<u>Thoracic imaging</u> <u>THE LUNGS</u> <u>THE CENTRAL AIRWAYS</u> <u>THE LUNGS BEYOND THE HILA</u>

Pulmonary segments:

Right Upper Lobe

Apical segment - Posterior segment - Anterior segment **Right Middle lobe**

Lateral segment - Medial segment

Right Lower Lobe

Superior segment - Medial basal segment - Anterior basal segment - Lateral basal segment - Posterior basal segment.

Left Upper Lobe

Apicoposterior segment - Anterior segment *Lingula* Superior segment - Inferior segment

Left Lower Lobe

Superior segment - Anterior basal segment - Lateral basal segment - Posterior basal segment.

<u>Chest Wall</u> • Composed of soft tissues and bony structures

• <u>Soft tissues:</u> • Abnormalities or variants of the breasts and muscles, soft-tissue calcification and subcutaneous emphysema affect the radiological appearance of the chest wall.

• Tumours include:

- 1. benign causes (lipoma, neurilemmomas, neurofibromas, haemangiomas, lymphangiomas, elastofibroma)
- 2. malignant causes that may be primary (liposarcoma or fibrosarcoma, undifferentiated pleomorphic sarcoma, angiosarcoma) or
- Secondary (direct metastatic invasion, lymphoma).
- **Bone:** Abnormalities or variants of the ribs, sternum, clavicles, scapula and spine
- Tumours include
- 1. benign causes (chondromas, osteochondromas, fibrous dysplasia, eosinophilic granuloma haemangiomas and aneurysmal bone cysts) and
- 2. malignant causes which may be primary (chondrosarcoma, osteosarcoma, Ewing sarcoma, post radiation sarcoma, lymphoma) or
- 3. Secondary (myeloma or metastatic).

<u>PLEURAL EFFUSION</u>: transudate, exudate (thin or thick), blood and chyle.

All types of pleural effusion are radiographically identical,

Sometimes, CT and MRI can also help to specify the diagnosis.

Bilateral pleural effusions tend to be transudates.

Some bilateral effusions are exudates, and this is seen with metastatic disease, lymphoma, pulmonary embolism, rheumatoid disease, systemic lupus erythematosus (SLE), post–cardiac injury syndrome, myxoedema and some ascites-related effusions. Right-sided effusions are typically associated with ascites, heart failure and liver abscess, and left effusions with pancreatitis, pericarditis, oesophageal rupture and aortic dissection.

Massive effusions are most commonly due to malignant disease, particularly metastases (lung or breast), but may also occur in heart failure, cirrhosis, tuberculosis, empyema and trauma.

Imaging Pleural Effusion Chest Radiograph Free pleural fluid. A small amount of free fluid may be undetectable on an erect PA chest radiograph because it tends initially to collect under the lower lobes.

Such small sub pulmonary effusions can be demonstrated by ultrasound or CT. The superior margin of the opacity is concave to the lung and is higher laterally than medially. Above and medial to this meniscus there is a hazy increase in opacity owing to the presence of fluid posterior and anterior to the lungs.

A pleural effusion of approximately 1000 mL is usually present by the time the pleural effusion reaches the level of the fourth anterior rib.

Massive effusions cause dense opacification of the hemithorax with contralateral mediastinal shift.

Absence of mediastinal shift with a large effusion raises the strong possibility of obstructive collapse of the ipsilateral lung or extensive pleural malignancy, such as may be seen with mesothelioma or metastatic carcinoma.

Large effusions sometimes cause diaphragmatic inversion,

particularly on the left where the diaphragm lacks the support of the liver.

Paradoxical hemi diaphragmatic motion may occur as a result on the affected side.

For small effusions, a lateral decubitus radiograph can increase sensitivity for the detection of a pleural effusion as the pleural liquid moves with gravity and the lung effectively floats on the effusion.

However, ultrasound will often be an easier technique to demonstrate a small pleural effusion.

On a PA radiograph this sub pulmonary effusion presents as a 'high hemidiaphragm' with an unusual contour that peaks more laterally than usual, has a straight medial segment and falls away rapidly to the costophrenic angle laterally, which may or may not be blunted.

If occurring on the left, a separation of more than 2 cm of the stomach bubble from the lung, particularly if displaced inferomedially.

Loculated (encysted, encapsulated) pleural fluid:

Fluid can loculate between visceral pleural layers in fissures or between visceral and parietal layers, usually against the chest wall.

This often results from adhesions, and commonly an additional radiographic clue to the presence of pleural disease will be present.

Transudates may cause loculation without adhesions, particularly within the interlobar fissures mimicking masses, and have been called pseudotumor or vanishing tumours.

Occasionally, distinguishing between loculated pleural fluid and a pleural mass:

Helpful indicators are that the lesion is homogeneous, smooth when seen in tangent but poorly circumscribed when seen 'en face', and changes configuration between supine and erect films as a result of gravity.

Ultrasound Pleural fluid, especially when it is a transudate, is commonly echo free.

Exudative and haemorrhagic effusions may be echogenic and are often accompanied by pleural thickening.

The pattern of echoes may be homogeneous, complex or septated.

In addition, pleural lesions characteristically make an obtuse angle with the chest wall, whereas with intrapulmonary lesions the angle is often acute.

Ultrasound is widely used to localise pleural fluid for aspiration and identify any solid components to allow guided biopsy.

Computed Tomography

A pleural effusion appears on CT as a dependent sickleshaped opacity with a CT number lower than that of any adjacent pleural thickening or mass.

The fat-containing chylothorax does not have a CT number lower than normal, because of its protein content.

Magnetic Resonance Imaging

MRI has a limited role in the evaluation of pleural effusion,

although it may be helpful to distinguish a transudate from an exudate.

Pleural fluid has a low signal on T1 weighted sequences and a high signal on T2 weighted images, often with heterogeneous appearances as a result of motion within the effusion creating flow artefacts.

Complex exudates have greater signal intensity than simple exudates, with septations and nodularity showing late gadolinium enhancement. It may also be possible to differentiate transudates from exudates using triple echopulse sequence and diffusion-weighted imaging where transudates have been shown to have lower apparent diffusion coefficient (ADC) values. Although MRI is of limited value in detecting pleural infection, it is of value in assessing pleurocutaneous fistulae and associated osteomyelitis.

In the subacute and chronic stage, haematomas show bright signal intensity on T1 weighted images, surrounded by a dark rim caused by haemosiderin.

Positron-Emission Tomography/Computed Tomography

Increased uptake of glucose in malignant cells and those responding to inflammation and infection can help differentiate a transudate from an exudate on FDG PET/CT.

Some Specific Pleural Effusions

Exudates and Transudates

Pleural effusion is common in left ventricular failure and bilateral in approximately 90% cases, although occurring more frequently and larger on the right. All types of pericardial disease may be associated with pleural effusion, which is predominantly left sided.

Pulmonary embolism is commonly associated with a pleural effusion, which is seen in 25%–50% of cases but is usually small and may be haemorrhagic.

A number of drugs have been described as causing pleural effusions. The most common agents are cytotoxics (methotrexate, procarbazine, mitomycin, busulfan, bleomycin and interleukin-2), nitrofurantoin, antimigraine drugs (ergotamine, methysergide), amiodarone, propylthiouracil, bromocriptine and gonadotrophins. With a number of these agents, pleural thickening is more common than a pleural effusion.

Both acute and chronic pancreatitis are associated with pleural effusions which have high amylase levels. In acute pancreatitis, exudative and often blood-stained effusions form in 15% of patients, particularly on the left side, where the diaphragm is closely related to the pancreatic tail. Associated elevation of the hemidiaphragm and basal lung consolidation are common.

Exudative effusions may be seen in uraemia and are often accompanied by pericarditis.

Peritoneal dialysis can produce pleural effusions by the direct trans diaphragmatic passage of fluid, as occurs with cirrhotic ascites.

PNEUMOTHORAX

Air in the pleural space is a pneumothorax. When air and liquid are present the nomenclature depends on their relative volumes and the type of liquid. Small amounts of liquid are disregarded, and the condition is still called a pneumothorax; otherwise, the prefix hydro-, haemo-, pyo- or chylo- is added, depending on the nature of the liquid.

Imaging Pneumothorax

The diagnosis of pneumothorax is mostly made with the chest radiograph, although other techniques (e.g. CT) may be used for smaller pneumothoraces and detecting complications and predisposing conditions, as well as helping in management.

Chest Radiography

Typical Signs. These are seen on erect radiographs in which the pleural air rises to the lung apex. Under these conditions the visceral pleural line at the apex becomes separated from the chest wall by a trans radiant zone devoid of vessels.

Atypical Signs

These arise when the patient is supine or when the pleural space is partly obliterated. In the supine position. Signs that suggest a pneumothorax under these conditions are:

• Ipsilateral transradiancy, either generalised or hypochondrial.

• A deep, finger-like costophrenic sulcus laterally.

• A visible anterior costophrenic recess seen as an oblique line or interface in the hypochondrium; when the recess is manifest as an interface it mimics the adjacent diaphragm ('double diaphragm sign').

• A transradiant band parallel to the diaphragm and/or mediastinum with undue clarity of the mediastinal

border.

• Visualisation of the undersurface of the heart, and of the cardiac fat pads as rounded opacities suggesting masses.

• Diaphragm depression.

In a patient who cannot stand, the presence of a pneumothorax can

be confirmed with a lateral decubitus view or a supine decubitus projection with the cassette placed dorsolaterally at 45 degrees and the x-ray tube angled perpendicular to the cassette.

Ultrasound

Normal pleura is seen as an echogenic line, the 'pleural stripe'.

'A lines' are horizontal reverberation artefacts that are equally spaced lines caused by reflection from the pleura in the presence of pneumothorax.

Computed Tomography

CT is the most sensitive investigation for the detection of pneumothoraces.

CT can help guide chest

drain insertion.

Primary Spontaneous Pneumothorax

Iatrogenic causes apart, the most common type of pneumothorax.

A pneumothorax occurring without an obvious precipitating event is spontaneous.

PSP occurs predominantly in young adults (65% are between

20 and 40 years of age), and it is five times more common in men than women, nearly always caused by the rupture of an apical pleural bleb.

Secondary Spontaneous Pneumothorax

A large number of conditions predispose to pneumothorax.

Spontaneous, Primary

- 1. Airflow obstruction Asthma
- 2. Chronic obstructive pulmonary
- 3. disease (COPD)
- **4.** Cystic fibrosis
- 5. Pulmonary infection Cavitating pneumonia
- **6.** Tuberculosis
- 7. Fungal disease
- 8. AIDS
- 9. Pneumatocele
- **10.** Pulmonary infarction
- **11.** Neoplasm Metastatic sarcoma
- **12.** Diffuse lung disease Histiocytosis X
- **13.** Lymphangioleiomyomatosis
- **14.** Fibrosing alveolitis
- **15.** Other diffuse fibroses
- **16.** Hereditable disorders of fibrous
- **17.** connective tissue
- **18.** Marfan syndrome
- **19.** Endometriosis (catamenial

pneumothorax)

Traumatic, No iatrogenic

- 1. Ruptured oesophagus/trachea
- **2.** Closed chest trauma (± rib fracture)
- **3.** Penetrating chest trauma

Traumatic, Iatrogenic

- 1. Thoracotomy/thoracocentesis
- 2. Percutaneous biopsy
- 3. Tracheostomy
- 4. Central venous catheterization

Tension Pneumothorax

This life-threatening complication is present when intrapleural pressure becomes positive relative to atmospheric pressure for a significant part of the respiratory cycle. Tension has an adverse effect on gas exchange and cardiovascular performance, causing a rapid deterioration in the patient's clinical condition. The diagnosis is usually made clinically and treatment instituted without a radiograph. Should a chest radiograph be taken, it will show contralateral mediastinal shift and ipsilateral diaphragm depression.

Pyopneumothorax

This unusual complication is seen most commonly following necrotizing pneumonia or oesophageal perforation.

Adhesions

These generate straight band shadows extending from the lung margin to the chest wall. They limit collapse but at the same time may account for continued air leakage from the lung surface, and if they tear they may bleed. They can be identified with CT.

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PLEURAL THICKENING AND TUMOURS

Pleural thickening may be benign or malignant and, if benign, usually represents the organised end stage of various active processes such as infective and non-infective inflammation (including asbestos exposure and pneumothorax) and haemothorax.

Malignant processes include mesothelioma and metastatic deposits.

Imaging Pleural Thickening and Tumours

Chest Radiography

The chest radiograph remains the initial investigation of pleural thickening and provides a starting assessment of whether localised or diffuse, smooth or nodular, the presence of any calcification and whether associated with volume loss or pleural effusion. Pleural thickening appears as fixed opacification of water/soft-tissue density, which if viewed en profile, appears more or less parallel to the chest wall and with a sharp lung interface. En face, it causes ill-defined, veil-like shadowing.

Ultrasound

Normal pleura is seen as a bright echogenic line (the 'pleural stripe') that represents the air–visceral pleural interface. Diffuse or smooth thickening is often challenging to visualise on ultrasound, having a variable echogenicity and only appreciated when >1 cm in depth.

In some cases small loculated effusions can themselves be mistaken for pleural thickening. In such cases, colour Doppler may demonstrate fluid movement in effusions with cardiac pulsation. Where visualised, parietal, visceral or diaphragmatic nodularity is strongly suggestive of pleural malignancy.

Computed Tomography

CT is very sensitive in the detection of pleural thickening, which is most easily assessed on the inside of the ribs, where there should normally be no soft-tissue opacity.

The most useful signs on CT that indicate malignant as opposed to benign pleural thickening are circumferential thickening, nodularity, parietal thickening of more than 1 cm and involvement of the mediastinal pleura.

Magnetic Resonance Imaging

MRI is particularly useful to help problem-solve in cases where there is uncertainty between benign and malignant disease and tumour stage.

Signal hypointensity with long repetition time (TR) sequences has been shown to be a reliable predictive sign of benign pleural disease.

Particular benefit over CT has been seen in assessing diaphragmatic invasion and assessment of resectability of solitary tumour foci.

The diagnosis of thoracic endometriosis may also be strongly suggested by detecting T1 and T2 hyperintensity and susceptibility artefact from degradation blood products on implants at the diaphragm or in the pleural cavity. Meanwhile, functional sequences may aid differentiation between benign and malignant pleural disease—the presence of multiple hyperintense pleural spots on high b-value diffusion-weighted MRI (DW-MRI; 'pleural pointillism sign') has been shown to potentially be a useful marker of malignant disease and may help to guide biopsy. DW-MRI may also suggest the tumour subtype in mesothelioma because the sarcomatoid subtype of malignant pleural disease has been shown to have significantly lower ADC values than the epithelioid subtype, although biopsy is still required because of the considerable overlap of the biphasic subtype.

Positron-Emission Tomography/Computed Tomography

FDG PET/CT currently has a significant role in both the diagnosis and management of malignant pleural disease, particularly in patients with suspected or proven mesothelioma, with increased FDG activity on PET/CT helping to differentiate benign from malignant pleural disease.

However, false-positive FDG activity can occur due to inflammation of the pleura in infection, inflammatory pleurisy or talc pleurodesis.

Talc pleurodesis presents a particular challenge, resulting in intense FDG uptake which can persist for several years, with FDG uptake mostly correlating with areas of high density on CT.

False negatives may occur due to small tumour size or depth, or metabolically inactive tumours, with epithelioid subtype mesothelioma being less FDG-avid than sarcomatoid mesothelioma.

Nodal status and the detection of unsuspected extrathoracic

metastases, which may alter treatment planning.

Pleural Plaques

Fibrous pleural thickening can be induced by asbestos exposure. They almost always involve the parietal pleura alone and are most commonly found along the lower thorax and on the diaphragmatic pleura.

In extensive disease the anterior and ventral part of the thorax may also be involved. Pleural plaques need to be large before they become visible on a chest x-ray, where they may be unilateral (more frequently on the left) and asymmetrical if bilateral.

When calcified, pleural plaques are visualized as opaque lines on tangential views parallel to the chest wall, diaphragm or cardiac border, and when seen en face, they produce irregular linear or stippled uneven calcifications ('holly leaf' calcification).

On CT they are visualized much earlier.

On MRI, pleural plaques are low signal on T1 and T2 weighted sequences with areas of signal void where there is calcification.

Diffuse Pleural Disease

The radiographic definition of diffuse pleural thickening is somewhat arbitrary. It has been suggested that uninterrupted pleural density that extends over at least one-quarter of the chest wall.

On CT, it has been defined as a continuous sheet of pleural thickening that extends more than 8 cm in the craniocaudal direction and 5 cm laterally and with a thickness of more than

3 mm. It may be caused by asbestos exposure or other causes.

Common causes of *non–asbestos*-related diffuse pleural thickening are empyema, tuberculosis and haemorrhagic effusion. The CXR changes are generally unilateral, affecting the lateral and posterior costophrenic recesses and appear as smooth, often angular thickening.

In post-talc pleurodesis there is a 'sandwich' of parietal pleural thickening, high attenuation talc and visceral pleural thickening on CT.

Pleural Tumours

These may be localised or diffuse; benign or malignant, in which they may be primary or secondary in origin.

Localised tumours are relatively uncommon, with diffuse malignant disease accounting for the vast majority of pleural tumours.

Pleural Fibroma

Also known as solitary fibrous tumour of the pleura (SFTP), these lesions most commonly present in middle age, approximately half the patients being asymptomatic. Hypertrophic osteoarthropathy (HPOA) is a well-recognised complication (10%–30% of patients), and rarely the tumour is associated with hypoglycaemia.

The **CXR** findings are of a pleurally based, well-demarcated, rounded and often slightly lobulated mass (2–20 cm diameter) which may, because of pedunculation, show marked positional variation with changes in posture and respiration.

Pleural fibromas usually make an obtuse angle with the chest wall and may reach enormous sizes. They are usually seen in the lower third of the chest and may be in a fissure (30%), along the mediastinal pleura (18%), the thoracic pleura (46%) or adjacent to the hemidiaphragm (6%).

CT findings are similar to those observed on plain radiography: a mass, which is often heterogeneous because of necrosis and haemorrhage, frequently enhancing after contrast medium administration with a characteristic swirling pattern, with calcification most commonly seen when they are large. The adjacent lung parenchyma may be displaced with atelectasis, with bowing of the bronchi and pulmonary vessels around the mass.

Malignant types are usually larger than 10 cm and may invade the chest wall or have associated pleural or pulmonary metastases, or an effusion.

Typically, on **MRI** these tumours show low signal on **T1** weighted images and heterogeneous high signal on **T2** weighted images, occasionally with a peripheral rim of low intensity seen on T1 weighted images.

PET/CT may be of value in identifying sarcomatous change within a pleural fibroma, by demonstrating significantly increased FDG avidity.

Pleural Lipoma

Lipomas are asymptomatic benign tumours usually discovered incidentally on chest radiographs as sharply defined pleural masses.

Diagnosis is straightforward with CT delineating its pleural origin and fatty composition, which is usually homogeneous.

Pleural lipomas have.

MRI high signal intensity on T1 weighted images.

On T2 weighted images the signal is moderately increased.

PET/CT is rarely used to image them but may be used to confirm suspected sarcomatous change, as they usually demonstrate FDG avidity less than that of background activity when benign.

Malignant Mesothelioma (Primary Pleural Malignancy)

Diffuse malignant mesothelioma is an uncommon primary neoplasm, and its development is strongly related to asbestos exposure. It is usually indistinguishable from metastatic disease on imaging, although the presence of calcified or noncalcified pleural plaques, alongside interstitial disease or asbestosis, may provide evidence of prior asbestos exposure.

It most commonly presents on a **chest radiograph** as irregular and nodular pleural thickening with an associated pleural effusion.

On **CT**, malignant mesothelioma presents as a nodular softtissue mass sometimes with hypodense areas corresponding with necrosis.

Metastatic enlargement of hilar and mediastinal nodes is seen in up to 50% of patients. The epithelioid subtype has a better prognosis than sarcomatoid.

On **MRI** Malignant mesothelioma has minimally increased signal on T1 and moderately increased signal on T2.

MRI may be superior to CT in determining the extent of local disease because it allows better evaluation of the relationship of the tumour to the structures of the chest wall, mediastinum and diaphragm.

Ultrasound may be a supplementary method for biopsy and

surgery planning.

Advances in the use of functional MRI and PET/CT to differentiate benign from malignant disease, to provide clues as to the subtype, stage, assessment of treatment response and prognosis and to plan biopsy.

Pleural Metastases (Secondary Pleural Malignancy)

Pleural metastases are the most common pleural neoplasm.

Common sites of origin including the ovary, stomach, breast and lung.

Pleural metastatic disease can present as a solitary mass but is more often seen as multiple pleural lesions or diffuse pleural thickening. Pleural metastases are very often accompanied by a pleural effusion, which may be the only finding on a **chest radiograph**.

CT, MRI and ultrasound are more sensitive.

Bronchogenic carcinoma may directly invade the adjacent pleural surface and chest wall or may have metastasized to it.

Tumour-Like Conditions of the Pleura

Erdheim–Chester disease should be considered in patients with pleural or

pericardial thickening and retroperitoneal/renal abnormalities along with musculoskeletal features such as osteosclerosis; diffuse pulmonary lymphangiomatosis has accompanying pulmonary findings predominantly affecting the upper lobes, including smooth symmetrical interlobular septal and peribronchovascular interstitial thickening, pericardial and pleural effusion and mediastinal fat infiltration. Thoracic splenosis, thoracic endometriosis and extrapleural hamartomas are rare tumour-like focal lesions of the pleura, which again may be suggested as a diagnosis because of an appropriate clinical history and possible extrapleural abnormalities.

Pleural Calcification

Pleural calcification is most commonly seen following asbestos exposure, empyema (usually tuberculous) and haemothorax. Most common in the lower posterior half of the chest and is usually unilateral. However, in silicosis, particularly of the asbestos-related type, calcification occurs as more discrete collections within plaques and is usually bilateral.

INTERVENTION

Interventional procedures of the chest wall and pleura may be performed for both diagnostic and therapeutic reasons. Ultrasound or CT guidance is most commonly used, although fluoroscopy and, rarely, MRI have also been used. PET/CT is now increasingly performed before chest wall or pleural biopsy to guide the procedure to the most metabolically active and therefore most likely diagnostic site.

Chest Wall Intervention

Haemorrhagic diatheses are the main contraindication to pleural intervention. Patients unable to control their breathing and/or coughing pose relative contraindications.

Pleural Intervention

Pleural Aspiration

The main indications are in malignant pleural effusion, in

which pleural fluid is sampled for diagnosis or larger-volume aspiration is performed to relieve symptoms of dyspnoea, and in pleural effusion associated with sepsis (suspected empyema), where sampling guides the diagnostic decision to drain.

All pleural aspirations should be guided by **ultrasound** intervening time period.

Chest Drains

Patients with symptomatic pneumothoraces, large-volume pleural effusions, infected effusions and symptomatic malignant effusions require chest drain insertion.

Chest drainage should not be performed in hepatic hydrothorax.

Pleural Biopsy

Although the aetiology of pleural thickening (or a combination of thickening and pleural effusion) will be determined in most patients by a combination of clinical history and imaging features, making biopsy unnecessary, some patients require further investigation and histological confirmation.

This may either be by percutaneous biopsy or under direct visualisation at medical or video-assisted thoracoscopy.

Image-guided percutaneous biopsy can be performed using ultrasound or CT guidance. Ultrasound guidance offers the advantage of real-time imaging, ready availability and no radiation risk. CT guidance permits access to regions difficult to visualise on ultrasound, in particular pleural lesions behind ribs or along paravertebral surfaces.

Complications of Image-Guided Pleural Intervention

Documented image-guided pleural complications include intercostal nerve artery damage, iatrogenic infection, iatrogenic pneumothorax, procedure failure, pain, solid organ puncture, diaphragmatic injury and haemorrhage, although the actual complication rates remain low.

Factors increasing the risk of complication are poor supervision and low levels of clinical experience, poor position and selection of the insertion site, excessive insertion of dilators and inadequate imaging.

Intercostal artery injury.

Iatrogenic pneumothorax.

Iatrogenic infection.

DIAPHRAGM

The diaphragm is the dome-shaped muscle-tendinous barrier separating the thorax and abdomen, with its upper surface covered by the pleura and the inner surface by the peritoneum. Its attachments are sternal (xiphoid process), costal (6-12th ribs) and lumbar (arcuate ligaments, right crus to L3 and left crus to L2).

IMAGING THE DIAPHRAGM

Chest Radiograph

The diaphragm is only visualised where there is air-containing lung adjacent to it superiorly. It is 2–3 mm thick, but this will be appreciated only if there is air immediately beneath it, as with a pneumoperitoneum.

Localised loss of clarity usually indicates adjacent pulmonary

or pleural disease; for example, the costophrenic or costovertebral angles are obliterated by pleural fluid and much of the diaphragmatic outline may be obliterated by basal pneumonia.

When the diaphragm is flat, as in emphysema.

Prominent fat pads at the cardiophrenic angles are an occasional cause of overestimation of the transverse cardiac diameter.

On correctly exposed radiographs, the relatively low radioopacity of the fat pad enables it to be distinguished from the cardiac apex.

On the lateral radiograph. Localisation of disease requires the correct identification of each leaf on the lateral radiographs. The left diaphragm is obscured anteriorly by the heart and usually has an air-distended gastric fundus beneath it; whichever leaf is nearer the detector is related to the ribs least magnified by the diverging beam. In most people the diaphragm in the midlung field lies at the level of the fifth or sixth anterior rib interspace. It may lie at a lower level in normal young individuals, particularly those of an asthenic build and at a slightly higher level in the obese, the elderly and young infants.

In more than 90% of normal people the right hemidiaphragm is higher than the left. This difference in height on the PA radiograph is usually approximately 15 mm but may be as much as 30 mm.

Depression of the diaphragm occurs in emphysema and in acute severe asthma, but flattening occurs only in emphysema.

Inversion of the diaphragm is sometimes seen with a tension pneumothorax and with large basal bullae.

It is also a common accompaniment of pleural effusions.

Causes of Unilateral Elevation of the Diaphragm

Posture—lateral decubitus position (dependent side)

Gaseous distension of stomach or colon

Dorsal scoliosis

Pulmonary hypoplasia

Pulmonary collapse

Phrenic nerve palsy

Eventration

Pneumonia or pleurisy

Pulmonary thromboembolism

Rib fracture and other painful conditions

Subphrenic infection

Subphrenic mass

Causes of Bilateral

Symmetrical Elevation of the Diaphragm

Supine position

Poor inspiration

Obesity

Pregnancy

Abdominal distension (ascites, intestinal obstruction, abdominal mass)

Diffuse pulmonary fibrosis

Lymphangitis carcinomatosa

Disseminated lupus erythematosus

Bilateral basal pulmonary emboli

Painful conditions (after abdominal surgery)

Bilateral diaphragmatic paralysis

Elevation of a single hemidiaphragm is usually secondary to adjacent pleural, pulmonary or subphrenic disease or to phrenic nerve palsy. A minor degree of diaphragmatic elevation is a common accompaniment of pleurisy, lower lobe pneumonia and pulmonary thromboembolism. In the latter there may be no visible change in the affected lung. Upper abdominal inflammatory processes and rib fractures may also cause a high diaphragm. A high hemidiaphragm may be mimicked by a subpulmonary pleural effusion, a large well defined tumour adjacent to the dome or combined middle and lower lobe collapse.

Ultrasound

When no pleural disease is present a thick hyperechoic line is usually present, but this line is not the diaphragm itself but is caused by the interface between the abdominal structures and the strongly reflecting air in the lung. Becoming atrophic when paralysed.

Diaphragmatic motion can be quantified using B- or M-mode imaging, the excursion between inspiration (towards transducer) and endexpiration (away from transducer) normally being 2.5 cm.

Computed Tomography

Volumetric CT with multiplanar reconstructions has facilitated assessment of the diaphragm and is useful particularly in cases of trauma.

Magnetic Resonance Imaging

Multiplanar reconstructions with MRI allows further assessment with excellent resolution of soft tissue, where the diaphragm has low signal intensity relative to other skeletal muscles on all MRI sequences.

Diaphragmatic motion may lead to significant artefact and impair assessment.

Eventration

In eventration a part of the normal diaphragmatic muscle is replaced by a thin layer of connective tissue and a few scattered muscle fibres.

The unbroken continuity differentiates it from diaphragmatic hernia.

Localised forms of the condition are relatively common, particularly in the elderly, and predominantly affect the right hemidiaphragm at.

The distinction between a localised eventration and a small diaphragmatic hernia or a mass arising from the lung, pleura or

diaphragm is best made using coronal/sagittal CT or MRI (especially useful when subdiaphragmatic fat is present or when the liver is steatotic).

Causes of Focal Elevation

(Bulge) of the Diaphragm

Partial eventration

Diaphragmatic hernia

Diaphragmatic tumour

Pleural tumour

Pulmonary tumour

Focal diaphragmatic dysfunction

Focal diaphragmatic adhesions

Movement and Paralysis

Although normal young adults can move the diaphragm over at least 30 mm, this range is greatly reduced in the elderly.

As the chest radiograph is exposed at the end of a full inspiration, any severe unilateral limitation of diaphragmatic movement will be apparent on this static examination. However, diaphragmatic movement is better assessed by fluoroscopy (or ultrasound), which should ideally be performed in both the AP and lateral projections. Restriction of diaphragmatic movement occurs secondary to disease of the phrenic nerve and secondary to inflammatory and painful conditions adjacent to the diaphragm, such as lower lobe pneumonia and subphrenic infection.

Phrenic palsy is most commonly secondary to involvement of

the phrenic nerve by tumour—usually a bronchial carcinoma. Phrenic nerve paresis may be caused by trauma (road accidents, birth injury, brachial plexus block and phrenic crush), irradiation and a variety of neurological conditions such as poliomyelitis, herpes zoster and cervical disc degeneration.

The recognition of phrenic paresis depends upon finding a high hemidiaphragm which exhibits absent, restricted or paradoxical movement.

Diaphragmatic motion can also be examined with ultrasound

An important mimic of phrenic paresis is eventration (usually

left-sided).

Bilateral paralysis may not be recognised by fluoroscopic examination, for passive descent of the diaphragm may occur with inspiration.

On CT, decreased diaphragmatic thickness may be evident.

Diaphragmatic Hernias

Intrathoracic herniation of abdominal contents occurs through congenital defects in the muscle, through traumatic tears or, most commonly, through acquired areas of weakness at the central oesophageal hiatus.

Bochdalek defects through the pleuroperitoneal canal occur along the posterior aspect of the diaphragm, and the hernia usually contains retroperitoneal fat or a portion of kidney or spleen. The majority occur on the left. A well-defined, domeshaped, soft-tissue opacity is seen midway between the spine and lateral chest wall on the frontal view and above the posterior costophrenic recess on the lateral view.

It may appear to 'come and go' on serial PA radiographs because of varying degrees of inspiration and differences in transdiaphragmatic pressure.

On **CT** and **MRI** the diagnosis can be made when a soft-tissue or fatty mass is seen protruding through a small defect in the posteromedial aspect of either hemidiaphragm.

A Morgagni hernia presents in adulthood as an anterior opacity at the right cardiophrenic angle. It frequently contains omentum and may contain bowel.

It is more difficult to differentiate from a low-lying pericardial cyst.

Hernias through the oesophageal hiatus are extremely common, particularly in the elderly, in whom they may be an incidental finding on chest radiography (retrocardiac mass with or without a fluid level) or on CT.

The rare congenital defect of the diaphragm, either total or partial, particularly affects the lateral part of the diaphragm. It may lead to a large hernia formation, and, on the left, the small bowel may fill the left hemithorax.

Diaphragmatic Trauma

Because diaphragmatic rupture is often associated with thoracic or abdominal injuries that require surgical treatment, many cases are diagnosed during surgery.

The **chest x-ray** and coronal/sagittal reformats on **MDCT** should be evaluated carefully. Now that the use of CT is so widespread, barium studies are rarely warranted.

An artificial pneumoperitoneum can be established by introducing a small amount of air into the abdominal cavity. If air shifts through the diaphragmatic tear and a pneumothorax develops, the test is diagnostic for diaphragmatic rupture.

Ultrasound can be diagnostic if both the diaphragm and the herniated organs can be visualised.

However, this technique is limited by the often-minimal visualization of the diaphragm itself, the tenderness over the upper abdomen and the presence of gas in herniated bowel.

The **MDCT** diagnosis of diaphragmatic rupture is largely based on the fact that abdominal organs are seen in the pleural space outside the diaphragm.

Neoplasms of the Diaphragm

Primary tumours of the diaphragm are rare (Fig. 3.35). Both benign and malignant varieties are mostly derived from muscle, fibrous tissue, blood vessels or fat. They are usually well defined and on the right may mimic an elevated diaphragm or local eventration. Calcification has been described in lipomas. Malignant tumours may present as a pleural effusion. Secondary invasion of the diaphragm by malignant tumours of the lung, pleura, stomach or pancreas may occur.

Imaging with **CT** or **MRI** is particularly helpful in such patients.

MEDIASTINAL DISEASES

MEDIASTINAL MASSES

Incidence

Neurogenic (17%-23%), thymic (20%-25%) or lymph node (10%-20%) origin (usually neoplastic).

Developmental cysts, thyroid masses and germ-cell tumours constitute the next most frequent group (approximately 10% each). In children, neuroblastoma/ganglioneuroma, foregut cysts and germ-cell tumours account for over three-quarters of cases, whereas thymoma and thyroid masses are rare.

The mediastinum is divided into.

The mediastinum is divided into three parts: anterior, middle and posterior.

A line that extends from the thoracic inlet to the diaphragm along the anterior pericardial surface and anterior to the trachea separates the anterior from middle compartments.

The middle and posterior compartments of the mediastinum are separated by a line that runs 1 cm behind the anterior margins of the vertebral bodies.

A new classification system: divides the mediastinum into prevascular, visceral and paravertebral compartments based on anatomical structures seen on cross-sectional imaging such as multidetector computed tomography (CT).

All three compartments are superiorly bound by the thoracic inlet and inferiorly by the diaphragm.

The anterior compartment is bound anteriorly by the posterior cortex of the sternum and posteriorly by the anterior pericardium. The prevascular compartment contains the thymus, lymphnodes, fat and the left brachiocephalic vein.

The visceral compartment is bound anteriorly by the anterior

pericardium and posteriorly by a vertical line connecting a point 1 cm posterior to the anterior margin of the thoracic vertebral bodies.

The visceral compartment contains most of the vascular structures.

Those not contained within the visceral compartment include the left brachiocephalic vein, lymph nodes, trachea, carina, oesophagus and the thoracic duct.

The extrapericardial pulmonary arteries and veins are considered pulmonary structures and not part of the visceral mediastinum.

The paravertebral compartment is bound anteriorly by a vertical line connecting a point 1 cm posterior to the anterior margin of the thoracic vertebral bodies and posteriorly by a vertical line against the posterior margin of the chest wall at the lateral margin of the transverse processes of the thoracic spine.

The paravertebral compartment contains the paravertebral soft tissues and the thoracic spine.

Most of the abnormalities in the paravertebral compartment are neurogenic neoplasms.

Imaging Techniques

Radiography

Mediastinal masses are often incidentally detected on chest radiograph (CXR).

Computed Tomography

CT is the most useful technique for localising, characterising

and demonstrating the extent of a mediastinal mass and its relationship to other structures.

CT following intravenous (IV) contrast medium with multiplanar reformats provides an excellent assessment of mediastinal structures, including vessels in the coronal and sagittal planes, and the presence or absence of enhancement in the mediastinal mass.

CT can guide biopsy, plan resection and follow response to therapy.

Magnetic Resonance Imaging

Magnetic Resonance Imaging (MRI) is very useful in differentiating cystic from solid lesions (e.g. thymic cyst from solid neoplasms), identifying septations and solid components in cystic neoplasms and differentiating benign cysts from cystic neoplasms.

Ultrasound

Ultrasound (US) of the mediastinum, including echocardiography and endoscopic US, may be of use in selected patients, in particular for distinguishing cystic from solid mediastinal masses and for distinguishing cardiac from paracardiac masses. US is increasingly being used to guide mediastinal biopsy.

Radionuclide Examinations

Radionuclide examinations have a limited role in assessing mediastinal masses.

Positron emission tomography (PET) and PET/CT using

[F-18]2-deoxy-D-glucose (18F-FDG) have proven useful in

evaluating mediastinal lymph node involvement in lung cancer and lymphoma.

One of the limiting factors of PET/CT in characterising mediastinal masses is the presence of both false positives and false negatives.

Thymic hyperplasia can have a variable fluorodeoxyglucose (FDG) uptake and may be as high to overlap with malignant lesions in the mediastinum.

Fibrosing mediastinitis can also have high FDG uptake and thus confound with malignant lesions.

Approach to Mediastinal Masses

- 1. Localise to the mediastinum
- 2. Localise within the mediastinum
- 3. Characterise on CT or MRI

Localise to the Mediastinum

The CXR is the first step in evaluating mediastinal diseases.

Localise Within the Mediastinum

Chest CT examination.

Characterise on Computed Tomography or Magnetic Resonance Imaging

Mediastinal masses can be further characterised by CT or MRI, depending on whether they contain fat, fluid or are vascular.

Thyroid Masses

Most thyroid masses in the mediastinum represent downward

extensions of either a multinodular colloid goitre or, occasionally, an adenoma or carcinoma. Intrathoracic thyroid masses usually have a well-defined spherical or lobular outline.

Rounded or irregular, well defined areas of calcification may be seen in benign areas, whereas amorphous cloud-like calcification is occasionally seen within carcinomas.

Almost all intrathoracic thyroid masses displace the trachea and may cause tracheal narrowing. The direction of displacement depends on the location of the mass.

Thyroid masses are most commonly anterior and lateral to the trachea. Posteriorly masses often separate the trachea and the oesophagus.

CT imaging features of mediastinal thyroid goitres include continuity of the mediastinal mass with the thyroid gland in the neck, foci of calcifications and cystic areas, high attenuation (higher than muscle) on unenhanced CT reflecting high iodine content and intense and prolonged enhancement following IV injection of iodinated contrast medium administration.

The most important of these features is to demonstrate continuity of the mass with the cervical thyroid.

It is not possible to distinguish between a benign and malignant mass on CT unless the tumour has clearly spread beyond the thyroid gland.

MRI of intrathoracic goitre, like CT, can identify cystic and solid components, and in addition can demonstrate haemorrhage.

In most practices, evaluation of the abnormal thyroid usually

relies on **US** with biopsy.

Radionuclide imaging with 123I or 131I demonstrates the presence of thyroid tissue within the mediastinum in almost all intrathoracic goitres.

Although radionuclide imaging is a sensitive and specific method of determining the thyroid nature of an intrathoracic mass, CT is more useful as the initial technique because it provides more information should the mass prove to be something other than a thyroid lesion and is almost as specific as nuclear medicine in diagnosing a thyroid origin. CT optimally demonstrates the shape, size and position of the mass.

Parathyroid Masses

A parathyroid tumour is a rare cause of an anterior mediastinal mass.

The parathyroid glands may migrate into the chest during fetal development. Mediastinal parathyroid tumours causing hyperparathyroidism are most commonly located in or around the thymus.

The role of **CT or MRI** is for detection of ectopic adenoma, which is suspected when no lesion is detected by US, or the hyperparathyroidism persists despite parathyroidectomy. The adenomas tend to be small and enhance homogeneously.

Often, the CT is used in conjunction with **99mTc-sestamibi imaging**.

Thymic Tumours

The thymus is a bilobed, triangular-shaped organ that occupies
the retrosternal space and varies widely in size and shape depending on the age. After 25 years of age, the thymus is no longer discretely recognized but seen as islands of soft-tissue attenuation within a background of fat.

Anterior mediastinal masses of thymic origin include thymomas, thymic carcinoma, thymolipoma, thymic lymphoma, thymic carcinoid and thymic hyperplasia. Thymic cysts may be simple cysts and occur in an otherwise normal gland, may lie within a thymoma or may follow thymic irradiation for Hodgkin disease.

Thymomas

Thymomas are the most common tumour of the thymus in adults, and the most common primary tumour of the anterior mediastinum in adults. Thymomas are usually benign or low-grade malignant tumours of thymic epithelium. The average age at diagnosis is approximately 50 years, earlier in those who present with myasthenia gravis. Thymomas are extremely unusual below the age of 15 and rare under 20. Up to 50% of patients with thymoma have myasthenia gravis, and approximately 10%–20% of patients with myasthenia gravis have a thymoma.

Thymomas may be encapsulated (non-invasive) or may extend beyond their capsule (invasive). A variety of other syndromes are seen in patients with thymoma, including hypogammaglobulinaemia and pure red cell aplasia.

Most thymomas (90%) arise in the superior aspect of the anterior mediastinum. A few are situated more inferiorly, projecting from the left or right heart border, or lying close to the cardiophrenic angles. They are usually spherical or oval in shape and may show lobulated borders. Thymomas may demonstrate cystic changes, haemorrhage or necrosis. A few thymomas are predominantly cystic and some thymomas may demonstrate punctate or curvilinear calcifications.

СТ

Is the most sensitive technique to detect all of these features and to help detect a thymoma in patients with myasthenia gravis?

Thymomas as small as 1.5–2.0 cm in diameter are readily identified in men and women over the age of 40, largely because the rest of the thymus is atrophic.

Diagnosing a small thymoma in those patients younger than age 40, and particularly younger than 30, can be difficult because the normal gland is variable in size and in myasthenia gravis the associated hyperplasia may cause a bulky gland.

Thymomas usually show homogeneous density and uniform enhancement after contrast media injection and may occasionally be cystic.

Most thymomas are completely encapsulated but approximately 30%–60% show degrees of invasion of the tumour capsule.

On **MRI**, the normal thymus in children and young adults characteristically demonstrates homogeneous and intermediate

T1 and T2 weighted signal intensity, less intense than mediastinal fat but greater than muscle. In older patients after puberty, the T1 and T2 signals increase with age because the thymus begins to involute and is replaced by fat. Thymomas typically demonstrate low T1 signal intensity similar to muscle and relatively high T2 signal intensity.

MRI can be useful for showing mediastinal involvement when CT is not definitive.

SUMMARY BOX: Thymoma

- Most common thymic tumour in adults
- Usually benign or low-grade malignant thymic epithelial tumours
- Average age of diagnosis is age 50
- Myasthenia gravis develops in up to 50%
- Less commonly develop hypogammaglobulinaemia and pure red cell aplasia

• Absence of, or extension into, the capsule indicates an invasive nature

• Complete obliteration of the adjacent fat planes suggestive of mediastinal invasion

• Absence of obliteration of adjacent fat does not exclude capsular invasion

• MRI more sensitive than CT in showing mediastinal involvement when CT is not definitive

• Pleural thickening, nodularity or the presence of an effusion generally indicates invasion.

Thymic Carcinoma

Thymic carcinoma is a thymic epithelial tumour with a high degree of anaplasia, cell atypia and increased proliferation.

It accounts for about 20% of thymic epithelial tumours and

predominantly occurs in adults.

Thymic carcinomas have a poor prognosis despite treatment with surgery and radiotherapy.

Thymic carcinomas are aggressive, locally invasive malignancies that have frequently metastasised to regional lymph nodes and distant sites at presentation.

They are typically large, heterogeneous masses, containing areas of necrosis and calcification, often demonstrating evidence of invasion of adjacent structures, in particular the mediastinum, pericardium and pleura.

Thymic carcinomas lack a well-defined capsule, whereas twothirds of thymomas are encapsulated.

On **MRI**, thymic carcinoma demonstrates intermediate signal intensity, slightly higher than muscle on T1 weighted sequence, and high signal intensity on T2 weighted sequence. Thymic carcinomas are more commonly associated with mediastinal node and extrathoracic metastasis, but less commonly associated with pleural implants compared with invasive thymomas. In general, before considering a diagnosis of thymic carcinoma on imaging, more common metastatic carcinomas should be considered.

Thymic Neuroendocrine Tumour (Thymic Carcinoid)

Primary neuroendocrine tumours (carcinoids) of the thymus are rare.

Well-differentiated neuroendocrine tumours and account for less than 5% of anterior mediastinal tumours.

Unlike pulmonary carcinoids, these tumours are aggressive

and at least 20% of patients have distant metastasis at presentation to the liver, lung, bone, pleura and pancreas.

Approximately 40% of patients have Cushing syndrome because of adrenocorticotrophic hormone secretion by the tumour, and up to 20% have multiple endocrine neoplasia (MEN) syndromes I and II.

On **CT** or **MRI**, the tumours appear as a lobulated thymic mass with heterogeneous enhancement and central areas of low attenuation secondary to necrosis or haemorrhage; local invasion may also be seen. Bone metastasis is typically osteoblastic.

Thymic carcinoids are more aggressive than thymomas and cause more frequent superior vena cava (SVC) obstruction.

Thymolipomas

Thymolipomas are rare, benign, well-encapsulated tumours composed of a mixture of mature fat and normal-looking or involuted thymic tissue.

The reported age range is 3–60 years. The average age of the patient is 22–26 years and most patients are asymptomatic. These tumours occur low in the anterior mediastinum, and often extend to the cardiophrenic angle as their pliability allows them to conform to adjacent structures.

Thymolipomas can grow to a very large size before discovery and, being soft, mould themselves to the adjacent mediastinum and diaphragm, and may mimic cardiomegaly or lobar collapse.

Individual cases have been reported in association with a variety of conditions, including myasthenia gravis, aplastic

anaemia, Graves disease and hypogammaglobulinaemia.

CT shows the fatty nature of the mass, with islands of thymus and fibrous septa running through the lesion.

On **MRI**, fat within the tumour appears as high signal intensity and soft tissue appears as low signal intensity bands coursing through the mass. CT and MRI generally reveal a connection between the tumour and the thymus.

Lymphofollicular Thymic Hyperplasia and Rebound

Thymic Hyperplasia

Also seen in conditions, such as thyrotoxicosis, systemic lupus erythematosus (SLE), Hashimoto thyroiditis and Addison disease.

Thymic Cyst

Thymic cysts are uncommon.

They can be congenital or acquired. Congenital thymic cysts are derived from a patent thymopharyngeal duct and are usually unilocular.

Approximately 50% of thymic cysts are discovered in those under 20 years old.

Acquired thymic cysts are multilocular and occur in association with thymic tumours, Langerhans cell histiocytosis or radiation therapy for Hodgkin disease.

On **CXR**s, thymic cysts are indistinguishable from other thymic masses.

On CT, simple congenital thymic cysts are seen as well-

defined water attenuation masses with imperceptible walls.

Multilocular thymic cysts appear as well-defined heterogeneous masses with imperceptible walls.

On **MRI**, thymic cysts demonstrate typical characteristics of fluid with low T1 and high T2 signal intensity. If haemorrhage or infection occurs, then the cysts can demonstrate high signal on both T1 and T2 weighted images.

Germ-Cell Tumours of the Mediastinum

Germ-cell tumours; mediastinal masses in adults and in children.

Most germ-cell tumours present during the second to fourth decades of life.

Mediastinal germ-cell tumours include teratoma and a number of malignant forms, chiefly seminoma and non-seminomatous germ-cell tumours such as embryonal carcinoma, choriocarcinoma, endodermal sinus tumour and tumours with mixtures of these cell types. Malignant germ-cell tumours secrete human chorionic gonadotrophin and α -fetoprotein, which can be used as markers to diagnose and monitor the tumour. Malignant germ-cell tumours are almost always seen in male patients.

Teratomas

Teratomas contain elements of all three germinal layers: ectoderm (skin, teeth and hair), mesoderm (bone, cartilage, muscle) and endoderm (bronchial or gastrointestinal epithelium).

Teratomas are the most common mediastinal germ-cell tumour

and most are cystic.

Teratomas are found at all ages, particularly in adolescents and young adults, with women slightly outnumbering men. They are usually asymptomatic and diagnosed incidentally on chest radiography or CT, but may give rise to cough, dyspnoea or chest pain if they compress the bronchial tree or SVC, or if they rupture into the mediastinum or lung.

Teratomas are usually stable, but haemorrhage or infection may lead to a rapid increase in size.

Teratomas are classified as mature, immature and malignant.

<u>Mature</u> teratomas represent approximately 60%–70% of all mediastinal germ-cell tumours.

<u>Immature</u> teratomas contain various adult tissues, but also contain foci of primitive, less well-organised tissue. Teratoma with malignant transformation contains frankly malignant tissues. Teratomas usually have a benign course and surgical resection is the treatment of choice on the small chance that few malignant elements are present.

Malignant teratomas have a poor prognosis.

On **CXR or CT** most teratomas present as a well-defined, rounded or lobulated mass, localised to the anterior mediastinum.

Teratomas may have variable appearances on CT. Combinations of fat, fluid, soft-tissue components and calcification may be seen in teratomas.

MRI is useful in differentiating teratoma from thymoma and lymphoma. Soft-tissue elements in the teratoma are isointense

to muscle, cystic elements demonstrate low T1 intensity and high T2 intensity, and fat appears as high T1 intensity with signal loss on fat-saturation sequence.

Fat is virtually diagnostic of teratoma.

Seminoma

Seminoma is the most common malignant mediastinal germcell tumour.

Seminomas occur almost exclusively in males during the second through fourth decades. They are usually well-defined solid masses with possible small foci of degenerative changes representing haemorrhage and necrosis.

Seminomas are usually asymptomatic, but when symptoms do occur they are usually caused by mass effect on adjacent structures.

On **CT** and **MRI**, seminomas have homogeneous attenuation and signal intensity and may have areas of haemorrhage and necrosis.

Non-Seminomatous Germ-Cell Tumours

Non-seminomatous germ-cell tumours include embryonal carcinoma, choriocarcinoma, endodermal sinus tumour and tumours with mixtures of these cell types.

Malignant non-seminomatous germ-cell tumours are usually seen in young adults and are much more common in men than in women.

They are usually more symptomatic than teratomas, either from mass effect or invasion of adjacent structures.

Their **plain radiographic** findings are similar, except that the

malignant tumours are more often lobular in outline.

Fat density and visible calcifications are rare.

Because these are malignant tumours, they grow rapidly and metastasise readily to the lungs, bones or, less often, pleura. **CT** often shows a lobular, asymmetric mass. The adjacent mediastinal fat planes may be obliterated, and the tumours either are of homogeneous soft-tissue density or show multiple areas of contrast media enhancement interspersed with rounded areas of decreased attenuation caused by necrosis and haemorrhage.

On **MRI**, these tumours may demonstrate heterogeneous intensities with areas of high T2 signal intensity corresponding to degenerative cystic changes.

Mediastinal Lymphadenopathy

Malignant Lymphoma and Leukaemia

Malignant lymphoma often involves mediastinal and hilar lymph nodes, multiple nodal groups usually being involved, particularly in Hodgkin disease.

Any intrathoracic nodal group regarding plain radiograph,

CT and MRI findings can be made:

1. The prevascular, para-aortic and paratracheal nodes are the groups most frequently involved. The tracheobronchial and subcarinal nodes also may be enlarged in many cases.

2. Hilar node enlargement is usually seen with mediastinal node enlargement.

3. The posterior mediastinal nodes are infrequently involved the enlarged nodes are often low in the mediastinum and contiguous retroperitoneal disease is likely.

4. The paracardiac nodes are rarely involved but become important as sites of recurrent disease because they may not be included in the initial radiation therapy fields.

Lymph node enlargement is also seen occasionally with leukaemia, the pattern being the same as with lymphoma.

Lymph Node Calcification

Extensive lymph node calcification is common following tuberculosis and fungal infection, and is occasionally seen with other infections.

It may also be encountered in a variety of other conditions, notably sarcoidosis, silicosis and amyloidosis. Although it may be seen in lymph node metastases from primary malignancies, such as osteosarcoma, chondrosarcoma and mucinous colorectal and ovarian tumours, lymph node calcification is rare in metastatic neoplasm. It is virtually unknown in untreated lymphoma.

CT is the most sensitive technique for the detection of lymph node calcification.

Low-Attenuation Nodes

On CT, areas of low attenuation within enlarged nodes, corresponding to necrosis, may be seen in a variety of conditions. This is particularly seen in tuberculosis and occasionally in fungal disease, infections in immunocompromised patients, metastatic neoplasm (notably from testicular tumours) and lymphoma.

Necrotic lymph nodes are common in patients with active

tuberculosis.

Enhancing Lymph Nodes

Castleman disease is a rare cause of strikingly uniform enhancing lymph nodes. Castleman disease (also referred to as angiofollicular lymph node hyperplasia) is a specific type of lymph node hyperplasia of uncertain aetiology which can cause substantial lymph node enlargement in many sites in the body.

In addition to Castleman disease, marked lymph node enhancement may occur in hypervascular metastases from melanoma, renal cell carcinoma, carcinoid tumours, papillary thyroid cancer and Kaposi sarcoma.

Lymph Node Enlargement

Normal-sized nodes are demonstrable at **CT/MRI** but are not easily visible on **CXR**.

Sarcoidosis. Sarcoidosis is a common cause of intrathoracic lymph node enlargement. Hilar nodes being enlarged in almost all cases.

One important diagnostic feature of lymphadenopathy in sarcoidosis is its symmetry. Lymph node calcification may have a stippled or eggshell appearance.

Tuberculosis and histoplasmosis. Lymph node enlargement caused by tuberculous or fungal infection may affect any of the nodal groups in the hila or mediastinum.

.Lymph node enlargement is usually seen ipsilateral to the side of lung disease, but involvement of the contralateral nodes may be present.

Dense nodal calcification is frequent whether the nodes stay enlarged or shrink.

The enlarged nodes, together with surrounding fibrosis, may compress the SVC or pulmonary veins and cause obstruction.

Metastatic carcinoma. Mediastinal lymph node metastases can occur from primary bronchogenic carcinoma or from extrathoracic primary carcinomas. The extrathoracic tumours likely to metastasise to the mediastinum are head and neck cancer, breast cancer, genitourinary cancers and melanoma. In Half the cases of mediastinal lymph node enlargement from extrathoracic primary carcinomas arose from tumours of the genitourinary tract, particularly the kidney and testis.

Reactive hyperplasia. Reactive hyperplasia in nodes draining infection/inflammation may cause mild enlargement, recognisable on **CT** but not easily with **CXR**.

Thoracic lymphadenopathy in AIDS. Mediastinal lymphadenopathy is seen in 35%–40% of patients infected with human immunodeficiency virus (HIV) and may raise concern for infection or malignancy.

Foregut Duplication Cysts

'Foregut duplication cyst' is a term that covers various congenital cysts derived from the embryological foregut, including bronchogenic and enteric cysts.

Bronchogenic Cysts

Bronchogenic cysts are thought to result from abnormal budding of the developing tracheobronchial tree with

separation of the buds from the normal airways. A good majority of bronchogenic cysts (65% to 90%) are mediastinal. Bronchogenic cysts are usually solitary asymptomatic mediastinal masses which may present at any age.

Most bronchogenic cysts are located adjacent to the trachea or main bronchi.

On conventional **CXR**s, a bronchogenic cyst usually appears as a well-defined solitary spherical or oval mass with homogeneous opacity just inferior to the carina and often protruding slightly toward the right hilar shadow.

Most are unilocular and do not have a lobulated outline.

They usually contact the carina or main bronchi but may be seen anywhere along the course of the trachea and larger airways, and frequently project into the middle mediastinum.

Calcification of the wall is rare.

Occasionally, duplication cysts can contain milk of calcium which creates a cyst–liquid calcium level within the cyst.

Foregut duplication cysts frequently push the carina anteriorly and the oesophagus posteriorly—displacements that are almost never seen with other masses (the exceptions being thyroid masses and an aberrant left pulmonary artery).

CT is an excellent method of demonstrating the size, shape and position of a bronchogenic cyst and defining its extent and relation to key structures.

In some cases, it may demonstrate a thin-walled mass with contents of uniform CT attenuation close to that of water, thereby effectively making the diagnosis of a fluid-filled cyst. In other cases, the CT attenuation is similar to soft tissue, and therefore to tumour, in which case the differential diagnosis becomes wider.

Rarely, the cyst may show uniformly high density, probably caused by high protein content within the fluid. In these cases, unenhanced CT images might be helpful.

Calcification occurs occasionally in the wall or within the cyst contents.

T1 weighted **MRI** show that the intrinsic signal intensity varies from low to high, depending on the cyst contents. T2 weighted images demonstrate high signal intensity. The possibility of malignancy should be considered when a solid component is seen in the cyst.

One advantage of MRI is the ability to obtain fat-suppressed images before and after enhancement. The unenhanced images can be used as a mask, and subtraction images can be created. Subtraction images can be helpful in identifying subtle areas of enhancement and thus making duplication cyst unlikely.

Oesophageal Duplication Cysts

Oesophageal duplication cysts are uncommon. They usually present first in childhood but may not present until adulthood; initial presentation up to the age of 61 has been reported mass on thoracic imaging, they may cause dysphagia, pain or other symptoms caused by the compression of adjacent structures, or perforation The imaging features of oesophageal duplication cysts on **CT** and **MRI** are identical to those of bronchogenic cysts except that, in the former, the wall of the lesion may be thicker, the cyst may assume a more tubular shape and it may be in more intimate contact with the oesophagus.

Neurenteric Cysts

Neurenteric cysts result from incomplete separation of the foregut from the notochord in early embryonic life and are far less common than oesophageal and bronchogenic cysts.

There is usually a fibrous connection to the spine or an intraspinal component. There are typically associated vertebral body anomalies such as butterfly vertebral deformity or hemivertebra.

Radiologically, a neurenteric cyst is a well-defined, round, oval or lobulated mass in the posterior mediastinum between the oesophagus (which is usually displaced) and the spine. Appearances on **CT** and **MRI** are similar to those of other foregut duplication cysts, with MRI being the investigation of choice for demonstrating the extent of intraspinal involvement.

Mediastinal Pancreatic Pseudocyst

On rare occasions, pancreatic pseudocysts extend into the mediastinum.

Most patients are adults and have a history of pancreatitis; in children, the usual cause of the pseudocyst is trauma. Most patients also have left-sided or bilateral pleural effusions. Having gained access to the chest via the oesophageal or aortic hiatus.

CT is the optimal method of demonstrating these thin-walled cysts, which may show continuity with the pancreas and any

peripancreatic fluid collections. **MRI** demonstrates the cystic nature of the mass.

Isolated pancreatic mediastinal cysts are very rare.

A history of pancreatitis will usually be present.

Neurogenic Tumours

Neurogenic tumours are the most common tumours to arise in the posterior mediastinum (paravertebral space), and most neurogenic tumours occur in this location.

They can be classified as tumours arising from peripheral nerves, including neurofibromas and malignant tumours of nerve sheath origin (neurogenic sarcomas), or as tumours arising from sympathetic ganglia such as neuroblastomas and ganglioneuroblastomas.

MRI is the best technique for imaging these tumours. Neurofibromas or schwannomas are more common in adults, whereas neuroblastomas and ganglioneuroblastomas are more common in children.

Peripheral Nerve Sheath Tumours

Peripheral nerve tumours are the most common mediastinal neurogenic tumours. They typically originate in an intercostal nerve in the paravertebral region and most are benign. **Radiologically**, the benign tumours (neurofibromas and schwannomas) present as well-defined round or oval posterior mediastinal masses.

On **CT** the tumours may be homogeneous or heterogeneous,

usually enhancing heterogeneously. Punctate foci of calcification may be seen.

Care must be taken on CT, however, as these lesions are often homogeneous and low in attenuation (from the myelin content).

The net effect is a lesion that can mimic a duplication cyst.

As a general rule, a posterior mediastinal lesion should not be called a cyst unless there is a clear vertebral anomaly or communication with the spinal canal.

On MRI, neurofibromas and schwannomas have low-tointermediate signal intensity on T1 weighted images and may have characteristic high signal intensity peripherally, low signal intensity centrally (target sign) on T2 weighted images and enhance after gadolinium. Ten per cent of paravertebral neurofibromas extend into the spinal canal and appear as dumb-bell–shaped masses with widening of the affected neural foramen.

Malignant tumours of nerve sheath origin are rare spindle cell sarcomas, typically occurring in the third to fifth decades, although they may occur earlier in patients with neurofibromatosis type 1.

Radiologically, the masses are usually larger than 5 cm in diameter. Although **MRI** cannot reliably differentiate benign from malignant neurogenic tumours, sudden change in size of a pre-existing mass, the development of heterogeneous signal intensity (caused by haemorrhage and necrosis) or infiltration of adjacent mediastinum or chest wall is cause for concern. Hematogenous metastases to the lung have been reported, but lymph node metastasis is rare.

Sympathetic Ganglion Tumours

Sympathetic ganglion tumours are rare neoplasms representing a biological continuum ranging from benign ganglioneuroma to malignant neuroblastoma, with ganglioneuroblastoma being an intermediate form.

They originate from nerve cells rather than nerve sheaths and can occur in sympathetic ganglia and adrenal glands.

Ganglioneuromas are benign neoplasms usually occurring in children and young adults.

Ganglioneuroblastomas exhibit variable degrees of malignancy and usually occur in children.

Neuroblastomas are highly malignant tumours that typically occur in children younger than 5 years of age.

The posterior mediastinum is the most common extraabdominal location of a neuroblastoma.

Ganglioneuromas and ganglioneuroblastomas usually arise from the sympathetic ganglia in the posterior mediastinum and therefore usually present **radiologically** as well-defined elliptical masses, with a vertical orientation, extending over the anterolateral aspect of three to five vertebral bodies. Calcification occurs in approximately 25% and **CT** appearance is variable.

On **MRI**, ganglioneuromas and ganglioneuroblastomas are usually of homogeneous intermediate signal intensity on T1 and T2 weighted images.

Neuroblastomas are typically more heterogeneous, caused by

areas of haemorrhage, necrosis, cystic degeneration and calcium.

They may be locally invasive and have a tendency to cross the midline.

Mediastinal Paragangliomas

Paraganglioma is a rare neuroendocrine tumour of chromaffin cell origin.

Intrathoracic paragangliomas are of two types: chemodectomas

or phaeochromocytomas (functioning paragangliomas), either of which may be benign or malignant.

Almost all intrathoracic chemodectomas

are in a location close to the aortic arch and are classified as aortic body tumours.

Other mediastinal chemodectomas are very rare. They are

usually single, but multicentric cases are reported.

Most intrathoracic phaeochromocytomas are found in the posterior mediastinum or closely related to the heart, particularly in the wall of the left atrium or the interatrial septum.

Findings of overproduction of catecholamines.

The various paragangliomas have similar appearances on chest

radiography, **CT** and **MRI**. They form rounded, soft-tissue masses, which are usually very vascular and therefore enhance intensely on CT. On MRI, phaeochromocytomas usually show a signal intensity similar to that of muscle on T1 weighted images and very high signal intensity on T2 weighted images.

Radio-iodine MIBG

(131I-metaiodobenzylguanidine) and somatostatin receptor scintigraphy both show increased activity in paragangliomas and are useful techniques for identifying extra-adrenal phaeochromocytomas.

Lateral Thoracic Meningocele

Lateral thoracic meningoceles are rare posterior mediastinal cystic lesions characterised by redundant meninges (dura and arachnoid with small amounts of neural tissue within the wall) that protrude through the spinal foramen and are filled with cerebrospinal fluid (CSF).

Like neurofibromas, they are commonly associated with neurofibromatosis.

They present as an asymptomatic mass, often with pressure deformity of the adjacent bone, indistinguishable on **plain radiographs** from neurofibromas. **CT** and **MRI** can both indicate the correct diagnosis

by showing the mass to be fluid filled rather than solid and demonstrating continuity between the CSF in the meningocele and that contained in the thecal sac.

If necessary, the diagnosis can be established by CT with

intrathecal contrast medium demonstrating flow into the lesion.

Extramedullary Haematopoiesis

Extramedullary haematopoiesis can result in paravertebral masses caused by compensatory expansion of bone marrow in patients with severe anaemia caused by inadequate production or excessive destruction of blood cells. Red blood cells are produced in the bone marrow of the long bones, pelvis, vertebrae, ribs, sternum and the skull.

In conditions such as thalassaemia and sickle cell disease, there is a problem with erythropoiesis and red blood cells are produced in extramedullary sites such as the liver and spleen.

Radiographically, lobulated

paravertebral masses, usually multiple and bilateral and in the

lower thoracic vertebra, are typically seen.

The bones may be normal or may show an altered lace-like trabecular pattern caused by marrow expansion. The masses are usually of homogeneous soft-tissue attenuation on CT, although, occasionally,

when the anaemia resolves, a fatty component may be visible. Usually the masses are bilateral and reasonably symmetrical.

Mesenchymal Tumours and Tumour-Like Conditions

Lymphangiomas (Cystic Hygromas)

Lymphangiomas are rare, benign congenital malformations consisting of focal proliferations of well-differentiated lymphatic tissue comprising complex lymph channels or cystic spaces containing clear or strawcoloured fluid.

Most lymphangiomas are present at birth and are detected in the first 2 years of life.

Lymphangiomas are most common

in the neck and axilla.

Lymphangiomas can occur in any part of the mediastinum but

are most common in the anterior or superior mediastinum.

Most cervicomediastinal lymphangiomas present in early life as a neck mass, whereas the purely

mediastinal lymphangiomas usually present in older children and adults as an asymptomatic mediastinal mass.

Complications include airway compromise, infection, chylothorax and chylopericardium.

On **CT**, a lobulated smooth mass envelopes the adjacent mediastinal structures rather than displaces them. This feature can be useful in distinguishing lymphangiomas from other mediastinal cysts.

Usually they have a homogeneous fluid attenuation but can have a combination of fluid and soft tissue. Thin septations can sometimes be seen within the mass. On **MRI** the lesions may have heterogeneous T1 signal intensity but usually have high T2 signal intensity.

Haemangiomas

Haemangiomas are rare vascular tumours composed of interconnecting vascular channels with varying areas of thrombosis and fibrous stroma.

Haemangiomas can be capillary, cavernous or venous, with cavernous haemangiomas accounting for approximately 75% of the cases.

Haemangiomas occur in young patients, with half of the patients being asymptomatic. Symptoms, when they occur, are caused by compression.

On CT, enhancement following contrast media administration

can be dense, focal or diffuse and peripheral or central. Phleboliths or punctate calcifications are seen in 10% to 20% of the cases.

Fatty Lesions in the Mediastinum

Fat is normally present in the mediastinum and its amount increases with age.

Normal fat is equally distributed throughout the matrix of

the mediastinum and is not encapsulated.

Abnormalities of fat distribution in the mediastinum can be diffuse (mediastinal lipomatosis) or focal (fat-containing diaphragmatic hernia or mediastinal lipoma).

Relatively large collections of fat are often present in the cardiophrenic angles, particularly in obese subjects. These cardiophrenic fat pads may resemble a mass.

Mediastinal Lipomatosis

Mediastinal lipomatosis is a benign accumulation of excessive amount of redundant unencapsulated histologically normal fat in the mediastinum.

Mediastinal lipomatosis is a phenomenon seen particularly in

Cushing disease, in patients on steroid therapy and in obese subjects.

The excess fat deposition is most prominent in the

upper mediastinum, resulting in a smooth symmetrical mediastinal widening on **CXR**. Chest **CT** shows exuberant, unconfined tissue of homogeneously low-attenuation fat that sharply outlines anatomical structures in all mediastinal compartments.

The diffuse nature of the fatty mediastinal infiltration helps to differentiate this entity from a focal mediastinal tumour.

Fatty Tumours of the Mediastinum

Fatty tumours of the mediastinum are rare. On **chest radiography**, regardless of whether they are benign or malignant, fatty tumours are seen as well-defined round or oval mediastinal masses.

Benign lipomas are soft and do not compress

surrounding structures unless they are very large.

On CT they show uniform fat attenuation.

Mediastinal liposarcomas are rare malignant fat-containing tumours. They may occur anywhere in the mediastinum.

In contradistinction to benign lipomas, they usually contain large areas of soft-tissue density material.

CT findings include inhomogeneous attenuation with significant soft tissue within a mass with fat attenuation, poor definition of adjacent mediastinal structures and infiltration or invasion of mediastinal structures.

Lipoblastoma, a benign tumour of childhood, contains fat and soft tissue.

CT findings are similar to liposarcomas.

Angiomyolipoma and myelolipoma are both benign tumours which may show a combination of soft-tissue and fat attenuation on CT and therefore can be indistinguishable from liposarcoma on imaging. Angiomyolipomas and myelolipomas are rare in the mediastinum.

Fat-Containing Hernias

Herniation of omental fat is a common cause of a localised fatty mass in the mediastinum. Omental fat can herniate through the foramen of Morgagni and give the appearance of a cardiophrenic angle mass on the right. Fat herniation through the foramen of Bochdalek occurs most frequently on the left side posteriorly. The fat may herniate through the oesophageal hiatus as well.

On CT or MRI, appearances

consistent with fat eliminate confusion with other mediastinal masses.

OTHER MEDIASTINAL LESIONS

Acute Mediastinitis

Acute mediastinitis is a rare but a life-threatening condition with high mortality and morbidity.

The most common causes of acute mediastinitis are postoperative complications and oesophageal perforation. Forceful vomiting may result in oesophageal perforation (Boerhaave syndrome) and a leak into the mediastinum can result in acute mediastinitis.

Such tears are almost invariably just above the gastrooesophageal junction.

Other causes of acute mediastinal infection are leakage from the oesophagus into the mediastinum through a necrotic neoplasm, and extension of infection from the neck, retroperitoneum or adjacent intrathoracic or chest wall structures into the mediastinum.

The **CXR** may show widening and ill-defined mediastinal outline adjacent to the oesophagus. Streaks or collections of air may be seen within the mediastinum, and there may even be mediastinal air–fluid levels. Air may also be seen in the soft tissues of the neck. Pleural effusions are frequent and are usually on the left.

The radiographic picture is often complicated by lower lobe pneumonia or atelectasis.

Radiologically, detection of oesophageal perforation relies on the presence of indirect signs, including pneumomediastinum, left pleural effusion and pneumothorax. An oesophagram using water-soluble contrast medium may show the site of perforation, with extravasation of orally ingested contrast agent into the mediastinum.

CT is the optimal technique in evaluating suspected mediastinitis and mediastinal abscess. Common CT findings of acute mediastinitis include increased attenuation of mediastinal fat, free gas bubbles in the mediastinum, localised fluid collections, enlarged lymph nodes, pleural effusions and empyema. Additional findings that depend on the cause

of the condition are obliteration of the normal mediastinal fat planes, oesophageal thickening and extraluminal gas bubbles within the mediastinum. In advanced cases there may be walled-off discrete fluid or air–fluid collections indicating abscess formation. There

may be an associated pleural effusion, empyema, subphrenic or pericardial collection.

Distinguishing a retrosternal haematoma

from reactive granulation tissue or cellulitis is difficult, as is distinguishing osteomyelitis from the direct effects of the surgical incision. It should

be remembered that substernal fluid collections and tiny pockets of air are normal in the first 20 days following sternotomy. Therefore, before gas-forming infections can be diagnosed, the air collections must appear de novo or must progressively increase in the absence of any other explanation. In descending necrotising mediastinitis, CT shows solitary or multiple fluid collections, which may be contiguous with other fluid collections in the cervical region and diffuse obliteration of normal fat planes related to fasciitis.

Fibrosing Mediastinitis

Fibrosing mediastinitis (sclerosing mediastinitis or mediastinal fibrosis) is a disorder that results in proliferation of fibrous tissue and collagen within the mediastinum. It is usually caused by previous infection from histoplasmosis or tuberculosis. Other causes include sarcoidosis,

autoimmune diseases, retroperitoneal fibrosis, radiation and drugs such as methysergide maleate. The most common clinical consequences are obstruction to the SVC and, occasionally, obstruction to the central pulmonary arteries or veins.

The **CXR** is non-specific and often underestimates the extent of mediastinitis. In fibrosing mediastinitis caused by previous tuberculous or fungal infection, the CXR may show calcification of mediastinal or hilar lymph nodes. **CT** typically shows an infiltrative, often extensively calcified, hilar or mediastinal process, which may be relatively focal when disease is caused by previous histoplasmosis or tuberculosis, and more diffuse in the idiopathic form.

CT is excellent for the evaluation of the extent of mediastinal soft-tissue infiltration and identification of the degree of narrowing of the mediastinal structures.

Two patterns of fibrosing mediastinitis have been described: a focal pattern and a diffuse pattern. The focal pattern caused by histoplasmosis, seen in 82% of cases, manifests as a mass of soft-tissue attenuation that is frequently calcified (63% of cases) and is usually located in the right paratracheal, subcarinal or hilar regions. The diffuse pattern, not related

to histoplasmosis, often occurs in the setting of retroperitoneal fibrosis, seen in 18% of cases, and manifests as a diffusely infiltrating, non-calcified mass that affects multiple mediastinal compartments.

Fibrosing mediastinitis typically demonstrates a heterogeneous, infiltrative mass of intermediate signal intensity on T1 weighted **MRI**.

On T2 weighted MRI it is more variable, with areas of both increased and markedly decreased signal intensity seen in the same lesion.

Areas of decreased signal intensity represent calcification or fibrous tissue, and areas of increased signal intensity may indicate more active inflammation.

Extensive regions of decreased signal intensity within the lesion, when present, help differentiate fibrosing mediastinitis

from other infiltrative lesions of the mediastinum, such as metastatic carcinoma and lymphoma, that typically have increased T2 signal intensity.

Heterogeneous enhancement of the mass may be seen after administration of a gadolinium-based contrast medium.

MRI lacks sensitivity for detection of calcification, which is an important feature for differentiating fibrosing mediastinitis from other infiltrative disorders of the mediastinum, such as lymphoma and metastatic carcinoma.

Mediastinal Haemorrhage

Mediastinal haemorrhage is most commonly caused by trauma to the arteries and veins within the mediastinum, with other causes including rupture of an aneurysm, aortic dissection and complications of central venous catheterisation.

Radiologically, haemorrhage produces an increase in the mediastinal diameter, which is maximal at the point of bleeding. Blood may track through the mediastinum, frequently running over the apex of the left lung to produce a smooth and well-defined apical cap. When haemorrhage

is severe, blood may rupture into the pleural cavity or dissect into lung along peribronchovascular sheaths, resulting in a radiographic pattern resembling interstitial oedema.

On unenhanced CT, acute haemorrhage

may appear of relative high attenuation.

The appearance of mediastinal haematoma on MRI varies with

the age of the haemorrhage.

Pneumomediastinum

Pneumomediastinum is characterised by the presence of free air around the mediastinal structures.

Common causes of pneumomediastinum include blunt or penetrating trauma, oesophageal perforation, recent

interventions in the oesophageal or tracheobronchial tree, pulmonary infections, gas-forming infections in the mediastinum, cocaine inhalation, and extension of air from a pneumothorax.

The radiographic signs of pneumomediastinum depend on the

anatomical structures outlined by the air. Air around the pulmonary artery (usually the right pulmonary artery) results in the 'ring around

the artery sign'. Elevation of the thymus causes the 'sail sign'.

Air anterior to the pericardium is best seen on the lateral radiograph.

The 'continuous diaphragm sign' is seen because of the air trapped posterior to the pericardium, giving the appearance of a continuous collection of air on the AP projection.

The 'tubular artery sign' occurs when there is air adjacent to the major branches of the aorta, the mediastinal air outlines the medial side and the aerated lung outlines the lateral side of the vessel. The 'double bronchial wall sign' is seen when the air adjacent to the bronchus allows clear depiction of the bronchial wall.

Air can also dissect through the perivascular tissues

and may track up into the neck, supraclavicular areas and axillae, as well as down into the retroperitoneum.

The differential diagnosis of a pneumomediastinum on **CXR** includes a medially located pneumothorax and a 'Mach effect' caused by the abrupt change in density between the lung and the adjacent heart and mediastinum. The Mach band effect is associated with convex surfaces, appearing as a region of lucency adjacent to structures with convex borders.

The absence of an opaque line, which is typically seen in pneumomediastinum, can aid in differentiation.

PERICARDIUM

The pericardium is a compliant sac that consists of two layers, the parietal and visceral pericardium, separated by a small amount of fluid, which is normally less than 50 mL.

The pericardium envelops the cardiac

chambers and the origins of the great vessels. The left atrium is partially covered by the pericardium. The thickness of the normal pericardium, as measured on CT and MRI, is less than 2 mm. Pericardial sinuses may be seen on CT and MRI, containing small amounts of fluid in normal healthy individuals. The oblique pericardial sinus behind the left atrium may be misinterpreted (e.g. bronchogenic cyst).

The transverse pericardial sinus posterior to the ascending aorta may also be misinterpreted (aortic dissection,

lymphadenopathy, etc.).

The superior pericardial recess lies posterior to the ascending aorta.

IMAGING PERICARDIAL DISEASE

Chest radiography is of limited use in the assessment of pericardial disease although pericardial effusions, calcification and secondary signs and complications of pericardial disease may be evident.

Interval enlargement of the cardiac silhouette should raise the suspicion of pericardial effusion.

Transthoracic echocardiography (TTE) is usually the initial investigation of suspected pericardial disease.

It is inexpensive and widely available and has high accuracy for detecting pericardial effusions and signs of tamponade. TTE is also helpful for guiding diagnostic or therapeutic

pericardiocentesis.

Restricted acoustic windows limit evaluation of the

entire pericardium; loculated collections, intrapericardial blood clot and pericardial thickening may be difficult to assess.

TTE is not very accurate for depicting pericardial thickening, because echogenicity of the pericardium is similar to adjacent tissues.

Transoesophageal echocardiography

is limited by a narrow field of view.

CT and **MRI** have distinct advantages over echocardiography, including larger field of view, higher contrast media resolution, excellent anatomical delineation and multiplanar reformats.

CT with multiplanar reformats, particularly

if ECG gated, provides excellent motion-free assessment of the pericardium; advantages include speed and wide availability and accessibility.

CT can also detect pericardial calcifications that may be indicative of constrictive pericarditis.

Disadvantages of CT include ionising radiation

and the need for IV iodinated contrast agent.

MRI can provide a comprehensive assessment of the pericardium. When T1 and T2 weighted sequences (some with ECG-gated breath-hold techniques) are combined with cinebased functional cardiac imaging, both pericardial disease

and its impact on cardiac function can be assessed.

MRI has some advantages over US and CT in detecting and

characterising pericardial collections and masses.

Limitations of MRI include its inability to reliably

depict calcification, and relatively long data acquisition times, especially with regard to breath-holding. Arrhythmias, which commonly occur in association with pericardial disease, may affect image acquisition and quality.

Nevertheless, CT or MRI should be used when findings

on echocardiography are difficult to interpret or nondiagnostic.

DEVELOPMENTAL ANOMALIES

Congenital Absence of the Pericardium

Compromise of the vascular supply to the pleuropericardial membrane during embryological development is associated with congenital defects in the pericardium.

Pericardial defects are rare and are usually asymptomatic.

The defects vary in size from small communications between

the pleural and pericardial cavities to complete (bilateral) absence of the pericardium. The most common form is complete absence of the left pericardium, with preservation of the pericardium on the right.

Bilateral and isolated right-sided lesions are very rare. Absence of the pericardium is rarely associated with congenital anomalies of the heart and lungs, including atrial septal defect, tetralogy of Fallot, patent ductus arteriosus, bronchogenic cysts and pulmonary sequestration. Pericardial defects are frequently associated with large defects in the parietal pleura, through which the left lung can herniate and surround the intrapericardial vascular structures.

Complete absence of the pericardium is usually asymptomatic,

whereas partial or localised absence of the pericardium may be complicated by herniation and entrapment of a cardiac chamber, in particular the left atrial appendage in left-sided defects.

CXR findings are frequently subtle and non-specific.

In complete absence of the left pericardium they include displacement of the heart into the left chest and interposition of lung between the aorta and pulmonary artery (as well as between the left hemidiaphragm and cardiac

silhouette). Both the medial and lateral borders of the main pulmonary artery may be visualised more clearly, caused by absence of the anterior pericardial reflection between the aorta and the pulmonary artery.

CT and **MRI** can depict herniation of cardiac structure through the defect.

Discontinuation of the pericardial line can occasionally be detected in the partial form. The most reliable signs of complete absence of the left pericardium are interposition of lung between the aorta and main pulmonary artery (in the aortopulmonary window), and a rotation of the cardiac axis to the left side (rather like a right anterior oblique view).

Pericardial Cysts

Pericardial cysts are formed when a portion of the pericardium is pinched off during early development and are thought to be
the result of persistence of blind-ending ventral parietal pericardial recesses.

Those cysts that communicate with the pericardial space are termed pericardial diverticula. With increase or decrease in pericardial fluid, diverticula can change in size. They almost invariably appear as a well-defined, oval or occasionally lobulated mass attached to the pericardium. More occur in

the right cardiophrenic angle $(\sim 70\%)$ than on the left $(\sim 20\%)$; some are seen higher in the mediastinum.

They contain clear fluid and can be recognised as fluid-filled cysts surrounded by normal pericardium on **echocardiography**, **CT** or **MRI**.

On MRI they have low to-

intermediate T1 signal intensity and homogeneous high T2 signal intensity. They do not enhance following IV gadolinium administration.

ACQUIRED PERICARDIAL DISEASE

Pericardial Effusion

Pericardial effusions are transudative or exudative accumulations of fluid in the pericardial space.

Common causes of pericardial effusion include heart failure, renal insufficiency, infection (bacterial, viral or

tuberculous), neoplasm (carcinoma of lung, breast or lymphoma) and injury (trauma and myocardial infarction).

Transudative pericardial effusions may develop after cardiac surgery or in congestive heart failure, radiation, uraemia, postpericardiectomy syndrome, myxoedema and collagen–vascular diseases.

Haemopericardium may be caused by trauma, aortic dissection, aortic rupture or neoplasm.

Interval enlargement of the cardiac silhouette on a **radiograph** over a short period of time should raise the suspicion of pericardial effusion. Filling in of the retrosternal space, effacement of the normal cardiac borders, development of a

'flask' or 'water bottle' cardiac configuration and bilateral hilar overlay are features of pericardial effusion.

The epicardial fat pad sign may be seen on the lateral projection that demonstrates an anterior pericardial stripe (bordered by epicardial fat posteriorly and mediastinal fat anteriorly) thicker than 2 mm. This sign represents pericardial thickening or fluid.

TTE is highly sensitive and specific for evaluating pericardial disease although visualisation may be limited in some obese

or emphysematous patients; loculated collections and intrapericardial clot in postoperative patients may be difficult to detect.

CT and **MRI** are indicated when TTE is inconclusive or when loculated or haemorrhagic effusion or pericardial thickening is suspected.

Increased attenuation in a pericardial effusion on CT suggests haemorrhage. When pericardial effusion is seen in patients with malignancy, the pericardium should be carefully evaluated for nodular (possibly metastatic) thickening

of the pericardium.

MRI is useful to differentiate small pericardial effusion from pericardial thickening.

On spin-echo MRI, the signal characteristics of pericardial collections vary, depending on the composition of the fluid. In the absence of haemorrhage, effusions are typically

of predominantly low T1 signal intensity, although intermediate signal intensity may be seen in inflammatory conditions such as uraemia, tuberculosis or trauma, possibly reflecting high protein content and, when more focal, the presence of adhesions limiting normal flow of pericardial fluid in the pericardial space. In haemorrhagic effusions, signal intensity varies, depending on the age of blood products.

Cardiac Tamponade

Gradual accumulation of pericardial fluid may fail to produce clinical signs or symptoms for an extended period of time. However, *rapid* accumulation of as little as 100–200 mL of fluid can cause a haemodynamically significant compression of the heart, which severely impedes diastolic filling, resulting in pericardial tamponade.

Because acute tamponade may occur with

small effusions, clinically important pericardial enlargement may be difficult to detect on **CXR**.

Subtle changes in cardiac contour may only be detectable by comparison with previous studies.

CT and **MRI** are frequently useful for determining the cause of the effusion, some of which include haemorrhage, neoplastic involvement, inflammation caused by tuberculosis, or other infectious processes.

Pericarditis

Inflammation of the pericardium (pericarditis) may occur in response to a variety of insults. Viral infection is the most common cause of myocardial infarction (acute or postmyocardial infarction referred to as Dressler syndrome), pericardiotomy, mediastinal irradiation, infection (viral or bacterial), connective tissue disease (rheumatoid arthritis, SLE), metabolic disorders (uraemia, hypothyroidism), neoplasia and AIDS.

The most common imaging manifestation of acute pericarditis is a pericardial effusion.

Thickened, inflamed pericardium can appear as moderate-tohigh signal intensity on spin-echo **MRI**, and pericardial enhancement may be seen on either MRI or **CT** performed after IV contrast medium administration.

Delayed images on contrast media-enhanced CT are useful for demonstrating pericardial enhancement.

Constrictive Pericarditis

Constrictive pericarditis presents with symptoms of heart failure such as dyspnoea, orthopnoea and fatigue.

The most common causes of

constrictive pericarditis are cardiac surgery and radiation therapy.

Other causes include infection (viral, tuberculous), connective tissue disease, uraemia, neoplasm or idiopathic.

The aetiology is unknown in many cases, presumed to be secondary to an occult viral pericarditis and other causes of pericarditis.

Any insult to the pericardium can progress from an acute pericarditis with pericardial effusion to a subacute stage

of resorption of the effusion with organisation, and then to a chronic phase of fibrous scarring, pericardial thickening and obliteration of the pericardial cavity.

CT and **MRI** are significantly more sensitive, with CT having the advantage over MRI of being able to demonstrate the

presence of calcification, which is associated with pericardial constriction.

Both CT and MRI may show the secondary effects of

constriction on the central cardiovascular structures.

Cardiac MRI can also be used to provide a more detailed assessment of cardiac function.

Diastolic septal bounce can be seen on cardiac MRI. A freebreathing sequence on cardiac MRI in which a patient performs a 'sniff' while the images are acquired, which demonstrates an exaggerated septal bounce (often referred to as ventricular interdependence), is helpful in leading to the diagnosis.

SUMMARY BOX: Constrictive Pericarditis

- Presents with dyspnoea, orthopnoea and fatigue
- Most common cause in the USA is iatrogenic (radiation and cardiac surgery)
- Most common cause in the world is infectious
- Pericardial thickening >4 mm

• Pericardial thickening can be localised adjacent to right ventricular free

wall or the right atrioventricular groove

• Pathophysiology based on restricted diastolic filling of the cardiac

chambers

- CT more sensitive in depicting pericardial calcification
- MRI can show ventricular interdependence on a free breathing sequence
- Cardiac cirrhosis may ensue and can be reversible with pericardectomy

Pericardial Neoplasms

Pericardial metastases are as much as 20 to 40 times more common than primary pericardial neoplasms.

The most common malignancies encountered are lung, lymphoma, breast, melanoma and colon.

Primary pericardial neoplasms are rare, with approximately equal incidence of benign versus malignant pericardial neoplasms.

Benign tumours include teratomas, fibromas, neurofibromas, lipomas, haemangiomas and lymphangiomas. Although these patients are usually symptom free, pericardial effusion or constriction, particularly in the case of childhood teratomas, may occur.

Malignant mesothelioma is the most common primary pericardial malignancy and is almost certainly related to

asbestos exposure.

Mesothelioma may present as a well-defined single mass, multiple nodules or diffuse plaques involving the visceral and parietal pericardium and wrapping around the cardiac chambers and great vessels.

A pericardial effusion is the most common finding in pericardial malignancy, whether primary pericardial or metastatic.

CXRs are often abnormal but are non-specific. Alteration of fat-pad contours, cardiac enlargement, mediastinal widening, hilar adenopathy or a hilar mass may be seen.

Echocardiography is usually the initial technique for evaluating a suspected pericardial neoplasm, with **MRI** and **CT** being useful for further evaluation. Both MRI and CT are excellent at providing information regarding the size, location and extent of pericardial neoplasms, but are not tissue specific. Fatty tumours (lipomas, fat-containing teratomas)

are the exception, because of their typically low attenuation on

CT and increased signal intensity on spin-echo T1 weighted MRI.

Mtastatic melanoma may have high

signal intensity on T1 and T2 weighted images, a feature that may be useful in differentiating it from other metastatic neoplasms, which are frequently of low signal intensity on T1 weighted images and high signal intensity on T2 weighted images.

Primary lipoma, liposarcoma and lymphoma of the

pericardium typically appear as large heterogeneous masses frequently associated with a serosanguineous pericardial effusion.

Pulmonary Infection in Adults

TYPES OF PNEUMONIAS

Currently accepted classifications of pneumonia include communityacquired pneumonia (CAP), hospital-acquired pneumonia (HAP),

ventilator-associated pneumonia (VAP) and health careassociated pneumonia (HCAP).

Community-Acquired Pneumonia (CAP)

The diagnosis of CAP is based on the presence of select clinical features (e.g. cough, fever, sputum production and pleuritic chest pain) and is supported by imaging of the lung, usually by chest radiography.

The spectrum of causative organisms of CAP includes grampositive bacteria such as *Streptococcus pneumoniae* (pneumococcus), *Haemophilus influenzae* and *Staphylococcus aureus*, as well as atypical organisms such as *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, or *Legionella*

pneumophila, and viral agents such as influenza A virus and respiratory syncytial viruses. Pulmonary opacities are usually evident on the **radiograph** within 12 hours of the onset of symptoms.

Hospital-Acquired Pneumonia (HAP)

Hospital-acquired pneumonia (HAP) may be defined as one

occurring after admission to hospital and was neither present nor in a period of incubation at the time of admission. Hospital-acquired pneumonia (nosocomial) is the leading cause of death from hospital-acquired infections and a serious public health problem. It occurs most commonly among intensive care unit (ICU) patients, predominantly in individuals requiring mechanical ventilation.

Ventilator-Associated Pneumonia (VAP)

Microorganisms responsible for VAP may differ according to the population of patients in the ICU, the duration of hospital and ICU stays, and the specific diagnostic method(s) used.

The spectrum of causative pathogens of VAP in humans is *S. aureus*, *Pseudomonas aeruginosa* and Enterobacteriaceae.

Health Care–Associated Pneumonia (HCAP)

When pneumonia is associated with health care risk factors such as prior hospitalisation, dialysis, residing in a nursing home, and immunocompromised state, it is now classified as health care–associated pneumonia (HCAP).

Aspiration Pneumonia

Infectious pneumonia needs to be differentiated from aspiration pneumonia, which also presents with patchy consolidations typically in the dependent portions of the lung (superior segments of the lower

lobes and posterior segments of the upper lobes).

The pattern is very variable, dependent on the quantity and quality of aspirated material,

and ranges from tree-in-bud to patchy consolidations, usually

multilobar and bilateral in distribution, though more frequently and more extensively to the right side due to the vertical position of the right-sided central airways.

CLINICAL UTILITY AND LIMITATIONS OF CHEST

RADIOGRAPHY AND COMPUTED TOMOGRAPHY

Although different patterns of pneumonia are associated with certain

underlying microorganisms, it has to be clearly stated that there is no

specific radiological pattern of pneumonia caused by one particular

microbe. Overlap of imaging findings also with respect to course over

time makes the differentiation of aetiologies based solely on the radiograph

unreliable.

The spectrum of causative pathogens of pneumonia in humans

includes gram-positive bacteria (S. pneumoniae and S. aureus), gramnegative

bacteria (H. influenzae, Escherichia coli and Klebsiella pneumoniae),

atypical bacteria (Mycoplasma pneumoniae, C. pneumoniae

and *L. pneumophila*), oral anaerobes and viral agents, fungi, protozoa and parasites.

Differentiation of aetiologies based solely on the radiograph is

not reliable, yet the pattern of abnormalities can be very useful in formulating a differential diagnosis of the nature of the disease.

New emerging pathogens have been recognised such as community-acquired methicillinresistant *S. aureus*, human metapneumovirus (hMPV), avian influenza A viruses (H5N1), coronavirus associated with severe acute respiratory

syndrome (SARS), swine flu (H1N1) and Middle East respiratory syndrome coronavirus (MERS-CoV).

Chest radiography remains an important component of evaluating a patient with a suspicion of pneumonia, and is usually the first examination to be obtained.

Although chest radiographs are of limited value in predicting the causative pathogen, they are of good use to determine

the extent of pneumonia and to detect complications (e.g. cavitation, abscess formation, pneumothorax and pleural effusion).

Computed Tomography

High-resolution computed tomography (HRCT) with thin < 2 mm thick slices, has been shown to be more sensitive than the radiograph in the detection of subtle abnormalities and may show findings suggestive of pneumonia up to 5 days earlier than chest radiographs High-resolution CT is recommended in patients with clinical suspicion of infection and normal or non-specific radiographic findings and in patients with increased risk of pulmonary infections (e.g.

neutropenia) (Fig. 5.1). CT is also indicated in patients with pneumonia and persistent or recurrent pulmonary opacities to

diagnose or rule out underlying or alternative disease processes.

PATTERNS OF PULMONARY INFECTION

Pneumonia is usually divided according to the chest imaging appearance into *lobar pneumonia, bronchopneumonia, and interstitial pneumonia.*

Common associated findings include hilar and mediastinal lymphadenopathy, pleural effusion, cavitation, and chest wall invasion.

An air bronchogram is frequently seen.

S. pneumoniae is by far the most common cause of complete lobar consolidation. Other causative agents that produce complete lobar consolidation include *K. pneumoniae* and other gram-negative bacilli, *L. pneumophila*, *H. influenzae*, and, occasionally, *M. pneumoniae*.

Characteristic manifestations on **CT** are lobar or sublobar consolidations,

sharply demarcated by the interlobar fissure.

Bronchopneumonia (lobular pneumonia) is characterised histologically by predominantly peribronchiolar inflammation. Although initially patchy, progression of disease results in lobular and segmental consolidation.

An air bronchogram is usually absent. The most common

causative organisms of bronchopneumonia are S. aureus, H. influenzae, P. aeruginosa and anaerobic bacteria.

Characteristic manifestations of bronchopneumonia on **HRCT** include centrilobular ill-defined nodules and branching linear

opacities, airspace nodules, and multifocal lobular areas of consolidation.

Many causative organisms are identified as bacteria, albeit unusual types (Mycoplasma is a type of bacteria).

COMPLICATIONS OF PNEUMONIA

Lung abscess is defined as a localised necrotic cavity containing pus and the most common cause is aspiration. A lung abscess occurs most commonly in the posterior segment of an upper lobe or the superior segment of a lower lobe. Common causes of lung abscess

include anaerobic bacteria (most commonly Fusobacterium nucleatum and Bacteroides sp.), S. aureus, P. aeruginosa and K. pneumoniae and radiologically manifest with single or multiple masses that are often cavitated.

Differential Diagnosis of

Cavitating/Necrotising Community-Acquired

Pneumonia in Immunocompetent Patients

Staphylococcus aureus, including methicillin-resistant S. aureus

- Anaerobic aspiration syndrome
- Klebsiella spp.
- Streptococcus milleri
- Right-sided endocarditis
- Tuberculosis
- Nontuberculous mycobacteria

Pulmonary gangrene is a rare complication of pneumonia characterized by the development of fragments of necrotic lung within an abscess cavity (pulmonary sequestrum). **Radiological manifestations**

consist initially of small lucencies within an area of consolidated lung, usually developing within lobar consolidation associated with enlargement of the lobe and outward bulging of the fissure (bulging fissure sign).

Pneumatocele is a thin-walled, gas-filled space that usually develops in association with infection.

The complication is caused most often by S. aureus in infants and children and P. jiroveci in patients who have acquired immune deficiency syndrome (AIDS).

Septic emboli to the lungs originate in a variety of sites, including cardiac valves (endocarditis), peripheral veins (thrombophlebitis), and venous catheters or pacemaker wires. On cross-sectional **CT** images the nodules often appear to have a vessel leading into them ('feeding vessel' sign). Dependent on the underlying organism, nodules cavitate typically at different time points, resulting in the simultaneous

appearance of solid nodules and nodules with varying sizes of cavitations.

Empyema occurs in less than 5% of pulmonary infections. The pathogens traditionally associated with empyema are *S. pneumoniae*, *Streptococcus pyogenes* and *S. aureus*. Radiographically, early signs include obliteration of the costophrenic angle.

Complete opacification of a hemithorax and contralateral

mediastinal displacement may occur in large effusions. Typically, an infected pleural effusion is encapsulated.

Other CT features include

(1) pleural enhancement and thickening of

the parietal pleura (split pleura sign),

(2) increased density of extrathoracic

fat and

(3) thickening and increased density of the extrapleural

subcostal fat.

Bronchopleural fistula is a sinus tract between the bronchus and the pleural space that may result from necrotising pneumonias, lung surgery, lung neoplasms and trauma. **Imaging features** consist of

- (1) increase in intrapleural air space,
- (2) (2) appearance of a new air-fluid

level,

(3) changes in an already present air-fluid level,

(4) development

of tension pneumothorax and

(5) demonstration of actual fistulous communication by CT.

INTEGRATING CLINICAL AND IMAGING FINDINGS

The clinician evaluating the patient with a known or suspected diagnosis of pulmonary infection faces a diagnostic challenge. This is because most processes present with similar signs and symptoms, and the radiographic findings of an individual pneumonia do not provide a specific aetiological diagnosis. Furthermore, radiographic manifestations of a given infectious

process may be variable, depending on the immunological status of the patient as well as the pre- or coexisting lung disease.

The most useful imaging techniques available for the evaluation of the patient with known or suspected pulmonary infection are chest radiography and CT.

Lobar Pneumonia

Most Common Organisms

Streptococcus pneumoniae. S. pneumoniae is responsible for

approximately one-third of all cases of CAP.

Pneumoccocal infections occur predominantly in the winter and early spring and are often associated with prior viral infection.

Risk factors for the development of pneumococcal pneumonia include the extremes of age, chronic heart or lung disease, immunosuppression, alcoholism, institutionalisation and prior splenectomy.

In the elderly, classic features of disease may be absent and pneumonia may be confused with or confounded by

other common medical problems, such as congestive heart failure, pulmonary thromboembolism or malignancy.

The typical **radiographic** appearance of acute pneumococcal pneumonia consist of an homogeneous consolidation that crosses segmental boundaries (nonsegmental) but involves

only one lobe (lobar pneumonia).

Occasionally, infection is manifested as a spherical focus of

consolidation that simulates a mass (round pneumonia). Complications such as cavitation and pneumatocele formation are rare. Pleural effusion is common and is seen in up to half of patients.

The **CT** 'angiogram sign', initially described in the lobar form of lepidic adenocarcinomas as the enhancement of branching pulmonary vessels in a homogeneous low-attenuation consolidation of lung parenchyma, may also occur in lobar pneumonia.

Klebsiella. *K. pneumoniae* is among the most common gramnegative bacteria, accounting for 0.5%–5.0% of all cases of pneumonia.

The **radiographic** features include *bulging fissures* due to volume increase of the infected lobe, sharp margins of the advancing border of the pneumonic infiltrate and early abscess formation. **CT** findings consist of ground-glass attenuation, consolidation and abscess formation.

Legionella *sp. Legionella* is one of the most common causes of severe CAP in immunocompetent hosts. Human infection may occur when *Legionella* contaminates water systems, such as air conditioners and condensers.

Risk factors for the development of *L. pneumophila* pneumonia include immunosuppression, post-transplantation, cigarette smoking, renal disease and exposure to contaminated drinking water.

Imaging findings include peripheral airspace consolidation

similar to that seen in acute S. pneumoniae pneumonia.

In many cases, the area of consolidation rapidly progresses to occupy all or a large portion of a lobe (lobar pneumonia) to involve contiguous lobes or to become bilateral.

Occasionally, Legionella pneumonia may result in a

round area of consolidation simulating a mass (round pneumonia).

Pleural effusion may occur in 35%–63% of cases.

Chlamydia. *C. pneumoniae* (strain TWAR) is the most commonly occurring gram-negative intracellular bacterial pathogen.

It is frequently involved in respiratory tract infections and has also been implicated in the pathogenesis of asthma in both adults and children.

On **CT**, *C*.

pneumoniae pneumonia demonstrates a wide spectrum of imaging findings that are similar to those of *S. pneumoniae* pneumonia and *M. pneumoniae* pneumonia, consisting of areas of consolidation, bronchovascular bundle thickening, nodules, small pleural effusion, lymphadenopathy, reticular or linear opacities and airway dilatation.

Moraxella catarrhalis. *Moraxella catarrhalis* (formerly known as *Branhamella catarrhalis*) is an intracellular gramnegative coccus now recognised as one of the common respiratory pathogens.

M. catarrhalis causes otitis media and sinusitis in children and relatively mild pneumonia and acute exacerbation in older

patients with chronic obstructive pulmonary disease (COPD).

Most patients with this type of pneumonia (80% to 90%) have underlying chronic pulmonary disease and their clinical illness may be difficult to distinguish from exacerbations of lung disease by other causes.

Chest radiographs show bronchopneumonia or lobar pneumonia that usually involves a single lobe.

Additional **CT** findings include ground-glass opacities, bronchial wall thickening and centrilobular nodules. Small effusions occur in one-third of patients.

Immunocompromised Host

Nocardia *sp.* Nocardia is a genus of filamentous grampositive, weakly acid-fast, aerobic bacteria that affects both immunosuppressed and immunocompetent patients. Nocardiosis usually begins with a focus of pulmonary infection and may disseminate through haematogenous spread to other organs, most commonly to the central nervous system

(CNS).

Imaging findings are variable and consist of unifocal or multifocal consolidation and single or multiple pulmonary nodules.

Cavitation is common and lymphadenopathy or chest wall involvement may occur.

Nocardia asteroides infection may complicate alveolar proteinosis.

Actinomyces *sp*. Thoracic actinomycosis is a chronic suppurative pulmonary or endobronchial infection caused by

Actinomyces sp., most frequently *Actinomyces israelii*, which is considered to be a gram-positive branching filamentous bacterium. Actinomycosis has the ability to spread across fascial planes to contiguous tissues without regard for normal

anatomic barriers.

On CT, parenchymal actinomycosis is characterised

by airspace consolidation with cavitation, or central areas of low attenuation and adjacent pleural thickening. Endobronchial actinomycosis can be associated with a foreign body (direct aspiration

of a foreign body contaminated with *Actinomyces* organisms) or a broncholith (secondary colonisation of a pre-existing endobronchial broncholith by aspirated *Actinomyces* organisms).

Endemic in Certain Geographic Areas

Coxiella burnetii (*Rickettsial Pneumonia*). The most common rickettsial lung infection is sporadic or epidemic Qfever pneumonia caused by *Coxiella burnetii*, an intracellular, gram-negative bacterium.

Affected patients are invariably debilitated by a chronic medical or pulmonary disease.

These bacteria are generally aspirated from a colonised

upper respiratory tract or may be inhaled or spread haematogenously.

The lower lobes predominantly tend to be affected and the radiographic pattern is similar to that seen with *S. aureus* infections in adults.

Infection is mainly acquired by inhalation from farm livestock or their products, and occasionally from domestic animals. **Imaging findings** consist of multilobar airspace consolidation, solitary or multiple nodules surrounded by a halo of 'groundglass' opacity and vessel connection, and necrotising pneumonia.

Other rickettsial infections such as Rocky Mountain spotted fever are usually tick-borne and occasionally demonstrate diffuse heterogeneous or homogeneous opacities on **chest radiographs**, perhaps representing vasculitis or cardiogenic pulmonary oedema.

Francisella tularensis. Tularaemia is an acute, febrile, bacterial zoonosis caused by the aerobic gram-negative bacillus *Francisella tularensis*.

It is endemic in parts of Europe, Asia and North America.

Primary pneumonic tularaemia occurs in rural settings. Humans become infected after introduction of the bacillus by inhalation, intradermal injection or oral ingestion. **Chest radiographic** findings are scattered multifocal consolidations, hilar adenopathy and pleural effusion.

Bronchopneumonia

Most Common Organisms

Staphylococcus aureus. Pneumonia caused by *S. aureus* usually follows aspiration of organisms from the upper respiratory tract.

Risk factors for the development of staphylococcal pneumonia include underlying pulmonary disease (e.g. COPD, carcinoma), chronic illnesses (e.g. diabetes mellitus, renal failure) or viral infection. A severe CAP caused by associated methicillin-resistant *S. aureus* (MRSA) carrying genes for Panton–Valentine leukocidin has been described in immunocompetent young adults.

This bronchopneumonia (lobular pneumonia) is bilateral in

approximately 40% of patients.

Other features are cavitation, pneumatoceles, pleural effusions and spontaneous pneumothorax.

The **CT** manifestations of *S. aureus* pneumonia include centrilobular nodules and branching opacities (tree-in-bud

pattern) and lobular, subsegmental or segmental areas of consolidation with or without abscess formation.

Escherichia coli. *E. coli* accounts for approximately 4% of cases of CAP and 5%–20% of cases of HAP or HCAP. It occurs most commonly in debilitated patients.

The **radiographic manifestations** are usually those of bronchopneumonia; rarely, a pattern of lobar pneumonia may be seen.

The pneumonia involvement is usually multilobar and predominantly in the lower lobes.

Pseudomonas aeruginosa. *P. aeruginosa* is a gram-negative bacillus that is the most common cause of nosocomial pulmonary infection.

It causes confluent bronchopneumonia that is often extensive and frequently cavitates.

The radiological manifestations are non-specific and consist

most commonly of patchy areas of consolidation and widespread poorly defined nodular opacities.

CT findings consist of multifocal, predominantly

upper lobe, airspace consolidation, random large nodules,

tree-in-bud opacities, ground-glass opacity, necrosis and pleural effusion.

Haemophilus influenzae. *H. influenzae* is a pleomorphic, gram negative coccobacillus that accounts for 5% to 20% of CAP in patients in whom an organism can be identified successfully.

Factors that predispose to *Haemophilus* pneumonia include COPD, malignancy, human immunodeficiency virus (HIV) infection and alcoholism.

The typical radiographic appearance

of *H. influenzae* pneumonia consists of multilobar involvement with lobar or segmental consolidation and pleural effusion.

Atypical Pneumonia

Mycoplasma pneumoniae. M. pneumoniae is one of the most

common causes of CAP. It occurs most commonly in younger persons and infection is particularly common among military recruits.

Patients with COPD appear to be more severely affected with *M. pneumoniae* than normal hosts.

The **radiographic findings** in *M. pneumoniae* are variable and, in some cases, closely resemble those seen in viral infections of the lower respiratory tract.

A focal reticulonodular opacification confined to a

single lobe is a radiographic pattern that seems to be closely associated with *Mycoplasma* infection.

Although lymphadenopathy is uncommon in *Mycoplasma* pneumonia, unilateral hilar lymph node enlargement has been described. These

findings may be indistinguishable from those seen in children with primary tuberculosis.

CT findings consist of patchy segmental and lobular

areas of ground-glass opacity or airspace consolidation, centrilobular nodules and thickening of the bronchovascular bundles.

Viral

Acute bronchiolitis is a term most often used to describe an illness in infants and children.

Viral infections predispose to secondary bacterial pneumonia.

Influenza A.

They are more common during infancy and may often lead

to severe lower respiratory tract disease. In adults, infections are usually mild and restricted to the upper respiratory tract. Influenza A virus is transmitted from person to person by aerosolised or respiratory droplets.

The predominant **HRCT findings** are ground-glass opacities, consolidation, centrilobular nodules and branching linear opacities.

Adenovirus.

Swyer–James–MacLeod syndrome is considered to be a postinfectious bronchiolitis obliterans (BO) secondary to adenovirus infection in childhood.

CT findings in post-infectious BO consist of sharply marginated focal areas of increased and decreased lung opacity with reduced vessel size in lucent lung regions, bronchial wall thickening and bronchiectasis.

Air-trapping is commonly visible on expiratory CT as lucent areas that represent regions of lung that are poorly ventilated and perfused.

In children, adenovirus may result in lobar collapse, especially of the right upper lobe.

The **CT** findings consist of patchy bilateral areas of consolidation in a lobular or segmental distribution and/or bilateral ground-glass opacities with a random distribution.

Respiratory syncytial virus (RSV). Respiratory syncytial virus (RSV) is the most frequent viral cause of lower respiratory tract infection in infants. The major risk factors for severe RSV disease in children are prematurity (<36 weeks' gestation), congenital heart disease, chronic lung disease, immunocompromised status and multiple congenital abnormalities.

CT findings consist of small centrilobular nodules, airspace

consolidation, ground-glass opacities and bronchial wall thickening. The abnormalities are located in the central and peripheral areas of the lungs with a predominantly bilateral and asymmetric distribution. *Epstein–Barr virus (EBV).* Primary infection with Epstein– Barr virus (EBV) occurs early in life and presents as infectious mononucleosis with the typical triad of fever, pharyngitis and lymphadenopathy, often accompanied by splenomegaly.

Mild, asymptomatic pneumonitis occurs

in about 5% to 10% of cases of infectious mononucleosis.

The **CT** manifestations of EBV pneumonia are similar to those of other viral pneumonias.

Varicella-zoster virus. Varicella-zoster virus is a common contagious infection in childhood with increasing incidence in adults. Clinically, it presents in two forms: varicella (chickenpox) representing a primary disseminated disease in uninfected individuals and zoster (shingles) representing reactivation of latent virus (unilateral dermatomal skin

eruption).

Pneumonia, although rare, is the most serious complication affecting adults with chickenpox. Varicella pneumonia is estimated to occur in one of every 400 cases of adulthood chickenpox infections, being more common in pregnant and immunosuppressed patients.

Predisposing conditions include underlying leukaemia and lymphoma and other causes of immunodeficiency.

Thin-section CT appearances in varicella pneumonia largely reflect the multicentric haemorrhage and necrosis centred on airways.

CT findings include numerous nodular opacities measuring 5 to 10 mm in diameter, some with a surrounding halo of

ground-glass opacity, patchy ground-glass opacities and coalescence of nodules.

A miliary distribution may also occur and nodules may calcify, presenting as well-defined, randomly scattered, 2 to 3 mm densely calcified nodules.

Herpes simplex virus type 1 (HSV 1). Herpes simplex virus type 1 (HSV-1) pneumonia may be a life-threatening infection seen almost exclusively in immunocompromised and/or mechanically ventilated patients, usually as a component of polymicrobial infection.

The **radiographic findings** include airspace consolidation, predominantly lobar or more extensive and always bilateral, or a mixed airspace and interstitial pattern.

During the course of disease, pleural effusions can also develop.

CT findings consist of patchy lobular, subsegmental or segmental consolidation and ground-glass opacities; associated small centrilobular nodules and tree-in-bud pattern have been described in patients infected with herpes simplex virus type 2; nodules surrounded by a 'halo' of ground-glass opacity may also occur.

Hantaviruses.

Hantavirus infection may cause diffuse airspace disease, termed hantavirus pulmonary syndrome (HPS).

The mortality rate of treated patients can approach 35%. Histologically, changes are characteristic

for exudative and proliferative stages of diffuse alveolar

damage.

Imaging findings may be initially normal, but progressively worsen, displaying signs of pulmonary oedema and acute respiratory distress syndrome (ARDS).

The chest radiograph findings may represent differences

in the extent of alveolar epithelial damage seen in HPS and

ARDS.

The **CT** appearances of HPS consist of extensive bilateral ground-glass opacities, thickened interlobular septa, a few

poorly defined small nodules, bronchial wall thickening and small bilateral pleural effusions.

Cytomegalovirus (CMV). Cytomegalovirus (CMV) pneumonia is a

major cause of morbidity and mortality following haematopoietic stem cell (HSC) and solid organ transplantation, and in patients with AIDS in whom CD4 cells are decreased to fewer than 100 cells/mm3.

CMV infection occurs in up to 70% of bone marrow transplant (BMT) recipients, and approximately one-third develop CMV pneumonia.

This complication characteristically occurs during the postengraftment

period (30 to 100 days after transplantation), with a median time onset of 50 to 60 days post-transplantation.

Chest radiographs demonstrate focal and diffuse hazy opacification and multiple small (less than 5 mm) nodules, and

less commonly focal consolidation.

CT features of CMV pneumonia consist of lobar consolidation, diffuse and focal ground-glass opacities, irregular reticular opacities, and multiple miliary nodules or small nodules with associated areas of ground-glass attenuation ('halo').

New Emerging Viruses

Human metapneumovirus (hMPV). Human metapneumovirus

(hMPV) is a recently identified RNA virus, genus *Metapneumovirus*.

It is usually associated with acute respiratory tract infections including upper airway disease, lower airway bronchitis and bronchiolitis, influenzalike syndrome and pneumonia.

An increased risk for severe illness occurs in premature infants with or without chronic lung disease and infants and young children with congenital heart disease.

In adults, epidemiological studies have demonstrated that hMPV infection accounted for 4% of patients with CAP or COPD.

CT findings consist of patchy areas of ground-glass attenuation, small nodules and multifocal areas of consolidation in a bilateral asymmetric distribution.

Pulmonary parenchymal involvement during the course of hMPV pneumonia infection may result in interstitial lung

disease and fibrosis.

Severe acute respiratory syndrome coronavirus. Severe acute

respiratory syndrome (SARS) caused by SARS-associated coronavirus (SARS-CoV) is a systemic infection that clinically manifests as progressive pneumonia.

The **CT** imaging features of SARS-CoV infection consist of unilateral or bilateral ground-glass opacities, focal unilateral or bilateral areas of consolidation or a mixture of both.

In the areas of ground-glass opacification, thickening of the intralobular interstitium or interlobular septamay be present. If marked septal thickening occurs, a 'crazy paving' appearance results.

Middle East respiratory syndrome. Middle East respiratory syndrome (MERS) is a viral disease caused by a coronavirus (MERS-CoV).

Chest radiography may reveal pulmonary opacities and consolidation, with a peripheral predominance in the mid and lower lung zones in the initial stages of the illness.

As the disease progresses, parenchymal abnormalities may spread to the central areas and become diffuse.

Within

the first week of the disease, **CT** may depict ground-glass opacities, consolidation, interlobular thickening and pleural effusion.

During the subsequent weeks, other findings may be present such as centrilobular nodules, a 'crazy-paving' pattern, obliterative bronchiolitis, peribronchial air trapping and organising pneumonia.

Avian flu (H5N1). Avian influenza is caused by the H5N1

subtype of the influenza A virus.

Most

chest radiographs are abnormal at the time of presentation, with multifocal consolidation the commonest radiographic finding.

The most common **CT** findings consist of focal, multifocal or diffuse ground-glass opacities or areas of consolidation. Pseudocavitation, pneumatocele formation, lymphadenopathy and centrilobular nodules are often seen.

Swine influenza (H1N1).

The **predominant CT** findings are unilateral or bilateral ground-glass opacities with or without associated focal or

multifocal areas of consolidation.

On CT, the ground-glass opacities and areas of consolidation have a predominant peribronchovascular and subpleural distribution, resembling organising pneumonia.

Multifocal areas of air trapping may also be observed.

CHANGING SPECTRUM OF HUMAN

IMMUNODEFICIENCY VIRUS INFECTIONS:

40 YEARS LATER

Aetiologically, S. pneumoniae predominates,

followed by *H. influenzae. Mycobacterium tuberculosis* is still a major threat; its **imaging** patterns may vary depending on CD4 count.

Immune reconstitution inflammatory syndrome (IRIS) in

HIVinfected patients with mycobacterial infections starting HAART is defined as an exacerbation of symptoms, signs or radiological manifestations of a pathogenic antigen, which are not due to relapse or recurrence.

The **most common imaging features** of IRIS consist of mediastinal lymph node enlargement, with central low attenuation, diffuse and bilateral pulmonary nodules, organising pneumonia and small pleural effusions.

Mycobacterium tuberculosis

Mycobacterium tuberculosis accounts for more than 95% of pulmonary mycobacterial infections. Other mycobacterial spp., mainly *M. kansasii* and the *Mycobacterium avium– intracellulare complex* (MAC), account for the remainder.

Factors that contribute to the large number of cases seen worldwide are HIV infection, inner-city poverty, homelessness and immigration from areas with high rates of infection.

Other predisposing conditions

are diabetes mellitus, alcoholism, silicosis, malignancy, immune compromise from a variety of causes and living in closed institutions.

The imaging findings of patients with tuberculosis take many

forms and are best discussed as primary, reactivation and reinfection tuberculosis.

Primary Tuberculosis

This form is commonly seen in infants and children. With improved control of tuberculosis in Western societies, however, more people reach adulthood without exposure and primary patterns of disease are being seen with increasing frequency in adulthood.

It represents approximately 23%–34% of all adult cases of tuberculosis.

Although primary tuberculosis typically presents with **radiographic manifestations**, chest radiography may be normal in 15% of cases.

Parenchymal disease manifests as homogeneous lobar consolidation, which may occur in any lobe, and is often indistinguishable from that of other bacterial pneumonia, although the clinical evolution is usually different.

Lymphadenopathy is the most common manifestation of primary tuberculosis in children and occurs with or without pneumonia.

Pleural effusion is often large and unilateral in children with parenchymal or nodal disease, or in teenagers and young adults, when it is frequently isolated.

Usually, the primary pneumonia resolves completely.

In one-third of patients a residual well-defined rounded or irregular (linear) opacity, with or without calcification, remains.

This is a Ghon lesion or focus.

Nodal calcification may occur in the ipsilateral hilum or mediastinum and is heterogeneous and irregular.

When a Ghon lesion or focus and ipsilateral lymph node calcification are seen together, the combination is termed a Ranke complex.

Reactivation and Reinfection Tuberculosis

Most cases are due to reactivation of quiescent lesions but, occasionally, a new infection from an exogenous source occurs.

The **radiological** manifestations may overlap with those of primary tuberculosis, but the absence of lymphadenopathy, more frequent cavitation and a predilection for the upper lobes, are more typical of post-primary tuberculosis.

Cavitation indicates active disease and is seen in the region of

abnormality in 40%-80% of cases.

Air-fluid levels.

A Rasmussen aneurysm is a rare life-threatening complication of cavitary tuberculosis caused by granulomatous weakening of a pulmonary arterial wall.

Endobronchial spread can occur with or without cavitary disease and is similar to that seen with primary tuberculosis, leading to the appearance of the typical images of 'tree-inbud'.

After antituberculous treatment, healing results in scar formation, often with evidence of severe volume loss and pleural thickening.

Residual thin-walled cavities may be present in both active and inactive disease.

Although classically a manifestation of primary disease, miliary tuberculosis is now more commonly seen as a postprimary process in older patients. Multiple small (1-2 mm), discrete nodules are scattered evenly throughout both lungs. A tuberculoma may occur in the setting of primary or postprimary tuberculosis and represents localised parenchymal disease that alternately activates and heals. It usually calcifies and frequently remains stable for years. Satellite nodules around the tuberculoma may be present.

Chest wall involvement may be due to haematogenous seeding or direct spread from the lung and may affect soft tissue, rib or costal cartilage ('empyema necessitatis').

Pulmonary Non-Tuberculous Mycobacteria (NTMB)

As mentioned above, 13% of pulmonary mycobacterial infections are caused by agents other than *M. tuberculosis*: usually MAC and, less commonly, *M. kansasii*.

The severity of disease depends on the presence of underlying lung disease and the status of immunocompetence.

The most typical form of pulmonary non-tuberculous mycobacteria (NTMB) infection is seen in elderly men with underlying lung disease.

Another form of NTMB infection affects elderly white women without underlying lung disease (Lady Windermere syndrome).

HRCT findings consist of mild to moderate cylindrical bronchiectasis and multiple 1–3 mm diameter centrilobular 'tree-in-bud' opacities usually affecting the middle lobe and lingula.

Fungal Infection

Fungi involved in pulmonary infections are either pathogenic fungi, which can infect any host, or saprophytic fungi, which

infect only immunocompromised hosts.

Pathogenic fungi cause coccidioidomycosis, blastomycosis and histoplasmosis.

Saprophytes cause PCP, candidiasis, mucormycosis and aspergillosis.

Aspergillus Infection

Aspergillosis is a fungal disease caused by *Aspergillus* sp., usually *A. fumigatus*. Classically, pulmonary aspergillosis

has been categorised into saprophytic, allergic and invasive forms.

Aspergillus mycetomas are saprophytic growths that colonise a preexisting cavity in the lung (usually sarcoidosis or tuberculosis).

Most cavities and, therefore, mycetomas are in the upper lobes or superior segments of the lower lobes.

The great majority of aspergillomas are asymptomatic. Haemoptysis is the most important complication.

Bronchial artery embolisation may sometimes be helpful in management.

At **CT**, saprophytic aspergillosis (aspergilloma) is characterised by a mass with soft-tissue attenuation within a lung cavity.

The mass is typically separated from the cavity wall by an airspace ('air crescent'sign).

Bilateral involvement may occur and multiple nodules

have been reported.
The **radiographic** appearances consist of non-segmental areas of opacity most common in the upper lobes, lobar collapse, branching thick tubular opacities due to bronchi distended with mucus and fungus ('finger-in-glove sign', 'Y' shape) and,

occasionally, pulmonary cavitation.

On **CT**, although the mucous plugs are generally hypodense, in up to 20% of cases they can be hyperdense.

Angioinvasive aspergillosis is almost exclusively seen in immunocompromised hosts, mainly in patients with severe neutropenia.

This form is characterised by invasion and occlusion of small to medium pulmonary arteries, developing necrotic haemorrhagic nodules or infarcts.

The most common pattern seen in **CT** consists of multiple nodules surrounded by a halo of ground-glass attenuation ('halo sign') or pleural-based wedge-shaped areas of consolidation.

The bronchial cut-off sign refers to the central necrosis. The nodular opacities are usually widespread in several lobes as opposed to clusters of peribronchial opacities seen in bacterial infections.

An air crescent sign—though not specific for angioinvasive *Aspergillus* infection—indicates recovery of the immune system and is actually quite a late sign.

Radiologically, the appearances are variable, but a common pattern is of one or more rounded, poorly marginated areas of homogeneous opacification with or without air bronchograms.

Candidiasis

Candida sp. has been increasingly recognised as an important source of fungal pneumonia in immunocompromised patients, particularly in those with underlying malignancy (acute leukaemia and lymphoma), intravenous drug abuse and AIDS, and following BMT.

The usual **thin-section CT** findings of pulmonary candidiasis consist of multiple bilateral nodular opacities, often associated with areas of consolidation and ground-glass opacity.

Less common CT findings are pleural effusion, thickening of the bronchial walls and cavitation.

Pneumocystis jiroveci

P. jiroveci (formerly *Pneumocystis carinii*) is a unique opportunistic fungal pathogen that causes pneumonia in immunocompromised individuals such as patients with AIDS (CD4 counts below 100 cells/mm3), patients with organ transplants and with haematological or solid organ malignancies who are undergoing chemotherapy and in patients receiving immune-suppressive treatments, particularly systemic corticosteroids (e.g. patients with rheumatoid arthritis).

Reportedly >90% of patients show **radiographic** abnormalities, mainly the classical findings of diffuse bilateral interstitial infiltrates in a perihilar distribution, although normal radiographs do not exclude the diagnosis.

In these patients, **CT** may be helpful in confirming the diagnosis of PCP when clinical suspicion is high, typically showing images with perihilar ground-glass opacities,

occasionally combined with focal consolidation, with a patchy or geographical distribution.

In the acute phase there may be subpleural sparing and in the subacute phase, cysts may develop during treatment.

Mucormycosis

Mucormycosis is an opportunistic fungal infection of the order Mucorales.

The most common **radiographic** findings consist of lobar or multilobar areas of consolidation and solitary or multiple pulmonary nodules and masses; associated cavitation is found in 26% to 40% of cases.

An air-crescent sign, highly suggestive of an invasive fungal infection.

CT features are non-specific and consist of solitary or multiple areas of consolidation and solitary or multiples nodules surrounded by a halo of ground-glass attenuation ('halo sign') and cavitation.

A pattern of multifocal pneumonia.

Cryptococcosis

Cryptococcosis is caused by inhaling spores of *Cryptococcus neoformans*, a fungus of worldwide distribution found in soil and in bird droppings.

Cryptococcal pneumonia is a common pulmonary

infection in AIDS patients with CD4 counts below 100 cells/mm3.

The most **typical radiographic** manifestation consists of

pulmonary masses, homogeneous segmental or lobar opacifications, and miliary, reticular or reticulonodular interstitial patterns.

The masses, ranging from 5 mm to very large size, are usually ill-defined and may show a halo similar to an invasive *Aspergillus* lesion, which may eventually

cavitate.

Histoplasmosis

Histoplasma capsulatum is a fungus found in moist soil and in bird or bat excreta in many parts of the world.

Though nodules greater than 3 cm may be seen, the most

common radiographic findings consist of diffuse nodular opacities of 3 mm or less in diameter, nodules greater than 3 mm in diameter, small linear opacities and focal or patchy areas of consolidation.

CT is requested as a more sensitive imaging investigation. Hilar and mediastinal lymph nodes are frequently enlarged.

Chronic pulmonary histoplasmosis radiologically resembles **post-primary tuberculosis**, with upper lobe contraction, calcification and cavitation.

In some cases, fibrosing mediastinitis may develop and can lead to constriction of mediastinal structures, including the airways, superior vena cava, pulmonary arteries and

pulmonary veins.

Coccidioidomycosis

Coccidioidomycosis is caused by Coccidioides immitis, a

fungus.

In primary coccidioidomycosis, unifocal or multifocal homogeneous opacities resembling community-acquired bacterial pneumonia may be seen.

Cavitation and hilar/mediastinal adenopathy may be seen. Primary disease almost invariably

resolves spontaneously or reveals only small residual linear or nodular scars.

A characteristic CT appearance consisting of a central area of soft-tissue attenuation with a surrounding halo of ground-glass attenuation may be seen around these nodules. Disseminated coccidioidomycosis may cause miliary nodules.

Chronic fibronodular cavitary disease may resemble **postprimary tuberculosis**.

Paracoccidioidomycosis (South American Blastomycosis)

Paracoccidioidomycosis (PCM), an endemic disease caused by the dimorphic fungus *Paracoccidioides brasiliensis*. The **predominant HRCT** findings consist of areas of groundglass opacities, nodules, the 'halo' and 'reversed halo' signs, interlobular septal thickening, airspace consolidation, cavitation and fibrosis.

North American Blastomycosis

North American blastomycosis is due to *Blastomyces dermatiditis*. Pulmonary infection may be accompanied by infection of the skin, bones and genitourinary tract.

The chest radiograph reveals homogeneous unifocal or

multifocal segmental or lobar opacification indistinguishable

from acute pneumonia.

Cavitation occurs.

Sometimes, the pneumonia is spherical in shape, closely resembling bronchial carcinoma.

Pleural thickening or pleural effusion may accompany the pneumonia. Blastomycosis may cause miliary nodules, particularly in immunocompromised patients.

A chronic fibrocavitary form of the disease is also seen.

PARASITIC INFECTIONS

Parasitic infections of the lung occur worldwide among both immunocompetentand immunocompromised patients.

Protozoa

Amoebiasis

Pleuropulmonary amoebiasis caused by *Entamoeba histolytica* is usually secondary to liver involvement.

The lung is the second most common extraintestinal site of amoebic involvement after the liver.

Pleuropulmonary amoebiasis is a significant complication of amoebic liver abscess.

Right-sided abnormalities are found in 86% of cases and consists of hemidiaphragmatic elevation, pleural effusion or empyema and/or thickening and plate-like atelectasis.

Liver abscess can extend directly into the lung. Causing pulmonary consolidation. If communication

with a major bronchus occurs, haemoptysis can develop, containing the 'anchovy paste' pus coming from the amoebic abscess.

Malaria

Malaria is transmitted by the bite of *Anopheles* mosquito. The microorganisms *Plasmodium vivax*, *P. falciparum*, *P. malariae* and *P. ovale* are responsible for the disease, and *P. falciparum* is the deadliest type of infection.

Adult respiratory distress syndrome is the most common

lung-finding manifestation.

Septal thickenings, pleural effusions and airspace consolidations are seen on **HRCT** and are consistent with

noncardiogenic pulmonary oedema.

Cryptogenic organising pneumonia has also been reported.

Nematodes

Dirofilariasis

Although not common in humans, dirofilariasis is occurring with increasing frequency as the canine population grows. *Dirofilaria immitis*, or the dog heartworm, is a rare cause of pulmonary nodules in humans.

The majority of patients with dirofilariasis are asymptomatic.

Ascaris immitis is transmitted by mosquitoes from dogs to humans.

An immature adult worm unable to mature in the accidental human host can reach a peripheral vein and travel in the bloodstream until it lodges in a pulmonary vein.

The disease has been reported predominantly in the temperate climates of the east and south coasts of the United States, but sporadic cases have been found worldwide.

Ascariasis

Ascariasis is one of the most common parasitic infections, affecting 1.3 billion people worldwide.

The disease is caused by ingestion of food or fluids contaminated with faeces with *A. lumbricoides*.

Strongyloidiasis

Strongyloidiasis is a chronic parasitic infection caused by *Strongyloides stercoralis*. *S. stercoralis* filariform larvae invade the lungs and small intestine through the skin from the soil.

Trypanosomiasis

Caused by *Trypanosoma cruzi*, which is acquired through the bite of a triatomine insect, trypanosomiasis is also known as Chagas disease, being endemic in South America.

A nodular lesion or furuncle, usually called chagoma,

can appear at the site of inoculation. Chronic manifestations include cardiomyopathy, bundle branch blocks, complete atrioventricular block and ventricular aneurysms. Late gastrointestinal compromise is caused by damage to neurones of the myenteric plexus, with achalasia, megaoesophagus and megacolon.

Oesophageal manifestations are similar to those of idiopathic achalasia. **Radiographically**, oesophageal

dilatation shows a shadow projecting to the right of the mediastinum, with or without the presence of an air-fluid level.

Cysticercosis

Cysticercosis is a common parasitic disease in Latin America caused by infection with the larval stage of the pork tapeworm *Taenia solium*.

CT may depict cystic lesions, commonly with a hyperdense central nodule, which represents the parasite head, called the scolex.

Pulmonary cysticercosis mimics many other diseases

presenting with nodules, cavitary lesions and pleural effusion. If association of chest wall and cardiac muscles lesions is seen, cysticercosis should be the first diagnosis to be considered.

Toxocariasis

Humans can be accidental hosts or may develop the disease, which is caused by the larvae of *Toxocara*

canis or T. cati.

In humans, the larvae do not develop into adult worms

but migrate through host tissues. Therefore, the disease is also called visceral larva migrans.

CT findings consist of ground-glass opacities, solid nodules, areas of consolidation and linear opacities.

Cestodes

Echinococcosis (Hydatid Disease)

Hydatid disease (echinococcosis) is caused by the larval forms of *Echinococcus granulosus, E. multilocularis* and *E. vogeli. E. granulosus* (unilocular cystic echinococcosis) is the most common form affecting man and is seen in the Mediterranean area, Eastern Europe, Africa, South America, the Middle East, Australia and New Zealand.

Humans are accidental hosts and acquire infection by ingesting ova from fomites or contaminated water and by direct contact with dogs.

Hydatid cyst has been reported in almost all human tissues and organs.

Cysts in the mediastinum, heart and pulmonary arteries are rare.

Hydatid cysts are usually solitary but may be multiple and/or bilateral in 10% of cases. They may be ruptured (two-thirds) or unruptured (one-third) at the time

of presentation.

Aggressive invasion of vascular structures such as

bronchial and pulmonary arteries may result in massive haemoptysis and haemorrhage.

The **radiological findings** in patients with unruptured pulmonary cysts are one or more homogeneous, roughly spherical or oval, sharply demarcated lesions with mass effect. Cyst rupture is usually associated with secondary infection and may spread into the airways or pleural space.

The radiographic appearance resembles the air crescent of a mycetoma.

Should there be disruption of the inner layers, a complex cavitary lesion results with one or more of the following radiographic features: an air-fluid level, a floating membrane (water lily sign, camalote sign), a double wall, an essentially dry cyst with crumpled membranes lying at its bottom (rising sun sign, serpent sign) and a cyst with all its contents expectorated (empty cyst sign).

Secondary infection of a hydatid cyst may produce a lung abscess with or without surrounding lung opacity.

Rupture into the pleural space causes an effusion or, if

there is airway communication, a hydropneumothorax.

Trematodes

Paragonimiasis

Pleuropulmonary paragonimiasis is a disease caused by a fluke (*Paragonimus westermani*) characterised by migration of a juvenile worm in the early stage and by formation of cysts around the worm later on.

Water snails and crustaceans are intermediate hosts and infestations are acquired from eating raw or incompletely cooked fresh water crabs and crayfish. The disease mainly occurs in the Far East, southeast Asia and Africa.

Radiological changes tend to be bilateral, including a mixture of consolidation, nodules and band, tubular and ring opacities.

In the lower lobes, parenchymal changes mimic bronchiectasis, and in the upper lobes, tuberculosis.

The constellation of focal pleural thickening and subpleural

linear opacities leading to a necrotic peripheral pulmonary nodule is another frequent **CT** finding of paragonimiasis.

Schistosomiasis

Schistosomiasis is an acute and chronic parasitic disease caused by a trematode worm of the genus *Schistosoma*. Chronic granulomatous inflammation of pulmonary arterioles can result in arteriolitis obliterans, pulmonary hypertension and cor pulmonale Formation of a pulmonary

artery aneurysm is a common complication related to this disease.

Large Airway Disease and Chronic

Airflow Obstruction

TRACHEAL DISORDERS

The trachea may be affected by a variety of extrinsic or intrinsic processes.

Extrinsic processes, particularly masses, displace and distort the trachea, while intrinsic ones cause narrowing, widening, or a mass effect.

Tracheal narrowing may affect a short or a long segment and may extend to the mainstem bronchi.

Tracheal disease, though commonly missed on the

chest radiography, is usually evident on careful evaluation of the frontal and lateral radiograph. Computed tomography (**CT**) allows precise

delineation of the intratracheal and extratracheal extent of the abnormality.

Multidetector CT, by combining helical volumetric CT acquisition and thin collimation during a single breath hold, provides an accurate assessment of proximal airways, allowing multiplanar reformations and 3D rendering of very high quality. Complementary CT acquisition at

suspended or continuous expiration demonstrates tracheal collapsibility.

This expiratory acquisition may be performed at reduced dose or even better at ultra-low dose, by using thin slices reconstructed with iterative reconstruction or a soft kernel when using filtered back projection

mode.

Post-Traumatic Strictures

Strictures of the trachea are usually secondary to damage from a cuffed endotracheal or tracheostomy tube or to external neck_trauma. The lesions consist of granulation tissue followed by the development of dense mucosal and submucosal fibrosis associated with the distortion of cartilage plates.

The two principal sites of stenosis following intubation

or tracheostomy tube are at the stoma or at the level of the endotracheal or tracheostomy tube balloon.

On **radiographs**, the stenosis may be seen as a focus of circumferential or eccentric narrowing associated with a segment of increased soft tissue.

The size of the narrowing is usually easily seen at **CT**.

The narrowing is often concentric. Post-intubation stenosis

can extend for several centimetres and typically involves trachea above the level of the thoracic inlet.

Post-tracheostomy stenosis typically begins 1 to 1.5 cm distal to the inferior margin of the tracheostomy stoma and involves 1.5 to 2.5 cm of tracheal wall.

Multiplanar reformations are particularly helpful

in defining accurately the site, the length and the degree of the stenosis.

In selected cases, the degree of stenosis may also be shown

by virtual bronchoscopy.

Infectious Tracheobronchitis

A number of infections, both acute and more often chronic, may affect the trachea and proximal bronchi, resulting in both focal and diffuse airway disease.

Subsequent fibrosis may result in localised airway narrowing.

The most common causes of infectious tracheobronchitis are

bacterial tracheitis in immunocompromised patients, tuberculosis, rhinoscleroma (Klebsiella rhinoscleromatis), and necrotizing invasive aspergillosis.

On **CT**, the extent of irregular and sometimes circumferential tracheobronchial narrowing is clearly demonstrated, and in some patients an accompanying mediastinitis (opacification of the mediastinal fat) is evident. In active disease, the narrowed trachea and frequently one or more main bronchus have an irregularly thickened wall. In the fibrotic or healed phase, the trachea is narrowed but has a wall that is smooth and of normal thickness.

Primary Malignant Neoplasms

These are uncommon tumours, accounting for less than 1% of all thoracic malignancies.

On **CT**, they appear as a soft-tissue mass, usually in the posterior and lateral wall. Often sessile and eccentric, resulting in asymmetric luminal narrowing, they may appear

rarely circumferential.

They can be polypoid and mostly intraluminal with mediastinal extension. The surface of tumour is often irregular in squamous cell carcinoma, whereas it is smooth

in adenoid cystic carcinoma. Multiplanar reformation and volumetric rendering images are recommended for a precise pre-therapeutic assessment of tumour extent.

Secondary Malignant Neoplasms

The large airways may be involved secondarily by malignant neoplasms as a result of either haematogenous metastasis or direct invasion from the oesophagus, thyroid, mediastinum or lung.

Neoplasms that have a propensity to metastasise to the trachea and major bronchi include renal cell carcinoma and melanoma.

On **CT**, the abnormalities are usually focal and include intraluminal soft-tissue nodules and wall thickening.

Distal bronchoceles may also be seen.

Benign Neoplasms

The most common are hamartoma, leiomyoma, neurogenic tumour and lipoma. They are usually well-demarcated, round and less than 2 cm in diameter.

The **radiologic** appearance typically consists of a smoothly marginated intraluminal polyp.

Hamartomas and lipomas may demonstrate fat attenuation on CT.

Tracheobronchial papillomatosis is a particular entity caused by human papillomavirus infection usually acquired at birth from an infected mother. The larynx is most commonly affected, with occasional extension into the trachea and proximal.

Exceptionally, the infection spreads into the lung parenchyma. The **typical radiological** findings consist of multiple small nodules projecting into the airway lumen or

diffuse nodular thickening of the airway wall.

Although benign, papilloma may undergo transformation to squamous cell carcinoma.

Wegener Granulomatosis

Involvement of the large airways is a common manifestation of Wegener granulomatosis.

Inflammatory lesions may be present with or without subglottic or bronchial stenosis, ulcerations and pseudotumours.

Radiological manifestations include thickening of the subglottic region and proximal trachea with a smooth

symmetric or asymmetric narrowing over variable length. Stenosis may also be seen in any main lobar or segmental bronchus.

Nodular or polypoid lesions may also be seen on

the inner contour of the airway lumen.

Relapsing Polychondritis

Relapsing polychondritis is a rare systemic disease of autoimmune pathogenesis that affects cartilage at various sites, including the ears, nose, joints, and tracheobronchial tree.

Symmetric subglottic stenosis is the most frequent

manifestation in the **chest**.

As the disease progresses, the distal trachea and bronchi may be involved. **CT** shows smooth thickening of the airway wall associated with more or less diffuse narrowing.

In the early stage, the posterior wall of the trachea is spared but in advanced disease circumferential wall thickening occurs.

The trachea may become flaccid with considerable collapse at expiration.

Gross destruction of the cartilaginous rings with fibrosis may cause stenosis.

Tracheobronchial Amyloidosis

Deposition of amyloid in the trachea and bronchi may be seen in association with systemic amyloidosis or as an isolated manifestation. As a result, the amyloid forms are either multifocal or diffuse submucosal plaques or masses.

The overlying mucosa is usually intact.

Dystrophic calcification or ossification is frequently present. **CT** shows focal or, more commonly, diffuse thickening of the airway wall and narrowing of the lumen.

Calcification may be seen.

Narrowing of the proximal bronchi can lead to distal atelectasis, bronchiectasis, or both, or to obstructive pneumonia.

Sarcoidosis

Involvement of the trachea is rare and when it occurs, it is associated with laryngeal involvement.

The proximal and distal parts of the trachea may be affected, and the appearance of the stenosis may be smooth, irregular

and nodular, or even mass-like.

Bronchial involvement is much more common as a manifestation of sarcoidosis.

The most **common** signs at **CT**

are regular or nodular bronchial wall thickening, reflecting the presence of granulomas and fibrous tissue in the peribronchial interstitium.

This bronchial wall thickening may result in smooth or irregular bronchial narrowing, which correlates with the presence of mucosal thickening at bronchoscopy and presumably reflects prominent inflammation in this location. Obstruction of lobar or segmental bronchi may occur

as a result of granulomata, airway wall fibrosis, peribronchial lymph node compression and conglomerate fibrosis or some combination of these phenomena.

Bronchial stenosis may clear spontaneously or with

steroid treatment.

Inflammatory Bowel Disease

Ulcerative tracheitis and tracheobronchitis are rare complications and occur more often in association with ulcerative colitis than Crohn disease.

In most but not all cases, the diagnosis of inflammatory bowel disease precedes the presence of airway disease.

Cartilaginous plates are not destroyed. On CT, the

tracheobronchial walls are thickened and produce irregular luminal narrowing.

Bronchial wall thickening and bronchiectasis may

also be present with or without mucoid impaction.

Tracheobronchopathia Osteochondroplastica

This rare disorder is characterised by the presence of multiple cartilaginous nodules and bony submucosal nodules on the inner surface of the trachea and proximal airways. Men are more frequently involved than women and most patients are more than 50 years of age

The **chest radiograph** may be normal or may demonstrate lobar collapse or infective consolidation.

If the tracheal air column is clearly seen, multiple sessile nodules that project into the tracheal lumen extending over a long segment of the trachea can be appreciated.

On **CT**, tracheal cartilages are thickened and show irregular calcifications.

The nodules may protrude from the anterior and lateral walls into the lumen; they usually show foci of calcification.

Sabre-Sheath Trachea

Characterised by a diffuse narrowing involving the intrathoracic trachea, this entity is almost always associated with COPD.

The pathogenesis of the lesion is obscure, but probably it is an acquired deformity related to the abnormal pattern and magnitude of intrathoracic pressure changes in COPD.

On **radiographs and CT**, the condition is easily recognised by noting that the internal side-to-side diameter of

the trachea is decreased to half or less than the corresponding sagittal diameter.

On the postero-anterior radiograph and CT multiplanar

reformations, the narrowing usually affects the whole intrathoracic trachea, with an abrupt return to normal calibre at the thoracic inlet.

The trachea usually shows a smooth inner margin but

occasionally has a nodular contour.

Calcification of the tracheal cartilage is frequently evident.

Tracheobronchomegaly (Mounier-Kuhn Disease)

This refers to patients who have marked dilatation of the trachea and mainstem bronchi.

It is often associated with tracheal diverticulosis, recurrent lower respiratory tract infection and bronchiectasis.

Atrophy affects the elastic and muscular elements of both the cartilaginous and membranous parts of the trachea.

The diagnosis is based on **radiological** findings.

The immediately subglottic trachea has a normal diameter, but it expands as it passes to the carina and this dilatation often continues into the major bronchi.

Atrophic mucosa prolapses between cartilage rings and gives the trachea a characteristically corrugated outline on a plain radiograph. Corrugations may become exaggerated to form sacculations or diverticula.

On **CT**, a tracheal diameter of greater than 3 cm (measured 2 cm above the aortic arch) and diameter of 2.4 and 2.3 cm for the right and left bronchi respectively are diagnosing criteria. Additional findings include tracheal scalloping or diverticula (especially along the posterior membranous tracheal wall).

Tracheobronchomalacia

Resulting from weakened tracheal cartilages, this abnormality may be

seen in association with a number of disorders including tracheobronchomegaly,

COPD, diffuse tracheal inflammation such as relapsing polychondritis, as well as following trauma. On chest than

50% can occur at expiration with normal tracheal compliance.

As a result, only a decrease in cross-section area of the tracheal lumen greater than 70% at expiration indicates tracheomalacia.

Dynamic expiratory multislice **CT** may offer a feasible alternative to bronchoscopy in patients with suspected tracheobronchomalacia.

Dynamic expiratory **CT** may show complete collapse or collapse of greater than 80% of airway lumen.

Involvement of the central tracheobronchial tree may be diffuse or focal.

The reduction of the airway may have an radiographs, a

reduction by almost 300% of the sagittal diameter at expiration is an excellent indicator of the diagnosis.

At **CT**, the diagnosis is based on a narrowing of the lumen of diameter by more than 70% on expiration compared with that on inspiration.

The increase in compliance is due to the loss of integrity of the wall's structural components and is particularly associated with damaged or destroyed cartilage. The coronal

diameter of the trachea becomes significantly larger than the sagittal one, producing a lunate configuration to the trachea. The flaccidity of the trachea or bronchi is usually most apparent during coughing or forced expiration.

In patients with COPD with high downstream resistance,

particularly high dynamic pressure gradients can be

generated across the tracheal wall and it is likely that calibre changes of more oval or crescentic shape.

The crescentic form is due to the bowing of the posterior membranous trachea.

Tracheobronchial Fistula and Dehiscence

Multidetector computed tomography (MDCT) with thin collimation is the most accurate technique to identify peripheral bronchopleural fistula that are most commonly caused by necrotising pneumonia or secondary to traumatic lesions.

Minimum intensity projection oval or crescentic shape. The crescentic form is due to the bowing of the posterior membranous trachea.

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fistula that are most commonly caused by necrotising pneumonia (Fig.

6.13) or secondary to traumatic lesions. Minimum intensity projection (minIP) reconstructions provide good delineation of the fistulous tract.

Nodobronchial and nodobronchoesophageal fistulas caused by mycobacterium tuberculosis infection, are depicted by the presence of gas in cavitated hilar or mediastinal lymphadenopathy adjacent to the airways. Tracheobronchoesophageal fistula may also be diagnosed even in adults.

Malignant neoplasia, particularly oesophageal, is the most common cause of tracheoeosophageal fistula in adults.

Occasionally congenital fistulas are first manifested in adults.

Infection and trauma are the most frequent non-malignant causes.

MDCT has a high degree of sensitivity and specificity for depicting bronchial dehiscence occurring after lung transplantation.

Bronchial dehiscence is seen as a bronchial wall defect associated with extraluminal air collections.

BRONCHIECTASIS

Bronchiectasis is a chronic condition characterised by local, irreversible dilatation of bronchi, usually associated with inflammation.

Despite its decreased prevalence in developed countries, bronchiectasis remains an important cause of haemoptysis and chronic sputum production.

Although the causes of bronchiectasis are numerous, there are **three mechanisms** by which the dilatation can develop: bronchial obstruction, bronchial wall damage, and parenchymal fibrosis.

In the first two mechanisms, the common factor is the combination of mucus plugging and bacterial colonisation. Cytokines and enzymes released by inflammatory cells plus

toxins from the bacteria result in a vicious cycle of increasing airway wall damage, mucus retention and bacterial proliferation.

In cases of parenchymal fibrosis, the dilatation of bronchi

is caused by maturation and retraction of fibrous tissue located in the parenchyma adjacent to an airway (traction bronchiectasis).

As the extent and degree of airway dilatation increase, the lung parenchyma distal to the affected airway shows increasing collapse of fibrosis.

Radiographic Findings

Chest radiography reveals abnormalities in most cases. Thickened bronchial walls are visible either as single thin lines or as parallel line opacities (tramline).

When seen end-on, bronchiectatic airway appears as a poorly defined ring or curvilinear opacities.

Dilated bronchi filled with mucus or pus result in tubular or ovoid opacities of variable size.

Cystic bronchiectasis manifests as multiple thin-walled ring shadows often containing air-fluid levels.

Pulmonary vessels may appear increased in size and may be indistinct because of adjacent peribronchial inflammation fibrosis.

In generalised bronchiectasis, such as that associated with cystic fibrosis, overinflation is often present.

Localised forms are frequently accompanied by atelectasis which may be mild and detected only because of vascular crowding, fissure displacement, or obscuration of part of the diaphragm.

Computed Tomographic Findings

The major sign of bronchiectasis on thin collimation high resolution computed tomography (HRCT) scan is dilatation of the bronchi (with or without bronchial wall thickening). The CT findings of bronchial dilatations include lack of tapering of bronchial lumina (the cardinal sign of bronchiectasis), internal diameter bronchi greater than that

of the adjacent pulmonary artery (signet ring sign), visualisation of bronchi within 1 cm of the costal pleura or abutting the mediastinal pleura, and mucus-filled dilated bronchi.

In varicose bronchiectasis, the bronchial lumen assumes a beaded configuration.

Cystic bronchiectasis is seen as a string of cysts caused by sectioning irregular dilated bronchi along their lengths, or a cluster of cysts, caused by multiple dilated bronchi lying adjacent to each other.

Clusters of cysts are most commonly seen in the atelectatic lobe.

Air fluid levels, caused by retained secretions, may be present in the dependent portion of the dilated bronchi. Secretion accumulation within bronchiectatic airways is

generally easily recognisable as lobulated glove-finger, -V or -Y shaped densities.

When oriented perpendicular to the avail acquisition

plane, the filled dilated bronchi are visualised as nodular opacities and recognised by the observation of the homologous pulmonary arteries, whose diameters are smaller than those of the dilated filled bronchi.

CT may show a completely collapsed lobe containing bronchiectatic airways.

Subtle degrees of volume loss may be seen in lobes in relatively early disease.

This is most evident in the lower lobes on the basis of

crowding of the mildly dilated bronchi and posterior displacement of the oblique fissure.

Multiplanar reformations along the long axis of airways may help in assessing the dilated bronchi, recognising

clusters of cystic bronchiectasis and differentiating them from lung abscess.

Associated CT findings of bronchiolitis are seen in about 70% of patients with bronchiectasis.

Small centrilobular nodular and linear branching opacities (tree-in-bud sign) express inflammatory and infectious

bronchiolitis.

Areas of decreased attenuation and vascularity, mosaic perfusion pattern, and expiratory air trapping reflect

the extent of obliterative bronchiolitis.

These abnormalities are very common in patients with severe bronchiectasis and can even precede the development of bronchiectasis. The obstructive defect found at pulmonary tests in patients with bronchiectasis seems not to be related to the degree of collapse of large airways on expiratory CT or to the extent of mucus plugging of the airway but is the consequence

of an obstructive involvement of the peripheral airways (obliterative bronchiolitis).

The extent of CT evidence on small airway disease

(decreased lung attenuation, expiratory air trapping) and bronchial wall thickening commonly present in patients with bronchiectasis have proven to be the major determinants of airflow obstruction.

The bronchial wall thickening assessed by CT has been demonstrated to be the primary determinant of subsequent major functional decline.

Pulmonary hypertension (PH) may be reflected by pulmonary arterial enlargement on CT scans and is a

highly significant prognostic indicator in the evaluation of patients with bronchiectasis.

Accuracy of Computed Tomography

By combining helical volumetric CT acquisition and thin collimation, CT has gained greater advantages by circumventing the limitations of HRCT, particularly the risk of missing bronchiectasis strictly localised within the intervals between slices.

At the present time, multidetector CT with thin collimation is a highly recommended technique for assessing the presence and extent of bronchiectasis. A CT Dose Index (CTDI) of less than 1 may be proposed with iterative reconstruction or filtered back projection with soft kernel, especially for young people.

Multiplanar reformations increase the detection rate and the reader's confidence, with regard to the distribution of bronchiectasis, and improve agreement between observers, with regard to the diagnosis of bronchiectasis.

In addition, maximum intensity projections (MIPs) improve the detection and display of both mucoid impactions and small centrilobular and linear branching opacities (tree in bud sign) characteristic of infectious bronchiolitis.

minIP performed on a slab reconstructed with a soft-tissue

kernel or iterative reconstruction help detect hypoattenuated lung areas reflecting obstruction lesion in the small airways (obliterative bronchiolitis) associated with bronchiectasis. The reliability of CT for distinguishing between the causes of bronchiectasis is somewhat controversial.

An underlying cause for bronchiectasis is found in fewer

than half of patients and CT features alone do not usually allow a confident distinction between idiopathic bronchiectasis versus other causes of bronchiectasis. However, bilateral upper lobe distribution is most commonly seen in patients with cystic fibrosis and allergic

bronchopulmonary aspergillosis (ABPA), while unilateral upper lobe distribution is most common in patients with tuberculosis, and a lower lobe distribution is most often seen in patients after childhood viral infections.

Cystic Fibrosis

Cystic fibrosis results from an autosomal recessive genetic defect in the structure of the cystic fibrosis transmembrane regulation protein, which leads to abnormal chloride transport across epithelial membranes.

Although the mechanisms by which this defect leads to lung disease are not entirely understood, an abnormally low water content of airway mucus is at least partially responsible for decreased mucus clearance, mucus plugging of airways, and an increased incidence of bacterial airway infection. Bronchial wall inflammation progressing to secondary bronchiectasis is always present in patients with longstanding disease.

In patients with early or mild disease, **chest radiographs** may be quite subtle.

Hyperinflation reflects the presence of obstruction of the small airways.

Thickening of the wall of the upper lobar bronchi can

also be seen on the lateral film.

In more advanced disease, the radiographs can be diagnostic, showing increased lung volume, accentuated linear opacities in the upper lung areas, resulting from bronchial wall thickening or bronchiectasis, proximal bronchiectasis and mucoid impaction.

Additional findings include cystic regions of the upper lobes, representing cystic bronchiectasis, healed abscess cavities, bullae, atelectasis, findings of PH or cor pulmonale, pneumothorax or pleural effusion.

Chest radiography may be sufficient for clinical management, but there is often little visible radiographic change during clinical exacerbation. These studies consistently document a close correlation between HRCT findings and both clinical and pulmonary functional evaluation of these patients.

On **CT**, peripheral and/or central bronchiectasis is present in all patients with advanced cystic fibrosis.

All lobes are typically involved, although early in the disease abnormalities are often predominantly distributed in the upper lobes, and sometimes with right upper lobe predominance.

Bronchial wall and/or peribronchial interstitial thickening is also commonly present.

It is generally more evident than bronchial dilatation in patients with early disease.

Mucus plugging is present in 25–50% of patients and may be seen in all lobes.

Collapse or consolidation is visible in up to 80% of patients. Lobar volume loss is often present in patients with advanced disease.

Bullae may be difficult to distinguish from cystic bronchiectasis, particularly in fibrotic upper lobes. Abscesses may be difficult to distinguish from cystic bronchiectasis, particularly as both may contain air fluid levels. Pleural thickening, often apparent on chest radiography, is better demonstrated by CT.

Small centrilobular nodular and branching linear opacities (tree in bud sign) can be an early sign of disease.

They reflect presence of mucous impactions in dilated bronchioles associated with peribronchiolar inflammation. Focal areas of decreased lung attenuation are frequently present, representing air trapping and mosaic perfusion

due to obstruction of the small airways (obliterative bronchiolitis).

At an early stage of disease, CT can demonstrate abnormalities of the airways in patients who are asymptomatic and have normal pulmonary functions and normal chest radiographs.

In patients with more advanced disease, CT is superior to chest radiograph in detecting bronchiectasis and mucus plugging.

Magnetic resonance imaging has been recommended as a substitute for CT in the assessment of patients with cystic fibrosis in order to avoid the use of ionising radiation. Although the spatial resolution of pulmonary MR is lower than that of CT, it has the advantage of being able to distinguish different aspects of tissue on the basis of different contrast on T1 weighted and T2 weighted images as well as enhancement after contrast media administration. Perfusion defects assessed by contrast enhanced perfusion MR imaging show good correlation with the degree

of tissue destruction in patients with cystic fibrosis.

If applied to therapeutic monitoring, it might be possible to differentiate between lung areas with reversible and irreversible disease. The recent development of ultrashort TE sequences provides the differentiation between bronchial

wall thickening and mucus and permits the visual assessment of bronchiolar abnormalities.

In addition, the ultrashort TE (time of echo) sequences can detect air trapping areas (making gadolinium administration

unnecessary).

Allergic Bronchopulmonary Aspergillosis

A hypersensitivity reaction to aspergillus species, ABPA is characterized by asthma, blood eosinophilia, **radiographic** pulmonary opacities and evidence of allergy to antigens of aspergillus species.

It may also occur in patients with cystic fibrosis.

Recurrent acute episodes cause progressive lung damage that can be controlled by steroids.

The **radiological** features can be classified as acute and transient, or chronic and permanent.

The most common acute changes are transient consolidation, mucoid impaction, and atelectasis.

Consolidation ranges from massive and homogeneous to lobar or segmental in configuration, or, to subsegmental

or smaller.

When consolidation clears, it often leaves residual bronchiectasis that creates a favourable condition for fungal

recolonisation, a finding that accounts for the fact that consolidation recurs often in the same area.

Mucoid impaction obstructs the airway lumen which becomes distended by retained secretions.

At the same time, lung parenchyma remains aerated by collateral drift, permitting the visualisation of the impacted airway.

Bronchoceles appear as opacities of a variety of shapes

(linear, branched or unbranched, bandlike opacities that point to the hilum, tooth-paste opacities, V- and Y-shape opacities, glove finger opacities).

These opacities disappear once their airway contents

have been coughed up, leaving ring or parallel linear opacities.

Atelectasis can be subsegmental, segmental, lobar or even affecting a whole lung, with a tendency to recur in the same area.

Permanent changes indicate irreversible lung damage and provide the clue that an asthmatic has ABPA when he/she is in remission.

Bronchiectasis is responsible for most of the permanent radiological changes.

It affects lobar bronchi and the first- and second-order segmental bronchi. Beyond the proximal bronchi, more distal airways remain normal and patent, though small airway abnormalities are present on **CT**.

These abnormalities include a tree-in-bud appearance

reflecting mucoid impaction in dilated bronchioles and focal areas of decreased lung attenuation and air trapping reflecting obstruction of the small airways.

Compared with other bronchiectatic diseases, bronchiectasis

in ABPA is more commonly widespread and central, and more likely to contain cystic or varicose components.

Mucus plugs within the ectatic airways are frequently seen. High attenuation within the plugs is also relatively frequently seen, reflecting the presence of calcium salts and metals (the ions of iron and manganese).

Hyperattenuated mucus plugs may be depicted within the areas of consolidation.

Parenchymal scarring represents the fibrotic stage of the disease.

It commonly follows bronchiectasis and manifests by linear opacities and lobar shrinkage.

Mirroring the distribution of bronchiectasis, these features have a strong upper zone predilection.

Despite this upper lobar shrinkage, the lung volume is frequently increased, reflecting overinflation in the lower lobes due to obstruction of the small airways and the presence of bullae and cavitation in the upper lobes.

Diskinetic Cilia Syndrome

Resulting from a genetic abnormality having autosomal recessive transmission, dyskinetic cilia syndrome is characterised by abnormal ciliary structure and function, leading to a reduced mucociliary clearance and chronic airway infection.

Bronchiectasis and sinusitis are common manifestations. About half of patients also have situs inversus.

The combination of bronchiectasis, sinusitis and situs inversus is termed Kartagener syndrome. Men and women are equally affected, but in men the syndrome may be associated with immotile spermatozoa and infertility.

Bronchiectasis develops in childhood and adolescence and

is associated with recurrent pneumonia.

Both **radiography** and **CT** typically show bilateral bronchiectasis with a basal (lower or middle lobe) predominance, similar to that seen in patients with other causes of postinfectious bronchiolitis.

Cylindrical bronchiectasis is most common, and a diffuse bronchiolitis may be present.

BRONCHOLITHIASIS

Broncholithiasis is a condition in which peribronchial calcified nodal

disease erodes into or distorts an adjacent bronchus. The underlying

abnormality is usually granulomatous lymphadenitis caused by mycobacterium

tuberculosis or fungi such as histoplasma capsulatum. A few

cases have been reported with silicosis. Calcified material in a bronchial

lumen or bronchial distortion by peribronchial disease
results in airway

obstruction. This leads to collapse, obstructive pneumonitis, mucoïd

impaction, or bronchiectasis. Symptoms include cough, haemoptysis,

recurrent episodes of fever and purulent sputum. Broncholithiasis is

more common on the right, and obstructive changes particularly affect

the right middle lobe.

On chest radiographs, three major types of changes may be seen:

- disappearance of a previously identified calcified nidus
- change in position of a calcified nidus
- evidence of airway obstruction, including segmental or lobar atelectasis,

mucoïd impaction, obstructive pneumonitis, obstructive oligaemia

with air trapping.

Calcified hilar or mediastinal nodes are a key feature.

CT and fibreoptic bronchoscopy complement each other in this

condition. Broncholithiasis is recognised at CT by the presence of a

calcified endobronchial or peribronchial lymph node,

associated with

bronchopulmonary complication due to obstruction (including atelectasis,

pneumonia, bronchiectasis, and air trapping), in the absence of

an associated soft-tissue mass.

OBLITERATIVE (CONSTRICTIVE) BRONCHIOLITIS

Inflammation of the bronchioles (bronchiolitis) is very common, although it is rarely extensive enough to cause clinical symptoms.

Obliterative bronchiolitis is a condition characterised by bronchiolar and peribronchiolar inflammation and fibrosis that ultimately leads to luminal obliteration affecting membranous and respiratory bronchiolitis.

Obliterative bronchiolitis is the result of a variety of causes and only rarely idiopathic.

Radiological Findings

The **chest radiograph** is often normal. In a small number of patients, mild hyperinflation, subtle peripheral attenuation of the vascular makings, widespread and conspicuous abnormalities in lung attenuation, and central bronchiectasis may be seen.

Thin section **CT** is superior to radiography in demonstrating the presence and extent of abnormalities.

The main CT findings usually consist of areas of decreased lung attenuation associated with vessels of decreased calibre during inspiration and air trapping on expiratory CT. Because the lesions of bronchiolar narrowing or obstruction are heterogeneously distributed throughout the lungs, redistribution of blood flow to areas of normal lung or less diseased areas results in a pattern of mosaic perfusion. Bronchial wall thickening and bronchiectasis, both central and peripheral, are also commonly present.

Although the vessels within areas of decreased attenuation on thin-section CT may be of markedly reduced calibre, they are not distorted as in emphysema.

The lung areas of decreased attenuation related to decreased perfusion can be patchy or widespread.

They are poorly defined or sharply demarcated, giving a geographical outline, representing a collection of affected secondary pulmonary lobules.

Redistribution of blood flow to the normally ventilated areas causes increased attenuation of lung parenchyma in these areas.

The patchwork of abnormal areas of low attenuation and normal lung or less diseased areas, appearing normal in attenuation or hyper-attenuated, gives the appearance of mosaic attenuation. The vessels in the abnormal hypoattenuated areas are reduced in calibre, whereas the

vessels in normal areas are increased in size, and the resulting pattern is called 'mosaic perfusion'.

The difference in vessel size between low- and highattenuation areas allows one to distinguish the mosaic perfusion pattern from mosaic attenuation due to an infiltrative lung disease with patchy distribution, in which the vessels have the same calibre in both high-attenuation and normalattenuation areas.

The areas of decreased lung attenuation and perfusion may be confined to or predominant in one lung, particularly in Swyer-James or MacLeod syndrome, that is a variant form of post-infectious obliterative bronchiolitis in which the

obliterative bronchiolar lesions affect predominantly one lung.

Usually the regional heterogeneity of the lung density seen at end-inspiration on thin-section CT is accentuated on sections obtained at end, or during, expiration because the high-attenuation areas increase in density and the lowattenuation areas remain unchanged.

In the case of more global involvement of the small airways, the lack of regional homogeneity of the lung attenuation is difficult to perceive on inspiratory CT images, and as a result, mosaic perfusion becomes visible only on expiratory

scans.

In patients with particularly severe and widespread involvement of the small airways, the patchy distribution of hypoattenuation and mosaic pattern is lost.

Inspiratory CT shows an apparent uniformity of decreased attenuation in the lungs, and CT at end-expiration may

appear unremarkable.

In these patients, the most striking features are paucity of

pulmonary vessels and lack of change of the cross-sectional areas of the lung at comparable levels on inspiratory and expiratory CT.

In such a situation, there is a risk of misdiagnosis

between obliterative bronchiolitis and panlobular emphysema.

Both conditions are characterised by bronchial wall thickening and generalized decreased attenuation of the lung parenchyma and bronchial dilatation.

However, patients with panlobular emphysema demonstrate parenchymal destruction with higher frequency and to a greater extent than those with obliterative bronchiolitis. Long lines reflecting limited thickened interlobular septa were significantly more frequent in patients with panlobular emphysema.

Computed Tomography Assessment of

Air Trapping

The most commonly used technique for the assessment of air trapping is post expiratory thin section CT obtained during suspended respiration following a forced exhalation. Each of the post expiratory images should be compared with the inspiratory image that most closely duplicates its level to detect air trapping.

Dynamic expiratory manoeuvre performed during helical CT acquisition has been described.

It permits a small increase in the degree of expiration, which leads to a better detection of air trapping. This technique is recommended when patients have

difficulty performing the suspended end-expiration manoeuvre adequately.

Using MDCT with thin collimation over the lungs and low

dose or ultra-low dose with iterative reconstruction or softtissue kernel with filtered back projection has become routine in many institutions to improve the conspicuity and the apparent extent of air trapping.

Multiplanar volume rendering slab associated with the technique of minIP increases the contrast between areas of normal lung attenuation and areas of lung hypoattenuation. This helps the depiction of mosaic perfusion pattern.

Its applications on expiratory CT can also facilitate

assessment of the presence and extent of air trapping.

The extent of air trapping present on expiratory images can be measured using a semiquantitative scoring system that estimates the percent of lung that appears abnormal on each section.

In the scoring system proposed by Stern et al., estimates of air trapping were made at each level and for each lung on a four-point scale:

0: no air trapping;

1: 1% to 25%; 2: 26% to 50%; 3: 51% to 75%; and 4: 76% to 100% of cross-sectional areas of lung affected.

The air trapping score is the summation of these numbers for the different levels studied. This scoring system provides good interobserver and intraobserver agreement.

The extent of expiratory air trapping at CT has proved to be correlated with the degree of airflow obstruction at pulmonary function tests in patients with obliterative bronchiolitis.

Objective measurement of air trapping can be done using CT densitometry.

In the density mask technique, all the pixels included in

areas of air trapping are segmented by thresholding at -910 HU and are highlighted and automatically counted.

Density changes between full inspiration and full expiration can be compared, and expiratory/inspiratory ratios can be calculated.

The density mask has the advantage that it combines density measurement with the visual assessment of pathology.

Using multislice CT with thin collimation over the lungs

performed at full expiration, an exhaustive assessment of the volume of air trapping may be provided as well as a 3D visualisation of distribution of air trapping.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Characterised by functional abnormalities, COPD is a slowly progressive airway obstructive disorder resulting from an exaggerated inflammatory response to cigarette smoke or other inhaled pollutants that ultimately destroy lung parenchyma (emphysema) and induce irreversible reduction of the calibre of the small airways (obstructive bronchiolitis).

Both lesions may be associated in the same patient.

On the other hand, narrowing and loss of terminal bronchioles clearly precede the appearance of microscopic emphysematous destruction.

That explains why the use of **CT** in evaluation of patients with COPD has made it clear that individuals with identical severity of airflow obstruction may exhibit different morphological appearances.

Some have extensive emphysema while others have minimal emphysema suggesting more significant small airway disease.

As a result, CT imaging may be employed to objectively classify individuals as having either emphysema or airway predominant disease.

This better phenotyping of COPD patients may help select stratify patients in clinical trials and in given individuals help optimise treatment.

Emphysema is defined as a condition of the lung characterised by permanent abnormal enlargement of airspaces distal to the terminal bronchiole, accompanied by the destruction of their walls without obvious fibrosis.

The most important aetiologic factor by far is cigarette

smoking.

There is also a causal relationship between HIV infection and the development of early emphysema.

Various genetic disorders may be associated with

emphysema including α 1-antitrypsin deficiency,

heritable diseases of connective tissue such as cutix laxa, Marfan syndrome and familial emphysema.

Emphysema is thought to result from the destruction of elastic fibres caused by an imbalance between proteases and protease inhibitors in the lung and from the mechanical stresses of ventilation and coughing.

Proteases are normally released in low concentration by phagocytes in the lung.

Protease inhibitors, mainly α 1-protease inhibitor (α 1-

antitrypsin), prevent them from causing structural damage to the lung.

Imbalance in the protease-antiprotease activity may result from antiprotease deficiency (α 1-antitrypsin deficiency), from excess release of protease stimulated by environmental agents, or from the defective repair of protease-induced damage.

Tobacco smoke increases the number of pulmonary macrophages and neutrophils, reduces antiprotease activity,

and may impair the synthesis of elastin.

As emphysema develops, lung destruction progresses, airspaces enlarge and elastic recoil declines, reducing radial traction on bronchial walls and on blood vessels and allowing airways and vessels to collapse.

Emphysema is traditionally classified on the microscopic localization of disease within the secondary pulmonary lobule.

The principal types are centrilobular, panlobular, paraseptal and irregular emphysema.

Centrilobular (centriacinar) emphysema affects mainly the proximal respiratory bronchioles and alveoli in the central part of the acinus.

The process tends to be most developed in upper parts of the lungs.

It is strongly associated with cigarette smoking.

Paraseptal emphysema

selectively involves the alveoli adjacent to connective tissues in septa and bronchovascular bundles, particularly at the margins of the acinus and lobule but also subpleurally and adjacent to the bronchovascular bundles.

Airspaces in paraseptal emphysema may become confluent

and develop into bullae, which may be large.

Panlobular (panacinar emphysema) is characterised by a dilatation of the airspaces of the entire acinus and lobule. With progressive destruction, all that eventually remains are thin strands of deranged tissue surrounding blood vessels.

It is the most widespread and severe type of emphysema with changes distributed throughout the lungs although often basely predominant.

Panlobular emphysema is the type occurring in α 1-antitrypsin deficiency and in familial cases.

Radiographic Findings

Chest radiography may be normal in COPD. When

radiographic abnormalities are present, they can include hyperinflation, oligaemia, bronchial wall thickening and accentuation of linear lung markings.

Thickening of the bronchial walls leads to tubular and ring shadows.

Increased lung markings cause the appearance of 'dirty

chest', a term widely used for describing a loss in clarity of the lung vessels.

Sabre-sheath trachea may be present.

Cor pulmonale is a recognised complication which is seen most exclusively in hypoxic patients.

With the onset of heart failure, the heart and hila and

intermediate lung vessels become enlarged. Enlargement of vessels is present in all zones and affects particularly segmental vessels and a few divisions beyond.

Signs of overinflation

are the best predictors of the presence and severity of emphysema.

Signs of overinflation include the height of the right lung being greater than 29.9 cm, location of the right hemidiaphragm at or below the anterior aspect of the seventh rib, flattening of the hemidiaphragm, widening of the sternodiaphragmatic angle, narrowing of the transverse cardiac diameter and enlargement of the retrosternal space on the lateral view.

Alterations in lung vessels include arterial depletion, whereas vessels of normal, or occasionally increased, calibre are present in unaffected areas of the lung, absence or displacement of vessels caused by bullae, widened branching angles with loss of side branches and vascular redistribution.

With the development of cor pulmonale, or left heart failure, the radiographic appearances will alter and may become less obviously abnormal.

The heart may then appear to be normal in size, or sometimes enlarged, and the diaphragm becomes less flat while the pulmonary vessels less attenuated. Bullae may be as small as 1 cm in diameter or may occupy the whole hemithorax causing marked relaxation collapse of the adjacent lung.

Bullae caused by paraseptal emphysema are much more common in the upper zones, but when they are associated with widespread panlobular emphysema, the distribution is much more even.

Occasionally the wall is completely absent and in such a case bullae can be difficult to detect.

The presence of emphysema associated with large bullae is referred to as *bullous*

emphysema.

An entity mainly seen in young men, characterised

by the presence of large progressive upper lobe bullae which occupy a significant volume of a hemithorax and are often asymmetrical, is referred as *giant bullous emphysema*, *vanishing lung syndrome* or *primary bullous disease of the lung*. Large bullae may be seen as avascular transradiant areas, usually separated from the remaining lung parenchyma by a thin curvilinear wall.

They can cause marked relaxation collapse of the adjacent lung and can even extend across into the opposite hemithorax, particularly by way of the anterior junctional area.

Spontaneous pneumothorax commonly occurs in association with localised areas of emphysema or bullae affecting the lung apices.

Bullae may enlarge progressively over months or years; a period of stability may be followed by a sudden expansion. Bullae may also disappear, either spontaneously or following infection or haemorrhage.

The main complications of bullae include pneumothorax, infection and haemorrhage.

In case of infection or haemorrhage, bullae contain fluid

and may show an air-fluid level.

When a bulla becomes infected the hairline wall becomes thickened and may mimic a lung abscess.

Carcinoma arising in or adjacent to bullae should be suspected when there is a mural nodule, mural thickening, a change in diameter of the bulla, pneumothorax, and the accumulation of fluid within the bulla.

Computed Tomographic Findings

The Fleischner Society published a statement in 2015 on CT-definable subtypes of COPD.

The purpose of this statement was to describe and define the phenotypic abnormalities that can be identified on the visually and quantitative evaluation of CT images in subjects with COPD, with the goal of contributing to a personalised approach to the treatment of patients with COPD.

The classification system provides a structured approach to visual and quantitative assessment of COPD.

Emphysema is classified as centrilobular, panlobular and paraseptal.

Additional important visual features include airway wall thickening, inflammatory small airway disease, expiratory gas trapping, and associate features.

Visually Defined Computed Tomography Pattern

of Emphysema

It is possible to recognise the subtypes of emphysema on the basis of their CT appearances.

Centrilobular emphysema is characterised by poorly defined local lucencies without visible walls and surrounded by normal lung and having a predominant distribution in the upper lobes.

According to the Fleischner Society subclassification, centrilobular emphysema is regarded as mild when scattered centrilobular lucencies, usually separated by large regions of normal lung, involving an estimated 0.5–5% of an upper lung zone.

It is regarded as moderate centrilobular emphysema when

many well-defined centrilobular or lobular lucencies are occupying more than 5% of any lung zone.

Small vessels, often seen traversing the hypoattenuated focal areas, are centrilobular pulmonary arteries or arterioles marking the centre of each lobule.

Centrobronchovascular bundles are preserved.

As emphysema becomes more severe, the areas of hypoattenuation appear confluent and multiple regions of lucencies span several secondary pulmonary lobules but do not involve extensive hyperexpansion of the secondary pulmonary lobules or gross distortion of pulmonary architecture.

Advanced destructive emphysema represents very

severe centrilobular emphysema, characterised by panlobular lucencies with hyperexpansion of the secondary pulmonary lobules and distortion of pulmonary architecture most often with upper lung predominance.

On maximal intensity projection CT images, the pulmonary

vessels located in the emphysematous parenchyma are straightened and splayed with decreasing branching.

In case of lung destruction involving the lung bases, long lines reflecting the thickening of the interlobular septa by slight fibrosis may be seen crossing the hypoattenuated destroyed lung parenchyma.

Panlobular emphysema is a term that is associated with

 α -1-antitrypsin deficiency characterised by a lower lobe predominant pattern involving generalised destruction of all

acini more or less equally.

On CT, the visual pattern is characterised by a generalised decrease of lung attenuation involving the lower lobes with an increase of lower lobes volume with anterior displacement of the major fissures.

Paraseptal emphysema is characterised by welldemarcated rounded juxtapleural lucencies, aligned in a row along a pleural margin, sometimes including an interlobular fissure, and along the peribronchovascular bundles. Paraseptal emphysema is characterised as mild when the rounded lucencies are small (<1 cm), and as substantial when many large (>1 cm) cystic-like lucencies or bullae are present (Fig. 6.34).

Bullae may be large enough to compress the adjacent lung parenchyma.

Although such compression is usually relatively mild, it may occasionally result in compressive atelectasis appearing as a parenchymal band or mass-like opacity.

Bullous emphysema is a pattern characterised by multiple large avascular lucencies partly bordered by a thin wall. Most patients with bullous lung disease have concomitant centrilobular or paraseptal emphysema.

The term 'giant bullous emphysema' has been used to describe the presence of bullae occupying at least one third of a hemithorax.

Giant bullae may be compressive not only on the lung

parenchyma but also on the diaphragm and the right atrium with a risk of tamponade. Visual assessment of emphysema may be done at the lobar level.

Several different subtypes may be present in different

lobes due to heterogeneous severity of disease. Kim et al. showed that visual subtypes can be reliably estimated at a lower lobar level with good agreement between readers.

Visually Defined Computed Tomography Patterns of Airway Diseases

These include bronchial wall thickening and features of small airway diseases.

Bronchial wall thickening is a feature often observed on CT

of smokers with or without COPD.

Bronchial wall thickening is recognised as a relative increase in the thickness of the bronchial wall be comparison with the bronchial lumen and the diameter of the homologous PA.

Unfortunately, this feature suffers from interobserver variability and is better assessed by comparison with visual standards obtained from subjects with normal and abnormal findings.

At the earlier stage of the disease, inflammatory changes in the small airways are seen on CT as multiple areas of ground glass attenuation and small centrilobular ill-defined nodular opacities.

These abnormalities, predominant in the upper lobes or sometimes more diffuse in distribution, have been reported to be present in about 22 to 25% of asymptomatic smokers. At a later stage of the disease (obstructive bronchiolitis), the CT findings include mosaic perfusion pattern (low attenuation and low perfusion areas where the terminal

bronchioles are obstructed) and expiratory air trapping in the same areas.

Obstruction of the small airways may also be suggested

in patients presenting airflow limitation at spirometry in the absence of emphysema at CT.

Associated Features

They include bronchiectasis, large airway disease, interstitial lung abnormalities and PH.

Evidence of moderate **tubular bronchiectasis**, mostly in the lower lobes, may be present and is usually associated with most severe airflow obstruction and with hospitalizations for

exacerbation.

Varicose and cystic bronchiectasis are often associated with panlobular emphysema in patients with α -1-antitrypsin deficiency.

In smokers, **bronchial diverticula or outpouchings** may be seen as small airway collections in the wall of the main and lobar bronchi particularly well displayed on coronal reformations with minimal intensity projection.

They express the fusion of multidepressions and dilatations of the bronchial gland ducts forming a diverticulum which herniates between and through the smooth muscle cellular

bundles.

An increased number of diverticula is associated with

cigarette smoking and with symptoms of cough.

An **expiratory central airway collapse**, defined by a 50% reduction of cross-sectional area of tracheal lumen at expiration in a large study of current and former smokers, was reported in 5% of subjects.

This feature was more prevalent in those with COPD and its presence was associated with worse quality of life as well as greater frequency of acute respiratory events. Tracheobronchomalacia, defined as a reduction in the tracheal luminal cross-sectional area by more than 80% at dynamic expiratory imaging, was found in about 20% of COPD patients but was not correlated with physiological impairment.

The presence of non-dependent interstitial lung abnormalities, including ground glass and reticular abnormalities that affected more than 5% of any lung zones, were reported in 8% of smokers with or without COPD.

The prevalence of these **interstitial lung abnormalities** rises with age, tobacco exposure, and current smoking.

They are associated with the lower total lung capacity and a lesser degree of emphysema. They were independently associated with reduced exercise capacity and higher mortality.

Pulmonary hypertension frequently complicates COPD and its presence is often seen in early disease.

Pulmonary arterial enlargement may be measured as a surrogate for PH.

A ratio of the trunk of pulmonary artery to aorta diameter

(PA/AA) greater than 1.0 correlates with PH and independently predicts future severe exacerbations requiring hospitalisation.

Quantitative Computed Tomography Image Analysis

Quantitative CT (QCT) is useful for identifying and sequentially evaluating the extent of emphysematous lung destruction, changes in the airway walls, and expiratory air trapping.

The goals of QCT in COPD are to quantify the presence and percentage of emphysema-like lung (low-attenuation areas), the lobar and zonal distribution of the low-attenuated regions, changes in airway walls and luminal calibre, and the severity of gas trapping at expiratory CT.

Volumetric thin section CT is generally recommended for characterization of COPD.

Submillimetric z-axis resolution with overlapping section reconstruction is recommended for optimal airway analysis. A high spatial resolution algorithm is better for visual assessment of the lung whereas a smooth reconstruction algorithm facilitates computerized analysis by reducing image noise.

The CT radiation dose delivery is driven by the balance between radiation dose and image quality.

Excessive image noise with a reduced CT dose can simulate emphysema and may impair segmentation of the airways and quantitative evaluation of the airway dimensions. Expiratory CT is required for determining the severity of airway obstruction.

It is performed as suspended full expiration. It may be performed at a lower CT radiation dose.

Quantitative Analysis of Emphysema Extent

So far the most commonly used technique for QCT analysis of emphysema remains lung densitometry.

It consists of automatically segmenting

voxels having an attenuation value below a given threshold cut off of the CT density histogram to generate CT density mask.

Although the highest correlations between QCT metrics and histology were found when using thresholds of -960 and -970 HU on MDCT and thin collimation CT, the threshold of -950 HU is commonly used in the interest of balancing between sensitivity and specificity.

An alternative is to use the percentile density, that is, a density value below which a given percentage of the lung pixels falls.

Although correlations with histology have shown the 1st percentile to be the optimal percentile for this determination, most studies used the 15th percentile because of concern regarding the presence of noise and artefact at the 1st

percentile.

The 15th percentile has proven to be the most sensitive index to detect disease progression in longitudinal studies. As emphysema is a regionally distributed disease, it makes sense to provide 2D and 3D colour display in longitudinal reformats with automatic extraction of proximal airway lumens and segmentation of the lungs with automatic

calculation of lung volume and percentage of emphysema. Specific software may divide the lung into upper, middle and lower parts of equal height or volume.

Other software may segment the lobar boundaries automatically and calculate the percentage of lobar

emphysema.

Sources of variations in density-based measures include inspired lung volume, CT system used (make and model),

increased body-mass index and increased lung density in individuals who are currently smoking.

Precise calibration of the CT system, ideally with a standardised phantom, is important for ensuring the accuracy of the CT number.

When different CT models are used, the results should be adjusted for tracheal air attenuation.

Adjustments for demographic factors are needed.

Other sources of variation deserve specific attention. Differences in emphysema measurement at varying

inspiration levels are not clinically relevant above 90% of vital capacity.

Spirometric control of lung volume is not necessary but careful coaching of the patient by the radiographers is important.

Lung densitometry is highly reproducible when it is

corrected for differences in lung volume (percentage of emphysema on the follow-up CT studies corrected using

the same achieved lung volume on the baseline study).

Patients referred for QCT of emphysema should be allowed to rest before the examination to increase the reliability of emphysema volume or index values.

Variation in technical parameters should be minimised by

using standardised acquisition and reconstruction parameters and using the same equipment and the same software. Differences in reconstruction algorithms have a large effect (9.5%) in CT measurement of a low attenuation area. Excessive image noise with a reduced CT dose can

simulate emphysema at QCT.

It is recommended to not use less than 60 mAs.

Iterative reconstruction algorithm improves consistency between low dose CT and standardised dose CT for emphysema quantification.

The extent of emphysema is more consistent across different tube currents when using iterative reconstruction algorithm.

The extent of emphysema appears to increase quite rapidly after smoking cessation, reflecting a fall in lung attenuation due to the decrease of inflammatory changes.

Moreover, emphysema measurements increase with increasing body mass.

As a result, longitudinal analysis of emphysema must adjust for both smoking status and body-mass index both of which may change over time. QCT analysis of emphysema extent correlates significantly with both FEV1/FVC as well as FEV1 and predicts COPD exacerbations that require hospitalisations.

Quantitative emphysema is associated with respiratory quality of life and with increased all-cause mortality in patients with COPD.

When the main sources of variations are minimised or under control, QCT has ability to detect progression of emphysema.

According to Gietama et al, a change of 1.1% in the emphysema extent may be detected with 95% probability by using MDCT.

Quantitative Computed Tomography Analysis of Gas Trapping

Gas trapping on expiratory CT has been used as a surrogate for small airway disease.

The expiration to inspiration ratio of mean lung density (E/I-ratioMLD) has been shown to be the most suitable.

As opposed to other gas trapping severity metrics, E/IratioMLD is not influenced by iterative reconstruction techniques. The percentage of low attenuation area at -856or -850 HU at end-expiration CT has proved to provide

remarkable high correlations with predicted force expiratory volume (FEV)1% and FEV1/forced vital capacity (FVC) ratio.

However, both these metrics are influenced by underlying emphysema.

Patients with similar values of emphysema extent (percentage of low attenuation area <-950 HU at inspiration) have different values in gas trapping extent

measured as percentage of low attenuation areas (<-856 HU at expiration).

Total gas trapping includes both emphysematous and nonemphysematous contribution.

To quantify the contribution of functional gas trapping in non-emphysematous lung, investigators compute the percentage of low attenuation area (<-856 HU at expiration) minus percentage of low attenuation (<-950 HU at inspiration).

Unfortunately, this metric does not provide spatial localisation of small airway disease.

Deformable registration techniques of the inspiration and expiration images to calculate a voxel-by-voxel ventilation map based on the change in CT attenuation between inspiration and expiration provide parametric response maps (PRM).

Double thresholding of lung densities allows to separate voxels of emphysema (<-950 HU insp and <-856 HU exp),

voxels of functional small airway disease (fSAD) (>-950 HU insp and <-856 exp) and voxels of normal lung (\geq -950 HU insp and \geq -856 exp).

PRMs may provide spatial information on the distribution of

emphysema and small airway disease, thus permitting the measurement and tracking of these disease component

separately.

Emphysema and gas trapping regional distribution may play a role in the assessment of symptoms severity and in the selection of patients for surgical and endoscopic lung volume reduction.

The PRM of fSAD is significantly associated with subsequent FEV1 decline, particularly in mild-to-moderate

stage disease.

However, PRM-derived values are most sensitive to lung

volume levels and mismatched reconstruction kernels. PRM metrics varied by 6.5% of total lung volume for PRM normal and PRM fSAD and only 1% for PRM emphysema when testing 30-day repeatability.

Thus, these variations are negligible when CT acquisitions and reconstructions were consistent an inspiration/expiration lung volumes are near the target volumes.

Quantitative Analysis of Airway Dimensions

As there is a significant association between the dimensions of the small and large airways in COPD patients, measurements of airway dimension in the larger bronchi can provide an estimate of small airway remodelling.

Bronchial wall thickening in cigarette smokers has been related to lung function (FEV1).

In COPD patients, bronchial wall thickening, and the

percentage of emphysema extent are both the strongest determinants of FEV1.

Both bronchial wall thickening and the percentage of emphysema extent have been demonstrated to be associated with COPD exacerbation frequency.

Several software have developed 2D and 3D methods for QCT analysis of airway dimensions.

Such software register the lumen of tracheobronchial

tree and extract the central axis of the airway on which any

given subsegmental bronchus may be interactively selected. Reformations of successive cross sections of airway strictly perpendicular to its central axis are obtained followed by automatic registration of the inner and outer contours of the airway wall sections.

Different metrics may be measured: airway luminal area (LA), airway wall area (WA), airway wall thickness (WT), wall area percentage (WA%).

The most commonly used summary measures for a given patient are Pi10 and Pi15, which are the square roots of the WAs of theoretical airways with 10 and 15 mm luminal perimeter respectively, calculated from linear regression of all measured bronchi.

These airway metrics are independently associated with respiratory quality of life.

These measures of airway thickness are also associated

with chronic bronchitis with bronchodilator responsiveness and with a paradoxical response to bronchodilators.

Moreover, CT studies have consistently showed reduced airway lumen dimensions and fewer peripheral airways in COPD. Increases in WA% with progressively greater disease stage are due to a greater reduction in overall airway size with a more modest decrease in WT.

This suggests that the increase in WA% with worsening COPD is likely due to a combination of reduced airway size and luminal encroachment by thickened airway walls.

In summary, QCT analysis of emphysema extent and the severity of fSAD as well as CT measurements of airway dimensions may provide better understanding of pathophysiology of COPD and better phenotyping

of COPD patients.

They contribute to improve the stratification of patients in clinical trials and to predict outcomes following intervention.

They may be used to assess the progression of the disease during followup according to a strict control of variation sources.

Standardisation remains operative for multicentre studies.

ASTHMA

Asthma is a chronic inflammatory condition involving the airways that causes bronchial hyper-responsiveness and induces recurrent episodes of wheezing, breathlessness, chest tightness and coughing, usually associated with widespread but variable airflow obstruction that is often

reversible either spontaneously or after bronchodilator inhalation.

Asthma is also a heterogeneous condition and approximately

5 to 10% of asthmatic subjects have severe disease, characterised by permanent airflow obstruction, frequent exacerbations and hospitalisations, and significant morbidity and mortality.

Severe asthma is associated with structure changes of the airways that may develop overtime or shortly after the onset of disease.

These structural changes identified at bronchial biopsies include thickening of reticular basal membrane hypertrophy

and hyperplasia of smooth muscle, mucous hyperplasia, dysregulated extracellular matrix deposition and increased vasculature.

As biopsy specimens are limited in size and depth and limited to the central airway—and the procedure is too invasive to be repeated—CT imaging plays a role in the noninvasive assessment of airway structure.

Radiographic Findings

Chest radiography is usually recommended in all asthmatic patients who are ill enough to justify admission to a hospital. Hyperinflation may be seen in both relapse and remission. The prevalence of hyperinflation is generally higher in children and in patients needing hospital admission.

While hyperinflation is often transient, it may be a permanent change.

Bronchial wall thickening is more frequent in children, but in adults when it becomes visible it is usually an irreversible phenomenon. The walls of end-on segmental airways become thickened and the normally invisible airways parallel to the radiographs appear as parallel or single line opacities.

It may be present in up to two thirds of patients.

Chest radiograph may depict complications including consolidation, atelectasis, mucoid impaction, pneumothorax or pneumomediastinum.

Consolidation is commonly infective but, in some cases, it is due to eosinophilic consolidation, probably associated with allergic aspergillosis.

Collapse ranges from subsegmental to lobar and occasionally involves the whole lung. Collapse is due to mucoïd impaction in large airways or, more commonly, mucus plugging in many small airways.

Computed Tomography Findings

So far, the clinical indication of CT in asthma has been restricted to the identification of associated conditions, such as ABPA and detection of condition that may mimic asthma, such as hypersensitivity pneumonitis, obliterative bronchiolitis, Churg-Strauss syndrome or chronic eosinophilic pneumonia. Qualitative assessment of CT findings in asthma has been performed by a number of studies using HRCT technique (incremental acquisition with 10 mm interval).

The findings observed are variably bronchial wall thickening, bronchiectasis, mucus plugging, decreased lung attenuation and gas trapping.

In asthma, the small airways are also affected with

significant inflammation and remodelling.

Small airway remodelling can be detected on CT as indirect changes.

The small airways dysfunction results in reduced ventilation of part of the lung which induces reflex vasoconstriction

highlighted as an area of decreased attenuation on CT images.

Heterogeneity of lung attenuation on inspiratory CT is accentuated in expiration due to regional differences in small airway closure (mosaic perfusion, and gas trapping). Mosaic perfusion and gas trapping in moderate persistent asthmatics may be observed without a significant change in

gas trapping scores after the inhalation of a bronchodilator. This demotes the hypothesis of bronchoconstriction to explain gas trapping in these patients and reinforces the role of airway remodelling.

Quantitative Computed Tomography Imaging

of Airways in Asthma

The extent of low attenuation areas on expiratory CT expressing obstruction in the small airways can be quantitatively assessed using the lung densitometry that consists of calculating the % of pixels in lung parenchyma having an attenuation value below a predetermined threshold.

Different indices to quantify gas trapping in asthma have

been developed, including the -850 HU attenuation as a threshold at functional residual capacity, the -900 HU as a

threshold at full expiration, the mean lung density expiratory to inspiratory ratio, the difference between inspiratory and expiratory lung attenuation, and the lowest 10th percentile lung attenuation frequency distribution at expiration.

CT assessment of gas trapping in asthma has been associated with airway hyperresponsiveness, disease duration, and airflow limitation, and has been used for the evaluation of response to inhaled steroids.

In addition, gas trapping has been shown to correlate with asthma severity.

Subjects with gas trapping are significantly more likely to have a history of asthma related hospitalisations, ICU visits and mechanical ventilation.

New QCT imaging has enabled us to study the large airway architecture in detail and indirectly assess the small airway structure.

The advent of multidetector row CT and advances in postprocessing techniques have made quantitative assessment of the airway tree and lung parenchyma possible.

Various studies have utilised CT for non-invasive quantitative assessment of proximal airway structural changes in asthmatics.

Airway wall thickening in asthma has been shown to correlate with hyperresponsiveness, airflow limitation, gas trapping on expiratory CT, and asthma control.

So far only few studies have demonstrated a correlation

between QCT assessed airway remodelling and asthma

severity. Severe asthmatics have thicker airway walls on MDCT than mild asthmatics and normal subjects.

The percentage of wall thickness (%WT) or percentage

of wall area (%WA) correlates with pathologic measurements of remodelling obtained from bronchial biopsies.

Airway lumen narrowing is another characteristic of proximal airway morphology in severe asthmatics, demonstrated by QCT assessment.

The bronchus lumen area corrected for body surface is significantly narrowed in severe asthmatics compared with healthy subjects. 2D and 3D analysis of airway wall volume, luminal narrowing and bronchial stenoses should be regarded as the imaging criteria to assess morphologic

remodelling of large airways in severe asthmatics.

Although airway narrowing is correlated with airflow obstruction, two identified clusters of severe asthmatics differ for parameters characterizing airway narrowing. Furthermore, investigators showed that using CT indices of proximal airway remodelling and air trapping, three asthma

phenotypes with different clinical and radiological features may be identified.

Assessment of proximal dimensions was made on CT performed at full inspiration and full expiration.

Delta lumen of airways was determined as the percentage difference between inspiration and expiration.

They showed that delta lumen values were significantly

lower for segmental airways in subjects undergoing hospitalisations because of exacerbation and in patients with refractory asthma requiring treatment with systemic corticosteroids, making this new metric a potential outcome biomarker of unstable refractory asthma.

In summary, although the standardisation of image analysis procedures needs to be improved, the identification of remodelling patterns in various phenotypes of severe asthma and the ability to relate airways structures to important clinical outcomes should help target treatments more effectively.

Pulmonary Lobar Collapse:

Essential Considerations

Collapse and atelectasis are terms which are often used synonymously and refer to loss of volume within the lung. In North America, the term collapse is often reserved to denote complete loss of volume within an entire lobe or lung.

Atelectasis can be described according to extent (linear, plate-like or subsegmental atelectasis, sublobar and lobar atelectasis) or due to the underlying aetiology: compression or passive atelectasis (e.g. by pleural effusion, pneumothorax or bulla) and obstructive or post-stenotic atelectasis.

Rounded atelectasis refers to a specific type of a sublobar atelectasis associated with previous (often haemorrhagic)

exudative pleural effusion (e.g. post-thoracotomy, trauma and asbestos exposure).

It is associated with adjacent visceral pleural thickening and

has characteristic computed tomography (CT) appearances which are described elsewhere.

MECHANISMS AND CAUSES OF LOBAR COLLAPSE

Broadly, lobar collapse can be divided into those due to endobronchial obstruction (either intrinsic or extrinsic) and those without obstruction.

The common causes differ slightly between adults and children.

In adults the frequent causes of intrinsic obstruction are tumours and mucous plugs.

More rarely, foreign bodies, broncholiths and focal bronchostenosis due to inflammation or trauma may be encountered.

In children, causes such as inhaled foreign bodies or mucous plugs are common, with tumours being very rare.

RADIOGRAPHIC CONSIDERATIONS

The cardinal radiographic features of lobar collapse are increased opacity of the affected lobe and volume loss.

The latter can be inferred by direct and indirect signs.

Direct signs of volume loss refer to displacement of

interlobar fissures, pulmonary vessels and bronchi, whereas indirect signs include compensatory shifts of adjacent structures such as hyperinflation of other lobes.

The effects of a lobar collapse are often maximal on

immediately adjacent structures; for example, an upper lobe collapse often results in a shift of the superior mediastinum, whereas a lower lobe collapse often demonstrates elevation of the posterior part of the diaphragm in particular. However, the general principles and fundamental radiographic signs are similar for all lobes.

A collapsed lobe appears radiographically dense due to a combination of retained secretions or fluid within the lobe and reduction in aeration of the lobe.

However, retained fluid is the dominant process, resulting

in increased opacity of a partially collapsed lobe, as virtually complete collapse is required to displace sufficient air for the normally radiographically hyperlucent lung to appear dense.

Direct Signs of Volume Loss

Displacement of fissures is a reliable feature of lobar collapse, and is generally characteristic depending on the affected lobe.

The pulmonary vessels and bronchi become crowded together in the affected lobe as the lung loses volume.

The sign may be one of the earliest seen in lobar collapse and can often be readily appreciated by comparison with previous radiographs.

Hilar elevation on the posteroanterior (PA) chest radiograph is a well-known sign of upper lobe collapse; the ipsilateral interlobar and lower lobe arteries remain visible as these structures are still outlined by aerated lung. It would seem logical to consider 'hilar depression' to be a sign of lower
lobe collapse, but some authorities believe the small

hilum to be a more accurate description.

This is due to the fact that when a lower lobe collapses, the opaque, collapsed lobe obscures the lower lobe artery that lies within it, and the interlobar artery is usually rotated so the margin is no longer in profile to the frontal x-ray beam.

Consequently, it is difficult to recognise the hilum as being depressed and, instead, smaller vascular structures are noted at the expected position of the hilum.

Occasionally, confusion with a central hilar mass/ adenopathy can arise if the convex margin of an interlobar artery remains visible due to minimal rotation.

As well as vascular reorientation, hilar bronchial alterations also occur.

The central large bronchi undergo characteristic changes in

position with collapse of either the upper or lower lobe. When either upper lobe collapses significantly, the ipsilateral main bronchus becomes more horizontally orientated than usual; hence the bronchus intermedius

and the left lower lobe bronchus swing laterally. Conversely, when either lower lobe collapses, each main bronchus is more vertically orientated than usual, with a medial swing of the bronchus intermedius on the right and the lower lobe bronchus on the left.

Indirect Signs of Volume Loss

Compensatory hyperinflation of adjacent lobes occurs with lobar collapse, resulting in fewer vessels per unit volume of lung.

It is often easier to detect a paucity of vessels, which are more widely spaced than on the unaffected side, than subtle increased radiolucency.

In isolation, the sign may be due to causes other than lobar collapse and other confirmatory features should be sought before making the diagnosis. The normal lung parenchyma should expand proportionally to compensate for the degree of collapse and often the greater the degree of lobar collapse, the greater the compensatory overinflation. Therefore when small lung volumes are involved, the hyperinflation usually only involves the remainder of the ipsilateral lung, whereas with larger volumes, the contralateral lung may expand across the midline. On a frontal radiograph the lung may expand across the midline superiorly, thus displacing the anterior junctional line to the contralateral side. On a lateral view, the anterior mediastinum appears hyperlucent.

Displacement of the azygo-oesophageal line and posterior

junctional line on the PA radiograph, which denote protrusion of contralateral lung through other weak areas between the oesophagus and vertebral column and the retrocardiac space, respectively, may be more difficult to recognise.

Although the term 'mediastinal herniation' is sometimes used, some authorities emphasise that there is no actual

mediastinal defect or hiatus and the sign more accurately denotes *displacement* of mediastinal structures.

A divergent or parallel pattern of vascular reorientation seen near the hilum has been described in marked upper lobe collapse.

The pattern is seen more commonly on the left than on the right, as a result of the different degree of compensatory overinflation in the superior segment of the ipsilateral lower lobe on each side.

The right middle lobe can also overinflate in compensation, which further explains the lesser degree of overinflation of the superior segment of the right lower lobe.

The sign of vascular reorientation can be helpful when unusual patterns of upper lobe collapse are present. Hyperexpansion may also result in a change in position of lung lesions, such as granulomas resulting in the so-called shifting granuloma sign.

Of particular note, the Luftsichel sign (from German, meaning air crescent) is due to the overinflated superior segment of the ipsilateral lower lobe occupying the space between the mediastinum and the medial aspect of the collapsed upper lobe, resulting in a paramediastinal translucency.

The sign is more common on the left than on the right and is regarded as a typical appearance of left upper lobe collapse. CT demonstrates the increased paramediastinal lucency to be due to a wedge shape of the collapsed upper lobe, with the apex of the V resulting from tethering of the major fissure by hilar structures.

Mediastinal shift is another indirect sign of volume loss and the degree varies according to the position of the affected lobe.

Usually the least mediastinal shift occurs in right middle lobe collapse, whilst the greatest shift, particularly of the inferior mediastinum, is seen with lower lobe collapse.

The amount of mediastinal shift due to upper lobe collapse is often dependent on the chronicity; in acute upper lobe collapse there is often little shift, whereas in chronic upper lobe volume loss with fibrosis, the shift may be greater.

The position of the trachea may be a useful indicator of superior mediastinal shift as it should be central in the superior mediastinum between the anterior ends of the clavicles or slightly deviated to the right by the aortic arch. Inferiorly within the mediastinum, anywhere between onehalf and one-fifth of the cardiac outline normally lies to the right of the midline and greater or lesser variations indicate mediastinal shift.

However, because of the wide variation in normal subjects, displacement of the cardiac outline may be more difficult to assess than changes in position of the trachea.

The hemidiaphragms may be elevated in lobar collapse, particularly involving the left upper lobe and to a lesser extent the right upper and both lower lobes.

However, the sign is of limited value because the position of the right hemidiaphragm is highly variable (0–3 cm higher

than the left on the frontal chest radiograph). A useful ancillary sign of upper lobe collapse (or a combination of right upper and middle lobe collapse) is a juxtaphrenic peak of the diaphragm. The sign refers to a small triangular density at the highest point of the dome of the hemidiaphragm, due to the anterior volume loss of the affected upper lobe, resulting in traction and reorientation of an inferior accessory fissure.

Reduction in the volume of a hemithorax may result in relative reduction of the spaces between the ribs by comparison to the unaffected side.

Rib crowding or approximation may be recognisable on the frontal radiograph in cases of chronic lobar collapse, but in acute collapse it may be more difficult to appreciate. Furthermore, the sign is considered to be unreliable as patient rotation and minor degrees of scoliosis may result in apparent rib crowding.

Ancillary Features of Lobar Collapse

Occasionally the cause of a lobar collapse may be apparent and an endobronchial lesion may be clearly demonstrated radiographically.

However, although the actual endobronchial component is

often not directly visualised, lobar collapse due to a central obstructing bronchogenic carcinoma is most likely when Golden's S sign is seen.

The sign refers to the S shape (or more accurately, reverse S

on the right) of the fissure due to the combination of collapse and mass centrally resulting in a focal convexity with a concave outline peripherally.

Although the sign was originally described in the right upper lobe, it can be seen in any lobe.

The CT equivalent is discussed later.

Generally, absence of air bronchograms within the affected lobe should also raise the suspicion of a central obstructing lesion as there is absorption of air from both the lung parenchyma and airways.

The sign may be useful for distinguishing a central obstructing mass from a consolidative process

such as bacterial pneumonia.

The rare important caveats are when a mass results in only partial obstruction of the airways or in cases of acute bronchopneumonia where the airways are filled with an

inflammatory exudate.

However, the sign is not as reliable on CT, and

often distal air bronchograms are visible in part of a collapsed lobe due to a central neoplasm.

COMPUTED TOMOGRAPHY OF LOBAR COLLAPSE

CT has become an invaluable method for investigating patients with lobar collapse.

The obvious benefits are a lack of superimposition of

overlying structures with the added advantage of demonstration of anatomical structures in the axial and, with computer reformatting, coronal and sagittal planes.

Not only does CT aid the understanding of the radiographic appearances of lobar collapse but also it provides invaluable information about the cause, which may not be apparent on chest radiography.

The most common indication for CT in adults with

lobar collapse is to identify an endobronchial or compressing lesion.

Technique

Careful attention to CT technique is required to accurately demonstrate an obstructing lesion resulting in lobar collapse despite the advances in multidetector CT; reconstruction and reformatting of volumetric data now provide routine display of tracheobronchial anatomy.

Three dimensional (3D) and virtual endoscopic images can provide an extremely useful adjunct to routine multiplanar images.

Utility

In some cases, the aetiology of lobar collapse can be determined from the patient's clinical history, examination and chest radiographic features.

Using fibreoptic bronchoscopy as the reference standard, CT is clearly more sensitive than chest radiography for the detection of an obstructing carcinoma.

Reported sensitivities for detection by CT range from 83%

to 100%, but generally, when an endobronchial lesion is sufficiently large to cause lobar collapse, CT is a reliable method for detection.

False-positive diagnoses may be due to bronchial strictures, plugs of mucous or secretions and compression by large pleural effusions. CT is not histologically specific, however, as bronchogenic carcinoma, endobronchial metastases, bronchial adenomas and lymphoma may all have similar appearances.

The accuracy of CT on axial images is limited to some extent and it may be difficult to demonstrate endobronchial

lesions in the right middle lobe and lingular bronchi owing to their oblique orientation relative to the axial plane; this is much less of a problem with multiplanar images.

Accurate delineation of a tumour mass from a surrounding collapsed lobe may be problematic, but collapsed lung usually enhances to a greater degree than tumour with contrast-enhanced CT.

The difference in attenuation value is maximal between 40 seconds and 2 minutes after a bolus injection of intravenous contrast; these numbers, however, vary with contrast administration and CT technique.

Golden's S sign on chest radiography has a CT equivalent that may be helpful in identifying an obstructing tumour. Usually, a collapsed lobe is associated with concavity of the adjacent fissure and a localised convexity is highly suggestive of an underlying mass.

The sign is not entirely specific, but it is strongly indicative of a bronchogenic carcinoma.

Unlike the frontal chest radiograph, in which the S sign is only helpful in the right upper lobe and to a lesser extent the right and left lower lobes, the S sign can be applied to all lobes on CT.

Another CT sign that is highly suggestive of an obstructing

lesion causing lobar collapse is the CT mucous bronchogram sign. Histopathologically, the lobar and segmental bronchi are filled with inspissated secretions and are usually dilated. The airways are optimally demonstrated as tubular, lowattenuation branching structures within the enhancing collapsed lobe following intravenous contrast enhancement.

Obstructing lesions such as bronchogenic carcinoma or benign causes, including tuberculous bronchostenosis, should be considered.

The sign may also result from excessive mucous production combined with decreased mucociliary function in conditions such as allergic bronchopulmonary aspergillosis, asthma and cystic fibrosis.

CT also has a role in complicated or atypical lobar collapse as their appearances may be confusing on chest radiography. In particular, combined right middle lobe and right upper lobe collapse may be difficult to diagnose on chest radiography when the collapse is nearly complete.

CT is useful for demonstrating mediastinal anatomy and provides information about mediastinal lymph nodes and the staging of a tumour causing lobar collapse.

Additional signs of lobar collapse, such as compensatory overinflation and the Luftsichel sign (described above),

are also well demonstrated, providing explanations for the radiographic appearances of lobar collapse.

In addition to findings indicative of volume loss, the usually strong and homogeneous enhancement of atelectatic lung parenchyma as opposed to consolidated lung parenchyma due to inflammation provides a useful sign for discriminating pneumonia from atelectasis.

Potential Pitfalls

The increased sensitivity of CT by comparison with radiography means that the presence of an air bronchogram within a lobar collapse does not necessarily exclude a central obstructing lesion.

In this context, an air bronchogram may be seen in the peripheral part of a collapsed lobe due to collateral air drift or tumour necrosis. Similarly, a proximal obstructing lesion may not cause complete lobar collapse when a fissure is incomplete, allowing ventilation by collateral air drift.

Occasionally the parenchyma and airways become filled with fluid owing to the presence of a central obstructing lesion with little or no associated volume loss, and the lobe may even be expanded, giving rise to the appearance termed 'drowned lobe'.

The CT equivalent of the Golden's S sign is particularly well demonstrated with right-sided lobar collapse and, on the left, care should be taken in interpretation owing to the

fact that normal mediastinal structures may mimic a mass (e.g. thoracic aorta).

The accurate determination of the reversibility and chronicity of a lobar collapse may be problematic. Relatively acute collapses may show apparent bronchiectatic dilatation of the airways and may mimic a long-standing irreversible event; a meaningful evaluation of the airways in the context of a lobar collapse is therefore often difficult.

OTHER IMAGING TECHNIQUES IN

LOBAR COLLAPSE

Magnetic resonance imaging (MRI) is still surpassed by CT in the investigation of lobar collapse largely due to the superior spatial resolution of lung parenchyma in the latter, but also due to cost, availability and speed of acquisition.

In particular, endobronchial tumours and smaller bronchi are less well demonstrated by MRI than CT, even though some

studies have investigated the ability of MRI to differentiate a tumour mass from post-obstructive collapse by utilising differences in signal characteristics.

Sometimes the distinction can be made on T1 weighted

images, but it is generally accepted that T2 weighted images are superior as the tumour yields lower signal intensity than the obstructed lung, which has higher water content. Nevertheless CT is still the imaging investigation of choice.

On ultrasound of a large pleural effusion, the underlying collapsed lung is often visible as a hyperechoic wedgeshaped area within hypoechoic or anechoic fluid.

In practice, the main utility of ultrasound is to readily distinguish pleural effusion from a collapsed and consolidated lung when radiographic appearances are equivocal, but ultrasound may also be used to guide biopsy of a peripheral lesion within a collapsed lobe.

On positron emission tomography (PET), a collapsed lobe demonstrates less uptake of 18F-fluorodeoxyglucose (18F-FDG) than tumour. PET/CT may provide more accurate delineation of tumour from post-obstructive collapsed lung than CT alone, which may be useful for guiding biopsy and treatment: for example, radiotherapy.

PATTERNS OF LOBAR COLLAPSE

Right Upper Lobe Collapse

On the frontal radiographic view of a right upper lobe collapse, the collapsed lobe forms increased density at the apex of the hemithorax adjacent to the right side of the mediastinum, with the elevated horizontal fissure resulting in a concave inferior outline depending on the degree

of collapse.

Even in cases where there is no obstructing lesion, there is often a small convexity at the hilum due to the pulmonary

veins and artery where the apex of the lobe is attached to the hilum.

On the lateral view, the horizontal and oblique fissure approximate and are both displaced superiorly and medially with the collapsed lobe, forming a superior ill-defined wedge-shaped density.

In cases where the collapse is very severe, the horizontal fissure parallels the mediastinum and appearances may simulate an apical cap of pleural fluid or mediastinal widening on the frontal radiograph.

There is also usually compensatory hyperinflation of the right middle and lower lobes, resulting in elevation and a more horizontal course of the lower lobe pulmonary artery and right main bronchus.

The vascular reorientation can be recognised on the frontal view, but the right main and lower lobe bronchial displacement can be difficult to appreciate on both the frontal and lateral view.

On **CT** the right upper lobe forms a roughly triangular density with the base anteriorly against the chest wall and the apex at the hilum.

A focal bulge of the lateral border usually indicates an

underlying mass.

Compensatory hyperinflation of not only the right middle and right lower lobes but also the left upper lobe is often more easily appreciated on CT.

Left Upper Lobe Collapse

The cardinal features of left upper lobe collapse are fundamentally different from right upper lobe collapse as there is very rarely a horizontal fissure on the left. Consequently, the main direction of volume loss is anteriorly and medially rather than superiorly, and the entire oblique fissure is displaced in that direction parallel to the chest wall on the lateral view.

On the frontal view the signs may be variable, depending

on the degree of collapse, but there is a 'veil-like' increased density of the whole of the affected hemithorax in most cases.

The increased density is often greatest at the hilum and it gradually fades out laterally, superiorly and inferiorly

without the clear inferior demarcation of the horizontal fissure as seen in right upper lobe collapse.

The difference in transradiancy may be relatively subtle and therefore overlooked by the unwary.

The other features that aid diagnosis on the frontal view

are loss of the normal silhouette of structures adjacent to the collapse, such as the left heart border, mediastinum and aortic arch, as these structures are no longer adjacent to aerated lung.

There is some variability in which outlines are obscured, depending on the degree of collapse.

In cases of relatively less severe collapse, the left heart border, left mediastinal outline and aortic knuckle are obscured on the frontal radiograph, whereas in more severe cases the apical segment of the left lower lobe is hyperexpanded superiorly adjacent to the aortic arch and somewhat paradoxically the aortic knuckle outline is therefore visible in more severe cases as it is adjacent to aerated lung.

The Luftsichel sign is a particular manifestation of the hyperexpansion, and literally describes an 'air crescent' which may be seen between the aortic arch and the

medial border of the collapse.

On the lateral view the anterior outline of the ascending thoracic aorta can be seen with unusual clarity and

this is due to compensatory hyperinflation of the right upper lobe across the midline and rotation of the mediastinum so the anterior aspect of the aorta is outlined by aerated lung tangential to the x-ray beam.

On the frontal radiograph the left main bronchus is reorientated and has a more horizontal course than usual. The superior displacement of this structure results in angulation between the left main bronchus and the left lower lobe bronchus.

The **CT** appearances of left upper lobe collapse are similar to that of the right upper lobe with a triangular soft-tissue density, the apex at the origin of the upper lobe bronchus and the base against the anterior chest wall, adjacent to the left border of the mediastinum.

However, in the left upper lobe the lingular segment is seen as a density closely opposed to the left heart border.

Rarely, left upper lobe collapse may mimic right upper lobe collapse.

The appearance is due to collapse of the apicoposterior and

anterior segments of the left upper lobe with sparing of the lingular portion resulting in a concavity to the inferior border of the collapse, even in the absence of a left minor fissure.

Apart from being on the left, isolated collapse of the lingula has a very similar appearance to that of right middle lobe collapse.

Right Middle Lobe Collapse

The features of right middle lobe collapse may be extremely subtle on the frontal view and consequently easy to overlook.

The collapsed lobe lies adjacent to the right heart border and there is loss of the silhouette of this structure to a variable degree.

There may or may not be a recognisable increase in density, depending on the orientation of the collapse relative to the x-ray beam.

When the collapse is orientated roughly parallel to the beam or if the patient is in a lordotic position, a triangular, sailshaped density may be seen adjacent to the heart border (Fig. 7.26). However, if the collapsed lobe lies obliquely

in the chest, more parallel with the major fissure, the only sign on the frontal radiograph may be indistinctness of a portion of the right atrial border.

By comparison, the triangular density of the collapsed right middle lobe is relatively easy to identify on the lateral view, with approximation of the minor and inferior portion of the

major fissure, the apex of the triangle being at the hilum.

In increasingly severe collapse the triangular shape is less marked as the fissures become almost parallel with only a thin wedge of density separating them.

The **CT** appearances are characteristically of a triangularshaped density of varying size adjacent to the heart border. Depending on the orientation of the collapse, only a small portion may be identified on each section as the collapse represents a relatively flat sheet of tissue.

The so-called 'middle lobe syndrome' refers to a collapsed

right middle lobe with bronchiectasis due to a focal bronchostenosis secondary to pulmonary tuberculosis. Although in theory any lobe may be affected, the middle lobe is the most common.

Right and Left Lower Lobe Collapse

The features of right and left lower lobe collapse are very similar and will be considered together.

In collapse of the lower lobes, the oblique fissure is displaced posteriorly and medially, and the collapsed lobe lies in the posteromedial portion of the chest, a feature readily appreciated on CT.

On the frontal radiograph, the collapsed lower lobes usually form a triangular density behind the heart.

The medial portion of the hemidiaphragm may be obscured as it is no longer outlined by aerated lung, but if the inferior pulmonary ligament is incomplete and does not attach to the diaphragm, the medial contour of the diaphragm may still be visualised.

On the lateral radiograph, a posterior portion of the hemidiaphragm may not be seen, but in more severe collapse the contour may reappear as it becomes outlined by aerated lung from the hyperexpanded upper lobe.

In addition, the vertebral column appears progressively denser inferiorly in lower lobe collapse, whereas normally the converse is true.

On the frontal radiograph the lower lobe pulmonary artery is usually not seen in lower lobe collapse as it is no longer outlined by aerated lung. The major airways, including the right and left main

bronchi, are also displaced more vertically in lower lobe collapse and often the relevant air-containing bronchus can be identified as leading directly into the triangular density of the collapsed lobe.

There are several features involving the upper mediastinum which are sometimes helpful in diagnosing lower lobe collapse.

The **first** of these is the 'superior triangle sign' and refers to a triangular density to the right of the mediastinum seen in right lower lobe collapse due to displacement of anterior junctional structures.

The appearance should not be confused with right upper lobe collapse.

The **second**, 'flat waist sign' is seen in extensive collapse of the left lower lobe and describes flattening of the contours of the aortic knuckle and main pulmonary artery due to cardiac rotation and displacement to the left.

Third, the outline of the superior aortic knuckle may be lost in severe left lower lobe collapse.

On **CT**, the collapsed lower lobes form a triangle of softtissue density posteromedially in the thorax, adjacent to the spine.

On the left, the collapsed lower lobe is seen to drape over the descending aorta, giving a focal convexity to the lateral border, a feature which potentially can cause confusion with an underlying mass on an unenhanced CT summarises the schematic radiographic appearances of the various individual lobar collapses.

Whole Lung Collapse

Collapse of an entire lung results in complete opacification, or 'white-out', of the affected hemithorax.

In adults, the cause is often an obstructing neoplasm in the right or left main bronchi or mucous plugging.

There is marked volume loss with compensatory hyperinflation of the contralateral lung across the midline. The cardinal feature of volume loss can help discriminate between collapsed lung and a large pleural effusion, the latter usually resulting in mediastinal shift to the contralateral side.

The lateral radiograph shows accentuation of the retrosternal space as the displacement of the contralateral lung is greatest anteriorly.

By comparison, the opacity of the hemithorax is more uniform on the lateral view in large pleural effusion and may

be a useful discriminating feature in equivocal cases.

Combinations of Lobar Collapse

Occasionally, various combinations of lobar collapse occur. Collapse of the right middle and right lower lobes is often due to an obstructing.

lesion or mucous in the bronchus intermedius.

The features are similar to right lower lobe collapse with the exception that the opacity extends laterally to the costophrenic angle on the frontal view and from the front to the back of the hemithorax on the lateral view.

Collapse of the right upper and right middle lobes is more unusual as these lobes do not have a common bronchial origin which spares the lower lobe.

In adults the cause is often a carcinoma which obstructs

one bronchus and causes extrinsic compression of the other due to mass effect.

Combined collapse of the right upper and right middle

lobes results in an appearance very similar to left upper lobe collapse on both frontal and lateral radiographs and CT.

Both bilateral lower lobe and upper lobe collapse are exceedingly rare and may occur as a result of metachronous bronchial neoplasms or mucous plugging.

Pulmonary Neoplasms

Anaplastic Lymphoma Kinase

Fusions in the ALK gene (gene rearrangements) result in aberrant activation of the transcribed ALK kinase protein and transformation into malignancy.

ALK fusions are more often seen in never-smokers and in younger patients, but with an equal sex distribution. ALK+ NSCLC has a high predilection to central nervous system (CNS) metastases, seen in around 40% of patients at presentation.

ALK+ NSCLC is an aggressive poor prognosis cancer if treated with standard chemotherapy.

However, ALK TKIs are highly effective, resulting in rapid and durable responses in most patients. The first ALK inhibitor used and proven to be markedly superior to chemotherapy was crizotinib.

Since then, a number of second-generation ALK inhibitors are now licensed (ceritinib and alectinib) with even better duration of response than crizotinib and importantly marked intracranial penetration, obviating the use of upfront cranial radiotherapy for patients with CNS metastases. Third generation ALK inhibitors are near approval (brigatinib and lorlatinib), with potentially more effective CNS control. Through effective use of upfront ALK inhibitors the median survival of ALK+ metastatic NSCLC is now 4.5 years, again comparing favourably with around 1 year for those without ALK fusions.

ROS1

Patients with tumour ROS1 fusions are rare, occurring in up to 2% of NSCLCs, predominantly seen in adenocarcinomas, never-smokers and usually patients below the age of 55. ROS1 fusions result in an activated tumour ROS1 kinase. Crizotinib, as well as being an effective ALK inhibitor, is also a highly active ROS1 inhibitor. Due to its rarity, no

randomised trials of drugs in ROS1+ NSCLC have been performed.

BRAF

Mutations in BRAF are activating and result in an intracellular signalling cascade leading to carcinogenesis. The typical BRAF mutation observed is BRAF V600E and is most often observed in malignant melanoma, seen in around 40% of cases. BRAF V600E mutations are also observed in NSCLC but in around 1% of cases. These tumours are sensitive to BRAF kinase inhibitors (viz. dabrafenib or vemurafenib) and activity is enhanced with downstream MEK inhibitors (e.g. trametinib).

Thus, the combination of dabrafenib–trametinib results in near doubling of progression-free survival compared with that expected of more conventional chemotherapy.

Programmed Cell Death Ligand 1

Tight regulation of the immune system is required to prevent

autoimmunity and eradicate malignant cells as they are formed.

Cancer cells evade the immune system through several different mechanisms.

One of these is by strongly expressing PDL1. This protein is expressed on tumour cells and on immune cells (e.g. macrophages and other antigen-presenting cells).

It binds to PD1 (an immune checkpoint) on the T-cell surface, inducing T-cell exhaustion and tolerance. PD1

or PDL1 inhibitors (ICPIs) disrupt this balance and shift T cells to a more activated phenotype, resulting in antitumour immune activity.

The greater the extent of PDL1 expressed on tumours, the greater the potential benefit from ICPIs, in some cases potentially above that of chemotherapy.

Indeed, in patients with PDL1 levels \geq 50% starting treatment with the ICPI pembrolizumab, median survival is currently around 3 years compared with 18 months for conventional chemotherapy.

Re-biopsy

Tumours evolve over time and are usually heterogenous at the time of diagnosis.

Clear evidence now shows that treatments-especially

molecular targeted therapy—place selection pressures on tumours for them to evolve with the acquisition or outgrowth of new mutations that result in the translated protein becoming resistant to the drug treatment.

Examples of these include an EGFR T790M mutation that

results in resistance to afatinib, erlotinib and gefitinib, but introduces sensitivity to osimertinib.

Similarly, resistance to alectinib can be mediated through an acquired ALK G1202R mutation, which is sensitive to lorlatinib.

Moreover, the histological subtype of NSCLC can markedly change with treatments.

Thus, mechanisms of resistance to EGFR and ALK TKIs include transformation to high-grade neuroendocrine carcinomas including SCLC or pleomorphic subtype NSCLC.

The transformed SCLCs harbour the native tumour mutation (EGFR L858R) but are rapidly progressive, requiring chemotherapy for treatment.

Finally, another acquired drug resistance mechanism is loss of the molecular target through genomic deletion. Thus, ALK+ tumours with acquired resistance to ALK TKIs have been demonstrated to have lost the ALK fusion and become ALK wild type, meaning that further next-generation ALK inhibitors would not be active whereas conventional chemotherapy would be.

Therefore it is worthy of note that re-biopsy series in patients previously demonstrated to be without treatable tumour mutations have demonstrated changes in histological subtype.

For example, adenocarcinoma may change to squamous cell carcinoma or vice versa, resulting in changes in drug options for chemotherapy and molecular testing.

For these reasons, it has become routine to re-biopsy

clinically progressing lesions where clinically feasible in patients with molecularly driven tumours.

LUNG CANCER AND OTHER

ENVIRONMENTAL FACTORS

Smoking

Smoking, by a large margin, is the major risk factor for lung cancer, and a dose relationship has been reconfirmed several times since the hallmark study of Doll and Hill.

Cigarettes have changed in composition since the 1950s. Cigarette smoke is complex in nature and there are up to 60 identified carcinogens in tobacco smoke.

Filters are now commonplace and nicotine levels have fallen in the tobacco varieties now produced.

Nicotine itself is not thought to cause tumours, but seems to promote their growth.

As nicotine is the major dependent pharmacological agent in cigarettes, lowering levels combined with the introduction of perforated filters may have resulted in a habit of greater

depths of inhalation and in total numbers of cigarettes consumed.

As a consequence, the prevalence of adenocarcinoma is rising markedly and squamous cell carcinoma (and small cell carcinoma) falling in parts of the world where 'light' cigarettes are more prevalent.

Passive Smoking

Passive smoking has received considerable attention and is now recognized as a major contributor to worldwide morbidity and mortality related to lung cancer.

A number of studies have demonstrated that non-smoking

spouses of smokers have a 20%–30% increase in lung cancer and a dose–response relationship has been demonstrated.

Huge efforts have been made to reduce smoking rates, and clearly never commencing smoking is the aim.

There are now almost as many former smokers as active smokers in the United States, and cessation of smoking reduces all lung cancer risk, especially those most strongly

associated with smoking, namely SCLC and squamous cell carcinoma.

It is estimated that the risk of lung cancer will have dropped by 50% 15 years after ceasing to smoke.

General Environmental Pollutants

General environmental pollutants have been suggested as a further risk factor for lung cancer development.

The influence of air pollutants has been long recognised as an environmental issue.

More recently, attention has been paid to air quality and particularly to the concentrations of fine particles within the air that we breathe. Particles of less than $2.5 \ \mu m$

in diameter are strongly associated with lung cancer, especially in non-smokers.

These particles are particularly associated with diesel engine exhaust.

Asbestos

Asbestos has also long been associated with increased lung cancer risk as well as being a known trigger for nonmalignant lung and pleural disease.

Chrysotile fibres are most closely linked with lung and pleural malignancy.

The exposure to both asbestos and tobacco is particularly

carcinogenic and estimates of a 15- to 50-fold increased risk of developing lung cancer are frequently quoted.

Radon

Perhaps the forgotten aetiological agent is 222Radon, second only to smoking as a cause of bronchogenic carcinoma.

As radon is in the earth's crust, there is little that can be done to alter exposure levels. Certain geographical areas, for geological reasons, result in greater exposure levels.

Data related to radon risk largely come from underground workers, where levels are high.

LUNG CANCER SCREENING

Chest Radiographic Screening

There is considerable literature on the use of chest radiography as a screening tool for early lung cancer.

These trials have been of all varieties, including randomised controlled trials (RCTs).

Some have been undertaken in conjunction with sputum cytology.

Two early important trials were performed in Japan. Although designed differently and coming to slightly different conclusions in large numbers of patients, these mass screening programmes concluded there was a benefit associated with chest x-ray screening and sputum cytology compared with non-screening.

These studies were both case-controlled studies.

The next landmark study was the Mayo Lung Project performed between 1971 and 1983, a RCT on nearly 11,000 patients.

Rather than a case-control study, this RCT also set out to determine whether chest x-ray and sputum cytology provided an effective means of screening for lung cancer. Perhaps unusually, patients were randomised into two different screening regimes, screened annually or every 4 months for 6 years, with further follow-up.

This study demonstrated a clear stage shift in the more frequently screened patients, resulting in a better 5-year survival, but at 20-year follow-up there was no overall survival benefit.

Further large studies from the Memorial Sloan Kettering Hospital, the Johns Hopkins lung project and a Czechoslovakian study all had insufficient statistical power to demonstrate a reduction in mortality between screened and non-screened patients.

As the question remained open, the prostate, lung, colorectal and ovarian (PLCO) cancer screening trial, recruiting between 1993 and 2001 at 10 screening centres across the United States, attempted to resolve whether chest x-ray could be used as an effective screening technique for lung cancer and result in subsequent reduction in mortality. Unlike previous studies, many of the enrolees were neversmokers (45%), or non-smokers (42%), and

only about 10% were current smokers. Of the total 154,000 men and women enrolled, only 24,000 were considered to be of high risk for lung cancer.

In this study, despite a slight stage shift in the screening

group, there was no difference in lung cancer deaths between the screened group and the usual care group. From these various trials, providing some contradictory data, it can be reasonably concluded that chest x-ray alone has no useful role in lung cancer screening.

Although lung cancers may be detected, often at a slightly

earlier stage, the eventual outcome between screened and non-screened groups is almost identical.

Computed Tomography Screening

Latterly the debate has concentrated on lung cancer screening with computed tomography (CT), more recently using a low-dose technique.

Again, it was the Japanese that led the way with two early trials.

These studies set the pattern of subsequent CT screening projects.

High-risk patients were identified, and volumetric CT was undertaken.

Detected nodules were followed up according to protocol. Very small nodules were not followed up, intermediatesized nodules would continue along a screening pathway and subsequent CT at varying intervals, to detect growth. Larger nodules would be immediately sampled.

Subsequent studies, including the landmark Early Lung Cancer Action Project (ELCAP) concluded that low-dose CT results in lung cancers being diagnosed at an earlier stage and with a higher cure rate than lung cancers detected as a result of symptoms. Since then, there have followed

at least 20 subsequent studies using CT as a screening tool. A full discussion of these trials is beyond the scope of this chapter.

However, some have had a greater impact than others, most importantly the US National Lung Cancer Screening Trial (NLST).

This large and well-funded trial, by the National Cancer Institute, enrolled 53,454 smokers or ex-smokers between the ages of 55 and 74, randomised to low-dose CT or posteroanterior (PA) chest radiography on an annual basis for 3 years.

This design is slightly unusual, because there is no nonscreening arm, but compares two different screening methods.

There have been a number

of important findings to come out of this large trial:

• Many patients have a positive screening test, either by x-ray (16%) or CT (39%), at least once over the course of 3 years.

• More cancers were detected in the CT arm than the chest x-ray arm.

• Investigation of possible lung cancers resulted in complications in both the CT and chest x-ray arms, described as major complications in approximately 10% of both groups, undergoing invasive evaluation.

• Screen-detected cancers are at an earlier stage in the CT arm compared with the chest x-ray arm.

• Adenocarcinomas are more common in the screening population than in the symptomatic population.

• There is a 20% reduction in lung-cancer-specific mortality in the CT group.

This study, it is generally agreed, has demonstrated that CT

screening applied to a carefully targeted group of patients can reduce lung cancer mortality.

The cost of this approach looms large amongst the other

questions that await a definitive answer. Cost-effective analyses are still underway.

This is not the end of the story—there are a number of ongoing or recently completed European RCTs underway or in preparation from Italy, France, Netherlands, Denmark and the UK.

All of these trials have been designed slightly differently, but the question, as yet unanswered, is whether this form of screening should be rolled out across the general at-risk population.

Amongst the many other questions that require consideration are the issues around the psychological burden of telling a patient they have a small nodule that requires follow-up to exclude lung cancer, with no answer likely for at least 2 years.

CT screening techniques are not perfect and the accuracy of CT as a detection technique has resulted in considerable debate.

In the early days, 10-mm contiguous slices were utilised. Technology has since evolved, with multidetector CT (MDCT) being routine and the ability to produce contiguous 1-mm collimation images now being commonplace.

A simple, cheap but very effective technique, now widely employed on these narrow section data sets, has been the use of maximum intensity projection image (MIP) reconstructions.

This technique can be used on all CT workstations and most picture archiving and communication system (PACS) workstations and has been demonstrated to greatly improve conspicuity of nodules.

There has also been considerable resource expended on the development of computer-assisted diagnosis (CAD). Scrolling through many hundreds of images in an attempt to detect small nodules leads fairly rapidly to reader fatigue. CAD systems have been shown to augment the ability of a radiologist to detect all relevant lesions, by highlighting candidate lesions and allowing the radiologist to include or dismiss them as appropriate.

The corollary of CAD utilisation is high initial false-positive rates: many lesions that are highlighted by the CAD system

are subsequently dismissed by the radiologist. This may not necessarily result in a faster assessment, but does improve accuracy overall.

In both the screening studies and in general practice, once a nodule has been detected, typically between 5 and 8 mm in size, the usual practice is to undertake follow-up CT studies and most radiologists will follow the Fleischner guidelines or the British Thoracic Society (BTS) guidelines for the follow-up of lung nodules.

Key differences between the systems are highlighted in for solid nodules and for subsolid nodules.

The vast majority of detected lung nodules, at least 98%, will be of no clinical significance, particularly in low-risk

patients.

Most of these nodules will not increase in size.

However, being small, reproducible measurements are potentially problematic and therefore accurate determination of genuine increase becomes of critical importance in

managing further follow-up intervals. Most radiologists routinely employ 2D caliper measurements, but for small nodules this is notoriously inaccurate, and is not reproducible either across different readers or between the same readers on different occasions, and the technique

also does not lend itself to non-spherical lesions. Therefore, as well as being able to assist in the detection of nodules, computer-assisted characterisation tools have also become commonplace, through automatic segmentation and volume calculation.

This technique, of producing a semi-automated nodule volume, is much more reproducible than 2D caliper techniques even though others have shown that the technique itself, when repeatedly measuring the same nodule, may give varying results.

However, the practice of routine volumetric assessment is

beginning to become routine as CT workstation vendors provide the relevant software as a standard.

Radiation Dose Considerations

It is important, at all times but particularly in a screening population, where there is a high likelihood of detected nodules being of no significance, to reduce radiation exposure to a minimum. The use of a 'low-dose' CT technique should be automatic. This can be achieved by

reducing tube current and tube voltage and increasing pitch. It is also important not to over-investigate screening or incidentally detected nodules, and to time follow-up studies appropriately.

Furthermore, it is sometimes preferable to target the followup examination to only examine the nodule in question, rather than repeating the CT study of the entire thorax.

The Future of Screening

The NLST screening study has demonstrated a decrease in mortality from lung cancer in patients undergoing low-dose CT assessment.

The resources required to roll out a CT screening programme are huge.

The medical communities in many countries were waiting to see if the results from the NLST trial would be confirmed by one or more of the other ongoing studies in Europe, before the implementation of screening programmes. Recently presented data from the Dutch-Belgium NELSON lung cancer trial also showed a reduction in lung cancer mortality, suggesting the benefits of screening may indeed be reproducible outside of the NLST trial.

What is not yet defined is how wide the screening net should be cast and which screening frequency is most costeffective.

While the NLST screened participants based on age and smoking history, it is generally agreed in Europe that a risk-

model-based approach should be used to target screening, incorporating a number of lung cancer risk factors beyond age and smoking.

Currently, both in Europe and the United States, it is agreed that the patients undergoing screening CT should do so according to agreed guidelines.

These guidelines also advise in detail about the management of screening results.

The American Lung Association has also recently issued guidance on lung cancer screening to patients and physicians.

In Europe a recent opinion piece from the investigators of European screening neatly sets out a framework

for implementing lung cancer screening programmes, as well as defining some of the outstanding issues that require further work.

The document also emphasises the importance of evidencebased nodule management guidelines in reducing harm in lung cancer screening, including minimizing recall rates, unnecessary invasive investigations for benign nodules

and overdiagnosis.

PULMONARY NODULES

Management of Small Pulmonary Nodules

Nodule detection, now an everyday occurrence in patients undergoing multislice CT, raises a series of management problems for the referring physician and reporting radiologist. The widely adopted Fleischner Society Recommendations from 2005 have now been updated (2017) and supplemented by the BTS (2015).

In evaluating a pulmonary nodule, it is helpful to bear in mind likely causes.

Assessment of nodular morphology and characteristics

can also provide useful information, though nodule size is often the dominant parameter in guiding management. Regardless of guidelines, the management of incidental pulmonary nodules can be categorized into one of three options: (1) no further action required;

(2) CT surveillance;

or (3) further investigation with, for example, positron emission tomography (PET)/CT and biopsy.

Nodule Size and Growth Rate

Small nodules are very unlikely to be due to malignancy. Indeed, screening studies have demonstrated that malignancy in nodules of less than 5 mm in size (or 80 mm3) is so low, and these nodules are so common, that follow-up is not generally recommended.

However, this does not necessarily hold true in patients with a known primary malignancy elsewhere.

Most benign nodules measure less than 2 cm in diameter

and the smaller the nodule is, the more likely it is to be benign.

The use of volumetry to measure nodule size is advocated in the BTS guidelines not only to measure nodule size at detection, but also to enable calculation of volume doubling
time (VDT) at follow-up.

Growing nodules with a VDT of less than 600 days are significantly more likely to be malignant that slowergrowing nodules, although some indolent

adenocarcinomas (usually manifesting as subsolid nodules) are recognized to have considerably prolonged VDTs. Because of the impact of CT acquisition parameters, such as reconstruction kernel and slice thickness on volumetry algorithms, the use of volumetry applications to measure nodule size does require use of reproducible CT protocols at baseline and follow-up.

Location, Shape and Morphology

Perifissural nodules are a recognised entity following CT screening studies.

These small subpleural nodules have been shown to frequently represent intrapulmonary lymphoid tissue or complete intraparenchymal lymph nodes.

Characteristic features of intraparenchymal lymph nodes are nodules less than 15 mm from the pleural surface, being ellipsoid in shape and usually being connected to the pleural surface by a fine linear opacity and usually in the lower lobes.

Follow-up studies of nodules of this variety, detected during the Nelson Screening Trial, demonstrated that no perifissural nodules developed into lung cancer.

Nodule outline can also be helpful when other features typical of intrapulmonary lymphoid material are absent. Concave surfaces on all sides or a straight surface of contact with the pleura has also been shown to represent benign features.

The less spherical a nodule is, particularly on volumetric assessment, the less likely a malignant aetiology.

Flat or tubular nodules are more likely to be benign than round nodules.

Therefore, solid, subpleural, polygonal nodules with a low

sphericity index are highly unlikely to be malignant. Cavitation within a nodule can occur in both benign and malignant processes.

Malignant cavitation is often associated with a thick and

irregular internal cavity wall, compared with the more uniform cavitation associated with benign nodules, although this is not a reliable distinguishing feature.

Nodule Contour

Nodules without obvious benign morphology may be smoothly marginated, lobulated or spiculated.

Smoothly marginated nodules are more likely to be benign. Lobulated nodules are more likely to be malignant, but there is considerable overlap.

Therefore the presence of smooth borders is of little practical value.

In distinction, spiculation is predictive of a malignant aetiology.

The presence of central air bronchograms or soap bubble lucency centrally within a nodule has been previously evaluated.

Multiple spherical areas of air may be present in adenocarcinoma, due to the lepidic growth pattern of these lesions, where tumour cells have grown along the alveolar

walls and adjacent airways without filling the alveolar spaces.

In comparison, the presence of air bronchograms, rather than bubble-like lucencies, also may be seen in lymphoma, organising pneumonia and alveolar sarcoidosis.

Nodule Density

Certain patterns of calcification are recognised as being highly predictive of a benign aetiology.

Recognised benign patterns are lamellated, solid, central and popcorn-like. Central or lamellated calcification is typically

indicative of previous granulomatous disease and, similarly, dense solid calcification is likely to indicate previous granulomatous infection.

Popcorn calcification usually indicates the presence of a hamartoma and these lesions may also contain convincing evidence of internal fat density.

When fat is present in a lesion of less than 2.5 cm in diameter, then, particularly if the lesion is PET negative, further evaluation is not required, but most hamartomas do not demonstrate this helpful characteristic.

Calcification, which is eccentric or stippled within an area of soft-tissue density, may be seen in malignancy. Very occasionally metastases from bone-forming or cartilage-

forming tumours may present a benign pattern of calcification, but usually there is a relevant history.

Subsolid Nodules

A focal area of increased lung attenuation, which may be well or poorly defined but through which normal structures can still be discerned, is typically referred to as a groundglass density. If localised and round, the opacity may be described as a ground-glass nodule (GGN). If an area of ground-glass density includes a solid component that does obscure lung architecture, this may be termed a part-solid nodule.

In the literature both **pure ground-glass nodules** and **part-solid ground-glass nodules** may be grouped together under the term subsolid nodules. The Fleischner Society and BTS have now published guidelines on the management of these **subsolid nodules**, recognising that such subsolid nodules may represent early forms of adenocarcinoma.

Because of the relevance of the current classification of lung adenocarcinoma to the management of subsolid nodules, the new classification will be considered here.

The new classification eliminates the term bronchoalveolar carcinoma and mixed subtype adenocarcinoma and now divides adenocarcinoma into the following categories:

• **Pre-malignant lesions.** This includes atypical adenomatous hyperplasia and adenocarcinoma in situ.

These lesions are 1 cm or less in diameter and histology manifests pure lepidic growth with no solid components. These will appear as pure GGN on CT. Both the Fleischner and BTS guidelines recommend that small GGNs (<5 or 6 mm) do not require surveillance.

• Malignant lesions, divided into the following:

• **Minimally invasive** adenocarcinoma, with predominantly (in distinction to pure) lepidic growth, 3 cm or less, and with invasive components of no more than 5 mm.

These are generally subsolid nodules on CT, with a solid component usually less than 5 mm.

Because these types of lesion may grow slowly, both the Fleischner and BTS guidelines recommend longer-term follow-up (up to 5 years) for part-solid nodules (see Fig. 8.5B).

The presence of new or enlarging solid components within a GGN or part-solid nodule is typically regarded as a marker of nodule growth requiring further investigation and/or treatment.

• **Invasive** adenocarcinomas, subclassified as predominantly lepidic, acinar, papillary, micropapillary and solid types.

• Invasive mucinous adenocarcinoma, an entity formerly described

as mucinous bronchioalveolar carcinoma and considered as a

separate group from the non-mucinous types above.

Prognosis of patients with adenocarcinoma in situ or minimally

invasive adenocarcinoma (characterised on CT as pure ground-glass

lesion) is excellent; these patients should have almost 100% disease-free survival.

Invasive adenocarcinoma has a variable outlook, and to some extent this depends on the histological subtype.

Pericystic Tumours

Malignant nodules developing in the walls of cystic areas of lung destruction may result in delayed diagnosis.

The presence of a subtle soft-tissue element in the wall of a cystic space may be difficult to recognise initially.

These lesions are usually due to adenocarcinoma.

The cystic component may be due to an emphysematous bulla, fibrotic cavity, bronchiectatic airway or subpleural bleb.

As the neoplastic component of these lesions is small, percutaneous or bronchoscopic confirmation of malignancy may be problematic and biopsies are relatively high risk. The entity of a pericystic tumour has become more widely recognised because of the various lung cancer screening programmes, but as yet there are no specific guidelines for the management of this morphological subtype.

Detailed discussion of nodule assessment and follow-up is beyond the scope of this chapter but there are excellent reviews of the Fleischner

Society and BTS 2015 guidelines for managing pulmonary nodules.

OTHER FORMS OF NODULE ASSESSMENT

Nodule Enhancement

Contrast-enhanced CT is an effective management tool in the assessment of lung nodules.

In essence, malignant nodules will demonstrate enhancement, as will some benign nodules.

If there is no enhancement, malignancy is effectively excluded.

This technique works well in soft-tissue density nodules, but is less applicable to nodules containing calcification, cavitation or ground-glass opacity. The possibility of generating a virtual unenhanced data set, using dual-energy CT, has been investigated as a means to reduce radiation exposure yet provide similar information to acquisitions before and after intravenous contrast administration.

Although nodule enhancement has been demonstrated to be practical, in practice it has largely been superseded by PET/CT evaluation.

Positron Emission Tomography/Computed Tomography

PET/CT is now an essential tool in the management and the work-up of patients with possible pulmonary malignancy. It forms part of the standard staging in patients with proven or suspected lung cancer but is also a frequently utilised tool in the work-up of patients with an indeterminate lung nodule. The commonest isotope utilised is 2-deoxy-2-[18F]fluoro-D-glucose, a glucose analogue, with the positron-emitting

radioactive isotope fluorine-18 substituted for the normal hydroxyl group at the 2' position in the glucose molecule, commonly referred to as FDG.

The technique relies on increased uptake in neoplastic

nodules.

Increased uptake also occurs within many inflammatory processes.

Nevertheless, the utility of PET/CT has been documented,

in a number of studies, to have sensitivities of 90% and specificities of 83% for a diagnosis of malignancy. However, in the context of small nodules, FDG results must be interpreted with some caution, as nodules of less than 1 cm are more likely to result in a false-negative interpretation, particularly with certain lower-grade adenocarcinoma subtypes and carcinoid tumours.

The application of PET/CT for nodules of less than

6 mm is currently not justified.

In the context of lung disease, sarcoidosis, granulomatous infection and a number of inflammatory processes are recognised as resulting in significant PET FDG avidity. A risk prediction model called the Herder model integrates PET/CT results along with nodule size and other risk factors to predict the likelihood of nodule malignancy in lung nodules.

The use of the Herder model to guide further management is recommended in the BTS guidelines.

Tissue Sampling

Tissue sampling of nodules that are both accessible and of a size, shape and morphology to suggest the possibility of malignancy may be undertaken transbronchially, surgically or percutaneously with radiological guidance.

Central lesions may be amenable to bronchoscopic biopsy but even perihilar nodules, in the absence of an endoluminal component, remain very challenging for bronchoscopic diagnosis.

Bronchoscopic biopsy of peripheral lung cancer using conventional techniques is also highly problematic. Percutaneous fine-needle or cutting-needle biopsy has been demonstrated as an accurate technique for the identification

of malignancy, but not all nodules are suitable for this approach. When a final diagnosis of lung cancer is eventually established, a previous aspiration biopsy has a 90% likelihood of providing confirmation of a malignant diagnosis.

There is a very low false-positive rate but there is a recognised and troubling false-negative rate. Transthoracic needle biopsy remains an essential tool in the management part of indeterminate nodules.

Multidisciplinary team discussion of the relative merits of a

follow-up strategy, further imaging, percutaneous or bronchoscopic diagnostic procedures or surgical resection for an individual lung nodule remains the ideal management step in this common problem.

Decisions regarding further investigation of pulmonary nodules also can be helpfully guided by the pre-test probability of malignancy: most importantly, previous known malignancy, patient age and smoking history.

The use of risk management modelling has been previously

studied, incorporating various risk factors, but all methods

reported to date confirm that a significant current or previous smoking history in an elderly patient with a nodule diameter of more than 1 cm are all highly suggestive of a malignant aetiology.

LUNG CANCER STAGING—THE 8TH EDITION OF THE TNM STAGING SYSTEM

The new 8th edition of the TNM staging system (2016) has introduced a number of changes from the 7th edition.

With features that have changed in bold.

As before, the TNM classification may be based on clinical assessment (cTNM), imaging features (iTNM), or definitive pathological staging (pTNM).

There are even designations for restaging after treatment (yTNM), and restaging after recurrence (rTNM).

These prefixes can be combined; for example, a patient pathologically restaged after treatment has a

ypTNM classification.

Changes from the 7th edition include refinement of the T descriptor, which is now subdivided into 1 cm increments up to 5 cm (T2b).

T3 tumours are 5–7 cm and T4 tumours greater than 7 cm. The measurements relate to the largest dimension of the solid portion of the tumour.

There are also qualifiers based on invasion into adjacent structures.

Visceral pleural or main bronchus invasion (not carina), as

well as atelectasis to the hilum, are T2 descriptors.

Chest wall, pericardial sac and phrenic nerve invasion, as well as separate tumour nodules in the same lobe, are T3 descriptors.

Tumours invading the mediastinum, diaphragm, heart, great vessels, recurrent laryngeal nerve, carina, trachea, oesophagus and spine are T4 lesions, as are less-extensive lesions with tumour nodules in a different ipsilateral lobe. Therefore a 3.5 cm tumour in the mid part of the right lower lobe would be a T2a tumour, but if the same tumour was associated with pericardial invasion it would become a T3 tumour.

If the tumour had involved the oesophagus, despite no change in size, it would instead be designated a T4 tumour.

For the radiologist, the distinction between a T3 tumour and a T4 tumour requires careful thought in certain locations. For example, any invasion of the mediastinum is a T4 descriptor.

Phrenic nerve involvement is a T3 descriptor, yet many radiologists would consider that the phrenic nerve lies within the mediastinum.

However, the TNM 8th edition clearly states that the fibrous pericardium and phrenic nerve involvement indicates T3 stage.

Assessment of pleural and chest wall invasion has long been recognized as a difficult task for CT analysis. Where there is obvious soft-tissue extension into the intercostal muscles or bone destruction, the issue is easily resolved. Subtle chest wall parietal pleural invasion is more difficult

to define and magnetic resonance imaging (MRI), highresolution targeted ultrasound and even diagnostic artificial pneumothorax may be helpful.

Pancoast (superior sulcus) tumours are individually staged according to the involved tissues.

For example, an apical tumour with parietal pleural involvement is defined as a T3 lesion, but a similar tumour

extending into a vertebral body or involving subclavian vessels becomes a T4 lesion.

Because of the importance of this differentiation, the utility

of multiplanar reformatted images on CT and targeted MRI examination has been highlighted.

Additional Pulmonary Nodules in the Presence

of Lung Cancer

In the 7th edition, nodules in the same lobe as the primary tumour conferred T3 status (unchanged in the 8th edition).

A nodule in the ipsilateral lung but in a different lobe, whilst predicting a poor 5-year survival, confers a slightly better outlook than M1 disease of other types.

Therefore, the combination of a primary lesion with a further nodule within an ipsilateral different lobe remains described as T4 disease in the 8th edition.

N Descriptors

Nodes are described as either N0 (no involvement), N1 (nodes up to and including hilar stations), N2 (ipsilateral

mediastinal nodes) or N3 (contralateral mediastinal or hilar nodes and supraclavicular or scalene nodes).

Nodes beyond these stations are designated M1 nodes. The

nodal mapping system used by the American Thoracic Society (ATS) is given in Fig. 8.8. Note the following:

• Supraclavicular and sternal notch nodes are designated station 1.

• There is a shift of the midline for designation of right and left level 2 and level 4 nodes such that the 'midline' lies at the left lateral border of the trachea.

Therefore a lymph node lying directly anterior to the trachea using the 8th edition nodal map would be designated as a right paratracheal lymph node.

• Station 7 is defined by the undersurface of the carina superiorly.

The lower border of station 7 is the upper border of the lower lobe bronchus on the left and the lower border of the bronchus intermedius

on the right.

• Hilar lymph nodes are those adjacent to the mainstem bronchus and hilar vessels, including the proximal portions of the pulmonary veins and main pulmonary artery, with station 10R on the right and station 10L on the left.

The upper border of station 10R is the lower rim of the azygos vein, and the upper border of station 10L is the

upper rim of the pulmonary artery on the left.

The lower borders of stations 10R and 10L are the interlobar regions bilaterally.

For more detail, readers are referred to El-Sherief et al. 2013.

M Descriptors

M disease is now divided into:

• M1a, indicating additional tumour nodule(s) in the contralateral lung or pleural or pericardial nodules or malignant effusions.

• M1b, indicating a single extrathoracic metastasis, including in a non-regional lymph node, and

• M1c, indicating multiple extrathoracic metastases in one or more organs.

These staging changes are related to more comprehensive examination of survival patterns, a direct result of the larger databases from which the 7th edition, and now the 8th edition, have been derived.

The stage groups from the 8th TNM classification are shown in Table 8.4.

Small Cell Lung Cancer

SCLC presents a different phenotype to NSCLC. It is relatively common (15%–20% of all lung cancers).

The disease is characterised by rapid growth rate, early metastatic spread and an association with smoking.

Characteristically, these tumours are initially responsive to radiation and chemotherapeutic treatment but are also

associated with early recurrence.

In the 7th edition of the lung cancer TNM staging, SLCLC was divided simply into limited disease and extensive disease groups.

1. Low cervical, supraclavicular and sternal notch nodes. From the lower margin of the cricoid to the clavicles and

the upper border of the manubrium. The midline of the trachea serves as border between 1R and 1L. Superior Mediastinal Nodes 2-4: 2R.

Upper Paratracheal. 2R nodes extend to the left lateral border of the trachea. From upper border of manubrium to the intersection of caudal margin of innominate (left brachiocephalic) vein with the trachea. 2L.

Upper Paratracheal. From the upper border of manubrium to the superior border of aortic arch. 2L nodes are located to the left of the left lateral border of the trachea. 3A. Prevascular. These nodes are not adjacent to the trachea like the nodes in station 2, but they are anterior to the vessels. 3P. Pre-vertebral. Nodes not adjacent to the trachea like the

nodes in station 2, but behind the esophagus, which is prevertebral.

4R. Lower Paratracheal. From the intersection of the caudal margin of innominate (left brachiocephalic) vein with the trachea to the lower border of the azygos vein. 4R nodes extend from the right to the left lateral border of the trachea.
4L. Lower Paratracheal. From the upper margin of the aortic arch to the upper rim of the left main pulmonary artery. Aortic Nodes 5-6: 5.

Subaortic. These nodes are located in the AP window lateral to the ligamentum arteriosum.

These nodes are not located between the aorta and the pulmonary trunk but lateral to these vessels. 6. Para-aortic. These are ascending aorta or phrenic nodes lying anterior and lateral to the ascending aorta and the aortic arch.

Inferior Mediastinal Nodes 7-9. 7. Subcarinal. 8. Paraesophageal. Nodes below carina. 9. Pulmonary Ligament. Nodes lying within the pulmonary ligaments. Hilar, Lobar and (sub)segmental Nodes 10-14:

These are all N1-nodes. 10. Hilar nodes. These include nodes adjacent to the main stem bronchus and hilar vessels. On the right they extend from the lower rim of the azygos vein to the interlobar region.

On the left from the upper rim of the pulmonary artery to the interlobar region.

Limited disease indicates disease confined to one hemithorax but includes contralateral mediastinal and supraclavicular nodes and malignant pleural effusions. Patients with disease beyond these parameters are described as having extensive disease.

Patients with limited disease typically receive chemotherapy and possibly radiotherapy.

Patients with extensive disease will have chemotherapy alone.

It is possible to stage SCLC using the same TNM system utilised for NSCLC, but this is not likely to be important for decision-making purposes. Surgery is sometimes an option for SCLC in localised disease.

Bronchopulmonary Carcinoid Tumour

Bronchopulmonary carcinoid tumours are staged in the same way as NSCLC and is also classified under the 8th edition of the American Joint Commission on Cancer (AJCC) TNM staging system.

Carcinoid tumours are potentially malignant neuroendocrine tumours.

The spectrum of disease ranges from low-grade typical carcinoids, through atypical carcinoids to higher-grade large cell and small cell carcinomas.

The distinction between these neuroendocrine tumours is based on pathological analysis.

The field is also slightly complicated by the relatively small

numbers available for analysis and the phenomenon of preinvasive lesions seen in diffuse idiopathic pulmonary neuroendocrine-cell hyperplasia (DIPNECH), to be distinguished from genuine metastatic disease.

The presence of multiple small nodules of less than 5 mm in size in association

with mosaic attenuation pattern within the lungs in the setting of a known carcinoid tumour should raise the possibility of DIPNECH.

Bronchial carcinoids are uncommon, constituting less than 5% of pulmonary tumours.

The peak age at diagnosis is in the fifth decade, but the age

range is wide and includes children.

Two forms of bronchial carcinoid are described: typical (85% to 90%) and atypical (10% to 15%).

Typical carcinoids most commonly arise in central airways. Atypical carcinoids usually arise in the lung periphery. Bronchial carcinoids can invade locally and may metastasise to hilar and mediastinal lymph nodes as well as to the brain, liver and bone.

The atypical carcinoids have histological and clinical features intermediate between typical bronchial carcinoid and small cell carcinoma of the lung and have a poorer prognosis.

Bronchial carcinoid may present with wheeze, pneumonia or haemoptysis.

Even when small, tumours may secrete adrenocorticotrophic

hormone (ACTH) in sufficient quantities to cause Cushing syndrome.

Carcinoid syndrome is very rare if the tumour is still confined to the lung.

Radiographic appearances vary with location of the tumour. There is no lobar predilection and on rare occasions carcinoids may arise in the trachea.

Bronchial carcinoids, particularly those located centrally,

may calcify and occasionally ossify. Calcification is seen on CT in up to one-third of cases, but is only occasionally visible on chest radiography.

Marked contrast enhancement may be seen on CT.

Carcinoids arising in central bronchi (80%–90% of cases) often show a larger mass external to the bronchus than within the lumen (so-called 'iceberg' lesions), and the extrabronchial component may be visible as a hilar mass. Central lesions usually produce partial or complete bronchial obstruction, resulting in atelectasis with or without

pneumonia. Central bronchial obstruction may be complicated by development of distal bronchiectasis or lung abscess.

Occasionally, a bronchial carcinoid in a segmental or subsegmental bronchus may obstruct bronchial secretions, thereby causing a mucocele.

Peripheral lesions (10%–20% of carcinoids) present as solitary spherical or lobular nodules, 2–4 cm in diameter, with a well-defined smooth edge.

Non-calcified peripheral bronchial carcinoid tumours closely resemble bronchial carcinomas, both radiologically

and cytologically, and are therefore frequently removed surgically in the belief that they are carcinomas.

Summary

The use of the 8th edition of the AJCC TNM staging system in NSCLC, SCLC and bronchopulmonary carcinoid informs the stage grouping system that guides treatment choices. Since the adoption of the 8th edition TNM descriptors, the group staging has become more complex.

These stage groupings are of relatively little importance for the thoracic radiologist in day-to-day practice but will have a significant effect in some patients in determining treatment options and trial eligibility.

IMAGING PROTOCOLS FOR LUNG

CANCER STAGING

Clinical features vary with cell type and extent of disease. Approximately 25% of patients are asymptomatic at the time of diagnosis, following the discovery of an abnormality on a chest radiograph or CT.

Pneumonia is another common presentation.

Cough, wheeze, haemoptysis, symptoms of pneumonia and paraneoplastic syndromes, such as the inappropriate secretion of antidiuretic hormone or a peripheral neuropathy, are the cardinal symptoms at a stage when lobectomy or pneumonectomy may be curative.

Hoarseness, chest pain, brachial plexus neuropathy and

Horner syndrome (Pancoast tumour), superior vena caval obstruction, dysphagia and the problems of pericardial tamponade indicate invasion of the mediastinum or chest wall and a much poorer prognosis.

The **chest radiograph** will remain the initial investigation in all patients suspected of lung cancer. As the lung cancer screening studies have shown, the ability of a chest radiograph to detect all lung cancers is distinctly limited. Therefore the mainstay of staging investigation for a patient with suspected lung cancer (in distinction to patients undergoing lung cancer screening) is contrast-enhanced CT supplemented by PET/CT and MRI when required.

In certain circumstances ultrasound assessment of peripheral

tumours and supraclavicular lymph nodes adds further useful information.

The Current Standards of Computer

Tomography Technology

The current standard of CT technology is a multislice (usually at least 64 detector rows) CT system, able to acquire submillimetre collimation images through the thorax in a short breath-hold.

The decision to include abdominal, pelvic and intracranial assessment varies from centre to centre.

However, a comprehensive brain, chest, abdomen and pelvis acquisition can be undertaken in very short order and the main rate-limiting steps are now patient identification, preparation and documentation rather than the acquisition of the data sets.

Most institutions will routinely use intravenous contrast agents, although this is not mandatory.

Not infrequently, difficulty with venous access, asthma, allergy or previous contrast reaction and impaired renal function will prevent contrast administration.

A standard thoracic CT will be undertaken with the

patient in the supine position and the arms elevated.

Imaging planning and dose reduction optimisation require an anteroposterior (AP), and sometimes a lateral scout projection. If contrast medium is administered,

then image acquisition is timed to optimise opacification of central pulmonary vasculature (usually 20–30 seconds).

If an abdominal and pelvic study is also undertaken, this component is best acquired during the portal venous phase of contrast enhancement (65 seconds).

This will require two short breath-holds and two pre-planned acquisition ranges with some overlap at the lung bases. Alternative injection protocols combined with fast CT scanners now allow a single volumetric acquisition with both arterial and portal venous phase enhancement simultaneously.

The ability to produce isotropic voxels allows multiplanar reformatting to be undertaken as a routine, either by the radiographic staff or at the time of reporting by the radiologist.

The PET/CT technique is similar for the CT acquisition of the study, which is usually obtained from skull base to upper thigh.

If the patient is also undergoing a conventional CT, the CT acquisition for PET coregistration can be low dose and unenhanced.

As the PET component of the acquisition takes considerably longer than the CT acquisition, in this situation the unenhanced low-dose CT will usually be undertaken during gentle respiration, to allow optimum co-registration with the

PET data. Usually the PET acquisition takes between 5 and 7 bed couch positions, with each position taking up to 5 minutes, and therefore the whole study may take up to 35 minutes to acquire.

More modern systems achieve the entire study in

considerably less time.

MRI of the thorax is usually undertaken to answer a particular question as a problem-solving tool. In the context of lung cancer staging, the MRI study is often to assess superior sulcus tumours, chest wall or thoracic invasion or to assess the integrity of the diaphragm.

Usually triplanar examinations are untaken with respiratory gating and T1 and T2 weighting.

A variety of more refined techniques, including dynamic

contrast-enhanced MRI sequences for the evaluation of lung nodules as well as use of diffusion-weighted imaging, are commonplace.

Diffusion weighted imaging can differentiate tumour from surrounding lung and may be helpful in assessing response to treatment before clear dimensional changes are evident. Dynamic cine acquisitions can be utilized to assess fixation of a peripheral tumour to chest wall or mediastinal structures.

IMAGING FEATURES OF

BRONCHOGENIC CARCINOMA

The thoracic imaging features of bronchial carcinoma are discussed under three headings: (1) peripheral tumours; (2) central tumours (arising in a large bronchus at or close to the hilum); and (3) staging intrathoracic spread of bronchial carcinoma.

Peripheral Tumours

Approximately 40% of bronchial carcinomas arise beyond

the segmental bronchi, and in 30% a peripheral mass is the sole radiographic finding.

Tumour Shape and Margins

Tumours at the lung apex (Pancoast tumours, superior sulcus tumours) may resemble apical pleural thickening; however, most peripheral lung cancers are approximately spherical or oval in shape. Lobulation, a sign

that indicates uneven growth rates in different parts of the tumour, is

common. Occasionally, a dumb-bell shape is encountered or two nodules

are seen next to one another.

The term 'corona radiata' is used to describe numerous fine strands radiating into the lung from a central mass, sometimes with transradiant lung parenchyma between these strands.

While not specific, this sign is highly suggestive of bronchial carcinoma.

Absolutely spherical, sharply defined, smooth-edged nodules due to carcinoma of the lung are rare.

A peripheral line shadow or 'tail' may be seen between

a peripherally located mass lesion and the pleura, a phenomenon that occurs in both benign and malignant lesions.

When associated with carcinoma of the lung, the 'tail' probably represents either plate-like oedema due to lymphatic obstruction.

Although the edges of a tumour are frequently well defined, some peripheral cancers, notably some types of adenocarcinoma, have ill-defined edges similar to pneumonia.

Cavitation

Cavitation may be identified in tumours of any size and is best demonstrated by CT.

Squamous cell carcinoma is the most likely cell type to show cavitation.

The walls of the cavity are of irregular thickness and may contain tumour nodules, but sometimes the wall has smooth inner and outer margins.

The cavity wall is usually 8-mm thick or greater. Fluid levels are common.

Calcification

Calcification within bronchogenic carcinomas is rarely seen on chest radiography but is identified on CT in 6% to 10% of cases.

Some foci of calcification represent pre-existing calcified granulomatous disease engulfed by tumour.

However, amorphous or cloud-like calcification consistent with dystrophic tumour calcification is still seen in a small proportion of cases (<10%) (Fig. 8.16).

Most calcified tumours atelectasis secondary to bronchial obstruction beyond the mass or septal are large, with a diameter of 5 cm or more, but calcification also can be seen in small peripheral tumours.

Other Findings

Air bronchograms and bubble-like lucencies or pseudocavitation may be seen within lung cancers, in particular with adenocarcinoma.

Occasionally, dilated mucus-filled bronchi (bronchocele, mucocele, mucoid impaction) are seen distal to a carcinoma obstructing a segmental or subsegmental bronchus.

Ground-glass attenuation may be seen as a component of nodules and is associated with a greater risk of malignancy than that of purely solid nodules.

It is more commonly associated with adenocarcinoma, which may present as a purely ground-glass opacity.

Central Tumours

The cardinal imaging signs of a central tumour are collapse/consolidation of the lung beyond the tumour and the presence of hilar enlargement, signs that may be seen in isolation or in conjunction with one another.

Although the concept of a central tumour seems simple, a recent survey of practitioners involved in staging found that there is no consensus as to what constitutes a central tumour, some using contact with the hilum, others the inner third of the lung and others still the inner two-thirds of the lung as defined by concentric rings related to the hilum. Alternatively, there is a school of thought that favours anatomical divisions based on sagittal planes spaced evenly from the midline to the outer third of the lung.

Suffice to say there is no universally agreed guidance.

Collapse/Consolidation in Association With

Central Tumours

Obstruction of a major bronchus often leads to a combination of atelectasis and retention of secretions with consequent pulmonary opacity, but collateral air drift may partially or completely prevent these post-obstructive changes. Secondary infection may occur beyond the obstruction.

The following features suggest that pneumonia is secondary to an obstructing neoplasm:

1. The shape of the collapsed or consolidated lobe may be altered because of the bulk of the underlying tumour.

In cases with lobar collapse due to a central tumour mass, the fissure in the region of the mass is unable to move in the usual manner and, therefore, the fissure may show a bulge (the Golden S sign if involving the right upper lobe).

The description has become extended to include the CT equivalent appearance of a hilar mass and collapsed distal lobe and also to describe the phenomenon in other lobes.

2. The presence of pneumonia in an at-risk patient, confined to one lobe (or more lobes if there is a common bronchus) that persists unchanged for longer than 2 to 3 weeks, or a pneumonia that recurs in the same lobe, particularly if the lobe shows loss of volume and no air bronchograms.

Simple pneumonia often clears or spreads to

other segments within a few weeks. In practice, complete resolution of pneumonia virtually excludes an obstructing neoplasm as a cause of infection.

Although consolidation may improve partially on appropriate antibiotic therapy, it almost never resolves completely if secondary to an underlying carcinoma. Occasionally, the opacified lobe may appear larger than normal because of the build-up of infected secretions beyond the obstructing carcinoma, an appearance that has been labelled the 'drowned lobe'.

3. A visible mass with irregular stenosis of a mainstem or lobar bronchus.

Careful analysis of CT images may demonstrate the presence of an obstructing tumour when there is obstructive atelectasis.

4.Simple pneumonia rarely causes radiographically visible hilar adenopathy, though enlarged central nodes may be seen on CT or MRI.

Lung abscess can occasionally be confused with bronchial

carcinoma because it may result in hilar or mediastinal adenopathy.

5. Mucus-filled dilated bronchi may be visible within collapsed lobes on a CT examination as branching, tubular low-density structures, and when seen should prompt a search for a centrally obstructing tumour.

Staging Intrathoracic Spread of Bronchial Carcinoma Hilar Enlargement Hilar enlargement is a common presenting feature in patients with bronchial carcinoma.

It may reflect a proximal tumour, lymphadenopathy,

consolidated lung, or a combination of these phenomena.

A mass superimposed on the hilum may lead to increased density of the hilum, owing to summation of the opacity of the mass and that of the normal hilar shadows.

This sign may be the only indication of lung cancer on a frontal chest radiograph; when suspected,

it is essential to inspect the lateral radiograph with care.

Mediastinal Invasion **Plain radiograph** evidence of mediastinal invasion relies on demonstrating phrenic nerve paralysis.

However, caution is needed before deciding that a high hemidiaphragm is caused by phrenic nerve invasion, because lobar collapse can also lead to elevation of a hemidiaphragm, a subpulmonary effusion may mimic it, and diaphragmatic eventration is common.

The **CT and MRI** signs of mediastinal invasion include the demonstration of visible tumour deep within the mediastinal fat, particularly if tumour surrounds the mediastinal vessels, oesophagus, or proximal mainstem bronchi.

Associated pneumonia or atelectasis may make it very difficult to determine whether or not mediastinal contact is present. Even clear-cut contact with the mediastinum is not enough for the diagnosis of invasion, and the apparent interdigitation of tumour with mediastinal fat can be a misleading sign on both CT and MRI.

- 1. Glazer et al. showed that the presence of (1) less than 3 cm of contact with the mediastinum, (2) less than 90 degrees of circumferential contact with the aorta or
- 2. (3) a visible mediastinal fat plane between the mass and

any vital mediastinal structures indicated a very high likelihood of technical resectability, even if the tumour had crossed into the mediastinum, and that most tumours in their series conforming to this description had no mediastinal invasion at surgery.

- 3. However, when the question is turned around to enquire as to the criteria for unresectability, the answer is less certain.
- 4. Tumours that obliterate fat planes or show greater contact than that described above are not necessarily unresectable, though the greater the degree of invasion and the extent of contact, the more likely it is that there is significant mediastinal involvement.
- 5. MRI does not appear to offer any advantages over CT for the routine diagnosis of mediastinal invasion, its role being limited to problem solving in specific cases. Before the advent of MDCT, the multiplanar capabilities of MRI could be used to advantage to identify involvement of major mediastinal blood vessels and the tracheal carina.
- 6. MDCT has largely obviated the need to proceed to MRI to take advantage of multiplanar imaging alone; however, MRI sequences optimised for evaluation of the heart and vessels may still offer advantages where there is concern about invasion of hilar or mediastinal vessels, the heart or pericardium.

Chest Wall Invasion

The presence of chest wall invasion alone does not preclude surgical resection, though it does adversely affect prognosis. The necessarily more extensive surgery is associated with increased morbidity and mortality and it therefore greatly helps the surgeon to know the extent of any chest wall invasion preoperatively.

The diagnosis of chest wall involvement adjacent to a tumour is unreliable on CT, unless there is clear-cut bone destruction or a large soft-tissue mass.

Local chest wall pain remains the single most specific indicator of whether or not the tumour has spread to the

parietal pleura or chest wall. Contact with the pleura on CT examination, even if the pleura is thickened, does not necessarily indicate invasion, though the greater the degree of contact and the greater the pleural thickening, the more likely it is that the parietal pleura has been invaded, particularly if the extrapleural fat plane is obliterated.

A definite extrapleural mass that is not explicable by previous chest trauma is likely to be the result of invasion by tumour, but even this sign may be misleading because soft-tissue swelling may be due to inflammation

and fibrosis rather than neoplasm. Conversely, a clear extrapleural fat plane adjacent to the mass may be helpful, but again not definitive, in excluding chest wall invasion.

Previously, in selected cases, MRI proved to be better than CT in demonstrating chest wall and diaphragmatic invasion.

MRI was regarded as the optimal technique for

demonstrating the extent of superior sulcus tumours (Pancoast tumour), reliably diagnosing mediastinal invasion, extension into the root of the neck and involvement of vascular and neural structures. With the ability of CT to provide routine multiplanar reformatted images, routine MRI assessment is not usually required.

Transthoracic ultrasound can identify chest wall invasion (tissue fixed to pleura) with a high degree of accuracy; however, in many centres the technique is rarely used.

99mTc radionuclide skeletal scintigraphy is a sensitive technique with which to assess bone invasion and it may be positive when the plain radiograph still shows no bony abnormality.

However, as discussed above, 18F-FDG PET/CT is now the examination of choice for detection of distant spread (outside the CNS) and has been shown to provide assessment of skeletal as well as soft-tissue spread.

Generally, chest radiography is insensitive for nodal staging.

However, the presence of enlarged hilar or paratracheal nodes has been shown to be specific (92%) for N2 to N3 disease.

Lymph node assessment on CT and MRI is limited to size, shape and location, with size being the major criterion used to predict metastatic involvement.

Normal mediastinal lymph node size on CT or MRI varies according to the location of the nodes within the mediastinum, but a simple and reasonably accurate rule is

that nodes with a short-axis diameter of less than 10 mm fall within the 95th percentile and nodes above this size

should, therefore, be considered enlarged.

The problem with using size as the only criterion for malignant involvement is that intrathoracic lymph node enlargement has many non-malignant causes, including previous tuberculosis, histoplasmosis, pneumoconiosis, sarcoidosis and, most importantly, reactive hyperplasia

to the tumour or associated pneumonia/atelectasis: it has

repeatedly been shown that one-half to two-thirds of enlarged nodes draining post-obstructive pneumonia/atelectasis are free of tumour.

Conversely, microscopic involvement by tumour can be present in normal-sized nodes.

Therefore there is no measurement above which all nodes can be assumed to be malignant and below which all can be considered to be benign.

The sensitivity and specificity of CT for diagnosing metastatic involvement of mediastinal lymph nodes vary

greatly in different published series, reflecting different size criteria and the methods used to confirm or exclude lymph node metastases.

A reasonable generalisation in the United States (where fungal infection is endemic) is that both sensitivity and specificity are in the 50% to low 60% range when the cutoff point for normal is a short-axis diameter of 1 cm. Better specificity figures have been obtained in Europe and Japan, probably because the prevalence of coincidental histoplasmosis is much lower than in the United States.

The positive predictive value for nodal metastatic disease may be improved (to up to 95%) by ensuring that nodes draining the tumour are larger than nodes elsewhere in the mediastinum.

The accuracy of MRI, despite its improved contrast resolution, is limited by the same constraint as for CT of overlap of features of benign and malignant causes of node enlargement.

Although it is generally considered that the MRI signal within nodes is not a useful predictor of involvement, it has been reported that short tau inversion recovery (STIR) imaging produces sufficient signal difference between normal and pathological nodal tissue to detect metastases with 93% sensitivity and 87% specificity.

The previously cited advantage of MRI over CT in nodal detection because of its ability to distinguish small nodes from vessels without intravenous enhancement has been effectively negated by the advantages of MDCT.

Endobronchial ultrasound (EBUS) can be used to assess the size and morphology of, and to guide fine-needle or small-core needle biopsy of, aortopulmonary, subcarinal and posterior mediastinal nodes, achieving greater sensitivity and specificities for nodal involvement than CT and PET in some series.

Ultrasound assessment with or without fine-needle aspiration)

of supraclavicular lymph nodes improves sensitivity for detection of supraclavicular lymph node involvement; its routine use has been suggested as a method to improve the accuracy of preoperative staging.

18F-FDG PET/CT imaging is routinely utilised for staging lung carcinoma, with published studies consistently demonstrating greater accuracy compared with CT and MRI in the detection of nodal disease.

False-positive results still occur, most commonly due to

inflammation and reactive hyperplasia. Fused PET/CT imaging provides registration of FDG metabolic activity with the anatomical detail of CT.

Decision analysis studies have shown that PET can

be incorporated into the work-up of lung cancer in a costeffective manner, with savings derived from identifying inoperable patients before thoracotomy.

Mediastinoscopy (and mediastinotomy for nodes not accessible to mediastinoscopy) remain widely employed for mediastinal lymph node sampling but are now generally utilised as a second-line technique when EBUS is either not available or has not provided a definitive result.

They have high sensitivity and specificity for detecting malignant disease and, although invasive, are indicated before thoracotomy when other forms of imaging suggest nodal involvement.

Current practice has struck a balance between PET/CT and tissue sampling for the assessment of mediastinal

nodes. In essence,

• When the CT assessment and the PET assessment are negative, the

patient is offered resection without preoperative nodal sampling.

• When the CT is negative but the PET is positive, the mediastinal nodes will require sampling by EBUS or mediastinoscopy to assess resectability or guide presurgical therapy with a view to downstaging and reassessment.

• When CT and PET are positive, tissue confirmation is required, assuming there are no distant metastatic sites.

Pleural Involvement

Pleural involvement may occur as a result of direct spread, lymphatic involvement or tumour emboli.

On occasion, adenocarcinoma takes the form of a sheet of lobular pleural thickening indistinguishable from malignant mesothelioma.

A pleural effusion in association with a primary lung cancer designates the tumour as being M1a.

The exception is the few patients who have clinical evidence of another cause for the effusion (e.g. heart failure) and in whom cytology examinations of multiple pleural fluid samples are negative for tumour cells, in which case the effusion can be disregarded as a staging criterion.

Attempts to characterise the nature of the pleural fluid
based on density measurements at CT or signal intensities at MRI have not so far proven useful. Several studies suggest PET may have a role in the evaluation of pleural effusion in patients with lung cancer.

Summary

Staging the intrathoracic extent of lung cancer is a multidisciplinary process utilising imaging, bronchoscopy and biopsy.

Chest radiography, CT and 18F-FDG PET/CT are currently the routine imaging procedures for assessing intrathoracic spread and determining resectability, with

MRI and ultrasound reserved for specific indications.

The essential points to establish when staging the intrathoracic extent of non-small cell cancers are:

(1) whether the tumour has spread to

hilar or mediastinal nodes;

(2) if it has, which nodal groups are involved;

(3) whether the tumour has invaded the chest wall or mediastinum;

and (4) if it has, whether it is still potentially curable surgically.

If chest radiography and CT with or without } PET show no evidence of spread beyond the lung (other than to ipsilateral hilar nodes) in a patient who is suitable for surgery, and in whom bronchoscopy shows the tumour to be resectable, then that patient should be offered surgical resection without further preoperative invasive procedures.

Spread to ipsilateral nodes, whilst not necessarily precluding surgical resection, has a significantly adverse effect on prognosis and even if surgery is undertaken,

it is performed with the understanding that 5-year survival rates are poor.

The poor specificity of **CT** in determining nodal involvement must be appreciated.

Nodal enlargement, whilst probably due to metastatic

carcinoma, may also be due to coincidental benign disease, reactive hyperplasia to the presence of the tumour, or to any associated obstructive consolidation/atelectasis. Thus, biopsy confirmation of neoplastic nodal involvement by mediastinoscopy, mediastinotomy or needle aspiration is usually essential before a patient is denied surgery.

Positive **PET** findings for nodal involvement do not obviate the need for histological confirmation of nodal involvement.

However, in patients with no enlarged lymph nodes on CT and normal findings on PET, the likelihood of nodal

involvement is so low that mediastinoscopy can be omitted for peripheral tumours (but see the comment above about the definition of central versus peripheral location).

For lung cancers that have invaded the mediastinum or

chest wall, it is important to decide whether the tumour is nevertheless resectable for possible cure, again recognising that the prognosis will be poorer than for tumours confined to the lung.

CT may show definitively that the tumour is too extensive for resective surgery (i.e. that it is a T4 lesion). Alternatively, CT may leave the issue in doubt and **MRI** may then help to solve the problem.

Extrathoracic Staging of Lung Cancer

Lung cancer is commonly associated with widespread haematogenous dissemination at the time of presentation. Sites of spread include the adrenal glands, bones, brain, liver and more distant lymph nodes.

Detection of metastatic disease precludes surgical resection of the primary tumour.

In most centres, chest CT is extended to include the liver and adrenals (with appropriate timing for portal venous enhancement).

Further imaging is usually only undertaken if there are clinical features suggesting metastatic disease. In many European countries it is now routine to undertake PET/CT in any patient who is to be offered radical therapy for lung cancer.

In patients initially selected for curative resection using standard tumour staging, PET/CT has been reported to detect occult metastatic disease in 11%–14% of patients, and to alter management in up to 40%.

PULMONARY SARCOMA AND OTHER

PRIMARY

MALIGNANT NEOPLASMS

Most pulmonary sarcomas in the lungs are metastases from extrathoracic primary tumours.

Primary pulmonary sarcomas are rare, the most common primary forms being fibrosarcoma and leiomyosarcoma.

Chondrosarcoma, fibroleiomyosarcoma, rhabdomyosarcoma, pleomorphic undifferentiated sarcoma, carcinosarcoma, liposarcoma and osteosarcoma are among the other sarcomas that may occasionally

arise as primary airway or pulmonary tumours.

All the above neoplasms present as a solitary pulmonary nodule or as a tracheal or endobronchial mass indistinguishable radiologically from bronchial

carcinoma. Angiosarcomas of the pulmonary artery extend or arise intravascularly.

The acquired immune deficiency syndrome (AIDS) epidemic led to an increased number of cases of Kaposi sarcoma involving the lung, a situation largely redressed by effective anti-retroviral therapy.

Kaposi sarcoma in the respiratory tract is rare in the absence of cutaneous involvement.

Coincidental involvement of the tracheobronchial tree is

relatively frequent but parenchymal involvement may occur in the absence of endobronchial disease.

Imaging may show the disease to be focal or widespread.

Focal segmental or lobar opacities are usually due to the tumour itself, but endobronchial Kaposi sarcoma may result in atelectasis or post-obstructive pneumonia. **Radiographically** widespread disease is the more frequent pattern, with a tendency to perihilar predominance of linear, rounded or reticulonodular shadowing, reflecting a bronchocentric distribution of the lesions.

The pulmonary opacities of Kaposi sarcoma do not fluctuate in severity, whereas the major differential diagnoses—pulmonary oedema and opportunistic

infections-may do so.

Intrathoracic hilar/mediastinal lymphadenopathy

has been detected in 25%–60% of cases in some series. Pleural involvement is frequent pleural effusions, which are most commonly bilateral and may on occasion be large.

Other rare malignant pulmonary neoplasms include haemangiopericytoma,

pulmonary blastoma, plasmacytoma, choriocarcinoma,

teratoma and Askin tumours.

BENIGN PULMONARY TUMOURS

There are a variety of relatively rare lesions that may present as an asymptomatic solitary pulmonary mass. Imaging plays a key part in the characterisation of these lesions and will guide the need for further investigation or surgery.

HAMARTOMA

Hamartomas are tumour-like malformations composed of an abnormal mixture of mature tissues normally found in the organ in which the tumour occurs.

Pulmonary hamartomas consist predominantly of masses

of cartilage, with clefts lined by bronchial epithelium, and may contain large collections of fat.

Malignant transformation is either non-existent or extremely rare.

Pulmonary hamartomas are very occasionally multiple.

A triad of pulmonary chondroma(s) (often multiple), gastric epithelioid leiomyosarcoma (leiomyoblastoma) and functioning extra-adrenal paragangliomas, known as Carney triad, has been reported, as has a form with just pulmonary chondromas and gastric smooth muscle tumours.

The age range for hamartoma is from young adulthood to old age, with presentation peaking in the seventh decade; they are only occasionally

seen in children.

The distribution of pulmonary hamartomas is opposite to that

seen with bronchial carcinoid: 90% are peripheral and present as a

solitary pulmonary nodule, while the remaining 10% arise within a major bronchus.

Central lesions may lead to major airway obstruction

and the features are then identical to those seen with bronchial carcinoids.

On **plain chest radiography** the tumour is seen as a spherical or slightly lobulated, well-defined nodule, usually less than 4 cm in size, with normal surrounding lung.

Some hamartomas show calcification, which may be spotty or linear or show the characteristic 'popcorn' configuration associated with calcification in cartilage. The frequency of calcification increases significantly with the size of the lesion.

Popcorn calcification, if present, is virtually diagnostic of a hamartoma (the only differential diagnosis is a chondrosarcoma).

Central fat density on CT is another important finding, which, if present, establishes the diagnosis.

The lesions grow slowly, usually much more slowly than carcinoma of the bronchus, and cavitation is almost unknown.

OTHER BENIGN PULMONARY NEOPLASMS

Fibroma, chondroma, lipoma, haemangioma, benign clear cell tumours, neurogenic tumours, chemodectoma and granular cell myoblastoma are benign neoplasms that are occasionally encountered in the trachea, bronchi or lungs. The **plain radiographic and CT** findings vary with

the size and location of the tumour mass, but no features

distinguish any one of these lesions from any other, and therefore the specific diagnosis has to be made histologically.

They are indistinguishable radiologically from carcinoid tumour and solitary metastasis.

Leiomyoma

Leiomyoma of the lung may be a solitary lesion, **radiographically** indistinguishable from the other benign connective tissue neoplasms.

Multiple leiomyomas present as multiple discrete nodules in the lungs.

They are given a wide variety of names, including benign metastasizing leiomyoma.

In women these tumours may be very slow-growing

metastases from a uterine leiomyoma; women with multiple pulmonary leiomyomas often have a history of previous hysterectomy for uterine fibroids.

Intrapulmonary teratomas are very unusual. Most are benign, though malignant lesions are occasionally encountered.

Radiographically, and on **CT**, intrapulmonary teratomas appear as lobulated masses that may show calcification or cavitation.

Inflammatory Myofibroblastic Tumour

Inflammatory myofibroblastic tumour (IMT)—also known by a variety of other names, including plasma cell granuloma, inflammatory pseudotumour and fibrous histiocytoma—is a lesion that is presumed to be reactive inflammatory granulomatous tissue. It is still unclear if

these lesions, which can be locally invasive, represent a purely inflammatory process or a low-grade malignancy with a marked inflammatory response.

The age range is wide and includes children. Indeed, IMT is one of the commonest paediatric primary lung tumours. Most patients present with an asymptomatic solitary pulmonary nodule.

Cavitation and calcification have both been described. These lesions are PET positive and mimic bronchogenic carcinomas. Similar lesions can develop elsewhere in the body.

Sclerosing Haemangioma

Sclerosing haemangioma is a benign neoplasm, which almost always presents as an asymptomatic solitary pulmonary mass.

Calcification may be seen.

Squamous Papillomas

Squamous papillomas of the trachea, bronchi and lungs are most commonly associated with laryngeal papillomatosis, a disease that usually commences in childhood and is caused by the human papilloma virus.

Rarely, these papillomas are also present in the lung and are seen on **plain chest radiography** or **CT** as multiple, small, widely scattered and well-defined, round pulmonary nodules, frequently showing cavitation.

BENIGN LYMPHOPROLIFERATIVE DISORDERS LYMPHOCYTIC INTERSTITIAL PNEUMONIA

Lymphocytic interstitial pneumonia (LIP) is an uncommon nonneoplastic lymphoproliferative disorder characterised by diffuse infiltration of the pulmonary parenchymal interstitium by lymphocytes and plasma cells.

It is more commonly seen in association with an underlying immunological abnormality such as Sjögren

syndrome and AIDS. The main imaging findings are of bilateral areas of ground-glass opacification and thin-walled cysts.

FOLLICULAR BRONCHIOLITIS

Follicular bronchiolitis, also known as diffuse lymphoid hyperplasia, is characterised by hyperplasia of bronchial mucosa-associated lymphoid tissue (MALT) in relation to airways.

Reticular or reticular nodular

shadowing with centrilobular nodules and ground-glass opacity and occasionally bronchial wall thickening, bronchial dilatation, interlobular septal thickening and peribronchovascular airspace consolidation is seen.

MALIGNANT LYMPHOPROLIFERATIVE

DISORDERS

LYMPHOMA

Only pulmonary parenchymal involvement by lymphoma

is considered.

Pulmonary parenchymal involvement can be broadly

divided into that occurring in association with existing or previously treated nodal disease, and that due to primary lymphoma of the lung (Hodgkin or non-Hodgkin). Parenchymal involvement is comparatively rare at initial presentation (10% to 15% of cases), but it becomes

considerably more common as the disease progresses. It is particularly frequent in patients who relapse after treatment.

Involvement of the lung appears to be three times as frequent in Hodgkin lymphoma as it is in non-Hodgkin lymphoma.

In Hodgkin lymphoma the lung disease is almost invariably accompanied by visible intrathoracic adenopathy, whereas in the non-Hodgkin lymphomas, isolated pulmonary involvement is not uncommon.

If the mediastinal and hilar nodes have been previously irradiated, then recurrence confined to the lungs may be

seen in both Hodgkin and non-Hodgkin lymphoma.

The radiographic appearances of lung involvement in malignant lymphoma vary.

The usual patterns are (1) one or more areas of pulmonary

consolidation resembling pneumonia,

(2) multiple pulmonary nodules and, occasionally,

(3) miliary nodulation or reticulonodular shadowing

resembling lymphangitis carcinomatosa.

The areas of pulmonary consolidation, which may contain air bronchograms, may be segmental or lobar in shape but often they radiate from the hila or mediastinum without conforming to segmental anatomy, in keeping with the concept that extension into the lungs is by direct invasion from involved hilar or mediastinal nodes. However,

peripheral subpleural masses or areas of consolidation without any visible connection to enlarged nodes in the mediastinum and hila are common in both Hodgkin disease and non-Hodgkin lymphoma.

Very rapid increase in the size of lymphomatous deposits in the lung, so rapid that the disease may be confused with pneumonia, has been reported with high-grade non-Hodgkin lymphoma.

Primary lymphoma of the lung (i.e. lymphoma isolated

to the lung at initial presentation) is very uncommon, non-Hodgkin lymphoma of MALT type, being the most frequently encountered form.

These are low-grade B-cell lymphomas of MALT (also called bronchusassociated lymphoid tissue or BALT), which consist of mucosal lymphoid follicles located in distal bronchi and bronchioles, particularly at airway

bifurcations.

The second most common primary tumour, known as

angiocentric immunoproliferative lesion or lymphoid granulomatosis, is high grade and may have a B- or T-cell

phenotype.

Primary pulmonary Hodgkin disease is notably rare.

The imaging features of MALT lymphomas are solitary or multifocal, round or segmental areas of pulmonary consolidation.

There is no lobar predilection and the consolidations may be placed centrally or peripherally in the lung parenchyma.

Air bronchograms are frequently visible and may be a striking feature.

A few of the lesions show cavitation, but calcification does not occur.

MALT lymphomas are relatively rarely associated with pleural effusions despite contact with the pleura.

Other Findings in Pulmonary Lymphoma

Lobar atelectasis caused by endobronchial lymphoma is occasionally encountered, but, somewhat surprisingly, atelectasis as a result of extrinsic compression by enlarged lymph nodes is rare, with encasement rather

than obstruction being the usual pattern of disease.

Pleural effusions are common except in MALT lymphoma.

They are usually unilateral and accompanied by visible intrathoracic adenopathy.

They frequently disappear once the mediastinal nodes have been irradiated; in such cases they are probably due to venous or lymphatic obstruction rather than neoplastic involvement of the pleura.

The usual radiographic problem is in deciding whether the pulmonary abnormality is due to involvement by lymphomatous tissue, infection or a complication of therapy.

It should be remembered that the pattern of pulmonary infection in patients with lymphoma is modified because

they are immunocompromised hosts, owing either to their disease or, more often, to the drugs used for treating the disorder.

In many instances, a biopsy is the only way to establish the precise diagnosis.

As Hodgkin disease is believed to spread from nodal sites, a useful guideline is that if a patient presents with Hodgkin lymphoma and a pulmonary opacity, but no evidence of hilar or mediastinal disease, it is more likely that the opacity represents something other than Hodgkin lymphoma.

A caveat here is that the patient should not previously have received radiation therapy to the mediastinum.

LEUKAEMIA

The incidence of leukaemic infiltration of the lungs, mediastinal lymph nodes and pleura varies with the course of the disease.

Pulmonary infiltration by leukaemic cells is found at autopsy in nearly two-thirds of patients who have leukaemia.

However, provided those patients with leukostasis (see later) are considered separately, leukaemic infiltration

of the lungs, though very common pathologically, is usually asymptomatic and is rarely a cause of significant pulmonary opacity on a chest radiograph.

When respiratory impairment is present, pulmonary

infection, oedema or haemorrhage is a more likely cause of the patient's symptoms.

Imaging features include diffuse bilateral reticulation and

patterns resembling interstitial oedema; lymphangitic carcinomatosis, small nodules, ground-glass opacification and consolidation have also been described.

Radiographically visible hilar and/or mediastinal lymph node enlargement may be present and pleural effusions are common, though it is not possible to state the cause of the effusion with any confidence.

The distribution of nodal enlargement closely resembles that of the lymphomas.

T-cell leukaemias may show massive mediastinal adenopathy that responds rapidly to chemotherapy or radiation treatment.

Huge mediastinal masses of T-cell leukaemia may disappear within a few days following appropriate treatment.

Pleural thickening due to a mass of leukaemic cells in patients with myeloid leukaemia, so-called granulocytic

sarcoma or chloroma formation (because of its green appearance), may be encountered on rare occasions.

Leukostasis is seen in patients with acute myeloid leukaemia with very high white blood cell counts in the order of 100,000 to 300,000 cells/mm3.

The patients may be dyspnoeic because of the obliteration

of their small pulmonary blood vessels by the leukaemic cells.

The **chest radiograph** may be normal or show airspace shadowing, which is probably due to pulmonary oedema rather than directly to the accumulation of leukaemic cells in the lungs.

METASTASES

Pulmonary metastases in adults are usually from breast, gastrointestinal tract, kidney, testes, head and neck tumours or from a variety of bone and soft-tissue sarcomas.

The basic sign of haematogenous pulmonary

metastasis is one or more discrete pulmonary nodules, usually in the outer portions of the lungs, a distribution that is most evident on CT.

The nodules are usually spherical and well defined,

but they may be almost any shape and can occasionally have a very irregular edge.

Such irregular edges are seen particularly with metastases from adenocarcinomas.

Cavitation is occasionally seen in pulmonary metastases; it is a particular feature of squamous cell carcinoma.

Calcification is very unusual except in osteosarcoma and

chondrosarcoma. Even if the primary tumour shows calcification (e.g.in breast and colon), visible calcification in the pulmonary metastases is rare.

The rate of growth of metastases is highly variable; in some choriocarcinomas and osteosarcomas, for example, it may be explosive and double the volume of the lesions in less than 30 days.

Alternatively, metastases can remain unchanged in size for a long time, as in some cases of thyroid carcinoma.

A solitary pulmonary metastasis may be the presenting feature in a patient without a known primary tumour. However, a metastasis is a rare cause of the asymptomatic pulmonary nodule in patients who do not have a known extrathoracic primary neoplasm, comprising no more than 2% to 3% of most series.

The simplest technique for diagnosing pulmonary metastases is the plain PA and lateral chest radiograph. High-kV techniques are often used routinely, because substantial portions of the lungs are obscured on low-kV radiographs by overlying structures such as the diaphragm, heart, mediastinum, hila and ribs.

Such radiographs will detect most lung metastases above 1 cm in diameter.

Increasing sensitivity can be obtained with MDCT. However, the increase in sensitivity for small nodules is at the cost of decreasing specificity.

On CT, lesions smaller than 1 cm are regularly demonstrated, together with most lesions above 3 mm in diameter.

Below 1 cm, and particularly below 6 mm, the differential diagnosis from granulomas due to tuberculosis, histoplasmosis or other fungi becomes difficult.

Where calcification can be identified, metastases (except from osteogenic sarcoma or chondrosarcoma) can

effectively be dismissed from consideration.

If the nodules are not calcified, the best that can be done in most instances is to give a statistical probability of the nodules being metastases.

With a plain chest radiograph showing multiple noncalcified nodules, the probability is high, well over 90%, even in areas endemic for fungus granulomas, and approaches 100% in areas where fungus granulomas are rare or non-existent.

With the smaller lesions detectable on CT, this probability diminishes.

Depending on the prevalence of infectious granulomas in the community and the likelihood of a particular tumour metastasising to the lung, the probability that a pulmonary nodule seen solely on CT is indeed a metastasis may drop to as low as 50%.

LYMPHANGITIC CARCINOMATOSIS

Lymphangitic carcinomatosis is the name given to permeation of pulmonary lymphatics and/or their adjacent interstitial tissue by neoplastic cells.

The most common tumours that spread in this manner are

carcinomas of the bronchus, breast, stomach and prostate. Lymphangitic carcinomatosis may develop secondary to blood-borne emboli lodging in smaller pulmonary arteries and subsequently spreading through the vessel walls into the perivascular interstitium and lymphatic vessels.

Such spread tends to give rise to bilateral symmetric pulmonary abnormality.

Alternatively, lymphangitic carcinomatosis may result from direct extension of tumour from hilar lymph nodes into peribronchovascular interstitium, from the pleura into adjacent interlobular septa, or from a

primary carcinoma of the lung into the adjacent peribronchovascular interstitium.

Tumour spreading by these mechanisms tends to be

more localised.

The radiological findings are fine reticulonodular shadowing and/or thickened septal lines.

These signs occur because of a combination of dilated lymphatics and interstitial oedema, together with shadows due to the tumour cells themselves along with any desmoplastic response that may have been induced by the tumour.

Another useful sign of lymphangitis carcinomatosa is

subpleural oedema resulting from lymphatic obstruction by tumour cells, a feature that is most readily visible as thickening of the fissures.

Pleural effusion is common, and is seen in about 30%.

As would be expected, CT is more sensitive than plain radiography in the detection of lymphangitic spread and may show changes in patients whose chest radiograph is normal.

CT, particularly high-resolution CT, shows non-uniform, often nodular, thickening of the interlobular septa and irregular thickening of the bronchovascular bundles in the central portions of the lungs.

Small, peripherally located, wedgeshaped densities are sometimes seen as well; these may represent volume

averaging of the thickened septa.

There is often patchy airspace shadowing, but an important differential diagnostic feature from pulmonary

oedema is that many of the acini subtended by thickened interlobular septa are normally aerated.

Nodular shadows may be seen scattered through the parenchyma. The abnormalities may involve all zones of

both lungs or they may be centrally or peripherally predominant; sometimes, particularly when lymphangitis is due to bronchial carcinoma, they are confined to a lobe or one lung.

Hilar lymph node enlargement is seen in only some of the patients.

UNUSUAL PATTERNS OF METASTATIC CANCER

Endobronchial Metastases

Endobronchial metastases are most unusual. Melanoma and renal, colorectal and breast carcinomas are the primary tumours that most frequently give endobronchial submucosal metastases.

In such cases the effect of airway obstruction is the dominant feature.

Miliary Metastases

Occasionally, innumerable tiny nodules closely resembling miliary tuberculosis are seen throughout both lungs, with no large masses and no evidence of lymphatic obstruction, such as is seen in lymphangitis carcinomatosa.

However, metastases are one of the rarest causes of this

pattern. The primary tumours that are most likely to produce miliary nodulation of the lungs are thyroid and renal carcinomas, bone sarcomas and choriocarcinoma.

Tumour Emboli

Radiologically recognisable pulmonary arterial hypertension may occur on rare occasions as a result of tumour emboli blocking small pulmonary arteries. Many tumours can embolise in this fashion, particularly hepatoma, carcinoma of the breast, kidney, stomach and prostate, and choriocarcinoma.

High-Resolution Computed

Tomography of

Interstitial and Occupational Lung Disease

The pulmonary interstitium consists of the connective tissue fibres that

support the lung. It includes the intralobular interstitium beneath the

alveolar epithelium, the interlobular septa and the peribronchovascular

interstitium. The term interstitial lung disease (ILD) is used to refer to

a group of disorders that mainly affects these supporting structures.

The *predominant* abnormality is usually thickening of the interstitium,

which may be due to the accumulation of fluid, cells, or fibrous tissue.

Air spaces are also often involved in ILDs due to the tight reliance of

the alveolar epithelium in the interstitial network.

The chest radiograph remains part of the initial assessment of ILD,

but the radiographic pattern is often non-specific, observer variation

is considerable, and it has low sensitivity for the detection

of early ILD.

High-resolution computed tomography (HRCT) has revolutionised the

imaging of ILD, as it enables early detection of disease, allows a histospecific

diagnosis to be made in certain cases, and provides insights

into disease reversibility and prognosis.

HIGH-RESOLUTION COMPUTED TOMOGRAPHY

PATTERNS OF DIFFUSE LUNG DISEASE

Before considering the individual HRCT patterns related to each ILD, an understanding of normal lung anatomy is needed.

In addition, radiologists should refer to a common terminology outlined in the Fleischner Glossary to describe HRCT abnormalities.

Diffuse abnormalities of the lung on HRCT may be broadly classified into one of the following main four patterns: (**A**) reticular;

(B) nodular; (

C) mosaic

attenuation pattern; and

(**D**) cystic pattern. It is common to see overlap between the established HRCT patterns.

Reticular Pattern

A reticular pattern on computed tomography (CT) almost always represents significant ILD.

Morphologically, a reticular pattern may be caused by thickened intralobular or interlobular septa or honeycomb

(fibrotic) destruction.

Although intralobular and interlobular septal thickening often coexist, there is a morphological distinction: intralobular thickening is mostly below the spatial resolution of HRCT, thus appearing as faint ground-glass opacification rather than distinct fine reticulation.

Intralobular septal thickening is seen in all ILDs, but it is most common in fibrosing lung disorders.

Numerous thickened interlobular septa indicate an extensive interstitial abnormality; causes include infiltration by fluid (e.g. pulmonary oedema) and/or abnormal cells (e.g. lymphangitis carcinomatosa).

Although thickened interlobular septa can be a consequence of infiltration by fibrosis, this feature is not a frequent finding in fibrosing lung disorders (e.g. idiopathic pulmonary fibrosis [IPF]).

Interlobular septal thickening is usually described as smooth (seen in pulmonary oedema and alveolar proteinosis) or irregular/beaded (e.g. lymphangitic spread of tumour, and seldom sarcoidosis), but the distinction is not always easily made.

In some diseases, a perilobular distribution may give the

spurious impression of thickening of the interlobular septa.

However, such a pattern reflects a pathological process that is 'smeared' around the internal lobular surface and is most frequently associated with organising pneumonia.

Severe pulmonary fibrosis usually results in a coarse reticular pattern made up of interlacing irregular linear opacities.

The reticular pattern of end-stage fibrotic lung is characterised by cystic air spaces surrounded by irregular walls, also known as honeycombing.

The certain identification of honeycombing, as opposed to other forms of reticulation, is not always straightforward but is of particular relevance, as it may influence patient care.

Honeycomb is a distinctive feature for the radiological

definition of usual interstitial pneumonitis (UIP). The extensive fibrosis accompanying honeycomb is oftentimes associated with distortion of normal lung morphology, resulting in irregular dilatation of segmental and subsegmental airways (traction bronchiectasis/bronchiolectasis);

in the periphery of the lung, it can be difficult to distinguish dilated

airways from true honeycomb destruction.

Nodular Pattern

A nodular pattern is a feature of both interstitial and

airspace diseases.

The distribution and density of nodules may help refine what can be a lengthy differential diagnosis. Nodules within the lung interstitium, especially those related to the lymphatic vessels, are seen in the interlobular septa and in the subpleural and peribronchovascular regions; this distribution is seen most frequently in sarcoidosis but also in lymphangitis carcinomatosa.

Centrilobular nodules are seen in several acute or chronic conditions affecting terminal bronchioles, including

infection, hypersensitivity, or cigarette smoke.

The distinction between subacute hypersensitivity pneumonitis (HP) and respiratory bronchiolitis–interstitial lung disease (RB–ILD) can be difficult, because both cause relatively low-density, poorly defined centrilobular nodules which may look identical on HRCT.

A random distribution of very small well-defined nodules is seen in patients with haematogenous spread of tuberculosis, pulmonary metastases, pneumoconiosis and,

rarely, sarcoidosis.

Mosaic Attenuation Pattern

The term 'mosaic attenuation pattern', or more simply mosaic pattern, refers to regional attenuation differences demonstrated on HRCT with well-defined borders corresponding to interlobular septa. The attenuation

of a given area of lung depends on the amount of blood, parenchymal tissue, and air in that area, and thus the sign

of a mosaic attenuation pattern is non-specific. It is the dominant abnormality in three completely different types of diffuse pulmonary disease: small airways disease,

chronic occlusive vascular disease and infiltrative lung disease.

In the first two processes, the decreased attenuation ('black') lung is abnormal; in infiltrative lung disease it is the 'grey' lung with increased attenuation that is abnormal.

In patients in whom a mosaic attenuation pattern is

the dominant abnormality, small airways disease and infiltrative lung disease are usually correctly identified but the mosaic attenuation pattern caused by occlusive vascular disease can be misinterpreted.

Bronchial abnormalities and, to a lesser extent, the presence of air trapping on expiratory CT are the most useful discriminatory features in identifying small airways disease as the cause of mosaic attenuation.

In chronic thromboembolic disease the mosaic pattern is caused by regional perfusion inhomogeneity.

The phenomenon of hypoxic bronchodilatation causes vasoconstriction in the hypoperfused areas. Normally, expiratory CT scans help to exclude air trapping as the underlying cause.

In addition, signs of pulmonary hypertension (enlarged pulmonary trunk and pathological arterio-bronchial ratio) point towards chronic thromboembolic pulmonary hypertension (CTEPH). However, in a subset of patients, coexistence of air trapping and vasoconstriction may be seen and can complicate interpretation.

Infiltrative lung disease manifesting as ground-glass opacification is the most frequent cause of the mosaic attenuation pattern.

Borders between regional attenuation differences may be less well defined in infiltrative lung disease. Typically, no vascular calibre differences are present.

A ground-glass pattern on HRCT is defined as a generalized increase in opacity that does not obscure pulmonary vessels and bronchial walls.

At a microscopic level, the changes responsible for ground-glass opacity are complex and include partial filling of the air spaces, considerable thickening of the interstitium, or a combination of the two.

Ultimately, though, the pattern of ground-glass opacity on HRCT results from subtotal displacement of air from the lungs.

Indeed, ground-glass opacity may be found in many conditions, either as the predominant pattern or as an ancillary one.

A predominant ground-glass pattern may be seen in subacute HP, acute respiratory distress syndrome (ARDS), pulmonary oedema, acute interstitial pneumonia (AIP), non-specific interstitial pneumonia (NSIP), and some infections, notably viral pneumonias and *Pneumocystis jiroveci*.

Cystic Pattern

A cyst appears as a round parenchymal area of low attenuation with well-defined interface against the normal lung.

The cyst wall is usually thin (<2 mm); epithelial or fibrous wall of variable thickness are found at pathology. Cystic abnormalities are depicted both by radiography

and HRCT, the latter being significantly more sensitive. They usually occur independent from pulmonary emphysema, which is one among several differential diagnoses.

On **HRCT**, bronchiectasis is a pitfall for overcalling cysts; volumetric acquisition with multiplanar reformation clearly differentiate bronchiectasis from cysts.

Cysts in the lung usually contain air but occasionally can be filled by fluid or solid material.

A cavitated lesion might resemble a simple cyst, but an exceedingly thick wall should suggest a differential diagnosis (metastasis, septic emboli, pneumatocele after *Staphylococcus aureus* pneumonia, etc.).

Lymphangioleiomyomatosis (LAM) and Langerhans cell histiocytosis (LCH) are the classical diseases with a cystic pattern.

Nevertheless cysts are seen also in *Pneumocystis jiroveci* pneumonia (PJP), lymphoid interstitial pneumonia (LIP), Birth–Hogg–Dubé syndrome, HP and even in the

normal ageing lung.

IDIOPATHIC INTERSTITIAL PNEUMONIAS

The term idiopathic interstitial pneumonia (IIP) is applied to a group of disorders with no known cause, and with more or less distinct histological and radiological appearances.

The term 'pneumonia' should not mislead the physician towards infectious origin of such pulmonary diseases, which otherwise are sustained by idiopathic pulmonary damage with allegedly self-maintaining chronic course. In the 2013 American Thoracic Society (ATS)/European Respiratory Society (ERS) consensus classification of the IIPs, the overall architecture of the classification is preserved but the clinical entity, rather than the histopathological label, is given pre-eminence.

In addition, an entity termed idiopathic pleuroparenchymal fibroelastosis (IPPFE) is included. The authors of the updated classification again stress the importance of a multidisciplinary and dynamic approach to the diagnosis of the IIPs which requires interaction among clinicians, radiologists and pathologists.

Usual Interstitial Pneumonia/Idiopathic

Pulmonary Fibrosis

The term idiopathic pulmonary fibrosis is applied to patients with a histological and/or CT pattern of usual interstitial pneumonia (UIP) and compatible clinical and imaging features.

However, the UIP pattern may be also secondary to other conditions such as chronic HP, asbestosis, connective

tissue disease (CTD; especially rheumatoid arthritis [RA]), and rarely, drugs.

Thus the interpretation of the UIP pattern requires

a multidisciplinary discussion with clinicians and, sometimes, pathologists in order to obtain the final diagnosis.

The pathological features of UIP are the presence of fibroblastic foci, normal areas, dense fibrosis and honeycombing; another crucial finding is areas of fibrosis at different stages of maturity, the so-called temporal

heterogeneity.

The temporal heterogeneity of UIP–IPF is macroscopically depicted by CT, whilst it can be a source of low accuracy at pathology.

This makes CT a pivotal player for planning pulmonary sampling. After exclusion of an underlying (systemic) disease, HRCT plays a central diagnostic role for the diagnosis of UIP in the context of IPF.

Guidelines, most recently updated in 2018, have defined various levels of radiological confidence.

The 'typical UIP' pattern on HRCT is characteristic and virtually pathognomonic; it appears as a predominantly subpleural bibasal reticular pattern within which there are areas of honeycomb destruction.

As the disease progresses, it often appears to 'creep' around the periphery of the lung to involve the anterior aspects of the upper lobes (also known as 'propeller blade distribution').

The presence of ground-glass opacification is not a dominant feature and, when present, there is usually obvious traction bronchiectasis and bronchiolectasis that indicate fibrotic irreversible substrate.

A 'probable UIP' pattern on HRCT is characterised by predominantly subpleural bibasal reticular pattern with peripheral traction bronchiectasis or bronchiolectasis, without honeycombing. The 'probable UIP' pattern on HRCT reflects pathological probable or definite UIP

pattern in 82%–94% of cases.

The estimate of the clinical probability of IPF (e.g. age above 60 years, smoking history and no history of other

potential causes of fibrosis) must be integrated to assess the likelihood of UIP in these patients.

As opposed to the two aforementioned patterns associated with IPF, the 2018 white paper from the Fleischner Society and the most recent ATS/ERS/JRS/ALAT Clinical Practice Guideline 2018 define two other of an alternative diagnosis: namely, the 'CT pattern indeterminate for UIP' and the CT features most consistent with an 'alternative diagnosis'.

In an indeterminate pattern for UIP, no features 'inconsistent with UIP' are seen; however, distribution of fibrosis may be very heterogeneous or asymmetric and various amounts of ground glass can be seen.

Features inconsistent with UIP/IPF include nodules,

cysts, consolidations, air and a bronchocentric distribution.

In patients whose HRCT does not demonstrate either a typical or a probable UIP pattern, a surgical lung biopsy may still demonstrate UIP pattern onHRCT patterns that demand pathological confirmation or consideration histopathology. Most recent ATS/ERS/JRS/ALAT guidelines suggest the option for biopsy for all subclasses except for the 'typical UIP', though the recommendation is not strong and leaves room for individual decision.

Mediastinal lymphadenopathy (up to approximately 2.5 cm in diameter), unrelated to infection or malignancy, is a frequent finding in UIP–IPF.

The rapid development of a diffuse increase in the attenuation of lung parenchyma in patients with IPF should suggest the possibility of an accelerated phase (also known as acute exacerbation) of the disease, concurrent pulmonary oedema, or an atypical infection. Other complications include lung cancer and pulmonary tuberculosis; the latter usually has atypical appearances on CT caused by the presence of underlying lung fibrosis.

Classical HRCT Findings

- Subpleural basal honeycombing
- Ground-glass opacity not predominant
- Subpleural disease in the upper lobes (if present) tends to be anterior
- Traction bronchiectasis and bronchiolectasis

Non-Specific Interstitial Pneumonia

NSIP is characterised by varying degrees of interstitial inflammation and fibrosis without the specific features that allow a diagnosis of UIP.

While NSIP may have significant fibrosis, it is usually temporally uniform (in comparison with UIP), and fibroblastic foci and honeycombing are absent or scanty. Although the clinical features of idiopathic NSIP resemble those of UIP, prognosis is considerably better. Non-idiopathic NSIP is most often found on lung biopsy in patients with CTD and may be the predominant histopathological pattern in some cases of drug-induced lung disease and chronic HP.

On **HRCT**, ground glass with or without associated distortion of airways is usually the dominant pattern. Reticular abnormalities are common, but honeycombing

is sparse or absent even when other signs of fibrotic changes are evident.

Abnormalities are usually peribronchovascular or peripheral, although they may sometimes spare the subpleural lung.

In general, NSIP may be distinguished from UIP on CT by a more prominent component of ground-glass attenuation and a finer reticular pattern in the absence of honeycombing.

However, the variability of CT appearances reflects the heterogeneity of the pathological processes encompassed

by NSIP and a confident diagnosis of NSIP based on CT

alone is less readily made than in cases of UIP. Consolidation is reportedly a highly variable feature (0%–98%) and this discrepancy probably reflects the

fact that some patients with non-idiopathic NSIP have significant amounts of histological organising pneumonia, making classification of individual cases difficult.

Classical HRCT Findings

• Bilateral ground-glass opacities and superimposed fine reticulation

- Predominantly peripheral, but also patchy or band-like
- Honeycomb pattern minimal or absent
- Traction bronchiectasis and bronchiolectasis

Cryptogenic Organising Pneumonia

This is considered in the section on airspace disease.

Respiratory Bronchiolitis–Interstitial Lung Disease and

Desquamative Interstitial Pneumonia

These two entities are considered together because of their strong association with cigarette smoking. All cigarette smokers have, to some degree, inflammation around their small airways ('respiratory bronchiolitis'),

but this is clinically unimportant and not considered further here.

Patients with RB–ILD generally present with an insidious onset of dyspnoea and cough.

Chest radiography is relatively insensitive for

the detection of RB–ILD and desquamative interstitial pneumonia (DIP) and a normal chest x-ray (CXR) has been reported in up to 20% of patients with RB–ILD and 25% in DIP.

On HRCT, the features of RB–ILD include areas of patchy groundglass opacification (resulting from macrophage accumulation within alveolar spaces and alveolar ducts) and poorly defined low-attenuation

centrilobular nodules.

In addition, upper lobe centrilobular emphysema, usually of very limited extent, and areas of air trapping may be present, the latter reflecting the bronchiolitic element of this entity.

In RB-ILD, scattered thickening of the interlobular septa and features of interstitial fibrosis can be seen, but this is not the dominant pattern.

Ground-glass opacification is the dominant feature seen in DIP. The distribution is typically lower zone, peripheral, and may be patchy or geographic.

In some patients there are HRCT features of established fibrosis (in the form of architectural distortion with

dilatation of some bronchi), usually of limited extent. Most patients with DIP or RB–ILD have a relatively stable clinical course and the two entities variably coexist.

Smoking cessation is remarkable in the management of
patients, but the influence of smoking on the clinical course of these patients has not been fully delineated; some patients have persistent abnormalities on HRCT even with smoking cessation and corticosteroid therapy. Because of the significant overlap between the clinical, imaging and histological features of DIP and RB–ILD and to a lesser extent between these two patterns and LCH and interstitial fibrosis, the global term 'smokingrelated interstitial lung disease' (SR-ILD) has been proposed to encompass DIP, RB–ILD, LCH and interstitial fibrosis.

Classical HRCT Findings

• Inconspicuous poorly defined centrilobular nodules of ground-glass

opacification in symptomatic smokers are suggestive of RB–ILD

• Non-specific extensive ground-glass opacities, usually lower zone, with or without associated mild reticulation, are typical features of DIP

Acute Interstitial Pneumonia/Diffuse Alveolar Damage

AIP can be regarded as an idiopathic form of ARDS and is histologically (and clinically) distinct from the other interstitial pneumonias.

The histological pattern seen in AIP is that of diffuse alveolar damage (DAD), which is also found in infection, CTD, drug toxicity and toxic fume inhalation. DAD has an acute exudative phase and a subsequent organising and fibrotic phase.

Lung biopsy shows diffuse involvement with temporal homogeneity, which implies lung injury due to a single

event. The chest radiograph shows bilateral patchy airspace opacification.

HRCT demonstrates a combination of ground-glass opacification, consolidation, bronchial dilatation and architectural distortion. Ground-glass opacification on HRCT is found in all three phases of AIP, but coexistent traction bronchiectasis probably reflects the early

incorporation of established fibrosis. Follow-up CT shows reticular opacities consistent with residual fibrosis. Anterior non-dependent fibrotic damage in survivors secondary to barotrauma has also been reported.

Classical HRCT Findings

• Patchy or diffuse ground-glass opacities and consolidation/collapse (the latter mainly in dependent lung)

• Traction bronchiectasis and reticulation may become evident after several days

Lymphoid Interstitial Pneumonia

The term 'lymphoid interstitial pneumonia' was proposed by Liebow and Carrington to describe a disease entity characterised by a widespread interstitial lymphoid infiltrate of the lung, resembling lymphoma but with a clinical course more akin to a chronic interstitial pneumonia. Although in the past LIP has been considered by some to be a pulmonary lymphoproliferative disorder, evolution to frank lymphoproliferative disease is rare and thus LIP remains within the group of interstitial pneumonias. Classically, LIP occurs in association with autoimmune

diseases, most often Sjögren syndrome (SjS).

Other diseases associated with LIP include dysproteinaemias, autologous bone marrow transplantation and viral, mycobacterial and human immunodeficiency virus (HIV) infections.

LIP is approximately twice as frequent in women and symptoms of progressive cough and dyspnoea usually predominate.

Common HRCT findings are nodules of varying sizes (which may be ill-defined), areas of ground-glass opacification, thickened bronchovascular bundles, interlobular septal thickening and thin-walled cysts

(1 to 30 mm).

Airspace disease, large nodules, and pleural effusions are rare in these patients.

The cysts in LIP are usually discrete, sometimes clustered and tend not to be subpleural.

Classical HRCT Findings

• Patchy ground-glass opacities, indistinct nodules and thin-walled cysts.

Idiopathic Pleuroparenchymal Fibroelastosis

Little is known regarding aetiology of IPPFE, but

recurrent infections are a feature in some patients and a few cases have been reported in association with previous bone marrow or lung transplantation. IPPFE is characterised by dense established intra-alveolar fibrosis containing prominent elastosis, and dense fibrous thickening of the visceral pleura; these changes have a striking upper zone predominance.

Such apical caps tend to continue leaning against the posterior visceral pleura.

HRCT appearances consist of irregular pleural thickening and 'tags' in the upper zones that merge with fibrotic changes in the subjacent lung.

In 2012, Reddy et al. suggested radiological criteria

for 'definite' (pleural thickening, almost exclusively confined to the upper lobes), 'consistent with' (not necessarily requiring upper lobe predominance) and 'inconsistent with' (none of the above features).

Such classification was intended for integration with histopathology.

Unfortunately, surgical biopsy is rarely granted because persistent postsurgical pneumothorax is a common complication.

Restrictive functional impairment is seen in IPPFE as a fibrotic ILD per se; moreover, other ILD patterns might associate: UIP pattern was reported in about 5% to 10% of cases.

Classical HRCT Findings

• Bilateral upper lobe irregular pleural thickening with posterior continuity and subjacent reticular pattern.

SARCOIDOSIS

Sarcoidosis is a multisystem granulomatous disorder of unknown aetiology.

As a consequence, the diagnosis of this syndrome is defined by the presence of characteristic clinical and radiological data along with histological evidence of noncaseating granuloma.

Granulomas in the lung have a characteristic distribution along the lymphatics in the bronchovascular sheath and, to a lesser extent, in the interlobular septa and subpleural lung regions.

Sarcoidosis is a disease of young adults, with a peak incidence in the second to fourth decades.

The hilar and mediastinal nodes and the lungs are affected clinically much more commonly than any other organ or system.

They are followed in decreasing order of frequency by the skin (26%), peripheral lymph nodes (22%), eyes (15%), spleen (6%), central nervous system (4%), parotid glands (4%) and bones (3%).

Pulmonary involvement accounts for most of the morbidity and mortality associated with sarcoidosis. Chest radiography was traditionally used for sarcoidosis staging according to the modified Scadding method:

stage I, lymphadenopathy; stage II, lymphadenopathy

with parenchymal opacity; stage III, parenchymal opacity alone; stage IV, pulmonary fibrosis.

Low stages at presentation are reported to have a better prognosis than high stages, although the precision and clinical usefulness of such 'staging' is questionable.

Lymphadenopathy

Sarcoidosis is characterised by bilateral, symmetrical hilar and paratracheal lymphadenopathy.

Some degree of lymphadenopathy is evident on chest radiography in about 70%–80% of patients at some time

during the course of the condition. Hilar lymph node enlargement ranges from the barely detectable to the massive and gives the hila a dense lobulated and usually well-demarcated outline.

Occasionally hilar lymphadenopathy appears to be asymmetrical or, in 1%–5% of cases, may even be strictly unilateral although this is distinctly unusual.

Paratracheal lymphadenopathy may be bilateral or unilateral and in the latter instance is usually right-sided. The most common manifestation of left-sided lymphadenopathy is enlargement of the aortopulmonary

window nodes—a common and characteristic feature on the chest radiograph.

Other mediastinal nodes (anterior prevascular, posterior

and subcarinal) are often not identified as being enlarged on the chest radiography but on CT are seen to be affected in about half of patients. In 90% of patients with lymphadenopathy, nodal enlargement is maximal on the first radiograph and usually disappears within 6–12 months.

Recurrence of lymphadenopathy is exceedingly rare.

The affected lymph nodes may calcify, sometimes in a characteristic eggshell fashion.

This latter feature is shared by only a few conditions,

such as silicosis and histoplasmosis. The calcification is of variable intensity and may even be relatively light with homogeneous representation over the whole lymph node, into the so-called 'icing sugar' pattern.

Such a pattern of calcification is common in relatively small lymph nodes with even distribution throughout the mediastinum and hila (very different from calcified nodes due to tuberculous infection, which usually follow a drainage path).

About 40% of patients presenting with nodal enlargement will develop parenchymal opacities, usually within a year, and of these about one-third will go on to have persistent (fibrotic) changes.

Usually, nodal enlargement does not develop after parenchymal opacities have appeared.

Parenchymal Changes

Parenchymal changes probably occur histologically in most patients but are only detected on the chest radiograph in 50%–70% of cases.

Characteristically, parenchymal abnormalities appear as

the nodal enlargement is subsiding (in lymphoma such abnormalities tend to progress in unison).

Rounded or irregular nodules 2–4 mm in diameter and with sharp edges are the most common radiographic pattern, seen in 75%–90% of patients with parenchymal opacities.

Smaller or larger opacities are not uncommon, though they rarely exceed 5 mm.

All zones can be affected but there is usually a mid and upper zonal predominance.

Patchy airspace consolidation is the second most common

pattern, seen in 10%–20% of patients with parenchymal opacity.

Opacities sometimes contain air bronchograms and have ill-defined margins that commonly break up into a nodular pattern.

Nodules tend to involve predominantly the peribronchovascular regions of the middle and upper

lung zones, although they may be diffuse or, occasionally, have a subpleural predominance.

The parenchymal opacities described above will clear completely in about two-thirds of cases and progress to fibrosis in one-third.

Permanent fibrotic shadowing is unusually coarse, with a mid and upper zone predominance.

The radiographic pattern consists of coarse linear opacities with evidence of volume loss mainly of the

upper lobe with displacement of the hila and ring shadowing caused by bullae or traction bronchiectasis.

Occasionally a conglomerate opacity develops, resembling progressive massive fibrosis (PMF).

Pulmonary hypertension, bullous disease with or without mycetoma formation, and pneumothorax are all recognised complications of this fibrotic stage.

High-Resolution Computed Tomography Features

Despite the better delineation of parenchymal disease on HRCT, it is not recommended as part of the initial diagnostic work-up in patients with suspected sarcoidosis; its greatest use is in patients who present with an atypical chest radiograph.

Parenchymal opacities are well demonstrated on HRCT, with remarkable sensitivity and specificity for the diagnosis of sarcoidosis.

The most consistent pulmonary parenchymal abnormality is the presence of nodular opacities (1-5 mm) distributed in a perilymphatic fashion, predominantly along the

bronchovascular bundles, pleura (including fissures) and, to a lesser extent, interlobular septa. Other findings include irregular and beaded interfaces, larger ill-defined nodules with/without an air bronchogram, patchy groundglass opacities and occasional interlobular septal thickening.

In advanced disease there is evidence of fibrosis, predominantly in the perihilar regions of the middle and upper lung zones. Air trapping is a common HRCT feature of sarcoidosis and its presence shows a good correlation with indices of small airways disease on pulmonary function tests. Less common parenchymal changes seen in sarcoidosis evolve if the small nodules are confluent to form larger nodules (nodular sarcoidosis, galaxy sign) or if the nodules are so small, being below the resolution of the HRCT, that they appear as areas of ground glass (alveolar sarcoidosis).

Areas of parenchymal consolidation and ground-glass opacity are usually reversible, whereas resolution is not expected in patients showing reticulation and architectural distortion.

Classical fibrotic changes include linear opacities (radiating laterally from the hilum), fissural displacement

(volume loss in upper lobes), bronchovascular distortion (bronchiectasis) and honeycombing concentrated in the upper zones.

Despite this distinction between reversible and irreversible disease on HRCT, studies comparing HRCT assessment of disease activity to clinical, scintigraphic and bronchoscopic findings have yielded contradictory results.

Hence, HRCT is not generally used to guide prognosis in patients with sarcoidosis.

18-Fluorodeoxyglucose Positron Emission Tomography can be used to accurately assess inflammatory activity for example, in patients with persistent disabling symptoms without serological inflammatory activity. PET has also been described as helpful in predicting pulmonary deterioration at 1 year and to monitor therapy response.

Inhibition of the physiological myocardial FDG uptake for example by appropriate diets—enables the detection of cardiac sarcoidosis active lesions.

Recently an integrated clinico-radiological staging system has been proposed to identify patients with poor prognosis and at risk for mortality (50% in 5.5 years): while initial separation between the two prognostic groups was done by applying a weighted combination of lung function parameters, further separation was yielded if extent of fibrosis on CT exceeded 20% and/or an abnormal diameter ratio of the main pulmonary and ascending aorta (>1) was seen, indicating pulmonary

hypertension.

Classical HRCT Findings

• Well-defined, smooth or irregular nodules, measuring 2–4 mm, in a perilymphatic distribution (i.e. mainly along interlobar fissures, peribronchovascular interstitium and interlobular septa), most extensive in the upper lobes.

• Nodules may be grouped in clusters or coalesce to larger nodules.

• Bilateral hilar and mediastinal enlarged lymph nodes.

• Fibrosis may occur and typically involves the upper lobes.

HYPERSENSITIVITY PNEUMONITIS

HP, also called extrinsic allergic alveolitis (EAA), is an immunologically mediated lung disease characterised by an inflammatory reaction to specific antigens contained in a variety of organic dusts.

Common causes include avian proteins (e.g. bird breeder's lung) and thermophilic bacteria present in mouldy hay (farmer's lung), mouldy grain (grain handler's lung), or heated water reservoirs (humidifier or air conditioner lung).

These antigens reach the alveoli where they provoke an immunological reaction that includes both type III (immune complex response) and type IV (cell-mediated) mechanisms.

The cell-mediated response results in a delayed hypersensitivity reaction and the presence of granulomatous inflammation within the pulmonary interstitium.

The clinical features of HP are characteristic. Approximately 6 hours after exposure the patient develops fever, chills, dyspnoea and cough.

There is no eosinophilia, and wheeze is not a prominent feature.

The radiological findings are influenced by the stage of the disease.

Typical HRCT findings of subacute phase include centrilobular nodules 5 mm in diameter, which are typically poorly defined, and mostly spread throughout the lung (mid to lower lung zone predominance has been variably reported).

Ground-glass opacity is most common in the acute phase but may also be a feature of subacute and chronic

HP, especially if there is ongoing exposure. A mosaic attenuation pattern is common in HP; the presence of lobular areas of decreased vascularity that show air trapping on expiratory HRCT reflect the coexisting

bronchiolitis caused by antigen deposition in the small airways.

The combination on HRCT of features of infiltrative (illdefined nodules and ground-glass opacity) and small airways disease may be remarkably similar to that seen in patients with RB–ILD; however, the distinction can usually be made with knowledge of the smoking history. The presence of thin-walled lung cysts is also an occasional feature in subacute HP. Cysts range in size from 3 to 25 mm and resemble those seen in LIP, although their pathogenesis remains uncertain.

Emphysema is a reported sequel of farmer's lung and a study has demonstrated that in hypersensitivity caused by farmer's lung, emphysema was a more prominent feature than honeycombing/fibrosis (even in never-smokers) and was seen in approximately one-third of patients.

This is in comparison to bird breeder's disease, where lung fibrosis is the major complication.

The chronic stage of HP is characterised by fibrosis, although evidence of active disease is often present. HRCT findings include intralobular and interlobular interstitial thickening, traction bronchiectasis and honeycomb destruction.

In some cases, there is a mid-zone predominance, but the fibrotic appearance may be seen in the upper or lower lobes.

Nonetheless, the radiological differential with UIP is sometimes impossible.

Indeed, patients with HP may exhibit histological and imaging features of NSIP or UIP.

Imaging features that favour HP over IPF include an upper- or mid-zone predominance, the presence of abundant ground-glass opacity, centrilobular nodules, a bronchocentric distribution of fibrotic changes and air

trapping.

In late 2018, a radiological diagnosis model was proposed by Salisbury which included mosaic attenuation and air trapping as predominant features over reticulation, along with diffuse axial distribution of the disease.

Such a model was designed and validated with a 90%

specificity for diagnosis of HP, yet the authors declared decreased positive predictive value in a low-prevalence setting.

Classical HRCT Findings

• In the subacute phase, poorly defined centrilobular nodules,

background ground-glass opacification and lobular areas of air trapping.

• Chronic HP results in a pattern of fibrosis which may resemble NSIP or UIP; ancillary findings such as coexisting areas of mosaic attenuation and air trapping suggest the diagnosis of chronic HP.

• Axial distribution and upper-lobe predominant disease and not subpleural but bronchocentric distribution of fibrosis.

LANGERHANS CELL HISTIOCYTOSIS

LCH is a granulomatous disorder characterised histologically by the presence of large histiocytes containing rod- or racket-shaped organelles (Langerhans cells).

The male-to-female ratio is about 4 : 1, and there is strong association with cigarette smoke. In the early stages, patients are often asymptomatic.

Otherwise, symptoms include dyspnoea, cough, constitutional symptoms or a spontaneous pneumothorax (from complication of cystic abnormalities).

Parenchymal findings are bilateral and mostly symmetrical. In adults, pulmonary involvement is predominantly located in upper lungs with pathognomonic sparing of lower zones.

At symptomatic presentation, usually because of dyspnoea or a pneumothorax, the chest radiograph is abnormal.

On chest radiograph, reticulonodular shadowing is commonly depicted in the mid and upper zones of the lungs.

The nodules vary in size from micronodular to

approximately 1 cm in diameter and, although histopathological examination will often demonstrate cavitation, this feature is often difficult to appreciate on chest radiography.

The classical pattern of LCH on HRCT includes nodules (ranging in size from a few millimetres to 2 cm, but mostly small, in the mm range) of both subsolid and solid density with natural evolution towards cavitation (this feature often clinches the diagnosis), finally becoming

cysts, often with bizarre shapes (Fig. 9.16). Different types of nodules and cysts can coexist at the same time, representing the expression of different evolution phases likely in continuously active disease within a chronic setting.

Reticular opacities may be also seen in the background

of the cystic abnormalities in the late stage, thus representing signs of supervening pulmonary fibrosis.

Classical HRCT Findings

• Progression from ill-defined nodules (which cavitate) to a combination of cysts and nodules.

• The typical distribution of parenchymal abnormalities spares the

costophrenic recesses even in advanced disease; however, exception

to this is seen in paediatric onset.

LYMPHANGIOLEIOMYOMATOSIS

LAM shows two histological key features: cysts and proliferation of atypical smooth muscle cells (LAM cells) of the pulmonary interstitium, particularly in the bronchioles, pulmonary vessels and lymphatics.

Thoracic and extra-thoracic findings reflect the anatomical consequence of the variable systemic proliferation of LAM cells.

LAM can occur with or without evidence of other disease, such as tuberous sclerosis complex.

LAM is a rare disease seen almost exclusively in women, the vast majority of cases being diagnosed during childbearing age.

However, there are case reports of women developing LAM after menopause, including women in their eighth decade.

The most commonly described radiographic manifestation of LAM is a pattern of generalised, symmetrical, reticular or reticulonodular opacities with normal or increased lung volumes. Pleural effusions

(chylous) occur in 10%–40% of patients (these may be unilateral or bilateral) and pneumothoraces in approximately 50% of cases (as a complication of pulmonary cysts).

The main HRCT sign of LAM is represented by numerous thin-walled cysts randomly distributed

throughout the entire lungs with no zonal predilection.

Imaging features that help distinguish LAM from LCH include a more diffuse distribution of cysts, typically with no sparing of the bases, more regularly shaped spherical cysts and normal intervening lung parenchyma. Thus there are no associated signs of fibrosis in LAM.

Occasionally HRCT may demonstrate interlobular septal thickening (attributed to dilatation of lymphatic channels secondary to obstruction of pleuropulmonary lymphatics and/or septal veins) or patchy areas of ground-glass attenuation (presumably the result of pulmonary haemorrhage).

Classical HRCT Findings

• Diffuse thin-walled cysts throughout the lungs with no zonal predominance

CONNECTIVE TISSUE DISEASES

The CTDs form a heterogeneous group of chronic inflammatory and immunologically mediated disorders, all of which affect the lung and pleura to a variable extent. Although the lung is a particularly vulnerable target organ, the frequency of pleuropulmonary involvement varies widely within the spectrum of disease and also in each disease separately, depending upon whether imaging, physiological or histological criteria are used to judge involvement.

Although the radiographic and HRCT appearances are not specific for any of the CTDs, they frequently provide

good corroborative evidence in substantiating what is often a difficult clinical diagnosis.

Pulmonary abnormalities can either precede or follow the diagnosis of a specific CTD. Patients with CTD-associated ILD (CTD–ILD) are thought to have a more favourable clinical course when compared with those with IPF.

Several patients with ILD do not meet CTD diagnostic

criteria even though they show some clinical or serological features suggestive of a CTD. The ERS and the American Thoracic Society termed this category of ILDs as interstitial pneumonia with autoimmune features

(IPAF) and indicated a number of clinical, serologic and morphologic domains for its definition.

Subjects with IPAF oftentimes evolve towards a mature form of CTD. Therefore, IPAF raised a number of questions, and it is still an 'interim' category that is continuously refined using the evolving scientific evidence.

Rheumatoid Disease

RA is associated with a broad spectrum of pleural and pulmonary abnormalities. In a significant minority of patients with RA, pleuropulmonary disease antedates the development of arthritis and, in general, pleuropulmonary involvement is not related to the severity of the

arthritis.

The most frequently encountered manifestations of rheumatoid disease in the chest are listed in Table 9.5. Pleural involvement, either manifesting as effusion or thickening, is common.

Pleural effusions can be unilateral or bilateral, are usually small or moderate in size, and the majority resolve spontaneously.

ILD in RA is more common in men, particularly cigarette smokers with seropositive disease.

The most common histopathological patterns in RAassociated ILD are UIP followed by NSIP with HRCT features that are indistinguishable from idiopathic cases. UIP is more prevalent than in the other CTD. Although data are still controversial, it is thought that the prognosis for RA–ILD is better than for idiopathic cases.

Other pulmonary abnormalities seen in RA include follicular bronchiolitis, bronchiectasis (in up to 30% of cases), obliterative bronchiolitis (this can occur in patients who are on penicillamine, gold, or no treatment) and organising pneumonia. Obliterative bronchiolitis

(causing extensive air trapping on HRCT) can cause considerable respiratory functional impairment requiring lung transplantation.

Acute exacerbations (representing histologically with findings of DAD, radiologically of ARDS) may also occur in RA, and discrimination from other conditions (e.g. opportunistic infections, pulmonary oedema)

may be problematic.

Rheumatoid (necrobiotic) pulmonary nodules are an uncommon feature of the disease.

They are usually associated with the presence of subcutaneous nodules and, like them, may wax and wane.

They may be single or multiple, may vary in size from a few millimetres to several centimetres, are well circumscribed and may cavitate; if they are subpleural they may cause a pneumothorax.

They show increased FDG uptake on PET, which should not be misinterpreted as metastatic disease.

They are usually asymptomatic and may occur in association with pulmonary fibrosis and pleural changes.

Follicular bronchiolitis (discussed here because of its frequent association with rheumatoid disease) is part of the spectrum of lymphoproliferative disease and is characterised histologically by a diffuse peribronchiolar proliferation of hyperplastic lymphoid follicles and mild, if any, alveolar interstitial inflammation. Clinically, the patients usually present during young adulthood or middle age with insidious dyspnoea.

Most cases of follicular bronchiolitis are associated with

CTD, especially RA and SjS, but it is also seen in association with immunodeficiency syndromes including AIDS, pulmonary infections or ill-defined

hypersensitivity reactions. On HRCT, follicular bronchiolitis mostly shows centrilobular nodules measuring 1–12 mm in diameter, variably associated with peribronchial nodules and patchy areas of ground-glass

opacity. Nodules and ground-glass opacities are generally bilateral and diffuse in distribution.

Mild bronchial dilatation with wall thickening and a treein-bud pattern are less frequent findings.

Classical HRCT Findings

- Pleural effusions are common
- UIP is more frequent than NSIP

• Other findings include necrobiotic nodules, organising pneumonia, bronchiectasis and evidence of small airways disease

Sjögren Syndrome

SjS is a chronic autoimmune inflammatory disease characterised by a triad of clinical features: dry mouth (xerostomia), dry eyes (keratoconjunctivitis sicca) and arthritis. SjS can occur alone as primary SjS or in

association with other autoimmune diseases—as secondary SjS.

One study evaluating the radiological and pathological manifestations of lung diseases associated with primary SjS found that NSIP was the most common entity; other features included bronchiolitis, lymphoma, amyloidosis and atelectasis. HRCT studies have demonstrated LIP in

patients with SjS, the imaging findings of which are described under the section on the IIPs.

The association of LIP and amyloidosis (manifesting

on HRCT as multiple irregular nodules with cysts) in patients with SjS is recognised, but as these patients are also at increased risk of pulmonary lymphoma, the finding of LIP on HRCT in conjunction with multiple nodules or consolidations in a patient with SjS should

at least prompt further diagnostic ascertainment.

Classical HRCT Findings

• The most frequent interstitial pneumonias in SjS are NSIP and LIP

• Mild bronchiectasis is common

• Lymphoproliferative disease may occur on a background of LIP

Progressive Systemic Sclerosis (Scleroderma)

Progressive systemic sclerosis (SSc) is a collagen vascular disease characterised by the deposition of excessive extracellular matrix with vascular occlusion involving several organs.

It commonly affects the skin (scleroderma), peripheral vasculature, kidneys, oesophagus and lungs.

ILD is common in patients with SSc and causes considerable morbidity and mortality.

Nonetheless, absence of parenchymal abnormalities

may be associated with pulmonary hypertension and poor prognosis.

The interstitium and pulmonary vasculature are the predominant sites that are affected.

The HRCT findings of interstitial fibrosis in SSc include

peripheral reticular opacities, ground-glass attenuation associated with traction bronchiectasis and (seldom) honeycomb destruction.

Hence, fibrotic NSIP is the most prevalent histological pattern in patients with SSc, whereas the UIP pattern is reported in some 5-10% of cases.

Pulmonary arterial enlargement out of proportion to the severity of the lung fibrosis may indicate an independent vasculopathy akin to primary pulmonary hypertension, and a markedly dilated oesophagus is a frequent accompaniment.

Pleural disease is much less common in SSc than in other CTD; pleural thickening is seen on HRCT in only 10% of patients.

As in other diffuse fibrosing lung diseases, enlarged mediastinal lymph nodes are a frequent finding on CT (with reactive hyperplasia at histology).

Classical HRCT Findings

• Fibrotic NSIP is the most common pattern of lung involvement

• Dilated oesophagus is usual

• Signs of pulmonary hypertension, often without fibrotic ILD

Polymyositis/Dermatomyositis

Polymyositis (PM) is an idiopathic autoimmune inflammatory myopathy that results in proximal muscle weakness.

Dermatomyositis (DM) is similar, except that it is accompanied by a skin rash. Pulmonary complications

of PM/DM are important determinants of the clinical course.

Aspiration pneumonia owed to respiratory muscle weakness is an important pulmonary complication, with relatively high prevalence as well as high associated morbidity and mortality.

ILD in PM/DM occurs in an up to 47% of patients. Initial clinical presentation includes cough, dyspnoea and fever. Arthralgia, myalgia and weakness are the musculoskeletal manifestations of PM/DM; they show later onset in 30% of cases and simultaneous occurrence in only 20%. NSIP and OP are the most common histological patterns seen in PM/DM.

The ILD can be acute and aggressive, similar to AIP, with some series reporting up to 10% mortality, or more slowly progressive.

The lung disease is variably responsive to steroids and immunosuppression.

At presentation, the most common HRCT features of

PM/DM are linear opacities with a lower lung predominance, ground-glass opacities, irregular interfaces and areas of consolidation. Honeycombing is less frequently observed.

Histologically, organising pneumonia is the correlate of consolidation and ground-glass opacification seen on HRCT. DAD is demonstrated in some cases and is associated with widespread involvement, dense

dependent consolidation and extensive diffuse groundglass opacification.

Organising pneumonia in PM/DM can also be admixed with interstitial fibrosis with a predominance of reticular elements and architectural distortion, traction bronchiectasis and honeycombing, and this overlap entity is associated with a poor prognosis.

Classical HRCT Findings

• Diffuse ground-glass opacities may represent either NSIP or DAD

• Consolidation is common and represents organising pneumonia frequently admixed with NSIP and DAD patterns

Systemic Lupus Erythematosus

Pleuropulmonary disease will occur in more than half of patients with systemic lupus erythematosus (SLE). Notably, pleuritis is the most common manifestation of SLE.

Diverse thoracic manifestations of SLE range from

diaphragmatic dysfunction (shrinking lung syndrome) to

life-threatening pneumonitis or pulmonary haemorrhage.

Pleural effusions are the most common radiographic abnormality.

They are frequently bilateral, usually only small in volume, and, unlike those in rheumatoid disease, are often associated with pleuritic pain.

On radiography, thick horizontal band shadows at the lung bases reflect linear atelectasis allegedly secondary to the pleurisy or, more likely, restricted diaphragmatic movement.

Pericardial effusion is quite common, too.

Pulmonary consolidation in patients with SLE may cause diagnostic difficulty as it may be a consequence of infection (high incidence of respiratory tract infection because of immunological abnormalities, immunosuppression from steroids and respiratory muscle weakness), pulmonary oedema, lupus pneumonitis or pulmonary haemorrhage.

Acute lupus pneumonitis is a well-recognised but rare manifestation of the disease that is characterised by fever, severe hypoxaemia and diffuse pulmonary infiltrates. **Radiological features are typically** patchy consolidation and focal atelectasis seen predominantly in the lower lung zones with concomitant pleural effusions. Histological findings are not diagnostic but include alveolar wall damage, inflammatory cell infiltration and haemorrhage.

Compared with many other CTDs, SLE is not commonly

associated with chronic diffuse ILD (around 15%, though possibly underdiagnosed according to autopsy studies). When present, HRCT findings include irregular linear and band-like opacities (in part atelectasis), ground-glass

opacities and interlobular septal thickening. Honeycombing, which can resemble IPF, is extremely rare. Diffuse alveolar haemorrhage (DAH) is a rare but dramatic complication of SLE, which manifests radiologically as widespread ground-glass opacity and consolidation.

SLE is associated with increased risk of malignancy, with lymphoma being the most common.

Classical HRCT Findings

• Pleural abnormalities and decreasing lung volumes ('shrinking lung

syndrome')

• Chronic ILD is less frequent than other CTDs

• Diffuse ground-glass opacities may represent DAD or pulmonary haemorrhage

Intrathoracic Manifestations of

Systemic Lupus Erythematosus

- Pleural effusion
- Segmental or subsegmental collapse
- Lupus pneumonitis
- Pulmonary infection

- Pulmonary oedema
- Diaphragmatic dysfunction
- Interstitial fibrosis (rare)
- Pericardial effusion
- Pulmonary vascular disease
- Pulmonary arterial hypertension
- Vasculitis/capillaritis
- Pulmonary embolism
- Pulmonary veno-occlusive disease

SYSTEMIC VASCULITIDES

Systemic vasculitides are determined by deposition of immune complexes in the walls of blood vessels.

The size of the vessels predominantly involved strongly influences the clinical and radiological features of the

different forms of vasculitis and is therefore one major criterion for classification, according to the 2012 revised Chapel Hill Consensus Conference Nomenclature.

The systemic vasculitides that most commonly affect the pulmonary interstitium are granulomatosis with polyangiitis (GPA, formerly Wegener granulomatosis), eosinophilic granulomatosis with polyangiitis (EGPA,

former Churg–Strauss syndrome) and microscopic polyangiitis (MPA).

Circulating antineutrophilic cytoplasmatic antibodies (ANCAs) are seen in these diseases, which are often

referred to as ANCA-associated vasculitis. GPA is more often seen with cytoplasmatic ANCA (c-ANCA), whereas EGPA and MPA show predominant perinuclear ANCA (p-ANCA) expression.

As GPA will be considered in Chapter 11, 'Airspace Diseases', only EGPA and MPA will be covered in this section.

Eosinophilic Granulomatosis With Polyangiitis

(Formerly Churg–Strauss Syndrome)

EGPA is determined by necrotising vasculitis and extravascular granulomatous inflammation rich in eosinophils.

Clinical features include asthma, fever, blood eosinophilia and peripheral neuropathy.

HRCT appearances largely reflect the eosinophilic infiltrate and are largely non-specific.

Features include ground-glass opacities, areas of airspace

consolidation, centrilobular nodules and airways abnormalities attributable to asthma. Histologically, the airspace disease is due to eosinophilic infiltrate or organising pneumonia. Interlobular septal thickening may be seen as a result of interstitial pulmonary oedema

secondary to cardiac involvement. However, a significant proportion (up to 25%) of patients with EGPA have few or no imaging abnormalities and imaging is often of little help in making this somewhat elusive diagnosis.

Even when HRCT abnormalities exist, they are not

specific, with diagnostic accuracy reported less than 50% in one study.

The presence of asthma at any time within the disease course is obligatory for the diagnosis of EGPA

Classical HRCT Findings

• Non-specific patchy ground-glass opacities or consolidation

• Interlobular septal thickening (particularly with cardiac involvement)

• Pleural and pericardial effusion

Microscopic Polyangiitis

MPA is a non-granulomatous vasculitis of small vessels. This is a systemic disease with notable involvement of the kidneys by segmental necrotizing glomerulonephritis. DAH is the most frequent manifestation (10%–30%);

chest radiography may be negative or show diffuse parenchymal shadowing.

On HRCT, patchy ground glass and consolidations or centrilobular faint nodules are seen.

Other common thoracic radiological findings of MPA are pleural effusion (15%) and pulmonary oedema (6%). Lung fibrosis is uncommon in MPA, yet it is a negative prognostic factor.

Classical HRCT Findings

- Patchy ground-glass opacities
- Subsolid centrilobular nodules with faint margins

DRUG-INDUCED LUNG DISEASE

The lung is less commonly the site of drug-induced disease than other organs such as the skin and gastrointestinal tract.

Nevertheless, many drugs can cause injury to the lungs, and the list of drugs and patterns of involvement continues to increase.

Notably, subjects with lung cancer treated by target therapy or immune checkpoint inhibitors show pulmonary toxicity.

Susceptibility to lung toxicity might be promoted by

chronic pulmonary damage in smokers. Respiratory disease secondary to drugs may be the result of the pharmacological action of the drug in normal or excessive dosage, or caused by an allergic or idiosyncratic reaction. The radiological manifestations of drug-induced ILD are

heterogeneous and non-specific; therefore, a number of alternative diagnoses need to be excluded before suspecting drug-induced lung disease.

The most important of these are infections, but also cardiac oedema or other systemic diseases must be ruled out.

In the early stages

of disease, symptomatic patients may have a normal chest radiograph.

Furthermore, data based on a small number of cases suggest that the different histological patterns of drug

reaction are not always reflected by characteristic HRCT findings.

Despite these limitations and the fact that only very rarely is a biopsy for histological proof of the diagnosis carried out, it is reasonable to interpret the radiological manifestations of drug-induced lung disease according to disease manifestations known from other interstitial and airspace-related lung diseases: namely, DAD, chronic interstitial pneumonia (a term used by histopathologists which incorporates drug-induced lung disease with histological features that resemble either NSIP or less commonly UIP), HP, organizing pneumonia, eosinophilic pneumonia and sarcoid-like reaction.

Most drugs typically cause more than one type of histological pattern.

Diffuse Alveolar Damage

Chemotherapeutic drugs such as busulfan, cyclophosphamide, carmustine (BCNU) and bleomycin constitute the largest group of drugs associated with this pattern of lung toxicity.

Nonetheless, precision cancer therapy aiming to a specific oncogenic pathway may result in DAD; for instance, vascular endothelial growth factor (VEGF) inhibitors and epidermal growth factor (EGFR) inhibitors. DAD usually develops a few weeks or months after initiating therapy, and disease onset is heralded by progressive dyspnoea. The corresponding radiological features are similar

to those found in ARDS, with bilateral patchy or homogeneous airspace consolidation involving mainly

the middle and lower lung zones. HRCT demonstrates extensive bilateral ground-glass opacities and dependent

areas of airspace consolidation.

Severe DAD with AIP evolution can be seen in patients treated with immune checkpoint inhibitors or EGFR inhibitors.

In most circumstances there are no histological features that allow separation of drug toxicity from other potential

causes of DAD, and the diagnosis of drug-induced lung disease requires vigorous exclusion of other potential aetiologies, most importantly opportunistic infection.

Interstitial Pneumonia

A variety of patterns, in particular NSIP and OP, are associated with drug-induced lung disease. Of these, the NSIP pattern is the most common.

Drugs reported to cause an NSIP-type pattern include

amiodarone, busulfan, carmustine, methotrexate, phenytoin, simvastatin, programmed death 1 (PD-1) inhibitors and EGFR inhibitors.

Descriptions of HRCT findings are available for a limited number of agents, but demonstrate the same range of abnormalities described in patients with the idiopathic form of NSIP.

With disease progression, there may be evidence of fibrosis with development of a reticular pattern and traction bronchiectasis.

The fibrosis is patchy in distribution and predominantly

peribronchovascular, a pattern sometimes seen in patients receiving nitrofurantoin.

In some cases, however, HRCT features suggestive of

irreversible fibrosis may show complete resolution on cessation of nitrofurantoin.

NSIP is the most common manifestation of amiodaroneinduced lung disease.

HRCT features that have been described with

amiodarone-induced lung disease include ground-glass opacities in association with fine intralobular reticulation predominantly in a peripheral distribution.

Foci of consolidation have also been described, and represent areas of organising pneumonia. The diagnosis of amiodarone toxicity can occasionally be made on HRCT by virtue of the high-attenuation values of amiodarone deposited in the lung and liver.

Organising Pneumonia

An organising pneumonia-like reaction has been reported most frequently in association with methotrexate, cyclophosphamide, gold, nitrofurantoin, amiodarone, bleomycin and busulfan.

The chest radiograph shows patchy bilateral areas of consolidation, masses or nodules, which may be asymmetric.

HRCT shows patchy ground-glass opacity and areas of

consolidation which often have a predominantly peripheral or peribronchiolar distribution.

Eosinophilic Pneumonia

Eosinophilic pneumonia is characterised histologically by the accumulation of eosinophils in the alveolar air spaces and infiltration of the adjacent interstitial space by eosinophils and variable numbers of lymphocytes and plasma cells.

Peripheral blood eosinophilia is present in around 40% of patients.

Eosinophilic pneumonia secondary to drug

reaction is seen most commonly in association with methotrexate, sulfasalazine, para-aminosalicylic acid, nitrofurantoin and non-steroidal anti-inflammatory drugs (NSAIDs).

Chest radiography and HRCT show

bilateral airspace consolidation, which tends to involve mainly the peripheral lung regions and the upper lobes.

The diagnosis of drug-induced disease will be missed unless specifically sought as a cause of unexplained diffuse pulmonary shadowing in patients at known risk with clinical symptoms of lung disease.

It is particularly important, though often difficult, to differentiate between drug-induced disease, infections (particularly of the opportunistic variety) and metastatic malignancy in patients who are susceptible to these processes.

Classical HRCT Findings

• Imaging findings of most drug reactions are non-
specific and mimic those of various acute and chronic lung diseases

• A drug-specific diagnosis is rarely possible

• The main role of HRCT in this setting is the exclusion of other diseases

OCCUPATIONAL LUNG DISEASE

Diseases of the lung caused by workplace and environmental exposures are common throughout both developed and developing worlds, and as industrial techniques continue to evolve, new occupational diseases

will be recognised (e.g. sandblasting).

The following section highlights the imaging features of the main pneumoconioses—silicosis, coal worker's pneumoconiosis (CWP) and asbestos-related pulmonary disease.

HP is covered in the preceding section on ILD.

Work-related asthma is one of the most frequently

reported occupational lung diseases in a number of industrialised countries but as these patients are not frequently imaged (and the contribution of imaging is negligible), this topic is not further discussed.

The International Labour Office Classification

The International Labour Office (ILO) International Classification of Radiographs for the Pneumoconioses is a system used for the recording of chest radiographic abnormalities related to the inhalation of dusts. In the ILO system, the size, shape and profusion of opacities on radiographs are classified in a detailed manner by trained observers using a set of standard radiographs.

Rounded or nodular opacities are graded as p (<1.5 mm diameter), q (1.5–3 mm) or r (3–10 mm).

Irregular opacities are classified as s, t or u, using the same size criteria.

Large opacities (>10 mm) are graded as A, B and C based on the combined dimensions of all large opacities present.

The classification also scores the extent and thickness of pleural plaques, pleural thickening, fissural thickening and calcified nodules. Profusion of the opacities is classified into four categories (0–3); category 0 indicates that there is no excess of small opacities above normal. The use of two profusion categories is useful when appearances lie between those of the standard radiographs.

Despite acknowledged limitations and problems with the ILO classification (interobserver variability, the presence of background opacities that are unrelated to dust exposure, the relative insensitivity of the chest radiograph to early disease and the misuse of the classification in legal settlements for compensation), it remains a useful shorthand whose meaning is widely understood for epidemiological studies.

Silicosis/Coal Worker's Pneumoconiosis

Silica causes three distinct clinical patterns of lung disease which are related to both level and duration of exposure.

The earliest radiographic changes of silicosis and CWP are nearly identical.

Typical appearances are a profusion of small (1–3 mm) round nodules distributed in the posterior aspects of the upper two-thirds of the lung. **Radiologically**, the only difference between simple CWP and simple silicosis is that the nodules in CWP are often smaller.

With advancing disease, the nodules increase in size and number to involve all lung zones.

The nodules are sometimes calcified.

Hilar and mediastinal lymph node enlargement with calcification of the eggshell type is not uncommon and may be seen on the chest radiograph or CT. On CT, the micronodules are sharply defined and distributed throughout the lungs but are frequently most numerous in the upper lung zones.

The nodules may be centrilobular or subpleural in location; the subpleural micronodules may become confluent into the so-called 'pseudo-plaque'.

PMF refers to the coalescence of large nodules and is much more common in silicosis than in CWP.

On the chest radiograph, PMF is seen as mass-like opacities, typically in the posterior upper lobes and

associated with contraction of the upper lobes and hilar

elevation.

Sequential evaluation of these masses often demonstrates migration towards the hila, leaving a peripheral rim of traction emphysema.

The outer margins of PMF often parallel the contour of the adjacent chest wall.

CT confirms the architectural distortion associated with PMF. Large lesions (>5 cm) often show irregular low-attenuation regions on CT indicative of necrosis.

Frank cavitation is a less frequent finding; it should always be put in differential with tuberculosis (conventional or atypical). Unilateral or asymmetric PMF may be distinguished

from lung cancer by the presence of lobar volume loss and peripheral emphysema.

Classical HRCT Findings

• Well-defined dense centrilobular and subpleural nodules, upper and posterior lung predominance

- Hilar and mediastinal lymph node enlargement, with or without calcification
- Upper lobe irregular masses characterise PMF

Asbestos-Related Disease

Asbestos is the generic term for a group of fibrous silicates that share the property of heat resistance. They are classified into two groups: the serpentines and the amphiboles. The only serpentine asbestos used commercially is chrysolite, which accounts for more than 90% of the

asbestos in the USA.

The pathological hallmark of asbestos exposure is the asbestos body consisting of a fibre (2–5 μ m in width) that is inhaled and accumulated in the lung.

These bodies can be identified in tissue sections in interstitial fibrous tissue and intra-alveolar macrophages

in bronchoalveolar lavage (BAL).

The effects of asbestos on the lung are diverse. Clinical onset of disease is usually delayed by some 20 years or more after initial exposure.

The exception is asbestos-related pleural effusions, which may be present as early as 5 years after first exposure.

Benign Pleural Effusions

The exact prevalence of benign pleural effusions is unknown, as many are subclinical.

The effusions are typically haemorrhagic exudates of

mixed cellularity and usually do not contain asbestos bodies.

Their diagnosis is mostly made on exclusion of other causes.

The development of effusions is thought to be exposuredependent.

The effusions are often small, may be persistent or recurrent, and may be simultaneously or sequentially

bilateral.

Diffuse pleural thickening, with or without areas of subjacent folded lung, is the usual consequence.

Pleural Plaques

The most common manifestation of asbestos exposure is the presence of pleural plaques that, macroscopically, are discrete foci of pearly white fibrous tissue (2–5 mm thick).

They involve the parietal pleura almost exclusively and are classically distributed under the anterior ends of

the upper ribs, the paravertebral gutters and the diaphragmatic surface.

Calcification is reported in 10%–15% of cases. CT is undoubtedly more

sensitive for the detection of pleural plaques. Only 50%–80% of cases

of documented pleural thickening are detected by chest radiography;

on chest radiography, pleural plaques were most commonly missed in

the paravertebral and posterior regions of the costal pleura. Studies

have suggested that pleural plaques are not associated with significantly

impaired lung function.

Diffuse Pleural Thickening

The frequency of diffuse pleural thickening increases with time from first exposure and is thought to be doserelated.

It results from thickening and fibrosis of the visceral pleura, which leads to fusion with the parietal pleura and may be caused by extension of interstitial fibrosis to the

visceral pleura, consistent with the pleural migration of asbestos fibres.

Diffuse pleural thickening superimposed on circumscribed plaques has been observed, often after a pleural effusion.

CT is more sensitive and specific than chest radiography in the detection of diffuse pleural thickening and can make the distinction between mild pleural disease and extra-pleural fat.

Round Atelectasis

Round atelectasis, also known as folded lung, is a form of parenchymal collapse that occurs in association with pleural thickening, most commonly in the peripheral lung in the dorsal regions of the lower lobes.

Pathological examination shows pleural fibrosis overlying the abnormal parenchyma as well as invaginations of fibrotic pleura into the region

of collapse.

Because of the pathogenetic association with fibrosis, the areas of atelectasis are always seen adjacent to the

visceral pleura.

A characteristic finding is the presence of crowding of bronchi and blood vessels that extend from the border of the mass to the hilum ('comet tail' sign).

In most cases, the collapsed lung has a rounded or oval shape; however, wedge- and irregularly-shaped masses can also occur.

Volume loss of the affected lobe is a key sign. Serial examinations show a relatively stable appearance, and the differentiation from a lung neoplasm is usually straightforward on CT by characteristic findings such as the subpleural location, comet tail sign and the strong and homogeneous enhancement after intravenous contrast medium, the latter indicative

of atelectasis rather than tumour.

Asbestosis

Asbestosis is defined as pulmonary parenchymal fibrosis secondary to inhalation of asbestos fibres.

The time lag between exposure and onset of symptoms is usually 20 years or longer.

In the most severe cases there is diffuse interstitial

fibrosis associated with parenchymal remodelling and honeycombing.

Asbestos bodies are almost always identifiable microscopically in the fibrous tissue or macrophages in residual air spaces. Early CT changes indicative of asbestosis are the presence of subpleural curvilinear lines and dots, pleural-based nodular irregularities, parenchymal bands and septal lines.

The fine reticulation eventually progresses to a coarse linear pattern with honeycombing.

These abnormalities are usually most severe in the subpleural regions of the lower lobes.

HRCT–pathological correlation studies have shown that subpleural dots and branching structures correspond to peribronchiolar fibrosis.

The sensitivity of HRCT over the chest radiograph for the identification of early fibrosis in asbestos-exposed individuals is well established; however, sensitivity is not 100% and a histopathological diagnosis of asbestosis

can be present in patients with normal or near-normal HRCTs.

The diagnosis of asbestosis is prognostically relevant, including work ability and the possibility of receiving legal compensation.

Although both the chest radiograph and HRCT can confirm previous exposure, the diagnosis of asbestosis is largely inferential from critical investigation of exposure history and exclusion of other plausible conditions associated with pulmonary fibrosis. It is noteworthy that subjects exposed to asbestos likely have risk factors for IPF (male gender, smoking habit and age).

Distinguishing asbestosis from IPF is also desirable, as asbestosis is associated with a much slower rate of progression and hence a better prognosis. Although it may be difficult to differentiate between asbestosis and IPF on HRCT, the presence of pleural disease may provide a pointer: Akira et al. reported pleural disease in 83% (66/80) of patients with asbestosis but only in 4% (3/80) of patients with IPF. Copley et al.

found no statistically significant differences in the coarseness of fibrosis between individuals with asbestosis and a cohort of individuals with biopsy-proven UIP, although the CT findings of asbestosis were strikingly

different from NSIP; the quality of fibrosis was coarser, there was a lower proportion of ground-glass opacification, and a higher likelihood of a basal and subpleural distribution.

Classical HRCT Findings

• Asbestos-related benign pleural disease consists of either parietal pleural plaques in characteristic locations or diffuse visceral pleural thickening

• The presence of such pleural disease in individuals with HRCT findings compatible with UIP/NSIP pattern suggests the diagnosis of asbestosis in patients with an appropriate exposure history.

Airspace Diseases

INTRODUCTION

Diseases of the air spaces are remarkably common, yet, the radiological approach to diagnosis is often considered challenging.

In part, this is because a pattern of airspace opacification

is non-specific.

However, at its simplest, this radiological pattern simply indicates that air has been displaced, to a greater or lesser degree, from the lung.

In clinical practice, airspace opacification is most commonly a manifestation of pulmonary oedema or infection.

This chapter considers not only some of the common but also a few of the more unusual causes of airspace opacification in clinical practice.

Airspace diseases caused by infection and cancer are considered in detail elsewhere.

SUGGESTED APPROACH TO THE RADIOLOGICAL

DIAGNOSIS OF AIRSPACE DISEASES

The plain chest radiograph (CXR) is usually the first imaging test requested by clinicians.

In patients with an abnormal CXR, radiologists should aim to formulate a sensible diagnosis or, at most, a short list of differential diagnoses. To this end, the radiologist must pay heed to the following: the clinical background, the distribution of radiographic abnormalities and serial changes (i.e. progression/resolution, time course etc.) on repeat studies where available.

Clinical context is, of course, important when reporting imaging studies. For instance, the most likely cause of lobar consolidation in a patient with pyrexia and a productive cough is infection, whereas the same radiological pattern (only bilateral) in a critically ill patient is most likely to indicate noncardiopulmonary oedema/acute respiratory distress syndrome (ARDS).

The distribution of airspace opacities on imaging studies can also provide important clues: in cryptogenic organising pneumonia (COP), for instance, areas of consolidation tend to be most obvious in the periphery and lower zones.

By contrast, upper zone infiltrates parallel to the chest are typical in chronic eosinophilic pneumonia.

A review of serial radiographs should be considered de rigeur in the radiologist's routine.

Rapid clearing—occurring over a period of hours or, at most, a few days—suggests oedema fluid or pulmonary haemorrhage as the likely cause as opposed to, say,

pneumonia.

Opacities that are transient and migratory in a patient

with constitutional symptoms should make the radiologist consider an eosinophilic pneumonia in the differential diagnosis.

Computed tomography (CT) is frequently requested in patients with airspace disease and, occasionally, the CT features will be helpful; the so-called 'crazy-paving' pattern is an example that immediately comes to mind, which, at least in its classical form, should be considered

pathognomonic of pulmonary alveolar proteinosis (PAP).

In other instances, the radiologist may only be able to limit the list of diagnostic possibilities despite the additional information from CT (e.g. cavitation that may not have been evident on plain radiographs). Therefore, except in certain circumstances, the advantages of CT over plain radiography in the diagnosis of airspace diseases are not clearly defined.

Anatomical Considerations

The air spaces are defined as the air-containing part of the lung, which includes the respiratory bronchioles but *excludes* the terminal bronchioles; the latter are the last purely conducting airways of the bronchial tree and the region of lung subtended by a terminal bronchiole is the acinus.

Important pathways of collateral ventilation (the pores of Kohn) link different alveolar units and maintain lung inflation in the presence of proximal airway obstruction. These normal collateral pathways also facilitate the spread of certain diseases (most notably infections) into

adjacent alveolar units.

An important unit of lung structure is the pulmonary lobule, defined as the smallest unit of lung bounded by connective tissue septa.

Individual lobules are irregular polyhedrons, best seen in the subpleural lung and measuring between 5 and 30 mm in diameter, incorporating between 3 and 24 acini.

The lobular bronchiole and accompanying artery form

the core structures. Normal centrilobular arteries (with a

maximum diameter of 0.2 mm) can be resolved on highresolution computed tomography (HRCT), but the wall of the accompanying bronchiole is too thin to be seen.

The implication is that when bronchioles are visible within 2 cm of the subpleural space (either because of wall thickening, dilatation and/or mucous plugging of the lumen) there is disease.

Infiltration of the interlobular septa by oedema fluid or malignant cells, or thickening caused by fibrosis, will also render individual pulmonary lobules visible on HRCT.

Radiological Signs of Airspace Disease

One of the principal limitations of imaging airspace diseases is that a multitude of pathological processes manifest as a limited number of patterns; thus, for most airspace diseases, a nodular pattern, ground-glass

opacification and consolidation represent the range of radiological abnormalities.

1. A *nodular pattern* as a sole manifestation of airspace disease is relatively uncommon.

The term 'acinar nodules' or 'acinar rosettes' has been

used in the past to describe the appearance of poorly defined infiltrates on a CXR and HRCT. However, the diagnostic value of localizing disease to the acinus is questionable; in pathological studies, the acinar pattern on plain radiographs, as described in radiology reports, does not generally correspond to the filling of acini as per strict anatomical definitions. This notwithstanding, the so-called acinar pattern is most frequently encountered in the context of bacterial infection or pulmonary haemorrhage.

2. *Ground-glass opacification* is a relatively common sign that can reflect airspace disease.

3. On plain radiography, ground-glass opacification

is seen as hazy, increased lung opacity in which the margins of pulmonary vessels are obscured. Because of the greater contrast resolution, ground-glass opacification **on CT** appears as a hazy increase in lung attenuation but *without* obscuration of bronchial

and vascular markings.

It is important to remember that ground-glass opacification can be a manifestation of airspace and/or interstitial disease.

Sometimes, particularly when there is diffuse disease, ground-glass opacification on CT may be subtle and barely perceptible.

In such cases, a noticeable difference between the density of air in the lumen of an airway and that in the adjacent

lung (the 'black bronchus' sign) might be the clue needed

to confirm the suspicion of lung infiltration: in the normal lung, the two densities will be roughly equal.

3. *Consolidation* refers to the increase in lung density on a CXR or CT in which the margins of vessels and airways are obscured.

An air bronchogram may or may not be seen. This

radiological pattern indicates that air in the air spaces has been replaced (e.g. by inflammatory cells, blood or tumour).

In some patients, the distribution of consolidation in relation to the pulmonary lobule is an important diagnostic pointer: a perilobular distribution in

which there is dense opacification apparently 'smeared' around the lobule is a characteristic finding in organising pneumonia.

PULMONARY OEDEMA

Pulmonary oedema—defined as an excess of extravascular lung water—is caused either by an increase in hydrostatic pressure (sometimes termed 'cardiogenic' oedema) or increased vascular permeability (or 'noncardiogenic' oedema).

However, despite the attraction of simplicity, the clinical utility of this dichotomous classification of pulmonary oedema is debatable. That said, hydrostatic oedema occurs when there is a shift of fluid out of the vascular compartment caused by an increase in venous/capillary pressure.

Perhaps the commonest cause of increased hydrostatic pressure is left heart failure.

A reduction in plasma osmotic pressure (as in hypoalbuminaemic patients) will have the same effect. Non-cardiogenic pulmonary oedema occurs in conditions where the permeability of the alveolar-capillary barrier is increased.

The archetypal example of increased permeability oedema is ARDS.

Chest Radiography in Pulmonary Oedema

Plain CXR is undoubtedly more sensitive than clinical examination for the early detection of pulmonary oedema.

Accordingly, on CXRs, the signs of interstitial oedema generally precede frank airspace opacification.

In the following sections, the radiographic features of pulmonary oedema are considered; for clarity, the vascular, interstitial and intra-alveolar

changes are discussed separately.

Vascular Alterations

The signs of raised pulmonary venous pressure on a CXR are well documented, although the mechanisms causing blood flow 'redistribution' are not entirely clear.

Signs of vascular redistribution (from bases to apex), namely balanced flow or inverted flow, often suggest elevation of the pulmonary venous pressure.

Both vascular dilatation and redistribution are more appreciable in chronic or, at least, subacute left heart dysfunction.

The ratio of the diameter of adjacent pulmonary arteries and bronchi seen end-on, particularly at the level of the upper lobes, is useful when judging whether vessels are abnormally enlarged.

Interstitial Oedema

Thickening of the interlobular septa is a classical chest xray sign of interstitial oedema; prominent septal (Kerley B) lines, indicating fluid in the interlobular septa (typically 1–2 mm wide and 30–60 mm long), are only really seen in the subpleural lung, perpendicular to the pleural surface.

By contrast, Kerley A lines are longer (up to 80–100 mm), are occasionally angulated and cross the inner two-thirds of the lung in varying directions, but tend to point medially towards the hilum.

In practice, Kerley A lines are more difficult to see.

In left heart failure, septal lines become visible as they distend with extravascular fluid. Naturally, thickened oedematous septal lines will not be seen if neighbouring alveoli are also opacified.

It should also be remembered that the demonstration of thickened interlobular septa is *not* diagnostic of pulmonary oedema; fibrosis and malignant infiltration

(as in lymphangitis carcinomatosa) will also render interlobular septa visible.

Another useful sign of interstitial oedema on frontal chest radiographs is peribronchial cuffing, in which the normally thin and well-defined wall of the airway becomes thickened and indistinct.

A loss of conspicuity of the central pulmonary vessels (termed a perihilar haze) also occurs and, as with peribronchial cuffing, is believed to be caused by oedema of the perivascular interstitium. Oedema fluid can also collect in the potential space between the visceral pleura and lung; on a CXR this may be seen as thickening of the interlobar fissures or as a lamellar 'effusion' in the costophrenic recesses (Fig. 11.14). The latter (admittedly

something of a misnomer) indicates fluid between the lung and visceral pleura.

Alveolar Oedema

Airspace opacification becomes apparent on the CXRs as oedema fluid passes from the interstitium into the alveoli. The distribution of oedema is variable and bilateral opacification is the norm.

However, an asymmetric distribution or oedema restricted to one lung on CXRs also occurs.

Not infrequently, oedema fluid spares the apices and extreme lung bases.

Sparing of the lung peripheries with involvement of the

central lungs produces the so-called 'bat's wing' distribution.

As oedema progresses, opacities may coalesce to produce a general 'white-out' and an air bronchogram or alveologram may be seen.

The density of airspace opacification caused by pulmonary oedema can change relatively quickly; indeed, the speed of change (i.e. sometimes over hours as opposed to days or weeks) is a useful pointer to the

diagnosis of oedema fluid rather than another airspace

disease.

In specific settings, the radiographic signs of intraalveolar oedema may be modified. For instance, as hinted above, the distribution of pulmonary oedema can vary with posture so that in patients lying on one side for a prolonged period, the dependent lung becomes more

oedematous and there is unilateral airspace opacification. Coexisting diseases (e.g. fibrosis or emphysema) will also influence the distribution and appearance of oedema fluid.

Radiographic Differentiation of Cardiogenic and

Non-Cardiogenic Oedema

Making the distinction between hydrostatic and permeability oedema is of clinical value and, for this purpose, a CXR is certainly more reliable than physical examination.

However, whether a CXR can consistently differentiate between cardiogenic and non-cardiogenic oedema is

doubtful.

Moreover, in clinical practice, both patterns of oedema not infrequently coexist.

This notwithstanding, the distribution of blood flow (i.e. upper vs lower zone) and oedema (i.e. peripheral vs central) together with the width of the vascular pedicle may be discriminatory:

in patients with hydrostatic oedema, upper lobe blood diversion is said to be more common.

By comparison, in patients with non-cardiogenic oedema caused by ARDS, a minority show this inverted pattern. A peripheral distribution of oedema is uncommon in hydrostatic oedema, being seen more frequently in ARDS.

The discriminatory value of signs of interstitial fluid accumulation and pleural effusions, when distinguishing

cardiogenic from non-cardiogenic causes, is questionable. In summary, analysis of the radiographic pattern will sometimes allow a distinction to be made, but the inconsistency of radiographic signs suggests that radiographic distinction between the various forms of

pulmonary oedema is unreliable.

Computed Tomography in Pulmonary Oedema

Not surprisingly, CT is more sensitive to small changes in lung water than CXR: CT may demonstrate clinically 'silent' oedema or help to differentiate oedema from other disease processes.

The latter is of particular value in critically ill patients with multiple co-morbidities.

The typical CT signs of pulmonary oedema are. However, the appearances of pulmonary oedema on CT can vary.

Because of excellent contrast resolution, CT may detect abnormalities before the transudation of fluid into the interstitium and air spaces: in an animal model of fluid overload there was an increase in background lung attenuation, attributed to an expansion of intra-capillary volume.

Vascular dilatation, particularly in the perihilar regions, may be observed in association with other CT abnormalities before the development of frank pulmonary oedema.

The CT equivalent of radiographic upper lobe blood diversion may be seen with preferential dilatation of vessels in the anterior (non-dependent) lung.

It is likely that the earliest detectable findings associated with enlarged vessels are scant, thickened interlobular septa and ground-glass opacification.

Smooth septal lines are often limited to the lung apices reflecting engorged septal veins.

With more florid transudation of oedema fluid, peribronchovascular cuffing, prominent interlobular septa, ground-glass opacification and consolidation become more obvious.

The absence of any lung parenchymal distortion and the more linear, smooth septal thickening should differentiate cardiogenic interstitial oedema from other causes including lymphangitis carcinomatosis and sarcoidosis.

As with a CXR, the changes on CT are usually bilateral but, occasionally, confined to one lung, and the appearances may be modified by coexistent disease such as emphysema. A perihilar, 'bat's wing' appearance

is seen in some patients but it is important to stress that this is not specific and also occurs in other diseases including PAP or pulmonary haemorrhage. An important ancillary finding in congestive heart failure

is the enlargement of mediastinal lymph nodes and a hazy increase in the attenuation of mediastinal fat. Overall, ~50% of patients with heart failure have nodal enlargement on CT and this rises as the ejection fraction falls. Enlarged lymph nodes may have blurred margins.

With medical therapy, a significant reduction in the volume of nodes occurs, often within days.

DIFFUSE PULMONARY HAEMORRHAGE

Bleeding into the lungs is a relatively common—albeit sometimes subclinical—event. It is known, for instance, that patients with pneumonia and lung cancer frequently aspirate blood into the air spaces.

However, because the bleeding tends to be localised and there is often an established underlying cause, the diagnosis is generally straightforward.

In addition to these more common clinical settings, there are numerous pulmonary haemorrhage syndromes characterised by diffuse intra-alveolar bleeding.

The severity of haemorrhage is variable, ranging from small subclinical episodes to catastrophic, life-threatening haemorrhage.

One scheme for classifying diffuse pulmonary haemorrhage (DPH) categorises the various syndromes according to the presence/absence of immunocompromise.

In immunocompetent subjects, DPH may be

immunologically mediated (e.g. antiglomerular basement membrane disease), have a presumed immunological basis (e.g. systemic lupus erythematosus, Wegener's granulomatosis), or be unrelated to immunological mechanisms (e.g. idiopathic pulmonary haemosiderosis (IPH), drug reactions).

In immunocompromised patients, infection, tumours and blood dyscrasias account for most cases.

The clinical presentation of the DPH syndromes also varies but many patients give a history of recurrent haemoptysis, dyspnoea and chronic cough.

Non-specific clinical features include intermittent fever,

headache, lethargy, basal crackles on auscultation and clubbing.

With repeated episodes there is thickening of alveolar septa, indicating fibrosis, which, in occasional patients, may be florid.

The chest x-ray and CT appearances of DPH are fairly stereotypical and differentiation between different causes of DPH, on the basis of radiological findings alone, is not possible. Following acute bleeding the CXR is usually, but not invariably, abnormal.

On chest x-ray there may be small acinar nodules or patchy consolidation and ground-glass opacification more pronounced in the perihilar region of the mid/lower zones.

A useful diagnostic clue is that compared with other causes of widespread airspace opacification (but with the notable exception of pulmonary oedema), the changes of diffuse intra-alveolar haemorrhage will generally clear quickly (i.e. over a few days) as blood is removed by lung macrophages.

With repeated episodes, ill-defined nodular or reticulonodular opacities are seen and there may be enlargement of hilar lymph nodes.

On CT there may be poorly defined centrilobular

acinar nodules and patchy ground-glass opacities. Abnormal thickening of interlobular septa may be present and, in some patients, a combination of ground-glass opacities with thickening of inter- and intralobular septa (the crazy-paving pattern) is seen.

Of the many DPH syndromes, IPH and antiglomerular basement membrane antibody disease (Goodpasture's syndrome) usually receive the greatest attention and are considered briefly below.

Idiopathic Pulmonary Haemosiderosis

Idiopathic pulmonary haemosiderosis (IPH) is a rare disorder of unknown aetiology.

The majority of patients are children (typically in the first decade), although sporadic cases in older subjects have been recorded.

The clinical picture is that of episodic intra-alveolar haemorrhage, haemoptyses, iron-deficiency anaemia and airspace opacification on CXRs.

Repeated bouts of bleeding may lead to lung fibrosis.

The outlook for patients with IPH varies with survival, ranging from a few days (following massive haemorrhage) to years. The pathogenesis of IPH is not clear, although a number of hypotheses have been proposed.

The imaging findings are non-specific and, as for other haemorrhage syndromes, the clue to a radiological diagnosis may only come after a thorough review of clinical features and the exclusion of other causes

of widespread pulmonary haemorrhage.

Antibasement Membrane Antibody Disease

(Goodpasture's Syndrome)

A link between renal disease and diffuse intra-alveolar bleeding has long been known.

Although the eponymous title Goodpasture's syndrome

was, until relatively recently, in common use, the pathogenetically accurate term antibasement membrane (anti-BM) antibody disease is preferred.

Anti-BM antibody disease typically affects young men, with a male-to female ratio of around 3 : 1. On histopathological examination there is glomerulonephritis with circulating serum antibodies directed against

components of basement membrane in the lungs and kidneys.

The pulmonary manifestations of anti-BM antibody disease often dominate the clinical presentation, though renal disease is present in the majority.

Granulomatosis With Polyangiitis

(GPA; Formerly Wegener's Granulomatosis)

Granulomatosis with polyangiitis (GPA), together with microscopic polyangiitis, eosinophilic GPA (Churg– Strauss syndrome) and isolated pauci-immune pulmonary capillaritis, is best classified as one of the primary (idiopathic) small vessel vasculitides.

GPA is multisystem disorder with necrotising granulomatous inflammation of small vessels in the

upper and lower respiratory tracts.

There is an equal gender predilection and a wide age range of presentation (from childhood to >70 years).

The lungs are affected in approximately 90% of patients with GPA.

Most patients present with symptoms referable to the nose, paranasal sinuses or chest; in some patients, the disease manifests solely in the respiratory tract and is termed 'limited' GPA.

Chest symptoms include cough, dyspnoea, pleuritic chest pain and haemoptysis.

The aetiology of GPA is unclear but there is a strong link with a cytoplasmic-staining pattern of anti-neutrophil cytoplasmic antibodies (c-ANCA) directed against proteinase-3 (PR3-ANCA).

The spectrum of morphological abnormalities in GPA is potentially legion.

Bilateral nodules or masses are the most prevalent

finding, seen in 70%–90% of patients. Nodules range in size from a few millimetres up to 10 cm in diameter, are frequently multiple and can increase in size and number as the disease progresses.

Nodules have no specific zonal predilection and generally cavitate when more than 2 cm in diameter.

Cavitation is generally regarded as the classical

radiological finding in pulmonary GPA.

However, cavitation is by no means an invariable feature and the absence of this sign does not preclude a diagnosis of GPA. On CT, a halo of ground-glass opacification

(believed to reflect surrounding haemorrhage) may be seen around nodules.

In some patients there may be a 'feeding' vessel leading to a nodule; linear bands, spiculation and pleural tags may also be seen.

With treatment, nodules generally regress, but it should be noted that CXRs may not return to normal for up to a month after the start of treatment.

Moreover, there may be residual parenchymal scarring on

CT despite resolution of nodules and consolidation. Interestingly, the converse is apparently true in children, in whom nodules are seen less frequently.

Consolidation and ground-glass opacities are recognised

features on CT but are less common than nodules.

The distribution of consolidation is variable and might

include peripheral wedge-shaped foci abutting the pleura (mimicking pulmonary infarcts), a peribronchovascular

predilection, a 'reverse halo' pattern, or multifocal areas of consolidation with or without cavitation.

Airway disease is also reported in GPA. Stenoses of large airways leading to subglottic, tracheal or bronchial narrowing are well documented.

Bronchiectasis is an additional feature and seen in ~40% of cases.

CT has also highlighted some of the less common features of GPA, including areas of lobar or segmental atelectasis, pleural effusions or thickening and, rarely, hilar and mediastinal lymph node enlargement.

ORGANISING PNEUMONIA

The historical aspects of cryptogenic organising pneumonia (COP) are worth discussing briefly.

The pattern of COP was first reported as a clinicoradiological-pathological entity by Davison and colleagues in 1983.

In their paper, the authors described the case studies of eight patients presenting with an illness of insidious onset characterised by cough, night sweats, generalised malaise and weight loss. On chest x-ray, there were bilateral patchy areas of consolidation and, on biopsy, buds of fibrous connective tissue ('bourgeons conjunctifs') were seen in the alveoli and alveolar ducts and, crucially, only infrequently in the airways.

Despite thorough investigation—specifically for infections—the investigators found no cause.

Another key aspect was that there was a striking response to corticosteroid treatment.

The authors noted that organizing pneumonia per se is simply a histological response to 'injury' and that the label 'cryptogenic' should be used only when other potential causes of an organising pneumonia pattern have been excluded, since organizing pneumonia occurs in a variety of clinical contexts.

Unfortunately, the more confusing term 'idiopathic bronchiolitis obliterans organising pneumonia (BOOP)', now, thankfully, confined to the historical waste-bin, was also used to describe the same clinicoradiological-

pathological entity described by Davison, based on the

findings of a paper published two years later. However, because the airway changes are secondary to the dominant process in the air spaces and there is no evidence of a 'bronchiolitis obliterans', the term organizing pneumonia is now preferred.

The **typical chest x-ray and CT signs** of COP may be predicted from knowledge of the histopathological changes.

Bilateral patchy areas of consolidation, which tend to be peripheral, are the characteristic findings on chest x-ray and CT.

Although earlier series suggested a predilection for the mid and lower zones, it is clear that all lung zones may be affected. The changes of COP may be confined to one lung but this is uncommon.

Consolidation in COP has a propensity for the subpleural and/or peribronchovascular regions in approximately twothirds of patients.

Cavitation is not a feature of COP but multifocal areas of ground-glass opacification with a surrounding rim of consolidation (termed the 'reverse halo' or 'Atoll' sign), has been described.

Needless to say, the radiological distinction from pure infection (e.g. bacterial pneumonia) may be difficult, particularly when abnormalities are unilateral.

Nodules, sometimes measuring up to 1 cm in diameter and representing focal areas of organising pneumonia, are seen in some patients and, occasionally, these may be the sole radiographic manifestation of COP as with areas of consolidation, there is no definite zonal predilection. In

rare instances, a large solitary nodule or mass with irregular margins may be seen, usually prompting investigations for lung cancer. Linear opacities may be the dominant CT pattern in some patients with

COP.

Two types of opacity (termed types I and II) are

recognized.

Type I opacities are intimately related to bronchi, extend

radially towards the pleura, measure 2-4 cm in length and are 1-2 mm in thickness.

Areas of consolidation may coexist with type I linear opacities.

Type II linear opacities are subpleural and, unlike the type I pattern, are not related to airways.

Type II linear opacities also tend to parallel the pleural surface and are frequently associated with multifocal airspace consolidation.

A perilobular distribution of consolidation, giving rise

to a distinctive CT appearance, is also recognised in COP and, unlike a multitude of other radiological signs, may be regarded as pathognomonic of an organizing pneumonia pattern.

Eosinophilic Lung Disease

The eosinophilic lung diseases are a diverse group of disorders associated with peripheral or tissue eosinophilia.

Infiltration of the lung by eosinophils is surprisingly common, and reported in conditions as diverse as asthma, opportunistic infections and certain cancers.

However, by common convention, such processes are not usually considered to be eosinophilic lung diseases per se. A simplified classification of the pulmonary eosinophilias is given in and a few of the disorders under the broad category of eosinophilic pneumonia are discussed below.

Simple Pulmonary Eosinophilia (Löffler's Syndrome)

The term Löffler's syndrome (first described in 1932 and synonymous with simple pulmonary eosinophilia) describes patients with transient radiographic infiltrates, minimal constitutional upset and an elevated eosinophil count in peripheral blood.

The airspace opacification in Löffler's syndrome is classically fleeting and may be either uni- or bilateral.

Resolution of opacities within a period of days and, by definition, within a month is the rule. In many cases, no underlying cause is found but there is an association with parasitic infection, in particular infestation with *Ascaris lumbricoides*.

CT findings include ground-glass opacities or consolidation principally in the periphery of the middle/upper lung zones, as well as single or multiple acinar nodules.

Acute Eosinophilic Pneumonia (AEP)

In rare patients with pulmonary eosinophilia there is a more fulminant clinical illness beginning with a short febrile episode (<1 month duration) but followed by significant respiratory distress. Strict criteria for

a diagnosis of acute eosinophilic pneumonia (AEP) have been difficult to define but currently the modified Philit criteria are the most widely accepted. The four principal features are:

(1) an acute respiratory illness

 ≤ 1 month duration;

(2) a widespread pulmonary infiltrate on imaging

(CXR or CT);

(3) pulmonary eosinophilia with >25% eosinophils in

lavage fluid (with or without variable increase in lymphocytes and neutrophils) or evidence of an eosinophilic pneumonia on biopsy; and

(4) the exclusion of other specific eosinophilic diseases (e.g. eosinophilic GPA (formerly, Churg-Strauss syndrome) and allergic bronchopulmonary aspergillosis).

AEP may be idiopathic but an aetiological link with cigarette smoke seems very likely.

On this note, an important finding is the observation that AEP has been reported in subjects who have just started to smoke or in those with an established habit but which may have changed recently.

Exposure to other inhaled 'toxins' (e.g. cocaine, marijuana, firework dust and tear gas), certain drugs (e.g. antimicrobials, antidepressants, non-steroidal antiinflammatory drugs (NSAIDs) and infections (parasitic, fungal and viral) have also be implicated. Spontaneous

regression of AEP is reported but most patients respond relatively quickly to corticosteroid treatment. Treatment of the underlying cause (in particular, those cases linked to infection) is important. Disease relapses tend to be rare, except in smokers who continue to smoke.

On CXR, there is bilateral airspace opacification and/or reticular infiltrates.

Pleural effusions are common. Areas of ground-glass opacification and consolidation are seen on CT and there may be smooth thickening of interlobular septa.

The CT signs are similar to those seen in patients with pulmonary oedema or diffuse alveolar damage and the

initial serum eosinophil count may be normal.

Therefore, establishing a confident diagnosis of AEP can be difficult.

Chronic Eosinophilic Pneumonia

The clinical and radiological features of chronic eosinophilic pneumonia are strikingly different from the entities described above.

As the term suggests, the clinical course of chronic eosinophilic pneumonia is generally more protracted and symptoms often more marked than in patients with simple pulmonary eosinophilia.

There is frequently mild to-moderate eosinophilia and increased serum IgE levels in the peripheral blood. The prognosis is good and most patients respond to steroid therapy. **The plain radiographic** abnormalities in chronic eosinophilic pneumonia can be characteristic with patchy, non-segmental areas of consolidation typically in the mid and upper zones.

A distinctive feature is that the opacities are peripheral and seem to parallel the chest wall, a finding that was considered to be the '*photographic negative of pulmonary*

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oedema' by Gaensler and Carrington.
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Not surprisingly, the peripheral location of the consolidation and ground-glass opacity is more readily appreciated on CT.

Other disorders may mimic chronic eosinophilic pneumonia at CT, including organising pneumonia.

In one study, the most helpful distinguishing feature was the presence of nodules, seen in 32% of patients with COP but only 5% of patients

with chronic eosinophilic pneumonia.

PULMONARY ALVEOLAR PROTEINOSIS

PAP (also called alveolar lipoproteinosis and alveolar phospholipoproteinosis) is a rare disease characterised by the accumulation of a periodic acid–Schiff-positive lipoproteinaceous material in the alveoli.

Abnormal surfactant clearance from the lungs caused by a fault in macrophage function is at the heart of the pathogenesis of adult forms of PAP.

The most common cause of such impairment is a fault in granulocytemacrophage colony stimulating factor (GM-
CSF) signalling. Historically, most cases were regarded as 'idiopathic' but those patients are now believed to have an autoimmune form of PAP in which anti-GM-CSF antibodies lead to inadequate macrophage maturation/function.

Secondary PAP occurs in association with other disorders, most notably haematological diseases (e.g. myelodysplasia, lymphoma, myeloid leukaemia), dust inhalation (e.g. silica) and infections.

PAP usually affects adults aged 20–50 years, with a male preponderance, but has been described in children (in whom the outlook tends to be worse).

A definitive diagnosis usually requires bronchoscopic lavage and/or biopsy, supported by imaging findings. Although spontaneous resolution is reported, most patients require therapeutic (whole lung) bronchoalveolar lavage, a technique that has improved the outlook of patients with PAP.

The chest radiographic changes of alveolar proteinosis are nonspecific.

In general, both lungs are affected and airspace opacification is most pronounced in the central lung, sometimes producing a 'bat's wing' appearance.

The CT features are much more suggestive of alveolar

proteinosis: a 'crazy-paving' pattern (comprising geographical areas of ground-glass opacification with thickened inter- and intralobular septa) is the characteristic feature, which, in its classical form, is virtually diagnostic of PAP.

However, it is worth remembering that from time to time, a similar CT appearance is seen in some patients with adenocarcinoma, exogenous lipoid pneumonia and pulmonary oedema.

ALVEOLAR MICROLITHIASIS

Pulmonary alveolar microlithiasis is a rare cause of airspace disease characterised by the deposition of tiny stones or calcipherites (measuring $250-750 \mu m$ in diameter and composed mainly of calcium phosphate)

in alveoli.

There is a high familial incidence and a genetic abnormality has been identified: mutations in the *SLC34A2* gene (which codes for a sodium-dependent phosphate transporter in alveolar type II cells) leads to phosphate accumulation. A wide age range (the peak incidence is between 30 and 50 years) has been reported but it is believed that alveolar microlithiasis begins in early life.

Most patients are asymptomatic at the time of diagnosis and disease progression is variable.

However, there is a tendency for pulmonary fibrosis and the development of cor pulmonale.

The fibrosis of alveolar microlithiasis is associated with the formation of bullae, particularly at the apices.

The classical finding on chest radiography is the widespread discrete high-density opacities (resembling

grains of sand) seen in both lungs; when the infiltration is profuse there may be a 'white-out', with obscuration of the heart borders and diaphragm and the tiny stones may then only be seen on an overexposed radiograph. A telltale line of black subpleural lung (caused by 5–10 mm diameter small cysts or paraseptal emphysema) may be seen and there may be thickening or beading of fissures. Less commonly, apical blebs and thickened septal (Kerley B) lines may be seen.

On CT, the characteristic finding is of widespread ground-glass opacification and/or a micronodular pattern. The changes are more pronounced in the lower zones and posteriorly.

In about half of cases, calcification is uniform, producing

a pattern of dense parenchymal opacification.

Thickening of fissures and interlobular septa may be present and, in rare patients, a crazy-paving

pattern has been reported.

<u>Cardiac Anatomy and Imaging</u> <u>Techniques</u>

CHAPTER OUTLINE

Knowledge of the cardiac anatomy is essential for identifying and understanding cardiovascular disease in patients and is therefore important in clinical practice. To date, various imaging techniques such as conventional chest radiography, cardiac magnetic resonance (CMR),

computed tomography (CT) and echocardiography are all used to assess aspects of cardiac and vascular anatomy. This chapter contains an overview of the techniques used and provides examples of the anatomy identified with these techniques.

NORMAL CHEST RADIOGRAPHY

Postero-anterior and lateral chest radiographs are commonly obtained in patients with cardiovascular disease. The chest radiograph provides an impression of the size of cardiovascular structures and the lung parenchyma. Specific cardiac chambers and large vessel anatomy can

be appreciated on chest radiography. Evaluation of the lung parenchyma and lung vasculature is helpful for assessing and grading heart failure.

Valvular calcifications may be recognised as a clue for specific valvular disease.

CARDIAC MAGNETIC RESONANCE

An advantage of choosing magnetic resonance for cardiac imaging is the free choice in obtaining imaging planes of cardiovascular anatomy in any arbitrary view, since this technique is not hampered by the limited availability of acoustic windows, as with ultrasound.

This benefit is especially advantageous when imaging the morphology of the right ventricle (RV), which is excellently delineated by CMR, whereas in echocardiography the assessment of RV geometry and function is challenging because of the particular crescentic shape of the RV as it wraps around the left ventricle (LV). Furthermore, the unrestricted field of view of CMR allows superior visualisation of extracardiac and large vessel anatomy.

Single-plane two-dimensional (2-D) or multiple-plane 2-D or three-dimensional (3-D) imaging is possible with CMR.

Dynamic functional information can be obtained by synchronising image acquisition to the interval of the R-

waves on the electrocardiogram, using either prospective triggering or retrospective gating.

With prospective triggering, the operator needs to set the expected heart rate before the acquisition and triggering will then be performed according to this defined heart rate.

With retrospective gating, imaging is performed continuously and the ECG signal is stored additionally.

In retrospect, image reconstruction is synchronised to the stored ECG, providing time-resolved imaging in multiple phases of the cardiac cycle, which can then be presented in cine mode.

Imaging planes in CMR are usually obtained in the orientation to the axes of the heart, or oriented to the major axes of the body.

Therefore, the standard CMR planes of the heart are comparable to the standard cardiac views, well-known and established in other non-invasive imaging techniques such as echocardiography, cardiac CT, x-ray LV angiography and nuclear medicine.

The choice for a specific CMR protocol is mainly determined by the clinical questions that need to be answered.

Standardised nomenclature for cross-sectional anatomy has been described, facilitating comparison between different techniques and proper communication between imaging specialists.

Another important issue in clinical CMR imaging is the

ability of the patient to collaborate during the examination and to perform breath-holding repeatedly and consistently.

If a patient is capable of performing breath-holding, successive imaging planes are obtained with accelerated imaging, with the patient usually performing breathholding in end expiration, as the anatomical level may be more reproducible than planes that are examined in inspiration.

CMR techniques for anatomical evaluation include bright-blood and black-blood imaging, which essentially determines the contrast in signal intensity between myocardium and the intracardiac blood pool.

For the assessment of left and right ventricular function, fast-gradient echo sequences are usually performed in combination with steady-state free-precession (SSFP) technique (balanced-Turbo Field Echo [TFE], True-Fast Imaging Steady state Precession [FISP], Fast Imaging Employing Steady-state Acquisition [FIESTA]) for optimal contrast.

On these bright-blood images, the blood pool is presented with bright signal, whereas the myocardium is represented dark with low signal.

This results in an excellent definition of the left ventricular endocardial and epicardial borders, which is required for accurate image segmentation during cardiac volume and function quantification. Typically, SSFP images should be acquired with slice thickness of 6–8 mm and temporal resolution less than 45 ms to obtain optimal accuracy in ventricular function

assessment.

Additionally, cardiac morphology can be evaluated by double inversion, black-blood, spin-echo sequences with fat suppression, providing gated, static images of the heart with high spatial resolution (optimally, in-plane-acquired resolution of less than 2×2 mm2 and slice thickness of 5–8 mm) in the orientation of the heart or the patient's body axes.

Multiple other magnetic resonance imaging techniques are available for tissue characterisation (e.g. T2 weighted sequences, delayed gadolinium-based contrast enhancement), extending the capabilities of CMR beyond anatomical and functional evaluation of the cardiovascular

system.

Cardiac Axis Imaging Planes

To acquire imaging planes in the direction of the cardiac axes, SSFP scout views are used for planning.

If available, free-breathing images obtained during realtime imaging can be used instead.

Perpendicular to an anatomical transverse image, which displays the heart's four chambers, an acquisition plane is chosen through the middle of the atrioventricular junction at the level of the mitral valve and running through the apex. This plane is the so-called vertical long-axis (VLA) plane.

On this VLA view, a plane is defined intersecting the apex and the middle of the mitral valve, resulting in the horizontal long-axis (HLA) view (see Fig. 12.2D). This HLA view is almost comparable to the four-chamber view; however, often only a part of the left ventricular outflow tract is visualised in this HLA view.

On the acquired HLA plane, the short-axis (SA) views

covering the entire LV are planned parallel to the ring of the mitral valve and perpendicular to the line intersecting the apex.

For reproducibility and comparison purposes, the true two- and four-chamber views can still be obtained.

The two-chamber view is planned perpendicular to the anterior and inferior wall of the LV through the centre of the left ventricular cavity on a mid-ventricular SA image intersecting the apex.

On the two-chamber view the apex, anterior and inferior wall of the LV, the mitral valve and left atrium can be evaluated.

The four-chamber view is also planned on a midventricular SA image by a plane through the centre of the left ventricular cavity and the acute margin of the RV, also intersecting the apex.

The four-chamber view depicts the interventricular septum, the lateral wall of the LV, the free wall of the

RV, the left and right atrium as well as the interatrial septum and both the mitral and tricuspid valves.

Routinely, the three-chamber or so-called left ventricular outflow tract view is planned on a basal SA plane,

and also intersects the apex.

The left ventricular outflow tract view depicts the apex, the anteroseptal interventricular wall, the left ventricular

outflow tract, the inferolateral wall, and the aortic and mitral valve.

The standard SSFP cine CMR protocol for assessing left ventricular function should include the two-, three and four-chamber views in combination with SA images covering the entire LV, resulting in images covering all described 17 left ventricular segments in two directions.

Additionally, the right ventricular outflow tract (RVOT) can be obtained.

This view can be planned on a coronal image, depicting the outflow tract of the RV. Alternatively, an optimised view of the RVOT view can be obtained from a plane outlining the tricuspid valve plane and the outflow tract. On this plane the outflow tract, pulmonary valve tricuspid valve and the basal (diaphragmatic) part of the right ventricular wall are all visualised.

Body Axes Imaging Planes

For the evaluation of cardiac morphology, the pericardium, the great thoracic vessels and (para-) cardiac masses, imaging planes oriented to the main body axes are obtained.

Also, the transverse (or axial), coronal (frontal) and sagittal planes are well known to clinicians, as these anatomical orientations are similar to clinical (cardiac) CT.

Black- and bright blood sequence approaches can be used in optimally adjusted planes to answer specific clinical questions.

Black-blood images provide only static information in a single phase and are not suitable for quantification of left or right ventricular dimensions.

For this analysis, SSFP multiphase images with appropriate temporal resolution are necessary.

Transversely orientated planes are especially useful for

the evaluation of thoracic vascular structures including the ascending and descending thoracic aorta, the superior and inferior vena cava, the pulmonary trunk and right and left pulmonary artery.

The right and left pulmonary veins entering the left atrium are also well depicted.

Images in transverse orientation through the heart allow the evaluation of morphology of the ventricles and atria. Also, the right ventricular free wall, the RVOT, the pericardium and mediastinum are well depicted.

It has been suggested that right ventricular volume and function quantification by planimetry can be performed more accurately on transversely oriented images instead of SA images.

Coronal or frontal anatomical views can be instructive for analysing the connection between the heart and the great vessels.

An advantage of the frontal view is the similarity to the well-known anatomy from chest radiography.

On sagittal images, the RVOT in relation to the pulmonary valve is well outlined and the connection of the right atrium with the superior and inferior vena cava can be studied.

Normal Anatomy on Cardiac Magnetic

Resonance Images

CMR images present distinct anatomical features of both atria and ventricles.

For evaluating anatomy, either cardiac axes or body axes imaging planes can be chosen.

The pericardial sac encloses the heart and the roots of the great vessels.

The pericardial cavity is outlined by the parietal and visceral layer of the inner pericardium.

Normal pericardium has a longer T1 than fat tissue and, therefore, yields low-signal intensity on T1 weighted MR

images and can be well visualised due to the surrounding epicardial and pericardial fat.

Normally, the thickness of the pericardium measures

less than 4 mm on CMR images.

In normal cardiac anatomy, the right atrium can be recognised by identifying the corresponding broad-based triangular appendage.

At the base, the tricuspid valve, positioned between the right atrium and the RV, is located closer to the apex compared with the mitral valve.

The right atrium receives venous blood from the superior and inferior vena cava and the coronary sinus.

The coronary sinus enters the right atrium in the posterior atrioventricular groove.

The appendage of the morphological left atrium has a narrow attachment to the atrium and is more tubular shaped.

Characteristically, the left atrium receives four pulmonary veins in total—two on either side—although several

variations occur.

To date, imaging the venous anatomy of the heart is becoming more relevant. For example, during preablation work-up for supraventricular arrhythmias, the clinician needs to be informed about the exact anatomy of the left atrial morphology and number of the pulmonary ostia, as the left atrium and pulmonary veins are used to guide the interventional procedure. The interatrial septum separates the two atria.

As part of the interatrial septum, the fossa ovalis is very

thin and can hardly be depicted on CMR images due to the limited spatial acquisition resolution. The RV is normally triangular in shape and anteriorly located relative to the LV, directly behind the sternum. Morphologically, the RV has typical features that can be depicted on CMR images.

The RV shows a muscular moderator band carrying branches of the conducting system.

Furthermore, the RV contains a muscular outflow tract (infundibulum or conus arteriosus) and typically, the RV wall is more trabeculated than the left.

In normal anatomy, the LV is positioned posteriorly and to the left.

The septum is smooth with no trabeculae and the left ventricular outflow tract lacks a muscular part.

The interventricular septum consists of a muscular and a membranous part. In particular, the membranous part is very thin and is sometimes not depicted on CMR images. It is important to recognise these normal anatomical features of atrial and ventricular morphology because the position of the atria and ventricles may be inversed in complex congenital heart disease.

At the outlet of each of the heart's four chambers, oneway valves are positioned to ensure that blood flows in the proper direction.

The blood flow through the atria into the ventricles is regulated by the atrioventricular valves (the tricuspid

valve is related to the morphological RV, the mitral valve to the morphological LV). The pulmonary valve connects the outflow tract of the RV to the pulmonary trunk and the aortic valve connects the left ventricular outflow tract to the thoracic aorta.

The normal tricuspid valve consists of three cusps, whereas the mitral valve consists of two cusps. Both the normal pulmonary and the aortic valve normally consist of three cusps.

Opening of the atrioventricular valves is predominantly determined by pressure differences between the atria and ventricles, which are the result of the isovolumetric relaxation of the ventricles during diastole.

Furthermore, the motion of the valves is regulated by papillary muscles, which originate from the inferolateral and anterolateral left ventricular myocardial wall

and are connected to the valve leaflets by chordae tendineae.

During contraction of the ventricle, the papillary muscles also contract, pulling on the chordae tendineae, closing the valves and preventing blood flow from the ventricles into the atria (i.e. regurgitation).

Normally, in the RV three small papillary muscles can be depicted: the anterior, posterior and septal papillary muscle.

The LV reveals two larger papillary muscles, the anterior and posterior papillary muscle; however, there is quite a

wide variation in this standard morphology.

Cine SSFP long-axis and SA images, as well as transverse images, are all well suited for depicting morphology and function of the valvular apparatus.

The valve leaflets can be depicted if spatial resolution is adequate. Dedicated acquisitions of specific valvular planes are used to image the valve area, which is especially useful when studying aortic valve stenosis or incompetence. Both SSFP and fast gradient-echo sequences are used for valvular imaging. Papillary muscles are well visualised on both cine bright- and black-blood sequences. Chordae tendineae, on the other hand, are difficult to visualise on CMR due to the limited spatial resolution.

COMPUTED TOMOGRAPHY IMAGING TECHNIQUES

With the introduction of ≥ 64 slice CT imaging devices, CT has been accepted as a diagnostic imaging tool for the evaluation of patients with suspected coronary artery disease and for several other cardiac indications.

This includes evaluation of cardiac structures and function in adult congenital heart disease, evaluation of ventricular morphology, left and right ventricular systolic function, the pericardium and evaluation of intra- and extracardiac structures such as valves, masses and pulmonary veins.

Stress CT myocardial perfusion may be used for evaluating myocardial perfusion for the detection of functionally significant coronary artery disease.

Cardiac CT requires intravenous injection of iodinated contrast agent, with the exception of CT calcium scoring,

which requires unenhanced cardiac CT.

Various cardiac CT imaging techniques are applied in clinical practice, depending on the CT device used, on the clinical question that must be answered and on patientrelated parameters.

Imaging can be performed with helical acquisition, with step-and-shoot 'sequential' acquisition or with widevolume acquisition.

With helical and with

step-and-shoot acquisition, multiple heart beats are needed for cardiac imaging, requiring a breath-hold of approximately 10 seconds.

Images are reconstructed with a slice thickness down to 0.5 mm, with a temporal resolution down to 83 ms.

Also, fast dual-source helical techniques and widevolume detectors that cover the whole heart allow for imaging of the heart within a single heart beat at a radiation dose below 5 mSv.

In some protocols, the dose can be as low as 1 mSv.

ECG recording is central in all cardiac CT techniques to avoid motion artefacts.

For optimal coronary artery imaging, after assessment of blood pressure, patients are generally prepared with β -blockers to slow the heart rate to below 65 beats/min and with nitroglycerine to dilate the coronary arteries.

In patients with a regular heart rhythm, the acquisition

is preferably performed with prospective ECG triggering.

This allows imaging during a predefined cardiac rest phase with least motion, which is at mid-diastole at approximately 75% of the cardiac -R cycle.

In patients with high heart rates that are susceptible to motion artefacts, image acquisition may be performed, with a wider acquisition interval during the cardiac cycle, allowing for selection and reconstruction of multiple cardiac phases for optimal motion-free imaging of each coronary artery.

Functional acquisition may be needed such as in patients with valvular disease (e.g. before trans-catheter aortic valve implantation), or in patients with congenital heart disease and with contraindications for magnetic resonance imaging. For functional imaging, including calculation of the end-diastolic and end-systolic volumes and ejection fraction, data acquisition throughout the cardiac cycle is required.

The current prospective triggering acquisition techniques have effectively reduced patient exposure to radiation. With the older retrospective gating techniques, CT data were continuously acquired throughout several consecutive cardiac cycles with simultaneous recording of the ECG.

This allows any cardiac phase to be reconstructed but at the expense of a relatively high radiation dose in the range of 12–21 mSv.

The technique may be used for combined imaging of the coronary arteries and ventricular function (ejection fraction), or in patients with irregular heart rhythm or

high heart rate.

Radiation dose for functional analysis may be reduced by ECG-dose modulation techniques if coronary artery information is also needed, or by low-dose CT data acquisition throughout the cardiac cycle if only functional information is required.

Cardiac CT imaging is a three-dimensional volume technique, which implies that any imaging plane can be reconstructed.

Therefore, the use of 'standard views' is less critical than with projection invasive coronary angiography or echocardiography, or than with image-stack CMR.

CT investigations are evaluated by reviewing the appropriate (multiplanar) image reconstructions that depend on the topic of interest and the clinical question that must be answered.

Computed Tomography Imaging of Ventricles

and Myocardial Tissue

The myocardial tissue can be visualised in any plane. The RV can be best evaluated by scrolling through the transverse images.

Two-, three- and four-chamber views, and especially SA views, are helpful for visualising the LV and left ventricular myocardium.

The SA views can be used for 17-segment evaluation of the left ventricular myocardium, and enable good correlation with echocardiography, CMR and nuclear medicine techniques.

Coronary Arteries by Computed Tomography

Because of the good spatial and temporal resolution, the main coronary arteries and large side branches can be well visualised by coronary CT angiography.

CT can establish the dominance of coronary circulation.

The location of origins and courses of the coronary arteries can be visualised, along with coronary anatomical anomalies.

CT allows evaluation of coronary lumen and vessel wall for assessing coronary artery stenoses.

Dominance of the coronary arteries refers to the artery that gives rise to the posterior descending artery.

The right coronary artery is dominant in approximately 80% of the population and the left circumflex artery in approximately 10%.

The circulation is balanced (co-dominant) in the remaining population.

Evaluating the dominancy of the coronary arteries prevents confusion with branch occlusion, as in right dominant circulation a relatively small circumflex artery can be expected and in left dominant circulation a small right coronary artery is expected .

The right coronary artery arises from the right sinus of Valsalva and courses in the right atrioventricular groove (between the right atrium and RV).

Its side branches are usually visualised by scrolling

through the transverse image stack: the conus branch coursing along the RVOT, the atrioventricular branch coursing posteriorly to the sinus node (at the junction

of the superior vena cava and right atrium), the acute marginal/right ventricular branches along the right ventricular free wall, the posterior descending branch in the posterior interventricular groove and a posterolateral branch that continues in the left atrioventricular groove.

The left main coronary artery arises from the left sinus of Valsalva. It divides into the left anterior descending artery that runs in the anterior interventricular groove (between the LV and RV) and the circumflex artery that runs in the left atrioventricular groove.

In about one-third of the population, an intermediate artery arises from the left main artery which courses along the left ventricular wall between the left anterior descending and circumflex artery.

The left main coronary artery may be absent in 1% of

the population. In these cases, the left anterior descending and circumflex arteries arise from a common origin or separately from the left sinus

of Valsalva. The left anterior descending artery gives rise

to septal branches that run straight down into the interventricular septum, and to diagonal branches (usually one to three) that course along the anterolateral left ventricular wall.

The circumflex artery gives rise to obtuse marginal branches (usually one to three) supplying the lateral free wall of the LV.

In approximately one-third of the population, the sinus node branch arises from the left circumflex artery instead of the right coronary artery.

Furthermore, a left atrial circumflex branch that supplies part of the left atrium may be observed.

The coronary arteries and their major side branches can be classified by location, by segment numbers or segment names for locating coronary artery stenosis.

As several numeric classification systems are used in clinical and research practice, using numbers may be confusing.

Therefore, it may be more practical to use the segment names.

Evaluation of the coronary arteries is done on original standard transverse views or orthogonal reconstructions because these images contain all information without risk of reconstruction artefacts. (Curved) multiplanar and surface rendering reconstruction can be additionally helpful for overview and fast reading by projecting larger parts of the coronary arteries within single images.

For comparison with CT, show views of the coronary anatomy obtained with invasive angiography. Invasive angiography is still considered the gold standard for evaluation of the coronary anatomy.

It has a high temporal and spatial resolution and provides lumen evaluation that is not limited by the presence of calcium. The main disadvantage of invasive angiography is its invasive fashion, although at low risk of complications.

Valves

Echocardiography and CMR are the preferred imaging techniques for evaluating the cardiac valves, as these techniques provide advanced functional imaging with superior temporal resolution without the use of ionising radiation.

However, CT allows detailed information on aortic

and mitral valve morphology and can provide functional information as well.

The pulmonary and tricuspid valve can also be visualised but have thinner cusps and are, therefore, more difficult to appreciate on CT.

For each valve, multiphase cine views may be helpful for evaluation.

The normal aortic valve is composed of a fibrous annulus, three cusps (right coronary cusp, left coronary cusp, posterior or non-coronary cusp) and three commissures that separate the cusps.

The dilatations in the aorta at each cusp are the sinuses of Valsalva.

The aortic cusps open at systole and close at diastole with a small area of overlap.

The normal aortic valve area at opening is 3.0–4.0 cm2. The aortic valve is well visualised on coronal view and

with multiplanar reconstruction (MPR) on coronal threechamber view and parallel at the valvular plane itself.

A bicuspid aortic valve is present in 1–2% of the population and often results in complications such as aortic valve stenosis and/or regurgitation.

The mitral valve is composed of a saddle-shaped fibrous annulus, two leaflets (a semicircular anterior leaflet and a rectangular posterior leaflet), two commissures, two papillary muscles (anterolateral and posteromedial) and chordae tendineae, which are fibrous tendons that arise from the papillary muscles and insert on the free edges of the leaflets.

The normal mitral valve area during opening in diastole is

4.0-5.0 cm2.

The mitral valve leaflets close with some overlap to prevent regurgitation.

The mitral valve can be visualised on two-, three- and

four-chamber views and on SA MPR (Fig. 12.20).

The pulmonary valve contains a fibrous annulus, three cusps and three commissures separating the cusps. Optimum imaging views are the sagittal plane showing the RVOT and pulmonary valve, and with MPR at the valvular plane itself.

If the pulmonary cusps are easily visible, they are likely to be thickened.

The tricuspid valve has three cusps (anterior, superior, inferior).

The tricuspid valve is usually moderately visualised, due to the thin cusps; its optimal views are transverse or fourchamber long- and short-axis views.

Pulmonary Veins

CT provides excellent view on the left atrium and pulmonary veins that can be used as a road map for guiding radiofrequency catheter ablation therapy.

Volume rendering and transverse views show the pulmonary vein and left atrium anatomy well. Orthogonal

sagittal views may be used for pulmonary vein ostium evaluation.

Other Structures

CT also visualises other (cardiovascular) structures in the same acquisition, including cardiac veins (see Fig. 12.13) and the normal pericardium

being visualised as a thin line.

Pulmonary CT angiography is the imaging test of first choice in patients with suspected pulmonary embolism and aortic CT angiography is the preferred imaging technique for evaluating patients with suspected acute aortic syndrome.

Other thoracic structures beyond the heart and great vessels—the hilum, lungs, chest wall and bones—can be optimally visualised by viewing the images at the appropriate window-width and window-level settings.

ECHOCARDIOGRAPHY

Cardiac ultrasound is currently one of the most important

imaging techniques in clinical cardiology because it is quickly performed, readily available (even at bedside) and bears low costs.

Echocardiography has evolved from M-mode ultrasound to 2-D and, recently, to 3-D image orientation. Echocardiography uses high-frequency ultrasound (2.0– 7.5 MHz), and the nature of the ultrasound waves are such that the use of echocardiography is harmless and no x-rays are involved.

Ultrasound waves do not traverse interfaces with air (lung) or bone (rib/sternum) and are attenuated by body fat.

Therefore, in patients with chronic obstructive pulmonary disease and in obese patients, suboptimal windows with limited quality are almost inevitable.

Cardiac and vascular anatomy can be assessed with 2-D echocardiography and cardiac and vascular function can be assessed with ECG traced cine images.

The temporal resolution of the cine images depends

on the various settings and ranges typically from 30 to 100 frames per second (temporal resolution: 10–33 ms). With the use of the Doppler technique, blood-flow velocities can be measured to estimate pressure gradients in a non-invasive fashion and colour Doppler allows for non-invasive assessment of blood flow.

The Doppler techniques are particularly important for the assessment of valvular function.

Since the focus of this chapter is mainly on cardiac

anatomy, functional and Doppler aspects are not addressed.

Trans-thoracic echocardiography consists of several standard views and usually starts with the patient in the left lateral decubitus position at the left parasternal position at the third to fourth intercostal space.

Then, apical views are performed from the apex of the heart.

In the supine position, subcostal views and suprasternal views can be obtained.

Additional customoriented views may be obtained depending on the clinical questions.

The parasternal position enables LA and SA views. The parasternal long-axis view (Fig. 12.24) shows the anteroseptal and the inferolateral/posterior wall of the LV.

This view is used to assess end-diastolic and

end-systolic LV dimensions and normal values are derived from this orientation.

The dimensions of the left atrium, the aorta and the RVOT and left ventricular outflow tract can also be measured from this view.

Furthermore, identification of the aortic valve and mitral valve is possible.

By rotating the transducer 90 degrees, the parasternal SA view at the level of AV allows assessment of the right atrium, left atrium, tricuspid valve, RVOT (in transverse

orientation from the parasternal long-axis view), pulmonary veins, pulmonary valve and the interventricular septum.

Of note, the view of the AV is a transverse orientation

from the parasternal long axis and provides clear identification of the aortic leaflets and also the pulmonary artery branches may be identified. At the level of the basis of the LV, all six basal segments of the myocardium referring to the 17-segment model can be identified. Furthermore, a part of the RV, mitral leaflets and, occasionally, the moderator band are shown.

At the mid-level of the LV, the six mid-segments of the myocardium from the 17-segment model are identified, as well as a mid-portion of the RV and the papillary muscles.

The last parasternal SA view is the apical view and shows the four apical segments.

The apical views show the apex of the heart usually on top and the atria on the bottom of the image. The first apical view shows the LV, RV, left atrium and right atrium and is, therefore, named the 'fourchamber'

view, although the left atrium and right atrium are not real chambers.

Furthermore, the interatrial septum (consisting of the primary and secondary parts; Fig. 12.30B), the pulmonary veins, mitral valve, tricuspid valve and the septal and lateral myocardium are identified.

With a 90-degree rotation of the transducer from the

four-chamber view, the two-chamber view is obtained,

showing the LV with the anterior and inferior myocardium, and the left atrium as the second 'chamber'. From the four-chamber view, the five-chamber view is then obtained, showing the four chambers and the aorta as the fifth chamber.

This view identifies the anteroseptal- and inferolateralposterior myocardium, the aortic valve and the left ventricular outflow tract.

When the regular four-chamber view is angulated towards the RV, the apical RV view is obtained, showing a greater part of the RV, and allows assessment of

right ventricular function.

The subcostal views are performed via a sub-xiphoid approach with the transducer in the direction of the heart and show again a four chamber view, which has the advantage of a detailed view on the pericardium and the pericardial space to assess pericardial effusion.

This view is often used after thoracic operations in which the apical and parasternal windows are usually limited. Also, the inferior vena cava is seen and the inferior vena cava dimension, indicative of right atrial pressure, can be measured.

The last standard view is the suprasternal view obtained from the suprasternal notch and this view enables assessment of the proximal ascending aorta, the aortic arch and its upper side branches and the descending aorta.

Valves

Apart from the above-mentioned structures, echocardiography is particularly suitable for assessing valvular anatomy and function with Doppler techniques. All four cardiac valves can be assessed with regular

2-D echocardiography but in clinical practice, most lesions affect the aortic valve and mitral valve. Echocardiographic example of a normal

aortic valve (a detail from the parasternal SA aorta view;

allows identification of the three leaflets.

In case of a bicuspid aortic valve, echocardiography can distinguish the anatomy of a true bicuspid valve or a bicuspid valve with fused leaflets with a raphe.

Also, the mitral valve anatomy can be looked at with 2-D

echocardiography in the parasternal long-axis view, the apical fourchamber view and the two-chamber view.

For detailed assessment of the cardiac valves, transoesophageal echocardiography can also be performed. Compared with trans-thoracic echocardiography, transoesophageal echocardiography provides closer views on the valves and atria with less attenuation since the oesophagus is situated posteriorly to the heart with almost no interposed tissue.

The main disadvantage is discomfort for the patient, sometimes even requiring light anaesthesia.

Three-dimensional echocardiography was introduced for identifying valvular anatomy, and examples are.

Three-dimensional images provide a better orientation of

the valve anatomy in relation to the surrounding structures.

However, acquisition and spatial and temporal resolution of 3-D images are still to be improved.

Congenital Heart Disease:

General Principles and Imaging

INTRODUCTION

Although rare, with an incidence of 8 per 1000 births, congenital heart disease (CHD) has increased in prevalence due to the success of surgical and medical management in childhood.

A significant proportion of patients with repaired CHD surviving to adulthood fall under the care of cardiologists outside tertiary centres for congenital cardiac care.

Specialist cardiovascular and general radiologists require an understanding of the underlying morphological abnormalities and their physiology, methods of repair and how potential complications may be detected and assessed in their practice, using appropriate imaging techniques, such as echocardiography, magnetic resonance imaging (MRI), cardiac magnetic resonance (CMR) and computed tomography (CT).

CHD is *any* developmental malformation of the heart. The spectrum of disease falling into this classification ranges from simple lesions—for example bicuspid aortic valve—through to more complex diseases involving single ventricle lesions, such as hypoplastic left-heart syndrome.

The underlying causes of CHD remain relatively poorly understood, although the epidemiology suggests a genetic basis contributing to the majority of CHD. Aneuploidies—for example, trisomy 21 (Down syndrome, septal defects) and monosomy X (Turner syndrome, bicuspid aortic valve and coarctation)—are the earliest identified causes and account for 10%–20% of CHD.

Copy number variations (small to large deletions or duplications) lead to altered dosage of genes and may

represent another important mechanism; an example is Del22q11, which causes DiGeorge syndrome (interrupted aortic arch, tetralogy of Fallot (TOF), truncus arteriosus). Unfortunately, the cause of CHD in most

patients remains unknown.

CLINICAL PRESENTATION

The clinical presentation of CHD in infancy may be dominated by a number of physiological states.

1. Left-to-Right Shunts: Redirection of blood from the systemic (left) to the pulmonary circulation (right) may occur at atrial, ventricular or great vessel level.

A proportion of already oxygenated blood is recirculated to the lungs with each heartbeat, resulting in inefficiency.

The volume of the shunt and its location accounts for the observed signs.

Chambers and vessels receiving the excessive volume

enlarge and high pulmonary blood flow results in pulmonary plethora.

Typical examples include atrial septal defects (ASDs), ventricular septal defects (VSDs) and patent ductus arteriosus (PDA).

Patients are pink but increasingly breathless with larger shunts.

2. Compromised Systemic Perfusion: This may result from low stroke volume of a systemic ventricle (hypoplastic left-heart syndrome), outflow tract obstruction (critical aortic stenosis (AS)) or aortic

obstruction (interrupted aortic arch or coarctation). The clinical picture is one of poor peripheral perfusion, with low-pulse volume; patients may be pink or blue (cyanotic).

The ductus arteriosus may provide an effective temporary bypass for the obstruction, facilitating systemic perfusion with deoxygenated or mixed blood; however, as the duct closes (some days after birth), life-threatening systemic or

lower body hypoperfusion ensues and, often, pulmonary venous hypertension.

Therapy is directed at maintaining the patency of

the arterial duct using intravenous prostaglandins, intensive care for critically ill patients and planning for surgical relief of the obstruction.

2. Pulmonary Venous Congestion: Obstruction to pulmonary venous return results in increased

pulmonary venous pressure (elevated pulmonary capillary wedge pressure); at progressively higher transvascular gradients, oncotic pressure is exceeded and extravasation of fluid into the interstitial and alveolar space occurs.

Obstruction may occur in the pulmonary venous pathway (total anomalous pulmonary venous connection, TAPVD), in the atrium (cor triatriatum) or at the level of the left ventricle (LV) inflow (supravalvular, valvular or subvalvular mitral stenosis or mitral regurgitation).

Pulmonary venous congestion may also occur as a function of elevated left atrial pressure secondary to LV diastolic dysfunction; increased LV end diastolic pressure (valve disease, aortic coarctation, myocardial disease).

The degree of pulmonary venous hypertension determines

the clinical presentation.

Patients with severe obstruction may present with hypoxia, cyanosis and dyspnoea caused by pulmonary oedema, whilst patients with less severe obstruction may remain pink but may present later with failure to thrive.

The following three physiological states predominantly account for patients with cyanosis.

4. Low Pulmonary Blood Flow: Reduction in pulmonary blood flow is commonly caused by obstruction to outflow from the right ventricle (RV), e.g. TOF or severe pulmonary stenosis (PS).

The increased resistance to RV outflow results in a redirection of systemic venous return to the left heart

(right to left shunt) via an interatrial communication

(patent foramen ovale or ASD) or a VSD. Elevated

pulmonary vascular resistance (PVR) without anatomical obstruction may also result in shunt redirection. As lung function is normal, any pulmonary venous blood returns to the left atrium fully saturated and mixes with the shunted systemic venous blood; however, because

pulmonary flow is so low, there is insufficient oxygenated blood in the mix, resulting in cyanosis.

5. Parallel Circulations: This occurs in transposition of the great arteries (TGA), where the aorta arises from the morphological right ventricle and the pulmonary artery from the left ventricle.

In this condition, deoxygenated systemic venous return recirculates into the aorta and the oxygenated pulmonary venous return recirculates to the pulmonary artery, a situation clearly incompatible with life.

Patients can only survive if there is sufficient mixing of the streams (shunt); this can occur best at atrial level through a large interatrial communication, less well at ventricular level (via a VSD) and even less well at great vessel level (via a PDA).

Critical cyanosis may be managed medically by maintaining patency of the PDA by prostaglandins,

but may require the creation of an artificial interatrial communication using cardiac catheterisation until definitive treatment by surgically switching the great vessels. 6. Intracardiac Mixing: Complete intracardiac mixing of blood may occur at atrial level (common atrium), ventricular level (all univentricular hearts) or great artery level (common arterial trunk).

Patients are expected to be mildly cyanosed, depending on the relative amount of deoxygenated blood in the mix, and breathless, according to the amount of pulmonary blood flow.

Later Clinical Presentation

The majority of adult patients with CHD are survivors from childhood.

This group may present with an interesting array of problems related to residual lesions or deteriorations of their initial repair or palliation (heart failure, valve regurgitation, conduit stenosis, baffle leaks).

They require life-long surveillance for anticipated problems arising from the 'unnatural history' of their underlying disorder.

New presentations of CHD continue beyond infancy into adulthood, usually because the underlying disorder has not yet produced symptoms.

Common lesions include left-right shunts, such as ASDs,

VSDs or partial anomalous pulmonary venous drainage, which only begin to be symptomatic in older patients; milder forms of LV or aortic obstruction such as coarctation of the aorta or valvular AS, which did not

compromise systemic perfusion, may progress and
become symptomatic in later childhood or adulthood; and milder forms of RV obstruction such as PS.

A very rare late presentation of CHD is congenitally corrected TGA (atrioventricular (AV) and ventriculoarterial discordance).

Here, the right atrium connects to the left ventricle, then the pulmonary trunk, and the left atrium to the right ventricle, then the aorta.

Whilst blood flow is 'normal', the right ventricle is the systemic ventricle and may fail late in life or even found to be undiagnosed until a post-mortem study.

An important presentation for unrepaired CHD is that of pulmonary arterial hypertension (PAH).

PAH is a common complication of adult

congenital heart disease (ACHD), affecting up to 10% of patients.

PAH related to CHD is characterised by a rise in PVR with normal left atrial *ASDs*, Atrial septal defects; *PDA*, patent ductus arteriosus; *TAPVD*, total anomalous pulmonary venous connection; *VSDs*, ventricular septal defects.

SUMMARY BOX: Major Modes of Clinical **Presentation of**

Congenital Heart Disease

- Left-to-right shunt (e.g. ASDs, VSDs, PDA).
- Compromised systemic perfusion (e.g. critical aortic stenosis).

- Pulmonary venous congestion (e,g, obstructed TAPVD).
- Low pulmonary blood flow (e,g, tetralogy of Fallot).

• Parallel circulation (e,g, transposition of the great arteries).

• Intracardiac mixing (e,g, truncus arteriosus).

MORPHOLOGICAL DESCRIPTION AND SEQUENTIAL

SEGMENTAL ANALYSIS

A significant diversity of morphological abnormalities may be responsible for the physiological phenomena described above and although initial management of an infant simply requires correct classification of the initial physiological pattern, subsequent surgical correction and medical management requires a precise anatomical diagnosis.

The potential intrinsic complexity of CHD necessitates a systematic scheme of nomenclature that captures precisely the unique anatomy of each patient, called sequential segmental analysis.

Using this approach, the clinician describes how the components of the heart and blood vessels are connected.

This entails describing atrial situs (location of the atrial chambers and whether they are of left or right morphology), atrioventricular (AV) connections, ventriculo-arterial (VA) connections and other associated lesions in turn.

Any cross-sectional imaging technique may be used for

this purpose but transthoracic echocardiography is most

commonly used for routine inpatient and outpatient assessment.

In more complex lesions or when echocardiography provides an inadequate assessment (e.g. poor acoustic windows), CMR represents a powerful non-invasive technique giving morphological and haemodynamic

information that echocardiography alone cannot provide.

Sequential Segmental Analysis

Step 1—Atrial Situs

Atrial situs is determined by an assessment of the morphology of each atrial appendage.

Correct identification of the atrium allows the subsequent determination of the AV connection.

The atrial appendages are the most consistent feature of the atrial mass; indeed, the venous attachments to each atrial chamber can form a variety of combinations.

The right atrial appendage is a triangular shape, with a broad base.

In the normal heart the morphological right atrium is located to the right of the morphological left atrium (situs solitus).

The right lung is trilobed, with a shorter, early-branching bronchus and the left lung is bilobed.

In addition, the inferior vena cava (IVC) is to the right of

the abdominal aorta, with a right-sided liver and left-

sided spleen.

In situs inversus the mirror image of the normal anatomy is present.

Isomerism of the left atrial appendages is usually associated with bilateral bilobed lungs, polysplenia and IVC interruption.

Isomerism of the right atrial appendages is usually associated with bilateral trilobed lungs, asplenia and a midline liver.

In isomeric lesions there is often a common AV junction (instead of two separate and offset left and right junctions) with varying degrees of AV septal defect (AVSD).

Gut malrotation is associated with both right and leftsided isomerism.

Step 2—Ventricular Morphology

Determination of ventricular morphology allows analysis of AV and ventriculo-arterial connections.

An AV connection is described as 'concordant' when the atria are connected to the expected ventricle (i.e. left atrium with left ventricle and right atrium with right ventricle); 'discordant' if the left atrium is connected to the right ventricle and right atrium to the left ventricle; 'ambiguous' if there is isomerism of the atrial appendages (e.g. two morphologically right atria connected prominent pectinate muscles that extend around the right AV valve, whilst the left atrial appendage is a more elongated, tubular structure and has less extensive pectinate muscles that are confined within the appendage.

The most common lesions involve inversion of situs, or isomerism of the left or right atrial appendages.

The non-cardiac thoracic and abdominal organs usually (but not always) demonstrate a similar 'sidedness' to that of the atrial chambers.

to a left and right ventricle, respectively (one connection is concordant, the other discordant)); and, finally, 'univentricular' if both atria predominately connect to a single ventricle.

Irrespective of AV concordance,

the AV valve is always concordant with the ventricle that is the tricuspid valve connects to the morphological right ventricle and the mitral valve connects to the morphological left ventricle.

The most distinguishing feature of the tricuspid valve is the direct attachments to the septum of cords from the septal leaflet.

Unlike the tricuspid valve, the mitral valve has no direct septal attachments.

The septal insertion of the tricuspid valve is more apical (apically 'offset') than that of the mitral valve and these features aid determination of the ventricular morphology. The muscular structure of the ventricles also differs, with the RV being more trabeculated than the LV, with a

muscular infundibulum and mid-ventricular 'moderator band'.

Although they are different in normal subjects, the size, shape and degree of trabeculation of the ventricles are not good indicators of ventricular origin, as all are dependent on load effects.

Step 3—Ventriculo-Arterial Connection

Description of ventriculo-arterial connections represents the final element of sequential segmental analysis. This entails describing how each great vessel (aorta, pulmonary artery [PA], or common trunk) is connected to its respective ventricle. A ventriculo-arterial connection

may be concordant (RV-PA, LV-aorta), discordant (RVaorta, LV-PA), double outlet (e.g. RV-PA and aorta) or single outlet (e.g. LV and RV to common arterial trunk). The aorta and pulmonary arteries are defined by their typical branching patterns.

Three-dimensional balanced steady-state free-precession (b-SSFP) and contrast-enhanced magnetic resonance angiography (MRA) techniques are particularly useful in determining the arrangement of the great vessels and the

connections with their respective ventricles.

Step 4—Identification of Other Abnormalities

Other abnormalities to be considered include abnormal systemic and pulmonary venous connections, intracardiac shunts, valvar abnormalities and vascular abnormalities (PDA, right/left aortic arch, coarctation/ interruption or pulmonary arterial abnormalities).

In general, most congenital cardiac lesions are single abnormalities that are easily described; however, almost any combination of abnormalities and connections can occur, and using the sequential segmental analysis method, the description of all conceivable combinations

and diagnoses is possible.

PHYSIOLOGICAL AND FUNCTIONAL ASSESSMENT

Whilst the correct morphological analysis is a critical first step, it must be incorporated into a complete physiological assessment to understand the clinical problem.

It is helpful to briefly consider a few parameters

relating to normal cardiac function, which are commonly calculated by techniques such as CMR.

Stroke Volume: This is the volume of blood (mL) pumped (displaced) by a ventricle with each heartbeat. The displaced volume is calculated by subtracting the volume of the ventricular cavity at end diastole from the volume at end systole.

In the normal heart the stroke volume for each ventricle is the same and is also the same as the forward flow in the associated great artery.

It may not be the same in the presence of a shunt or a regurgitant valve.

Here, discrepancies in interventricular volumes or great artery flows help locate and quantify the severity of shunts and valve regurgitation.

Cardiac Output: This is how much blood each ventricular

chamber pumps in 1 minute (L/min).

It is calculated by multiplying the stroke volume (or great artery flow (mL)) by the heart rate (stroke (beat)/min). Cardiac output is increased by physiological stress (e.g.,

exercise that increases both heart rate and stroke volume) and depressed in conditions that reduce either heart rate (bradyarrhythmias) or stroke volume (dilated cardiomyopathy, heart failure).

Ejection Fraction: A useful assessment of gross systolic cardiac function is the percentage of blood ejected from the heart during each beat.

This is calculated by dividing the stroke volume by the end-diastolic volume.

Ejection fraction may be decreased if the systolic performance of the ventricle is impaired (cardiomyopathy).

Flow: Using phase-contrast MRI, blood flow and its direction (mL/beat) across valves and vascular structures can be quantified.

In valvar regurgitation, backward flow can be measured and expressed as a regurgitant fraction (backward flow/forward flow).

Combined with cine imaging, flow data can be used to calculate and localise intra-/extracardiac shunts.

NON-INVASIVE IMAGING TECHNIQUES

Imaging is fundamental to the diagnosis of CHD and is required at all stages of patient care.

An ideal non-invasive technique for imaging of CHD should be able to accurately and reproducibly delineate all aspects of the anatomy, including intracardiac abnormalities and abnormalities of extracardiac vessels; evaluate physiological consequences of CHD such as measurement of blood flow and pressure gradients across stenotic valves or blood vessels; be cost-effective and portable; provide data from fetal life to adulthood; not cause excessive discomfort and morbidity; and not expose patients to harmful effects of ionising radiation. No single technique has fulfilled these entire requirements and in the delivery of a CHD service, the imaging techniques discussed below play an important complementary role.

Echocardiography

Echocardiography is the initial imaging technique used in the evaluation of patients with suspected CHD and should always be performed before other techniques are used. In most patients, echocardiography alone provides sufficient information to complete the diagnostic evaluation

using a sequential segmental and functional analysis. In UK clinical practice, paediatric cardiologists have traditionally performed echocardiography;

however, more recently, neonatologists and radiologists have begun to use echocardiography in patients with suspected CHD where paediatric cardiology services are not immediately available.

Cardiac anaesthetists also increasingly perform perioperative assessment using transoesophageal

echocardiography.

For a more comprehensive discussion of echocardiography in CHD, the reader is referred to Lai et al.

Magnetic Resonance Imaging

As previously alluded, CMR probably provides the most comprehensive assessment available from a single noninvasive imaging technique but its immobility, cost and limited availability constrain its general applicability.

In our clinical practice it is used to define the morphology and physiology of the most complex CHD cases as well as providing routine surveillance for patients with repaired CHD such as TOF and TGA.

Extracardiac anatomy, including the great arteries and systemic veins, can be delineated with high spatial resolution.

Vascular and valvular flow can be assessed, shunts can be quantified and myocardial function can be measured accurately with high reproducibility, regardless of

ventricular morphology.

Finally, CMR provides high-resolution, isotropic,

three-dimensional data sets. This allows for reconstruction of data in any imaging plane, facilitating visualisation of complex cardiac anomalies without the use of ionising radiation.

The majority of CMR images are acquired using cardiac (vectorcardiograph) gating during a single breath-hold to

reduce the artefacts associated with cardiac and respiratory motion.

For a complex case, CMR is performed over approximately 1 hour, although this time can

be considerably reduced if a focused question is being addressed or by the incorporation of newer real-time sequences.

Imaging sequences can be broadly divided into:

• 'Black blood' spin-echo images, where signal from blood is nulled and thus not seen—for accurate anatomical imaging.

• 'White blood' gradient-echo or SSFP images, where a positive signal from blood is returned—for anatomical, cine imaging and quantification of ventricular volumes, mass and function.

• Phase-contrast imaging, where velocity information is encoded for quantification of vascular flow, including newer 4D (or 7D) phasecontrast imaging.

• Contrast-enhanced MRA, where non-echocardiogram (ECG)-gated 3D data are acquired after gadolinium contrast medium has been administered for thoracic vasculature imaging.

• Tissue characterisation imaging, where innate contrast between normal myocardium and disease can be imaged: T1 mapping and extracellular volume imaging, T2 oedema imaging, T2* iron deposition imaging, late gadolinium enhancement fibrosis and necrosis

imaging.

All these sequences can be acquired in a single breathhold, reducing the overall time in the CMR machine and enabling the acquisition of accurate data in the majority of patients.

Importantly, 'white blood' cine images can be acquired in a continuous short-axis stack along the heart, enabling accurate quantification of RV and LV function.

Imaging should be performed in the presence of a cardiovascular MRI clinician in conjunction with an MRI technician to ensure that the appropriate clinical questions are answered.

A comprehensive treatment of cardiovascular MRI is provided in the textbook by Bogaert and colleagues.

Computed Tomography

Cardiac CT is now well established for the assessment of the thoracic vasculature and large and small airways. Recent advances in multidetector CT (MDCT) with highpitch spiral and volumetric scan modes have resulted in significant advances in spatial and temporal resolution and a decrease in radiation dose, often less than 1 mSv.

Most studies are fully diagnostic without ECG gating. ECG-triggered and ECG-gated acquisitions should therefore only be utilised when cardiac motion may produce non-diagnostic images. Newer-generation scanners permit rapid imaging with minimal motion artefact and thus remove the need for gated scans and general anaesthesia.

General anaesthesia may still be needed to control breathing when detailed coronary artery imaging is required.

The route and contrast administration protocol are critical to successful imaging.

The right upper limb in most cases provides a good site of administration of contrast (avoiding streak artefact from contrast in the innominate vein, which can obscure head and neck vessels).

Generally, a biphasic injection protocol using a power injector will be appropriate, deploying a neat contrast bolus (1–3 mL/kg) followed by saline chaser.

In neonates and low-bodyweight children requiring small

absolute contrast doses, short contrast transit time increases the risk of suboptimal opacification of essential structures.

Using the full available contrast dose, reducing the injection rate and mixing the contrast bolus with saline increases the transit time. Empirically, dilution with saline to 70%–80% contrast concentration gives good opacification.

Visual bolus triggering from a low-resolution monitoring scan is our favoured approach for timing of acquisition because it more reliably ensures opacification of the appropriate cardiac structures. This does incur a small, added radiation dose, which can be minimised by delaying monitoring toward the end of the injection and reducing the frequency of monitoring scans.

A pre-scan timing bolus is often avoided because it

utilises part of the contrast bolus available and increases the radiation dose.

We currently use MDCT for the following indications in patients with CHD:

• Thoracic aorta disease, including vascular rings where airway information is critical.

Aim for a narrow bolus via right arm injection to avoid

streak artefact from innominate vein over head and neck vessels.

• Pulmonary arterial disease. Aim for a prolonged contrast transit time to ensure all sources of pulmonary blood supply are evaluated.

The infradiaphragmatic area should also be imaged because collateral vessels may arise here.

If thromboembolic disease must be excluded, a rapid undiluted bolus must reach the pulmonary arteries—this

can be extremely challenging in cavo-pulmonary connections.

• Coronary artery abnormalities. ECG-triggered or ECG-gated protocols may be necessary.

Pharmacological heart rate reduction may be required in

cases of very high heart rate.

• Pulmonary venous abnormalities. Aim for a prolonged contrast transit time to ensure there has been ample time for delayed filling of venous collaterals or slow flow segments.

Care should be taken to avoid very dense contrast that may cause streak artefact and obscure anomalous entry points into the systemic venous system.

The scan should include the hepatic inferior vena cava in suspected infra diaphragmatic total anomalous pulmonary anomalous connections or partial anomalous pulmonary venous drainage to the hepatic inferior vena cava.

• Patients with implants or devices that cannot be imaged by CMR.

Imaging should take account of the material to be imaged. Higher kVp, edge-enhancing reconstruction kernels and iterative reconstruction improve the diagnostic accuracy.

Conventional Radiology

Although CHD may be suspected on the basis of the chest x-ray (CXR), the technique precludes the detailed morphological assessment necessary for diagnosis and determination of specific underlying pathology.

The diagnostic accuracy of the CXR in the assessment of infants with asymptomatic murmurs is poor. Despite its

poor performance as a screening tool, CHD may be suspected on the basis of a CXR because of higher specificity, but false-positive rates are significant.

The CXR, however, is not dispensable and remains important in the subsequent management of patients with CHD, particularly in three

situations:

1. Postoperatively, for identification of the position of intravascular catheters, chest drains and endotracheal tubes.

2. Identification of postoperative complications: consolidation, collapse, pleural effusion, pneumothorax, pneumomediastinum or pericardial collections.

3. Perioperative, *physiological* assessment of the lungs and cardiomediastinal contour.

Diagnostic Features

The ubiquity of the CXR in clinical practice warrants discussion of the diagnostic features that should prompt suspicion of CHD.

It is suggested that when reporting images, the reader avoid such terms as 'boot-shaped' or 'snowman' typically associated with specific lesions because they can be misleading and often erroneous.

More appropriate is a descriptive consideration of the cardiomediastinal contour and lungs, attempting to evaluate the predominant physiological profile discussed above. The reader may find it helpful to read this section in conjunction with the section on clinical presentation.

The Pulmonary Vasculature

Radiologically normal pulmonary vascularity is present in CHD if the patient is not in heart failure, if no large shunt is present and if there is no significant reduction in pulmonary blood flow: for example, mild

PS.

The pulmonary vasculature may, however, look normal on the conventional radiograph even in the presence of significant CHD.

Increased pulmonary perfusion (pulmonary plethora) is recognised by enlarged central and peripheral pulmonary arteries and veins in all zones, as occurs in situations with increased pulmonary blood flow: ASD, VSD and PDA with large left-to-right shunts.

Decreased pulmonary perfusion (oligaemia) (Fig. 13.4) is caused by a reduction in pulmonary blood flow and is typically a phenomenon of cyanotic CHD.

Dark lungs and sparse pulmonary vascular markings suggest the diagnosis. Image acquisition must be optimal because overexposure will significantly confound correct interpretation.

Pulmonary blood flow may be impaired by obstruction to normal flow through the right heart: for example, tricuspid atresia, TOF and PS.

Pulmonary venous congestion and oedema in CHD

is caused by functional or anatomical obstruction to pulmonary venous return.

In addition to oedema formation caused by increased transvascular pressure gradients, consideration should be given to other pathological processes such as increased vessel leakiness caused by acute lung injuries.

The usual adult pattern of basal oedema, resulting in alveolar hypoxia and constriction of lower pulmonary vasculature and redirection to the apices does not apply to

the supine infant.

As pulmonary venous pressure increases, there is

progressive accumulation of radiological signs, beginning with redistribution (in older children/adults), progressing to interstitial oedema (perivascular haziness, peribronchial cuffing, Kerley B lines, subpleural effusions) and, finally, migration of extravasated fluid centrally, resulting in perihilar alveolar consolidation.

Systemic to pulmonary collateral vessels.

Abnormal systemic arterial connections to the pulmonary vasculature may occur as an adaptive mechanism to inadequate pulmonary blood flow. This usually occurs

in the setting of pulmonary atresia associated with VSD, in which the RV and pulmonary arteries are not in continuity; instead, discrete MAPCAs (major aortopulmonary collateral arteries) and non-discrete

networks of bronchial arteries are the source of pulmonary blood flow.

It may also occur during staged management of the single ventricle.

They may be recognisable by a nodular lung pattern in the central third of the lung parenchyma, with many small, rounded, opacities representing enlarged bronchial arteries seen end-on.

Pulmonary arterial hypertension may complicate unrepaired CHD.

Increased pulmonary blood flow caused by left-right shunting in unrepaired ASD, VSD or PDA gradually causes changes in the pulmonary vasculature, which, over time, leads to increased PVR and overt hypertension.

The central pulmonary arteries enlarge and the peripheral pulmonary arteries become smaller than normal. In cases where pulmonary pressure exceeds systemic pressure, shunt reversal occurs, resulting in cyanosis—as occurs in Eisenmenger syndrome.

Heart Size, Shape and Position

Abnormalities of the position of the cardiac apex, aortic arch, liver and stomach may be determined from examination of the CXR.

The presence of situs inversus and left aortic arch may be discerned; however, this may or may not be associated with underlying CHD.

Some assessment of global and regional heart size is possible and should be described; however, the limitations of CXR in this regard should be considered.

In a study comparing echocardiographical assessment of

cardiac enlargement in 95 consecutive paediatric outpatients, the sensitivity of the CXR to identify cardiomegaly was only 58.8% (95% confidence

index (CI): 32.9 to 81.6), specificity was 92.3% (95% CI: 84.0 to 97.1).

SPECIFIC LESIONS

In the following discussion lesions have been classed as acyantoic and cyanotic for convenience.

It is important to understand, however, that in various situations a lesion typically described in this way may present in the opposite manner, perhaps caused by the presence or absence of a particular morphological feature or the imposition of altered haemodynamics such as elevated PVR.

For example, TOF with minimal outflow tract obstruction may have no cyanosis or a VSD that is so large as to

facilitate complete intracardiac mixing may produce cyanosis.

Furthermore, certain lesions do not fit easily into either category: for example, Ebstein anomaly of the tricuspid valve when mild is acyanotic but in its severe form is cyanotic.

Similarly, congenitally corrected TGA, although

acyanotic, is better understood when discussed alongside its cyanotic relative, simple TGA. For further illustrations and images.

ACYANOTIC LESIONS

Septal Defects

Atrial Septal Defects

ASDs are the most common congenital heart defect detected in adults.

Irrespective of their type and location, isolated ASDs cause left-to-right shunting at the atrial level.

This leads to atrial dilation, predisposing to tachyarrhythmias, and RV volume overload.

The degree and direction of atrial shunting can be modified by AV valve function and ventricular compliance.

The presence of an ASD is an independent risk factor for

thromboembolic stroke. This is caused by the ability of thromboemboli,

originating either in the right atrium or venous vasculature, to pass

through the ASD into the systemic circulation.

ASDs are, anatomically and developmentally, a heterogeneous group of lesions.

The specific nature of the ASD influences the natural history and management of this disease.

Ostium secundum defects make up 80% of ASDs and are located in the fossa ovalis.

These defects are caused by failure of the septum

secundum to form closure of the ostium secundum.

Other forms of ASD are more properly termed interatrial communications because they do not occur in the true morphological atrial septum.

The ostium primum defect is actually a component of a common AV junction, also known as an AVSD.

This defect usually occurs together with some degree of AV valve abnormality.

The sinus venosus defect is found at the junction of the

right atrium and either one of the caval veins.

This type of ASD is less common and is always associated with partial anomalous pulmonary venous drainage.

The least common type of ASD occurs in the coronary sinus and is termed an unroofed coronary sinus.

In this case, there is deficiency of the coronary sinus wall as it passes behind the left atrium, allowing shunting from left to right through the coronary sinus itself.

The management of ASDs has changed in recent years, particularly with the increasing use of transcatheter ASD closure devices.

Previously, surgical closure was only considered when a large left-to-right shunt led to RV volume overload, atrial dilation and symptoms; however, with the advent of transcatheter techniques, management has become more aggressive.

Transcatheter techniques are only viable in patients

with small-to-medium-sized ostium secundum defects that have adequate margins with which to anchor the device.

Deficiency of the anterior or posteroinferior rim of the defect usually precludes transcatheter closure.

Patients with large ostium secundum defects, or defects with deficiency of the anterior or posteroinferior rim. or with sinus venosus lesions, usually require operative repair.

The clinical aim is to complete ASD closure before the development of cardiac failure or atrial dilation and

timing of intervention depends on the haemodynamic status of the patient; thus, evaluation of ASDs requires definition of type and location of the defect, quantification of the net shunt (pulmonary flow: systemic

flow (Qp:Qs)), detection of any intra-atrial thrombus, assessment of RV volume and systolic function and visualisation of the pulmonary venous anatomy.

Visualisation of most interatrial communications is possible by transthoracic echocardiography, although sinus venosus or coronary sinus defects are challenging without a high level of suspicion.

In addition, detection of pulmonary venous abnormalities is technically difficult using the transthoracic approach. Transoesophageal echocardiography is the main imaging technique used to assess ASDs (particularly at the time of catheter and surgical closure); however, transoesophageal echocardiography cannot be used to accurately quantify the shunt (Qp:Qs) and it can be difficult to delineate pulmonary venous anatomy.

CMR has, therefore, a significant role in the diagnosis and pre-interventional assessment of ASDs.

Three-dimensional whole-heart techniques, with isotropic resolution, allow accurate multiplanar reformatting with no loss of resolution.

These techniques allow 3D rendering of the atrial anatomy.

Multislice 2D gradient-echo techniques can be used to assess the dynamic 3D anatomy of the defect, and phasecontrast through-plane flow techniques can accurately size the cross-sectional dimensions of the defect.

Multiple or fenestrated defects may also be diagnosed.

Haemodynamic assessment is also an important part of the evaluation of ASDs.

Invasive catheterisation has historically been used to quantify left-to-right shunts.

Quantification of left-to-right shunts using velocityencoded phase-contrast MRI compares well to invasive catheterization results.

It has the benefit of being non-invasive and does not require exposure to ionising radiation.

Ventricular overload can also be accurately assessed using multislice b-SSFP short-axis imaging and can give important information influencing the timing of intervention.

Key imaging goals

• Assess defect location, diameter and margin size suitability for device anchorage.

• Quantify right heart volume and function—assess volume overload.

• Quantify shunt (see Fig. 13.5D).

• Look for sinus venosus defect, which has an associated partially anomalous pulmonary venous drainage.

• Look for signs suggestive of elevated PVR—RV hypertrophy, systolic flattening of the interventricular septum and notching of the pulmonary artery flow curve.

Atrioventricular Septal Defects

An atrioventricular septal defect (AVSD) is a lesion caused by a deficiency of the tissues that normally interpose the atrial and ventricular chambers.

The involved tissues include the atrial primum septum, the AV valves and the inlet portion of the ventricular septum.

The feature shared by all AVSDs is a common AV junction guarded by a common AV valve, which may have either one or two orifices.

The common AV junction can be discerned by the loss of the usual 'offset' of the tricuspid and mitral valves in the normal heart.

The valve, even when it has two orifices, is no longer

referred to as a mitral and tricuspid valve; instead they are called left and right AV valves.

The common valve typically has five leaflets, referred to as the superior bridging, right anterosuperior, right inferior/mural, inferior bridging and left mural leaflets.

The relative deficiency of the septal structures and the number of valve orifices give rise to the classification as complete (both ASD and VSDs and single valve orifice), intermediate/incomplete (VSD with two valve orifices) and partial (ASD with two valve orifices, also called

an ostium primum ASD).

Another clinically useful description is the

relative size of the ventricular chambers, allowing for classification as balanced (equal-sized ventricles) or unbalanced (disproportionate ventricles).

AVSD can be associated with other cardiac abnormalities, including TOF, subaortic stenosis, atrial isomerism and ventricular hypoplasia, which modify the presentation, prognosis and surgical management.

The diagnosis of AVSD is made in the neonatal period on the basis of a transthoracic ECG. Other imaging techniques are usually not required.

Surgical repair is carried out at approximately 3 to 4 months of age and certainly before 6 months of age to prevent the development of pulmonary vascular disease. The repair involves closing the septal defects and creating competent left and right valves from the common AV valve tissue. The association of AVSD with trisomy 21 is well known; repair in this group is associated with *lower* mortality than non-trisomy 21.

Additional imaging techniques including CMR may be useful in the long-term management of patients with repaired AVSD, including surveillance for important late complications such as AV valve regurgitation.

Ventricular Septal Defects

The ventricular septum is a complex, almost helical 3D structure.

VSDs are the commonest form of CHD in childhood. Physiologically, the defect causes left-to-right shunting and the magnitude of the shunt determines the signs and symptoms.

The volume of the shunt depends on the size of the defect and the relative resistances of the systemic and pulmonary circulations; at birth the PVR is high, reducing the magnitude of the shunt (it also remains high for longer in patients with left-to-right shunts, explaining why infants may initially be asymptomatic).

The degree of shunting is usually estimated by measuring the velocity of blood crossing the defect by ECG; if PVR is normal, higher-velocity jets indicate that the expected pressure difference between chambers is preserved and are termed 'restrictive' defects; low-velocity jets suggest

the LV and RV have similar pressures and that the defect is 'unrestrictive'.

The exact volume of the shunt cannot be determined

accurately by ECG, but can be qualitatively inferred by relative chamber dilatation.

As described above for ASDs, shunt volume can be measured using velocity-encoded phase-contrast CMR.

The commonest location is the perimembranous region, accounting for 80% of VSDs; many small perimembranous VSDs close spontaneously.

The rest of the ventricular septum is muscular and has three components: inlet, outlet (subarterial) and midmuscular regions.

The appropriate management depends on the type and size of the defect.

ECG is the mainstay of diagnosis but CMR can provide accurate 2D and 3D images, which are particularly useful in complex defects.

Multislice 2D gradient-echo techniques can be used to assess the dynamic 3D anatomy of the defect; however, multislice techniques suffer from poor through-plane resolution.

Three-dimensional b-SSFP techniques with isotropic resolution allow accurate multiplanar reformatting, permitting 3D rendering of the ventricular anatomy. Image acquisition during the diastolic period is useful in assessing the anatomy of a VSD and its relationship to valvular structures.

• Quantify shunt (note LV stroke volume contributes to the PA forward flow during systole).

• Look for signs suggestive of elevated PVR—RV hypertrophy, systolic flattening of the interventricular septum and notching of the pulmonary artery flow curve.

• Quantify ventricular volume.

• Assess aortic valve regurgitation and associated abnormalities.

• Post repair, assess integrity of VSD patch.

Abnormalities of the Great Vessels

Patent Ductus Arteriosus

The arterial duct, in fetal life, connects the pulmonary artery to the aortic arch, allowing blood ejected from the RV to bypass the highresistance pulmonary circulation and enter the descending aorta.

The ductal tissue constricts after birth in response to changes in the blood gas composition.

If the duct fails to close beyond the first few days of

life, it is termed a PDA. The PDA permits a left-to-right shunt from the aorta into the pulmonary artery throughout the cardiac cycle.

This leads to increased pulmonary blood flow and dilation of the left heart.

The length and diameter of the PDA and the relative resistances of the pulmonary and systemic circulations determine the volume of the shunt, which, in turn, determines the signs and symptoms of the lesion.

A common neonatal problem is the failure of the ductus

arteriosus to close in the premature infant. In this situation, a PDA can confound the management of the lung disease associated with prematurity and can prolong ventilation.

It can be comprehensively assessed using an ECG in infancy but in older patients the duct may not be easily demonstrated.

CMR may be required to visualise and quantify the shunt in the same way as described for ASD and VSD.

Coarctation of the Aorta

Coarctation of the aorta is a luminal narrowing of a short section of the aorta.

It occurs most commonly at the site of insertion of the ductus arteriosus and is thought to develop because of the presence of excessively integrated ductal tissue around the aortic isthmus, which contracts along with the ductus arteriosus at the time of birth.

In severe coarctation, systemic perfusion will be compromised with ductal closure in infancy caused by increased luminal narrowing and the loss of the

anatomical bypass provided by the duct itself. In less severe coarctation, the body maintains perfusion by renal mechanisms, resulting in systemic hypertension manifested proximal to the coarctation.

Collateral arterial vessels develop over time to maintain lower body perfusion as the patient grows.

Patients may present with unexplained hypertension as a

teenager or adult and are at increased risk of the attendant micro- and macrovascular complications.

Treatment in infancy is usually by surgical excision of the narrowing but in older subjects, balloon angioplasty may be undertaken.

Patients remain at increased risk of hypertension even if repaired in infancy.

An ECG is used in the initial diagnosis of infants, children and adults.

Typical ECG features include increased systolic and diastolic velocities across the stenosis.

CMR or CT may be required in the postoperative phase to establish if there is re-coarctation (up to 35% of patients in some series), aneurysmal dilatation or LV hypertrophy

secondary to hypertension. CMR is preferred to CT if there are no contraindications.

Imaging is crucial to establish the location and degree of stenosis, length of coarctation segment, associated aortic arch involvement (such as tubular hypoplasia), the collateral pathways (internal mammary and posterior mediastinal arteries), presence and relationship to an aberrant subclavian artery, post-stenotic dilatation and LV hypertrophy.

Three-dimensional contrast-enhanced MRA can show the severity and extent of involvement.

An assessment of collateral flow by measuring flows in

the proximal and descending aorta can be performed. Reassessment of collateral flow following treatment can

also be used to assess the success of the treatment.

In patients with metal stents, high flip angle gradientecho sequences can be used to overcome metal artefact and assess luminal narrowing.

CMR can also be used to assess secondary pathology in patients with coarctation: for example, aortic root for dilatation associated with a bicuspid aortic valve (frequency in coarctation of 15%), aortic valve incompetence and stenosis and ventricular function and LV mass (an indirect indicator of increased LV afterload).

Late after repair, imaging is used to assess for recoarctation (especially in hypertensive patients), pseudoaneurysm and dissection.

Thoracic aorta morphology is highly variable and represents the combination of repair-type residual hypoplasia, stenosis and dilatation.

Interrupted Aortic Arch

Interrupted aortic arch results from a structural discontinuity between the ascending and descending aorta.

The site of interruption relative to the brachiocephalic arteries forms the basis of classification.

There is a high incidence of DiGeorge syndrome, which is also associated with variable thymic hypoplasia, the presence of which can be examined.

Physiologically, systemic blood flow is provided distal to the interruption by deoxygenated blood via a patent arterial duct.

The lower body will be cyanosed and circulation may be compromised following duct closure.

The site and length of interruption and any associated anomalies can be demonstrated well by CMR. Following repair, assessment is similar to that of coarctation. It is important to interrogate the repair site for residual narrowing, assess for the presence of LV outflow tract obstruction due to posterior deviation of the outlet septum and look for residual intracardiac shunts.

Three-dimensional MRA and 3D whole-heart imaging are particularly useful.

Cine imaging will identify regions of flow acceleration.

Abnormalities of the Aortic Arch and Vascular Rings

The aortic arch connects the ascending aorta to the descending aorta.

Abnormalities of this vascular section include disorders of sidedness.

Arch sidedness refers to the side of the trachea that the aortic arch passes as it crosses a mainstem bronchus: namely, left, right and double.

In certain circumstances, the morphological pattern of the aortic arch and related structures (its branches or the ductus/ligamentum arteriosus) may produce a vascular ring, which can compress the trachea or oesophagus,

producing symptoms of stridor or dysphagia.

This usually involves the retro-oesophageal course of either the descending aorta or an aberrant subclavian artery combined with a ligamentum arteriosus on the opposite side of the arch, although non-ring structures such as anomalous origin of the left pulmonary artery from the right pulmonary artery or 'pulmonary artery sling' may also cause vascular compression.

Cross-sectional imaging (CMR or CT) can be regarded as the gold standard for the assessment of the aortic arch. For CMR, imaging begins with a simple transverse stack from the level of the larynx to the diaphragm.

This information is augmented by 3D MRA.

Using this information, patent vascular structures compressing the trachea/oesophagus can easily be identified.

It is important to remember that some important components of a vascular ring may not be patent and

thus remain invisible on imaging—for example, the ligamentum arteriosus; however, clues to these structures often remain and include dimples opposite the side of the aortic arch, a diverticulum opposite the side of the arch or if the proximal descending aorta descends on the opposite side of the arch.

Valvular Heart Disease

Aortic Valve Disease

Congenital aortic valve disease is predominated by stenosis, which may occur at subvalvular, valvular or supravalvular levels.

The haemodynamic consequence of AS is pressure loading of the LV and the development of secondary concentric hypertrophy.

Aortic regurgitation (AR) is usually a manifestation of treated AS (e.g. balloon angioplasty) or secondary to pathological dilatation of the aortic root, which can occur in connective tissue disease (e.g., Marfan syndrome, Fig. 13.10).

The haemodynamic consequence is volume loading of the LV and eccentric hypertrophy (dilatation).

Doppler ECG assessment of transvalvular pressure gradient is the commonest technique to assess severity of AS; however, transvalvular pressure gradients are flow dependent and measurement of valve area represents, from a theoretical point of view, the ideal way to quantify

AS.

Inaccuracies in both gradients and valve area, however, require consideration of a combination of flow rate, pressure gradient and ventricular function, as well as functional status that may require multimodality contributions.

AS with a valve area less than 1.0 cm2 is considered severe; however, in patients with either unusually small or large body surface area, indexed areas, with a cut-off value of 0.6 cm2/m2, is helpful.

The presence of valvular stenosis can be identified by loss of signal on CMR cine images.

Velocity mapping can be used to establish an accurate peak velocity across the stenosis, and planimetry can assess the aortic valve area.

An ECG is also used to routinely assess AR, in particular using colour Doppler (to determine extension and width of regurgitant jet) and continuous-wave Doppler (to assess the rate of decline of aortic regurgitant flow and holodiastolic flow reversal in the descending aorta);

however, these are semiquantitative measures. CMR permits precise assessment of the regurgitant volume and assessment of the volume and function of the eccentrically hypertrophied LV.

It also allows assessment of the effective regurgitant orifice area.

Subvalvular AS is the least common form of AS. It may be an isolated lesion, or associated with hypertrophic cardiomyopathy or, occasionally, following repair of AVSD.

Valvular AS covers a broad spectrum of anomalies, including critical AS presenting with compromised systemic perfusion in infancy sometimes associated with the hypoplastic left-heart syndrome, through to mild AS caused by a bicuspid aortic valve.

Supravalvular AS is a rare lesion that is typically associated with underlying Williams (Williams–Beuren) syndrome, a genetic disorder of the connective tissue
protein elastin.

Elastin is responsible for the normal distensibility of the aorta during systole and its subsequent recoil during diastole.

In Williams–Beuren syndrome, the reduced net

deposition of arterial wall elastin leads to increased proliferation of arterial wall smooth muscle cells and multilayer thickening of the medial of large arteries, resulting in the development of obstructive hyperplastic

intimal lesions.

A characteristic hourglass narrowing of the aorta develops at the sinotubular junction but in approximately 30% of cases there is a diffuse, tubular narrowing of the ascending aorta, often extending to the arch and the origin of the brachiocephalic vessels.

Pulmonary Valve Disease

Obstructive lesions dominate congenital pulmonary valve disease, similar to the aortic valve, whereas significant pulmonary regurgitation (PR) is most often iatrogenic following surgical or catheter-based interventions for obstructive lesions.

Trivial PR is commonly discerned on an ECG and can be considered physiological. Important congenital PR can occur in the absent pulmonary valve syndrome.

According to the site, PS is classified as valvular,

subvalvular (infundibular) or supravalvular.

It can occur as isolated finding or in constellation with other lesions such as VSDs or more complex lesions (TGA, TOF), which may significantly alter the clinical presentation.

PS and PR have physiological consequences analogous to aortic valve stenosis and regurgitation. In the former, RV pressure rises to overcome the obstruction and maintain stroke volume.

Compensatory mechanisms include RV hypertrophy.

In PR, volume loading of the RV results in progressive dilatation and dysfunction, which is associated with adverse clinical outcomes.

In pulmonary valve stenosis, the pressure gradient across the valve is used to assess severity of the lesion more so than in left-sided valve conditions due in part to the difficulty of obtaining an accurate assessment of pulmonary valve area.

The systolic pressure gradient is derived from

the transpulmonary velocity flow curve using the simplified Bernoulli equation (pressure gradient = $4 \times$ velocity2).

Mild stenosis is defined by a peak velocity under 3 m/s on continuous-wave Doppler, which corresponds to a peak gradient under 36 mm Hg; moderate stenosis is defined by a peak velocity from 3 to 4 m/s, corresponding to a peak gradient between 36 and 64 mm Hg; severe stenosis is characterised by a peak velocity above 4 m/s, corresponding to a peak gradient above 64 mm Hg.

CMR assessment of PS can be performed in a similar fashion as outlined for AS, above.

CMR is the gold standard for the assessment of PR. As described for AR, quantification of the regurgitant volume and its effect on the RV can be precisely determined.

RV volume and function cannot be accurately assessed by 2D ECG but CMR measurements have been shown to be associated with adverse outcomes and can aid decision making for timing of interventions.

Ebstein Anomaly of the Tricuspid Valve

Ebstein anomaly is a congenital abnormality of the tricuspid valve and right ventricle with the following components:

(1) adherence of the tricuspid leaflets to the underlying myocardium (failure of delamination);

(2) anterior and apical rotational displacement of the functional annulus;

(3) dilation of the 'atrialised' portion of the right ventricle with variable degrees of hypertrophy and thinning of the wall;

(4) redundancy, fenestrations and tethering of the anterior leaflet;

(5) dilation of the right AV junction (the true tricuspid annulus); and

(6) variable ventricular myocardial dysfunction.

The degree of displacement determines the clinical presentation.

In severe cases there is gross right atrial enlargement and raised right atrial pressure.

The anomaly is usually associated with an ASD and, therefore, right-to-left shunting at the atrial level and subsequent cyanosis may occur.

Ebstein anomaly results in gross enlargement of the cardiac contour with a prominent curved right atrial border on the plain chest radiograph.

Treatment is problematical, although expert surgical repair of the tricuspid valve is possible in some centres. Imaging should assess the valve morphology, quantify ventricular function and volume and quantify right atrial enlargement.

Coronary Artery Abnormalities

Anomalous Coronary Arteries

Coronary artery abnormalities are rare. They involve anomalous proximal and epicardial courses of the left coronary artery (LCA) and right coronary artery (RCA) or, rarely, anomalous *origin* of the LCA from the pulmonary artery (ALCAPA).

Anomalous course is increasingly important when interventions are carried out in close proximity to a coronary artery—for example, percutaneous pulmonary valve implantation into the pulmonary trunk and compression of the LCA. Similarly, the course of the coronary arteries are important during surgical repair of TOF; a transannular patch repair may not be possible if the LCA arises from the RCA and passes anterior to the RVOT tract.

ALCAPA results in the LCA territory being supplied with low-pressure deoxygenated blood; blood must therefore be supplied by collateralization from RCA.

Patients experience myocardial ischaemia and usually present approximately 4 to 5 months of age when PVR drops and LCA blood flow is reduced.

Patients with sufficient collateralisation may survive

to adulthood.

Treatment usually involves surgical reimplantation of the

coronary artery using a button transfer technique or coronary artery bypass grafting.

From an anatomical point of view, coronary anomalies are classified according to the coronary artery involved, the origin of the anomalous coronary artery and the anatomical course of the proximal segment.

From a clinical point of view, the anomalies are divided into 'benign' and 'malignant' lesions.

The latter, especially those of ALCAPA and in cases where the LCA arises from the RCA and passes between the aortic root and RVOT tract or pulmonary artery, have an increased risk for developing myocardial ischaemia and sudden cardiac death.

Even with multiple projections, the precise location of the

proximal course of the vessel in a patient with an abnormal origin of a coronary artery can be difficult to depict with conventional angiography and

echocardiography; however, CMR and CT angiography provide reliable visualisation of the root of the arteries and the coronary artery tree.

CYANOTIC CONGENITAL HEART DISEASE

Tetralogy of Fallot

TOF is the most common cyanotic congenital heart defect, with an incidence of approximately 420 per million live births.

It is caused by malalignment of the muscular outlet septum, which leads to RVOT obstruction, a subaortic VSD with aortic override and RV hypertrophy.

This produces the physiological pattern of low pulmonary

blood flow and right-to-left shunt as described above. Current management consists of early single-stage reconstructive surgery, with closure of the VSD, and relief of the RVOT obstruction, usually by the placement of a transannular patch (across the pulmonary valve annulus) to enlarge the RVOT.

Staged reconstruction is still required if there is

severe cyanosis caused by a very narrow RVOT or significant hypoplasia of the central pulmonary arteries. In such cases, a systemic-to-pulmonary anastomosis called a modified Blalock–Taussig (BT) shunt is placed

(usually) between the innominate artery and the right pulmonary artery.

This shunt is then taken down during subsequent

definitive repair.

A transthoracic ECG is the imaging technique of choice for the initial diagnosis and assessment of paediatric patients; however, CMR imaging does have a role in untreated or shunt-palliated patients in delineating pulmonary artery anatomy or excluding significant pulmonary artery distortion.

While early surgical mortality from complete repair

of TOF is very low in the modern surgical era, residual anatomical and haemodynamic abnormalities are almost universal.

These include right ventricle dilatation from PR, RVOT aneurysm, RVOT obstruction, pulmonary artery stenosis,

residual atrial or VSD, tricuspid valve regurgitation and aortic root dilatation.

CMR has emerged as the gold standard for the assessment of the right ventricle in patients with repaired TOF.

Two-dimensional b-SSFP sequences can be used to define RVOT anatomy and quantitatively assess RVOT dilatation or stenosis.

Velocity-encoded phase-contrast MR can accurately quantify the degree of PR and can be used to measure

peak velocities at the level of RVOT obstruction, as well as differential regurgitation in the branch pulmonary arteries.

MR assessment of RV function/volumes with multislice short-axis b-SSFP imaging is particularly important when determining the timing and evaluating the impact of invasive therapeutic strategies.

Transposition of the Great Arteries

TGA is the second-commonest cyanotic CHD diagnosed in the first year of life, with an incidence of 315 per million live births.

In this condition, the aorta arises from the right ventricle, and the pulmonary artery from the right ventricle (ventriculo-arterial discordance).

This produces the physiological pattern of parallel circulations described above, which is incompatible with life.

Treatment for TGA patients was revolutionised with the introduction of the Senning procedure, in which an intraatrial baffle was used to divert blood from the right atrium to the left ventricle, and the left atrium to the right ventricle.

A variation to the Senning procedure, the Mustard procedure uses a pericardial patch or prosthetic material to construct the intra-atrial baffle; however, although both these procedures produce a physiologically normal circulation, the patient is still left with a systemic RV. Patients surviving with these repairs may have unique complications, including pulmonary venous pathway or baffle obstruction, baffle leaks and failure

of the systemic RV.

Currently, the arterial switch operation has become

the procedure of choice. In this operation, the great vessels are transected above the valve sinuses and sutured to their appropriate ventricle; the coronary arteries arising below this transection level must also be transferred separately. I

n cases of TGA associated with a VSD and sub-PS, the Rastelli procedure (where blood from the LV is channelled through the VSD to the aorta) is preferred.

Congenitally Correct Transposition of the Great Arteries

Congenitally corrected transposition of the great arteries (CCTGA) is a rare disorder characterised by both AV discordance and ventriculoarterial discordance (right

atrium to left ventricle to pulmonary artery to lung and left atrium to right ventricle to aorta).

Therefore, although the heart is anatomically abnormal, it is physiologically normal in terms of the pulmonary and systemic circuits.

This lesion does not usually cause cyanosis; however, many of the problems are similar to those experienced by patients with TGA, particularly those treated by

an atrial switch operation, and thus a systemic RV. CCTGA may be asymptomatic and in some patients is an incidental finding; however, the majority of patients with CCTGA have associated cardiac lesions, the most common being VSD.

PS is present in approximately 50% of cases and tricuspid valve abnormalities (e.g.Ebstein abnormality) are found in 20% of cases.

Even without associated abnormalities, most patients with CCTGA eventually develop systemic ventricular failure. The main role of imaging is in evaluation of associated lesions, quantification of ventricular function and assessment of postoperative complications.

Pulmonary Atresia

Pulmonary atresia is the lack of luminal continuity and absence of blood flow from the RV to the pulmonary artery.

Pulmonary atresia can be separated into two groups depending on the presence of a VSD.

As the diagnosis and subsequent management of these two groups is different, it is useful to consider them separately.

Pulmonary atresia with a ventricular septal defect. This is the more common variant and is considered by some to be a severe form of TOF, with a subaortic VSD and overriding aorta.

Pulmonary blood flow is supplied via MAPCAs.

Surgical repair aims to establish RVOT to the pulmonary

artery continuity with a homograft (RV-PA conduit), repair the VSD and bring the aortopulmonary collaterals into the pulmonary circulation.

As with TOF, the main role of imaging in patients with pulmonary atresia and a VSD is assessment of postoperative complications.

The most common long-term complication is homograft failure: usually mixed stenosis and regurgitation leading to RV dysfunction.

Conduit stenosis is often secondary to calcification of the non-viable homograft and although calcified tissue is difficult to visualise using CMR, it is clearly seen on CT. Other long-term complications are similar to those found in TOF.

Pulmonary atresia with an intact ventricular septum. This is the lass common variant of pulmonary atrasia

This is the less common variant of pulmonary atresia. There is complete atresia

of the pulmonary valve in conjunction with a variable

degree of hypoplasia of the tricuspid valve and RV cavity.

The type of surgical repair depends on the size and shape of the RV cavity.

The presence of an RV infundibulum allows a biventricular repair.

If the RV cavity is small, then single ventricular physiology is established and angiography demonstrates large venous sinusoids in the RV wall.

Imaging assessment is considered in the section below on the single ventricle.

Double Outlet Right Ventricle

The term double outlet right ventricle (DORV) refers to any cardiac anomaly in which both the aorta and the pulmonary artery originate, predominantly or entirely, from the right ventricle.

In this situation the LV has no direct outlet to either great vessel and must eject blood into the RV through a VSD. Rarely there may be no VSD and then the LV

is very hypoplastic.

The physiological picture and type of surgical correction depend on the arrangement of the great vessels and the anatomy of the VSD.

Cyanosis is not invariably present and depends on the degree of PS.

The most common variant is a normal arrangement of the great vessels and a subaortic VSD.

This variant is often referred to as the 'Fallot's

type' because it is often associated with PS and has a similar presentation.

DORV may also be associated with an anterior aorta and a subpulmonary VSD known as the 'Taussig–Bing' anomaly.

Surgical correction for the 'Fallot type' variant consists of patch closure of the VSD, which redirects blood to the aorta, and correction of any PS.

For the 'Taussig–Bing' anomaly the surgical approach depends on the presence of pulmonary obstruction. In the absence of pulmonary obstruction, correction consists of patch closure of the VSD and arterial switch.

In the presence of obstruction, LV flow is tunnelled through the VSD to the aorta and an RV-PA pathway is established, known as the Rastelli procedure.

Imaging plays an important role in preoperative assessment.

The 3D anatomy of the VSD and the arrangement of the great vessels are well visualised by CMR and are particularly important when deciding

the type of surgery.

Black-bood spin-echo CMR of the VSD has been shown to compare well with surgical findings and is able to indicate the optimal type of repair.

Common Arterial Trunk

Common arterial trunk (truncus arteriosus) is defined as a

single arterial trunk arising from both ventricles, which overrides a large misaligned VSD.

The pulmonary, systemic and coronary arteries all

originate from the trunk. This produces the physiological pattern of cyanosis caused by intracardiac mixing as the simultaneous ejection of both ventricles into the common trunk merges streams.

The classification

of common arterial trunk relies on the branching pattern of the pulmonary artery.

In type I, a short main pulmonary artery arises from

the common trunk and subsequently divides.

In type II, the right and left pulmonary arteries originate from the posterior wall of the common trunk and, in type III, the right and left pulmonary arteries emerge from the lateral wall of the common trunk.

The truncal valve is often abnormal, with varying degrees of stenosis and insufficiency.

Approximately 40% of truncal arches are on the right side, with most truncal arches rising higher in the mediastinum than the normal aortic arch.

Surgical repair consists of reconstruction of the common trunk to produce a systemic vessel from the left ventricle, patch closure of the VSD and establishment of a right ventricle-to-pulmonary artery conduit.

The main role of CMR is in assessment of postoperative complications (homograft failure, truncal valve

regurgitation and VSD patch leak).

Imaging can be used to better delineate the vascular anatomy before surgery.

Anomalous Pulmonary Venous Connection/Drainage

Pulmonary veins may connect abnormally to a site other than the left atrium—usually the right atrium, systemic vein or coronary sinus.

If all the veins connect abnormally, then it is described as total anomalous pulmonary venous connection/drainage (TAPVD), and if less than all the veins connect abnormally (usually only 1) then it is termed partial

anomalous pulmonary venous connection/drainage (PAPVD).

In TAPVD, a complete left-to-right shunt causes all of the pulmonary venous return to mix with systemic venous return.

Survival is dependent on obligatory right-to-left shunting of the mixed pulmonary venous and systemic venous blood, usually at atrial level.

PAPVD is an acyanotic condition, which results in a physiology similar to an ASD.

The number of veins involved determines the magnitude of the shunt and the clinical symptoms.

It is associated with superior and inferior sinus venosus ASD.

In TAPVD the pulmonary veins coalesce posterior to the left atrium but do not drain into it.

Drainage from this venous confluence to the

right atrium may be:

(a) via either an ascending vein to the innominate vein and then to the superior vena cava (SVC) (supracardiac, 50% of patients;

(b) the coronary sinus directly into the right atrium

(cardiac, 15% of patients);

(c) via a descending vein, which passes through the diaphragm into either the IVC or portal venous system

(infracardiac, 25% of patients, Fig. 13.18); or

(d) a mixture of these routes may coexist (mixed, 10% of patients).

The infracardiac type is usually associated with a degree of obstruction as the descending vein passes through the diaphragm; thus, unlike the supracardiac and cardiac variants, which present with a left-to-right shunt, intracardiac mixing and cardiac failure, the clinical picture for infracardiac TAPVD is potentially more severe, with superimposed pulmonary venous hypertension, resulting in tachypnoea, tachycardia, liver enlargement, cyanosis, pulmonary oedema and respiratory distress.

Symptoms usually appear within 24 to 36 hours of birth. Importantly, the diagnosis of infracardiac TAPVD can be missed on a ECG and must always be considered in the differential diagnosis of pulmonary oedema on the neonatal chest radiograph. Associations of TAPVD are complex cardiac anomalies such as isomerism of the atrial appendages, AVSD, PS, DORV, hypoplastic left-heart syndrome (HLHS), common arterial trunk, TGA and aortic coarctation.

The anomalous pulmonary venous connection is easily

visualised with ultrasound but in patients with poor ECG acoustic windows, cross-sectional imaging with CMR and CT is very useful, often avoiding the need for a diagnostic x-ray catheterisation.

SINGLE VENTRICLES

The term single ventricle covers a wide range of different cardiac morphologies: for example, HLHS tricuspid atresia or pulmonary atresia with intact ventricular septum; however, pragmatically, the term can be used to describe a group of patients who, following surgical 'correction', have a circulation supported by one ventricle.

Modern palliative management has resulted in long-term survival for many patients who would otherwise have died as infants.

This division extends the narrower morphological classification to include also functionally single ventricle: for example, where two ventricles are connected by a large VSD, which cannot be surgically septated because of AV valve apparatus straddling the ventricular septum

(chordae tendinae attached to the septal crest or opposite ventricle) or when there is significant imbalance of the ventricular chambers, such as in double inlet left ventricle.

The ultimate management goal is the creation of a single ventricle circuit with separation of the systemic and pulmonary circulations—a Fontan or total cavopulmonary circulation (TCPC)—such that the single

ventricle pumps blood into the systemic circulation and systemic venous return is directed to the pulmonary circulation without a ventricular pump.

This is performed in a step-wise surgical fashion involving two or three stages.

Systemic to Pulmonary Artery Shunt

In patients with inadequate pulmonary blood flow caused by a hypoplastic RV (tricuspid atresia or pulmonary atresia with intact ventricular septum) and in patients with HLHS as part of the Norwood procedure, the first stage involves the creation of a systemic-to-pulmonary artery shunt such as a modified BT shunt (see Fig. 13.13D). This is a temporizing procedure in infants, in whom PVR is not low enough to proceed immediately with a bidirectional superior cavopulmonary connection (BCPC), known as the Glenn procedure.

Bidirectional Glenn Circulation

The second stage in the creation of a single ventricular circulation is the BCPC.

It is usually performed at approximately 3 to 9 months of age.

In this procedure, an anastomosis is created between the

SVC and the right pulmonary artery (such that the SVC blood flows into both arteries), and the SVC-RA junction oversewn.

Any previous surgical systemic-to-pulmonary artery shunts are also taken down at this time.

Imaging should be used to assess branch pulmonary

artery narrowing and pulmonary venous obstruction; otherwise.

The circulation may fail.

Fontan Circulation

The Fontan circulation can be completed by a number of different surgical methodologies, but in the current era it is performed by the creation of an intracardiac (lateral tunnel) or extracardiac conduit between the IVC and the pulmonary arteries.

This is known as a total cavopulmonary connection (TCPC).

It is usually performed between 18 months and 5 years of age.

The classical Fontan operation involved connection of the SVC to the RPA (non-bidirectional Glenn procedure) and connection of the right atrium to the LPA.

Right atrial dilatation is the major complication of the classical Fontan procedure and may cause arrhythmias,

thrombosis or pulmonary vein compression, which can lead to failure of the Fontan circulation. CMR allows evaluation of the branch pulmonary arteries and their systemic venous connections and can be used

to accurately assess ventricular function.

Despite optimal medical and surgical management, the intrinsic shortcomings of the TCPC invariably manifest as late attrition during follow-up.

This situation, known as a 'failing Fontan', is particularly difficult to manage because systemic venous hypertension and low cardiac output may result in peripheral oedema and unusual clinical syndromes of plastic bronchitis and

protein-losing enteropathy.

Ultimately, this may result in death or necessitate highrisk cardiac transplantation.

Recent Developments in Cardiac Magnetic

Resonance Imaging

Hybrid Catheter/Cardiac Magnetic Resonance

Imaging Laboratory

In a hybrid catheter/CMR lab (XMR), a cardiac catheterisation laboratory is connected to the CMR scanner via a shielded sliding door.

A mobile patient table facilitates seamless transfer between the two techniques.

As a diagnostic tool, XMR is particularly helpful in the evaluation of haemodynamic problems in which pressureonly or flow-only measurements result in an incomplete characterisation of the problem: for example.

In the assessment of PVR for pulmonary hypertension. XMR can also be used to guide structural intervention and electrophysiological studies and in these cases would reduce the radiation exposure, which is particularly important in children and infants.

Fetal Cardiac Magnetic Resonance Imaging

Fetal CMR is an emerging technique that may prove complementary to a fetal ECG.

As with other ultrasound techniques, a fetal ECG can

be affected by maternal body habitus or other situations that reduce acoustic windows.

Fetal CMR is affected by several technical challenges

related to the fetal cardiac dimensions and fast heart rate, fetal motion and the lack of fetal ECG trace for gating.

Post-Mortem Cardiac Magnetic Resonance Imaging

Perinatal and paediatric cardiac autopsies have an important role in the counselling of parents with regard to the cause and implications of death of their child. Recently, less invasive post-mortem MR has been proposed as an alternative for conventional autopsy and could be used as the first-line assessment for structural heart disease in this situation.

Post-mortem imaging allows an opportunity to investigate the heart in situ before dissection and both post-mortem CT and postmortem MRI have shown excellent accuracy in detecting most clinically significant cardiac lesions in the perinatal and paediatric population.

If all non-diagnostic and positive post-mortem CMR scans were referred for conventional autopsy, very few diagnoses would be missed based upon currently available evidence.

Three-Dimensional Printing

Three-dimensional-engineered replicas of different anatomical structures have been used extensively in different fields of medicine over the past 20 years.

As the manufacturing techniques, referred to as 'rapid prototyping, have become more refined over the years, medical researchers have used such 3D models for presurgical planning personalization of prostheses or testing of novel devices.

One of the other benefits of anatomical 3D models is being able to visualise the location and dimensions of the area of interest as an aid in communication, both

within a surgical team and, crucially, between the physician and the patient.

Any 3D cardiac images (CMR, CT or echo) can be used to create a 3D model.

The 3D data needs to be extracted from the images and

then converted into an *.stl* file that can be input into a 3D printer.

The 3D piece can be manufactured using a wide variety of materials to meet the needs of the model—rigid for

patient explanation, flexible for device pre-procedural planning and tissue-like for surgical practice with suturing.

CONCLUSION

CHD is a complex area of medicine that requires a wellintegrated understanding of anatomy and cardiovascular physiology.

Using the principles illustrated in this chapter, cardiovascular imaging can be successfully utilised to guide medical and surgical management of patients

with CHD. An ECG remains the first-line imaging technique; however,

when an ECG cannot provide a complete diagnosis, cross-sectional imaging with CMR and CT is the next line of investigation.

Catheter angiography is usually reserved for problem solving, coronary artery assessment, haemodynamics and for catheter-guided therapeutic procedures.

It is hoped that the complementary nature of imaging techniques has been demonstrated and that when used in combination, ECG, CMR, CT and x-ray catheter angiography can provide a comprehensive assessment of patients with CHD.

Nonischaemic Acquired Heart Disease

Nonischaemic heart diseases (NIHDs) account for nearly half of the cardiac deaths.

This group of diseases is extremely heterogeneous, including cardiomyopathies (CMPs), valvular problems, cardiac masses and pericardial disease.

Modern noninvasive imaging techniques have increased diagnostic accuracy for all these diseases, with consequent decrease in the number of invasive procedures.

ROLE OF IMAGING

In the past, NIHD diagnosis was based on chest radiography and invasive angiography; the introduction of echocardiography has deeply modified the diagnostic approach, as both myocardium and heart chambers are visualised noninvasively, in real time and with the same

examination.

Furthermore, magnetic resonance has increased the role of noninvasive imaging, with a wider field of view, higher contrast resolution and tissue characterisation capabilities, coupled with extremely accurate, operatorindependent functional assessment.

Finally, multidetector electrocardiographic (ECG)-gated computed tomography (CT) has had a deep impact on noninvasive coronary artery imaging; technological improvements have also made CT effective in the assessment and therapeutic planning of NIHDs, particularly in

valve diseases and cardiac masses.

Chest Radiography (CXR)

It still remains the first-line examination in both ischaemic and NIHD.

Its advantages are low cost, noninvasiveness, wide availability and unique information on pulmonary haemodynamics; its downside of course is that it is neither specific nor sensitive, particularly if disease

is not yet at an advanced stage.

Chest x-ray (CXR) interpretation is based on a stepwise procedure:

the chest wall anatomy may explain modification in heart contours; pleural or parenchymal disease may cause nonspecific symptoms such as chest pain.

Analysis of vessel size and distribution which reflect the

haemodynamic status is fundamental in assessing heart disease: size and distribution are strictly related to capillary wedge pressure and pulmonary venous pressure, that equalises left atrial pressure and, consequently, left ventricular end-diastolic pressure (LVEDP).

So, depending on acute or chronic development of the disease, it is possible to obtain a noninvasive qualitative assessment of LVEDP.

Furthermore, a general assessment of heart size determines whether there is cardiomegaly or not; this will help to create a list of possible diseases, with or without cardiomegaly, according to signs, symptoms and other clinical data.

The next step is the analysis of modifications of cardiac

contours in both the frontal and lateral views, which may be helpful in identifying specific chamber enlargement.

Echocardiography

Echocardiography is a noninvasive, portable ultrasound technique that allows high-resolution, two- and threedimensional (2D and 3D) views of the cardiac chambers, valves and pericardium.

These techniques, either using a transthoracic or transoesophageal approach, can assess cardiac anatomy and ventricular function.

When combined with Doppler and colour Doppler techniques, valvular regurgitation and stenosis and

transvalvular pressure gradients can also be assessed.

Echocardiography is the most commonly performed imaging examination in the assessment of NIHDs.

Magnetic Resonance Imaging

Cardiac magnetic resonance (CMR) imaging is rapidly becoming very useful in the assessment of NIHDs. Its role is most valuable in:

(A) serial measurement of ventricular function in patients with CMP (considered superior to echocardiography especially with respect to reproducibility);

(B) evaluation and quantification of valve function, including stenosis and regurgitation;

(C) morphology and extent of involvement in cardiac

tumours; and

(D) value of postcontrast delayed enhancement (also

called late gadolinium enhancement [LGE]) in assessing diagnosis and determining prognosis in many diseases, as hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), as well as many types of

infiltrative myocardial diseases, including sarcoidosis and myocarditis.

Recently introduced new CMR parametric techniques allow for a quantitative evaluation of myocardial tissue, based on changes in T1 (native and postcontrast agent), T2 and T2* (star) relaxation times.

Mapping sequences use different techniques to obtain a series of images at various inversion times, from which a recovery curve is derived; the result is a parametric image that shows the T1 or T2 relaxation values

pixel by pixel.

Changes of T1 relaxation times, although not specific for single disease, can be grouped into different patterns which reflect intracellular alterations of the cardiomyocyte (such us iron overload or glycosphingolipid accumulation in Anderson–Fabry disease [AFD]), extracellular changes in the myocardial interstitium (such us collagen or amyloid proteins accumulation, as seen in myocardial fibrosis or cardiac amyloidosis, respectively) or both (myocardial oedema with increased intracellular and/or extracellular water).

In particular, native T1 lengthens with an increase of

tissue water (as in cases of oedema in acute infarction or inflammation) or an increase of interstitial space (fibrosis or amyloid deposition) and conversely shortens in presence of an iron overload or an intracellular lipid accumulation (as in AFD).

Moreover, T1 mapping performed before and after injection of an extracellular T1-shortening contrast agent is used for calculating a parameter called the extracellular volume (ECV), a measure of the proportion of extracellular space within the myocardium.

Several pathophysiological processes can alter the ECV: it may increase with fibrosis, oedema or other protein deposition, such as amyloid.

Conversely, low ECV values occur in thrombus and fat/lipomatous metaplasia.

Regional myocardial T2 mapping has emerged to directly quantify local myocardial inflammation and oedema.

T2 parametric mapping overcomes some of the limitations of the qualitative evaluation of T2 weighted images such as image quality, low reproducibility and subjective assessment.

Finally, T2* mapping, derived from gradient echo (GRE) sequences, provides an accurate quantification of myocardial tissue iron overload, which is extremely important for clinical management of transfusion dependent haemoglobinopathies (e.g. β -thalassaemia major).

Computed Tomography

Until recently, conventional CT had a limited role in the evaluation of NIHDs.

However, the increasing use of ECG-gated multidetector (>16 slice) CT techniques currently makes cardiac CT a viable alternative in assessing cardiac function.

More recently, cardiac CT has also been shown to be useful in the assessment of valvular function.

However, as yet, CT has no demonstrable advantage over echocardiography and CMR in the evaluation of NIHDs. Furthermore, despite recent reconstruction advances, radiation dose remains an issue.

CARDIOMYOPATHIES

According to the 2006 American Heart Association (AHA) definition, CMPs are 'a heterogeneous group of diseases associated with mechanical and/or electrical dysfunction, usually exhibiting inappropriate hypertrophy or dilatation, due to a variety of causes, often genetic,

confined to the heart or part of systemic disorder'. This classification divided CMPs into primary and secondary; primary CMPs are subdivided into genetic, mixed or predominantly nongenetic and acquired, while secondary CMPs are a variety of diseases that can affect the myocardium.

In 2008, the European Society of Cardiology (ESC) proposed another classification based on different phenotypes (hypertrophic, dilated, etc.) that are subclassified into familial-genetic and nonfamilial-nongenetic.

The AHA classification is more based on pathology, whereas the ESC classification is more clinical, as, for example, a hypertrophic phenotype can be due to many diseases that cause myocardial thickening such as HCM, hypertensive CMP, Fabry disease, amyloidosis, etc.

In this chapter, the phenotype approach will be used, according to the ESC classification.

Hypertrophic Pattern

Increased myocardial thickness can be due to a variety of disease, both familial and nonfamilial.

Among the familial, the *classical HCM* is the most common; it is autosomal dominant and defined as a sarcomere disease (with a number of different mutations) that is characterised by an excessive hypertrophy of the myocardium (not explained by other causes) in a nondilated left ventricle.

Eleven mutations have been recognised, with the most common affecting the β -myosin heavy chain.

Pathologically there is disarray of myocytes with a variable amount of interstitial fibrosis, caused by microvascular bed damage.

Typically, increased septal thickness, exceeding 15 mm, is seen at echocardiography; in the presence of ECG abnormalities and symptoms (e.g. chest pain, shortness of breath and dizziness, but also presyncope, syncope and arrhythmias), increased thickness of the interventricular

septum is sufficient for diagnosis.

Another echocardiographic criterion is a ratio between septal thickness and inferior wall of the left ventricle

at midventricular level exceeding 1.3.

Chest x-ray is often unhelpful: in concentric hypertrophy there may be a rounded third left cardiac contour; this is different from that due to aortic stenosis and systemic hypertension, which both can cause concentric hypertrophy of the left ventricle.

Echocardiography can easily assess myocardial thickness; however, there are many patterns of hypertrophy distribution, not all of them easily recognisable by ultrasound.

Hypertrophy can be asymmetrical or septal, with or without left ventricle obstruction, symmetrical, apical, midventricular, mass-like and noncontiguous.

In asymmetrical or septal forms, 25% of cases show

a systolic obstruction of the left ventricle outflow tract, due to the movement of the anterior leaflet of the mitral valve toward the hypertrophic interventricular septum, caused by the Venturi effect.

This obstruction can be present at rest or only during/following physical exercise; it can easily be recognised at echocardiography and echo-Doppler.

Echocardiography has limitations particularly in apical forms close to the low-frequency probe, and in mass-like forms, where differential diagnosis with tumours can be difficult. In all these cases, and especially when the acoustic window is poor, **magnetic resonance imaging (MRI)** is extremely useful and accurate; it provides precise measurement of wall thickness, is more accurate in left ventricle mass quantification and can easily detect and

quantify right ventricle involvement.

Information on wall thickness can also be easily obtained by cardiac CT; modern CT equipment provides this information at a very low dose (1-3 mSv).

However, the most relevant information that only MRI provides is the presence of interstitial fibrosis; due to the increased extravascular bed of collagen and its impaired wash-out delayed enhancement after administration of contrast agent delineates fibrotic tissue as an area of

'bright' myocardium compared with normal 'dark' myocardium.

The distribution of delayed enhancement can be either diffuse or with selective localisation in the septum and relative sparing of the subendocardial layer (differently from myocardial infarct scar), at the anterior and

inferior septal insertion, or patchy with large foci of intramural enhancement.

Detection of fibrosis is extremely important because it is strictly related to prognosis: a variety of published papers reported the incidence of severe arrhythmias, due to reentry mechanisms, and sudden cardiac death in young patients (<40 years) or progression to heart failure in

older patients (>40 years) with HCM and severe fibrosis

demonstrated at MRI.

MRI findings suggest that the fibrotic tissue probably develops due to impairment of intramural myocardial blood supply: in patients presenting with acute chest pain and focal intramural areas of oedema (acute damage) with a nonischaemic pattern, vasodilator stress perfusion MRI often reveals a reduced myocardial flow reserve, corresponding to areas of fibrosis during late enhancement.

Finally, MRI permits recognition of associated findings, such as mitral regurgitation, and more sophisticated functional evaluation may reveal impairment of diastolic filling and radial or circumferential strains.

Histologically, fibrosis is often global and diffuse in these patients and it may be undetected on LGE imaging because of the absence of normal reference myocardium; furthermore, the evaluation of microscopic interstitial fibrosis is often hampered by the spatial resolution of LGE images; T1 mapping can be helpful in these cases.

Native T1 values are elevated in HCM (Fig. 14.6A) and correlate with wall thickness, suggesting potential clinical utility as a marker of disease severity.

In these patients, ECV is usually elevated, due to extracellular matrix expansion and myocardial disarray;

furthermore, this parameter can differentiate between HCM and athletic remodelling in athlete's heart as the latter shows reduced ECV values, probably due to an increase in healthy myocardium by cellular hypertrophy. In addition to its role in primary diagnosis, T1 mapping can be a valid tool for a quantitative follow-up of the degree of fibrosis, enabling an accurate stratification of risk for adverse events.

The hypertrophic phenotype, characterised by increased myocardial thickness, is also seen in other CMPs; delayed enhanced MRI is particularly useful for determining the differential diagnosis, which includes storage diseases such as AFD, amyloidosis and noninfectious granulomatous diseases (e.g. sarcoidosis).

In these cases, delayed enhancement patterns differ from those of HCM; in AFD it is typically subepicardic in the inferolateral wall, with different presentations in amyloidosis.

Due to the diffuse infiltration by amyloid and its link to gadolinium compounds, it is difficult to null myocardial signal, resulting in diffuse intermediate to-bright signal intensity; alternatively, a patchy intramural pattern can

be present, with small bright spots.

Sarcoidosis can also present with this hypertrophic phenotype; again, patchy pattern of distribution is more frequently seen with small foci, reflecting interstitial distribution of granulomas.

Dilated Phenotype

DCM is defined as a left ventricular dilatation with systolic dysfunction not caused by abnormal loading (as hypertension or valve disease) or coronary artery disease.

A dilated phenotype can be due to many different causes;

among familial forms, autosomal dominant ones are more frequent, due to mutations of cytoskeletal, sarcomeric and other protein genes.

Other forms are X-linked, as muscular dystrophia.

Nonfamilial DCM include end-stage inflammatory diseases (infective and noninfective myocarditis), nutritional deficiencies, endocrine dysfunctions and drug toxicity.

Chest x-ray has limited sensitivity, as cardiac contour abnormalities can be observed only in advanced stages; typically, on frontal view the third left cardiac arch is enlarged, heart size is increased and, eventually, there are signs of left atrium enlargement (carina widening and double contour of second right cardiac arch).

However, the most relevant role of chest x-ray is the evaluation of pulmonary vasculature;

due to increased left ventricular end-diastolic pressure (LVEDP), left atrium, pulmonary veins and capillary wedge pressures increase, with

consequent balanced distribution or caudocranial redistribution of pulmonary vessels.

In case of high-pressure values, further evolution causes pulmonary oedema (interstitial to alveolar). This is the only noninvasive tool to estimate LVEDP.

Echocardiography is considered the first-line examination in clinically suspected DCM; echocardiographic criteria are increased left ventricle end-diastolic diameter, exceeding normal values of 112% after age and body surface area correction, ejection fraction lower than 45% and fractional shortening lower than 25%. Another useful parameter is the spherical index that correlates the left ventricular end-diastolic volume with the long-axis diameter and is increased in DCM.

Furthermore, echocardiography is able to demonstrate regional diffuse hypokinesis, sometimes restricted to apical segments, decreased forward flow velocities across all the valves and dominant E wave (early diastolic filling) at mitral flow interrogation, as well as complications such as mitral and/or tricuspid regurgitation and left ventricle thrombi.

In patients with a poor acoustic window, cardiac MRI is extremely useful, because of the high intrinsic contrast resolution between blood and myocardium; planimetric and volume measurements are extremely accurate and more reproducible than echocardiographic ones even if, in clinical settings, ultrasound measurements are

commonly used.

One of the major contributions of MRI is the differential diagnosis between ischaemic and nonischaemic CMP that is crucial for decision making and treatment planning (revascularisation versus medical therapy and/or transplant); echocardiography in fact has a low specificity and this differential diagnosis is not always easy. Using delayed enhancement technique, MRI is able to easily differentiate an ischaemic DCM, demonstrating subendocardial or transmural scars, whereas in nonischaemic DCM, late
enhancement is absent or faint and limited to mesocardial layers, usually diffuse or septal.

Another important indication for MRI is the evaluation of the left ventricle before resynchronisation therapy. In clinical practice ECG and echocardiography with Doppler interrogation are mostly used, but the significant percentage of patients not responding to implantation—considering the high cost of the procedure—have increased the role of MRI in the preprocedural assessment of the presence of scar tissue in the inferior wall.

Finally, MRI is extremely accurate in thrombus detection;

contrast-enhanced images showed the highest sensitivity, also in areas where echocardiography has false negatives (e.g. close to the apex).

Differential diagnosis of nonischaemic forms is only partially feasible with delayed enhancement technique: in general, intramural or mesocardial enhancement is more frequent in postmyocarditis DCM that in the idiopathic form, but this has to be further investigated and confirmed. Histology is still mandatory in these cases; in other secondary forms, MRI is extremely useful: for example, in dilated end stage of HCM, the pattern and distribution of late enhancement help to establish the correct diagnosis.

The prognostic role of MRI in DCM is still under investigation; data are few and less robust than in HCM for risk assessment; left ventricular remodelling, ventricular tachycardia and sudden cardiac death seem to be related to the presence and amount of late enhancement.

Recently, several studies have investigated the value of T1

mapping.

Similarly to hypertrophic phenotype, DCMs are associated with the development of diffuse myocardial fibrosis during disease progression.

On **MRI** native T1 is increased in DCM (Fig. 14.14) and inversely correlated with wall thickness.

Furthermore, native T1 values were found to be increased not only in areas corresponding to LGE but also in areas without LGE, which suggests that this parameter can also detect interstitial myocardial fibrosis, allowing for initiation of timely management.

ECV measurement reflects myocardial collagen content in DCM and correlates with LV dysfunction, supporting its use as a noninvasive imaging biomarker to monitor therapy response.

ECV values in DCM have been shown to be increased

similar to hypertrophic phenotype; however, this overlap in

ECV between the two phenotypes is to be considered clinically irrelevant because DCM and HCM can be usually distinguished by their different morphological features and ventricular geometry.

When echocardiography proves difficult (e.g. poor acoustic window), cardiac CT can be used as an alternative to MRI to assess ventricular volumes and ejection fraction, but most important, it is useful in differential diagnosis between ischaemic and nonischaemic forms by means of its capability to exclude coronary artery disease. CT is also highly accurate in left ventricle thrombus detection, whereas late enhancement technique is not quite so useful in CT due to its lower contrast resolution compared with MRI.

Restrictive Phenotype

In this phenotype, the increased wall stiffness causes a rapid pressure increase with only small volume increase; this restrictive pattern can occur in a wide range of diseases; by definition, both diastolic and systolic are normal or reduced and wall thickness is normal.

Familial restrictive cardiomyopathy (RCM) is very rare and mostly autosomal dominant; nonfamilial forms are caused by systemic disorders, as amyloidosis, sarcoidosis, haemochromatosis, AFD, carcinoid heart disease, anthracycline toxicity, endomyocardial diseases, with or

without hypereosinophilia (as endomyocardial fibrosis) and endocardial fibroelastosis.

Chest x-ray is frequently unremarkable; only at an advanced stage does left atrial enlargement become evident with signs of increased pulmonary venous pressure, as in mitral stenosis (MS).

Echocardiography often shows normal-sized ventricles, enlarged atria and normal or decreased contractile function; in some cases, as in Löffler syndrome, or endomyocardial fibroelastosis or carcinoid syndrome, endocardial thickening is evident.

Doppler evaluation of mitral flow is particularly important, showing elevated early diastolic velocity, short deceleration

time and low and shortened atrial velocity.

However, these abnormal parameters can be present also in case of constrictive pericarditis, where pericardial stiffness does not allow ventricular filling; in this case, it is important to evaluate pericardial thickness, the interventricular septal kinetics and inferior vena cava flow during deep inspiration and expiration.

The pericardium is not easily assessed by ultrasound, and here either cardiac CT or MR plays a major role; a cut-off value of 4 mm is highly predictive of pericardial constriction, but it is important to remember that pericardial constriction without pericardial thickening can also occur.

MRI can easily assess morphological and functional abnormalities of restriction; T1 and T2 weighted images can help in tissue characterisation.

As previously described, unenhanced and delayed enhancement can be useful in differentiating some diseases, as amyloidosis, sarcoidosis and AFD.

Tissue characterisation with parametric mapping methods has also a promising value in the differential diagnosis of these forms.

Cardiac amyloidosis can be due mainly to transthyretin deficit Amyloid Transthyretin (ATTR) or to light chain disease (AL); LGE patterns are different between them, as light chain amyloidosis shows more frequently a global subendocardial distribution, whereas ATTR amyloidosis is characterised more frequently by a global transmural

distribution with failure in myocardial nulling at any given

inversion time.

This explains why native T1 and ECV may have more predictive power than LGE, providing a quantitative assessment of the diffuse extracellular expansion due to interstitial deposition of amyloid proteins.

In cardiac amyloidosis, abnormal proteins accumulate within the myocardial interstitial space modifying the composite relaxation time of the tissue, and resulting in elevated native T1 values that can be markedly increased in AL disease.

ATTR amyloidosis is more frequently associated with a higher ECV value compared with AL amyloidosis.

Furthermore, native T1 and ECV are also elevated when normal conventional clinical testing and LGE imaging suggested no cardiac involvement, representing a potential early disease marker.

In *AFD*, the low native T1 of fat can serve as an early biomarker of myocardial glycol-sphingolipid storage, even before the development of LV hypertrophy.

Conversely, the ECV is typically normal, because this parameter reflects an extracellular/interstitial disease, whereas AFD is an intracellular (lysosomal) storage disease.

The inferolateral wall, which is typically characterised by LGE in these patients, can show a pseudonormalisation or even elevation of T1 value, due to the effects of extensive fibrotic replacement which exceed the fatty-related T1 decrease.

Cardiac sarcoidosis is characterised by noncaseating

granulomatous infiltration that produces a patchy disorder which often involves small amounts of myocardial tissue, and in early stages it may not cause LV dysfunction. CMR appearance largely depends on timing of disease: in the acute phase a patchy increased T2 signal intensity can be due to oedema and inflammation and the LGE can show a patchy midmyocardial, subepicardial or epicardial pattern; in chronic disease, nodular foci of LGE without oedema on T2 weighted images are due to fibrosis and scar formation.

Although LGE imaging is a powerful predictor of risk in patients with sarcoidosis, the earlier stages of the disease can go undetected on LGE images; in these cases, abnormal myocardial T2 times can reveal an active inflammation before the development of myocardial scar, suggesting that T2 mapping may improve the detection of granulomatous active inflammation when it is potentially reversible with appropriate treatment.

Finally, cardiac MRI is extremely important in the assessment of iron overload of the myocardium as the measurement of T2* (transverse relaxation time in gradient-echo sequence) closely correlates with iron overload; consequently, it is possible to modulate chelation therapy in these patients, which helps to reduce the mortality for heart failure, the leading cause of death in this disease.

Cardiac CT, as well as MRI, can be used in differentiating RCM from constrictive pericarditis, by means of pericardium thickness measurement; a potential advantage over MRI is the assessment of pericardial calcification.

Arrhythmogenic Right Ventricular Cardiomyopathy

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a relatively uncommon familial disease, usually autosomal dominant, characterised by various desmosome proteins mutations.

These result in right ventricle dysfunction, global or regional, with or without left ventricle involvement, in the presence of histopathological evidence of right ventricular myocardial replacement with fatty and fibrous tissue

in various amounts.

There is preferential localisation in the so-called triangle of dysplasia (outflow tract, inflow tract and apex).

There are distinctive electrocardiographic abnormalities, according with previously published and recently revisited criteria.

ARVC is a frequent cause of sudden cardiac death in young people due to severe ventricular arrhythmias. For this reason, early diagnosis is crucial.

In 1994 a number of criteria were proposed: familial history,

ECG alterations, repolarisation abnormalities, arrhythmias (ventricular tachycardia with left bundle branch block, extrasystoles >1000/24 hours), right ventricle systolic dysfunction, fibrofatty replacement at endomyocardial

biopsy.

Based on the severity of the alterations, major and minor

criteria are distinguished and a certain combination of findings is needed to establish (or rule out) the diagnosis.

In doubtful cases, it is important to strictly follow the

patient.

In 2010 these criteria were revised, and, particularly, quantitative parameters for right ventricle enlargement and ejection fraction were introduced by means of ultrasound or cardiac MRI measurements with the aim to increase sensitivity.

MRI has been used in the past quite exclusively to demonstrate fatty infiltration of the right ventricle myocardium, particularly in the so-called triangle of dysplasia, the region between the subtricuspid area, the apex and the free wall of the outflow tract.

However, the capability to assess the presence of fat is strictly related to the amount of the fat, because of the limited spatial resolution: for this reason, it is possible to recognize only cases with extensive replacement.

Another issue is the relative difficulty in differentiating intramyocardial from subepicardial fat accumulation, partly because of limited spatial resolution but also because subepicardial fat accumulation is also seen in other physiological and pathological conditions such as obesity, steroid therapy and old age.

For the revised criteria, MRI has been included only for the assessment of ventricular size and global/segmental functional assessment because it has been demonstrated to be more sensitive than ultrasound for right ventricular systolic function evaluation; it is superior for volumes measurements as it uses a 3D approach (unlike ultrasound) that needs a geometrical assumption (not available for the right ventricle) to measure volumes.

In addition, regional function is superiorly evaluated by MRI: systolic bulging and aneurysms of the right ventricle anterior wall are easily detected and can be also seen in the free wall, which is not always assessable by echocardiography.

Recent data have been published on the use of delayed enhancement technique to demonstrate presence of fibrotic tissue, although this is not easy to visualise in the thin myocardium of the right ventricle.

Despite the fact that the typical fibrofatty replacement of ARCV should lead to alterations of both native T1 and ECV, the thin RV free wall hinders the use of parametric mapping techniques.

Cardiac CT is not important considering the pre-eminent role of MRI; however, in small series, CT has detected small foci of fat deposition/substitution even in the right ventricle due to its high spatial resolution

and good contrast resolution for fat. However, it is less easy to assess regional wall motion abnormalities of the right ventricle at CT, although new CT techniques may improve this.

Unclassified Cardiomyopathy

In this group, two entities are included: left ventricular noncompaction (LVNC) and takotsubo CMP.

LVNC is characterised by prominent left ventricular trabeculae and deep intertrabeculae recesses; this results in segments of thickened myocardium, composed of thin compacted epicardium with a thick endocardial layer.

It is unclear if LVNC is a separate CMP, a congenital

or acquired trait shared by other phenotypes; it can be isolated or associated with congenital anomalies (complex cyanotic, Ebstein) or muscular dystrophies.

It is frequently familial, with approximately 25% of asymptomatic relatives showing a wide range of ultrasound abnormalities.

Echocardiography is the first and often unique diagnostic tool to assess LVNC, especially in paediatric patients. Increased trabeculation is usually detected in midapical segments, both on lateral wall and septum, with the latter being normally nontrabeculated.

In difficult cases, MRI can be useful, using a cut-off value of 2.3 for the ratio between noncompacted and compacted myocardium.

Furthermore, delayed enhancement is able to demonstrate the presence of fibrotic tissue in the compacted myocardium, more often in forms associated with muscular dystrophies.

The native T1 values in LVNC patients with and without LGE were significantly higher than in the normal controls; furthermore, LVNC patients without LGE finding may show elevated native T1, suggesting that native T1 mapping can be used earlier than LGE imaging to detect myocardial fibrosis.

Takotsubo CMP or *transient left ventricular apical ballooning syndrome* is characterised by a reversible regional systolic dysfunction, associated with chest pain and a negative invasive coronary angiography; typically,

patients present with an acute coronary syndrome, mostly seen in postmenopausal women after a physical or emotional stress with norepinephrine acting as a neuromediator. Functional recovery usually occurs within days or a couple of weeks.

Echocardiography is usually able to detect the abnormal function and the ballooning but, because of the acute presentation, invasive coronary angiography is required to exclude obstructive coronary artery disease according to guidelines.

In these cases, after negative coronary angiography, there is a strong indication for cardiac MRI, with the aim to differentiate a myocardial infarction with normal coronary arteries, from an acute myocarditis and a takotsubo CMP. MRI is indeed able to detect the functional ballooning but, more importantly, the oedema of the myocardium

without any delayed enhancement, indicating the absence of necrosis and the reversibility of the damage.

T1 and T2 mapping can be used to confirm the presence of increased T1 and T2 relaxation times in the hypokinetic regions, and they show higher diagnostic accuracy than T2 short tau inversion recovery (STIR) images to detect oedema, because of their quantitative nature.

Myocarditis

Myocarditis is not included in the ESC CMP classification as a single definite category but is included in the acquired group as inflammatory CMP; in the ESC classification, chronic myocarditis is described as demonstrating the dilated phenotype, whereas acute myocarditis does not show a precise phenotype.

Consequently, myocarditis has to be treated apart from the classification, also considering its increasing incidence and the recently increased possibilities to define the diagnosis.

Myocarditis is an acute or chronic inflammatory process affecting the myocardium; underlying causes can be toxic, infective (viral, bacterial, rickettsial, fugal, parasitic) or a hypersensitivity reaction.

It typically evolves through an active, healing and healed stage with progression of inflammatory infiltrates, interstitial oedema, myocyte necrosis and finally scarring. In some cases, subclinical forms of viral myocarditis can trigger an autoimmune reaction causing immunological

damage to the myocardium and/or cytoskeletal disruption leading to a DCM phenotype with LV dysfunction. In these cases, viral persistence and chronic inflammatory infiltrates have been demonstrated.

Histology obtained through an endomyocardial biopsy is still considered the 'gold standard' for the diagnosis, based on the combination of leucocyte infiltration and necrosis defined by the so-called Dallas criteria, even if these criteria have been recently debated.

Substantial refinement of the diagnosis can be reached by using molecular analysis of the specimens, such as DNA– RNA extraction and polymerase chain reaction.

Acute presentation can often mimic an acute coronary

syndrome with chest pain, exertion dyspnoea, ECG abnormalities and mild enzyme elevation.

In this case there is an indication to invasive coronary

angiography to exclude obstructive coronary artery disease, even if the presence of a recent viral infection or unexplained fever is indicative of the correct diagnosis.

Echocardiography is usually performed to assess and quantify left ventricle systolic dysfunction; in case of associate pericardial effusion, ultrasound can suggest the suspicion of an inflammatory process, but need for further examination remains.

In the acute presentation, after negative coronary angiography, there is a strong indication to perform cardiac MRI, which can demonstrate oedema and delayed enhancement in the subepicardial layer, most frequently in the lateral and/or inferior wall.

This pattern easily allows differential diagnosis from acute myocardial infarction, where delayed enhancement is located in the subendocardial layer or is transmural.

In takotsubo CMP, delayed enhancement is typically absent.

However, a negative delayed enhancement study does not exclude an acute myocarditis, because there is not always macroscopic detectable necrosis; in this case it is important to acquire MR images before and immediately after administration of contrast agent (early enhancement) to demonstrate inflammatory hyperaemia. The combination of oedema imaging (T2 weighted sequences), early and late enhancement imaging constitutes the cornerstone for the diagnosis according to the so-called Lake Louise criteria.

Cardiac MRI is of course useful and accurate to evaluate biventricular global and regional systolic function and eventually associated pericardial effusion, with or without pericardial enhancement, in case of myopericarditis.

Acute fulminant forms or cardiogenic shock can represent other rare but possible acute presentations.

Clinical presentation can also be more subtle, e.g. as newonset cardiac failure or with tachyarrhythmias; these presentations are more often associated with chronic myocarditis.

In these situations, echocardiography is useful to exclude other diseases: for example, a new-onset heart failure. Cardiac MRI is particularly helpful to demonstrate fibrosis with late enhancement technique typically located in the mesocardium.

Enhancement is generally less intense than in the acute forms, diffuse rather than patchy and located in lateral wall

or in the septum, the latter being more frequent in tachyarrhythmias.

The presence of tissue oedema on MRI is usually detected visually on T2 weighted-STIR images or using a semiquantitative method such as the ratio of myocardial to skeletal muscle (T2 ratio) by drawing two distinct regions of interest in the same slice. However, these methods can be prone to errors due to a highly variable distribution of inflammatory foci into the myocardium, which range from solitary small infiltrates to a diffuse involvement of myocardial tissue.

Moreover, the contemporary presence of skeletal muscle inflammation with oedema, which is possible in coexisting myositis, can lead to false-negative results for myocardial oedema.

In this scenario, T1, ECV and T2 mapping have a crucial clinical value and may be used in conjunction with the Lake Louise Criteria.

In particular, myocardial T2 mapping provides a noncontrast quantitative assessment of myocardial oedema in patients with suspected myocarditis without the limitations associated with T2 weighted imaging such us signal heterogeneity and the need of reference tissue for signal

normalisation.

Furthermore, native T1 values are significantly elevated in these patients, and it has been proven to be superior to T2

weighted imaging and LGE, providing a high level of diagnostic accuracy with high positive and negative predictive values.

The elevated T1 relaxation time is likely due to both the increased water content in the intracellular and extracellular space, as well as an impaired electrolyte distribution in the inflamed tissue.

Lastly, ECV is also increased in acute myocarditis, reflecting both myocardial oedema and myocyte necrosis

with subsequent myocardial fibrosis; this parameter, together with LGE significantly improves the diagnostic accuracy compared with the

Lake Louise CMR criteria.

VALVULAR HEART DISEASE

Compared with the past, the aetiology of acquired valve disease is currently usually degenerative rather than due to rheumatic or infective causes; the prevalence of mitral regurgitation and aortic stenosis is higher than MS and aortic insufficiency.

In addition, the age of onset is increasing.

Findings on plain radiography are often minimal and

nonspecific, and the assessment is based on echocardiography.

Mitral Valve Disease

In Western countries, nonrheumatic mitral valve disease is the most common manifestation of mitral disease; in non-Western countries, rheumatic heart disease is still prevalent.

Among nonrheumatic diseases, mitral regurgitation is the most common, while nonrheumatic MS is very rare. Many conditions can result in significant mitral regurgitation, affecting the mitral leaflets (prolapse, endocarditis, mucopolysaccharidosis, lupus, rheumatoid arthritis) or the subvalvular apparatus (annular dilatation, chordae tendinae rupture, annular calcification, myocardial infarction, HCM).

In mitral regurgitation, a portion of the left ventricular stroke volume is directed retrogradely into the atrium during systole, returning to the left ventricle during diastole with consequent left ventricular volume loading. To maintain an adequate stroke volume, both the left ventricular stroke volume and the ejection fraction increase.

Acute regurgitation may result from infective endocarditis or rupture of chordae tendineae/papillary muscles.

Sudden volume loading into the noncompliant left atrium may result in markedly elevated atrial pressure, causing acute pulmonary oedema and symptoms of heart failure. Rupture or elongation of chordae tendineae, ischaemic and

nonischaemic CMP, hypertrophic obstructive CMP and rheumatic heart disease are all causes of chronic mitral regurgitation.

In response to the chronic volume load, both the left atrium and left ventricle dilate, thus serving as a reservoir for the regurgitant volume without necessarily increasing pulmonary vascular pressure.

However, if the left ventricle decompensates and the forward stroke volume decreases, heart failure is the result.

The appearances on chest radiography depend on the duration and severity of the mitral regurgitation and any other associated heart disease.

Acute, severe mitral regurgitation may present with pulmonary oedema but with a virtually normal heart size and shape.

After an interval, the heart usually decompensates by developing marked left ventricular dilatation.

Selective left atrial enlargement may be absent, slight or moderate, with or without left atrial appendage enlargement. Pulmonary vascular changes reflect the haemodynamic

derangement and the effects of treatment.

As previously described, mitral regurgitation can be due to many different causes such as mitral prolapse, chordae tendineae rupture (during bacterial endocarditis, collagen diseases, acute myocardial infarction) or be functional (DCM, ischaemic).

Mitral Valve Prolapse

The most common cause of severe (nonischaemic) mitral regurgitation is the mitral valve prolapse syndrome.

Mitral valve prolapse is defined as systolic bowing of the mitral leaflet more than 2 mm beyond the annular plane into the atrium, caused by rupture or elongation of the chordae tendineae.

The middle scallop of the posterior leaflet is most often affected.

Mitral valve prolapse is due to elongation of the chordae tendineae associated with myxomatous degeneration of the valve leaflets, occurring alone or in association with Marfan syndrome and in patients with atrial septal defect.

The diagnosis is typically made by echocardiography,

but is also possible with CMR with two- and three-chamber views preferred; associated imaging findings include leaflet thickening (thickness of >5 mm) and flail leaflet.

CT has also a good sensitivity for detecting mitral valve

prolapse, small vegetations and ruptured chordae; furthermore, cardiac CT may be useful to assess valvular and subvalvular calcifications.

Prolapse of the mitral valve may be associated with chest pain and ECG changes, which may suggest ischaemic heart disease.

Chordal Rupture

It may complicate bacterial endocarditis or, less frequently, myocardial infarction or connective tissue diseases, leading to flail of part of a leaflet; as a result there will be eversion of the mitral leaflet tip into the

atrium during systole, preventing proper closure in systole and producing

severe mitral regurgitation.

In case of an acute event, acute pulmonary oedema is detected at CXR usually without cardiomegaly.

Functional Mitral Regurgitation

This may occur in DCM or ischaemic cardiac failure. In this case the valve is normal, but regional wall motion abnormalities, left ventricular dilatation, tethering of chordae tendinae or annular dilatation, alone or in combination, lead to dysfunction of the mitral apparatus with 'functional' mitral regurgitation.

Mitral regurgitation in these situations is very common and severe.

Mitral regurgitation detection and severity are usually assessed by 2D Doppler echocardiography. This can detect

left atrial dilatation, increased atrial emptying volume and gradual closure of aortic valve during systole, coupled with visualisation of the systolic regurgitant, colour-coded flow within the left atrium.

Pulsed Doppler interrogation is extremely sensitive also to small amounts of regurgitant flow; the extent of penetration and the area of the regurgitant jet within the left atrium allow a semiquantitative estimation of the disease (mild, moderate, severe).

However, in case of asymmetrical jets (flail) this method underestimates the severity.

In addition, continuous Doppler is very sensitive, giving a characteristic high-velocity, parabolic, systolic spectrum of the flow.

MRI identifies mitral regurgitation in cine, as a retrograde jet through the mitral orifice from the left ventricle into the left atrium, due to turbulent flow and consequent spin dephasing.

Mitral valve regurgitation can be quantified as the difference between left ventricle stroke volume (LVSV) and right ventricle stroke volume (RVSV).

Every difference between the two measured stroke volumes indicates the amount of blood which comes back through the insufficient valve during diastole.

This estimation is valid only if the tricuspid valve is competent (tricuspid regurgitation is reported in up to 50% of patients with significant mitral regurgitation); moreover, the calculation of RVSV is less reproducible compared with LVSV due to the extensive trabeculation of the right ventricle.

In cases with combined aortic and mitral regurgitation, the difference represents the sum of regurgitant volume.

Phase-contrast MRI can discriminate between anterograde and retrograde flow during the cardiac cycle; the mitral regurgitant volume (MRV) can be measured by MRI as the difference between the LV stroke volume and the aortic forward flow.

The regurgitant fraction (RF) is the ratio of the MRV divided by the LVSV.

It may also be possible to directly measure mitral flow by phase-contrast velocity flow mapping at the tips of the mitral valve leaflets, but this is superiorly obtained with a specialised imaging sequence which tracks the motion of the mitral valve annulus during the cardiac cycle to adjust the plane of velocity encoding for diastolic mitral valve motion.

With cine-phase-contrast MRI, mitral regurgitation can be calculated as left ventricular inflow through the mitral valve minus left ventricular outflow in the ascending aorta.

This approach is also applicable in patients with mitral and aortic regurgitation, because diastolic left ventricular inflow (= left ventricular mitral inflow and aortic regurgitation volume) is equal to the systolic left ventricular outflow (= aortic outflow and MRV).

The AHA and the American College of Cardiology (ACC) have established echocardiographic criteria for grading the severity of mitral regurgitation.

Even in the absence of intersociety established criteria for MRI, the measurements of regurgitant volume and fraction

derived from LV volume and ascending aortic flow, allow to grade the regurgitation as:

mild = RV < 30 mL/beat; RF < 30%

moderate = RV 30 to 59 mL/beat; RF 30% to 49%

severe = RV > 60 mL/beat; RF > 50%.

For a comprehensive assessment of patients with mitral regurgitation, three components are mandatory:

(1) quantification of regurgitation,

(2) assessment of left ventricular adaptation to volume overload and

(3) anatomy of mitral valve and subvalvular apparatus. Whereas MR satisfies points 1 and 2, the method of choice for assessment of valve anatomy is echocardiography, although improvements in MR imaging strategies allow detection of morphological abnormalities such as flail

mitral valve leaflets.

Mitral Stenosis

MS is a structural abnormality of the mitral valve, which prevents proper opening during diastolic filling of the left ventricle.

Increased left atrial pressure is necessary to move blood

across the stenotic mitral valve and into the left ventricle. Chronic elevation of left atrial pressure causes atrial dilatation and pulmonary venous hypertension.

Atrial fibrillation (due to atrial dilatation) and dyspnoea (due to pulmonary venous hypertension) are common symptoms of MS.

Prolonged pulmonary venous hypertension may also lead to right ventricular dilatation and failure, as well as tricuspid regurgitation.

MS is highly prevalent in developing countries because of its association with rheumatic fever but is also seen in developed countries.

The most common cause of MS is rheumatic fever. Isolated MS is twice as common in women as in men; it occurs in 40% of all patients presenting with rheumatic heart disease; a history of rheumatic fever can be elicited from approximately 60% of patients presenting with pure MS.

Other causes of MS are very rare and include congenital anomalies, prior exposure to chest radiation, mucopolysaccharidosis, severe mitral annular calcification, ball valve thrombus and left atrial myxoma.

In cor triatriatum, the left atrium is divided by a membrane into two chambers; blood flow may be restricted before it reaches the mitral valve, mimicking MS.

The main features of a stenotic mitral valve are leaflet thickening, nodularity and commissural fusion, with narrowing of the valve to the shape of a fish mouth.

Leaflets might be calcified; chords may be fused and

shortened.

The normal mitral valve cross-sectional area is 4–6 cm2 and a gradient is rare unless the valve is less than 2 cm2. Symptoms correlate with increasing mean left atrial pressure, when mitral valve area (MVA) reduces to 1.5 cm2. The increase in left atrial pressure from obstruction across the mitral valve is transmitted to the pulmonary circulation,

causing dysphoea and leading to pulmonary oedema. Haemoptysis may occur.

In chronic severe MS, secondary pulmonary hypertension may cause right ventricular failure and tricuspid regurgitation.

Occasional embolic episodes are related to the atrial fibrillation.

Death is mainly due to heart failure or systemic embolism.

The standard for diagnosis and determination of the severity of MS is 2D/Doppler echocardiography.

Two-dimensional echocardiography evaluates the morphology of the mitral valve leaflets and the subvalvular

apparatus.

Leaflet thickening (Fig. 14.38) or calcification (hockey stick

deformity of the mitral valve leaflets is typical), leaflet mobility, commissural or subvalvular fusion can be seen. Narrowing of the MVA

can be appreciated.

Two-dimensional echocardiography helps assessment of the

suitability for mitral valve valvotomy: a pliable noncalcified valve could be suitable for balloon valvuloplasty or commissurotomy; a calcified fibrotic valve with subvalvular fusion that may preclude valvotomy.

Criteria for determining the severity of mitral valve obstruction are the mean mitral valve gradient and the MVA: mild MS is present when the area exceeds 1.5 cm2 and the mean gradient is less than 5 mm Hg; moderate stenosis is seen with an area 1.0 to 1.5 cm2 and a gradient of

5 to 10 mm Hg; severe stenosis occurs when the area is less than 1.0 cm2 and the gradient exceeds 10 mm Hg.

Mitral valve area (MVA):

• The most reliable method to calculate the valve area is planimetry from the short-axis view at the tip of the mitral valve leaflets; an even higher reliability might be achieved with 3D echocardiography.

• MVA is inversely related to diastolic half-time (T1

2): that is the time it takes for the maximal mitral gradient to decrease by 50%.

This can be obtained from the rate of velocity decrease during early and mid-diastole.

• MVA can be calculated with the continuity equation when the area derived from the half-time does not correlate with the mean transmitral gradient

Cine–MRI can be helpful in selected cases, however, with good visualisation of the restricted mitral leaflets and the anterograde jet due to turbulent flow across stenotic valve orifice, particularly on the two chambers and LV outflow tract views.

MS that is caused by rheumatic disease may have distinctive morphological features: restricted opening, thickened leaflets, commissural fusion, valve calcification, a 'fishmouth' appearance on short-axis images.

Bowing of a thickened and fibrotic anterior leaflet during diastole results in a 'hockey stick' appearance that is best seen on two- or fourchamber images.

Direct measurement of the orifice area can be performed in the same way as for aortic stenosis, by placing an imaging plane perpendicular to the direction of flow at the mitral valve tips during diastole and drawing a contour around the smallest valve orifice.

The technique has good agreement with echocardiography, but care needs to be taken in positioning the plane at the tips to obtain an accurate valve area, and multiple parallel thin slices may be helpful.

Diastolic flow and velocity can also be measured in this image plane; velocity-encoded cardiovascular magnetic resonance can be used as a robust tool to quantify MVA via mitral flow velocity analysis with the

pressure-half-time (PHT) method, although the frequency of atrial fibrillation in severe MS reduces the accuracy of the flow measurements.

MVA planimetry can be also determined by multidetector computed tomography (MDCT); can also be determined by CT which may provide reliable quantification of mitral valve stenosis (MVS) and allow accurate assessment of severity.

Mitral valve leaflet calcification on MDCT indicates mitral valve sclerosis or stenosis.

Cardiac catheterisation and angiocardiography is used in those rare situations where echocardiography has failed to elucidate the contribution of each valve lesion or when coexistent coronary artery disease needs assessment.

Nonrheumatic causes of MS usually produce nonspecific imaging features such as valve thickening or leaflet fixation. However, CT and MR imaging characteristics occasionally are suggestive of the cause of stenosis.

For example, radiation-induced valve disease is associated with mitral premature calcification of the apparatus, lung fibrosis and focal vertebral abnormalities.

Calcification of the mitral leaflets, a cause of senescent MS, may be depicted at CT.

Nonvalvular disease (e.g. ball-valve thrombus, left atrial myxoma) may also produce signs and symptoms of MS.

Rheumatic Mitral Valve Disease

Acute rheumatic disease can cause a pancarditis. During the acute phase, mitral regurgitation can be present; this is usually reversible.

Chronic rheumatic mitral valve disease often leads to stenosis, due to fusion of the commissures, thickening and shortening of the chordae tendineae and fibrosis of the papillary muscles. Severe mitral regurgitation results from leaflet destruction. However, there is usually a combination of MS and regurgitation, with the first limiting the amount of the

second, so that both cannot be severe at the same time.

Tricuspid Valve Disease

Tricuspid stenosis is generally rheumatic, more common in females than in males, and usually associated with tricuspid regurgitation and MS.

Most commonly, tricuspid regurgitation is functional and secondary to marked dilatation of the tricuspid annulus due to RV enlargement in the presence of pulmonary hypertension, mitral valve disease or mitral valve replacement, ischaemic heart disease or DCM.

Tricuspid valve regurgitation may be directly caused by rheumatic disease.

Severe tricuspid regurgitation can also occur in endomyocardial fibrosis and carcinoid heart syndrome (also responsible for stenosis).

In Ebstein anomaly, the insertion of the septal cusp of the tricuspid valve is displaced towards the apex of the right ventricle.

Endocarditis can also cause tricuspid regurgitation.

The clinical recognition of tricuspid valve disease can be difficult.

On **CXR**, **the main radiological sign** is right atrial enlargement that can be appreciated on frontal view as an increase of the second right cardiac; in the lateral view, an enlarged right appendage is seen as increased retrosternal opacity between the aortic arch and the outflow tract of the right ventricle.

Again, echocardiography is the most important diagnostic tool.

Colour Doppler can easily detect retrograde flow in the right atrium; by measuring the depth and the area of penetration of the jet, regurgitation can be semiquantitatively graded.

At pulsed Doppler, regurgitation appears as a pansystolic turbulent signal in the right atrium; if retrograde flow is appreciated also in inferior vena cava, regurgitation can be graded as severe.

The estimation of the peak velocity of regurgitant flow through the valve at continuous Doppler is not useful to grade the regurgitation but allows estimation of the peak systolic pressure in the right ventricle and pulmonary artery, applying the modified Bernoulli formula.

This parameter is extremely useful for evaluating the haemodynamic effect of all left chambers and myocardial diseases.

In tricuspid stenosis, echocardiography allows the visualisation of thickened valve leaflets and their limited motion, whereas Doppler permits visualisation and measurement of the jet.

Cardiac MRI, with steady-state free-precession cine sequences, is used to delineate abnormal valvular morphology such as in Ebstein anomaly or carcinoid heart disease. Tricuspid regurgitation signal void seen in the right atrium is less evident than mitral regurgitation for its lower velocity and turbulence.

The regurgitant volume can be quantified combining phasecontrast flow measurements at the pulmonary valve and RV stroke volume.

Aortic Valve Disease

Aortic Stenosis

The predominant cause of aortic stenosis in Western countries is degenerative calcific disease in middle-aged or elderly patients.

Compared with MS, where calcium is deposited on an already stenotic valve, calcific aortic stenosis results from calcification of relatively normal aortic cusps, which then cause obstruction.

Rheumatic disease is a rare cause nowadays.

Clinical presentation may include breathlessness, chest pain or syncope, with ECG signs of left ventricular hypertrophy.

CXR can detect rounding of the cardiac apex, suggesting left ventricular hypertrophy.

Prominence of the ascending aorta (first right cardiac arch) may indicate poststenotic dilatation, but in older patients the whole thoracic aorta may be widened from atherosclerosis.

In lateral view, it is easier to demonstrate the presence of

aortic valve calcification.

TTE is the first-line examination, assessing valve

morphology (leaflets number and thickening morphology, calcification) and function (leaflet mobility). The degree of calcification is related to the severity of stenosis and progression of the disease.

Doppler echocardiography allows stenosis quantification, in terms of maximal velocity, pressure gradient and aortic valve area (AVA); particularly, pressure gradient

is obtained by the modified Bernoulli equation ($\Delta p = 4v2$, where v is maximal velocity), while AVA is functionally obtained from continuous Doppler.

The 'anatomical' orifice area (AOA) is not equivalent to the valve effective orifice area (EOA).

The latter reflects the cross-sectional area of the transvalvular flow jet and is generally smaller than the valve area because there is a contraction of the flow downstream of the valve orifice.

The EOA is given by the continuity equation:

EOA = SV VTIAo where VTI is the velocity-time integral.

This estimation is based on the principle that the flow in the left ventricle outflow tract area must equal the flow in the subsequent valve leaflet area, in absence of shunts.

According to maximal velocity, pressure gradient and valve area, aortic stenosis is graded as mild, moderate and severe, with subtle differences between the guidelines of the ESC and the ACC–AHA.

To overcome acoustic limitations of the transthoracic approach, a transoesophageal echocardiography can be

performed, which allows a planimetric measurement of the valve orifice at maximal opening (mid-systole), especially if 3D technique is applied that overcomes off-axis 2D measurements at the tips of the valve (with consequent

overestimation of the area).

Coupled with quantitative stenosis grading, echocardiography assesses LV size and function that is mandatory for several reasons:

firstly, surgical or interventional corrections are indicated in asymptomatic patients with reduced function (EF <50%); **secondly**, severe stenosis can have low velocity and low pressure gradient because of flow reduction to reduced LV function.

Furthermore, the assessment of LV function is also crucial in case of coexisting MS (that reduces LV preload) or regurgitation (that reduces LV stroke volume).

Finally, estimation of RV function is due in case of severe aortic stenosis, where pulmonary hypertension and RV dysfunction can be present, increasing perioperative risk.

Calcification in the aortic valve leaflets and adjacent aortic root is well shown by echocardiography and CT; in

younger patients, it may be found in a congenitally bicuspid valve, whereas 'degenerative' calcifications are usually seen in patients older than 65 years.

Calcified deposits are commonly distributed along the

commissural edges of the leaflets. A valve calcium Agatston score of 150 is 100% sensitive for discriminating between

valve jet velocities less than 2.5 m/s and those greater than 2.5 m/s; however, 13.3% of patients with an increased gradient across the aortic valve at echocardiography

have an Agatston score of less than 50.

Cardiac CT diagnosis of aortic stenosis is based on the demonstration of left ventricular hypertrophy, mild to moderate poststenotic dilatation of the ascending aorta, calcification of the aortic valve, limited motion and reduced area of the aortic valve.

CMR can demonstrate impaired aortic valve opening, morphology of the valve (bicuspid or tricuspid) and assess stenosis; however, it is less sensitive than CT for calcium detection.

Coronal and oblique LV outflow tract views provide good qualitative assessment of the aortic valve.

In cine–MRI, the area of systolic flow dephasing seen in the aortic root has a poor relationship to the severity of aortic stenosis.

Direct planimetry of the aortic valve orifice, both with CT

and MRI, is the most useful technique for quantifying stenosis severity, achieved by placing an imaging plane through the valve tips in systole.

Transvalvar velocity can be measured with cine phasecontrast velocity mapping, although peak velocity may be less accurate (often underestimated) compared with continuous wave Doppler echo.

In-plane velocity mapping in the outflow tract is useful to

identify the location of maximal velocity, followed by through-plane velocity mapping in a plane perpendicular to the direction of flow, positioned at the identified location of maximal velocity.

There is a good agreement between CMR and Doppler echocardiography for the estimation of valve EOA.

CMR–cine imaging differentiates subvalvular and supravalvular stenosis and accurately evaluates the ascending aorta, which may be dilated particularly with bicuspid aortic valves.

Left ventricular function and hypertrophy are accurately measured by CMR, which is the most accurate method for determining ventricular volumes and mass. Late gadolinium enhanced MR imaging in patients with aortic stenosis has shown patchy midwall ventricular enhancement this likely reflects focal areas of fibrosis and is associated with a worse prognosis.

In older adults, aortic stenosis is frequently associated with coronary artery disease; imaging of coronaries is therefore indicated before surgery for valve replacement.

Rheumatic aortic stenosis is characterised by fusion of the commissures of the aortic valve cusps and is often associated with regurgitation and involvement of the mitral valve.

At CXR the main signs are related to accompanying mitral valve disease with left atrial enlargement. Poststenotic dilatation of the aorta is rare in rheumatic aortic stenosis but is seen in cases with associated aortic regurgitation.

Gross aortic valve calcification is rare.

Aortic Regurgitation

Aortic regurgitation may result from disease of the cusps of the aortic valve (bicuspid, endocarditis, rheumatic disease), or from disease of the aortic walls (aortic dissection, Takayasu arteritis, Marfan syndrome, rheumatoid arthritis, Elhers–Danlos syndrome, trauma).

Acute regurgitation can occur in bacterial endocarditis or, less frequently, can be traumatic or be related to aortic dissection.

Chronic aortic regurgitation may be the result of congenital abnormality as bicuspid aortic valve, or rheumatic heart disease.

Aneurysms of the ascending aorta may cause dilatation of the valve ring, leading to aortic regurgitation.

In a bicuspid valve the inadequately supported cusps allow progressive development of aortic regurgitation; a variable degree of stenosis can be present because of inadequate development of the valve commissures or dystrophic calcification.

In rheumatic aortic regurgitation, there is a slow destruction of the free edges of the cusps, often with commissural fusion.

The slow onset of chronic aortic regurgitation allows the left ventricle to adapt and dilate to receive the regurgitant flow; due to compliance increase, the end-diastolic pressure rises only when cardiac failure develops. Aortic regurgitation remains asymptomatic until the patient

develops heart failure. At CXR, chronic aortic regurgitation appears as enlargement of the left ventricle on both views, which is well related to the severity of the condition and is one factor suggesting the need for surgical intervention.

The enlargement can be reversible after treatment.

The thoracic aorta may be moderately enlarged. In acute regurgitation the left ventricle is not dilated, while the rapid increase of ventricular pressure can cause pulmonary oedema.

Echocardiography is the main imaging technique for most patients with aortic valve disease.

However, its most important role is the assessment of timing for valve replacement: a progressive increase in regurgitation

together with deterioration of ventricular function represent the best indicator for surgery.

Severity estimation is semiquantitatively obtained by means of Doppler; colour Doppler allows easy and immediate detection of regurgitation.

However, unlike the mitral regurgitant jet, the maximal length of the aortic jet does not correlate with severity;

the cross-sectional area of the jet shows a better correlation.

Another good indicator is the width of the narrowest central part of the jet; a width of 6 mm or greater is related to a severe regurgitation with a sensitivity of 95%
and specificity of 90%, whereas a width less than 3 mm represents a mild regurgitation.

Continuous Doppler allows the estimation of the transvalvular gradient, which drops rapidly in most

severe cases.

Pressure half-time is a very good indicator of severity:

400 ms is the cut-off value separating mild from significant forms, while 200 ms indicates severe regurgitation.

Finally, regurgitant volume and fraction can be measured comparing the total stroke volume, measured at the aortic level, and the forward stroke volume, obtained at the mitral valve level, using pulsed Doppler; however, this method shows some inaccuracies, particularly for mitral

flow measurements.

CMR allows for a good visualisation of the aortic valve and of the aortic root anatomy; the signal void jet of valvular insufficiency on cine sequences provides an approximate assessment of the severity of aortic regurgitation: a narrow jet width at the origin suggests

lower degree of regurgitation, whereas a wide jet suggests more severe regurgitation.

Cine sequences also help to identify the cause of the regurgitation: for example, an annuloaortic ectasia.

Velocity-encoded cine–MRI can quantify aortic regurgitation and RF with excellent accuracy.

The imaging plane for flow mapping is an axial oblique

one perpendicular to the flow and should be placed just above the aortic valve.

Placing the plane closer to the valve minimises underestimation of the regurgitation due to movement of the valve towards the LV apex during systole as blood between the imaging plane and the valve may return

back to the ventricle during diastole being lost to measurement.

Non-breath-hold flow sequences are recommended.

In the absence of other valve regurgitation or shunts, aortic regurgitation can also be quantified from cine imaging by assessing the differences in LV and RV stroke volumes, obtained from a volume study or from

aortic and pulmonary trunk flow measurements.

CMR reliably predicts the clinical course and outcome and is particularly useful for serial assessment.

A RF greater than 33% is an optimal threshold for identifying the need for valve surgery.

A dilated aortic root can also suggest the need for replacement at the time of valve surgery.

Cardiac CT is currently not used in the primary diagnosis of AR, but the aortic valve should be reviewed in all patients undergoing CT angiography (CTA) for possible concomitant underlying aortic regurgitation, particularly if echocardiography has not recently been performed.

Cardiac CT allows for measuring the aortic valve anatomical regurgitant orifice area (ROA) by direct planimetry: on end-diastolic CT scans the anatomical ROA can be visualised as 'central valvular leakage area', reflecting an incomplete closure of the cusps.

CT is thus able to detect the presence of AR and quantify the severity of AR with good correlation with the various echocardiographic parameters of AR.

However, the diagnosis of mild AR can be missed by CT in the presence of dense valvular calcification or bicuspid valves.

In case of an evident ROA, the patients should be further followed-up with echocardiography.

In the preoperative triage, CT allows for differentiating between bicuspid and tricuspid valve morphology; CT evaluates the aortic root, the ascending aorta and the coronary arteries within one imaging investigation.

Cardiac CT itself has recently shown promising results in depicting valvular abnormalities in infective endocarditis; in particular, evaluation of paravalvular involvement may be improved by CT.

CT may also provide a better morphological differentiation between valvular calcification and 'softtissue' lesions such as vegetations.

Complications of endocarditis such as a paravalvular abscess are well assessed by MR and CT; aortic root diseases such as annuloaortic ectasia or dissection are best investigated by CTA or MR angiography (MRA).

New Magnetic Resonance Imaging Techniques

In recent years a new sequence has been introduced for flow quantification, the so-called four-dimensional (4D) flow sequence, based on a cine 3D approach; its major advantage is represented by the acquisition of the entire heart volume in a single sequence; during the entire cardiac cycle off-line reconstructions of any possible plane within the volume allow calculation of flow volumes and velocities.

Flow measurements are possible in any given plane and in all spatial directions as well as valve tracking during the entire cardiac cycle.

The applications of this technique have been focused mainly on aortic diseases and congenital heart diseases; few data are available on adult valvular heart diseases, particularly on regurgitant volume and

fraction measurement, but the technique seems to be very promising also for other applications.

Prosthetic Cardiac Valves

There are two major types of artificial valves available for both aortic and atrioventricular placement, mechanical valves and bioprostheses.

Their specific characteristics should be structural durability, adaptation to the native valve annulus, chemically inert, free of thrombogenicity and without significant resistance to blood flow.

There are more than 40 types of cardiac valves that differ in inlet and outlet diameters and flow patterns, action and complication rates and availability for aortic, pulmonary, mitral and tricuspid replacement, as well as for vascular conduits.

The mechanical aspects all differ as well (central ball occluder valve, central caged disc occluder valve, eccentric monocuspid disc valve, bileaflet disc valve and bioprosthesis, etc.). More recently surgical techniques for valve reconstruction and annuloplasty have been introduced and developed.

The morphological differences and anatomical location of these types of valves should be known, to recognise them in the chest x-ray examination, at echocardiography or

CT.

Morphology is difficult to be assessed by MRI due to the

susceptibility artefact caused by metallic components of the prostheses.

Complications are relatively frequent and depend on the specific models of prosthesis; they including paravalvular leak, occluder variance or erosion, structural fracture, pseudoaneurysm, thrombosis, vegetations

or tissue overgrowth.

]In bioprostheses, infective endocarditis and primary

valve regurgitation can also occur.

Finally, further complications to be considered are those of anticoagulation, embolism and postpericardiotomy syndrome.

First-line examination of a prosthetic valve is echocardiography; other forms of radiology are used to identify the complications of prosthetic valves (chest radiography, fluoroscopy, CT and MR).

However, MR diagnostic performance may be limited by artefacts generated by the metallic components of the prosthesis.

Immediately after valve replacement, a baseline 2D and Doppler echocardiography should be

obtained to be able to compare findings in follow-up studies associated with malfunction or complication.

Transcatheter aortic valve replacement implantation (TAVI) is an emerging technique developed for nonoperable symptomatic patients with critical aortic stenosis; the device consists of an auto-expandable or a balloon-expandable stent with valve, which is delivered percutaneously by a transfemoral or a transapical approach.

CT is an essential tool for TAVI planning, aimed to assess: the size of the aortic root; the status of peripheral arteries (for the access); and the status of the coronary arteries. As alternative, CMR and MRA

can be used.

Complications of Prosthetic Valves

Structure Fracture

Structure fractures have been reported in some types of mechanical valves; chest radiography using microfocus, fluoroscopy and CT have been useful in identifying fractures of these radiopaque components.

Porcine Bioprosthesis

The major problem with porcine bioprostheses is their poor durability.

Cusp tears, degeneration, perforation, fibrosis and calcification appear from about the fifth postoperative year, and by the 10th year 20% have failed and require reimplantation.

Infective Endocarditis

Prosthetic valve endocarditis is an infrequent complication of cardiac valve replacement, with an overall incidence ranging from 0.9% to 4.4%; typically it occurs within 6 months of valve replacement.

Organisms most frequently involved are coagulasenegative staphylococci, *Serratia marcescens*, streptococci, *Candida albicans* and *Staphylococcus aureus*.

Diphtheroids are seen more frequently in early infective endocarditis, and there is a low incidence of gramnegative bacilli and fungal infections.

Infection typically develops in the coronary ostia, the ascending aorta and the aortic annulus, related to highpressure regurgitant jets of blood which damage valve attachments and cause development of local abscesses. Pannus and vegetations obstruct the flow through the

valve orifice or limit occluder motion. Sinus of Valsalva and perivalvar pseudoaneurysms may develop; they can be assessed by echocardiography, CT or MRI. Paravalvular insufficiency occurs as tissue fragments and sutures are destroyed by infection.

Two-dimensional echocardiography with transthoracic or, better, transoesophageal approach can demonstrate site, form and size of vegetations or thrombi.

However, also cardiac CT have been useful in identifying vegetations and particularly pseudoaneurysms; CMR is

limited for the detection of vegetations due to the artefacts generated by ferromagnetic components, while it is very useful for the assessment of pseudoaneurysms.

Valve Regurgitation

Minor regurgitation is relatively normal with many mechanical valves, but major regurgitation usually occurs as a result of ring dehiscence, thrombus, disc wear, and sticking, cocking or vegetations of the valve leaflets. Dehiscence with valve detachment may occur in case of infection, in a heavily calcified annulus or when there is underlying defective collagen as in Marfan syndrome. Perivalvular regurgitation or valve dysfunction should be suspected when sudden cardiac enlargement and pulmonary oedema occur.

Echocardiography is the preferred tool to assess dehiscence and regurgitation.

Thromboembolism

Thrombosis may occur spontaneously despite adequate anticoagulation; the involvement of the valve orifice reduces the excursion of the occluding ball, disc or leaflet and causes output reduction. Prosthetic mitral valve thrombosis is more common than aortic valve thrombosis.

The frequency of thrombosis has decreased markedly during the past few years.

With the early prostheses, the incidence of thromboembolism was 24% to 37%.

Since the introduction of cloth-covered prostheses, the incidence has decreased to 3% to 5%.

Echocardiography is extremely useful in assessing the presence of the thrombus, as CT and also CMR, if the thrombus is large enough.

Because this phenomenon is a surgical emergency, either immediate valve replacement or intervention by catheter remobilisation and intracardiac thrombolysis is required.

TUMOURS OF THE HEART

Cardiac tumours are rare. Metastases to the heart and pericardium are 40 times more frequent than primary tumours.

Approximately 75% of primary cardiac tumours are benign.

Some cardiac tumours remain clinically silent and are discovered incidentally; others present as heart failure, arrhythmia, chest pain or embolic disease.

The diagnosis is usually obvious when clinical evidence of cardiac involvement, arrhythmias or (haemorrhagic) pericardial effusion develops in a patient with a known primary malignant neoplasm.

Intrathoracic, extracardiac tumours—benign or malignant—may produce cardiac symptoms and signs by compressing the heart and great vessels and mimic obstructive lesions of these vessels.

Obstructive murmurs developing in the course of the malignant disease are well recognised.

Cardiac tumours and ventricular and aortic aneurysms may resemble each other radiographically.

The guiding criteria in differentiating cardiac masses are: age of the patient, chamber of origin, involvement of the interatrial septum, base of attachment, infiltrative growth, involvement of the valves and the pericardium and extension to extracardiac structures.

Echocardiography is the first-line imaging technique for the diagnosis of intracardiac tumours.

Real-time imaging can show tumour mobility and distensibility, features which are typically seen in atrial myxomas and less likely in sarcomas and metastases.

Because of MDCT's large field of view, the heart, paracardiac regions and lungs can be fully evaluated. This allows a better diagnosis of the site and extension of the lesions; MDCT is also useful in tumour staging by identifying metastases.

With CT, a densitometric evaluation of the lesion can also be performed, along with an assessment of the enhancement characteristics of the lesion: CT depicts calcifications and fat and also helps in identifying

the vascular supply of a cardiac mass. ECG-gated CT may be useful if more precise evaluation of tumour extent and relationships are required. MRI allows better softtissue characterisation than CT and can provide functional information such as flow direction and velocity, as well as a more reliable diagnosis of true invasion of cardiac structures by intrathoracic tumours. Although tissue characterisation is difficult, T1, T2 and Gadolinium enhanced images together with morphological analysis mostly allow at least for differentiation between benign and malignant lesions. In general, high cellular lesions intermediate-to-high

signal intensity both on T1 and T2 weighted images; postcontrast images show variable degrees of enhancement according to tumour vascularity, growth rate and necrosis.

Diffusion imaging can be useful, as restricted diffusion of water correlates with increased number of membranes

(cellular and intracellular) that can be roughly considered expression of high cellularity.

T1, T2 and ECV mapping are less useful for tumour characterisation; both T1 and T2 values are intermediate to high in

most tumours, with some exceptions, such as lipoma, fibroelastoma

or metastatic melanoma.

Metastasis

Secondary cardiac tumours are 30 to 40 times more common than primary malignant neoplasms.

The patterns of tumour spread are:

 (A) Direct extension from intrathoracic tumours; lung and mediastinal tumours can invade the heart directly and generally cannot be excised.

Lymphoma can extend into the pericardium

and heart, changing its staging.

(B) Intralymphatic dissemination; this is seen in patients with lung, oesophageal and breast carcinomas; invasion of the pericardium generally causes haemorrhagic exudate.

Due to their affinity for serous linings, adenocarcinomas frequently lead to pericardial metastases.

Mesothelioma can involve the pericardium and, less

frequently, the myocardium. Pericardial metastases are generally a sign of advanced disease and appear during tumour relapse;

(C) Haematogenous metastasis from a systemic tumour such as malignant melanoma, lymphoma, leukaemia, sarcoma or carcinoma.

(D) Intravascular dissemination: tumour thrombi from renal, adrenal or hepatic tumours may cause a transvenous spread via the inferior vena cava, whereas lung or thymic cancer may spread via the superior vena cava (SVC). Lung carcinoma can invade the left atrium via the pulmonary veins or spread to the right atrium via the vena cava.

In this case the formation of a mass in continuity with the systemic or pulmonary veins can be observed.

The evaluation of the atrial walls is important, because if there is no invasion tumour resection is not contraindicated.

CT is extremely useful in tumour localisation and staging for surgical resection.

CT features that suggest a malignant nature of a cardiac neoplasm are broad attachment to the wall of the heart, destruction of the cardiac chamber wall, involvement of more than one cardiac chamber, invasion of the pericardium with diffuse or nodular thickening and

pericardial effusion, especially if haemorrhagic. Pericardial effusion can be loculated or can give rise to cardiac tamponade, especially if it forms rapidly.

Nodular thickening is suggestive of secondary localisation.

CT is only moderately accurate for detecting direct invasion of mediastinal and cardiovascular structures by lung cancer, with sensitivity between 40% and 78% and specificity between 67% and 99%.

The contact area between the thoracic mass and adjacent mediastinal structure and the obliteration of intervening

fat are the commonly used CT features for local invasion, but neither is reliable.

The sliding motion between two contacting areas can be the helpful evidence of absence of invasion and this feature can be demonstrated by MRI.

Primary Cardiac Tumours

Primary tumours of the heart are rare and the great majority are benign, the malignant tumours being sarcomas.

Myxomas are by far the most common, followed by rhabdomyomas and fibromas.

The clinical features of these tumours depend on their sites of origin.

Intracavitary tumours are commonly pedunculated and may impact on and/or occlude the valves or fill cardiac chambers, leading to obstruction, arrhythmias and

cardiac failure.

Extension of tumours to the pericardium may produce haemorrhagic pericardial effusion that may lead to tamponade.

Benign Cardiac Tumours

Cardiac Myxoma

Myxomas are the most common benign tumour, accounting for 25% of primary cardiac neoplasms; they occur more commonly in women.

Patients may be asymptomatic or have the triad of

peripheral embolic phenomena, symptoms and signs of mitral valve obstruction and constitutional symptoms of fever, anaemia, raised erythrocyte sedimentation rate (ESR) and, sometimes, finger clubbing mimicking infective endocarditis.

However, blood cultures are sterile and splenomegaly does not occur.

Familial myxomas constitute less than 10% of all myxomas; they tend to present earlier (median age 20 years) and are more likely to have multiple myxomas at atypical locations and to develop recurrent tumours. Spotty skin pigmentation and endocrine abnormalities are

associated findings seen in the autosomal dominant condition of Carney complex.

Symptoms related to peripheral embolisation are frequent, prompting the need for early resection.

Approximately 90% are solitary lesions; they commonly arise in the left (75%) or right atrium (20%). In 85% of cases they are characteristically attached to the interatrial septum near the fossa ovalis.

Growth through the fossa ovalis with tumour in both atria is recognised.

Myxomas tend to be pedunculated or polypoid with a lobulated surface; the less common villous type has gelatinous, fragile surface extensions that are prone to fragmentation and embolisation. Owing to a pedunculated attachment, myxomas are often mobile but they can sometimes be broad based and relatively fixed.

Most are solitary and range in size from 1 to 15 cm.

On CXR, the heart can be enlarged and there is often evidence of selective left atrial enlargement, although rarely there is a large appendage, which would suggest rheumatic heart disease.

Pulmonary venous hypertension, pulmonary oedema or even pulmonary arterial hypertension may be present. However, the appearances of the chest radiograph may be normal.

The rare calcified myxoma may be identified on chest radiograph or CT.

The first-line examination, usually sufficient for diagnosis, is echocardiography.

It can assess the presence of a hyperechoic mass,

usually attached to the interatrial septum, with a heterogeneous texture in large lesions; the pedicle can be easily detected, as well as the fact that the lesion is crossing the mitral orifice.

Both MRI and CT are capable of demonstrating myxomas.

ECG-gated contrast-enhanced CT depicts an intracavitary mass with well-defined margins and a lobulated surface. Given their gelatinous nature, myxomas are heterogeneously hypodense. Foci of calcification are present in approximately 14%, more frequently in right-sided lesions.

Early arterial-phase contrast enhancement is usually not apparent, but heterogeneous enhancement due to the presence of cystic or necrotic areas is recognised on studies performed with a longer delay time.

The main differential diagnosis includes intracavitary thrombi, which usually have no pedicle and appear hypodense and nonenhancing.

On CT, prolapse through the mitral valve orifice is the only reliable discriminatory finding indicating myxoma. MRI is also useful; myxomas demonstrate an intermediate but variable signal intensity on spin-echo images similar to that of the myocardium.

A heterogeneous appearance is typical and caused by their complex architecture, with varying components of

myxoid, haemorrhagic, cystic, calcified, ossified and fibrous tissue.

They are predominantly hypointense compared with the myocardium on T1 and hyperintense on T2 weighted images.

On gradient-echo images, myxomas often have a low signal intensity caused by partial calcification.

Myxomas are usually hypointense relative to the blood

pool and hyperintense to the myocardium on steady-state free precession (SSFP) sequences.

Intratumoural subacute or chronic haemorrhage appears

as high or heterogeneous signal intensity on both T1 and T2 weighted sequences. Moderate enhancement after intravenous Gadolinium-DTPA is caused by increased vascularisation, but this can be heterogeneous due to cystic or necrotic areas.

Cine–MRI display may show the mobility of the tumour, including prolapse through the mitral or tricuspid valve orifice in diastole.

The attachment point for pedunculated lesions can be suggested on cine review.

First-pass enhancement is usually mild or not apparent; most lesions demonstrate at least some delayed enhancement, which is usually patchy, although some myxomas will have a homogeneous enhancement pattern.

MRI also helps to discriminate between a myxoma and atrial thrombus.

Thrombus usually occurs in an enlarged chamber; the atrial appendage is commonly involved and atrial fibrillation is likely to be present.

Myxomas can be sessile or pedunculated and are commonly attached to the interatrial septum.

Thrombi are usually sessile and readily distinguished by complete absence of both first pass and delayed

enhancement, which is seen to a variable degree in myxomas.

However, in some cases only surgical resection provides a definitive diagnosis.

Lipomas

Lipomas are slow-growing neoplasms composed of mature adipose tissue.

They may arise from the epicardium, myocardium or endocardial surfaces, including the interatrial septum. They occur commonly in the right atrium at the level of the interatrial septum.

An epicardial location, a narrow attachment point and growth into the pericardial space are typical.

Cardiac lipomas can have highly variable appearances

on echocardiography.

On CT, lipomas are well circumscribed lesions with homogeneous fat attenuation (-50 to -150 HU). Occasionally they may display internal soft-tissue septa. However, such lipomas must be differentiated from lipomatous hypertrophy of the interatrial septum, which consists of an accumulation of brown fat leading to a diameter greater than 2 cm; it characteristically spares the mid septum (the fossa ovalis), which gives a dumbbelllike appearance.

Lipomatous hypertrophy of the interatrial septum is often found incidentally on routine chest CT.

Lipomas have high signal intensity on MRI due to their short T1 and long T2 relaxation, consistent with fat. There should be no soft-tissue component and no contrast enhancement; both of these features are considered suspicious for the presence of sarcomatous elements.

Rhabdomyomas

These are the commonest (40%) benign cardiac neoplasms in infants and children and are typically found in patients less than 1 year of age.

They occur in association with tuberous sclerosis in up to 50% of cases, where they may be congenital and manifest in the neonatal period.

Arrhythmias, which may be fatal, are their main presenting feature.

They are usually intramural, may occur in any location in the heart but are more common in the ventricles.

They may be small and multiple, on average they measure 3 to 4 cm in diameter, but can be as large as

10 cm. These tumours are often inoperable because they are commonly deep seated, poorly demarcated and multiple; however, most cardiac rhabdomyomas regress spontaneously.

Echocardiographic appearance is variable, ranging from isoechoic (not easily differentiated brom normal myocardium) to hyperechoic (more often in neonates and children).

On CT, the lesions are enhancing, and when multiple may display diffuse thickening of the myocardium.

On MR, rhabdomyomas have signal intensity similar

to that of the adjacent myocardium on T1 weighted images and relatively increased signal intensity on T2 weighted images.

Fibroma

A fibroma is usually a solitary tumour of the ventricular wall, generally located on the left side.

It may be resectable.

It presents with arrhythmia or congestive cardiac failure, and plain radiographs can show an enlarged heart. Fibromas may calcify and then show characterising whorls of calcium, which may suggest the specific diagnosis.

On CT, a fibroma appears as a well-defined or infiltrative mass, usually large (at least 5 cm), with dystrophic calcification and very low enhancement.

On MRI fibromas are usually poorly vascularised, intramurally located with well-circumscribed margins and a surrounding rim of compressed myocardium.

On both T1 and T2 weighted images they have a low signal compared with the normal myocardium because of their dense fibrous composition.

They have variable signal intensity on steady-state free

precession (SSFP) and do not deform on tagged sequences.

Delayed enhancement may be homogeneous, peripheral or heterogeneous.

Fibromas that demonstrate little or no delayed enhancement may resemble a focal HCM.

Papillary Fibroelastoma

Papillary fibroelastoma is the second common benign cardiac tumour.

A fibroelastoma is nearly always solitary; it can arise from any endocardial surface, but the majority originate on the atrial surface of the mitral valve and aortic side of the aortic valve. Most are small (<1 cm), remain clinically silent and may cause systemic embolisation or sudden cardiac death secondary to coronary artery embolisation.

Echocardiography usually establishes the correct diagnosis, showing a small hyperechoic lesion attached to valve leaflets.

They are occasional findings on ECG-gated CT where they appear as a focal low-attenuation mass arising from a valve surface.

Detection with MRI can be difficult due to their small size; fibroelastomas are well circumscribed with intermediate signal intensity on T1 and T2 weighted images.

Usually there is no delayed enhancement; however, a uniform enhancement may reflect gadolinium accumulation within fibroelastic

tissue.

In SSFP cine sequences, they appear mobile, well circumscribed and of low signal with peritumoural turbulent flow.

Haemangioma

These are usually found in the ventricles; they may occur in multiple locations.

On CT they appear heterogeneous with intense enhancement; foci of calcification may be seen.

They are hyperintense on T2 and isointense or hyperintense on T1 weighted **MR** images.

Contrast enhancement is strong, sometimes heterogeneous due to calcifications and internal septations.

Hydatid Disease

Hydatid disease may involve the heart. The cysts behave as a benign myocardial tumour—well-circumscribed, loculated lesions; they may calcify.

Echocardiography can usually determine the correct diagnosis, but CT and eventually MRI can be useful.

MALIGNANT CARDIAC TUMOURS

Primary Malignant Tumours of the Heart

Primary malignant cardiac tumours can be broadly divided into sarcomas, lymphomas and primary pericardial malignancies.

Imaging findings suggestive of a malignant cardiac tumour include a right atrial location, involvement of more than one cardiac chamber, size greater than 5 cm, a haemorrhagic pericardial effusion, a broad base of attachment, extension into the mediastinum or great vessels and a moderate to strong, heterogeneous delayed enhancement pattern.

Sarcomas

Sarcomas account for nearly all primary malignant cardiac neoplasms and are the second commonest primary tumour after myxoma.

Angiosarcoma is the most common malignant tumour of the heart.

Peak incidence is in the fourth decade, and there is a strong male predominance.

They usually present with arrhythmias, symptoms of

right heart failure pericardial effusion, often haemorrhagic, cardiac tamponade, features of valvular or vena cava obstruction.

Diagnosis is usually late and metastases are present in most of the cases (lungs, liver, bones, lymph nodes and brain).

Most arise in the right atrium and are mainly intramural and infiltrating, although they may fill the chamber; they may extend to the pericardium, to the vena cava superior or inferior, tricuspid valve, right coronary artery and right ventricular free wall. Twenty-five per cent originate in other cardiac chambers or the pericardium. Involvement of the pericardium may lead to tamponade.

The heart is usually enlarged on the plain radiograph, and echocardiography will show a mass which is atypical of myxoma, with or without an effusion.

The following MR features are highly suggestive of an

angiosarcoma: a large infiltrating mass broad based with a cauliflower appearance; heterogeneous signal intensity (T1 isointense, T2 hyperintense) originating from necrosis and intratumoural haemorrhage; intralesional flow voids may be seen and reflect large vascular channels.

Homogeneous or heterogeneous strong enhancement, the last with a sunray appearance, is common on enhanced MRI.

On CT they appear as a heterogeneously enhancing mass.

A high attenuation pericardial effusion is frequent and caused by haemorrhage and/or tumour debris.

A left atrial location, even if rare, is possible.

Sarcomas with myofibroblastic differentiation.

These tumours include undifferentiated sarcoma, leiomyosarcoma, fibrosarcoma, liposarcoma and osteosarcoma; they occur in adulthood (fourth or fifth decade) and have slow infiltrative growth patterns. Most patients die of local effects.

Survival depends on effective surgical resection.

They originate most often from the posterior wall of the left atrial wall (fibrosarcoma in 30% of the cases from either ventricle and in 20% from the pericardium; liposarcoma from any chamber or pericardium).

MRI findings are relatively nonspecific. Liposarcoma rarely contains significant fat but necrosis and

haemorrhage predominate; osteosarcoma may present calcifications that appear as signal void in all sequences.

CT is better suited for the detection of the calcified components.

Rhabdomyosarcoma.

It predominates in childhood; only the much less frequent pleomorphic subtype occurs in adults.

This tumour appears as a large, bulky, infiltrative mass with central necrosis, has no chamber predilection and may involve the valves.

With echocardiography, the texture is variable, ranging from hyperechoic to very heterogeneous in larger lesions, often associated with pericardial effusion.

With **MRI**, signal intensity is heterogeneous on T1 and T2 weighted images.

At **CT**, attenuation is low, with peripheral enhancement after contrast injection.

Lymphoma

Primary cardiac lymphoma is an aggressive B-cell lymphoma, usually occurring in immune-compromised patients.

It is rare, confined to the heart or pericardium, with no evidence of extracardiac disease, and typically involves the right atrium and less frequently more than one chamber and pericardium.

On MRI, cardiac lymphoma may appear as multiple myocardial nodules that are isointense or slightly

hyperintense relative to the normal myocardium with heterogeneous enhancement or as diffuse pericardial

infiltration with haemorrhagic pericardial effusion.

On MDCT, it appears as a mass that is iso-attenuating relative to the myocardium.

PERICARDIAL DISEASES

Anatomy

The pericardium is a fibroserous, relatively inelastic sac that surrounds the heart and extends cranially to cover the pulmonary trunk, SVC and ascending aorta.

It is made up of an inner visceral and outer parietal

layer with a serosal lining; these layers surround a virtual cavity, which in normal conditions contains a small quantity of fluid (15 to 30 mL).

Its functions are:

• Mechanical: protecting the heart, acting as a barrier against local inflammation, limiting its movement within the mediastinum and maintaining ventricular compliance.

• Membranous: forming the serous pericardial fluid and producing surfactant and prostacyclins.

• Ligamentous: limiting cardiac displacement.

On CT, the pericardium appears as a thin line of fibrous tissue enveloping the heart, well contrasted by the surrounding low attenuation of the outer mediastinal fat and inner epicardial fat.

Visualisation of the pericardium on CT strongly correlates with the amount of fat present.

Although the pericardium is visible over the right atrium and right ventricle in most individuals, it often is not visible over the lateral and posterior walls of the left ventricle.

On MR, the pericardium is well demonstrated due to the high natural contrast between the two layers, fluid in the cavity, and the pericardial and epicardial fat.

On black-blood sequences, it appears as a thin low intensity line surrounded by the high signal of pericardial and subepicardial fat.

Its hypointensity is related to the fibrous structure of the layers, to the nonlinear movement of the fluid, and also to chemical-shift phenomena at the interface with the adipose tissue.

In these sequences, the layers appear hypointense in contrast with the marked hyperintensity of the pericardial fluid.

On MR angiographic sequences the pericardium may have intermediate signal.

Several studies have examined the normal thickness of

normal pericardium: 1.2 mm in diastole and 1.7 mm in systole, with a maximum of 4 mm.

The pericardium is best appreciated where it is well delineated from the surrounding fat (e.g. over the right ventricular surface), whereas it is more difficult to visualise near the lung, particularly along the posterolateral surface of the left ventricle, where it can be seen only in 61% of the cases.

The pericardium forms several recesses: these are cavities between the outer fibrous and inner serous layers of the pericardium, where small amounts of fluid may be present: knowledge of their anatomy can help to differentiate them from pathological findings.

The superior pericardial recess forms from the transverse sinus: it is wrapped around the right wall of the ascending aorta; its anterior extension can be seen between the ascending aorta and the pulmonary trunk with a characteristic triangular shape, its posterior extension is located directly behind the ascending aorta and has a crescentic shape; its right lateral part insinuates between the ascending aorta and the SVC.

The superior pericardial recess may be mistaken for an aortic dissection, mediastinal mass, lymph node or thymus.

The oblique pericardial sinus is the most posterior pericardial space; it is situated behind the left atrium and may be misinterpreted as an oesophageal lesion or a bronchogenic cyst.

On CT, the pericardial recesses are visible as defined

anatomical structures in up to 44% of the cases. Cine– MRI may help to differentiate the normal pericardial recesses from abnormal lesions.

Pericardial Cysts

Pericardial cysts are usually round or oval in shape; they occur most frequently at the cardiophrenic angles, especially on the right.

Pericardial cysts are rare congenital abnormalities; however, they are the most common benign pericardial mass.

Most often they are asymptomatic, representing an incidental finding on chest radiography; in some cases the cyst may cause compression on the cardiac chambers and right ventricular outflow tract obstruction.

Pericardial cysts usually have thin, smooth walls without internal septations and are attached to the pericardium directly or by a pedicle.

On CXR, pericardial cysts appear as a sharply demarcated mass causing a well-circumscribed, abnormal prominence of the cardiac border in the region of the right cardiophrenic angle.

CT correctly demonstrates the position and extent of this lesion that appears as a well-defined mass with fluid density and no enhancement after intravenous contrast agent.

Usually its size and shape alter with respiration or body position.

On MRI, pericardial cysts have low signal on T1 weighted images, but they can appear hyperintense when the cystic fluid has high protein content; signal intensity is homogeneously high on T2 weighted images; no enhancement is evident after intravenous gadolinium.

Pericardial cysts must be differentiated from other mediastinal cysts (e.g. bronchogenic or thymic) and from circumscribed fluid collections.

Hydatid pericardial cysts may be trabeculated with the presence of daughter cysts.

Pericardial Defects

Complete or partial pericardial defects are extremely rare; they result from an incomplete embryonic pericardial development, secondary to an insufficient intrauterine vascularisation.

Partial defects are more frequent than the complete absence; they may be associated with other complex anomalies, either cardiac (Fallot, interatrial septal defects, patent duct arteriosus) or extracardiac (bronchogenic cyst, hiatal hernia).

The absence of the pericardium may cause cardiac or left lung herniation through the defect.

Pulmonary tissue can be seen interposed between aorta and the pulmonary artery.

The clinical presentation is related to the site and entity of the defect: it may be asymptomatic or become symptomatic when herniation or strangulation through the defect leads to infarction of the left appendage or to coronary compression.

In the case of complete pericardial absence, CXR may show leftward displacement of the cardiac silhouette, a focal bulge in the region of the main pulmonary artery, lung interposition between aorta and pulmonary artery, and between the left hemidiaphragm and the inferior

cardiac border.

On CT or **MRI**, the pericardial defects can be more clearly defined:

in the complete absence of the left side of the pericardium, lung tissue is interposed between the main pulmonary artery and aorta; bulging of the left atrial appendage can occur through the defect.

The heart is usually rotated to the left. This abnormal location can change and becomes more evident in left lateral decubitus.

Pericardial defects may be difficult to directly diagnose even with CT and MR, as the left pericardium is not always well visualised.

Pericardial Diverticulum

A pericardial diverticulum is very rare; it can be congenital or acquired.

It is an evagination of the parietal serous layer through small gaps in the fibrous external layer, and it should be suspected when a complete wall cannot be identified in all parts of the lesion.

It is usually located at the right cardiophrenic angle; it tends to grow with time, requiring surgery.

The **chest radiograph** shows an abnormal shadow at the right side of the heart; **CT** demonstrates a well-circumscribed lesion with water attenuation.

Pericardial Effusion

In normal conditions the pericardium contains 15 to 35 mL of fluid; a quantity greater than 50 mL is considered abnormal.

The causes include cardiac failure, renal or hepatic insufficiency, infection (bacterial, viral or fungal) and neoplastic lesions (pulmonary, breast or lymphoma).

The **CXR** can be positive when the pericardium contains at least 200 mL of fluid: the cardiac silhouette enlarges symmetrically, resulting in a flask configuration. The cardiophrenic angles become acute.

On the lateral view, there is loss of the retrosternal clear space and water density separates substernal from epicardial fat; on the frontal view, a curvilinear

lucency can be seen along the left cardiac border.

Change in size can be rapid, with no changes in pulmonary vascular pattern.

Echocardiography is considered the primary imaging investigation for the evaluation of pericardial effusion. The normal small amount of fluid is not detectable with

echocardiography or is seen in systole as a thin posterior echo-free space.

A small pericardial effusion is usually seen only behind the LV free wall; moderate and large effusions surround

the heart.

The character of the effusion cannot be reliably diagnosed

by its echocardiographic appearance.

Pericardial fluid collections are usually well documented by ultrasound.

However, the accuracy of echocardiography can be significantly limited: anterior epicardial fat, pulmonary atelectasis or pleural effusion can all mimic a pericardial effusion; false negatives occur instead with small loculated collections.

In obese or emphysematous patients the heart may be difficult to examine and it becomes difficult to differentiate between thickened pericardium, fat and fluid.

The distribution of pericardial fluid is not uniform due to gravity; it is commonly localised along the posterolateral wall of the left ventricle, inferolateral to the right ventricle and in the superior pericardial recess.

The size, severity and extent of the pericardial effusion may be better assessed using CT or MRI than with transthoracic echocardiography.

Loculated effusions, especially those in anterior locations,

can be difficult to detect with echocardiography but are readily demonstrated with CT or MR imaging.

In general, a distance greater than 4 mm between the pericardial leaflets is considered abnormal; in moderate effusions (100–500 mL) the pericardial space anterior to the right ventricle is greater than 5 mm.

A more precise evaluation of the fluid quantity can be achieved by tracing the contours of the cavity.

A severe acute effusion can compress the cardiac chambers, limiting ventricular filling with decrease of the cardiac output.

This phenomenon is called cardiac tamponade. Symptoms depend on its severity and on

the time course of its development; it can be lethal, especially in cases of rapid development.

The diagnosis of tamponade is clinical and confirmed with echocardiography that shows right atrial compression, diastolic collapse of the RV free wall, increased respiratory variation of mitral and tricuspid diastolic blood flow velocities and abnormal right-sided venous flow with decreased inferior vena cava collapsibility in inspiration.

MR can help to assess the functional effects on diastolic filling and cardiac function.

CT or MR are indicated if the effusion is suspected to be complicated by haemorrhage, loculations, pericardial inflammation, thickening or constriction. A transudate typically has a low density (0–20 HU), whereas a higher CT attenuation value (up to 50 HU or more) indicates a purulent exudate or haemopericardium.

Pericardial effusions are in general hyperintense on T2 weighted, GRE and SSFP images.

Transudative or exudative effusions without debris are usually hypointense on T1 weighted images; proteinaceous or haemorrhagic effusions are T1 hyperintense but can be instead hypointense due to flowvoid effects.

GRE and SSFP images can show fibrinous strands of coagulated blood.

Accessory findings such as pericardial thickening or leaflet enhancement can suggest the inflammatory or neoplastic nature of the effusion.

When a pericardial effusion is secondary to a malignancy, there may be also associated irregularity and nodularity.

Pericardial Inflammation

Pericardial inflammation can be idiopathic (in 30% of the cases it is not possible to identify a cause). In most cases, its origin is infectious (viral, bacterial, mycobacterial or fungal): tuberculosis must be suspected in immunocompromised patients.

Pericarditis can be caused by systemic diseases (rheumatoid arthritis, lupus erythematosus, scleroderma) or be secondary to uraemia.

It can occur after an acute transmural myocardial
infarction (epistenocardic pericarditis), whereas the Dressler syndrome or postinfarct pericarditis arises later and has an autoimmune aetiology.

Direct or indirect thoracic trauma can result in pericarditis.

Radiotherapy for treatment of lung, breast or mediastinal cancer is another cause of pericarditis and constrictive pericarditis.

Symptoms vary in function of the severity of the inflammation.

In the acute phase, there is usually chest pain but a subclinical course is possible.

The acute inflammation of the pericardial leaflets is characterised by the presence of highly vascularised granulation tissue, pericardial fluid and initial fibrin deposits that later can cause the adhesion of the leaflets.

The chronic phase is characterised by a progressive sclerosis of the pericardial leaflets with the deposition of fibrin, fibroblasts and collagen fibres; the pericardium becomes thickened and inelastic, which is characteristic of constrictive pericarditis.

However, thickened pericardium does not always indicate constrictive pericarditis.

CT shows increased thickness and enhancement of pericardial layers, unsharp pericardial borders and

increased density of the surrounding fat.

It may not be easy to differentiate a small effusion from pericardial thickening.

In cases where a pericardial effusion is absent, CT abnormalities may be more subtle, consisting of a mild, diffuse thickening of the pericardium with increased enhancement after intravenous administration of contrast material. Calcification is best demonstrated by CT; on MR, calcification appears as focal hypointense areas, difficult to distinguish from the fibrous tissue.

MR signal intensity of the thickened pericardium can be highly variable, depending on the activity and nature of the inflammation.

In the chronic fibrous forms, on T1 and T2 weighted sequences, the pericardium appears as a low-intensity signal band; in subacute forms, signal intensity can be intermediate or high, not distinguishable from high signal effusion.

Late enhancement sequences are helpful to detect the acute inflammatory conditions and to better define the different components of the thickened pericardium delineating pericardial leaflets from the effusion. Saturation of the adipose tissue signal is in particular useful in cases of myocardial pericarditis as it separates the myocardial enhancement from the hyperintense contrasted pericardium.

Constrictive Pericarditis

Constrictive pericarditis is a chronic disease characterised

by the fusion of the visceral and parietal leaflets: the pericardial sac becomes a fibrous or fibrocalcific inextensible rind that envelops the heart and determines

a serious impairment of the diastolic filling. Patients with constrictive pericarditis have elevated systemic pressures and symptoms related to the low cardiac output, in particular with right cardiac failure such as dyspnoea, orthopnoea and fatigue and occasionally present with liver enlargement and ascites.

The inextensible pericardium determines the equalisation of the telediastolic pressure in the cardiac chambers with inversion of the interventricular septum convexity. Constrictive pericarditis can be idiopathic; more frequently it is a consequence of cardiac surgery and radiation therapy.

Other causes include subclinical acute viral infections,

connective tissue disease, uraemia and neoplasm; tuberculosis is rare nowadays.

As symptoms are nonspecific it is necessary to exclude the other causes of impaired ventricular filling (pulmonary hypertension, myocardial infarction, RCM). It is important to identify pericardial constriction as the cause of the impaired ventricular filling because these patients may benefit from pericardiectomy, whereas medical therapy is more appropriate in the restrictive forms.

This differentiation is particularly important in radiotherapy patients.

On CXR, the heart, in particular the left atrium, may be enlarged with dilatation of the SVC and of the azygos vein, so that the right and left cardiac borders appear straightened.

Pericardial calcification is seen in 40% to 50% of the patients as plaque-like or linear calcified densities

along the cardiac surface and in the atrioventricular grooves.

The main echocardiographic findings in constrictive pericarditis are pericardial thickening, abnormal motion of the interventricular septum, diastolic flattening of LV posterior wall, dilated inferior vena cava with reduced inspiratory collapse, increased respiratory variation of mitral and tricuspid blood flow. Constriction allows early diastolic filling but with abrupt termination in mid diastole.

Echocardiography may erroneously estimate pericardial thickness; moreover, some regions of the pericardium may not be easily accessible.

Transesophageal ultrasound, although limited by a narrow field of view and its more invasive nature, allows better visualisation of the pericardium.

Respiration-correlated Doppler techniques are particularly useful.

CT and MRI can aid the diagnosis of constrictive pericarditis.

Pericardial constriction appears as a more or less diffuse thickening of the pericardium that may present with irregular margins; it is more often localised along the free right ventricular wall and the atrioventricular junction.

A pericardial thickening greater than 4 mm is suggestive for pericardial constriction in those patients with corresponding clinical findings, while a thickness of greater than 5 to 6 mm is highly specific for constrictive pericarditis.

However, pericardial constriction can be present even in patients with normal pericardial thickness. MRI has

shown to be better than CT for differentiating between pericardial fluid and thickened pericardium, although CT superiorly shows calcifications.

MRI has a reported accuracy of 93% for differentiation between constrictive pericarditis and RCM on the basis of depiction of thickened pericardium

(≥4 mm).

Cardiac constriction symptoms depend mainly on the site of the lesions: focal lesions of the pericardial leaflets at the level of the atrioventricular junction or at the base of both ventricles can significantly impair ventricular filling: the haemodynamic impact is therefore related not only to the morphological criteria of the increased thickness but

mainly to the reduced compliance and the site of the lesion.

Pericardial constriction may be occult in normal conditions, because some patients develop symptoms only after a sudden water imbalance.

In other cases, myocardial constriction is related to the presence of pericardial effusion.

CT, unlike MRI, is very sensitive in demonstrating calcification of the pericardium.

On MR, fibrous or calcified pericardium is hypointense on T1 and T2 weighted images and cine sequences.

The altered filling pattern causes a particular tubular morphology of the ventricles (more often of the right ventricle) and consequent atrial dilatation that can be seen with both CT and MR imaging.

They also demonstrate the dilatation of the inferior vena cava and of the hepatic veins, as well as the presence of pleural effusion and ascites.

Cine–MRI can help to assess pericardial rigidity during the cardiac cycle and to document the reduced expansibility of the ventricles during the diastolic filling. Dynamic MR studies allow for differentiation of a normal pericardium from a rigid, sclerotic one: normal pericardium synchronously moves with the myocardium during the cardiac cycle; this characteristic is lost if the pericardium is thickened.

In pericardial constriction, the heart is isolated from the normal respiratory changes in intrathoracic pressure; reduced pericardial compliance accentuates coupling between the ventricles, meaning that each ventricle directly influences the volume and pressure in the other

ventricle; cardiac filling pressures are increased with pressure equalization in all four cardiac chambers.

In constrictive pericarditis, septal flattening or inversion is evident on early diastolic ventricular filling, and serpentine septal motion can

be seen on a cardiac long-axis view. Because of the respiratory-related variation in cardiac filling (enhanced RV filling in inspiration, enhanced LV filling in expiration), this paradoxical movement is most pronounced at onset of inspiration.

Assessment of these effects is usually performed

by echocardiography and cardiac catheterisation.

CMR, with the exception of intracardiac pressure measurements, may provide valuable information too, and has the intrinsic advantage that findings may be directly linked to morphological abnormalities.

Pericardial Masses

Primary tumours of the pericardium are rare, whereas pericardial metastases can be found in 22% of autopsies of patients with known metastatic disease. The most common primary malignant tumours of the pericardium are mesothelioma, sarcomas (fibrosarcoma, angiosarcoma, liposarcoma) and malignant teratoma.

Benign tumours include lipoma and teratoma.

Tumours that more frequently cause pericardial metastases are lung and breast carcinoma, leukaemia and lymphoma.

Metastatic pericardial implants are often small and difficult to identify; they cause a large effusion that is often haemorrhagic and disproportionate in size to the

tumour itself.

Invasion by contiguity from mediastinal masses can be identified by a focal disruption of the pericardial line and the presence of pericardial effusion; MR and CT can define the tumour implantation site and margins, demarcated by adjacent adipose tissue and effusion.

Tissue characterisation of pericardial tumours is not always possible, and biopsy is necessary for a definitive diagnosis.

A lipoma typically demonstrates low CT density and high MR T1 and T2 signal intensity; metastatic melanoma may demonstrate high signal intensity on T1 weighted images because of the paramagnetic effect of melanin.

Calcium or fat in a pericardial mass are suggestive of a teratoma.

Fibroma has low signal intensity on T2 weighted images

and no, or heterogeneous, enhancement. Mesothelioma of

the pericardium may manifest as pericardial effusion, occasionally accompanied by pericardial nodules or plaques.

Pleural mesothelioma also may invade the pericardium directly.

Lymphoma, sarcoma and liposarcoma typically appear as large heterogeneous masses, frequently associated with serohaemorrhagic pericardial effusion.

Pulmonary Circulation and Pulmonary

<u>Thromboembolism</u>

PULMONARY CIRCULATION

The function of the pulmonary circulation is both to support the lung's metabolic activities and to engage in gas exchange.

The pulmonary circulation should not be considered in isolation but, both anatomically and physiologically, as part of a functional unit which is intimately related to cardiac function and optimised to match ventilation and perfusion.

There are many examples of this unique interdependence,

including the pulmonary vascular response to hypoxia being arterial constriction as opposed to arterial dilatation in the systemic circulation; and venous congestion due to left heart failure requiring higher pulmonary arterial pressure (PAP) to maintain vascular flow potentially leading to pulmonary hypertension, right ventricular (RV) dysfunction and even failure.

The pulmonary circulation consists of both pulmonary

and bronchial circuits, of which the bronchial arteries normally contribute

only around 1%.

Appreciation of pulmonary anatomy and normal physiology enables a better understanding of abnormal conditions (and their relevant radiographic features).

Acute pulmonary embolism (PE) is common, can be life threatening, and has a high mortality if undiagnosed; chronic PE may lead to pulmonary hypertension and right heart failure.

As clinical symptoms are frequently non-specific, imaging plays a major role in diagnosing acute and chronic PE.

The second half of this chapter is therefore devoted

to demography, pathophysiology and imaging features of pulmonary thromboembolism.

PULMONARY CIRCULATION ANATOMY

Pulmonary Arteries

The *pulmonary trunk* originates from the right ventricle above the pulmonary valve. In adults, the main pulmonary artery (MPA) measures approximately 5 cm in length and is entirely enveloped within the pericardium. The pulmonary valve consists of three cusps preventing retrograde blood flow during diastole.

At the base of the pulmonary trunk there is a mild dilation forming the pulmonary sinuses, which lie between the valve cusps and prevent the valve leaflets from adhering

to the wall when open.

At about the fifth thoracic vertebral level, the pulmonary trunk divides into a longer right and shorter left pulmonary artery.

The *left pulmonary artery* runs superiorly over the left main bronchus to enter the left hilum.

Within the hilum, it may either continue directly

into the left interlobar artery, from which the segmental branches to the upper and lower lobe arise directly, or it may bifurcate into an ascending and descending branch. The ascending branch then divides almost immediately into the apicoposterior and anterior segmental branches which supply the left upper lobe.

The descending branch gives a branch to the lingula, which, in turn, divides into two segmental arteries (the superior and inferior lingular segmental artery).

The next branch from the descending branch is the superior segmental artery,

which supplies the superior segment of the left lower lobe (segment 6).

Subsequent branches supply the remaining four segments of the left lower lobe.

The right pulmonary artery runs under the aortic arch,

posterior to the superior vena cava and anterior to the right main bronchus; just before entering the hilum, it divides into the ascending (truncus anterior) and the descending (interlobar) branches.

The ascending branch divides into apical, anterior and posterior segmental branches, while the posterior

segmental branch may, however, also originate at the bifurcation of the right MPA or the right descending trunk.

The interlobar artery gives rise to the middle lobe artery (which further divides into the lateral and medial segmental branches) and the right lower lobe artery, which immediately gives off the artery to the superior segment of the right lower lobe.

As on the left side, subsequent branches supply the remaining four segments of the right lower lobe.

The arterial branching follows and runs parallel to the divisions of the bronchial tree (and using the same nomenclature), supplying each bronchopulmonary segment.

The branching pattern of the lobar and, especially, the segmental arteries show a high variation, whereas for

the more proximal arteries, it is fairly constant.

In addition, supernumerary

(accessory) branches exist that are not accompanied by bronchial branches and give additional arterial supply to the lung parenchyma.

These arteries are usually located in the periphery of the lung.

Normal sizes of the pulmonary arteries have been assessed with computed tomography (CT).

There are some contradicting data on the correlation between pulmonary artery diameter and height, weight.

Body Surface Index (BSI) and age; in general, diameters tend to be slightly larger in men.

According to the literature, in adults, the upper limit of normal for the pulmonary trunk diameter is 29 to 33 mm (for women 27 mm is suggested), and 23 and 22 mm for the right and left pulmonary arteries, respectively.

The pulmonary artery-to-aorta (PA-to-Ao) ratio is used for the screening and evaluation of pulmonary hypertension: A PA-to-Ao ratio

of greater than 1 or 1.1 has been proposed as being suggestive of pulmonary hypertension.

The PA-to-Ao ratio decreases with age because the ascending aortic diameter increases with age and body size, whereas the PA increases with body size only. In addition, the PA may enlarge in some diseases (e.g. pulmonary fibrosis) without a correlating increase

in PA pressure.

The pulmonary artery-to-bronchus ratio, which can be assessed on both plain chest radiography and CT, is especially helpful in the assessment of congestive heart failure and volume overload.

It has been also suggested to be used for the assessment of pulmonary hypertension.

Pulmonary Veins

The pulmonary veins, classically two on each side, transport the oxygenated blood from the lung back to the left atrium of the heart.

The veins run independently from the pulmonary arteries and bronchi towards the heart.

The superior pulmonary veins drain the blood from the

upper lobes, including the middle lobe on the right side; the inferior pulmonary veins drain the lower lobes.

In addition, the veins from the visceral pleura drain into the pulmonary veins, whereas the veins of the parietal pleura drain into the systemic circulation via the veins of

the thoracic wall.

There is great interest in pulmonary venous (PV)

anatomy variations with regards to ablation procedures for atrial fibrillation.

Bronchial Arteries

Bronchial arteries supply various structures in the intrathoracic region: they are responsible for the majority of oxygen supply to the bronchial tree from the central main bronchi to the respiratory bronchioles and lung parenchyma; the upper oesophagus; part of the pericardium; and the visceral pleura. The smallest, most peripheral branches anastomose

with branches from the pulmonary arteries in the walls of the bronchioles and the visceral pleura.

Systemic branches supplying the thoracic wall

also supply the parietal pleura.

The origin as well as the number of the bronchial arteries is subject to considerable variation.

In more than 70% of people, the bronchial arteries arise from the descending thoracic aorta, most commonly

between the levels of T5 and T6. In most individuals, there are two to four bronchial arteries present, arising either independently or from a common trunk.

The *right* **bronchial artery** usually (78% of people) arises within a common stem, with the first aortic intercostal (intercostobronchial artery) from the posteromedial aspect of the descending aorta.

On the *left* **side**, there is generally a superior and an inferior branch, both arising from the anterior aspect of the descending thoracic aorta.

The bronchial arteries run into the hilum, where they branch in a parallel manner and close to the bronchus to the peripheral airways.

The diameters of these arteries are small, usually 1-1.5 mm at its origin within the mediastinum.

Anomalous bronchial arteries, defined as bronchial arteries that originate outside the levels of T5 and T6, are found in up to 21% of patients with haemoptysis.

These anomalous arteries arise, in the majority of cases, from the aortic arch, and less frequently, from the lower part of the descending aorta, from major aortic branches such as the subclavian arteries, the thyrocervical trunk, the brachiocephalic artery, or the internal mammary artery.

Bronchial arteries course into the pulmonary parenchyma parallel to the bronchi, in contrast to the non-bronchial systemic collateral arteries.

In the periphery of the lung, bronchial arteries form anastomoses with the pulmonary arteries.

Venous return can occur via the bronchial veins into the azygos vein (right side), accessory hemiazygos vein, left superior intercostal vein (left side), or via the bronchopulmonary arterial anastomoses into the

pulmonary veins.

PULMONARY CIRCULATION PHYSIOLOGY

Unlike the systemic circulation, the pulmonary circulation is a low-pressure system with only a relatively small pressure difference between the pulmonary arteries (mean pressure 12 to 20 mm Hg) and the left atrium (7–12 mm Hg).

The pressure in the capillaries and the veins approximates the pressure in the left atrium.

That is the reason why the elevated pressure in the left ventricle/left atrium (e.g. mitral valve disease) leads via the capillary bed to an increased pulmonary artery pressure.

As with the airways, the combined cross-sectional area of the pulmonary vasculature increases at each generation of branching towards the periphery of the lung.

The resistance in the capillaries contributes considerably to the whole vascular resistance.

At rest, only one-third of the capillaries are perfused, but, with increasing cardiac output (CO) under stress, the remaining capillaries will be recruited by increasing pressure in order to contribute to gas exchange.

The hydrostatic pressure within the pulmonary capillaries drives fluid into the interstitium.

This is partly counteracted by the plasma oncotic (colloid osmotic) pressure, which draws fluid back into the

capillaries.

An imbalance in these pressures can lead to abnormal fluid shift and thus transudation of fluid into the pulmonary interstitium and alveoli.

Pulmonary lymphatic channels drain excess intersitital fluid and their capacity can increase by a factor of 10 if needed (e.g. chronic cardiac insufficiency).

However, if the rate of fluid accumulation exceeds

the lymphatic clearance capacity, fluid will begin to accumulate within the interstitium.

If this process continues, it leads to alveolar fluid

accumulation, which may compromise gas exchange

(which is not usually the case with isolated interstitial oedema).

Accumulation of interstitial fluid accounts for the bronchial wall thickening (cuffing) and subpleural

Kerley B lines seen in left heart failure.

An important difference between the pulmonary and systemic vasculature is the response to hypoxia. In the pulmonary system, hypoxia results in local vasoconstriction, causing diversion of blood to regions

of better ventilation.

Although contrary to the vascular response in the rest of the body, this mechanism serves to protect the alveolar–arteriolar pO2 balance and thus to minimise ventilation–perfusion (VQ) differences in cases of diffuse and regional disease; i.e. it supplies blood to regions of the lung that will most efficiently oxygenate it.

This homeostatic mechanism (Euler–Liljestrand reflex, hypoxic pulmonary vasoconstriction) is responsible for 'matched defects' seen in cases of pneumonic consolidation on VQ imaging. It is also responsible for different vascular calibres in patients with lobular air trapping.

The bronchial arteries primarily perfuse airways, pulmonary vessel walls, interstitium and pleura, while the more centrally localised bronchial veins drain into the right atrium; the peripherally located smaller bronchial veins drain into the left atrium.

The distribution of perfusion is influenced by gravity and

body position.

In the upright position, perfusion is greatest in the basal part of the lung, as illustrated by increased lung parenchyma density and larger vessel calibres.

In the apical part of the lung (zone I), the intraalveolar

pressure is larger than the intravenous and intra-arterial pressure independent of ventilation and blood volume.

In the basal part of the lung (zone III), intravenous and intra-arterial pressure exceed the intra-alveolar pressure. In the middle part (zone II), the intra-arterial

pressure is higher than the intra-alveolar pressure followed by the intravenous pressure. In a lying position, zone I is ventrally localised and zone III dorsally accompanied by an apicobasal gradient.

In case of acute volume overload or left cardiac failure, in particular, the vessels in zone III are affected.

PULMONARY VASCULAR PATTERNS

Pulmonary Venous Hypertension

PV hypertension is caused by increased resistance or flow in the pulmonary veins and is defined by an elevation of the mean pressure > 12 mm Hg.

An increased venous pressure automatically leads to an

increased capillary pressure. An increase of the mean PV pressure to 12–20 mm Hg results in a redistribution of blood volume (grade 1), a PV pressure of 20–25 mm Hg leads to interstitial oedema (grade 2) and a PVH of > 25-30 mm Hg to alveolar oedema (grade 3).

The most common cause of PV hypertension, by far, is left-sided heart disease due to left ventricular failure, mitral valve disease or aortic valve disease.

The severity of mitral valve stenosis can be noninvasively gauged by assessing the PV pressure.

In cases of aortic valve disease, however, the degree of PV hypertension is more indicative of myocardial failure than severity of stenosis.

It has to be noted that an increased left ventricular pressure load does not immediately result in PV hypertension.

Only an elevated end-diastolic left ventricular pressure leads to elevation of the left atrial pressure and subsequently to PV hypertension.

The PV pressure can be estimated from the pulmonary artery wedge pressure (PAWP) using a Swan–Ganz catheter and is usually < 12 mm Hg.

The radiological findings can be thought of as a progressive series of changes that occur in response to the underlying changes in physiology.

Three grades of severity of pulmonary congestion are differentiated.

Vascular Redistribution (Grade 1)

As PV pressure rises, the upper lobe veins distend.

They initially reach the size of, and eventually become larger than, the lower lobe vessels (thus reversing the normal 'gravity-dependent' pattern). This is described

as 'upper lobe venous diversion' and is often the first recognised radiological sign of PV hypertension.

Similar calibres of upper and lower lobe veins do not indicate increased PV pressure if seen in a bedside supine radiograph.

Patients suffering from their first episode of acute PV pressure elevation tend to immediately develop an interstitial or alveolar oedema.

Only recurrent periods or chronically increased PV pressure result in distended veins.

Interstitial Oedema (Grade 2)

If the PV pressure continues to rise and exceeds the plasma oncotic pressure, fluid will begin to accumulate in the lung interstitium.

This s known as interstitial pulmonary oedema.

Typical radiological signs of interstitial oedema are interstitial (Kerley) lines caused by thickening of the interlobular septa as a result of fluid accumulation.

Kerley B lines are the most obvious ones and are short (1 cm or less) interlobular septal lines, found predominantly in the lower zones peripherally, and parallel to each other but perpendicular to the pleural surface.

Kerley A lines are deep septal lines (lymphatic channels), radiating from the periphery (not reaching the pleura) into

the central portions of the lung and approximately 4 cm long.

Their presence normally indicates a more acute or severe degree of oedema.

Septal lines can be differentiated from blood vessels, as the latter are not visible in the outer 1 cm of the lung.

In addition, deep septal lines do not branch and are seen with a greater clarity than a blood vessel of similar calibre, as they represent a sheet of tissue.

Under normal circumstances septal lines caused by interstitial fluid overload would be expected to resolve after suitable reduction in PV pressure.

Exceptionally, however, they may persist, e.g. in longstanding PV hypertension, where haemosiderin deposition or fibrosis has occurred.

Alternative causes of persistent septal lines include idiopathic interstitial fibrosis, lymphangitis carcinomatosa and pneumoconiosis.

Other signs of interstitial fluid overload include perihilar haze (loss of visible clarity of the lower lobe and hilar vessels), peribronchial cuffing (apparent thickening of proximal bronchial walls as a result of interstitial fluid accumulating around their walls) and thickening of

the interlobar fissure due to thickened subpleural interstitium (to differentiate from interlobar pleural effusion).

Alveolar Oedema (Grade 3)

As the PV pressure continues to increase, fluid begins to accumulate in the alveolar spaces.

This is termed alveolar oedema.

Kerley B lines, airspace nodules, bilateral symmetric consolidation in the mid and lower lung zones and pleural effusions may be seen.

Depending on the amount of alveolar fluid overload, there are many variations of increased lung density, ranging from subtle haziness to dense consolidation with air bronchograms.

Certain patterns of opacification may suggest particular diagnoses.

The often-cited 'perihilar bat's wing' pattern of airspace consolidation is seen most commonly in left ventricular and renal failure, whereas alveolar oedema localised to the right upper zone is suggestive of severe mitral regurgitation.

The latter is thought to be a result of predominantly regurgitant blood flow in the right upper lobe pulmonary

vein, from the superiorly and posteriorly positioned mitral valve.

A predominantly upper lobe oedema is seen in patients with a severe head trauma (neurogenic oedema).

Alveolar fluid accumulation changes with patient position and gravity: asymmetric consolidations mimicking

a pneumonia may be the result of the left- or right-sided position of the patient.

Computed tomography (CT) findings of oedema are similar to the radiographic findings, although very atypical patterns are possible, causing differential diagnostic difficulties.

Interstitial oedema is characterised by smoothly thickened interlobular septa that do not follow the hydrostatic gradient.

The peribronchovascular interstitium is thickened, which is best seen in the perihilar area.

Commonly, there is also, at least subtly, increased

parenchymal density due to alveolar fluid overload.

Alveolar oedema may initially be recognised as peribronchovascular airspace nodules progressing to diffuse ground-glass or dense airspace consolidation. Increased density may follow a ventrodorsal gradient but can also be localised predominantly in the perhilar region

or in a patchy distribution, the latter causing sometimes quite atypical patterns.

In *chronic pulmonary venous hypertension*, signs of pulmonary arterial hypertension (PAH) may also develop. In addition, a fine nodular 'interstitial' pattern may appear throughout both lungs.

These nodules represent haemosiderin deposition.

This pattern was previously most commonly seen in patients with long-standing severe mitral stenosis.

Pre-existing underlying lung disease influences the pattern and distribution of oedema.

Patients with extensive emphysema do not develop

homogeneous consolidation; even though degree of PV pressure or fluid overload would otherwise lead to an alveolar oedema, the fluid remains within the interstitium, leading to thickened septa and a rather 'interstitial' fluid distribution, meaning that the radiographic appearance

may lead to underestimation of the severity of oedema in these patients.

Although most cases of PV hypertension are associated cardiomegaly resulting from valvular and/or myocardial dysfunction, the presence of cardiomegaly is not universal.

An important example of this is in the first 24–48 hours post myocardial infarction.

This is due to an acute decrease in myocardial compliance, which essentially resolves in the first week after infarction.

Other situations, where signs of pulmonary oedema

may be seen associated with a normal heart size, are in patients with non-cardiogenic pulmonary oedema, in patients with acute overhydration

or drug-induced lung oedema (e.g. heroin, aspirin, nitrofurantoin).

Cardiogenic oedema has to be differentiated from other underlying diseases that result in an imbalance of hydrostatic pressure, colloid osmotic pressure or capillary permeability, all of them resulting in pulmonary oedema.

Pulmonary Arterial Hypertension

PAH is defined by a mean pulmonary artery pressure of \geq 25 mm Hg at rest, as measured invasively at right heart catheterisation.

This can result from a broad spectrum of disease processes originating in the lungs, pulmonary vasculature or heart diseases with different pathophysiologies, treatments and prognoses.

Irrespective of its underlying cause, PAH is a progressive disease leading to substantial morbidity and mortality.

Because symptoms are non-specific and evaluation of pulmonary artery pressure is relatively inaccessible, there is often considerable delay between the onset of symptoms and the diagnosis of PAH.

Imaging, such as high-resolution computed tomography (HRCT), computed tomography pulmonary angiography (CTPA), magnetic resonance imaging (MRI) and echocardiography, plays a crucial role in the diagnostic work-up of patients with known or suspected pulmonary

hypertension.

Imaging also plays an important role in raising the possibility of PAH, both in those at risk of developing PAH due to comorbidities and in those presenting with non-specific cardiorespiratory symptoms where a de novo diagnosis may be suggested.

Imaging is particularly important for identifying patients with recurrent or chronic pulmonary thromboembolism where it is fundamental in assessing disease extent and distribution and evaluating the technical feasibility

of pulmonary thrombendarterectomy.

PAH is a clinical and haemodynamic syndrome that results from increased vascular resistance in the pulmonary circulation.

This may be secondary to raised PV pressures (left heart disease), chronic hypoxia resulting either from disease or altitude, or primary disease of either the large vessels (e,g, chronic thromboembolic disease) or the small vessels of the lung. In each of these disease processes exposure of the pulmonary circulation to persistently raised pressures results in ongoing small vessel remodelling and progressive PH.

Increase in pulmonary vascular resistance requires high driving pressure to maintain CO, which in turn leads to RV hypertrophy.

Ultimately, if untreated, the RV will fail initially during exercise, later at rest, with death from RV failure

occurring a medium of 2.8 years after diagnosis.

There are several different causes of PAH. The current PAH classification was developed at the Fifth World Symposium on Pulmonary Hypertension in Nice, France, in 2013 and represents a modification of the previous Dana Point classification.

The classification groups together diseases sharing similar pathophysiological mechanisms, clinical

presentation and therapeutic options.

Group 1 comprises diseases primarily affecting the pulmonary arterioles with vascular remodelling resulting in progressive luminal obliteration.

While collectively described as Group 1 or PAH, this group encompasses idiopathic and heritable PAH, PAH associated with drugs, connective tissue diseases, HIV infection, congenital heart disease, portal hypertension and schistosomiasis.

PAH is characterized clinically by the presence of precapillary PAH (a pulmonary capillary wedge pressure (PCWP) <15 mm Hg) and the exclusion of other causes

of PAH. The rare diseases pulmonary veno-occlusive disease (PVOD) and/or pulmonary capillary haemangiomatosis (PCH) are separated into a Group 1', which reflects the more distal anatomical location of

disease and potential adverse response to targeted vasodilator therapy used for Group 1.

Groups 2 and 3 are by far the most common causes of PAH.

Group 2 comprises patients with PAH secondary to left heart disease, causing an increased pulmonary artery pressure and an elevated PCWP greater than 15 mm Hg. Group 3 represents pulmonary hypertension due to lung disease or hypoxia. Group 4 is mainly comprises chronic thromboembolic pulmonary hypertension (CTEPH), which results from pulmonary arterial obstruction by an organised thrombus. In dedicated centres, removal of the obstruction, whether by surgical pulmonary endarterectomy or balloon pulmonary angioplasty, may result in cure of PAH in selected cases.

The diagnostic work-up of patients with suspected PAH includes a medical history, physical examination, chest radiography, echocardiography, right heart catheterisation and advanced imaging such as CT, MRI and scintigraphy.

Radiographically, cardiac enlargement (right atrial and RV enlargement), dilatation of the central pulmonary arteries (MPA and its branches down to the segmental level) and tapering of peripheral arterial branches (vessels beyond segmental level)—termed 'peripheral pruning'— are seen. In long-standing cases, the central pulmonary arteries may develop calcification due to atheroma, a feature absent in nonhypertensive pulmonary arteries. Central arterial enlargement may superficially mimic enlarged hilar lymph nodes, but the smooth outline

of arterial enlargement can usually be distinguished from the lobulated border of lymphadenopathy.

Measurement of the transverse diameter of the right descending pulmonary artery at its midpoint may be used

to suggest pulmonary hypertension. With a cut-off of greater than 17 mm being described.

However, while a relatively specific sign, the sensitivity of chest radiography for the diagnosis of (mild) PAH is low.

Transthoracic ultrasound (transthoracic echocardiography; TTE) is often used as a screening tool

that is recommended in all patients with suspected PAH. Echocardiography enables assessment of right- and leftsided cardiac chamber size and function, identification of intracardiac shunts and estimation of PA systolic pressure (by measuring the velocity of the tricuspid regurgitant jet).

When peak tricuspid regurgitation velocity is difficult to measure (trivial/mild tricuspid regurgitation), the use of contrast-enhanced ultrasound significantly increases the

Doppler signal, allowing for more precise measurement of the peak tricuspid regurgitation velocity.

However, the literature is not uniform with respect to the diagnostic accuracy of TTE; bedside measurements

show considerable user dependency and examinations may suffer from variable quality, especially in obese patients and those with chronic lung disease.

The *ventilation–perfusion (VQ) lung scintigram* is a nuclear medicine test widely performed in patients with suspected PAH to exclude CTEPH.

According to the European Society of Cardiology and the

European Respiratory Society guidelines published in 2009, it is recommended in all patients as the screening method of choice to diagnose or rule out CTEPH.

A normal or low-probability VQ result effectively

excludes CTEPH with a sensitivity of 90%–100% and a specificity of 94%–100%.

Unmatched perfusion defects may also be seen in PVOD

and sometimes in patients with PAH. In such cases. CTPA may be used as a complementary investigation.

As CTPA is more frequently being used as a first-line test in patients with unexplained symptoms, VQ may not be required if CT has already proven the presence of chronic

thromboembolic disease.

Traditional pulmonary angiography is still considered the reference standard in the anatomical assessment of the pulmonary arteries, though non-invasive imaging techniques are increasingly utilised.

In some centres, angiography is considered mandatory for the work-up of CTEPH to identify patients who may benefit from thrombendarterectomy.

Non-invasive imaging in many centres is playing an increasing role in the surgical evaluation or CTEPH. However, with increasing recognition of a potential role for balloon pulmonary angioplasty in CTEPH, a greater emphasis is being placed on angiography in inoperable

cases.

Angiography may also be helpful in the evaluation

of possible vasculitis or pulmonary arteriovenous malformations (PAVMs).

Right heart catheterisation is indicated in all patients with suspected PAH to confirm the diagnosis, to evaluate the severity and when PAHspecific drug therapy is considered.

Vasoreactivity testing is indicated in patients with

idiopathic pulmonary arterial hypertension (IPAH),

heritable PAH and other types of PAH; however, it should only be performed in specific centres and under controlled conditions.

This testing is not recommended for other PAH groups.

MRI plays an important role in diagnosis of PAH because of its ability to assess RV dysfunction caused by increased afterload.

Magnetic resonance angiography (MRA) of the pulmonary vasculature and parenchymal perfusion can be combined with dynamic quantitative assessment of ventricular volumes and function.

Cardiac MRI provides direct evaluation of the RV size, morphology and function, and allows non-invasive assessment of parameters including stroke volume, CO and RV mass, as well as evaluation of left ventricular

and valvular function.

Phase contrast MRI permits evaluation of flow in the PA and aorta and, therefore, quantification of any intracardiac shunt as well as dynamic evaluation of the distensibility of the PA.

The lack of ionising radiation and objective nature of cardiac MRI assessment of right heart haemodynamics are particularly valuable for follow-up purposes.

MRI data can be of prognostic importance—decreased stroke volume, increased RV end-diastolic volume and decreased LV end-diastolic volume being poor prognostic indicators.

Using temporally resolved MR perfusion techniques combined with spatially resolved MRA patients with CTEPH can be accurately differentiated from those with

PAH. Pulmonary arterial obstruction or stenosis leads to wedge-shaped perfusion defects or perfusion delay, while in PAH, the perfusion is reduced and heterogeneous. Quantitative evaluation of perfusion in patients with PAH has shown a significantly reduced pulmonary blood flow (PBF) and prolonged mean transit time (MTT) in patients when compared with healthy volunteers, but this did not correlate with the severity of pulmonary hypertension.

Computed tomography plays a major role in assessing patients with suspected or known PAH and may suggest the presence of PAH, even when clinically unsuspected. CT is widely available, non-invasive, inexpensive and well tolerated. CTPA permits comprehensive evaluation of the pulmonary vasculature, heart and lung parenchyma.

Systematic evaluation of each component is key to full pathophysiological understanding.

While 'CTPA's role in diagnosing acute and chronic PE is indisputable, the comprehensive evaluation that it provides also demonstrates the impact on the right ventricle, identifies any left heart comorbidity and evaluates the lung parenchyma for signs of chronic lung disease and features of vasculopathy or hypoperfusion (mosaic perfusion). CT may suggest the presence of PAH, independent of its cause when the 'generic signs' of PAH are present.

The generic signs can include both vascular and cardiac features, which are described below.

In the presence of known PAH, or CT signs suggesting its presence, a detailed evaluation of its potential cause should be sought.

This will include a systematic evaluation of cardiac causes (left ventricular dilatation, signs of prior infarct, presence of valvular disease or an intracardiac shunt),

large vessel obstruction (by chronic thromboembolic disease or rarely tumour or vasculitis) and the lung parenchyma (for primary lung disease, signs of vasculopathy/mosaic perfusion).

Vascular Signs

Dilatation of the pulmonary arteries is a useful sign which may suggest pulmonary hypertension.

The transverse diameter of the MPA at its bifurcation or the ratio of MPA and aortic diameter at the same level are the most commonly used parameters.

The upper limit of normal for the diameter of the pulmonary trunk is variously described as 29–33 mm and PA:Ao ratio less than 1. A PA:AA ratio greater than 1

carries a high specificity (around 90%) and acceptable sensitivity (around 70%) for the diagnosis of PAH > 25 mm Hg (Fig. 16.16). The dilatation

of segmental vessels also aids PAH diagnosis. If the segmental arterialbronchial ratio is greater than 1 in at least three lobes it suggests PAH with a specificity increased to 100% when seen in combination with a

dilated main PA.

A wide variation of the upper limit of the PA diameter is reported in the literature.

Although it is likely that the PA diameter is correlated to

patent size or stage in the cardiac cycle, neither the ratio of PA:AA nor normalisation of the PA to the body mass index (BMI) increased the correlation with the mean PAP. As the PA diameter can be considerably increased in patients with interstitial lung disease (e.g. up to 4 cm) in the absence of PAH, it should be interpreted with caution in this setting. From a practical point of view, the PA:AA ratio has become the most widely accepted sign for many radiologists.

Dilatation of bronchial arteries (>1.5 mm) is common in CTEPH when bronchial blood flow may account for over 20% of total blood flow to the lungs and may contribute to oxygenation.

Dilated bronchial arteries are most frequently seen in patients with CTEPH but may also be seen in patients with Eisenmenger syndrome or less frequently in IPAH. The enlarged bronchial collaterals are considered a good prognostic sign in CTEPH patients undergoing pulmonary endarterectomy, perhaps reflecting preserved vascular beds distal to pulmonary arterial obstruction.

Cardiac Signs

Straightening and later bowing of the interventricular septum towards the left ventricle are signs of RV dysfunction/strain and are common findings in PAH independent of cause.

RV dilatation is considered to be present when the maximal short-axis diameter of RV is greater than that of the LV (RV:LV >1).

This is also widely used in the setting of acute PE as a sign of RV dysfunction.

• Reflux of contrast medium into the inferior cava and hepatic veins is commonly seen in association with tricuspid regurgitation secondary to PAH but is not specific.

While reflux into the inferior vena cava can be seen in normal patients with injection rates exceeding 3 mL/s, reflux into the peripheral hepatic veins is considered abnormal.

• Pericardial effusions are common in patients with moderate or severe pulmonary hypertension; greater than 10–15 mm in fluid depth in the anterior pericardial recess has been reported in association with increased RV strain in PAH.

Parenchymal Signs
Mosaic perfusion is a hallmark of CTEPH, reflecting hypoperfusion of obstructed vascular beds and normal/hyperperfusion of patent beds. When seen in the presence of generic signs of PAH and the absence of signs of airways disease, it is highly suggestive of CTEPH, even on unenhanced images.

Small vessel vasculopathy in PAH may be associated with the presence of subtle diffuse centrilobular groundglass nodular opacities similar to those seen in non-PAH patients with hypersensitivity pneumonitis or respiratory bronchiolitis.

Imaging plays an important role in suggesting the diagnosis of PVOD and PCH, which are considered part of the spectrum in group 1'. Because the obstruction in PCH/PVOD is on the capillary/venous side of the

circulation, the use of PAH vasodilator therapy targeting the arterioles can result in life-threatening oedema. In PCH/PVOD, lung parenchymal findings are usually much more pronounced than in PAH; lymphadenopathy

and pleural effusion are frequent additional findings In PCH, diffuse centrilobular nodular opacities are more dense and may be associated with patchy ground-glass opacity and septal thickening. In PVOD, interlobular septal thickening is usually a prominent finding.

As smooth septal thickening is a feature most commonly seen in interstitial oedema, a review of the PCWP, cardiac morphology and function is required to exclude Group 2 disease.

In patients with Eisenmenger syndrome and IPAH, tiny

serpiginous intrapulmonary vessels may be seen (socalled neovascularity) arising from centrolobular arterioles not conforming to the usual pulmonary artery anatomy.

Pulmonary Arteriovenous Malformations

PAVMs may be diagnosed on clinical grounds and/or by familial screening in patients with hereditary haemorrhagic telangiectasia (HHT).

When acquired, they may be seen in conjunction with liver cirrhosis, schistosomiasis and metastatic thyroid carcinoma.

Clinically, they may produce systemic arterial desaturation and give

rise to signs of dyspnoea, hypoxia, cyanosis and heart failure.

If they rupture, massive haemoptysis and haemothorax occur.

Direct communication between a pulmonary artery and vein predisposes one to paradoxical embolism, which is responsible for two-thirds of neurological symptoms in patients with HHT.

Although 10% of cases present in the first decade, most do not manifest clinically until the third or fourth decade. Multiple lesions are seen in up to 50% of cases.

PAVMs can be treated non-invasively by embolotherapy or by surgery; the preference goes for the former in most cases. Precise understanding of the angioarchitecture, which is necessary before interventional procedures, can be achieved using modern computed tomography angiography (CTA) techniques and three-dimensional (3D) reconstructions.

Two types of PAVMs can be differentiated:

1. Simple PAVMs with a single feeding artery and one or several draining veins (80%).

2. Complex PAVM with more than one feeding artery and one or more draining veins (20%).

Radiographically, they may appear as round, oval or lobulated opacities with associated often serpiginous feeding and draining vessels, but if small and discrete, they may not be detected on plain chest radiography. They occur most frequently in the lower lobes.

Although pulmonary angiography has been considered the 'gold standard' for the diagnosis of PAVMs, it has been largely replaced by CTA using thin-slice acquisition and 3D reconstructions such as volume rendering technique (VRT) and maximum intensity projection (MIP), which permits excellent demonstration of the angioarchitecture : CT is more sensitive (approaching 100%) than pulmonary angiography (around 60%). MRI can also be used, but it has lower spatial resolution compared with the multidetector computed tomography

(MDCT) technique.

PULMONARY THOMBOEMBOLIC DISEASE

ACUTE PULMONARY THROMBOEMBOLISM

Background

Venous thromboembolism (VTE) encompasses deep venous thrombosis (DVT) and its most serious complication PE.

Acute PE is the third most common cause of acute cardiovascular disease after coronary artery disease and stroke, with an annual clinically detected incidence of around 50 per 100,000. As the incidence of acute PE increases with age, and both the size of the population and their life expectancy is increasing, the number of patients diagnosed is likely to significantly increase over time.

PE may result in significant morbidity both in the acute phase as well as later in the form of chronic thromboembolic disease.

PE is also a potentially lethal disease, directly causing or contributing to the patient's death in one-third of those diagnosed with the condition.

If treated with anticoagulants, mortality directly due to PE is reduced to 8%.

The causes of undetected PE are twofold: PE may remain clinically silent, or the non-specific clinical signs and symptoms fail to arouse suspicion of PE.

Most patients present with pleuritic chest pain, tachypnoea and/or dyspnoea.

The classic clinical triad of sudden chest pain, dyspnoea and haemoptysis is present in only a minority of cases. Other symptoms and signs include cough, syncope, tachycardia, fever and signs of DVT, but patients may also present with shock, hypotension, or even cardiac

arrest indicating severe PE.

Obstruction of the pulmonary artery may have several physiological effects which interfere with both the circulation and gas exchange, the severity being related to the extent of obstruction.

In order to raise the PAP significantly, it is estimated that at least 30%-50% of the pulmonary vascular bed needs to be obstructed.

Other factors resulting in vasoconstriction, such as humoral agents and reflex mechanisms, are considered to play an additional role.

The abrupt increase in pulmonary vascular resistance results in dilatation of the RV.

The increase in RV pressure and volume may eventually lead to RV failure, which is considered the primary cause of death in severe PE.

Factors predisposing one to the development of PE include: increasing age (the risk of VTE almost doubles with each decade after the age of 40 years); previous VTE; instrumentation (e.g. indwelling intravenous catheters); neoplastic disease; immobilisation; (orthopaedic) surgery; hypercoagulable state; and hormonal treatment (including oral contraceptives

and pregnancy). In some cases, the underlying cause remains unknown.

Over 90% of pulmonary emboli originate from thrombus in the deep veins of the legs or pelvis which becomes detached and migrates via the systemic veins to the right side of the heart and into the pulmonary arteries.

Emboli normally lodge either at the bifurcation of branching pulmonary arteries (a few are situated at the bifurcation of the MPA, so-called 'saddle emboli') or in the peripheral small pulmonary branches.

Once an embolus has lodged in a pulmonary artery, it is normally either lysed by the patient's fibrinolytic system (although this is frequently incomplete) or occasionally becomes organised with recanalisation.

The degree to which each of these processes occurs depends, to some extent, on the patient's fibrinolytic system, the amount of thrombus deposited

on the embolus, and the degree of organisation of the embolic material itself.

In cases of repeated thromboembolism without lysis of the embolic material, arterial hypertension (CTEPH) can develop.

Acute embolus results in either a reduction or a cessation of the distal perfusion.

Because of the collateral circulation offered by the bronchial arteries, which increases in the case of PE, lung viability is preserved in the majority of cases and pulmonary infarction usually does not occur in patients without pre-existing cardiovascular disease.

However, if an impaired circulation exists, e.g. due to chronic congestion, the presence of PE may result in local hypoxia, capillary damage, exudation, haemorrhage and coagulation necrosis.

Pulmonary infarction develops in only around 15% of thromboembolic events and is seen most commonly in the lower lobes.

When a part of the visceral pleura is involved in this process, ischaemia may result in inflammation, which

can irritate or adhere to the sensitive parietal pleura, resulting in pleuritic pain.

Pulmonary infarcts become revascularised from the periphery, leading to either complete resolution or the development of small scars.

Diagnosis

Accurate diagnosis of acute PE is essential, because if untreated, it carries high morbidity and mortality; furthermore, unnecessary anticoagulation may also result in increased morbidity and mortality due to the increased

bleeding risk.

Presentation is often non-specific—of all the patients

with clinically suspected PE, only around one-third are eventually diagnosed with thromboembolic disease.

Clinical (Pre-Test) Probability Estimate and

D-Dimer Testing

There are no reliable bedside tests available to diagnose PE.

Electrocardiogram (ECG) and measurement of arterial pO2 are not diagnostic for PE, and are more useful in suggesting other causes for the patient's symptoms, e.g. myocardial infarction.

A D-dimer blood test (a degradation product of fibrin in the process of fibrinolysis; an increased D-dimer suggests activation of the coagulation and fibrinolytic systems) has a very high negative predictive value (NPV).

However, the NPV is not 100%, meaning that a negative test cannot exclude PE.

On the other hand, the positive predictive value of a positive D-dimer test is low as there are many conditions in which the thrombolytic system is activated, such as inflammation, recent surgery, trauma, bleeding, neoplastic disease, during pregnancy, and in hospitalised patients.

In addition, the specificity of the D-dimer test decreases with increasing age.

A recent meta-analysis has shown that using age-adjusted cut-off values of the test (age \times 10 µg/L above the age of 50 years) instead of the standard value of 500 µg/L

increases the specificity while the sensitivity is maintained.

The D-dimer test generally is performed in combination with a clinical probability estimate (CPE), usually a clinical prediction rule.

Several clinical prediction rules, such as the Wells and revised Geneva rules, have been developed, of which, the original and the simplified Wells rule is the best evaluated and most frequently used.

However, the performance of these clinical prediction rules varies between

different patient groups and in different clinical settings. The combination

of a negative D-dimer test and a low or intermediate CPE reliably rules

out PE and no further testing is indicated. This combination is found

in up to 51% of outpatients or those seen via the emergency ward. In

all other circumstances (high clinical suspicion and/or positive D-dimer

testing) further diagnostic work-up using imaging is warranted. There

is insufficient evidence that it is safe to rule out PE in pregnant patients

based on D-dimer testing and CPE alone as this strategy is not validated

in this patient category.

Imaging Findings

Plain Chest Radiography

The chest x-ray may be normal (up to 40% of patients with PE) or show non-specific findings, even in extensive PE.

The chest x-ray is performed not to diagnose PE but to exclude other causes of the symptoms, such as pneumonia, pleuritis or pneumothorax. Several signs related to PE (and therefore suggestive of the diagnosis) have been described.

However, they are infrequently present and non-specific: i.e. its presence does not confirm the diagnosis of PE.

The most important ones are:

• *Hampton hump*. This is a pleural-based, wedge-shaped opacity with the apex of the triangle pointing towards the occluding vessel/hilum.

It is typically not seen in the first 24 hours after the embolus has lodged in the pulmonary artery and it represents a parenchymal infarction.

This condition may take from 3–5 weeks up to months to resolve, and a band-like opacity, due to scarring or focal pleural thickening, may remain.

The opacity may not always be triangular as the infarction may be surrounded by haemorrhage.

If the infarcted area becomes secondarily infected,

cavitation or abscess formation may occur. The latter may also be caused by septic emboli.

These opacities may not only be seen in case of infarction but can also be the result of oedema and haemorrhage.

The latter are usually found in the lower lobes, from 12 hours to several days after the thromboembolic event, and show relatively rapid resolution (7–10 days).

• *Westermark sign*, defined by a hyperlucent area with decreased vascularity due to oligaemia of the involved part of the lung.

Although this finding is not specific for PE, it should be considered, especially if newly found.

• '*Knuckle' or 'sausage' sign*, describing a dilatation of a central pulmonary

artery due to occlusion by the embolus with collapse or

constriction of the distal arteries, resulting in an abrupt tapering of these arteries.

Other secondary findings that may be present are: platelike atelectasis, (haemorrhagic) pleural effusion, and an elevation of the diaphragm, either due to pleuritic pain or as a result of decreased pulmonary compliance.

If PE is severe, signs of RV failure may be encountered, such as dilatation of the right heart, the superior vena cava and the azygos vein.

Transthoracic or Transoesophageal Ultrasound (Echocardiography).

This examination is the first imaging method of choice in

cardiorespiratory-unstable patients, in whom massive PE is suspected.

The RV function can be assessed and central pulmonary emboli be detected.

As this technique has a low sensitivity for peripheral emboli, its use is not recommended in stable patients.

The advantage of this technique is the assessment can be performed at the bedside and can diagnose other cardiovascular diseases that may explain the patient's

symptoms, such as cardiac tamponade or acute myocardial infarction.

Conventional Pulmonary Angiography

Until recently, pulmonary angiography was considered the gold standard for the diagnosis of PE. For several reasons (e.g. costs, limited availability and invasiveness of the procedure), it has not gained general acceptance.

In experienced hands it remains a valuable examination with a low complication rate (mortality 1% and non-fatal complications <5%); however, for diagnostic purposes, it may only have a role if CT is not available or a definite diagnosis cannot be obtained otherwise.

Thrombectomy or selective thrombolysis by conventional pulmonary angiography is performed in some centres as a treatment option in a subgroup of patients with PE.

Compression Ultrasound of the Legs

The majority of the PE originates from the deep venous system of the lower extremities and pelvis.

If DVT is diagnosed in a patient with clinically suspected PE, no further evaluation is needed and the patient can be treated for PE.

In skilled hands, compression ultrasound (CUS) achieves a 92%–95% sensitivity and 98% specificity for the diagnosis of acute DVT.

However, the presence of DVT can be confirmed in only

a minority of patients with proven PE. A negative CUS of the legs, the best investigation to evaluate DVT, does not exclude the presence of PE and further imaging is warranted.

Performing CUS may be an option in patients with symptoms and signs of DVT or in patients with relative

contraindications for CT.

Ventilation–Perfusion Scintigraphy

This is a nuclear investigation starting with the assessment of the PBF (perfusion (Q) scintigraphy) by intravenous injection of technetium (Tc)-99m-labelled macro-aggregated albumin (MAA) particles.

These particles are transported to the pulmonary circulation where they get trapped in a minor proportion of the small pulmonary capillary bed.

Currently there are three main lung perfusion acquisitions: planar imaging, single photon-emission computed tomography (SPECT) and a combination of SPECT and low-dose CT (SPECT/CT).

SPECT/CT has the highest spatial and contrast resolution and, with the additional anatomical information, it has a higher specificity.

Traditionally, in planar imaging, 6–8 static views are obtained by counting the radiation emitted by the particles in the lung with a gamma camera.

With SPECT and SPECT/CT a volumetric data set is obtained, but the latter increases the investigation time and the radiation dose, and often higher doses of technetium are used.

Data on this topic are limited, but there may be a higher diagnostic accuracy with SPECT and SPECT/CT as compared with planar imaging.

The choice of perfusion acquisition technique is dependent on user preference.

When thrombus is present, the particles cannot get into the small vessels, resulting in a perfusion defect.

A normal perfusion study rules out PE with almost 100% certainty and further investigation is not indicated.

If a perfusion defect is present and chest x-ray is normal, it is justified, in this situation, to consider the perfusion

defect as a mismatch. If the chest x-ray is not normal, further imaging is warranted.

Depending on the number and size of the perfusion defects, additional ventilation imaging can be performed to increase the specificity. Ventilation (V) scintigraphy is performed by inhalation of a radioactive gas.

Krypton-81m (81mKr) is the optimal imaging agent for this purpose as it emits high-energy photons (190 keV) and, owing to its short half-life, it can be continuously administered to the patient, including during perfusion imaging.

The disadvantage of 81mKr is that it is expensive to produce and its low-half-life limits its availability.

As an alternative, (Tc)-99m-labelled carbon microparticles (Technegas) is commonly used, but its use is not approved in the United States.

Once ventilation and perfusion images are obtained, they are then compared with observe for V/Q 'mismatches'. When segmental perfusion defects are present and ventilation is normal or the ventilation defect is smaller than the perfusion defect, there is a high probability for PE (>95%) and the patient can be treated for PE without further investigation.

All other V/Q results, i.e. subsegmental perfusion defects or ventilation defects matching the segmental perfusion defects (occurring in 60%–70% of the V/Q-scans), are called non-diagnostic or indeterminate, as other diseases, such as asthma and chronic obstructive pulmonary disease, may also cause these defects.

Further investigation therefore is indicated, as only up to 30%–40% of the patients with an indeterminate result

eventually have PE. Recently, it was proposed to use,

instead of the

probability-based interpretation of V/Q scinitigraphy, an alternative reporting system similar to CTPA examinations and more clinically useful.

V/Q scintigraphy results are reported as either PE positive or PE negative, with only a minority designated as indeterminate or nondiagnostic for PE.

As with CT, if the pre-test probability is discordant

with the V/Q result, further testing should be considered.

Perfusion scintigraphy is a good initial imaging investigation in patients with a normal chest x-ray and no history of pulmonary disease; in this setting a normal result or a segmental perfusion defect is a reliable finding that leads to few non-diagnostic results.

Perfusion scintigraphy should also be considered when a relative contraindication for CT (see below) exists, such as severe renal impairment.

Computed Tomography Pulmonary Angiography

In 1992 the first publication on the use of CTPA for the diagnosis of acute PE appeared.

Since then, CTPA has become the investigation of choice in the work-up of patients with suspected PE. Its preference is due to the continuous improvement of the CT technique, resulting in substantial improvement in the acquisition speed, spatial resolution,

image quality and, most importantly, diagnostic accuracy.

Together

with the broad availability, low cost and minimal invasiveness of this technique have led to a broad acceptance of it in clinical practice.

With modern MDCT reported sensitivities and specificities of 83%–100% and 89%–97% are comparable to those of the former gold standard of PE diagnosis, invasive pulmonary angiography of 98% and 97%, respectively.

This means that with a qualitatively good CT, PE can

be ruled out safely, at least in (out)patients without a high clinical probability of PE and further testing for PE is not warranted.

The advantage of CT (and to a lesser extent MRI) over other imaging techniques is the direct visualisation of the emboli as well as the other structures of the chest, including the lung parenchyma, mediastinum and chest wall, resulting in an additional or alternative diagnosis (e.g. pneumonia, pleuritis, aortic dissection, pneumothorax and lung tumours) in a significant proportion of patients with clinical symptoms suggestive of PE.

In patients with PE, CTPA can also provide parameters considered to be related to clinical outcome, such as right ventricular dysfunction (RVD), the total amount of thrombus present (although contradicting results for the latter are found) and, if available, pulmonary perfusion.

A RV/left ventricular (LV) diameter ratio greater than 1.0

measured on standard axial views has been shown to be directly correlated with RVD and to predict adverse outcome and early death.

Quantitative assessment of the thrombus load, for which several scoring systems have been proposed, is very timeconsuming, although this may be overcome with the use of computer-assisted detection (CAD) software in the future.

With the improvement of the CT technique, very small PEs are frequently detected that are at or even beyond the subsegmental level.

At the moment, it is uncertain whether the risk of having

a solitary very small PE outweighs the risk of anticoagulant treatment (minor to severe bleeding). Currently, treatment of a solitary small PE is considered indicated if patients have limited cardiopulmonary reserve, coexistent DVT or recurrent small PEs. In a subgroup of patients, especially those who have a good cardiopulmonary reserve, limited timeframe of risk factors and in whom DVT is excluded, treatment for

a shorter time period with anticoagulants or even withholding treatment may be considered.

Computed tomography pulmonary angiography protocol. Data

acquisition is performed during one breath-hold, preferably at total lung capacity.

The standard CT parameters are 100–140 kV, depending on patient habitus.

There is a general trend to decrease dose by lowering

the kV in slim patients to 70– 80 kV. The additional advantage of choosing lower kV is the increase in vascular enhancement (in HU) due to increased absorption of iodine at lower kV.

Dose modulation techniques should always be used to further reduce the dose.

Regardless of the number of detector rows, between 300 and 450 0.9- to 1.0-mm-thick slices using overlapping reconstruction should be obtained.

The injection protocol has to provide a constant and high degree of pulmonary arterial enhancement during the complete data acquisition, which has become a challenge with the very short acquisition times.

For an adequate assessment, an attenuation of at least 300 to 350 HU (i.e. 250 to 300 HU net contrast enhancement) in the pulmonary arteries is considered optimal. Suboptimal vascular opacification is one of the major causes of non-diagnostic images, and it compounds the effect of concomitant problems such as partial volume or movement artefacts.

Combined protocols: one-stop-shop procedure. CT venography has been considered as a part of a one-stop-shop procedure in order to diagnose VTE.

After administering one bolus of contrast medium, first

the pulmonary arteries are investigated followed by additional late-phase imaging of the deep venous system from the calves up to the inferior vena cava to detect DVT.

Although this combined procedure is feasible

and has the advantage of detecting DVT in pelvic veins and inferior vena cava (IVC), which is not possible with CUS, studies have shown that in comparison with CTPA alone, this combined technique results in only limited increase in sensitivity with a comparable specificity.

A major drawback of CT venography is the significant increase of radiation, which at this moment does not justify its routine use in patients with suspected PE.

Alternatively, CTA with ECG gating can be performed in patients presenting with acute chest pain without significant increase in radiation dose.

During one data acquisition, information can be obtained on the most important vascular diseases causing acute chest pain: acute coronary syndrome, aortic dissection and acute PE.

The use of dual-source CT or systems with high numbers of detector rows may overcome the initial limitations of ECG-gated CTPA, providing faster acquisition times,

better image quality in patients with abnormal cardiac rhythms, and lower radiation dose.

The downside of such a protocol is the increase in complexity both for the technician and the reader, with an increase in post-processing and interpretation time.

Computed tomography pulmonary angiography during

pregnancy.

During pregnancy and puerperium, the incidence of VTE is two- to fourfold higher and is one of the most important causes of maternal mortality.

As diagnosing DVT in patients with suspected PE justifies PE treatment, leg ultrasound is considered the first diagnostic test of choice as no radiation is used, at least if signs or symptoms of DVT are present.

Because of the concern about radiation, there is little

agreement about optimal imaging during pregnancy when leg ultrasound is normal. Either CTPA or perfusion scintigraphy can be obtained, the latter being useful if the chest radiograph is normal.

As an alternative, MRI has been proposed.

At any time during pregnancy (including the first 3 months) the radiation dose to the unborn child delivered by either V/Q scintigraphy or CTA is considered negligible, and the risks of a potential fatal ending

due to undiagnosed PE are substantial. If CTA is performed, the CT protocol should be adapted to reduce radiation dose and to the hypercirculatory state of pregnant women to limit the number of inconclusive

examinations.

Furthermore, it is advised that thyroid function should

be checked in the first week after birth, as the iodine in the CT contrast medium may decrease thyroid function.

In young women, either pregnant or not, the radiation

exposure to the radiation-sensitive breast tissue (in the order of 10 to 70 mGy) is an important issue, and to a lesser extent the exposure to the lung.

Perfusion scintigraphy produces a lower breast dose (1 mGy).

During pregnancy this would be at the expense of a slightly increased dose for the fetus as the radiopharmaceutical agent is excreted by the kidneys

and may give radiation from the bladder to the neighbouring uterus.

Flushing the bladder with saline via a catheter has been proposed to reduce the exposure.

Computed tomography pulmonary angiography assessment

The diagnosis of PE on CTA is based on the direct visualisation of the thrombus that may result in a partial filling defect or complete obstruction of the pulmonary artery.

Secondary findings of acute PE may help to point attention to a certain area, such as the presence of pulmonary infarcts.

Signs of acute pulmonary hypertension can also be present, usually as a result of extensive obstruction of the

arterial bed, such as dilatation of the pulmonary trunk and/or right heart. The direct and indirect signs of both acute and chronic PE.

Artefacts and pitfalls frequently occur and one should be aware of them to avoid false-positive and false-negative results.

Computed tomography perfusion. Introduction of the dual-energy CT (DECT) technique has led to several potential advantages, including novel image interpretation concepts without an increase in radiation dose.

The DECT technique uses the different absorption characteristics of iodine at different voltage levels.

Two data sets are (nearly) simultaneously acquired at different tube voltages, or using a relatively new technique with a single tube and multilayer detectors. Fusion of the two data sets results in a 'standard' CTA. Subtraction of the lower kV data set from the higher kV data can produce colour-coded CT regional iodine density maps of the lung which act as a surrogate for perfusion. The quantitative assessment of perfusion defects of the

lung parenchyma has been found to be an important determinant for patient outcome.

In addition, the presence of perfusion defects may

help in the detection of PE and therefore increase sensitivity, which can be beneficial, especially for less experienced readers.

However, this technique also has several pitfalls and artefacts, caused by underlying pulmonary disease such as emphysema, cardiac motion or diaphragm movement or beam hardening effects caused by dense contrast material in the thoracic veins.

Another post-processing technique possible with DECT is virtual monoenergetic imaging, which is the result of mixing the high- and low-energy data sets in a particular ratio that results in images at a specified virtual monoenergetic photon energy.

The potential of this reconstruction technique is optimisation of image contrast, improvement of the contrast-to-noise ratio and reduction of beam hardening. Both virtual monoenergetic and perfusion imaging may improve reader confidence and diagnostic accuracy. Although these techniques seem promising, their potential benefit for diagnosis, prognosis and therapy

monitoring still needs to be determined.

Magnetic Resonance Imaging

MRI is an attractive alternative to CTA as no ionising radiation is used and modern MRI contrast media yield less risk for the development of contrast-related nephropathy and contrast agent reactions as compared

with iodinated contrast media.

Due to the long data acquisition and limited availability, especially in the acute setting, MRI is still not widely performed.

On the other hand, recent improvements with respect to

spatial resolution and new sequences with shorter acquisition times make MRA a feasible technique for the acute setting.

Various MRI techniques are available (e.g. unenhanced and post-gadolinium angiography sequences, with or without MR perfusion sequences).

According to the literature, the accuracy of MRA is comparable to CTPA for central and segmental pulmonary arteries, but still limited for PE in the peripheral pulmonary vessels.

Reported overall sensitivity compared with MDCT and V/Q is 78%-85% and specificity 99%-100%.

However, the rate of inconclusiveness ranges from 25% to 30% and sensitivity drops down to 21%–33% for subsegmental PE.

As with the newest CT techniques, MRI offers the option to obtain additional functional information such as on cardiac function and lung perfusion.

At the moment, the technique is, however, less robust as compared with CTA and examination times remain long (up to 10–25 minutes for a combined technique protocol). However, further improvement in technique and acquisition speed is to be expected and, together with more experience, may result in better accuracies and a decrease in inconclusive results.

As the specificity of MRI is high, it should be considered as a viable alternative to CTPA, especially in patients with (relative) contraindications to CTA such as young and/or pregnant women.

Diagnostic Strategies

The most straightforward diagnostic approach as recommended in the 2014 ESC guidelines for patient with suspected acute PE.

This diagnostic algorithm is based on integrating clinical

data and laboratory and imaging tests. It should be noted that the choice of technique is also dependent on local availability and experience, user preference, and last but not least the patient studied.

CHRONIC PULMONARY THROMBOEMBOLISM

PE becomes chronic if the clots in the pulmonary arteries do not resolve adequately.

This may result in a progressively increased pulmonary arterial blood pressure and CTEPH, which is a serious and life-threatening complication, and if it occurs it is usually in the first 2 years after the thromboembolic event.

The estimated incidence of CTEPH after an episode

of acute PE varies, but figures as high as 4% have been described.

On the other hand, about half of the patients with CTEPH do not have a clinical history of acute PE.

Chronic PE is one of the few causes of pulmonary

hypertension that effectively can be treated by surgical resection of the thrombus (pulmonary thromboendarterectomy) if the thrombi are localised

in central vessels, up to the proximal segmental arteries. Percutaneous balloon angioplasty is emerging as a less invasive alternative that has been shown to be feasible and effective for a subgroup of patients, but its

exact role in the treatment of CTEPH is still to be determined.

Medical treatment is recommended in patients with persistent or recurrent CTEPH after surgical treatment, or who are considered inoperable.

CTEPH should be ruled out in patients who were treated for acute PE and suffer from persistent dyspnoea. In addition, chronic PE should be evaluated in every patient with pulmonary hypertension with a known history of PE or in whom the cause is unclear.

According to international guidelines, V/Q scintigraphy is the imaging method of choice to rule out suspected CTEPH, as a normal perfusion scintigram confidently

excludes the disease whereas multiple, bilateral segmental perfusion defects are suggestive but not specific for chronic PE.

DECT and perfusion MRI both permit maps of regional perfusion to be generated and show promise as a 'onestop shop' to evaluate both the pulmonary arteries

and parenchymal perfusion. Currently, pulmonary angiograpy is still considered the gold standard for the diagnosis of distal chronic PE, but as with acute PE, CTA has established a prominent role in many centres in the work-up of patients with pulmonary hypertension in general and suspected chronic PE in particular. CTA may effectively diagnose or rule out other causes, such as parenchymal disease, and diagnose and assess the location and extent of chronic thrombi.

Although, with MRI, important morphological and functional cardiac information can be obtained, it is not performed routinely, because of the known limitations:

cost, availability and examination time.

As for acute PE, at CT both direct and indirect

signs of chronic PE—which are partly related to the presence of pulmonary hypertension—have been

described.

It should be noted that in patients with recurrent PE both chronic and acute PE can coexist.

CONCLUSION

The investigation of changes in pulmonary vascular physiology has many facets.

The initial clinical assessment may significantly influence further investigations.

Chest radiography is still the primary method for assessing effects of PV hypertension.

CTA is the first imaging investigation in the diagnostic work-up of patients with suspected PE. In addition, CT may provide an alternative diagnosis in a significant percentage of patients in which PE is excluded. Pulmonary hypertension is a very serious

disease that can be caused by a number of different

diseases requiring different treatment and having varying prognosis. CT and MRI play a major role in determining the different types of PAH.

Ischaemic Heart Disease

INTRODUCTION

Ischaemic heart disease (IHD) is a complex, heterogeneous and incompletely understood disease that is usually caused by underlying coronary artery disease (CAD).

Worldwide, it is the single most common cause

of death and its frequency is increasing. Although the mortality associated with IHD has declined, due to therapeutic improvements and prevention campaigns reducing the incidence of fatal and non-fatal myocardial

infarction, the prevalence of IHD will continue to increase.

For instance,

in patients with STEMI (i.e. ST-segment elevation myocardial infarction),

mortality remains substantial, with in-hospital mortality and 1-year

mortality rates up to 10%. Moreover, survivors of a first myocardial

infarction are thought to die of IHD at later ages due to heart failure

and late cardiac deaths. Other contributing factors are an

increasing

prevalence of type 2 diabetes, physical inactivity and obesity.

Although catheter-based coronary angiography is the diagnostic

procedure of choice to diagnose and treat CAD, non-invasive cardiac

imaging—that is, echocardiography, nuclear medicine, cardiac computerised

tomography (CCT) and cardiovascular magnetic resonance

(CMR)—are key imaging techniques in unravelling the intricate relationship

between CAD and IHD, in preclinical detection of CAD and in

the assessment of patient prognosis.

PATHOPHYSIOLOGY OF ISCHAEMIC

HEART DISEASE

CAD, that is the process of atherosclerotic plaque formation, is the usual cause of IHD.

Symptoms of myocardial ischaemia occur when the coronary blood flow is significantly impaired.

This may happen when the coronary artery lumen is slowly and progressively impinged by an evolving atherosclerotic plaque (*chronic stable plaque*), or when a coronary artery plaque ruptures—or, less frequently, plaque erosion—and a thrombus is formed with a sudden occlusion of the lumen, causing an *acute coronary syndrome*.

Moreover, less common—or superimposed—causes of myocardial ischaemia are coronary artery spasm and microcirculatory dysfunction.

Acute coronary occlusion triggers in the myocardial perfusion territory distal to the occlusion, that is *the jeopardised myocardium* or *myocardium at risk*, an ischaemic cascade starting with metabolic disturbances followed by regional dysfunction, electrocardiographic (ECG) changes and, finally, onset of anginal symptoms. Systolic contraction typically ceases within seconds after coronary occlusion.

After approximately 20 to 30 minutes of sustained ischaemia, irreversible myocardial damage (i.e. *myocardial infarction*) occurs with myocardial cell swelling and apoptosis, ultimately leading to myocyte necrosis.

Cellular necrosis always initiates at the endocardial side of the myocardium with the lateral boundaries of infarction closely corresponding to the myocardium

at risk, and follows a transmural wave front progression taking 3 to 6 hours to reach the subepicardium.

As a consequence, the amount of necrosis is mainly determined by extent of myocardium at risk and degree of transmural progression. Current therapeutic strategies aim to timely restore coronary flow by percutaneous coronary intervention

or thrombolysis, which will stop the transmural progression of necrosis, and salvages the ischaemic, but still viable, myocardium; however, in spite of the beneficial effects of reperfusion, the process of cell death may continue during the first hours of reperfusion, a phenomenon called '*myocardial reperfusion injury*'.

This occurs in the infarct core and is characterised by a lack of reperfusion at myocardial capillary level (i.e. *microvascular obstruction* or *no-reflow phenomenon*) despite an effective recanalisation of the infarct-related artery.

Myocardial infarction can be recognised by clinical features, including ECG findings, elevated values of biochemical markers (biomarkers) of myocardial necrosis, and by imaging, or may be defined by pathology.

Infarctions are usually classified by

(a) location (anterior—inferior—lateral);

(**b**) size (focal necrosis, small (<10%), moderate (10% to 30%) and large (>30% of LV myocardium)); and

(c) temporally as evolving (<6 hour), acute (6 hour to 7 days), healing (7 to 28 days) and healed (>28 days). Although myocardial infarctions usually affect the left ventricle, extension toward the right ventricle may occur. Isolated right ventricular infarctions, conversely, are seldom.

In the days, weeks and months following the acute event, the heart undergoes a remodelling with changes in ventricular size, shape and function, with changes not limited to the infarcted myocardium but involving the remote myocardium as well.

In an early phase, tissue oedema, haemorrhage and acute inflammation lead to an expansion of the infarct size. This may lead to weakening of the myocardial wall, eventually resulting in an early ventricular rupture or rapid evolution towards an aneurysm. During infarct healing, an opposite phenomenon occurs, with a progressive replacement of the necrotic myocardium by a collagen-rich fibrous scar causing a thinning of the affected myocardial wall.

Depending on the extent of the infarct, part of the ventricle loses contractile force, and as a compensatory

mechanism, the ventricle usually dilates to maintain stroke volume.

This, however, is a potentially adverse event because it may trigger the evolution towards a dilated ischaemic cardiomyopathy and, ultimately, ischaemic heart failure (IHF).

If the duration of coronary occlusion is brief (<15 min), then no myocardial infarction occurs but recovery of the myocardial dysfunction is typically delayed and is closely related to the length of ischaemia, a condition known as

'stunned myocardium'.

This is typically encountered in patients with stable or unstable angina, and coronary vasospasm.

When a milder degree of ischaemia is persistent for a longer time, myocytes become chronically dysfunctional by down-regulation of energy consumption through a lower level of aerobic and/or anaerobic metabolism.

If perfusion is restored to these dysfunctional areas, function may return to normal, although the recovery is typically slow, taking up to more than 1 year in severe forms.

This condition, known as *'hibernating myocardium'*, should be differentiated from chronic myocardial dysfunction caused by irreversibly damaged myocardium. Patients typically present with moderate to severely reduced ventricular function, presence of several stenotic lesions on their coronary angiogram, and symptoms of heart failure.

Because of the cost of the revascularization procedure and the inherent risk related to these interventions, in

particular when performed in patients with poor cardiac function, it is crucial to determine preoperatively the potential benefit of a revascularization procedure.

It should be emphasised that IHD patients may present with a mixture of different ischaemic substrates (ischaemic, stunned, hibernating, necrotic/scarred myocardium), urging for accurate myocardial tissue characterisation to choose the best therapeutic option.

CORONARY ARTERY IMAGING

The process of atherosclerotic plaque formation usually involves the epicardial part of the coronary artery system. The diagnosis of CAD is made at conventional coronary angiography by impingement with narrowing or occlusion of the coronary artery (CA).

Significant CAD is considered in the presence of a diameter stenosis of \geq 70% in a major vessel or \geq 50% in the left main, and usually results in referral for intervention.

Although coronary angiography provides valuable information regarding the severity and length of stenosis, coronary artery (CA) occlusions, number of vessels affected, stenosis configuration (smooth, ulcerated), presence of thrombus, collateral vessels, CA anatomy and

variants, this technique faces several limitations.

Mild or non-stenotic CAD is not visualised and no or limited information is provided regarding the plaque composition or degree of vascular remodelling; thus a normal coronary angiogram does not exclude CAD, and a stenotic plaque may be just the tip of the iceberg in some CAD patients.

It should be emphasised that in most patients presenting with an acute myocardial infarction, it is caused by rupture of non- or minimally stenotic plaque.

Because of its invasive nature, the need to administer iodinated contrast agent, and radiation issues, the use of conventional coronary angiography should be limited to symptomatic patients with high pre-test likelihood

of obstructive CAD.

Finally, the relationship between myocardial ischaemia and CAD is complex, and many patients fulfilling the criteria of significant CAD turn out not to have a flowlimiting stenosis when measuring the fractional flow reserve (FFR).

While treatment should be reserved to patients with myocardial ischaemia, the oculo-stenotic reflex yields the risk of overuse of revascularisation.

Other issues such as collateral vessels and the number and length of plaques should also be considered in decision-making.

In a minority of patients presenting with typical angina and ST-segment depression on exercise testing, no

obvious abnormalities are found on conventional coronary angiography.

Diffuse subendocardial perfusion defects in these patients during stress perfusion imaging suggest that microvascular dysfunction rather than CAD is the causative mechanism of myocardial ischaemia.

Thanks to rapid technological advances in the field of CCT and CMR in recent years, non-invasive coronary angiography has become a reality and these novel techniques are now becoming integrated into daily clinical care.

Current state-of-the-art multidetector computed
tomography (CT) (at least 64 or more slices) affords coronary artery imaging with sufficient spatial and temporal resolution for clinical use.

A typical clinical examination consists of unenhanced CCT for detection and quantification of coronary calcium followed by contrast-enhanced CCT for coronary artery imaging, detection of coronary artery plaques and, to some extent, characterisation of the non-calcified plaques. The introduction of single x-ray source 256- and 320slice volumetric scanners and dual x-ray source 2×128 and 2×192 -slice CT systems has opened the door to 'single heartbeat' CCT in which the entire heart is imaged within one heartbeat.

Modern, single x-ray-source CT systems require approximately 125 ms to image the entire heart because only 180 degrees of gantry rotation (plus the fan beam angle) are required to reconstruct a CT image (the remaining 180 degrees are a mirror image of the first 180 degrees).

Dual x-ray-source CT systems have an even higher temporal resolution of up to 66 ms because only 90 degrees of gantry rotation are necessary (the two x-ray sources are mounted at a 90-degree angle and, therefore, only 90 degrees of gantry rotation are required to obtain a 180-degree view of the heart).

Using these state-of-the-art CT systems, high-quality CCT can be acquired in heart rates of up to 65 to 70 beats per minute, which are obtainable in the vast majority of subjects by administering β -blockers.

Patients are optimally suited if they have a regular heart rate, a body mass index below 40 kg/m2 and a normal renal function.

The examination is performed following intravenous injection of iodinated contrast agent (\sim 50–80 mL). Coronary vasodilatation can be achieved using sublingual nitroglycerin administration. Single heartbeat CCT has not only improved image quality but has also significantly reduced CCT radiation dose.

Where older CT systems used so-called retrospective

gating and acquired images throughout the cardiac cycle of multiple heartbeats, single heartbeat CT systems use prospective gating, where images are only acquired during a small fraction of the cardiac cycle (typically during end-diastole when cardiac motion is minimal). Further

reduction in radiation dose can be achieved with iterative reconstruction algorithms.

Using state-of-the-art CCT hardware with iterative reconstruction, routine, high-quality CCT examinations can be acquired with a dose of approximately 1 mSv. Coronary MR angiography is achieved using highresolution imaging targeted to each coronary artery separately, or using a whole-heart approach. Images are acquired during repeated breath-holds or during free breathing using a respiratory trigger algorithm.

Sequences are available for luminal and for wall imaging. Despite enormous efforts of CMR experts worldwide, coronary MR angiography has still not been incorporated into daily clinical care, mainly because of long acquisition times, lack of reliable image quality, and the comparative ready availability and ease of use of CCT; however, appropriate indications for coronary MR angiography include imaging of congenital anomalies of the coronary arteries, coronary artery imaging in (postoperative) patients with congenital heart disease and diagnosis (and follow-up) of patients with coronary aneurysms in Kawasaki disease.

Novel approaches such as coronary artery positron emission tomography/magnetic resonance (PET/MR) imaging and PET/CT imaging may open perspectives towards plaque inflammation imaging in the coronary arteries.

Calcification in the coronary arteries occurs, with exception of patients with advanced chronic kidney disease, almost exclusively in patients with coronary atherosclerosis.

As the amount of coronary calcium roughly correlates to the atherosclerotic plaque extent, detection and quantification of coronary calcium is of interest for patient risk stratification.

Most patients with an acute coronary syndrome (ACS)

show coronary calcium, and the amount of calcium in these patients is substantially greater than in age- and gender-matched subjects without CAD; however, coronary calcification is not related to plaque stability/

instability and only weakly related to the severity of

luminal stenosis.

In young symptomatic patients, negative coronary calcium findings do not exclude coronary artery stenoses. The Agatston score, less frequently volume or mass scores, is used to quantify the amount of calcium. Reference data sets stratified by age and gender are available for interpreting coronary calcium scans.

In the 2010 Appropriate Use Criteria for CCT, coronary calcium scoring was considered appropriate in asymptomatic patients without known CAD in low-risk patients with a family history of premature IHD, and to risk stratify intermediate risk patients.

Where previously CCT was typically not performed above a certain coronary artery calcium (CAC) score threshold (>400 or >1000 Agatston units) because the risk of a non-diagnostic CCT examination exposing the patient to a significant amount of radiation was too high,

this strategy has been abandoned.

Using state-of-the-art CCT equipment with iterative reconstruction algorithms, diagnostic CCT can be obtained in most patients with high CAC scores, yielding incremental prognostic value over CAC score alone.

Coronary CT angiography offers high accuracy for the detection of and, especially, for ruling out significant CAD.

In two recent multicentre trials, a sensitivity of 95%– 99%, specificity of 64%–83%, negative predictive value of 97%–99% and a positive predictive value of 64%–86% to identify patients with at least one coronary artery stenosis among individuals at low-to-intermediate risk for CAD.

The lower positive predictive value is explained by the tendency to overestimate the degree of stenosis by coronary CT angiography due to partial volume or blooming artefacts because the spatial resolution of current CT systems is limited to 0.5×0.5 mm2 or 0.6×0.6 mm2.

These systems use so-called energy-integrating detectors (EIDs) with an indirect conversion of x-ray photons into light photons by scintillator crystals and subsequent conversion of these light photons into an electric signal

by light sensors.

To prevent crossover of the light photons to adjacent

pixels, optically isolating septa separate EID pixels; however, because these septa have a finite thickness, the geometric dose-efficiency of EIDs is reduced with smaller pixels.

Therefore, there is a trade-off between EID spatial resolution and dose-efficiency.

New photon-counting detectors (PCDs) may overcome this limitation.

PCDs directly convert incident x-ray photons into an electric signal and measure their energy.

This direct conversion eliminates the need for optically isolating septa and allows for higher spatial resolution CT

without compromising dose-efficiency.

Prototype PCD CT systems with a spatial resolution of

 0.25×0.25 mm2 have demonstrated the potential of this technology to improve coronary stent visualisation and improve the diagnostic accuracy of CCT in coronary stenosis assessment.

Additionally, the lower sensitivity of PCDs to electronic noise may be used to improve CCT image quality at the same radiation dose or to maintain current image quality at reduced radiation doses.

Coronary CT angiography performs best in symptomatic patients with a low-to-intermediate likelihood of CAD.

In such patients, according to the 2010 Appropriate Use Criteria for CCT, coronary CT angiography was deemed appropriate to detect CAD in symptomatic patients without known heart disease, and also in those presenting with a clinical suspicion of ACS but having normal ECG and cardiac biomarkers, uninterpretable/non-diagnostic ECG or equivocal biomarkers.

Coronary CT angiography yields promise to determine and quantify the coronary plaque burden

and, to a certain extent, to characterise the plaque composition.

Using intravascular ultrasound (IVUS) as reference technique, lipid-rich plaques yielded result in attenuation values between 11 and 99 Hounsfield units (HU) versus 77–121 HU for fibrous plaques. With similar intra-reader, inter-reader, and inter-scan reproducibility to IVUS, serial CCT may

be used as a non-invasive alternative to IVUS for longitudinal plaque follow-up.

Finally, CCT is excellent to depict anomalous coronary arteries and myocardial bridging.

FUNCTIONAL IMAGING

Assessment of cardiac function is essential in the diagnostic work-up of IHD patients.

For instance, in acute myocardial infarction patients,

the dead myocardium ceases to contribute to the expulsion of blood, shifting the workload to the non-affected ('remote') myocardium.

Although a compensatory increase in contractility in the remote myocardium has been described, the net result is usually impairment in ventricular performance.

In patients clinically presenting with angina pectoris, the myocardium supplied by a haemodynamically significant

stenosis may become dysfunctional under stress conditions.

Also, in ischaemic heart failure patients, low-dose stress functional imaging may provide essential information with regard to the viability in dysfunctional parts of the heart.

A series of imaging techniques are available to assess function at the chamber (or global) or myocardial (or regional) level: that is, echocardiography, CMR, nuclear medicine (planar radionuclide ventriculography, gated blood pool single-photon emission computed tomography [SPECT]), catheter angiography and CCT.

Requirements are that these techniques are accurate, reproducible and preferably non-invasive. Global ventricular performance looks at the amount of blood expulsed by the ventricle in relation to the size of the ventricle.

Normalisation to body surface area enables comparison with gender- and age-matched normal subjects.

Typically, ventricular volumes are measured (or estimated) at end diastole (i.e. maximal filling) and at end systole (i.e. maximal emptying).

From the volumes, the ventricular stroke volume (i.e. end-diastolic volume minus end-systolic volume),

ejection fraction (i.e. stroke volume divided by enddiastolic volume) and cardiac output (i.e. stroke volume multiplied by heart rate) can be calculated.

In clinical practice two approaches are used:

(a) assumption comparing the ventricle to a geometrical model and

(**b**) volumetric techniques.

Whereas geometric assumption allows fast estimation of

ventricular size, it intrinsically depends on how well the model fits with the ventricle, which may not be the case in diseased ventricles.

Moreover, the complex geometry of the right ventricle

impedes easy use of geometric assumption.

In contrast, volumetric techniques use a slice summation,

cutting the ventricle in a set of (contiguous) slices. Summing up the volume of each of these slides yields an accurate estimate of the ventricular volume.

The downside is that this approach is more time

demanding for acquisition and analysis.

During systole, a complex deformation of the myocardium results in expulsion of approximately twothirds of the ventricular blood volume.

This myocardial deformation (also called '*myocardial strain*') is a direct consequence of the intricate myofibre anatomy, the interaction between deep and superficial myofibre layers and of a repositioning of fibre sheets during systole, resulting in a ventricular shortening in

long- and short-axis direction, wall thickening and, on top, a wringing motion of the ventricle in longitudinal direction—a phenomenon called ventricular torsion or twisting.

This deformation can be visually assessed and graded, and/or quantified and described.

Visual assessment describes (systolic) wall motion as *normokinetic* (preserved motion), *hypokinetic* (decreased but still present), *akinetic* (completely absent), *dyskinetic* (wall moving outward during contraction) and *hyperkinetic* (increased).

Systolic wall thickening can be visually graded as

normal, diminished, absent, as wall thinning, or as increased.

Strain imaging is used to quantify myocardial deformation, analysing deformation (or strain) in longitudinal, circumferential and radial directions. Quantification of ventricular torsion necessitates adapted approaches such as MR myocardial tagging.

Although beyond the scope of this chapter, it should be noted that the second part of the cardiac cycle, i.e. diastole, consisting of myocardial relaxation with subsequent ventricular filling, is also an essential of the cardiac performance.

Diastolic dysfunction may be the cause of heart failure or superimposed on systolic heart failure in IHD patients.

To describe regional myocardial morphology and function in a standardised and imaging-modality independent way, the American

Heart Association has promulgated a 17-segment model to map the left ventricle.

Because of conical shape of the left ventricle, it is divided

in longitudinal direction into four equal levels (or rings): that is a basal, mid and apical level, and a final level representing the LV apex.

Next, the basal and mid-level are divided in six equiangular segments, and the smaller apical level in four equiangular segments.

Finally, the segments are numbered starting with the

anterobasal segment and following a counter-clockwise direction (viewing the LV from apically): that is, basal level: segments 1 to 6, mid-level: segments 7 to 12, apical level: segments 13 to 16, and LV apex, that is segment 17.

Moreover, segments can be attributed to a coronary artery perfusion territory.

The left anterior descending (LAD) coronary artery typically supplies segments 1, 2, 7, 8, 13, 14, 17; the right coronary artery (RCA) segments 3, 4, 9, 10, 15; and the left circumflex (LCx) coronary artery segments 5, 6, 11, 12, 16.

Several variations, however, may occur depending on the

coronary artery anatomy and dominance. Despite the intrinsic advantages of using a standardised segmentation model, application in a myocardial infarction patient is often not ideal as the segments often only partially fit with infarct location, thus ending with segments consisting in a mixture of infarcted and viable myocardium.

Alternatively, a compartment model using the location and extent of the myocardial infarction may be more appealing to study the regional function as well as the

interplay between the infarcted, peri-infarct (or adjacent) and remote myocardium.

As right ventricular (RV) dysfunction in infarct patients

portends poor outcome, assessment of the ventricular performance is not complete without RV assessment.

Cardiac ultrasound is the first-line technique to assess cardiac function in IHD patients.

It can be performed at the bedside, provides valuable

information regarding cardiac structure and ventricular and atrial volumes and function, and allows the visualisation of complications such aneurysm or thrombus formation post-infarction.

Novel techniques such as speckle tracking echocardiography allow myocardial strain imaging

with good feasibility in the clinical setting; however, in many patients, image quality is suboptimal, and geometric assumptions are used in clinical routine to assess ventricular volume and function.

In recent years, CMR has emerged as an interesting alternative to echocardiography.

Compared with competing techniques, such as CCT or nuclear medicine, no iodinated contrast material nor radioactive tracer needs to be injected for volumetric/functional cardiac imaging. Moreover, as explained in more detail below, CMR offers a comprehensive view on the heart.

For volumetric and functional imaging, CMR relies on bright-blood CMR, nowadays using the balanced statestate free-precession sequence yielding a high intrinsic contrast between blood and surrounding myocardium. Dynamic information of the cardiac function is obtained when multiple images are acquired over the cardiac cycle. These can be played in cine-loops allowing to appreciate dynamic phenomena such as myocardial/valve motion, and to visualise infarct-related complications such as aneurysm formation and thrombus formation.

CMR images are typically acquired at breath-hold. In uncooperative patients or in patients with atrial fibrillation, non-ECG-gated real-time cine imaging

may be a valuable alternative.

Functional CMR imaging is typically performed using a combination of short- and long-axis planes: that is horizontal and vertical long-axis and three-chamber view.

For ventricular volumetric and functional imaging, the ventricles are completely encompassed by a set of contiguous slices, usually acquired in short-axis direction. In analogy to speckle-tracking echocardiography, CMRbased strain analysis is nowadays possible, based on optical flow technology (feature-tracking) or application of more complex elastic registration algorithms. Furthermore, magnetisation preparation pulses

enable to non-invasively create tag lines ('myocardial tagging') on the myocardium, allowing the unravel the intramyocardial deformation patterns in IHD patients. CCT is an alternative to echocardiography and CMR for ventricular volumetric assessment.

The administration of contrast agent should be adapted to obtain enhancement of both ventricular cavities.

Routine use of CCT for this purpose, however, is

hampered by the need to use radiation over the entire cycle.

In many hospitals, planar radionuclide ventriculography is an established technique to assess LV volumes and function.

Alternatively, gated blood pool SPECT can be used to assess wall motion and regional ejection fraction.

STRESS IMAGING

In patients with chronic stable CAD, treatment goals are threefold:

(a) relief of symptoms and ischaemia;

(**b**) prevention of premature cardiovascular death; and (c) prevention of progression of CAD leading to myocardial infarction, LV dysfunction and congestive heart failure.

Management of CAD, however, remains highly challenging as several studies have shown that revascularisation fails to improve mortality over medical treatment in randomised trials.

The explanation of this paradox lies most likely in the poor relation between stenosis severity in diffuse CAD and coronary flow physiology.

Whereas anatomical techniques (conventional coronary angiography, CCT) provide limited information regarding the impact of a stenosis on the coronary flow, stress testing can be recommended to assess the extent of myocardial ischaemia before coronary angiography. There is substantial evidence that a moderate-to severe ischaemic burden greater than 5%–10%, with or without angina, is an indication for revascularisation, whereas those patients without clear evidence of myocardial ischaemia likely benefit from an optimum medical treatment (e.g. high-dose statins—risk factor modification) to alter the natural history of CAD. At cardiac catheterisation, the functional severity of a stenosis can be determined by the FFR expressing the maximum achievable blood flow to the myocardium

supplied by a stenotic artery as a fraction of normal maximum flow.

A normal value is 1.0 and a value of 0.75 reliably identifies stenoses associated with inducible ischaemia. The diagnostic accuracy of FFR is greater than 90%. Although FFR may be helpful in determining in

patients presenting with diffuse CAD at cardiac catheterisation which stenoses may benefit from percutaneous coronary intervention (PCI),

non-invasive testing for reversible (or inducible) ischaemia is warranted to optimally stratify patients with stable CAD.

Non-invasive testing for reversible ischaemia is achieved by stressing the heart and evaluating whether, during stress, symptoms of angina, ECG signs of myocardial ischaemia, ischaemia-induced myocardial wall motion abnormalities (WMAs) or myocardial perfusion disturbances occur. Exercise ECG test (EET), although widely used in daily practice, has a low sensitivity (approximately 60%) and moderate specificity (nearly 80%), and a normal test does not exclude CAD.

In particular, EET is a poor diagnostic test in low-risk populations (such as women) owing to its low positive value in a population with a low prevalence of the disease.

The limited accuracy of EET in diagnosing CAD is also

due in part to its position near the bottom of the ischaemic cascade.

Therefore, the diagnosis of CAD may be improved by using non-invasive tests higher up in the ischaemic cascade than EET, assessing abnormalities in myocardial function or in myocardial perfusion during stress conditions.

While there is most experience with myocardial perfusion

scintigraphy and stress echocardiography for these purposes, several other single or hybrid techniques have emerged in the field of stress imaging, such as stress perfusion CMR, stress function CMR, stress perfusion CT, combined coronary and stress myocardial perfusion

imaging by CCT, and hybrid cardiac SPECT/CT or cardiac PET/CT.

Nuclear medicine is a cornerstone in the assessment of myocardial perfusion in CAD patients, and it has an established role in risk stratification for major adverse cardiac events.

Most often, SPECT is used to diagnose and evaluate the severity of CAD, while PET is more accurate but also

more expensive and less available.

SPECT measures the relative myocardial distribution of radionuclides, such as thallium-201 (201Tl), technetium 99m (99mTc) sestamibi (MIBI).

Study protocols are specific for the different tracers: for instance, MIBI SPECT is performed using an injection of tracer during stress and a second injection at rest (or vice versa), while 201Tl is injected during stress, and the redistribution of tracer is measured at rest after a delay (e.g. 4 hours).

In regions with impaired myocardial perfusion, the number of counts is lower than normally perfused myocardium, resulting in a 'defect'.

Reversible defects (i.e. present on stress but absent at rest) are caused by flow limiting stenoses and should be differentiated from *fixed* defects (i.e. present at rest/redistribution at rest), reflecting myocardial scarring

(Fig. 15.19).

The severity of the defect (i.e. reduction in counts) is

related to stenosis severity, while the extent of the defect is related to the myocardium supplied by the stenotic artery.

Although SPECT is widely used in clinical practice, yielding good sensitivity (approximately 90%) and moderate specificity (around 65%), certain pitfalls need to be mentioned.

Radiation exposure of the injected isotopes, depending

on the protocol used, ranges between 8 and 20 mSv. Subendocardial and small infarcts may be missed by SPECT because of the lack in spatial resolution.

To avoid false-positive readings and to improve the test specificity, use of attenuation correction methods and

gated analysis of wall motion is recommended.

Finally, in patients with multivessel CAD, hypoperfusion of the entire myocardium may mask regional abnormalities.

PET is very useful for assessing myocardial perfusion and metabolism.

Assessment of myocardial perfusion can be performed with 13N-ammonia, 15O-H2O, 82Ru or 11C-acetate. PET has several advantages over SPECT, such as a higher spatial resolution and the possibility to measure absolute myocardial blood flow.

This is advantageous in patients with balanced ischaemia caused by left main or three-vessel CAD in which maximal myocardial blood flow is reduced in all regions of the left ventricle, or in patients in whom the myocardial ischaemia is caused by microvascular dysfunction.

The reported sensitivity (and specificity) of PET for detecting angiographic stenosis ≥50% is approximately 90%. Drawbacks of PET are patient exposure to radiation (although less than SPECT), availability and limited half-life of PET tracers, cost

and availability of PET scanners, false-positive myocardial perfusion defects due to misregistration, and the limited spatial resolution when compared with CMR.

Perfusion CMR uses the changes in myocardial signal intensity during first pass of a contrast media bolus through the myocardium to assess myocardial perfusion.

This necessitates fast imaging sequences with saturation prepulses to suppress myocardial signal and obtain T1 weighting. Sufficient coverage of the left ventricle is obtained with three short-axis slices (possibly in combination with a long-axis view), enabling segmental perfusion assessment using the 16segment model.

Similar to nuclear imaging, myocardial hyperaemia (induced by a vasodilator such as dipyridamole or adenosine) enables depiction of haemodynamic significant stenoses.

Hypoperfused myocardium during stress conditions appears as a non- or slow-enhancing parts of the myocardium ('perfusion defect').

The defect, typically, obeys anatomical borders as well as the boundaries of the coronary artery perfusion territories, and the extent is determined by the position of the stenosis along the coronary artery.

Semiquantitative measures show a decline in the upslope during first pass of contrast, and when related to the upslope during resting conditions, the myocardial perfusion reserve (MPR) ratio is typically decreased in the hypoperfused areas. Similar to PET, absolute myocardial blood flow can also be quantified with CMR.

In a landmark paper by Greenwood et al. studying 752 prospectively included patients, stress perfusion CMR yielded a higher accuracy than SPECT.

This, and other recently published studies, emphasise the intrinsic value of CMR in assessing patients with stable CAD. As the spatial resolution of CMR is superior to SPECT,

smaller, subendocardial perfusion defects missed at SPECT can be shown at CMR. Moreover, CMR is not hampered by softtissue and attenuation artefacts.

In analogy to CMR, CCT can also be used to study myocardial perfusion under stress conditions; in particular, the combination with morphological depiction of the plaque and plaque stenosis severity at coronary CT angiography, this is potentially a very appealing application.

The downside of this approach remains the substantial radiation exposure.

In analogy to stress echocardiography, stress function studies can be performed safely in an MR environment. Dobutamine, a

 β -agonist, increases oxygen consumption by increasing myocardial contractility and heart rate.

A stepwise dose increment of dobutamine allows for the evaluation of the myocardial response at each stress level. Whereas normally supplied myocardium shows a progressive increase in myocardial contractility, myocardium supplied by a flow-limiting coronary stenosis becomes ischaemic when the compensatory increase in coronary blood supply is insufficient to match the increased demand in oxygen (therefore when the coronary flow reserve is superseded).

This, in turn, will cause a decrease in regional contractility and lead to WMAs. Using additionally administered up to 1 to 2 mg using fractionate doses of 0.25 mg every minute.

Dobutamine administration needs to be stopped on patient request, and is also discontinued if the systolic blood pressure decreases greater than 20 mm Hg below the baseline systolic blood pressure; the systolic blood pressure decreases greater than 40 mm Hg from a previous level; the blood pressure increases to above 240/120 mm Hg; or when severe arrhythmias occur.

As this is a potentially dangerous examination, haemodynamic parameters such as heart rate and blood pressure should be

closely monitored, cardiac resuscitation material should be available, and teams should be trained in case of cardiac complications for fast patient evacuation from the magnet; however, in experienced hands, high-dose dobutamine-atropine stress MRI is a safe examination with minimal side effects. Besides detecting flow-limiting coronary stenoses in patients suspected of obstructive CAD, low-dose stress function imaging ($\leq 20 \ \mu$ g/kg dobutamine) enables differentiation between viable and non-viable dysfunctional myocardium in patients with chronic CAD.

Also, in patients with a recent myocardial infarction, low-dose stress imaging can differentiate between stunned and irreversibly damaged myocardium.

High-dose dobutamine/atropine stress CMR yields good sensitivity (approximately 90%) and specificity (also approximately 90%) for detection of significant CAD. Novel CMR techniques such as sensitivity encoding (SENC)-CMR, which allows strain visualisation, provide incremental value for the detection of CAD compared with conventional wall motion readings, and have the strength to detect CAD at lower stress levels.

MYOCARDIAL INFARCT IMAGING

Assessment of the electrical cardiac activity using 12-lead electrocardiography and analysis of cardiac biomarkers are central diagnostic techniques in patients presenting with an ACS. Firstly, patient's triage and treatment are, to a large extent, based on ECG changes indicative of new ischaemia (new ST-T changes or new left bundle branch block), and development of new pathological Q waves (Fig. 15.23). The ECG allows the clinician to suggest the infarct-related artery, to estimate the amount of myocardium at risk, and to detect prior (healed) myocardial infarction. In infarcts presenting an ST-segment elevation, the degree of ST resolution post-reperfusion reflects the success of reperfusion.

Secondly, as myocardial cell death is characterised by a release of different proteins into the circulation from the damaged myocytes, increased cardiac blood biomarkers are indicative of recent myocardial necrosis.

The preferred biomarker at present is cardiac troponin (I or T), which has a nearly absolute myocardial tissue specificity as well as high clinical sensitivity.

If troponin assays are not available, the best alternative is creatine kinase-MB.

Because of the complex release characteristics of these cardiac proteins, it is still unclear whether the peak value, or a single point measurement of cardiac biomarkers, provides the best estimate of myocardial infarct size.

Moreover, neither blood biomarkers nor ECG provides a good insight in the evolving processes in the jeopardised myocardium.

Imaging techniques such as cardiac ultrasound and cardiac catheterisation visualise an acute myocardial infarction indirectly by the impact of the infarction on wall motion or wall strain, but do not visualise the necrotic myocardium. Gated SPECT shows a myocardial infarction as a fixed defect with loss in regional function; however, small (subendocardial) infarcts are frequently missed because of the lack in spatial resolution.

In recent years, CMR has become the in vivo reference technique for myocardial infarction imaging, providing an indepth, comprehensive view.

Although several groups have explored the use of CCT to assess acute myocardial infarctions, this technique has not yet entered the clinical arena. One major limitation of current CCT in the setting of myocardial infarction is the relatively low soft-tissue contrast between normal and infarcted myocardium.

Dual-energy and photon-counting spectral CT may overcome this limitation by imaging the contrast-to-noise ratio (CNR) of late iodine contrast material enhancement in the infarcted myocardium.

Additionally, photon-counting CT may allow for the simultaneous assessment of multiple phases of contrast enhancement (i.e. first-pass perfusion and late enhancement) during CCT, with a substantial reduction in radiation exposure. Myocardial tissue characterisation is probably the key feature where CMR excels and outperforms all other imaging techniques.

As T1- and T1 and T2 relaxation times are tissue specific, alterations in relaxation times are indicative of myocardial pathology.

Firstly, CMR sequences can be 'weighted', comparing the signal intensity of tissue deemed abnormal to the signal intensity of tissue deemed normal.

In the jeopardized myocardium, myocardial-free water increases as a consequence of prolonged myocardial ischaemia, resulting in a prolongation of both T1 and T2 relaxation times. Myocardial oedema is an early phenomenon that can be depicted as soon as 30 minutes after onset of myocardial ischaemia.

In particular, using T2-weighted sequences, the jeopardized myocardium will appear as an abnormally bright (hyperintense) area in clear contrast to the grey normal myocardium.

Currently, different optimised dark-blood and bright-blood T2weighted sequences are available.

Although well suited to depict areas of myocardial oedema, these sequences lack specificity, image quality may be suboptimal, and differentiation with hyperintense signal from stagnant blood adjacent may be challenging.

Moreover, in the bright-appearing jeopardized myocardium, differentiation between irreversibly damaged and reversible (viable) myocardium is not possible.

Fortunately, this issue can be solved by intravenously administering gadolinium chelates.

As these contrast agents have extracellular distribution properties, the distribution volume is the largest in the necrotic part of the jeopardised myocardium, resulting in a greater T1 shortening compared with the less-damaged, viable, parts of the jeopardised myocardium. The area of enhancement—in case of acute myocardial infarction—is typically subendocardial, located in the distribution territory of one of the coronary arteries, and the transmural spread of enhancement is variable. Using the relation of the extent of enhancement to the extent of myocardial oedema, a ratio can be calculated reflecting the myocardial salvage index.

For example, if no necrosis has occurred then no enhancement is present in the oedematous myocardium.

In this condition, also called aborted myocardial infarction, the myocardial salvage equals 100%. Assessment of myocardial salvage is important because it yields prognostic value. Over the years, the sequence design for T1-enhanced imaging has been modified and constantly improved, especially with the introduction of the inversionrecovery sequence, which has led to a paradigm shift in myocardial infarct imaging.

In brief, the difference in longitudinal relaxation time between normal and infarcted myocardium can be exploited to create, and to improve, the (differential) tissue contrast. Moreover, one should be familiar with the pharmacokinetics of gadolinium chelates. Within the infarcted myocardium, the optimum timing for accurate infarct imaging is approximately 10 to 25 minutes following administration of contrast agent.

Therefore, this sequence is called 'late' or 'delayed' gadolinium-enhanced CMR (LGE). This sequence has been extensively validated, and areas of irreversible myocardial damage as small as 1 mL can be depicted.

Moreover, the centre of the infarction may occlude the microvasculature—the so-called microvascular obstruction or no-reflow phenomenon—and is found in approximately 50% of successfully reperfused STEMI.

This can be visualised at contrast-enhanced

MRI as lack of enhancement ('dark area') in the centre of the area of enhancement.

Another sign of reperfusion injury is extravasation of red bloods ('haemorrhagic infarction') secondary to severe capillary damage. As deoxyhaemoglobin yields paramagnetic properties, intramyocardial haemorrhage can be recognised at T2-weighted imaging as a central dark area.

Both are considered to represent reperfusion damage incurred in the ischaemic myocardium and bear prognostic value.

In recent years, quantitative ('parametric') imaging has entered the front line for infarct imaging, with T1, T2 and T2* mapping providing a more objective means to tissue characterise the myocardium.

Mapping sequences acquire several images at different stages of the relaxation, allowing a pixel-wise fitting of the relaxation behaviour.

Colour-coded representation facilitates interpretation.

In a patient with an acute myocardial infarction, both T1 and T2 values increase in the jeopardised myocardium, and the extent of abnormal increase can be used to calculate the area at risk.

T1 mapping can be repeated following contrast administration (measurement performed 10 to 25 minutes post-contrast administration).

Lowest post-contrast T1 values will be found in the necrotic myocardium, less severe in the reversible damaged part of the jeopardised myocardium.

The extent of the extracellular space—ECV—can be estimated, relating the changes in T1 values before/after contrast

administration to the T1 blood values before/after contrast administration and correcting for blood haematocrit.

In normal myocardium, ECV values range from 22% to 29%, reversible damaged myocardium yields higher ECV values, whilst the highest values are found in necrotic myocardium. Moreover, as a haemorrhagic infarct shortens both T1 and T2* values, these mapping sequences can be used for this purpose as well.

In clinical routine, a combination of weighted and mapping sequences is used in acute myocardial infarction, allowing deep tissue characterisation of the jeopardised myocardium.

Also, in the non-infarcted ('remote') part of the ventricle, alterations in myocardial tissue characteristics, perfusion as function have been described, phenomena that are deemed to trigger ischaemic heart failure.

Furthermore, infarct-related complications of intraventricular thrombus and aneurysm formation, and epistenocardiac pericarditis, can also be visualised at CMR.

Finally, a substantial number of patients presenting with ACS and positive tropinins eventually show no significant abnormalities at cardiac catheterisation, causing a diagnostic dilemma.

In these patients, CMR provides valuable information, allowing differentiation between acute myocardial infarction, acute myocarditis, acute pericarditis and stress cardiomyopathy (or takotsubo cardiomyopathy).

The latter condition is usually triggered by emotional or physical stress, and causes temporary—often severe dysfunction, affecting the apical—less often the mid—part of the left ventricle.

The dysfunctional parts are oedematous but lack enhancement, allowing differentiation with acute myocardial infarction. Myocarditis patients typically show focal or diffuse myocardial oedema, usually associated with mild ventricular dysfunction. In these patients, the pattern of enhancement differs from acute myocardial infarction patterns, affecting the subepicardium usually in the inferolateral and lateral part of the left ventricle—or the mesocardium in the interventricular septum.

MYOCARDIAL VIABILITY IMAGING

IHF is one of the most challenging issues in cardiology today, posing an enormous medical and financial burden on our society.

Conceptually, it represents a maladaptive cardiac remodelling due to acute and/or chronic CAD with varying degrees of LV dilatation and dysfunction.

Onset of heart failure in these patients may be abrupt (e.g. following acute MI) or insidious (due to chronic or repeated ischaemia).

At coronary angiography they present with single or multivessel CAD and show dilated ventricles with focal or generalised ventricular dysfunction.

The histological substrate of the dysfunctional myocardium, however, can consist of non-viable (i.e. necrotic or scarred myocardium) and/or viable (i.e. stunned, ischaemic, hibernating) myocardium (Fig. 15.32).

Based on observational and retrospective studies, showing beneficial effects of coronary artery revascularisation on viable myocardium hereby

- (i) improves regional and global ventricular function,
- (ii) reverses the adverse remodelling process,

- (iii) improves exercise capacity,
- (iv) decreases symptoms of heart failure and
- (v) improves patient survival.
- (vi) Consequently, myocardial viability assessment has become an important tool in therapy planning of patients with IHF.

Myocardial viability can be assessed by analysing/evaluating myocardial wall thickness, myocardial contractile reserve, myocyte cellular integrity, myocardial metabolism and myocardial extracellular distribution volume.

Although these 'viability' parameters can be evaluated by a myriad of non-invasive imaging techniques such as dobutamine stress echocardiography (DSE), nuclear imaging (SPECT and PET), CCT and CMR, it should be emphasised that none of them are perfect to predict or rule out functional recovery post-revascularisation.

Moreover, in the famous STICH trial (Surgical Treatment for IHF), the value of preprocedural viability imaging was questioned as survival in patients receiving coronary artery bypass graft revascularisation was not different compared with medical treatment alone. Similarily, the PET and Recovery following Revascularisation (PARR-2) trial reported no benefit of assessing viability in guiding patient management; however, a recently published update of the STICH trial with longer follow-up (>10 years) showed a significant benefit for patients in the bypass group compared with the medical treatment group.

These above findings underscore the complexity of the myocardial viability issue as well as the quest for the ideal imaging technique to depict hibernating myocardium. Chronic dysfunctional myocardium recovery following successful coronary revascularisation is deemed to reflect hibernating myocardium, although reversed cellular differentiation has never been documented, but only assumed. Hibernating myocardium is therefore a post-hoc observation, and as such not useful to select those patients which might benefit from revascularisation.

A first approach is use of end-diastolic wall thickness. As scar formation in myocardial infarction causes wall thinning, preserved wall thickness is considered to reflect preserved myocardial viability and most workers use a cut-off of 5.5 to 6 mm; however, many segments with preserved wall thickness fail to functionally recover post-revascularisation. Conversely, thinned wall segments may functionally improve after revascularisation.

A second approach is based on myocyte membrane integrity and is used by both nuclear imaging and contrast-enhanced CMR. Both thallium-201 and technetium-99m

sestamibi/tetrofosmin SPECT techniques compare the uptake of radiotracer in the dysfunctional myocardium relative to remote (normal) myocardium.

A tracer activity greater than 50% of the maximum tracer uptake is used as threshold for viable tissue.

Although generally accepted and widely used, the downside is the low spatial resolution (i.e. 7 mm), limiting its ability to depict subendocardial infarcts.

A third approach is based on the principle of increased interstitial space (or extracellular volume) in scarred myocardium.

In particular, LGE-CMR is a well-validated, highly accurate and reproducible technique for sizing healed infarcts and has become the reference technique to depict infarct-related myocardial scarring (Fig. 15.33).

In a landmark paper by Kim et al. (2000), the likelihood of functional improvement after revascularisation was predicted by the transmural extent of enhancement. In dysfunctional segments without CMR evidence of scar, 78% of segments improved contractility post-revascularisation versus 2% of segments with a scar involving greater than 75% of wall thickness.

A fourth approach is imaging of myocardial metabolism using quantitative PET imaging. Combining a metabolism tracer (fatty acid or glucose analogs (e.g. 18F-fluorodeoxyglucose (18F-FDG) with a perfusion tracer (13N-ammonia), the myocardial viability can be accurately studied.

PET yields excellent sensitivity (approximately 90%) and moderate specificity (approximately 60%).

PET compared with SPECT has a superior spatial resolution, lower radiation burden and allows absolute quantification of myocardial blood flow.

Drawbacks are availability and short half-life of current available PET perfusion tracers, cost and the lower spatial resolution compared with CMR.

A fifth approach is assessment of contractile reserve. Dysfunctional myocardium that contracts (or improves contractility) is deemed viable if stimulated: for example, using dobutamine \pm atropine.

Non-viable myocardium, in contrast, shows no functional improvement or even a worsening in wall motion.

Myocardial contractility reserve is usually performed at echocardiography but can also be assessed by CMR.

The accuracy of viability imaging can be improved by combining approaches.

In particular, the likelihood of functional recovery is uncertain in patients showing dysfunctional myocardium with preserved end-diastolic wall thickness and in those presenting with intermediate grades of scar transmurality (i.e. 25% to 75%): for instance, by performing additional low-dose dobutamine stress imaging. Also, the emergence of hybrid PET–MR scanners may further improve diagnostic accuracy.

As many ischaemic heart failure patients have evidence of ventricular dyssynchrony, they may benefit from cardiac resynchronisation therapy

(CRT) as part of an effective therapy for heart failure. Although not yet included in the guidelines for CRT, imaging has an increasingly important role in determining those patients that might benefit from CRT.

Goals of imaging are threefold:

(a) assessment of the degree of mechanical dyssynchrony,

(**b**) myocardial scar imaging and

(c) coronary venous imaging.

Ventricular performance can be improved if the contraction of the different parts of the ventricle is synchronised.

The degree of mechanical dyssynchrony can be quantified using speckle-tracking echocardiography, strain-based cine CMR as well as more advanced techniques such as myocardial tagging, DENSE (displacement encoding with stimulated echoes) and tissue velocity mapping.

Secondly, correct placement of the CRT leads is crucial to improve mechanical dyssynchrony.

Thirdly, ventricular scar mapping can be achieved using LGE CMR, enabling to determine the presence, location and extent of myocardial scarring. Information regarding the coronary vein anatomy and patency, which may be important for CRT lead placement, can be achieved with CCT.

IMAGING OF COMPLICATIONS RELATED TO ISCHAEMIC HEART DISEASE

A series of potentially lethal complications is related to IHD, necessitating timely recognition and treatment (Fig. 15.34). Although echocardiography remains first in line and can easily be performed at the bedside, CMR and CCT are important when findings are equivocal. Acute myocardial rupture is a rare, but often lethal,

complication in patients with extensive transmural myocardial infarction.

If the rupture is contained by the pericardium, a false aneurysm is formed and the patient may survive the event.

Extensive thinning of the myocardial wall may lead to a true aneurysm.

Differentiation between false and true aneurysms is not always straightforward. In false aneurysms, the orifice is usually smaller than the maximal internal diameter, whereas in true aneurysms the dimensions are similar.

Moreover, pericardial enhancement is frequently found in false aneurysms while it rarely occurs in true aneurysms.

Ventricular thrombus formation is a frequent complication post myocardial infarction, and may be incidentally found in patients with ischaemic-dilated cardiomyopathy.

Early thrombus detection is of paramount importance to avoid neurological and peripheral embolic events, and to initiate anticoagulation therapy.

Small-sized thrombi are easily missed by transthoracic echocardiography, particularly when located in the apex or when trapped in the endocardial trabeculations.

CCT and LGE CMR facilitate the diagnosis of thrombi, as the blood pool is enhanced by the injection of contrast material, therefore improving the detection of intraluminal masses such as thrombi.

The myocardial damage (i.e. necrosis) incurred by the coronary artery occlusion—in particular in transmural infarctions—may cause pericardial inflammation early post-infarction, a condition that should be differentiated from late post-infarction pericarditi: that is, Dressler syndrome.

Pericardial abnormalities at CMR include enhancement of pericardial layers and pericardial effusion at the area of

myocardial infarction or more diffusely involving the pericardium.

Imaging biomarkers of pericardial injury are closely related to blood biomarkers of inflammation (i.e. C-reactive protein [CRP]).

Finally, mitral valve regurgitation in infarct patients can be caused by valve ring dilatation due to adverse LV remodeling and/or infarction of the papillary muscle(s).

PROGNOSIS ASSESSMENT IN ISCHAEMIC HEART DISEASE

In asymptomatic patients as well as in patients with suspected or known CAD risk, assessment and prediction of future cardiac events is important.

Traditional risk assessment classifies patients into those at high risk, intermediate risk and low risk. Although this classification helps patients to adapt their lifestyle (primary prevention) or medication (e.g. statins), most high-risk patients will never experience a cardiac event, while patients belonging to the intermediate or low-risk group will not be event-free; hence the need for approaches improving prognosis assessment. Coronary calcium score assessment is well known, well validated and widely used, reflecting the atherosclerotic burden in a patient.

In asymptomatic patients without evidence of CAD, coronary calcium scoring adds prognostic information beyond clinical risk factors.

In particular, asymptomatic adults belonging to the intermediate-risk group (i.e. 10% to 20% 10-year risk of events) can be 'upgraded' or 'downgraded', depending on the Agatston calcium score.

In symptomatic patients suspected of CAD, the severity of CAD and/or presence of myocardial ischaemia are important prognosticators for future events even though a negative

coronary calcium score in symptomatic patients does not exclude obstructive CAD.

The severity of CAD assessed by CCT, together with LV ejection fraction, predicts all-cause mortality. In the absence of myocardial ischaemia on SPECT, future cardiac events are highly unlikely.

In patients without a history of myocardial infarction but a clinical suspicion of CAD, evidence of ischaemia-related myocardial scarring carries an increased risk for future major adverse cardiovascular event (MACE) independent of the extent of LGE. In patients presenting an ACS in whom myocardial infarction is excluded by cardiac biomarkers and ECG, stress perfusion MRI is an accurate and independent predictor of future cardiac events.

Moreover, a substantial number of MRI studies have shown that several parameters other than ejection fraction are important in predicting adverse remodeling and patient outcome following an acute myocardial infarct; these include microvascular obstruction, post-infarction myocardial haemorrhage and myocardial salvage.

In patients with ischaemic cardiomyopathy, the extent of myocardial enhancement is a strong and independent predictor of all-cause mortality, even in the presence of traditional wellknown prognosticators such

as ejection fraction, congestive heart failure and age.

ROLE OF CONVENTIONAL CHEST RADIOGRAPHY IN ISCHAEMIC HEART DISEASE

Even though 'advanced' imaging techniques are nowadays central in the diagnosis of heart diseases, the contribution of conventional chest radiography in evaluating IHD patients should not be neglected.

Valuable information can be provided regarding the cardiac size, enlargement of a specific cardiac chamber, or pulmonary filling status, and the chest radiograph can help exclude some pulmonary, pleural or aortic disease such as aortic aneurysm. In ill cardiac patients, bedside radiography can readily be performed.

Left-sided cardiac decompensation in patients with recent myocardial infarction or ischaemic cardiomyopathy leads to an apical redistribution of pulmonary vascularisation, onset of pulmonary interstitial and alveolar oedema, and pleural effusion.

Chest radiography can closely monitor the effects of therapy, and to demonstrate concomitant pulmonary disease such as infection or acute respiratory distress syndrome (ARDS).

It also serves to check the correct positioning of devices such as endotracheal tubes, central venous catheters, pulmonary artery catheters and pacing leads. Infarct-related complications, such as pericardial effusion/hematoma or aneurysm formation, can be detected on chest radiography, although echocardiography, CMR and CCT are definitely superior.

DIFFERENTIAL DIAGNOSIS IN ISCHAEMIC HEART DISEASE

In patients suspected of having an ACS, the current American College of Cardiology (ACC)/American Heart Association (AHA)/Unstable Angina (UA)/STEMI guidelines recommend a classification into

(1) 'definite' ACS,

(2) 'possible' ACS,

(3) chronic stable CAD and

(4) non-cardiac cause of chest pain. This classification is based on the patient's history, physical examination, 12-lead ECG and initial cardiac biomarkers.

In patients with normal/non-diagnostic ECG or normal initial biomarkers, however, the question arises whether the symptoms arise from unstable angina pectoris, which is characterised by ischaemia without myocardial damage to release detectable quantities of markers of myocardial injury. These patients with 'possible' ACS are usually admitted for observation 12 hours or more from symptom onset and stress testing is usually performed to provide evidence of myocardial ischaemia.

As an alternative in these patients, CCT can be recommended to demonstrate or exclude significant CAD in those with low or intermediate pre-test probability of CAD, while the role of CCT in patients with a high pre-test likelihood is uncertain. A negative CCT, defined as no CAD or stenosis less than 50%, yields an excellent negative predictive value for ACS or MACE, while in those patients having a positive CCT, ischaemia testing can be subsequently performed. Cardiac CT is also of interest to rule out other causes of chest pain related to pathology of the pulmonary arteries (i.e. pulmonary embolism) and thoracic aorta (i.e. aortic dissection). This so-called 'triple rule out' approach needs an adaptation of the administration of contrast agent to assure sufficient enhancement of pulmonary arteries, coronary arteries and

thoracic aorta during CT data acquisition.

Although promising, the value of triple rule-out CCT in the emergency department is still uncertain.

In a small but important group of patients presenting with chest pain and elevated cardiac biomarkers, subsequent coronary angiography reveals normal appearances or non-flow limiting CAD, questioning the underlying cause of the clinical presentation.

Possible causes include non-cardiac aetiologies, myocardial infarction with a recanalised coronary artery and acute myocarditis.

In these patients, CMR is now recommended.

If patients have experienced an ischaemic event, T2-weighted imaging will show myocardial oedema while myocardial enhancement on LGE CMR is suggestive of myocardial
necrosis and the functional consequences can be evaluated with cine imaging.

Not infrequently, smaller coronary artery branches are affected that were not initially recognised at coronary angiography. The same CMR approach is of great help in depicting patients with acute myocarditis.

These patients show a different pattern of myocardial enhancement on LGE CMR than acute myocardial infarction patients: i.e. midwall/subepicardial enhancement instead of subendocardial enhancement with variable transmural spread. CMR is also of help in patients with takotsubo cardiomyopathy (also called stress cardiomyopathy).

The Thoracic Aorta: Diagnostic Aspects THE NORMAL AORTA

The aorta is the main artery delivering oxygenated blood from the left ventricle to all parts of the body. In common with other arteries, it has three histologically distinct layers: an intima consisting of a thin endothelial layer; a media containing an elastic lamella, smooth muscle and connective tissue; and a thin outer adventitia made of connective and elastic tissues also containing nerves, lymphatics and the vasa vasorum.

The aortic root begins at the upper part of the left ventricle and is approximately 3 cm in diameter.

A normal aorta passes superiorly and slightly to the right for approximately 5 cm, then arches posteriorly over the root of the

left lung, descending within the thorax beside the vertebral column, gradually achieving the median plane, and becoming the abdominal aorta, after it passes through the aortic hiatus in the diaphragm.

The abdominal aorta is approximately 2 cm in diameter; it ends slightly to the left of the median plane at the lower border of the fourth lumbar vertebra by dividing into the right and left common iliac arteries.

The aortic root and most of the ascending aorta are contained within the pericardium. The root consists of three sinuses: the right coronary artery arising from the right coronary sinus, the left coronary artery from the left coronary sinus and a noncoronary sinus which is usually located on the right posterolateral aspect.

The ascending aorta forms the right mediastinal border on a posteroanterior (PA) chest radiograph.

It becomes the aortic arch at the origin of the innominate artery and also gives rise to the left common carotid and left subclavian arteries (LSAs).

Approximately three-quarters of people show this 'normal' branch pattern of the supra-aortic arteries, but in 20% the innominate and left common carotid arteries have a common origin and in 6% the left vertebral artery arises directly from the aortic arch.

The aortic arch ends and the descending thoracic aorta begins immediately beyond the origin of the LSA. At this site the ligamentum venosum (the embryological ductus arteriosus, which closes within a few days of birth) joins the ninferior concavity of the aortic arch to the main pulmonary artery. The aorta is fixed at this point. Occasionally the duct may persist as a short diverticulum.

DIAGNOSTIC ASPECTS

The last few decades have seen an increasing recognition of thoracic aortic disease among Western people, partly due to greater longevity and an increased awareness of its clinical importance.

Recent technological advances in computed tomography (CT) and magnetic resonance imaging (MRI) have greatly contributed to the increased recognition and pathological understanding of aortic disease.

There are at least three main goals of imaging concerning thoracic aortic diseases: disease recognition, preoperative evaluation and imaging follow-up.

The appropriate imaging technique depends on which of these aspects is pre-eminent.

Aortic disease often presents as a clinical emergency, with patients becoming rapidly haemodynamically unstable over time.

Accordingly, noninvasiveness, diagnostic accuracy and speed are the main properties requested in this setting, together with a comprehensive evaluation of the thoracic aorta (crucial for an accurate assessment before any intervention).

Thus the choice of the optimal imaging technique should consider these aspects and various patient-related factors (namely, acute or chronic presentation).

Chest X-Ray and Echocardiography evaluation of the thoracic aorta has always been very difficult with first-line imaging techniques such as chest x-ray (CXR) and transthoracic ultrasound (except for proximal aortic segments) due to its anatomical location.

A CXR may identify only indirect signs of aortic aneurysm or dissection such as a widening of the upper mediastinum or an abnormal aortic contour increase, but it lacks sufficient sensitivity and cannot exclude significant aortic disease, especially in high-risk patients.

Therefore additional imaging is almost invariably required for clarification.

Moreover, a CXR does not give any information about anatomical details for surgical or endovascular planning. Transthoracic echocardiography (TTE) is limited by its restricted field of view, further reduced by acoustic window limitations in adult patients (e.g. due to chronic pulmonary diseases, surgical scars or obesity), and has a typical 'blind spot' at the level of the proximal aortic arch due to superposition of air in the right bronchus.

Transoesophageal echocardiography (TOE) is superior to TTE for thoracic aorta evaluation, and it can be easily performed at the bedside.

However, it is partially invasive and not well tolerated by patients. Although echocardiography is routinely used for follow-up of aortic root and proximal ascending aorta aneurysms in chronic diseases, its narrow field of view prevents a comprehensive evaluation of the thoracic aorta.

Furthermore, operator dependence limits the overall accuracy. However, ultrasound still plays the main role for valvular assessment in thoracic aortic diseases (coexisting valvular disease or valvular involvement in type A aortic dissection or ascending aortic aneurysm), whereas intraoperative TOE is often fundamental for endovascular or surgical aortic treatment. In summary, CXR and ultrasound, although easy to perform, noninvasive and inexpensive, provide some helpful information, but alone they cannot provide comprehensive information about aortic disease.

Angiography For many decades, angiography was the only available imaging technique for diagnosis and preoperative evaluation of aortic diseases.

It was intrinsically invasive, relatively costly and needed a well-organised and experienced team. It provided only limited information about the aortic wall, because angiography provides only 'luminographic' data. Thus it provided limited information about an intramural haematoma (IMH) and could be misleading in aortic dissection with a complete false lumen thrombosis.

Over the past 30 years, with the advent of CT and MRI and their technological evolutions, angiography has become progressively abandoned by physicians for diagnostic purposes. Computed Tomography and Magnetic Resonance Imaging CT and MRI combine noninvasiveness with high spatial and temporal resolution and can provide information about the entire length of the thoracic or thoracoabdominal aorta. Multiplanar images allow precise measurements of aortic diameters, preferably taken perpendicular to the longitudinal axis in more than one plane to avoid source of errors.

In fact, the aorta has such variable geometry that it cannot usually be entirely visualised in a single plane.

MR angiography (MRA) and CT angiography (CTA) have further enhanced the noninvasive visualisation of vascular structures with a high degree of spatial and contrast resolution in all three dimensions.

Different two-dimensional (2D) and three-dimensional (3D) processing techniques, such as multiplanar reformation (MPR), maximum intensity projection (MIP) and volume rendering (VR), play an important role for preoperative planning.

Although thin-slice MPRs in any arbitrary plane provide high anatomical resolution, they cannot visualise the entire aorta in a single plane.

MIP images of appropriate slab thickness, while demonstrating the whole aorta, yield information only of perfused lumina similar to digital subtraction angiography (DSA); as a threshold technique, MIP images may not discriminate lower-density intraluminal structures such as thrombus, plaque or IMH. MIP images also do not provide any information about adjacent structures and their important relationships. VR is a different 3D reconstruction technique where all tissues can be simultaneously represented.

Using adequate filters, metallic stents or clips do not create artefacts, and aortic wall lesions can be differentiated from the lumen.

VR provides 3D anatomical information displaying the spatial relationship between aortic lesions and branching vessels.

Finally, curved reformations can reconstruct even the most tortuous vascular structure in a single plane.

All these processing and display options make CT and MRI measurements highly reproducible and less operator-dependent than ultrasound.

CT and MRI currently form the backbone of thoracic aortic imaging.

Both techniques show comparable results in terms of diagnostic accuracy, measurement reproducibility and anatomical detail definition.

MRI does not use ionising radiation, and gadolinium is less nephrotoxic than iodinated contrast agents.

Consideration should only be given to patients with severe renal dysfunction (creatinine clearance <30 mg/ dL/min), where it is necessary to balance the clinical usefulness of gadolinium and the risk of nephrogenic renal sclerosis.

Some concerns have also been raised for MR contrast medium about the potential risk of gadolinium cumulative tissue deposition, especially in the brain, even if it seems to refer mainly to linear molecules, and there is still no evidence of a clear negative effect.

Anyway, the development of native 3D steady-state freeprecession (SSFP) sequences with electrocardiogram (ECG)-gated and navigator gating seems to overcome this limitation, allowing MRI to obtain angiographic images of the aorta without gadolinium administration with similar accuracy compared to traditional MRA imaging.

The main limitation of CT imaging is the potential radiation risk, especially in neonates, children and young adults. Although recent CT technologies (dual-source CT, prospective ECG gating, iterative reconstructions, low tube voltage protocols (80 to 100 kV) or tube dose modulation) are reducing radiation exposure, the dose cannot be considered negligible, especially for repeated follow-up examinations of chronic aortic disease. Moreover, the use of iodinated contrast medium requires careful consideration in patients with borderline renal insufficiency or a history of previous reactions.

Acute Diseases Disease presentation is another aspect that influences the choice of imaging investigation.

Thoracic aortic diseases frequently present acutely.

MRI requires longer examination times, is less readily available and usually has less favourable logistics/locations; these factors often make it less suitable for patients with acute disease. CT is rapid and very accurate and is particularly well-suited for the diagnosis and correct treatment planning of acute aortic problems.

Modern multidetector computed tomography (MDCT) allows for submillimetre, isotropic 3D data acquisition of extended anatomical ranges within comfortable (4 to 8 seconds) breathhold duration; dedicated software provides 2D and 3D artefactfree reconstructions from virtually any angle and in any desirable plane.

The introduction of ECG gating has minimized motion artefacts, increasing the sensitivity and specificity for type A aortic dissection, especially with respect to identifying intimal flaps and aortic valve morphology.

CT equipment is more widely available and often located close to the intensive care units or operating rooms. Moreover, when acute aortic dissection is suspected, MDCT is also able to exclude other potential causes of thoracic pain such as pulmonary embolism, other pulmonary diseases or coronary artery disease with high accuracy, although this requires choosing appropriate examination protocols.

Thus MRI, though highly accurate for acute aortic disease evaluation, is usually confined to cases of severe renal insufficiency or absolute contraindications to iodinated contrast medium; it is useful for subsequent follow-up studies. The high diagnostic accuracy of MR in patients with acute aortic syndrome is based on its high contrast resolution between the lumen and the vessel wall provided by black-blood fast spin-echo (BBFSE) and SSFP imaging, which allows differentiation of aortic wall alterations (e.g. IMH) from atheromatous plaques or aortitis.

Chronic Diseases

In patients with chronic aortic disease, follow-up and identification of findings requiring surgery are the main goals for imaging.

Both CT and MRI provide highly reproducible and accurate aortic measurements, but MRI may be preferred to CT to minimise radiation exposure, especially in young adults affected by congenital aortic anomalies and genetic syndromes associated with thoracic aneurysms such as Marfan or Turner syndrome.

MRI, with cine gradient-echo sequences and phase-contrast imaging, can also obtain functional information on the thoracic aorta and quantify aortic valve regurgitation or stenosis within the same examination.

CT is preferred to MRI only for aortic stent imaging follow-up. The stent material causes artefacts on MRI images, which reduce MRI's sensitivity for detection of small endoleaks or stent structure alterations.

ACQUIRED AORTIC ABNORMALITIES Acute Aortic Syndrome

The term 'acute aortic syndrome' comprises all aortic diseases characterised by a sudden clinical presentation that require acute hospitalization (within 15 days from symptom onset) and often need urgent surgical or endovascular repair.

It includes aortic dissection, IMH, penetrating aortic ulcer, traumatic aortic rupture, suture dehiscence and ruptured aneurysm.

Aortic Dissection

Aortic dissection is the most common nontraumatic acute aortic emergency, with an overall in-hospital mortality of 20% to 25%, which increases markedly in patients with complicated dissection.

The aetiology is frequently unknown but is related to advancing age and hypertension.

Cystic medial degeneration in connective tissue disorders such as Marfan syndrome and Ehlers–Danlos syndrome is a predisposing factor, as are coarctation, bicuspid aortic valve, aortitis, pregnancy and blunt chest trauma. Some authorities believe that dissection can progress from a penetrating aortic ulcer and IMH.

Aortic dissection is initiated by an intimal tear, which allows blood to penetrate into the medial layer, producing a cleavage plane (false lumen) between the inner two-thirds and outer onethird of media.

The true lumen is separated from the false lumen by an intimomedial flap.

The blood course through the medial layer can variably extend the dissection distal or proximal to the entry tear and eventually rupture through the adventitia or back through the intima into the true lumen, creating re-entry tears.

Branching vessels can be involved by the dissection process and may variably originate from the true lumen, the false lumen or both. The false lumen may thrombose completely or partially over time, whereas reduction in the amount of elastic tissue within the wall of the false lumen may lead to subsequent aneurysmal dilatation.

Classification

In the literature, there are various classification systems for aortic dissection, depending on the extent of the thoracic aorta involved.

The most frequently used is the Stanford classification, whereby an aortic dissection is called type A if it involves the ascending aorta, regardless of the site of entry tear.

Type B dissections only involve the aorta beyond the LSA. This classification is focused on prognosis and strongly influences treatment approach, because, if not surgically treated, type A dissection leads to death in most cases, whereas type B dissection can be successfully managed with medical therapy.

Even type B dissections, when unstable, may require intervention to avoid severe complications and mortality. The anatomy of the dissection indicates the type of surgery or endovascular technique and their feasibility, thus affecting the procedure success rate and the long-term results.

Therefore the goal of imaging is not only the identification of the intimal flap and the extent of dissection but also a clear definition of the presence and site of entry and re-entry tears, the relationship between true and false lumen and the aortic branches (visceral, epiaortic, iliac and femoral vessels) together with the presence and degree of aortic valve or coronary artery compromise.

Imaging

Aortography was traditionally the 'gold standard' in suspected aortic dissection even though catheter manipulation and directly high-flow contrast injection in a dissected aorta increased the risk of acute complications. The advent of noninvasive imaging also demonstrated its suboptimal accuracy, especially in terms of sensitivity (77% to 90%), while specificity was 90% to 100%. CT, MRI and TOE have rapidly substituted invasive angiography.

TOE can be performed at the bedside in patients too unstable for transportation and can give haemodynamic information about flow in the true and false lumen, with excellent sensitivity for the aortic dissection confirmation (85% to 90%). TOE also provides valuable information about the functional status of the aortic valve and can assess the degree of involvement of the coronary arteries in type A dissection. However, being operator-dependent, its specificity is reduced in the 'blind areas' of the distal ascending aorta and the aortic arch.

Besides, TOE cannot assess abdominal aorta and its visceral branches, so, in stable patients, a second imaging test is advisable for a comprehensive evaluation of the thoracoabdominal aorta.

Intravascular ultrasound (IVUS) at 12.5 MHz provides intraluminal cross-sectional images of vessels and is able to demonstrate the entry tear and extent of dissection but is particularly useful in differentiating the true and false lumen and demonstration of dynamic obstruction.

However, since the transducers are single use only and expensive, most departments have limited experience of IVUS as a diagnostic tool and its role is almost exclusively confined to interventional applications.

Magnetic resonance imaging. MRI is one of the most accurate tools for aortic dissection evaluation, with excellent sensitivity and specificity that approximate 100%.

On MRI the excellent contrast between the lumen and the aortic wall make the detection of the intimal flap very easy. In BBFSE sequences it appears linear inside the black vessel lumen. The false lumen can be differentiated from the true lumen by its higher signal intensity due to the slower flow.

The presence of cobwebs adjacent to the outer wall, which represent dissected media residual strands, are also useful for identifying the false lumen.

A fast spin-echo sequence in the sagittal plane should be performed to define the extension of the dissection in the thoracic and abdominal aorta, including the aortic arch branches.

The accurate definition of the anatomical details of the dissection (extension, site of entry and re-entry tear, aortic branch relationships) relies on gadolinium-enhanced 3D MRA and its reformatted images, also including a complete analysis of axial MRA images to confirm and improve spinecho information.

The SSFP technique generates images with a high-contrast resolution between the aortic lumen and the wall that may be used for morphological (2D or 3D images) or functional (cine sequences) analysis.

Cine sequences may be used as an additional tool to evaluate aortic valve involvement and to define the presence of an entry tear (flow turbulence). With more recent equipment, 2D images can achieve a complete study of the thoracic aorta within a few minutes while a patient's ECG, blood pressure and oxygen saturation can be monitored even during assisted ventilation. A 3D sequence may be an alternative to MRA in rare cases when gadolinium is contraindicated.

Despite these strong capacities, which virtually make MRI an ideal imaging technique for aortic dissection, its use in acute dissection is still very low because of restricted availability that limits its use in emergency situations. However, MRI is a powerful tool to investigate chronic dissection during follow-up.

The high contrast resolution of morphological sequences and the application of time-resolved 3D MRA (elevated number of volume acquisition of the aorta during contrast injection to visualise the aorta from the earliest arterial phase to the most late one with high temporal resolution) helps detecting the false lumen thrombosis without enhancing the radiation burden, as CT is forced to do with a late acquisition.

Moreover, the most recent MR flow imaging application, the four dimensional (4D) flow (a volumetric free breathing and ECG-triggering velocity-encoded cine acquisition to allow an entire aortic 3D flow analysis) is still under investigation. Such 4D techniques could potentially provide such comprehensive dynamic aortic information that aids prognosis and determination of optimal surgical timing for these patients in the near future.

Computed tomography

Despite the continuing improvement in MR techniques, modern MDCT provides high image quality with much shorter acquisition times.

In a few seconds MDCT can acquire data from a volume encompassing the supra-aortic vessels to the femoral arteries (as an aortic dissection study requires). Improved temporal resolution and ECG-gating acquisition minimise pulsation artefacts at the aortic root, with consequent sensitivity and specificity now approaching 100%.

The wide availability, the fast acquisition and reporting times and the high accuracy make MDCT the imaging method of choice for the diagnosis of aortic dissection.

Unenhanced CT may demonstrate internal displacement of intimal calcifications.

Contrast-enhanced CT allows detection of the intimal flap as a thin linear low attenuation separating the contrastenhanced true and false lumen.

Injection of contrast medium via the left upper limb should be avoided because the very high attenuation from contrast medium within the left brachiocephalic vein can produce streak artefact across the aortic arch, potentially causing diagnostic difficulties.

The differentiation of the false lumen from the true lumen is essential;

a number of imaging findings can be helpful, such as the cobweb sign, described before.

In most cases the true lumen is smaller and more medially located.

On most contrast-enhanced CT images it may be identified by its continuity with the undissected portion of the aorta.

An unusual type of aortic dissection is the intimointimal intussusception produced by circumferential dissection of the intimal layer, which subsequently invaginates like a wind sock; CT shows one lumen wrapped around the other one, with the inner lumen invariably being the true one.

A dissection with thrombosed false lumen should not be confused with an aneurysm with calcified mural thrombus. High attenuation within the false lumen on unenhanced images can help to identify the former.

In addition, a dissection tends to spiral as it passes along the aorta, whereas a thrombus maintains a constant relationship with the aortic wall.

A mural thrombus arising in an aneurysm also tends to have a more irregular internal border, whilst a dissection has a smooth internal border.

Finally, calcification of the intima may be identified at the periphery of the thrombus in an aneurysm.

Visceral and supra-aortic vessel involvement can account for high mortality, and MDCT can reliably diagnose these aspects, also with the use of MPR reconstructions. MIP and VR images greatly contribute to surgical planning and aortic segments measurements.

VR is preferred to MIP, as it preserves the variable enhancement patterns of the lumina and is more sensitive for visualisation of the flap.

Intramural Haematoma IMH was first described in 1920 as 'dissection without intimal tear', but clinical recognition of this pathological entity except for autopsy or surgical specimen was almost completely absent before CT and MRI.

In fact, IMH is a lesion confined to the aortic wall and invasive angiography is not able to detect it. It is considered the consequence of a hypertensive rupture of the vasa vasorum within the medial layer and eventually results in a circumferentially oriented blood collection.

IMH may occur spontaneously but may also arise from a penetrating aortic ulcer in a severely atheromatic aortic wall. It has also been described following trauma. An IMH is visualised by cross-sectional imaging as an aortic wall thickening, symmetric or asymmetric, variable in thickness from 3 mm to more than 1 cm, and it must be differentiated from mural thrombus or plaque.

Intimal displacement of calcification can aid in distinguishing these entities, because the IMH is a subintimal lesion, with calcifications displaced on top of the lesion facing the lumen. Acute IMH is hyperdense on unenhanced CT. Another

difference is the shape of the aortic wall thickening: in IMH the borders are generally smooth, while a thrombus or a plaque is typically characterised by irregular margins.

With TOE, false-positive and false-negative diagnoses have been reported.

Magnetic Resonance Imaging

In comparison with other imaging techniques, MRI had the best sensitivity for detecting IMH before the advent of MDCT. T1 weighted images reveal a typical crescent-shaped area of abnormal signal intensity within the aortic wall. MRI is also the only imaging technique able to assess the age of the haematoma, exploiting the influence on MRI signal intensity of the different degradation products of haemoglobin: in the acute phase (0 to 7 days after the onset of symptoms) on T1 weighted spin-echo images, oxyhaemoglobin shows intermediate signal intensity, whereas in the subacute phase (>8days), methaemoglobin shows high signal intensity. However, when the signal intensity is medium to low, it can be difficult to distinguish IMH from mural thrombus. T2 weighted spin-echo sequences may help in differentiating the two entities: signal intensity is high in recent haemorrhage but low in chronic thrombosis.

Computed Tomography

CT, like MRI, has proven to be highly accurate in the diagnosis of IMH, with comparable sensitivity and specificity. In the suspect of IMH, it is important to perform unenhanced CT: in the acute phase the haematoma appears as a crescent-like aortic wall thickening typically hyperdense on unenhanced CT with respect to the aortic lumen, whereas after enhancement the density of wall and lumen are reversed, with the IMH remaining unenhanced, unlike the false lumen in aortic dissection.

The differentiation between IMH and a completely thrombosed false lumen may be very difficult and the following findings are useful for differential diagnosis. IMH maintains a constant circumferential relationship to the wall (subintimal lesion), whereas the thrombosed false lumen tends to longitudinally spiral around the aorta.

Secondly, IMH does not reduce the lumen, which maintains its regular shape, whereas the false lumen can variably compress the true lumen.

MDCT is highly accurate for the detection of small circumscribed intimal defects that can appear at multiple levels of the IMH; they can enlarge over time, evolving towards aneurysmal dilation, and may eventually represent a patient subgroup with worse prognosis.

The diagnosis of IMH is mainly based on axial images, but 2D reformatted images may be useful to evaluate the extent of IMH and its relationships with aortic branches. MRA, like conventional angiography, has poor value in IMH diagnosis because it provides only luminal information.

An appropriate adaptation of the window level in reformatted images can help to identify the wall haematoma.

Penetrating Atherosclerotic Ulcer

An aortic ulcer is generated by erosion of an atheromatous plaque disrupting the internal elastic lamina, exposing the media to pulsatile arterial flow and subsequent haematoma formation.

This is distinguished from an atheromatous plaque by the presence of a focal, contrast medium–filled outpouching surrounded by an IMH. An atheromatous plaque does not extend beyond the intima, is frequently calcified and lacks an IMH.

The extension of the ulceration to the medial layer can also evolve in localised dissection or even break through into the adventitia, creating an aortic pseudoaneurysm. If the adventitia ruptures, only the mediastinal tissue can contain the haematoma; otherwise, the rupture is complete. Penetrating atherosclerotic ulcers (PAUs) are mainly located in the descending aorta but may be also seen in the aortic arch. Ulcers can be multiple and are frequently associated with a severe atherosclerotic aortic wall.

The imaging diagnosis of PAUs is based on the visualization of a crater-like, contrast-filled outpouching with jagged edges, of variable extension, which may result in a large pseudoaneurysm.

Mural thickening can be associated (localised haematoma), as well as aortic dissection. Differently from IMH, conventional angiography has a good sensitivity for PAUs, but both CT and MRI are better suited to evaluate the presence of associated lesions like atherosclerotic disease extent, localised haematoma and dissection.

Unenhanced CT has the advantage of visualising intimal calcification displacement.

MRA and CTA, including 2D and 3D reformatted images, are important for analysing the often-complex spatial relationships between the ulcers and the aortic branches.

The various aortic diseases as described so far are related to each other: PAU and IMH are both potential precursors of dissection.

Because they are lesions that involve a more external portion of the aortic wall, they are more prone to rupture than aortic dissection and need careful monitoring in the acute phase. Moreover, IMH can evolve into PAU and even dissection.

Traumatic Aortic Injury

Traumatic aortic injury (TAI) can result from both penetrating and blunt chest injuries.

Motor vehicles accidents are one of the main causes of TAI.

In the United States there are approximately 40,000 motor vehicle deaths yearly, and it has been estimated that 20% of deaths are caused by aortic rupture.

A number of mechanisms with an increased risk for TAI have been proposed, of which the most important is rapid and sudden deceleration during the impact (especially at speeds greater than 30 mph).

The aortic segment subjected to the greatest strain is the isthmus, where the relatively mobile thoracic aorta is fixed by the ligamentum arteriosum: 90% of traumatic aortic ruptures occur here.

Another mechanism leading to TAI consists of torsion caused by displacement of the heart to the left during anteroposterior (AP) compression, which typically involves the ascending aorta close to the innominate artery or immediately superior to the aortic valve; this is seen with vertical deceleration caused by falls from large heights (especially greater than 10 ft). Other aortic segments are less commonly involved like the distal descending (diaphragmatic) aorta or the abdominal infrarenal segment, suggesting underlying mechanisms other than the sudden deceleration strain: one process refers to the 'osseous pinch', leading to compression of the heart and aorta between the sternum and vertebral column with a trauma extended from the intima to the adventitia.

In most patients (80% to 90%) there is complete rupture of the aorta, with death occurring at the scene of the accident. Those patients that reach the hospital alive have injuries that vary from a simple intimal lesion, an IMH to a false aneurysm when the laceration extends through the media into the adventitia (which may be the only layer maintaining aortic integrity). Periaortic haemorrhage is frequently seen, irrespective of the type of lesion.

Imaging

The clinical diagnosis of TAI can be difficult due to the lack of specific symptoms or signs in many patients. CXR gives only indirect signs of an aortic lesion like haemomediastinum, which is insufficiently specific and is more likely the consequence of venous bleeding relative to the thoracic trauma.

Moreover, chest radiographs in patients with suspected TAI are taken in the supine position, so the interpretation of mediastinal widening can be problematic—especially in obese patients. Upper limits for a normal mediastinal width or the ratio of the mediastinal width to chest width at the level of the aortic arch (M/C ratio) have been proposed (8 cm and 25%, respectively) but have a wide range of reported sensitivities and specificities. In any case the initial CXRs performed as part of a trauma series may suggest an aortic involvement with satisfactory sensitivity (80% to 90%), showing the displacement of the nasogastric tube by the haematoma.

This makes chest radiography a useful screening tool for mediastinal haemorrhage, even though a normal mediastinum does not exclude a significant aortic injury.

Thoracic aortography is no longer the preferred diagnostic test: first because it provides less information than CT and MRI about wall alterations and anatomical preoperative evaluation and, secondly, because of its lower accuracy, with sensitivities ranging from 84% to 96%, with false positives caused by prominent ductus diverticulum, severe aortic atheroma or double densities from overlapping adjacent vessels and false negatives due to poor opacification of the aorta or small intimal defects. Examples are shown in Figs 17.21 and 17.22. TOE has a sensitivity of 91% and specificity of 98% for demonstration of isthmic aortic injuries.

TOE has the advantage that can be performed at the patient's bedside in 15 to 20 minutes, even in highly unstable patients. However, it may be contraindicated in the presence of severe facial injuries or unstable cervical spine fractures.

The entire aortic circumference may not be adequately visualised in approximately 30% of patients, while the aortic arch is not easily displayed, thus limiting preoperative evaluation.

On the other hand, TOE is extremely useful as an intraoperative assistant tool for guiding endovascular intervention, providing excellent visualisation of the proximal aorta for accurate placement of stent grafts in relation to aortic branch vessel origins.

With the exception of extremely unstable patients, CT and MRI are the ideal imaging investigations for TAI, with a diagnostic accuracy approaching 100%.

They can demonstrate both indirect signs such as mediastinal haematoma and direct signs of aortic trauma, especially giving high-definition images of the aortic wall alterations such as IMH, or small intimal lesions. In addition, CT and MRI provide primary information about endovascular treatment feasibility (relationships between epiaortic or visceral vessels and the aortic trauma, vascular access) and may also evaluate other organs and structures to search for associated traumatic lesions in the same examination.

Magnetic resonance imaging

The development of fast MRI techniques has shortened the examination time to a few minutes for TAI diagnosis, even less than TOE.

BBFSE images obtained in an oblique sagittal projection give a longitudinal view of the thoracic aorta, allowing for the distinction of a partial lesion (confined to the anterior or posterior aortic wall) from a lesion that encompasses the entire aorta (more than 270 degrees of circumference). MRI can provide this information even without contrast medium administration, but limited urgent access to MRI remains its main limitation.

MRI may be useful for identifying and dating an IMH, when present.

Computed tomography

CTA for TAI diagnosis is the most widely used imaging test, because of the extensive availability (location close to the intensive care units) and high acquisition speed, which are especially suitable in emergency conditions.

Moreover, CT allows quick assessment of the entire thorax and abdomen, as well as the head, which should be examined in any trauma for evaluation of head and/or abdominal injury.

Typical appearance of TAI on CT images is contrast agent extravasation or a defined pseudoaneurysm, but aortic injuries may also represent as dissection flap, a focal calibre change or a small aortic contour abnormality (representing intimal and media disruption), which may be more difficult to identify correctly.

But, as for aortography, false positives can arise from the presence of severe atheroma or a ductus diverticulum.

These can be first differentiated from a small pseudoaneurysm by the absence of surrounding mediastinal haematoma.

The superior intercostal vein, the bronchial artery infundibulum and movement artefacts are also sources of false-positive diagnoses.

Images can also be degraded by streak artefacts from nonelevated arms and shoulders, contrast medium injection into a left arm vein and monitoring lines.

The few cases with equivocal CT findings may eventually be resolved by IVUS, whereas aortography does not add substantial elements to the diagnosis.

Aortic Aneurysms

An aortic aneurysm is a localised or diffuse dilatation involving all layers of the aortic wall, exceeding the expected aortic diameter by a factor of 1.5 or more, whereas in a false aneurysm or pseudoaneurysm

the wall is represented only by the adventitial layer. This distinction is

relevant because false aneurysms result from a contained rupture and

should not be considered stable.

Aneurysm development is multifactorial in nature, with both a genetic

predisposition and environmental factors acting together to initiate a

cascade of arterial wall degeneration.

Most aneurysms are caused by atherosclerosis but can also be the result of a trauma, infection including tuberculosis and syphilis or genetic syndromes such as Marfan and Ehlers– Danlos, the latter most commonly affecting the aortic root, ascending aorta and arch.

Histologically, an inflammatory cell infiltrate has been demonstrated in all atherosclerotic aortic aneurysms. Matrix metalloproteinases (MMPs) play an important role in the remodelling process by degrading extracellular matrix proteins such as elastin and collagen, both of which are needed to maintain the structural integrity and mechanical properties of the aortic wall. In healthy tissue, MMP activity is tightly regulated by tissue inhibitors. Several MMPs have been identified, MMP-2 being most strongly associated with small aneurysms, and MMP-9 has been linked to medium-sized, large or ruptured aneurysms.

Furthermore, plasma concentrations of MMP-9 appear not only to be associated with aneurysms themselves but also with the size and expansion rate of abdominal aortic aneurysms (AAAs); plasma levels will fall after successful therapy of an AAA.

Atherosclerotic Aortic Aneurysms

As many as 95% of atherosclerotic aneurysms affect the abdominal rather than the thoracic aorta. The natural history of aneurysms is progressive remodelling, expansion and eventual rupture.

Because only 14% of patients have symptoms, a ruptured aneurysm is a major cause of death in Western populations. Patients usually have major comorbidities such as coronary disease, peripheral vascular disease, obstructive pulmonary disease, diabetes and renal failure.

Of patients who initially survive a ruptured aneurysm, more than 50% die during or following surgery.

The asymptomatic thoracic aortic aneurysm (TAA) is often detected as mediastinal widening or a calcified soft-tissue mediastinal mass on a chest radiograph taken for some other reason; not infrequently, it is confused with a tumour.

Likewise, AAAs can be detected incidentally on abdominal or lumbar spine radiographs because of their mass effect and wall calcifications.

Thoracic Aneurysms

The role of ultrasound in the evaluation of TAAs is confined to the proximal aortic segments (aortic root, sinotubular junction and proximal ascending aorta), whereas CT and MRI, with their unlimited access to the thoracic structures and the superior accuracy and reproducibility of measurements, have no limitations to the diagnosis and follow-up of these diseases.

Magnetic resonance imaging. Standard BBSE MRI sequences evaluate alterations of the aortic wall and periaortic space. Atherosclerotic lesions appear as areas of increased wall thickness, with irregular profiles and possible endoluminal projections.

The high tissue characterization of T1 and T2 weighted BBSE images allows accurate depiction of inflammatory changes or

the presence of a haematoma within the aortic wall or the periaortic spaces.

With a fat-suppression technique, the outer wall of the aneurysm can be easily distinguished from the periadventitial fat tissue, so that the aneurysm diameter can be accurately measured.

Mural thrombus and atheromatous plaques are well visualised in the axial plane, whereas sagittal and coronal views are used to define the longitudinal extension and location of the aneurysm and its diameters, avoiding projection effects in axial images, caused by the natural curvature and tortuosity of the aorta.

Contrast-enhanced 3D MRA can provide precise topographic information about the extent of an aneurysm and its relationship to the aortic branches.

Computed tomography

CT can detect thoracic aneurysms with 100% accuracy. It has the advantage over MRI of directly demonstrating aortic wall calcification, which is important when planning surgical or endovascular procedures.

MPR and 3D VR applications help for the assessment of calibre, length, angle, calcification and burden of mural thrombus, as well as length, shape and angle of the aneurysm necks.

Both imaging techniques have high reproducibility of measurements, but MRI is preferred to CT for monitoring expansion of chronic aortic aneurysms because it avoids ionising radiation.

This is particularly true for precise measurements in Valsalva sinus and ascending aorta aneurysms in patients with genetic disorders such as fibrillinopathies (e.g. Marfan disease). Although modern dedicated nongated CT protocols using modern CT equipment (gantry rotation time <0.3 second) show limited motion artefacts when cardiac frequency is reasonably stable, ECG gating is still frequently necessary to avoid aortic pulsation artefacts.

Abdominal Aneurysms

Unlike thoracic aneurysms, abdominal aneurysms are easy to show by ultrasound, which can be used for follow-up instead of CT.

Recent inversion recovery BBFSE breath-hold MRI sequences with adequate suppression of the blood pool can also provide the same information as CT, except for aortic wall calcification. Fast gradient-echo SSFP sequences may cover the whole abdomen within two or three breath-holds with good contrast resolution between the aortic lumen and the wall and optimal aneurysm thrombus visualisation.

Three-dimensional MRA can be helpful in planning surgical or endovascular therapy.

Abdominal aneurysms are usually monitored by ultrasound and CT. Ultrasound is the preferred imaging test for assessing abdominal aneurysm dimension; surveillance is associated with reduced mortality and no difference in long-term survival versus early endovascular

or surgical treatment for aneurysm diameters less than 5.5 cm.

Thus ultrasound is increasingly used as a screening test, with noninvasiveness and low cost.

CT is more accurate and widely used when dimensions are close to the cut-off values for surgical intervention.

Multiplanar reconstructions provide precise definition of the size and extent of the aneurysm and its relationships with visceral and iliac vessels, as well as the lumen, the wall, the extent of any inflammatory material and the position and degree of distension of all the important adjacent structures. For these reasons CT is used to evaluate AAAs, helping with decisions about endovascular treatment or surgery.

Advanced imaging techniques like 18F-Fluorodeoxyglucose Positron Emission Tomography (18-FDG-PET)-CT or MRI with ultrasmall superparamagnetic particles of iron oxide (USPIO-MRI) are still under review as potential predictors of aneurysm progression.

Inflammatory Aneurysms

Inflammatory abdominal aortic aneurysms (IAAAs) are defined as dilation of the aorta with a thickened aneurysm wall, marked perianeurysmal and retroperitoneal fibrosis and dense adhesions to adjacent abdominal organs.

IAAAs represent 3% to 10% of all AAAs and are more common in men.

Mean age of occurrence ranges from 62 to 68 years (5 to 10 years younger than patients with other atherosclerotic aneurysms).

Moreover, patients with IAAAs have a positive family history of aneurysms (17%) as compared with patients with noninflammatory aneurysms (1.7%). IAAAs are more often symptomatic.

In addition to abdominal or back pain, these patients also present with weight loss and elevated erythrocyte sedimentation rate (ESR).

The aetiology of IAAAs is the same as for other atherosclerotic AAAs, but the inflammatory component is more pronounced. Current aetiological thinking favours a single pathological process, with varying degrees of inflammation rather than a distinct clinical entity.

The importance of the IAAA lies in its potential treatment. Its true natural history is unknown, but the risk of rupture remains. Steroid therapy has been used to control the inflammatory process, but no controlled studies exist.

Surgery is technically difficult because the ureters can be involved in the inflammatory process and may need stenting for protection.

The duodenum and left renal vein are often adherent to the aneurysm sac. IAAA repair halts the progression of retroperitoneal fibrosis but does not cure it.

Complete regression of the retroperitoneal fibrosis is seen in 23% to 53% of cases after surgery, with partial regression or no change in the remainder.

In view of the technical difficulty of open IAAA repair and the increased morbidity and mortality, endovascular aneurysm repair is an attractive alternative.

However, the long-term regression of the perianeurysmal fibrosis, seen in up to 53% after open repair, is said to occur less frequently after endovascular repair, although the number of cases reported is small.

Computed tomography

Although ultrasound is very important, CT has become the mainstay of assessing IAAAs, showing a thick cuff of enhancing soft tissue around the aorta (Fig. 17.29). IAAAs can usually be differentiated from other diseases such as lymphoma surrounding an aneurysm, or a tumour reaction seen in liposarcoma or bladder cancer causing a strong periaortic inflammatory fibrous reaction.

Haemorrhage is another potential diagnostic pitfall. When an aneurysm has ruptured, the tissue planes within the retroperitoneum become poorly defined, which can make the identification of the inflammatory component difficult.

However, fresh blood has a higher CT attenuation than muscle and usually expands into the pararenal fat further away from the aneurysm itself, except at the very point of rupture.

Magnetic resonance imaging

MRI is optimal in patients with manifest or potential renal failure.

Spin-Echo (SE) T1 and T2 weighted sequences provide a good overall assessment of an inflammatory aneurysm.

On SE images the periaortic cuff of inflammatory aneurysms has intermediate signal intensity.

After intravenous administration of gadolinium, the periaortic cuff enhances significantly, so that intraluminal thrombus and aortic wall are clearly defined, along with the adjacent involved structures embedded in the inflammatory cuff.

Mycotic Aneurysms

Infection can cause thrombosis of the vasa vasorum with consequent destruction of the aortic intima and media.

Commonly, such infection is due to emboli from infectious endocarditis, septicaemia or local spread.

Imaging of mycotic aneurysms is similar to that of other aneurysms.

The results of surgical treatment can be poor and often the aorta must be tied off and axillobifemoral grafting performed.

More recently, stent grafting has been tried, with mixed results.

Aortic Sinus Aneurysms

These aneurysms can be congenital, particularly in Asian populations, but can also be seen secondary to infective endocarditis and in Marfan syndrome and ankylosing spondylitis.

The most common site is the right aortic sinus extending into the right ventricle or right atrium, but also the noncoronary sinus extending into the left atrium.

They may rupture into the heart and present subacutely with a left-to-right shunt and a continuous murmur.

When dilatation is confined to the aortic root, it will not be seen on the PA chest radiograph, although it may be revealed on the lateral radiograph. When the ascending aorta is involved, the right mediastinal border will be prominent and, on the lateral radiograph, the aorta will obliterate the retrosternal space above the heart. Left ventricular dilatation results from aortic regurgitation. The aortic root and ascending aorta are well shown by both MRI and CTA.

MRI has the advantage of adding functional information with cine gradient-echo, SSFP and phase-contrast imaging that show aortic regurgitation and fistulas as flow turbulence (signal void on bright-blood images) and may quantify aortic insufficiency. In emergency conditions, TOE is also very useful and can be carried out at the bedside. Angiography is avoided in these patients, particularly in the presence of infection.

Preoperative Evaluation of Acute Aortic Syndromes

The imaging techniques must first confirm or exclude the presence of impending aortic rupture or any other signs of severe instability that deserve immediate surgical or endovascular treatment (e.g. a visceral malperfusion in aortic dissection).

Secondly, the imaging test should define whether the anatomical conditions allow an endovascular or surgical treatment of the disease.

Impending Aortic Rupture

Aortic rupture appears on CTA images as a discontinuity of the aortic wall with contrast medium extravasation, and it is typically associated with a large, periaortic haematoma.

On unenhanced CT images the rupture can be suspected if there is a discontinuity of wall calcification.

In the absence of evident aortic disruption, an impending rupture is indicated by various indirect signs such as haemorrhagic pleural effusion, periaortic, pericardial and/or mediastinal haematoma.

A periaortic haematoma appears as a mass encompassing the aortic contour.

The haemorrhagic nature of a pleural or pericardial effusion is suggested by high density values on unenhanced CT (20 to 40 HU).

MRI is highly specific for the recognition of the haemorrhagic nature of a pleural or mediastinal effusion, exploiting the high tissue characterization power of BBFSE T1 and T2 weighted sequences.

Usually, the high signal intensity of the effusion, of periaortic tissue or the thrombus within the aneurysm, as well as a periadventitial enhancement on MRA or CTA images, indicate the presence of haemorrhage or acute inflammation (hyperintensity on T2 weighted images) and are signs of aneurysm instability.

An emerging right pleural effusion also indicates disease evolution, as does increasing diameter of the aorta over time. As a rule, imaging should be repeated after a few days in patients with suspected TAI, to rule out or diagnose changes over time.

Intraluminal contrast medium reaching to the very edge of the aneurysm is also a cause for concern.

There are two signs in patients with acute TAI representing a 'red flag' indicative of need for urgent aortic repair:

• The pseudocoarctation syndrome is a partial compression of the aorta by a pseudoaneurysmatic sac just distal to the traumatic injury of the aortic wall, leading to an aortic lumen reduction as in congenital aortic coarctation.

CT depicts this sign on MPR reconstructions in an oblique sagittal plane.

• A circumferential lesion is a traumatic injury of the aortic wall involving more than 270 degrees of the aortic circumference.

This lesion is a strong predictor of an impending rupture. It can be diagnosed on axial images but is best seen on 3D VR reconstructions.

Visceral Malperfusion

The instability of an acute aortic dissection is not only represented by signs of impending aortic rupture but also by the presence of partial or complete occlusion of branching vessels. The incidence of branching vessel compromise associated with aortic dissection ranges from 25% to 50%.

Restriction of flow into the aortic branch vessels is caused by two mechanisms leading to end-organ ischaemia.

1. Dynamic obstruction affects vessels arising from the true lumen.

Collapse of the true lumen is caused by bowing of the dissection flap into the true lumen, either proximal to or at the level of the ostium of the branching vessel, restricting or occluding flow.

2. Static obstruction is caused by extension of the dissection into the branching vessel without a re-entry point.

Increased pressure or thrombus formation in the false lumen produces a focal stenosis with subsequent end-organ ischaemia. Both dynamic and static obstruction can coexist, and identification of the mechanism of ischaemia is vital as the endovascular management of each differs.

Before or in addition to clinical or laboratory signs of malperfusion, CT and MR imaging can suggest or confirm the presence of this severe pathological condition, which deserves emergency treatment.

The CT features of malperfusion consist of both aortic and visceral findings: a thread-like true lumen is most suggestive, but a malperfusion mechanism must be already suspected when the intimal flap shows a convexity towards the true lumen even when its dimensions are not clearly reduced.

CT may overestimate the degree of compression: in fact, an absent opacification of the true lumen does not exclude the

possibility of passing the stenosis with a guidewire during an endovascular procedure.

CT readily depicts signs of renal ischaemia such as absent or reduced opacification of one kidney.

It is important to confirm the reduced opacification also in the venous phase, because if the renal artery arises from the false lumen, the renal perfusion may be delayed compared with the perfusion from the true lumen.

A delayed acquisition after contrast administration is therefore recommended to confirm or exclude a partial or total renal ischaemia.

Renal ischaemia is mostly accompanied by clinical signs such as anuria, haematuria, flank pain and uncontrolled hypertension.

Hepatomesenteric malperfusion is characterised by gastrointestinal bleeding, abdominal pain, abnormal hepatic laboratory findings and metabolic acidosis.

CT shows the oedematous infiltration of the mesenterial fat during bowel distress and gastrointestinal stretching, but the venous phase is crucial to show direct signs of hypoperfusion of the bowel such as thickening and decreased enhancement in the acute phase (shock bowel).

Static obstruction of a branching vessel is strongly indicated by an intimal flap entering the vessel with thrombus formation in the false lumen.

Preoperative or Preinterventional Evaluation

Both CT and MR are equally well suited for preoperative evaluation of aortic disease and have completely replaced conventional angiography.

Especially for planning of endovascular treatment, a number of anatomical details need to be assessed to evaluate procedure feasibility and choose the correct prosthesis. For TAAs the main features that should be assessed are:

• Size and extension of the aneurysm.

• Adequate distance (>15 mm) between the proximal neck of the aneurysm and the origin of the epiaortic vessels to ensure a sufficient sealing of the stent graft, although it should be noted that, especially in emergency conditions, the LSA can be covered, given that both vertebral arteries are patent. Overstenting of LSA may be performed in elective procedure after performance of revascularisation surgery.

• Distance of the peripheral neck of the aneurysm and its relationship to the origin of the visceral arteries (should be >15 mm) because preprocedural bypass operation or stenting is required if they have to be covered.

• Extent and type of wall alterations (e.g. amount of atheromatous material or calcium) at the proximal and distal neck that might affect the stent sealing (the oversize of the aortic diameter should be maintained by 10% to 20%).

• Diameter and condition of the abdominal aorta and vascular access (iliac and femoral arteries) and tortuosity of descending aorta which might prevent passage of the stent-graft delivery system.

• Any evidence for the presence of a large radicular artery supplying the spinal cord that could be covered by a stent graft. The incidence of paraplegia is much lower with thoracic stent grafts than with surgery but is still approximately 2%.

Expected length of coverage must be considered to evaluate the risk of such a complication, which can be partially prevented by cerebrospinal fluid (CSF) drainage before and after the procedure.

• Any other incidental findings in the chest, abdomen or pelvis that should contraindicate the procedure (e.g. metastatic tumour spread).

Endovascular treatment of an AAA needs to consider other anatomical relationships of the aneurysm because most AAA stent grafts are bifurcated, although aorto uni-iliac stent grafts with surgical femorofemoral cross-over grafting are also common, especially when the aneurysm has ruptured. Tube grafts are now the exception rather than the rule. Preprocedural CT evaluation is done to determine the following:

- Anteroposterior and transverse size of the AAA.
- Diameter of the aorta at the level of and just below the visceral arteries.
- Distance of the proximal aneurysm neck to the lowest renal artery (at least 15 mm).
- Shape of the neck (conical necks may lead to poor proximal seals or late endoleaks) and presence of excessive atheromatous wall changes potentially preventing a perfect seal.
- Angulation of the neck in the AP and lateral planes: an angle greater than 60 degrees aggravates stent sealing and harbours an increased risk for stent displacement.
- The presence of accessory renal arteries that will have to be covered may make a preprocedural assessment of split renal function necessary.
- Distance from the lowest renal artery to the aortic bifurcation determining the length of the stent-graft main body.

• Diameter, tortuosity, degree of calcification and morphology of the common iliac arteries. If they are aneurysmal, patients need to be informed with respect to possible buttock claudication following internal iliac artery embolisation and extension of the stent graft into the external iliac artery.

• Size of the common femoral and external iliac arteries and the presence of any stenoses that might prevent the stent-graft delivery.

• Any incidental findings, especially with respect to size and function of the kidneys or the presence of a doubled inferior vena cava, especially if open surgery is planned.

The following anatomical details need to be considered for planning of endovascular treatment of aortic dissection:

• The distance between the proximal neck, the entry tear and the origin of the epiaortic vessels.

• The origin of the visceral vessels in regard to the true or false lumen must be defined.

If one or more vessels arise from the false lumen, a re-entry tear ensuring vessel perfusion after stent-graft deployment has to be identified.

The recent introduction of branched/fenestrated devices allows endovascular treatment of thoracoabdominal anurysms. In these cases a comprehensive study with CT to accurately evaluate the whole aorta and the anatomical relationships among visceral and epiaortic vessels and the aortic lesion is needed to allow very precise measurements for custom-made devices.

• Careful evaluation of ascending aorta and aortic arch dimensions and degree of atheromatous wall changes are necessary.

Ascending aorta and arch aneurysms may favour a retrograde extension of the dissection if the proximal end of the stent graft (free flow extremity) is positioned in the distal arch. In patients with Marfan syndrome or a bicuspid aortic valve, endovascular treatment of type B dissection may be contraindicated for this reason.

The distal end of the stent graft is usually localised in a part of the dissected aorta which does not represent the true aortic diameter; thus the choice of the prosthesis calibre should not exceed 80% of the sum of true and false lumen to avoid aneurysmal degeneration of the false lumen.

CT provides optimal preoperative evaluation of stent-graft procedures under emergency conditions, as well as for elective
procedures, due to its rapid and accurate anatomical definition; MR, although adequate for preoperative evaluation, is not able to visualise calcification and is thus the less adaptable technique.

CT is preferred because it provides superior visualisation of the stent-graft material.

Despite high temporal resolution with time-resolved MRA, that could help differentiating endoleak type, metal artefacts on MR images limit the sensitivity for small initial endoleaks, as well as for stent fractures, as the latter represent a late complication. CXR and abdominal x-ray (AXR) may also be used to check for stent fracture in the long term.

MR provides accurate evaluation of the aorta distal and proximal to the stent graft, with reproducible measurements of the excluded aneurysmal sac; it is mainly reserved for the imaging follow-up of endovascular treatment of TAI, but it could also be used in aortic dissection after stent graft treatment, especially in young patients.

Another very useful tool for postoperative evaluation after endovascular treatment of AAAs is contrast-enhanced ultrasound (CEUS), which can be used during follow-up instead of CT, thereby reducing the radiation burden.

Complications may also occur after traditional surgical intervention, and regular imaging follow-up should be performed, although less frequently than after stent grafting. Ultrasound is satisfactory after proximal aortic interventions (involving the aortic valve and ascending aorta) because it provides both morphological and functional information (valve prosthesis function).

MR and CT are reserved for patients for whom ultrasound is inconclusive or to confirm the suspected complications (e.g. suture dehiscence).

MR is usually less affected by artefacts from surgical devices, except for old mechanical valve prostheses, and is the preferred

method for repeated postsurgical follow-up; moreover, it can also provide functional evaluation of the aortic valve.

Management of Aortic Diseases

Traumatic Aortic Injury

The traditional approach of immediate repair of TAI is based on the high mortality in the first 24 hours in patients who survive the initial traumatic event.

However, the outcome in these patients is related as much to associated injuries as it is to the TAI itself.

This led to the suggestion by some investigators to delay surgical repair or even consider conservative management of TAI, allowing time to manage other serious or potentially lifethreatening injuries.

Controlled hypotension is mandatory using β -blockers and vasodilators to keep the mean arterial pressure less than 70 mm Hg. β -Blockers reduce the rate rise of systolic ejection of the left ventricle, decreasing the shearing force on the aortic wall. This approach has been found to successfully reduce the overall morbidity and mortality in patients with other significant injuries.

Because surgery has a high morbidity and mortality, thoracic stent grafting (TSG) has been introduced for the management of TAI as a less-invasive alternative therapy.

Small cohort series have shown TSG to be a successful alternative treatment of TAI, with substantially reduced morbidity and mortality compared with surgical repair, and after 10 years of experience with endovascular treatment there is nowadays a definite management shift from surgery to endovascular approach.

Endovascular repair of TAI requires at least 15-mmlong distance of aortic wall proximal to the injury to achieve an adequate seal.

Given that the isthmus is the most common site of TAI and is usually very close to the origin of the LSA, the proximal distance is frequently insufficiently long.

This proximal 'landing zone' may be lengthened by intentionally covering the LSA origin and extending the stent graft to the origin of the left common carotid artery.

Initial concerns over acute upper limb ischaemia have not been confirmed; most patients have an adequate collateral supply via the circle of Willis and left vertebral artery and do not need carotid-to-subclavian bypass surgery.

However, the risk of adverse central neurological events after endovascular overstenting of the LSA without previous revascularisation is approximately 10% in multiple study series.

Aortic Dissection

Initial treatment in all patients presenting with a ortic dissection is aimed to eliminate pain, reduce systolic blood pressure and reduce systolic pressure rise during cardiac cycle. It is achieved by a combination of intravenous β -blockers and peripheral vasodilators.

Subsequent management is based on the Stanford type and the presence of complications.

Type A dissection

These dissections account for 75% of cases.

Immediate surgical repair is indicated in all patients, owing to the high mortality (>50% within 48 hours) if untreated. Fatal complications include aortic rupture, cardiac tamponade, acute aortic regurgitation and acute myocardial infarction. Involvement of the arch vessels harbours a high risk for

neurological complications.

Type B dissection

The current treatment of acute type B dissections is based on a complication-specific approach. In uncomplicated type B dissection (no evidence of rupture or branch vessel ischaemia), medical treatment is initiated because both medical

and emergency surgical management are associated with similar mortality rates.

Patients who fail under medical treatment (persistent pain and/or progression of dissection) or develop complications are referred for either surgical or endovascular intervention. Early surgery is recommended for patients with Marfan syndrome.

Endovascular treatment of type B dissection

Surgery for type B dissection is associated with mortality exceeding 50% with high risk for organ ischaemia. Endovascular techniques have been successfully used for the treatment of type B dissection with reduced morbidity and mortality. The three techniques used are stent insertion, stentgraft insertion and/or fenestration of the intimal flap.

The indications for stent or stent-graft placement in type B dissection are twofold:

1. Contained rupture.

Persistent flow in the false lumen is associated with aneurysmal dilatation and increased risk of rupture of the false lumen (20% to 50% of patients within 1 to 5 years). Placement of a stent graft covering the site of the entry tear can promote thrombosis of the false lumen and stabilisation of the dissection, thereby reducing the risk of rupture.

Acute type B dissections are the most appropriate group to treat as the dissection flap is thin and mobile, and will readily fuse with the aortic wall.

In chronic dissections, the flap becomes thickened and rigid and thus endovascular stenting is less likely to result in complete false lumen exclusion.

2. Occlusion of branching vessels

The treatment in patients with impeding branch vessel ischaemia is dependent on the cause.

Dynamic obstruction results from true lumen collapse.

Sealing the entry tear with stent-graft placement directs blood flow back into the true lumen, increasing the size of the true lumen, moving the dissection flap away from the branch vessel and in that way relieving branch vessel ischaemia.

Static obstruction can be successfully treated by direct stent insertion in the compromised vessel via the true lumen.

In cases where the dissection extends distally to cause lower limb ischaemia, direct access to the true lumen is gained by directly accessing the involved side with weakened or absent femoral pulse.

Currently, stent grafts are mostly used in patients who have indications for surgical intervention.

Given that the majority of patients undergo thrombosis of the false lumen following stent-graft placement, it is not inconceivable that, in the future, this may become the treatment of choice for all patients with acute type B dissection. More recent data on middle- and long-term results of endovascular treatment versus medical therapy for stable type B dissection seem to favour endovascular treatment.

However, more prospective and randomised comparative follow-up data are required about long-term patient outcome and device durability.

Since the introduction of stent grafts, percutaneous fenestration has been less frequently used in the management of branch vessel ischaemia due to true lumen compression.

Patients who are managed conservatively require long-term follow-up with either CT or MR to monitor the false lumen for aneurysmal dilatation and distal extension of the dissection over time.

Equally, all patients who undergo endovascular treatment require long-term follow-up to ensure integrity of the device. **Inflammatory Diseases of the Aorta and**

Midaortic Syndrome

A number of conditions can lead to an inflammatory aortitis, including ergotism, radiation fibrosis, syphilis, tuberculosis, giant cell arteritis and Buerger, Behçet, Cogan and Kawasaki disease.

There are also congenital inflammatory diseases that affect the aorta, such as Ehlers–

Danlos syndrome and Marfan syndrome, as well as neurofibromatosis.

In the acute phase, aortitis may mimic an acute aortic syndrome, especially an IMH.

Differential diagnosis can be difficult if based on clinical symptoms and laboratory tests alone. CT and MR imaging are very helpful for differentiating these two pathological entities: IMH has a typical crescent-like morphology, whereas in aortitis concentric wall thickening is usually observed.

Tissue characterisation with T1 and T2 BB sequences may aid to discern haemorrhagic products from mere inflammation.

Midaortic Syndrome

Midaortic syndrome is characterised by segmental narrowing of the proximal abdominal aorta and ostial stenosis of its major branches.

It is usually diagnosed in young adults but can present in childhood.

Clinical presentation and radiological findings are dependent on the underlying disease, but hypertension is a common feature in all patients.

Congenital aortic coarctation:

is a very uncommon cause of midaortic syndrome, in which the aortic narrowing occurs in the thoracic or abdominal aorta. It may be seen in fetal alcohol syndrome and then associated with intellectual disability.

Granulomatous vasculitis (Takayasu disease):

It is a chronic inflammatory disease that involves the aorta, its branches and the pulmonary arteries, causing varying degree of stenosis, occlusion or dilatation of the involved vessels; aetiology and precise pathogenesis are unknown.

It is more common in parts of the world with a high incidence of tuberculosis but also occurs more frequently in Japan.

It is predominantly a disease of young adults but may also affect children. It is very rare in infancy.

The female-to-male ratio varies from 9 : 1 in reports from Japan to

1.3 : 1 in India.

The pattern of vessel involvement also varies in different parts of the world.

The involvement of the aortic arch and its branches is common in Japan, whereas the thoracoabdominal aorta is mainly

involved in patients from Korea and India. It is not known whether this variation reflects differing causes of the disease or differing Human Leucocyte Antigen (HLA)-associated genetic subtypes.

Racial variation also occurs, the disease being relatively uncommon in Caucasians.

The initial site of inflammation is around the vasa vasorum in the media and adventitia but, later, nodular fibrosis in all layers of the arterial wall is seen and the intima can obliterate the lumen.

The diagnosis depends on typical angiographic morphology, a history or presence of constitutional symptoms suggestive of a systemic illness and the differential diagnosis of other, similar conditions as listed previously.

Atherosclerosis of the aorta is distinguished on clinical and morphological grounds, but secondary atherosclerotic changes may occur in older patients with Takayasu arteritis. The radiological features occur late in the course of the disease and include luminal irregularity, vessel stenosis, occlusion, dilatation or aneurysms in the aorta or its primary branches. Neurofibromatosis of the abdominal aorta and some other causes of midaortic syndrome may produce an identical angiographic picture in children.

Based on angiographic morphology, Takayasu arteritis is divided into type I (involving the aortic arch and its branches), type II (thoracoabdominal aorta and its branches) and type III (involving lesions of both types I and II).

Involvement of pulmonary arteries, in addition to any of the aforementioned types, is grouped as type IV.

The infrarenal aorta and the iliac vessels are usually not involved in Takayasu arteritis.

Similarly, the inferior mesenteric artery (IMA) is rarely involved.

Unlike coarctation of the aorta, intercostal collaterals rarely occur as the diffuse intimal disease in the aorta also involves the ostia of these intercostal vessels.

Aortic intimal calcification may be seen.

Saccular or fusiform aneurysms of the aorta occur in 2% to 26% of cases and usually coexist with stenotic lesions.

Aneurysms without stenosis occur in 1% to 2% of cases.

Pseudoaneurysm or dissection of the aorta is extremely rare. **Imaging**

CT, ultrasound and particularly contrast-enhanced MRI and MRA provide information on mural changes of the vessels and have largely replaced angiography for diagnostic and monitoring purposes.

FDG PET may be useful, especially in cases of fever of unknown origin, by illustrating increased FDG uptake in the involved vessels.

Prognosis and treatment. Takayasu arteritis in children has a mortality between 10% and 30%. The prognosis has

significantly improved due to interventional procedures for the treatment of renal and aortic stenosis.

Long-term follow-up data on children are not available. Fiveand ten-year survival in adults is 91% and 84%, respectively. Severe hypertension, aortic regurgitation, retinopathy, aneurysms or cardiac involvement are predictors of poor outcome.

In the absence of these complications, 80% of patients remain stable for years, but approximately 20% show progression. In the acute phase, treatment with corticosteroids leads to clinical remission in 60% of cases.

Cytotoxic drugs can also be used in resistant cases.

The major morbidity and mortality of Takayasu arteritis results from stenosis and occlusion of the aorta, renal and carotid arteries.

Interventional radiological techniques for stenosed segments have revolutionised the treatment of Takayasu arteritis. Surgical treatment is not preferred for Takayasu arteritis because of the diffuse, inflammatory and possibly progressive nature of the disease, except for otherwise therapy-resistant, symptomatic, stenotic lesions and large aneurysms.

Von Recklinghausen disease (type 1 neurofibromatosis)

It can be distinguished from other causes of midaortic syndrome by the presence of café au lait skin lesions and neurofibromas.

Approximately 2% of patients develop vascular abnormalities, including renal, aortic and mesenteric stenoses.

Vessels are surrounded by neurofibromatous or ganglioneuromatous tissue in the adventitia.

Alagille syndrome (a multisystem autosomal dominant disorder caused by mutations in the JAG1 gene on chromosome 20p12) and Williams syndrome (a rare genetic condition estimated to occur in 1 in 20,000 births) are both associated with aortic coarctation (thoracic or abdominal).

Aortic Occlusive Disease

Atherosclerosis is the predominant cause of chronic aortic occlusive disease (more than 90% of cases), with Takayasu disease (see earlier) accounting for the rest; acute occlusion may result from an aortic bifurcation 'saddle' embolus or in situ aortic thrombosis.

Chronic Aortic Occlusive Disease

Atherosclerotic aortic occlusive disease affects a younger population than this, generally presenting with lower limb arterial disease.

Patients are typically female, heavy smokers with hyperlipidaemia; they have a small infrarenal aorta and hypoplastic iliofemoral arteries (hypoplastic aortoiliac syndrome).

The infrainguinal arteries are 'protected' by the aortic lesion and are typically disease free.

Patients present with chronic lower limb ischaemia and are graded according to the severity of their disease.

Aortic occlusive disease is largely associated with Fontaine grade

I or II symptoms.

Symptoms of critical limb ischaemia (grade III or IV) are unusual at initial presentation as these are associated with both suprainguinal and infrainguinal disease.

Although the management of grade I and IIa patients is based solely on risk factor modification, patients with grades IIb–IV are investigated further and, in addition to risk factor modification, treated by revascularisation, if appropriate.

Investigation and management

In the presence of significant aortic disease, the femoral pulses are diminished or absent and there is a reduction in the Ankle Brachial Pressure Index (ABPI) (grade IIb, 0.5 to 0.8; grades III–IV, <0.5).

Duplex data acquisition plays very little role in the investigation of these patients because the aorta is often difficult to visualise and assess.

Angiography is currently the investigation of choice, although MRA offers major advantages.

It is noninvasive, avoiding a brachial puncture with its associated risks.

It provides excellent images of not only the aortic lesion but also the run-off and negates the need for large volumes of iodinated contrast medium.

It therefore allows planning of an appropriate management strategy with very little risk to the patient.

A number of key points need to be addressed, irrespective of the method of investigation, because these will have impact on the surgical and endovascular options considered:

1. What is the upper limit of the lesion? Is it infrarenal or juxtarenal?

2. What is the lower limit of the lesion? Is there involvement of the aortic bifurcation?

3. Are the coeliac axis (CA) and superior mesenteric artery (SMA) normal? This is important if intervention may potentially lead to compromise of the IMA.

In the past, aortic occlusive disease was treated by aortic bypass surgery or aortic endarterectomy. Although surgery is associated with excellent primary patency (75% to 90% and 90% to 95%, respectively), it is associated with considerable morbidity (9% to 27%) and mortality (1% to 7%).

Endovascular techniques have been used as an alternative since the early 1990s and are currently the treatment of choice.

Treatment options:

vary from angioplasty alone, angioplasty with selective stenting, to primary stenting.

Angioplasty alone is used in short focal stenoses

(<2 cm) and is associated with a primary patency of 85% and low incidence of major complications (3.6%).

Stenting has been reserved for flow-limiting dissection or residual stenosis following angioplasty.

Primary stenting has been advocated for the treatment of occlusions and complex lesions (eccentric, ulcerated or calcified plaques) if there is significant concern of distal embolisation.

Acute Aortic Occlusive Disease

Acute aortic occlusive disease is a vascular emergency resulting from either saddle embolus to the aortic bifurcation or in situ thrombosis of an aortic stenosis, aortic aneurysm or traumatic aortic dissection.

Given the proximal nature of the occlusion, patients often present with neurological deficits (including paralysis) of the lower limbs, which may be initially misinterpreted and lead to investigations to rule out or diagnose spinal cord compression with consequent delay in diagnosis.

If the vascular nature of the presenting symptoms is unrecognised, mortality is high (75%).

The key to the diagnosis is the absence of femoral pulses.

Imaging and management

The role of imaging is dependent on the severity of ischaemia. If there is major tissue loss, absent capillary return with marbling, profound paralysis and sensory loss or absent Doppler signals, the ischaemia is irreversible and amputation inevitable.

If any of the aforementioned findings is still missing, emergency surgery with no imaging may be appropriate. With less severe degrees of ischaemia, expedient imaging can provide useful information.

As for chronic occlusion, imaging may be done by catheter angiography or MRA, with similar risks and benefits.

The purpose of investigation is to determine the proximal location of occlusion, the state of the run-off vessels and to differentiate embolic from thrombotic occlusion.

If an embolic aetiology or thrombosis of an aneurysm/traumatic dissection is confirmed, surgical intervention with

embolectomy or bypass grafting is the treatment of choice. In situ thrombosis of a preexisting stenosis is suggested by the presence of collaterals.

Endovascular treatment with thrombolysis can also be considered if the severity of ischaemia allows us to allocate the necessary time for this.

Following successful thrombolysis, aortic angioplasty or stenting can be performed to treat the underlying lesion.

Even with appropriate intervention, overall in-hospital

mortality is high (21%), being higher in those with an embolic aetiology.

If the occlusion is embolic, following successful revascularisation, a search must be made for the underlying source.

Ultrasound will exclude a cardiac source, followed by careful examination of the thoracic aorta.

Emboli frequently originate from an aortic plaque or intimal flap.

CONGENITAL AORTIC ABNORMALITIES Vascular Rings

A vascular ring is a condition in which an anomalous configuration of the arch and/or its associated vessels completely or incompletely surrounds the trachea and oesophagus and causes compression of these structures. Neonates present with respiratory distress; older children present with stridor or dysphagia.

The two most common types of complete vascular rings,

accounting for 85% to 95% of cases, are double aortic arch and right aortic arch with a left ligamentum arteriosum.

Tracheomalacia may result from compression of the trachea by vascular rings.

The key to understanding vascular rings lies in the development of the arch.

Beyond 4 weeks' gestation there are paired ventral aortas joined to paired dorsal aortas by six pairs of arterial arches, although these are never all present simultaneously.

The fourth arch is the most important for the development of vascular rings.

Double Aortic Arch

Persistence of the right and left fourth arches leads to a double aortic arch.

In 75% the right arch is larger; in approximately

30% the smaller, or less dominant, the arch is atretic but remains in continuity with the descending aorta, maintaining a complete ring.

This may be difficult to identify radiologically.

The normally positioned left, or anterior, arch exits the pericardium and joins the left-sided descending thoracic aorta after giving off the LSA.

The ligamentum arteriosum is positioned normally.

The posterior, or right, arch joins the descending thoracic aorta at the same level as the anterior arch but reaches that point from an extreme posterior course behind the oesophagus.

Hence the descending aorta is more commonly on the left but can be on either side.

Other Vascular Rings Associated With Aortic Arch Abnormalities Involution of the left fourth branchial arch and persistence of the right branchial arch results in a right-sided aortic arch; it can occur in the absence of any other anomalies.

Its presence is suggestive of the existence of an associated anomaly, as persistence of the right arch with involution of the left creates a situation in which the origins of the LSA and ductus arteriosus can vary with possible development of a vascular ring.

Right aortic arch with aberrant left subclavian artery and left ligamentum arteriosum

In these cases, the right arch first gives off the left carotid artery, which runs anteriorly to the trachea. It then gives off the right carotid, followed by the right subclavian artery, and, lastly, the LSA, which courses in a retro-oesophageal position and gives rise to the ligamentum arteriosum from its base, completing the ring as it attaches to the pulmonary artery. Right aortic arch with mirror-image branching and retrooesophageal ligamentum arteriosum.

In these cases, only partial resorption of the distal left fourth arch occurs.

The first vessel originating from the right arch is a left innominate artery, which, in turn, branches into the left carotid and an LSA.

These course anteriorly to the trachea.

The right carotid artery and a right subclavian artery subsequently arise.

The ligamentum arteriosum is the final structure arising from the arch in this sequence.

It originates from the Kommerell diverticulum, which represents the nonresorbed remnant of the left fourth arch and is situated at the point of merging of the right arch and the proximal descending thoracic aorta. The ligamentum passes to the left, posterior to the oesophagus and then anteriorly to join the left pulmonary artery, thereby completing the ring.

Vascular Rings Associated With Left Aortic Arch

Two extremely rare complete rings occur in the presence of a left aortic arch, and both are associated with a right-sided descending thoracic aorta:

• Left aortic arch with right descending aorta and right ligamentum arteriosum.

• Left aortic arch, right descending aorta and atretic right aortic arch.

Aortic Arch Abnormalities

Without an Anatomical Ring there are also abnormalities of the aortic arch that produce compression symptoms without an anatomical ring.

Anomalous innominate artery

The innominate artery originates from a more distal and leftward position of the arch than normal.

As it takes its course from left to right, it crosses the trachea anteriorly and in doing so compresses the trachea.

Retro-oesophageal right subclavian artery with an otherwise normal left arch

This is the most common supra-aortic vessel anomaly, occurring in approximately 0.5% of the population.

In these cases, the right subclavian artery does not arise from an innominate trunk with the right carotid artery but originates as the last brachiocephalic branch from the descending aorta and takes a retro-oesophageal route to its destination.

Imaging

CXR is the first and most commonly performed imaging investigation.

The identification of a right aortic arch on a chest radiograph in a child with airway difficulties, respiratory distress or dysphagia should alert the radiologist to the likelihood of a vascular ring.

With a double aortic arch, the arch location is often ill defined. Findings on CXR include compression of the trachea and hyperinflation and/or atelectasis of some of the lobes of either lung.

Many authorities still consider barium oesophagography to be an important study in patients with a suspected vascular ring, and it is diagnostic in most cases.

A double aortic arch produces bilateral and posterior compressions of the oesophagus, which remain constant regardless of peristalsis.

The right indentation is usually slightly higher than the left and the posterior one is usually rather wide and courses in a downward direction from right to left.

If the right subclavian artery takes a retro-oesophageal course, there is a classical oblique posterior defect.

Ultrasound has been increasingly used for the diagnosis of a vascular ring using the suprasternal window, but there are limitations.

Structures without a lumen, such as a ligamentum arteriosum or an atretic arch, are difficult to identify, even with colour-flow echocardiography.

Identification of compressed midline structures and their relationship to encircling vascular anomalies may be difficult to detect.

However, associated congenital cardiac defects can be examined.

CT, MRI and Digital Subtraction Angiography (DSA) are all suitable diagnostic tools because they reveal the positions of vascular, tracheobronchial and oesophageal structures, and their relationships to one another. MRA is an excellent substitute for DSA, but young patients may require sedation/general anaesthesia, which can be a problem in patients with airway compromise and respiratory problems.

A potentially useful MR application in adult patients is a T2 weighted free-breathing real-time cine acquisition during patient water sip swallowing to obtain dynamic imaging similar to the oesophagography and identify the compression.

CT provides even better visualisation of the tracheobronchial tree and oesophagus and their relationship with vascular structures; sometimes it may identify the calcified ligamentum arteriosum.

Coarctation of the Aorta

Aortic coarctation most commonly affects the aortic isthmus (95% of cases) and much more rarely the more distal thoracic and abdominal aorta, where it is part of a midaortic syndrome (see earlier).

Presentation is characterised by hypertension and, in infants, failure to thrive.

The femoral pulses are usually delayed and weakened compared with the carotid and arm pulses, and there is a characteristic murmur, although this can disappear in older patients if the site of coarctation becomes occluded.

Eighty per cent of patients are male. In females, coarctation is associated with Turner syndrome.

Patients can present in infancy or adulthood.

The infantile type of coarctation is usually proximal to the ductus arteriosus, and 50% are associated with other congenital heart defects such as bicuspid aortic valve, ventricular septal defect (VSD) or hypoplastic left heart syndrome. Cystic medial necrosis of the aorta may be also associated.

At birth the ductus arteriosus closes, resulting in reduced blood supply to the distal aorta.

The consequent increased strain on the heart leads to heart failure because no collateral pathways are required in utero. The adult type of coarctation is usually located just distal to the ductus arteriosus and the LSA, and therefore collaterals develop in utero.

Consequently, infants present with hypertension and failure to thrive, whereas adults present with hypertension and the classical signs of collateral vessels on the chest radiograph.

Chest X-Ray

Rib notching usually takes several years to develop.

It is caused by pressure erosion of the inferior aspects of the upper adjacent ribs by enlarged and tortuous intercostal arteries.

It is usually bilateral but asymmetric and most often spares the first two ribs where intercostal arteries arise from the costocervical trunk proximal to the usual site of coarctation and therefore do not form part of the collateral circulation.

The rib notches may be shallow or deep and usually have a corticated margin.

Unilateral absence of rib notching may also be seen according to other anomalies.

Other radiographic features include cardiomegaly, particularly in older adults, a prominent ascending aorta (especially with a bicuspid aortic valve) and various aortic knuckle abnormalities. There may be a '3' sign due to enlargement of the LSA arising proximally of the coarctation, the narrowed segment itself and subsequently a localised segment with poststenotic dilatation of the aorta.

Occasionally this poststenotic dilatation simulates the picture of a low aortic knuckle.

The whole area of the aortic knuckle may appear small and flat. On the lateral radiograph an enlarged internal mammary artery may be seen behind the sternum. These CXR signs may already suggest the diagnosis. Demonstration of the coarctation may be difficult by transthoracic ultrasound in adults and older children but in infants it can demonstrate the degree of stenosis and associated congenital cardiac defects.

Continuous-wave Doppler measurements of flow velocities above and below the coarctation (and a modified Bernoulli equation) can also predict the degree of stenosis.

Magnetic Resonance Imaging

MRI is the imaging technique of choice in both infantile and adult coarctation.

It has considerable advantages because it is noninvasive, gives both morphological and functional information and is also useful for post-treatment follow-up.

T1 weighted spin-echo sequences willshow the whole of the aorta, the major branches and the larger collaterals.

Cine phase-contrast imaging can be used to visualise the turbulence through the stenosis, whereas phase-contrast imaging allows the quantification of the pressure gradient across the coarctation and the collateral circulation as percentage increment of flow from isthmic to diaphragmatic aorta. Gadolinium-enhanced 3D MRA provides high anatomical detail.

Computed Tomography

CT can also provide exquisite images but should be used sparingly in children and young adults because of the radiation involved. CT's strongest role is the follow-up of aortic coarctation corrected by stentgraft placement, because stent metal artefacts, together with a small aortic lumen, hampers MR visualisation of complications like stentfracture or in-stent restenosis.

The prevalent role of CT versus MR is still controversial.

Advocates of MR argue that MRI eventually is able to recognise all major complications like aortic dissection and identify stenosis by functional indirect signs (pressure gradient), while CT's major limitation is related to the radiation dose in the usually young population.

Angiography, previously the imaging procedure of choice, is currently rarely required unless cardiac catheterization is necessary for the investigation of associated cardiac abnormalities or for interventional purposes.

The coarctation can usually be crossed from the femoral arterial route, although, if impossible, brachial artery catheterisation is necessary.

Asymmetry of the stenosis may require the acquisition of multiple views.

Management

If undetected or untreated, death from cardiac failure, aortic rupture, infective endocarditis and intracerebral haemorrhage from associated cerebral aneurysms is inevitable, with only 50% of patients surviving into their 30s.

Surgery used to be the most common treatment for significant coarctation and is still often required.

If the lesion is short and the aorta can be adequately mobilised, resection and end-to-end anastomosis may be possible; this will give the best long-term result.

If this is not possible, the usual procedure is repair by a subclavian patch.

This involves resecting the lesion, transecting the LSA before the origin of the vertebral artery, incising longitudinally and turning it down as a patch repair.

This repair will grow with the patient. Collateral supply to the LSA, which will be mainly by the vertebral artery, may cause neurological symptoms.

Synthetic graft material is not suitable for children because it does not stretch.

There is a mortality of 2.6% to 3.1%, a 5.4% incidence of aneurysm formation and 1% risk of paraplegia.

Percutaneous transluminal angioplasty (PTA) was first used in 1982 to treat a recoarctation in a critically ill patient who had undergone previous surgical repair.

PTA is currently considered a successful treatment option of postsurgical recoarctation, with early success rates of 90% and restenosis rates of 16% to 30%.

The aorta is carefully measured proximal to the coarctation site, and a balloon is chosen with a diameter that is 2 mm smaller than this aortic diameter.

In view of the high success rate and the low complication rate compared with surgery, PTA is currently the primary method of treatment in adults, adolescents and children beyond infancy.

Some authors state that inserting stents at the coarctation site after balloon dilatation gives better long-term results.

However, there is currently insufficient evidence for this.

Stents should be reserved for initial failure of PTA due to recoil.

They should not be used in infants other than as a short-term treatment in the critically ill who are not eligible for immediate surgery.

Stent grafts should be available at all times to treat the very rare but invariably fatal complication of aortic rupture at PTA.

Pseudocoarctation

An elongated aortic arch will bulge posteriorly above the point at which it is fixed by the ligament.

This can produce the appearance of a '3' sign similar to true coarctation on the PA chest radiograph.

There is usually no significant haemodynamic obstruction. MR or CT will demonstrate the true anatomy.

Aortic Atresia

Aortic atresia is associated with the hypoplastic left heart syndrome.

The ascending aorta is variable in size but is usually very small and not larger than one of the brachiocephalic arteries.

Blood flow from the heart to the aorta is through the pulmonary trunk and the persistent arterial duct, with the aortic arch filling in a retrograde direction.

The brachiocephalic branches arise normally from the arch, and the coronary arteries are supplied via the diminutive ascending aorta.

Survival depends on maintaining patency of the duct by giving prostaglandin E1.

The 'Norwood' operation converts the morphological right ventricle into the systemic ventricle, by anastomosing the pulmonary trunk to the ascending aorta.

The atrial septum is excised.

Blood flow to the pulmonary arteries is maintained through a modified Blalock–Taussig shunt.

An interrupted aortic arch is rare and thought to be the result of faulty development of the aortic arch system during the 5th to 7th week of fetal development. It is almost always associated with a large VSD.

It can be located distally to the LSA (type A, 30%–40%), distally to the left common carotid artery (type B, 53%) or distally to the innominate artery (type C, 4%). Patients with type B often have a chromosomal abnormality called the DiGeorge syndrome.

<u>Current Status of Imaging of</u> <u>the Gastrointestinal Tract</u>

PLAIN ABDOMINAL RADIOGRAPH AND INTERPRETATION

The plain abdominal radiograph (AXR) was for generations the principal investigation in the acute abdomen. In most situations, either US or CT has replaced AXR as first imaging investigation after clinical assessment of the patient by a senior physician.

There are still several clinical settings where the AXR is very useful, and these will be discussed together with advice on interpretation, which can be difficult.

For non-acute situations, the relatively small diagnostic yield from a plain radiograph does not justify the radiation dose that it entails.

There are exceptions, such as in the follow up of ingested foreign bodies, urinary tract calculi and in assessment of bowel transit times in constipation.

In the acute abdominal setting, plain radiography should only be considered in situations where it is likely to yield useful information, which will impact diagnosis or patient management.

Plain radiography remains useful in diagnosing perforation of a viscus and for assessing bowel dilatation.

Plain AXR is not helpful in diagnosing common inflammatory conditions of the abdomen such as acute appendicitis, diverticulitis, cholecystitis and pancreatitis.

For this reason, plain radiography should be avoided in these situations.

Clinical assessment, US, CT and, in selected settings, MRI should replace AXR for investigation of these inflammatory conditions.

For the acute abdomen, a supine AXR and an erect chest radiograph (CXR) can be regarded as the basic standard radiographs.

The erect CXR is invaluable in diagnosing visceral perforation.

For this investigation, the patient should ideally remain in the erect position for 10 minutes before radiography to allow time for any free gas to rise to the highest point, although this may not be feasible in busy clinical practice.

The AXR should ideally be taken with an empty bladder and should include the area from the diaphragm to the hernial orifices, which, in practice, means that the obturator foramina should be included.

Other projections including the erect AXR, historically done to assess the number and length of air-fluid levels within the small or large bowel, have fallen out of favour because evidence shows that they can be misleading and unreliable for this. Occasionally, a left lateral decubitus radiograph may be performed, specifically to detect small amounts of intraperitoneal free air, which will be described later in this

ABNORMAL GAS DISTRIBUTION

Pneumoperitoneum

When reviewing a plain AXR, it is important to be able to attribute all the gas to normal anatomical structures, namely viscera.

There are numerous causes for gas in abnormal places; the most frequent is pneumoperitoneum but other causes include gas in the retroperitoneum, gall bladder, biliary tree, liver, kidneys, urinary bladder and within abscesses.

The presence of free intra-abdominal gas almost always indicates perforation of a viscus: for instance a perforated peptic ulcer.

Other causes of perforation include obstruction, inflammatory conditions, bowel ischaemia and injury during colonoscopy.

Approximately 70% of perforated peptic ulcers will demonstrate free gas, a phenomenon rarely seen in the case of perforated appendicitis.

Small amounts of gas are detectable under the right hemidiaphragm on an erect CXR, outlining the smooth surface of the liver clearly, but on the left it can be difficult to distinguish free gas from stomach and colonic gas. The diaphragm is seen as a relatively thin structure outlined by free gas below and lung above.

The free gas under the right and left hemidiaphragms may join across the midline (cupola sign).

There are many circumstances when interpretation of an erect CXR is difficult.

A lateral decubitus radiograph can resolve the problem by demonstrating gas between the liver and the abdominal wall, but nowadays CT is usually requested when there is doubt.

As interpretation of the plain AXR can be unreliable, it is important to consider clinical findings during interpretation of the plain AXR.

It is also important to be able to recognise the signs of pneumoperitoneum on supine AXRs: for example, in patients being monitored for colitis.

In many patients, particularly those who are unconscious, have suffered trauma, are old or critically ill or taking steroids, perforation may be clinically silent as it is overshadowed by other serious medical or surgical problems.

In approximately half of patients with pneumoperitoneum, gas may be detectable on the supine radiograph with free air in the right upper quadrant adjacent to the liver, lying mainly in the subhepatic space and the hepatorenal fossa (Morrison's pouch).

Visualisation of both sides of the bowel wall (outer and inner) is known as Rigler's sign, which can be difficult to appreciate if several loops of bowel lie close together. Pneumoperitoneum may also be detected on AXR, when the falciform or medial umbilical ligaments are outlined by free gas lying on either side or when air is seen in the fissure for the ligamentum teres.

Small volumes of free gas can be seen over the liver and anteriorly in the central abdomen or in the peritoneal recesses.

To not miss small amounts of free gas, the images should be reviewed on broad window settings (e.g. lung windows).

There are a number of causes of pneumoperitoneum without peritonitis, which are listed in.

Gas in Bowel Wall

If linear gas streaks are seen in the bowel wall, intestinal infarction should be suspected.

Intestinal infarction is a grave condition caused by thrombosis or embolism of the mesenteric vessels such as the superior mesenteric artery.

Other radiological signs are non-specific, consisting of slightly dilated loops of small bowel that may be gas filled, or poorly seen when mainly fluid filled. The walls of the small-bowel loops may be thickened due to submucosal haemorrhage and oedema.

Pneumoperitoneum may be present if perforation has occurred.

Intraluminal gas in the mesenteric veins or portal vein may be seen in advanced cases.

These features can be readily demonstrated on CT.

Pneumatosis cystoides intestinalis is an uncommon condition consisting of benign cyst-like collections of gas in the walls of hollow viscera.

The aetiology is unknown, but there is an association with obstructive airways disease.

The left hemicolon is the most common site and the term 'pneumatosis coli' is used to describe it.

Most patients are past middle age; symptoms include vague abdominal pain, diarrhoea, constipation and mucus discharge.

The cysts vary in size from 1 to 3 cm and lie both in the subserosa and submucosa.

Intermittently and subclinically, these cysts rupture, producing a pneumoperitoneum without evidence of peritonitis.

It is important to recognise pneumatosis as the cause of the pneumoperitoneum in such cases so as to avoid an unnecessary laparotomy.

One should also be aware of circumstances where intramural gas may be incorrectly suspected (pseudopneumatosis)—such as air trapped between mucosal folds or between bowel wall and luminal content—to prevent unnecessary intervention.

As with most findings in abdominal imaging, the finding of intramural air or portal venous gas must be correlated with the patient's condition, findings on clinical examination and on laboratory investigations (e.g. serum lactate, C-reactive protein levels or white cell count) before any major management decision is made.

Gas in Retroperitoneum

Gas can escape into the retroperitoneum and the causes of this include perforation of a posterior peptic ulcer, perforated sigmoid diverticular disease, colonoscopy and other iatrogenic causes.

The gas may be best visible in the flanks or around the kidneys.

Retroperitoneal gas can track superiorly into the mediastinum and inferiorly into the buttock and thigh.

Gas in the soft tissues of the left thigh is a classical site for gas from a diverticular perforation.

Gas in Other Organs

Gas may also be identified in the biliary tract, portal veins, renal collecting systems (emphysematous pyelonephritis, pancreas (infected necrosis or abscess), gall bladder wall and urinary bladder.

DILATATION OF BOWEL

Dilatation of the bowel occurs in mechanical intestinal obstruction, paralytic ileus and air swallowing.

The radiological differentiation of these different causes depends mainly on the size and distribution of the loops of the bowel and clinical correlation is essential.

Gastric Dilatation

Gastric dilatation may be caused by many conditions.

Mechanical gastric obstruction may be benign, malignant or from extrinsic compression.

It often leads to a huge fluid-filled stomach that retains its gastriform shape with little or no bowel gas beyond.

This compares with the normal small gastric air bubble, usually just enough for the stomach to be identified on AXR.

Paralytic ileus (often referred to as acute gastric dilatation) occurs mostly in elderly people, usually associated with considerable fluid and electrolyte disturbance.

Gastric volvulus is relatively rare and may result from twisting of the organ around its longitudinal or mesenteric axis.

There is usually a collapsed small bowel and virtually no gas is seen beyond the stomach.

The stomach loses its gastriform shape and becomes spherical.

If oral contrast medium is given, there may be complete obstruction in the lower oesophagus, or if contrast medium does enter the stomach, it may not pass beyond the obstructed pylorus.

Distinction Between Small- and Large-Bowel Dilatation

When a radiograph shows dilated bowel, it is important to determine whether it is small or large bowel, or both.

Useful differentiating features include the size and distribution of the loops.

Dilated small-bowel loops are usually more numerous and arranged centrally in the abdomen.

The loops show a small radius of curvature and rarely exceed 5 cm in diameter.

The small-bowel folds (valvulae conniventes) form thin, frequent, complete bands across the bowel gas shadow, prominent in the jejunum but becoming less marked in the ileum.

The valvulae conniventes are much closer together than colonic haustra and become thinner when stretched.

If the small-bowel blood supply is compromised, however, and the bowel becomes oedematous or gangrenous, the valvulae conniventes may become thickened.

It may be difficult to distinguish the distal ileum from the sigmoid colon as both may be smooth in outline and occupy a similar position, low in the central abdomen.

Although haustra usually form thick incomplete bands across the colonic gas shadow, they sometimes form complete transverse bands depending on the orientation of the loop.

Haustra may be absent from the descending and sigmoid colon but can usually still be identified in other parts of the colon, even when it is massively distended.

Small-Bowel Dilatation

Small-bowel dilatation may be due to mechanical obstruction or paralytic ileus/pseudo-obstruction.

In paralytic ileus, characterised by lack of an obstructing lesion, small and large bowel may be dilated.

Peritonitis and a postoperative abdomen are common causes but other causes include small-bowel ischaemia, metabolic disturbances, renal failure, drugs such as morphine and general debility.

CT is valuable in identifying an abrupt calibre change—the transition point—proximal to which bowel is dilated and distal to which bowel is collapsed.

Such features indicate small-bowel obstruction (SBO).

Careful inspection of the transition point at CT usually aids with defining the aetiology of SBO.

The causes of SBO are myriad but can be largely divided into mural lesions (e.g. tumour, stricture due to Crohn's disease, irradiation), luminal (bezoar, gallstone, Ascaris lumbricoides bolus, intussusception) and extrinsic (adhesions, hernia, volvulus, abdominal malignancy).

In the developed world, the most common cause of SBO is adhesions from previous surgery, with SBO resulting from strangulated hernia occurring in less than 10% of cases in the developed world compared with 75% in the underdeveloped world.

Mechanical obstruction of the small bowel normally causes small-bowel dilatation, with an accumulation of both gas and fluid and a reduction in the calibre of the large and/or small bowel, beyond the site of obstruction. On the plain radiograph, it is important to look for a hernia, which may be identified as a gas-filled viscus below the level of the inguinal ligament.

Visualisation of a hernia does not always mean that it is the cause of the SBO.

Dilated loops of small bowel are readily identified if they are gas-filled on the supine radiograph.

The string of beads sign, caused by a line of gas bubbles trapped between the valvulae conniventes, is seen only when very dilated small bowel is almost completely fluid filled, and is virtually diagnostic of SBO.

In a proportion of patients with SBO, the plain radiograph appears normal or only equivocally abnormal, since the dilated loops are mainly fluid filled.

Completely fluid-filled loops are not easily identified on plain radiographs, but are readily seen on CT.
Overall, the plain AXR has a sensitivity of approximately 66% for SBO.

Where a gallstone is the cause of obstruction, this is known as gallstone 'ileus' (technically an obstruction, not an ileus).

The gallstone passes into the duodenum by eroding the inflamed gall bladder wall, thereby bypassing the common bile duct.

This condition is well known to clinicians but relatively rare, accounting for approximately 2% of patients presenting with SBO.

The diagnosis is frequently delayed or missed even though the characteristic radiological features of gallstone ileus are present in 38% of cases.

Over half the patients will have plain radiographical evidence of intestinal obstruction and about one-third will have gas present in the biliary tree.

Gas in the biliary tree (pneumobilia) can be recognised by its branching pattern, with gas being more prominent centrally.

Gas in the portal vein, from which it must be distinguished, tends to be peripherally located in small veins around the edge of the liver.

The obstructing gallstone, which is frequently located in the pelvic loops of ileum, can be identified in approximately one-third of patients on plain AXRs.

Pneumobilia is more commonly caused by previous sphincterotomy or biliary surgery and may also be seen with perforation of a peptic ulcer into the common bile duct and a malignant fistula.

Pneumobilia is also seen in the elderly due to a lax sphincter of Odi, often due to the previous asymptomatic passage of a gallstone.

CT has a much higher sensitivity for pneumobilia of 95%–100%.

In gallstone ileus, obstructing gallstones tend to be 2–3 cm in size and are frequently found in the terminal ileum; they may be difficult to differentiate from bowel content as less than 15% are calcified.

Intussusception in adults nearly always develops as a result of a neoplasm of the bowel. Neoplasms arising in the submucosa such as lipoma, lymphoma and melanoma metastases may act as lead points for intussusception.

An intussusception may show on a plain radiograph as a softtissue mass, possibly part-outlined by gas (Fig. 18.15). If the intussusception is orientated end-on, a target sign may be seen comprising two concentric circles of fat density alternating with soft-tissue density.

In adults, intussusception when seen on CT (sometimes with the help of multiplanar 3D reconstruction) may show the characteristic feature of the intussusceptum bringing mesenteric fat into the lumen of the intussuscipiens. An underlying cause for the intussusception may also be apparent.

Intussusception is occasionally diagnosed on CT during investigation of abdominal pain, where the diagnosis has not been suspected.

US can detect fluid-filled loops of small bowel but is not usually definitive in diagnosing the cause of the obstruction; therefore, it is not usually recommended.

If complete SBO has been diagnosed and the patient is to undergo surgery, further radiological examination is not strictly necessary, although most surgeons now find a preoperative diagnosis by CT very useful.

If there is clinical doubt, partial obstruction or when conservative management is planned, CT has a valuable role.

CT will demonstrate dilated small-bowel loops, whether fluid or gas filled, and will add further information regarding the site and level of obstruction, and frequently the cause.

Importantly, CT can add information on strangulation of a small bowel loop, a sign that surgery is urgently required. The mortality of SBO with strangulation rises from 5%–8% to 20%–37% in comparison to SBO without strangulation, and mortality rises with treatment delay.

CT signs of a closed loop include small-bowel dilatation, Vshaped or radial fluid-filled loops, mesenteric vessels converging towards the point of obstruction and a triangular loop with or without a whirl or beak. Where there is strangulation, the bowel wall becomes thickened and may be of high attenuation due to haemorrhage. Gas may be seen within the bowel wall and mesentery and there may be congestion of the mesentery attached to the loop.

There may be free peritoneal fluid whether strangulation is present or not.

Where there is malignancy, additional staging information is gained by CT with the detection of lymphadenopathy, peritoneal deposits and other metastatic lesions.

Adhesions are not visualised with certainty by any imaging technique, and are usually diagnosed on the basis of clinical history and exclusion.

However, CT may demonstrate angulated and tethered loops, which suggest the presence of adhesions.

CT and MR enterography or enterocolysis represent more recent techniques used to evaluate the small bowel, and are more sensitive than conventional CT in detecting intraluminal lesions such as polyps, neuroendocrine lesions such as carcinoid tumours or metastatic lesions to the mucosa or submucosa.

Large-Bowel Dilatation

There are numerous causes of large-bowel dilatation without obstruction, including paralytic ileus and pseudo-obstruction.

Pseudo-Obstruction

Pseudo-obstruction usually occurs in elderly patients. It mimics intestinal obstruction clinically and on AXR. The plain radiographical appearances can be dramatic, showing a very dilated colon together with small-bowel distension.

CT or colonoscopy is usually required to exclude mechanical obstruction and to prevent unnecessary laparotomy.

The caecum may exceed the critical diameter of 9 cm, when perforation is imminent, and surgeons should be alerted to this possibility.

Large-Bowel Obstruction

Large-bowel obstruction is much less common than SBO. In the USA and Great Britain, carcinoma of the colon is the commonest cause of large-bowel obstruction, with approximately 60% of such carcinomas being situated in the sigmoid colon.

Diverticulitis is the second most common cause of obstruction.

In the USA, volvulus accounts for only 10% of cases of colonic obstruction, whereas for underdeveloped countries a figure of 85% is quoted.

Adhesive obstruction of the large bowel is very unusual and obstruction is much more common on the left side of the colon than the right.

The plain radiographic findings depend on the site of obstruction and whether the iliocaecal valve is competent.

In a minority of patients, the iliocaecal valve remains competent and despite increasing intracolonic pressure and marked distension of the caecum, the small bowel is not distended; however, in most cases even with a closed iliocaecal valve, the small bowel is distended.

In patients with an incompetent ileocaecal valve, the caecum and ascending colon are not unduly distended, but there is marked small-bowel distension.

The obstructed colon almost invariably contains large amounts of air and can usually be identified by its haustral margin around the periphery of the abdomen.

With distal large obstruction, when both small- and large-bowel dilatation is present, the radiographical appearances may be difficult to distinguish from paralytic ileus.

The plain radiographical appearances of large-bowel obstruction may be indistinguishable from pseudo-obstruction and any patient with suspected large-bowel obstruction therefore requires additional imaging to confirm the diagnosis.

CT has replaced contrast enema in this setting.

There are some large-bowel obstruction syndromes leading to more specific radiological appearances on a plain radiograph.

Sigmoid volvulus

Is the classical volvulus, occurring most frequently in old age or in patients with mental handicap or institutionalisation. The usual mechanism is twisting of the sigmoid loop around its mesenteric axis.

Although the classical radiographical findings may be present, in up to one-third of cases it is difficult to differentiate a twisted sigmoid from a distended but non-rotated sigmoid, or from more proximal colonic distension.

When sigmoid volvulus occurs, the inverted U-shaped loop of sigmoid is usually extremely distended and is commonly devoid of haustra, an important diagnostic point.

The anhaustral margin can often be identified overlapping, respectively, the lower border of the liver shadow (the liver overlap sign), the haustrated, dilated descending colon (the left flank overlap sign) and the left side of the bony pelvis (the pelvic overlap sign).

The top of the sigmoid volvulus usually lies very high in the abdomen with its apex on the left side.

As originally described on contrast enema, and now seen on CT, a smooth, curved tapering of the colon is observed at the torsion point, like a hooked beak (the bird of prey sign); a whirl sign is seen with twisting of the mesentery and mesenteric vessels.

Caecal volvulus

Can only occur when the caecum and ascending colon are mobile on a mesentery.

In comparison with sigmoid volvulus, it usually occurs in those aged 30–60 years.

In about half the patients, the caecum twists and inverts so that the pole of the caecum and the appendix occupy the left upper quadrant.

In other patients, the twist occurs in an axial plane without inversion and the caecum still occupies the right half of the abdomen.

The distended caecum can frequently be identified as a large viscus, which may be situated almost anywhere in the abdomen.

The attached gas-filled appendix may be seen.

There is often marked gaseous or fluid distension of the small bowel, which may sometimes obscure the caecal volvulus itself.

The left side of the colon is usually collapsed.

Distinction between caecal and sigmoid volvulus on CT may be difficult and careful scrutiny of the large bowel is essential to determine the type of volvulus.

Location of the obstructed loop and the 'swirl sign', if present, as well as location of anatomical appendages can certainly provide valuable clues.

The 'swirl' with caecal volvulus is usually located in the right lower quadrant, whereas the 'swirl' of sigmoid volvulus is typically located at the pelvic brim.

ABNORMAL BOWEL WALL PATTERN

The gas within the bowel profiles the mucosa, allowing appreciation of the mucosal surface on AXR.

Adjacent bowel loops and peritoneal fat can delineate the outer extent of the bowel wall and the wall thickness can, therefore, be judged.

Small-Bowel Ischaemia

Please see the above section Gas in Bowel Wall. The smallbowel wall becomes thickened if there is acute ischaemia, as a result of haemorrhage and oedema.

Thickened bowel wall outlined by gas and adjacent fat may be evident on plain radiographs, but CT is far more sensitive; furthermore, small amounts of gas in the bowel wall are better demonstrated using CT.

Large-Bowel Ischaemia

Ischaemic colitis is characterised clinically by the sudden onset of abdominal pain, followed by bloody diarrhoea.

The splenic flexure and proximal descending colon are most often involved, and an explanation for development of ischaemia in this distribution is that this section of colon is located at a 'watershed' between arterial supply from the superior and inferior mesenteric arteries. The wall, particularly the submucosa of the colon, is thickened as a result of haemorrhage and oedema.

This can sometimes be detected on plain radiographs, but in most cases CT is necessary.

The term 'thumbprinting' has been used to describe the plain radiographical appearance of the submucosal thickening.

The involved area of the colon acts as a functional obstruction so that the right side of the colon is frequently distended.

In the long term, the affected area could fibrose with development of a stricture.

Inflammatory Bowel Disease

The plain AXR can usually predict the extent of colonic involvement in acute inflammatory disease of the colon.

An assessment of the extent of colitis, the state of the mucosa and the presence or absence of toxic megacolon and/or perforation can be made.

The extent of faecal residue is related to the extent of the colitis.

The disease is likely to be inactive where there are formed faeces, while a complete absence of faecal residue suggests extensive colitis.

Intraluminal gas tends to accumulate as the colitis becomes more severe.

Severe mucosal changes can be missed, however, if there is no intracolonic air to delineate the mucosal outline.

When the bowel becomes dilated and the haustra disappear, the ulceration has penetrated the muscle layer and the patient moves into a high-risk group where urgent surgery must be considered.

This is known as toxic megacolon.

To identify the development of this situation, daily AXR may be justified in order to monitor progress.

Pseudomembranous Colitis

Pseudomembranous colitis may follow the administration of antibiotics, particularly clindamycin, lincomycin or antibiotics with similar pharmacological characteristics.

Clostridium difficile is frequently cultured in the stools.

AXR is abnormal in approximately one-third of cases: colonic dilatation (32%), thumbprinting, thickened haustra and abnormal mucosa (18%) may be identified. The whole colon may be involved, but the transverse colon is the most frequently affected segment.

The rectum is involved in most cases.

Appearances may mimic acute inflammatory bowel disease, and other forms of infectious colitis, with or without immunosuppression, can look similar.

CT is non-specific in the diagnosis of pseudomembranous colitis, and has been shown to be normal in 39% of cases, but CT can demonstrate markedly thickened mucosa, with oedema seen in the submucosa, and sometimes nodular mucosal thickening and the characteristic accordion sign.

There may also be mild pericolonic inflammatory change in the fat.

Peritoneal free fluid (ascites) may be seen in up to 40% of cases.

ACUTE ABDOMINAL

INFLAMMATORY CONDITIONS

The AXR still has a role in the acute abdomen in the scenarios described above but it offers very little information in the differential diagnosis of many causes of acute abdominal pain.

Patients with suspected appendicitis, diverticulitis and cholecystitis should not undergo plain radiography, since diagnostic signs are usually lacking and spurious findings may be misinterpreted.

Acute appendicitis is the commonest acute surgical condition in the developed world and carries an overall mortality rate of approximately 1%. Diagnosis is frequently difficult by clinical examination as there is a long list of alternative diagnoses that may mimic acute appendicitis.

Clinical diagnosis alone results in a normal appendix being found at appendicectomy in 10%-15%, and in young women the negative appendicectomy rate is higher still.

Many argue that this rate of preventable operative intervention is unacceptable and that this should lead to greater utilisation of US and CT.

Plain radiographs of the abdomen are not indicated for suspected appendicitis.

There are no specific plain radiographical signs of acute appendicitis but ileus can occur, and there may be obstruction as loops of small bowel become matted together or stuck to the inflamed appendix.

There is a high positive correlation between the presence of an appendiceal faecolith and acute appendicitis.

Ultrasound in Appendicitis

Graded compression US is a well-established technique for examining the appendix and is particularly well suited for children and thin patients.

The US probe is applied with gradually increased pressure over the right iliac fossa to displace bowel loops and examine the appendix. US signs of acute appendicitis include visualisation of a blindending tubular structure, which is non-compressible, with a diameter of 7 mm or greater.

An appendicolith may be seen as a hyperechoic focus casting an acoustic shadow and the surrounding inflammatory mass, which consists mainly of fat, is hyperechoeic.

An abscess or fluid around the appendix may be seen.

US of acute appendicitis has been reported to have a sensitivity of 78%–98% and specificity of 85%–98%.

There are interpretative pitfalls: false-negative results can arise in focal appendicitis of the appendiceal tip, retrocaecal appendicitis, gangrenous or perforated appendicitis, a gas-filled appendix and a massively enlarged appendix, which is very unusual in the inflamed appendix.

Pitfalls leading to a false-positive examination include a dilated fallopian tube, peri-appendicitis, inflammatory bowel disease and inspissated stool mimicking an appendicolith.

When the appendix has perforated it may be compressible at US.

This phenomenon has been reported in 38% of paediatric perforations and 55% of adult perforations.

The main drawback of US is that in most instances, and in most hands, a normal appendix is not visualised and, subsequently, a negative US result, where the appendix is not seen, is of little value. In a multicenter German study of 2280 patients with acute abdominal pain, US did not result in proven clinical benefit.

Similar results have been reported elsewhere.

US is more useful in patients considered clinically indeterminate for acute appendicitis rather than when the diagnosis is considered very likely or very unlikely.

Nevertheless, US can diagnose a number of conditions that mimic appendicitis clinically.

When an experienced radiologist is available, US is recommended in children where there is diagnostic doubt, in young women (due to the higher incidence of tubal disease) and in those patients who are pregnant.

Computed Tomography in Appendicitis

A number of large prospective trials have demonstrated that CT is a highly accurate investigation for confirming or excluding appendicitis.

CT signs of appendicitis include an appendix measuring greater than 6 mm in diameter, presence of appendicolith and enhancement of the wall of the appendix following intravenous contrast medium.

Surrounding inflammatory changes include increased fat attenuation, fluid, phlegmon, caecal thickening, abscess and extraluminal gas. Focal caecal thickening due to oedema at the origin of the appendix is referred to as a caecal bar. CT techniques for diagnosing appendicitis vary at different centres.

A focused technique examining the abdominopelvic junction exposes the patient to approximately one-third of the radiation dose of a full abdomen and pelvic examination (~3 vs 10 mSv).

However, this technique may not reveal other relevant diagnoses.

Although authors debate the figures, a normal appendix is seen more frequently at CT than US and thus CT carries a better true negative rate.

Much may depend on body habitus; US is well suited to thin patients and, especially, children.

Proponents of CT in acute appendicitis have reported sensitivities and specificities of 100% and 95%, respectively, while establishing an alternative diagnosis in 89%.

Several studies have reported overall accuracy of 93%–98%.

Excellent results such as these come from radiologists with expertise in CT of the acute abdomen, often examining patients where the diagnosis of acute appendicitis is deemed highly likely on clinical assessment.

It does not follow that CT will perform as well in the hands of general radiologists with less experience in abdominal imaging, especially when investigating patients where the differential diagnosis is still broad. The high radiation dose from abdominal CT should always be considered.

When performing CT in this setting, it must be remembered that performance of CT at some centres may result in delayed treatment of appendicitis, with potential impact on clinical outcome.

Imaging should not be a substitute for good clinical assessment.

Several studies have shown the negative appendicectomy rate to fall from over 20% to less than 9% with the liberal use of imaging.

In many institutions in the USA, CT is performed on almost all patients with acute right iliac fossa pain. Other studies have found that liberal use of CT and US does not reduce the negative appendicectomy rate.

A key strength of CT is its ability to make alternative diagnoses in right iliac fossa pain including mesenteric adenitis, terminal ileitis, Meckel's diverticulitis, typhlitis, epiploic appendagitis and omental infarction.

The use of CT versus US in the setting of suspected acute appendicitis is influenced by local expertise with US, availability of CT, and patient factors such as age and sex.

More recently, several studies have addressed the efficiency of low-dose CT and MRI in the assessment of suspected acute appendicitis, which is discussed later.

Other Inflammatory Conditions

CT is the accepted first investigation for suspected acute diverticulitis, due to its ability to assess extracolonic complications: namely, inflammation, abscess, perforation and fistula formation and the degree of bowel obstruction, if present.

CT also has the best chance of identifying alternative diagnoses in the clinical setting of left iliac fossa pain.

Ultrasound remains the investigation of choice in suspected acute cholecystitis because of its superior ability to detect gallstones and to assess sonographically for tenderness over the gallbladder (sonographic Murphy's sign).

IMAGING THE ABDOMEN WITH COMPUTED TOMOGRAPHY: RADIATION ISSUES

When imaging acute abdominal conditions, the choice of imaging investigation and technique is guided firstly by the clinical question at hand, secondly by accessibility to imaging equipment and economic issues and thirdly by the local expertise of the radiographer and radiologist who acquire and interpret the study.

The use of CT has increased exponentially in recent years; however, clinicians and their patients are becoming increasingly conscious of the exposure to ionising radiation associated with CT. This concern results partially from recent coverage in the scientific literature and media, which highlights the potential for increased cancer risk to patients as a result of increasing use of CT.

Carcinogenesis is the primary concern and it is a proven stochastic effect of exposure to ionising radiation. A stochastic effect occurs randomly and no lower threshold of ionising radiation exposure exists where cancer induction does not occur.

Carcinogenesis usually occurs many years remote from the exposure and is, therefore, of particular concern in patients who are young and in those with chronic disease who are subjected to repeated CT examinations over the course of their illness.

Young cohorts at particular risk for high cumulative effective dose include those with curable malignancies such as testicular cancer and Hodgkin's lymphoma, those with inflammatory bowel disease, particularly Crohn's disease, cystic fibrosis patients and patients who repeatedly present with renal colic.

Currently, there is a considerable research and industry drive to reduce radiation exposure during CT while preserving image quality and diagnostic yield.

One of the first technological steps towards CT dose reduction was to reduce inefficiencies of radiation delivery.

Fixedtube kilovoltage and amperage settings were commonly used in oldergeneration CT systems.

Using these fixed-tube settings for CT of the abdomen and pelvis resulted in wider areas such as the mid-abdomen receiving the same exposure as narrower regions such as the pelvis, frequently with no improvement in image quality. This inefficient method of dose delivery was the target of one of the most successful and now widely implemented dose-reduction technologies: namely, automatic exposure control or automatic tube current modulation (ATCM).

AUTOMATIC TUBE CURRENT MODULATION

Automatic tube current modulation tailors the output of the CT tube to the patient's size and shape based on the patient's diameter and the x-ray attenuation of the tissues through which the radiation beam is passing.

This automated process ensures that thicker regions of the body are imaged using higher tube currents than thinner, less attenuating areas.

Initial trials examining the utility of ATCM found that image quality could be preserved while radiation exposure was significantly reduced.

Early clinical trials demonstrated that dose reductions could be achieved in almost 90% of examinations and that the tube–current time product was reduced by an average of 32% while using ATCM.

Further reductions in CT dose, beyond the elimination of inefficiencies in dose delivery, are inherently associated with an increase in image noise.

Noise is defined as the statistical variation in attenuation values of CT images, which does not reflect anatomy and blurs image contrast.

Increased image noise is particularly problematic when imaging pathological changes with a low lesion–background contrast.

Accuracy in detecting small focal lesions of the liver, spleen and kidneys may be negatively influenced by even a slight increase in image noise, whereas when imaging the bowel or the renal tract (for potential urinary calculi), a higher amount of image noise is usually acceptable because of the higher lesion– background contrast.

In patient groups with Crohn's disease and with urinary calculi and also in patients with suspected appendicitis, clinical trials demonstrate preservation of diagnostic accuracy despite significant reductions in radiation dose and consequential increases in image noise.

Emerging CT noise-reduction strategies have provided new strategies for reducing CT dose while maintaining image quality.

These methods are already showing great promise in abdominopelvic CT and the widespread dissemination of technologies such as iterative reconstruction is likely to result in CT dose reductions on the order of 75% and greater in future years.

ITERATIVE RECONSTRUCTION ALGORITHMS

Iterative image reconstruction (IR) algorithms were used to generate images for the first commercial clinical CT systems but the limited processing abilities of computers in the early days of CT forced manufacturers to use a more computationally efficient method of IR known as filtered back projection (FBP).

The greater image noise associated with low-dose CT imaging is poorly handled by FBP alone and the use of IR has recently been revisited as a more appropriate method for low-dose imaging reconstruction.

Modern computers with improved computational capability and speeds have allowed iterative IR to enter the clinical domain and iterative IR techniques currently represent the most exciting dose-optimising developments in CT.

Multiple generations of IR are being developed and tested by CT manufacturers.

IR algorithms may operate on the image data or, preferably, on the raw projection data from the CT system itself.

Some IR algorithms operate on a combination of FBP and IR and are referred to as hybrid algorithms.

IR images were initially described as being 'waxy', 'plastic' or 'oversmoothened' in appearance in the case of early algorithms but later generations of IR have yielded more acceptable images, which are mildly 'mottled' or 'pixelated'. With time, radiologists have also become accustomed to images reconstructed with IR and are more accepting of these characteristics.

Expert opinion in this area suggests that imagers tend to adapt to the new quality of these images in a relatively short period of time.

Hybrid IR algorithms are typically noise efficient, computationally fast and studies have indicated that images have good low-contrast detail and preserved image quality even with radiation dose reductions of at least 30%.

Early investigations of the utility of IR systems from different manufacturers have shown that a diagnostically acceptable CT of the abdomen and pelvis can be acquired at approximately 50% less dose than was previously possible with FBP.

A recent prospective study investigating the diagnostic accuracy of low-dose CT, using hybrid IR, to detect active inflammation in Crohn's disease with doses comparable to plain AXR (~1.4 mSv), were as effective as conventional-dose CT in detecting clinically significant observations despite reduction in image quality.

In comparison to hybrid IR, pure iterative reconstruction algorithms result in diagnostically acceptable images de novo, which negates the requirement for blending with FBP data.

Pure or model based iterative reconstruction (MBIR) is now commercially available and models the physical characteristics of the focal spot, the x-ray fan beam, the three dimensional interaction of the x-ray beam within the patient and the twodimensional interaction of the x-ray beam within the detector. Pure IR is computationally demanding and despite the use of parallel processing technology, only three to four data sets can be reconstructed per hour, at present.

Several clinical trials suggest that both low-dose and, more recently, conventional-dose abdominal CT reconstructed with pure IR are superior to hybrid IR and also outperform FBP in both subjective image quality indices and objective image noise scores, facilitating dose reductions of approximately 80% in selected clinical settings.

In recent years, most CT manufacturers have incorporated IR into the latest generations of commercially available CT systems.

This raises an issue of widespread availability of this technology, as it is not feasible for all medical centres to replace their equipment with newer CT machines.

Also, the widespread availability of radiographers and radiologists trained in the optimal use of modern CT technology is challenging at many centres.

Current research is growing towards the development of 'vendor-independent' algorithms that may be applied to FBPreconstructed images obtained at lower doses to eliminate propagated image noise levels.

These are known as 'adaptive non-local means' (ANLM) algorithms and often require less computational time in comparison to de novo IR techniques.

Early clinical studies have validated this method and results are promising.

A study comparing ANLM to IR and, FBP suggests that image quality was not significantly compromised and, when applied with FBP, performance was as effective as IR techniques.

ROLE OF MRI IN THE ACUTE ABDOMEN

As previously discussed, current trends in CT imaging have led to increasing concern regarding patient radiation exposure, especially in patient subgroups with chronic illnesses who have the potential for high-lifetime cumulative exposures due to requirement for repeated CT imaging (e.g. Crohn's disease and cystic fibrosis patients).

Other groups for whom CT should be avoided include children and pregnant patients.

Avoidance of exposure to ionising radiation and the capability to produce excellent soft-tissue contrast in multiple imaging planes, without the absolute need for administration of intravenous contrast agents, make MRI an excellent alternative for an increasing number of indications.

MRI has been shown to supersede other investigations in certain abdominal: for example, complications and relapse of Crohn's disease (MR enterography), characterisation of solid visceral lesions (MRI liver and kidneys) and biliary abnormalities Magnetic resonance cholangiopancreatography (MRCP). Due to the aforementioned advantages, there is a growing demand for research for the potential expansion of the role of MRI in the acute abdomen.

A meta-analysis incorporating 30 studies of 2665 patients investigating the diagnostic performance of MRI for the evaluation of acute appendicitis in the general population, as well as paediatric and gravid subgroups, demonstrated high sensitivity and specificity (95%–97%) in comparison with CT.

However, replacement of CT with MRI has been limited in such cases due to its relatively high cost, longer acquisition times and limited access to MRI in comparison with CT.

Issues such as patient tolerance, claustrophobia and relative increased difficulty in performing MRI on critically ill patients also hinder its use.

Therefore, the current consensus by the American College of Radiology (ACR) ACR appropriateness criteria is that MRI utilisation in the acute setting should be reserved for selected patient groups as mentioned above and, in specific cases, usually as a second-line investigation or problem-solving tool following an inconclusive US or CT study.

A retrospective study of MRI used in the investigation of acute abdominal pain during pregnancy demonstrated an accuracy of almost 95% in identifying those who needed emergency intervention. Acute appendicitis is the commonest acute abdominal emergency encountered during pregnancy, with highest incidence in the second trimester.

Other relatively common indications for MRI in pregnancy include acute cholecystitis, choledocholithiasis and ureterolithiasis.

It also gives the advantage of excluding gynaecological disorders including ovarian torsion or pelvic abscess.

MRI has also been used in the evaluation of acute appendicitis, as well as Crohn's disease, in young patients presenting with acute pain.

For suspected appendicitis, graded compression US is usually the first-line imaging investigation and, when equivocal, an MRI of the pelvis is considered.

When choosing an MRI protocol for imaging of the acute abdomen, there is no fixed protocol or set of sequences. In many cases, MR protocols are tailored for the specific clinical question and to individual patients; in general, it is advised that a radiologist is on site to review studies and determine if further sequences are needed.

Several institutes have proposed the following basic sequences in assessment of acute abdominal pain: T2 weighted single shot fast spin echo with and without fat saturation (T2 SSFSE +/-FS) for detecting inflammatory change and oedema, T2 weighted fast spin echo +/- short inversion recovery (T2 FSE +/- STIR) for superior anatomical delineation and T1 weighted gradient echo including in and out-of-phase sequences. The use of IV contrast enhancement is also considered in special circumstances, particularly when abscess is suspected (diffusion weighted imaging (DWI) may also be useful).

Identifying the normal appendix on MRI may sometimes be difficult.

The paucity of intra-abdominal fat in children and the presence of a gravid uterus can pose additional challenges. Nonetheless, imaging features in acute appendicitis are quite similar to those in CT: that is, the demonstration of a dilated appendix (>6 mm) with thickened hypointense walls.

An appendicolith may be seen as a hypointense filling defect within the lumen.

T2 fat-saturated or STIR sequences usually demonstrate highsignal intensity within the appendix and the surrounding region, representing oedema and inflammatory change.

Fluid collections and abscesses may also be identified.

MRI findings in other acute and chronic abdominal conditions, including inflammatory bowel disease, choledocholithiasis and cholecystitis, are described in detail in their respective chapters.

MRI has many advantages, including equivalent diagnostic capability to CT in the diagnosis of acute appendicitis and/or alternative diagnoses in the acute setting.

Taking into account accessibility and other issues discussed earlier, MRI is currently not considered a first-line investigation for diagnosis of acute appendicitis but acts as a useful problem-solving tool in challenging or equivocal cases and in patients where exposure to ionising radiation should be avoided.

RADIATION DOSE REDUCTION IN CLINICAL PRACTICE

In practice, effective radiation dose reduction is best achieved by careful patient selection, rigorous justification of high-dose examinations and the application of suitable acquisition parameters particularly with CT.

The monitoring and audit of one's own practice is recommended and may serve to identify aberrant trends in patient management or imaging, which may result in an increase in patient cumulative effective dose.

It is important to involve CT radiographers in dose-reduction strategies to increase awareness and to prioritise dose reduction as part of routine practice. Variations in CT dose between, as well as within, individual institutions have been documented.

One study found a 32-fold variation in CT exposures among different centres, some even using the same CT machine.

Furthermore, the utilisation of alternative imaging techniques, which do not use ionising radiation, should be exploited when answers to clinical questions can be equally and effectively obtained.

Early recognition of patients that would require repeated imaging would often serve to guide future referrals and choice of examinations. For example, a recent study concluded that patients suffering from Crohn's disease who are receiving immunomodulating treatment or have had surgery for complications are prone to receiving greater cumulative radiation doses due to repeated CT imaging.

Patients such as these may, therefore, be considered 'at-risk' for high-lifetime, cumulative-effective doses and alternative imaging strategies should be prioritised.

Radiation dose management software is a new tool being developed in the era of 'big data'.

It allows continuous online monitoring of institutional radiation exposures from CT, nuclear medicine, plain radiography and fluoroscopy.

It also provides instant data regarding individual patient's recent and lifetime cumulative radiation exposures from diagnostic imaging studies and interventional radiology procedures.

In conclusion, radiation dose optimisation in abdominal imaging is a multidisciplinary process involving radiologists, radiographers, medical physicists and referring physicians.

This multidisciplinary focus on dose reduction will result in a systematic reduction in cancer risk.

Our responsibility is to first counsel patients accurately regarding the risks of ionising radiation exposure; second, to limit the use of those imaging investigations that involve ionising radiation to clinical situations where they are likely to change management; and third, to ensure that a diagnostic quality imaging examination is acquired with lowest possible radiation exposure when ever an imaging investigation that results in radiation exposure is deemed necessary.

The Oesophagus

ANATOMY AND FUNCTION

Anatomy

The oesophagus is a fibromuscular tube that connects the pharynx in the neck to the stomach in the abdomen, traversing the thorax via the superior and posterior mediastinum.

It begins below the cricopharyngeus muscle, at the lower edge of the cricoid cartilage and at the level of C6.

In the neck, the oesophagus lies posterior to the trachea. As it descends through the mediastinum, it passes posterior to the aortic arch, the left main bronchus and the left atrium, each of which causes an impression.

At the diaphragm the oesophagus passes through the diaphragmatic hiatus at T10, accompanied by the vagus nerves; it ends at the gastric cardia at the level of T11. The abdominal oesophagus lies posterior to the left lobe of the liver.

The oesophagus is therefore composed of a short cervical, a long thoracic and a short abdominal segment.

In health, the oesophagus is lined by stratified non-keratinising squamous epithelium. At the gastro-oesophageal junction (GOJ) there is an abrupt transition to columnar epithelium, termed the 'Z-line' because of the irregular interdigitations between pale pink squamous and darker columnar epithelia.

The GOJ is usually found at a surprisingly constant 40 mm from the teeth.

The wall of the oesophagus is made up of five layers: the mucosa, the muscularis mucosa, the submucosa, the muscularis propria and the adventitia.

Embryology

The stratified squamous epithelium of the oesophagus, together with its associated submucosal glands, is derived from the endoderm of the foregut.

The striated muscle of the upper oesophagus is derived from branchial arches 4 and 6, whereas the smooth muscle of the lower oesophagus is derived from somite mesenchyme.

The myenteric plexus is derived from neural crest cells.

Function

The oesophagus actively moves ingested material from the pharynx to the stomach and thus prevents reflux of stomach contents.

Passage of a food bolus is regulated by the upper and lower oesophageal sphincters.

The upper oesophageal sphincter is a high-pressure zone at the pharyngo-oesophageal junction and comprises the cricopharyngeus, the thyropharyngeus and the superior part of the cervical oesophagus.

The lower oesophageal sphincter is a 3-cm-high pressure zone at the GOJ and is composed of the lower oesophageal muscle fibres and the diaphragmatic hiatus.

The GOJ is anchored by the phreno-oesophageal ligament, which allows the oesophagus to slide a short distance longitudinally through the diaphragmatic hiatus while acting as a seal between the thoracic and abdominal cavities.

Unlike the upper and lower oesophageal sphincters, the oesophagus between these high-pressure zones is relaxed in the resting state.

The swallowing reflex induces so-called primary peristaltic (or stripping) waves that travel at 3 to 4 cm/s.

Secondary peristalsis occurs when oesophageal sensory receptors are activated by material persisting in the oesophagus after primary peristalsis.

Tertiary contractions are nonpropulsive and are seen in a variety of motility disorders.

EXAMINATION

The oesophagus can be examined with any of the commonly used imaging techniques.

The initial test of choice is usually endoscopy, with fluoroscopy reserved for frail patients or those who have had recent surgery.

Computed tomography (CT) is often the first-line test in the context of trauma.

Imaging is extensively used in the staging of oesophageal malignancy, particularly CT, positron-emission tomography–CT (PET-CT) and endoscopic ultrasound (EUS).

Plain Radiography

In most circumstances, plain radiographs reveal little useful information regarding the oesophagus except in the context of foreign body ingestion.

Foreign bodies tend to lodge at one of the following oesophageal constriction points:

- Cricopharyngeus
- Aortic arch
- Left main bronchus
- Diaphragmatic hiatus

Otherwise, a dilated, gas- or fluid-filled oesophagus B) may be identified incidentally during chest radiography for other indications.

Ultrasound

Most of the oesophagus is inaccessible to conventional ultrasound examination (but see 'Endoscopic Ultrasound', later).

The short cervical and abdominal segments are amenable to imaging in this way, but this is rarely used in clinical practice.

Fluoroscopy

Fluoroscopic examination of the oesophagus is performed for a wide variety of indications.

Barium suspensions are preferred for most indications; a preparation of 100% w/v is often used to provide good mucosal coating and an appropriate density.

If possible, double-contrast images should be obtained using an effervescent agent, usually with the patient in the erect position.

These are complementary to prone, single-contrast images.

Water-soluble contrast medium is used when a tear, perforation or anastomotic leak is suspected. Low osmolar agents such as iopamidol (Gastromiro) should always be used to prevent pulmonary oedema, which can occur following aspiration of high osmolar agents such as meglumine diatrizoate (Gastrografin).

In some institutions, when a leak is suspected, water-soluble contrast medium is followed with a barium suspension. Using barium in this way has been shown to be more sensitive for contained perforations, although it adds nothing in the detection of free leakage into the neck or mediastinum.

Fluoroscopic examination of the oesophagus is tailored to the indication, but a suggested technique is as follows: control images should be obtained if the patient has had oesophageal or gastric surgery.

With the patient in the erect position, double-contrast images are obtained in the lateral and posteroanterior (PA) projections of the cervical and upper oesophagus at four images per second.

Right anterior oblique images of the middle and lower oesophagus are obtained at two per second, also in double contrast.

The patient is then moved to the prone position and images are obtained at one per second during three separate single-bolus swallows to assess oesophageal motility and fully distend the GOJ.

This view is particularly important if wrap migration is suspected following fundoplication.

The images obtained in the prone position are usually single contrast.

Finally, a static image of the stomach to include the gastric fundus is obtained with the patient in the erect position.
The standard fluoroscopic examination may be augmented with additional procedures.

As an example, where a patient describes a clear history of dysphagia, but the images obtained appear normal, a swallow of biscuit dipped in barium or a barium tablet may uncover an occult stricture.

If there are pharyngeal symptoms, images of the pharynx obtained during phonation should be obtained.

Although no longer the first-line test for dysphagia, fluoroscopy remains an important test.

It is well suited to evaluate the oesophagus following trauma or surgery, in complex hiatal herniae and as a less invasive alternative to endoscopy in the frail patient.

Endoscopy

Oesophagogastroduodenoscopy (OGD/endoscopy) is the initial investigation of choice for most indications, particularly dysphagia.

It permits the direct visualisation of the mucosa and, crucially, biopsies can be taken.

In patients with high dysphagia, preliminary fluoroscopic assessment can be used to forewarn the endoscopist of a pharyngeal pouch, which if present, would potentially reduce the risk of perforation. An OGD is carried out with the patient in the left lateral position, under topical local anaesthesia or conscious sedation (usually with a benzodiazepine such as midazolam).

In addition to a detailed diagnostic assessment of the mucosa, a wide variety of therapeutic manoeuvres may be carried out endoscopically.

These include the treatment of upper gastrointestinal (GI) haemorrhage, balloon dilatation and/or stenting of strictures, radiofrequency ablation (RFA) of dysplastic epithelium and injection of botulinum toxin for motility disorders.

Endoscopic mucosal resection (EMR) deserves special note, as it is both therapeutic and the preferred method for staging early oesophageal tumours.

Computed Tomography

In the context of oesophageal disease, CT is most widely used in the staging of oesophageal cancer. A CT of the thorax, abdomen and pelvis should be acquired.

Good oesophageal and gastric distension is important: the patient should be given 1-1.5 L of water to drink as well as effervescent granules and should be imaged in the prone position.

Intravenous contrast medium should be used whenever possible, with the upper abdomen imaged in both the arterial and portal venous phases. For the investigation of patients with suspected oesophageal trauma (including Boerhaave syndrome) and in the postoperative setting, positive oral contrast medium is required.

As for fluoroscopic examinations, this should always be carried out with a low osmolar agent.

For suspected tracheo-oesophageal fistula, an initial acquisition without the use of oral contrast medium is usually diagnostic.

Magnetic Resonance Imaging

In current clinical practice, magnetic resonance imaging (MRI) is not used for imaging the oesophagus.

Image quality is hampered by motion artefacts from cardiac motion, breathing and peristalsis.

Whole-body MRI is under evaluation as an alternative to PET-CT for the staging of metastatic disease in oesophageal cancer but has not yet entered clinical practice.

Endoscopic Ultrasound

EUS is generally used to characterise abnormalities identified using other imaging techniques, in particular the staging of oesophageal cancer.

Less frequently, EUS is used for the assessment of submucosal lesions of the oesophagus.

The high frequency and close proximity of the ultrasound probe allow the delineation of five layers of the oesophageal

wall: mucosa, muscularis mucosa, submucosa, muscularis propria and adventitia.

The muscular layers are hypoechoic; hence, there is a fivelayered alternating pattern.

Endoscopic ultrasound/fine-needle aspiration (EUS-FNA) enables the sampling of structures deep to the oesophageal mucosa, particularly thoracic and upper abdominal lymph nodes.

This can be particularly useful in the staging of oesophageal and lung malignancy and in the diagnosis of tuberculosis.

In addition to sampling, EUS can be used to place fiducial markers to guide radiotherapy.

Radionuclide Radiology Including Positron-Emission Tomography–Computed Tomography.

For patients with oesophageal cancer, 18F-fluorodeoxyglucose (FDG) PET-CT is now the standard of care if radical treatment is intended.

The presence of FDG-avid lymph nodes on preoperative PET-CT is prognostically significant even within the group of patients with the same pathological stage.

The most important reason that PET-CT is used in oesophageal cancer staging is the high proportion of patients who have unsuspected metastatic disease at presentation and the superiority of PET-CT over other techniques for identifying it.

Technetium-based radionuclide imaging of the oesophagus can be used for the identification of oesophageal motility disorders and gastrooesophageal reflux disease (GORD).

Patients can be imaged swallowing both liquid and solid material (usually 99mTc-labelled sulphur colloid and scrambled egg, respectively) (Fig. 19.9).

PATHOLOGICAL FEATURES

Oesophageal Cancer

Oesophageal cancer is the sixth most common cause of death from cancer in the United Kingdom.

There are two major histological types: squamous cell carcinoma and adenocarcinoma.

Although the squamous type has been more common historically (and still is worldwide), in the United Kingdom, due to the rise in obesity, it has been overtaken by adenocarcinoma.

Accurate preoperative staging of oesophageal cancer is difficult.

The mobility of the oesophagus and its proximity to other organs make the assessment of local invasion problematic.

Malignant lymph nodes are usually not enlarged and may first arise some distance from the tumour.

Furthermore, unsuspected metastases may be present in up to 30% of patients at diagnosis. It is not surprising, then, that a variety of different tests are required for accurate staging.

The patient with oesophageal cancer can face a whirlwind of tests, including endoscopy, CT, EUS and PET-CT.

This combination is crucial for determining appropriate therapy.

Initial diagnosis is usually with endoscopy, as it permits histological confirmation with biopsy.

Despite this, a good-quality fluoroscopic examination can detect even early tumours.

If a stricture is identified using fluoroscopy and it appears unequivocally benign, with symmetrical, smooth narrowing and a gradual tapering to normal calibre, malignancy can be confidently excluded.

The converse is also true: strictures with an ulcerated, irregular mucosa and shouldered, shelf-like margins can be considered malignant on imaging appearances alone.

The vast majority of patients will go on to CT as their initial staging investigation. Although less sensitive than EUS and PET-CT, it is relatively specific for identifying locally advanced or metastatic disease.

Patients with these findings on CT are therefore spared further staging investigations.

In the case of early tumours that appear to be T1 endoscopically, EMR is the preferred initial staging technique.

The introduction of the 8th edition of the TNM (tumour–node– metastasis) classification has resulted in a single change to oesophageal cancer staging: type 3 junctional tumours are now considered gastric rather than oesophageal.

In other words, junctional tumours are classified as lower oesophageal tumours if their epicentre is within 2 cm of the junction and they extend to involve the oesophagus. Tumours with their epicentre more than 2 cm distal to the GOJ or cardial tumours that do not extend to involve the oesophagus regardless of site are classified as gastric tumours.

Computed Tomography for Oesophageal Cancer

The normal oesophagus when adequately distended should have a wall thickness of less than 5 mm on CT.

Tumours are seen as regions of wall thickening, which may be circumferential or asymmetric.

CT is rather limited in the local staging of oesophageal tumours because it is unable to delineate the layers of the oesophageal wall and is therefore useful only for distinguishing between T1–3 and T4 (invasion of other structures).

The sensitivity and specificity of CT for T4 disease in a study of 94 patients with oesophageal squamous cell carcinoma were 66% and 84%, respectively. Signs of T4 disease include tumour contact of more than 90 degrees with the aorta; loss of the triangle of fat between the oesophagus, aorta and spinal column; and nodular protrusion into the airways. For nodal staging of oesophageal cancer, CT is relatively insensitive, as the majority of involved nodes are not enlarged.

In a meta-analysis, the sensitivity and specificity for regional nodal disease were 50% and 83%, respectively.

In general, nodes with a short axis of greater than 1 cm are considered involved on CT.

Common sites of regional nodal disease include perioesophageal, subcarinal, left gastric and coeliac territories.

A key distinction for node groups is that between the perioesophageal cervical nodes, which are considered regional, and the supraclavicular lymph nodes, which are metastatic.

The anatomical landmark that distinguishes these sites is the vascular plane containing the common carotid artery.

The most frequent sites for oesophageal cancer metastases are nonregional lymph nodes such as the supraclavicular and retroperitoneal abdominal lymph nodes. As is the case with gastric cancer, the left supraclavicular node is more frequently involved than the right.

Visceral metastases are seen in the liver, the lungs, bones, muscles and the adrenal glands.

As for tumours arising elsewhere in the body, squamous cell carcinoma lung metastases are more likely to cavitate than is adenocarcinoma. In keeping with its performance for regional nodal involvement, CT is insensitive but relatively specific for metastatic disease.

Endoscopic Ultrasound for Oesophageal Cancer

EUS is superior to CT and PET-CT for T staging.

The sensitivity and specificity for identifying the various T stages of oesophageal cancer is high.

In some patients with advanced tumours, the stricture is too tight to permit passage of the standard radial echoendoscope.

An endobronchial ultrasound (EBUS) scope can be used in most of these cases if required. If the tumour is not traversable with the standard echoendoscope, the T stage is almost always T3 or T4. The number of abnormal lymph nodes seen on EUS correlates closely with patient survival.

For nodal disease, EUS has a sensitivity higher than that of PET-CT or CT, but it is less specific.

Although metastatic disease can be identified with EUS on occasion (for example, in the left adrenal gland or liver) it does not provide the whole-body coverage necessary and so is always used in conjunction with PET-CT.

Although previously a routine part of staging in some centres, the current National Institute for Health and Care Excellence (NICE) guidelines recommend against using EUS in this way and suggest that it should be reserved for cases where it will change management (for example, in patients with solitary FDG-avid lymph nodes outside the resection field).

Positron-Emission Tomography–Computed Tomography for Oesophageal Cancer

In T1 tumours of the oesophagus, it is usually not possible to identify the tumour with PET, which should therefore be omitted if this stage is suspected endoscopically.

If a tumour is not detectable by PET-CT, it will be T2 or less in 70% of cases.

PET-CT otherwise suffers the same limitations as CT in terms of depth of mural invasion; EUS is therefore the preferred technique for T staging.

Nodal disease can be assessed with reasonable sensitivity and specificity with PET-CT. The presence of FDG-avid lymph nodes is a negative prognostic marker and an indication for neoadjuvant therapy.

PET-CT is the technique of choice for identifying metastases to nonregional lymph nodes and other tissues such as the liver and skeletal muscle.

The ability of PET-CT to correctly upstage up to 20% of patients means that it should be used for all patients before radical treatment.

For single metastases, cytological or histological confirmation is recommended in view of the 4% false-positive rate with PET-CT.

Treatment of Oesophageal Cancer

Treatment for oesophageal cancer involves a broad range of interventions that are dependent on the stage and type of tumour as well as the fitness of the patient and local availability.

For the earliest oesophageal tumours (T1a) that do not invade the submucosa, EMR is the preferred technique for removal.

The EMR specimen is assessed histologically for deep invasion.

If present, further treatment would be considered, including oesophagectomy.

At the other end of the staging spectrum, patients with invasion of major structures (T4b) or metastatic disease are offered palliative treatment.

This includes a variety of manoeuvres for maintaining oesophageal patency, most commonly stenting.

Systemic treatment with palliative chemotherapy is used in patients with a good performance status. Radiotherapy has an important role, particularly for the more radiosensitive squamous cell carcinoma.

For patients with resectable disease, most will have nodal involvement or a tumour extending through the muscularis propria (T3 disease).

If a patient has disease staged clinically as cT2N0M0 or greater, the patient will likely benefit from neoadjuvant chemotherapy prior to surgery.

Radical chemoradiotherapy is an alternative treatment for squamous cell carcinoma.

A variety of surgical approaches are used.

The oesophagus is almost always substituted with a gastric conduit.

Both fluoroscopy and CT play an important role in the detection of postoperative complications.

If there is necrosis of the gastric conduit, a colonic interposition may be used, usually after an interval of several months, to allow the patient to recover before further surgery.

Other Oesophageal Neoplasms

Other than adenocarcinoma and squamous cell carcinoma, true neoplasms of the oesophagus are uncommon.

They can be categorised as benign or malignant and according to whether they are mucosal or submucosal.

Benign Lesions

Glycogenic acanthosis, though not a neoplasm, requires mention, as it is present in up to 30% of normal individuals.

It manifests as mural nodules, usually measuring 2 to 5 mm, which are more easily seen as white/yellow plaques on endoscopy.

These nodules/plaques are caused by the proliferation of glycogen-containing cells within the squamous epithelium.

Glycogenic acanthosis is of no clinical consequence, although it may be associated with GORD, coeliac disease and, rarely, Cowden syndrome.

The multiplicity of lesions is usually helpful in making the diagnosis at fluoroscopy.

Papillomata are uncommon benign tumours of the oesophagus and comprise hyperplastic squamous epithelium. A papilloma usually appears as a solitary sessile polyp and will rarely measure more than 10 mm.

In view of this non-specific appearance, biopsy is required to distinguish a papilloma from an early adenocarcinoma or squamous cell carcinoma.

The most common benign submucosal tumour of the oesophagus is the leiomyoma.

This is in contrast to the rest of the GI tract, where gastrointestinal stromal tumours (GISTs) predominate.

Endoscopically, and on fluoroscopic studies, a leiomyoma appears as a smooth submucosal mass.

On CT, a homogeneous well-defined soft tissue mass is the most common appearance, sometimes with a focus or two of punctate calcification.

These findings are rather non-specific, so EUS-FNA is needed to confirm the nature of the lesion.

Although not neoplastic, a congenital foregut duplication cyst may be identified as a submucosal mass on fluoroscopic or endoscopic examination of the oesophagus. Such cysts are very straightforward to characterise with MRI or EUS; both techniques will demonstrate a simple cyst.

Fibrovascular polyps are very rare pedunculated submucosal lesions that usually arise from the upper oesophagus.

As they tend to be rather

soft, they can reach a considerable size before causing dysphagia.

On CT they often have regions of both fat and soft tissue attenuation.

They are notable for their potentially unusual clinical presentation: regurgitation into the mouth, which can sometimes result in death by asphyxiation. Other submucosal lesions—such as schwannoma, neurofibromata and lipomata—are also rare.