Peripheral arterial disease

Peripheral arterial disease (PAD) has been estimated to affect about 20% of individuals aged 55–75 years in the UK. Only 25% of patients present with symptoms, the commonest of which is intermittent claudication (IC).

About 1%–2% of patients with IC per year progress to a point where amputation or revascularisation is required.

- However, the annual mortality rate of people with IC is about 5%, which is 2–3 times higher than the general population of the same age and sex. The cause of death is typically an MI or stroke, reflecting the fact that IC nearly always occurs in association with widespread atherosclerosis.

Pathogenesis

- In developed countries, almost all PAD is due to atherosclerosis and the risk factors are the same as described in patients with CAD. As the anatomical site, the presence or absence of a collateral supply, the speed of onset and the mechanism of injury

- Approximately 5%–10% of patients with PAD have diabetes but this proportion increases to 30%–40% in those with severe limb ischaemia. The mechanism of PAD in diabetes is atheroma affecting the medium to large-sized arteries rather than obstructive microangiopathy and so diabetes is not a contraindication to lower limb revascularisation. Nevertheless, patients with diabetes and PAD pose a number of particular problems

16.55 Factors influencing the clinical manifestations of peripheral arterial disease (PAD)

Anatomical site

Cerebral circulation
- TIA, amaurosis fugax, vertebrobasilar insufficiency

Renal arteries
- Hypertension and renal failure

Mesenteric arteries
- Mesenteric angina, acute intestinal ischaemia

Limbs (legs >> arms)
- Intermittent claudication, critical limb ischaemia, acute limb ischaemia

Collateral supply

- In a patient with a complete circle of Willis, occlusion of one carotid artery may be asymptomatic
- In a patient without cross-circulation, stroke is likely

Speed of onset

- Where PAD develops slowly, a collateral supply will develop
- Sudden occlusion of a previously normal artery is likely to cause severe distal ischaemia

Mechanism of injury

Haemodynamic
- Plaque must reduce arterial diameter by 70% ('critical stenosis') to reduce flow and pressure at rest. On exertion a moderate stenosis may become 'critical'. This mechanism tends to have a relatively benign course due to collateralisation

Thrombotic
- Occlusion of a long-standing critical stenosis may be asymptomatic due to collateralisation. However, acute rupture and thrombosis of a non-haemodynamically significant plaque usually has severe consequences

Atheroembolic
- Symptoms depend on embolic load and size
- Carotid (TIA, amaurosis fugax or stroke) and peripheral arterial (blue toe/finger syndrome) plaque are common examples

Thromboembolic
- Usually secondary to atrial fibrillation
- The consequences are usually dramatic, as the thrombus load is often large and occludes a major, previously healthy, non-collateralised artery suddenly and completely

(TIA = transient ischaemic attack)

Clinical features

Symptomatic PAD affects the legs about eight times more commonly than the arms. Several locations may be affected, including the aortoiliac vessels, the femoropopliteal vessels and the infrapopliteal vessels. One or more of these segments may be affected in a variable and asymmetric manner. In the arm, the subclavian artery is the most common site of disease. Peripheral artery disease can present clinically in a variety of ways.

Intermittent claudication

This is the most common presentation of PAD affecting the lower limbs.

- It is characterised by ischaemic pain affecting the muscles of the leg.
- The pain is usually felt in the calf because the disease most commonly affects the iliac arteries are involved. Typically, the pain comes on after walking, often once a specific distance has been covered, and rapidly subsides on resting

Resumption of walking leads to a return of the pain. Most patients describe a cyclical pattern of exacerbation and resolution due to the progression of disease and the subsequent development of collaterals. When PAD affects the upper limbs, arm claudication may occur, although this is uncommon.

Critical limb ischaemia

- Critical limb ischaemia (CLI) is defined as rest pain requiring opiate analgesia, or ulceration or gangrene that has been present for more than 2 weeks, in the presence of an ankle BP of less than 50mmHg

Rest pain only, with ankle pressures above 50mmHg, is known as subcritical limb ischaemia (SCLI). The term severe limb ischaemia (SLI) is used to describe the situation where either CLI and SCLI occurs. Whereas IC is usually due to single-segment plaque, SLI is always due to multilevel disease

- Many patients with SLI have not previously sought medical advice, principally because they have other comorbidity that prevents them from walking to a point where IC develops. Patients with SLI are at high risk of losing their limb, and sometimes their life, in a matter of weeks or months without surgical bypass or endovascular revascularisation by angioplasty or stenting.
- Treatment of these patients is difficult because most are older adults with extensive and severe disease and major multisystem comorbidities.

Acute limb ischaemia

- This is most frequently caused by acute thrombotic occlusion of a pre-existing stenotic arterial segment, thromboembolism and trauma that may be iatrogenic. The typical presentation is with paralysis (inability to wiggle toes or fingers) and paraesthesia (loss of light touch over the dorsum of the foot or hand); the so-called ‘Ps of acute ischaemia’ .
- These features are non-specific and inconsistently related to its severity.
- Pain on squeezing the calf indicates muscle infarction and impending irreversible ischaemia

- All patients with suspected acutely ischaemic limbs must be discussed immediately with a vascular surgeon; a few hours can make the difference between death/amputation and complete recovery of limb function. If there are no contraindications (acute aortic dissection or trauma, particularly head injury), an intravenous bolus of heparin (3000–5000IU) should be administered to limit propagation of thrombus and protect the collateral circulation.

- Distinguishing thrombosis from embolism is frequently difficult but is important because treatment and prognosis are different . Acute limb ischaemia due to thrombosis in situ can usually be treated medically in the first instance with intravenous heparin (target activated partial thromboplastin time (APTT) 2.0–3.0), antiplatelet agents, high-dose statins, intravenous fuids to avoid dehydration, correction of anaemia, oxygen and sometimes prostaglandins, such as iloprost. Embolism will normally result in extensive tissue necrosis within 6 hours unless the limb is revascularised.
- The indications for thrombolysis, if any, remaincontroversial. Irreversible ischaemia mandates early amputation or palliativcare.

Raynaud’s syndrome

This common disorder affects 5%–10% of young women aged 15–30 years in temperate climates. It does not progress to ulceration or infarction, and significant pain is unusual. The underlying cause is unclear and no investigation is necessary. The patient should be reassured and advised to avoid exposure to cold. Usually, no other treatment is required, although vasodilators such as nifedipine can may be helpful if symptoms are troublesome. More severe Raynaud’s syndrome can also occur in association with digital ulceration in patients with connective tissue disease

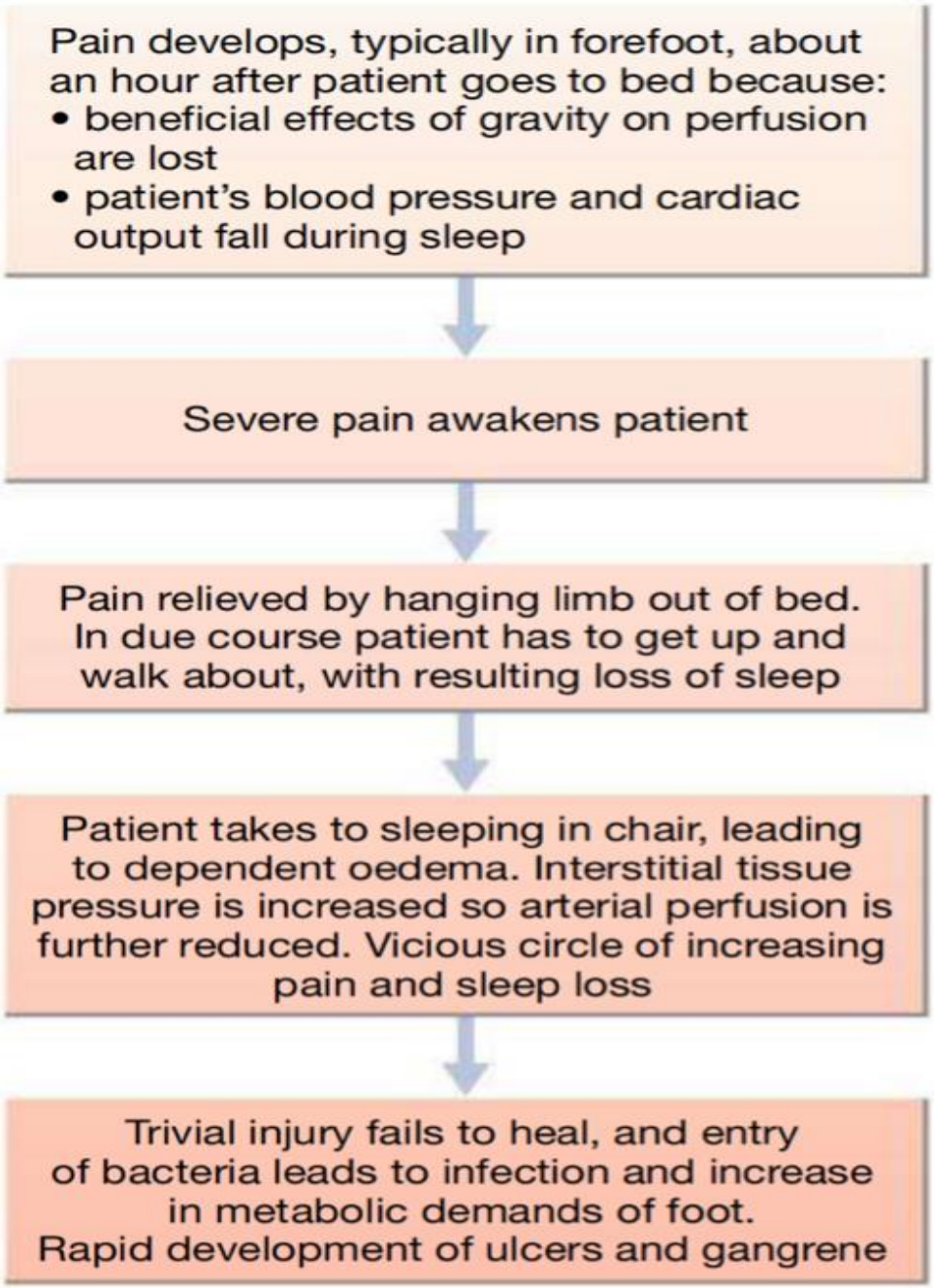

Fig. 16.70 Progressive night pain and the development of tissue loss.

16.57 Symptoms *and* signs of acute limb ischaemia

Symptoms/signs	Comment
Pain **Pallor** **Pulselessness**	May be absent in complete acute ischaemia, and can be present in chronic ischaemia
Perishing cold	Unreliable, as the ischaemic limb takes on the ambient temperature
Paraesthesia **Paralysis**	Important features of impending irreversible ischaemia

Atheroembolism

- This may be a presenting feature of PAD affecting the subclavian arteries. The presentation is with blue fingers, which are due to small emboli lodging in digital arteries. This may be confused with Raynaud's phenomenon but the symptoms of atheroembolism are typically unilateral rather than bilateral as in Raynaud's.

Subclavian steal

- This can be a feature of PAD affecting the upper limbs. The presentation is with dizziness, cortical blindness and/or collapse, which occurs when the arm is used and is thought to be caused by diversion (or steal) of blood from the brain to the limbs via the vertebral artery.

16.58 Distinguishing features of embolism and thrombosis in peripheral arteries

Clinical features	Embolism	Thrombosis
Severity	Complete (no collaterals)	Incomplete (collaterals)
Onset	Seconds or minutes	Hours or days
Limb	Leg 3:1 arm	Leg 10:1 arm
Multiple sites	Up to 15%	Rare
Embolic source	Present (usually atrial fibrillation)	Absent
Previous claudication	Absent	Present
Palpation of artery	Soft, tender	Hard, calcified
Bruits	Absent	Present
Contralateral leg pulses	Present	Absent
Diagnosis	Clinical	Angiography
Treatment	Embolectomy, warfarin	Medical, bypass, thrombolysis
Prognosis	Loss of life > loss of limb	Loss of limb > loss of life

Investigations

- The presence and severity of ischaemia can usually be determined by clinical examination and measurement of the ankle–brachial pressure index (ABPI), which is the ratio between the highest systolic ankle and brachial blood pressures. In health, the ABPI is over 1.0, in IC typically 0.5–0.9 and in CLI usually less than 0.5. Further investigation with duplex ultrasonography, MRI or CT with intravenous injection of contrast agents may be used to characterise the sites of involvement further. Intra-arterial digital subtraction angiography (IA-DSA) is used for those undergoing endovascular revascularisation. Other investigations should look for evidence of treatable secondary causes including a full blood count (for thrombocythaemia), lipids (for hyperlipidaemia) and blood glucose (for diabetes mellitus).

Management

- This consists of smoking cessation (if applicable), taking regular exercise, antiplatelet therapy with low-dose aspirin or clopidogrel, therapy with a statin, and treatment of coexisting disease such as diabetes, hypertension or polycythaemia. Recent evidence suggests that low-dose factor Xa inhibition (rivaroxaban 2.5 mg twice daily) when used in combination with aspirin can further reduce cardiovascular events, ischaemic limb events and mortality in patients with PAD although there is a modest increase in bleeding risk. The peripheral vasodilator cilostazol has been shown to improve walking distance and should be considered in patients

- Intervention with angioplasty, stenting, endarterectomy or bypass is usually considered only after medical therapy has been given for at least 6 months to effect symptomatic improvement, and then just in patients who are severely disabled or whose livelihood is threatened by their disability. Subclavian artery disease is usually treated by means of angioplasty and stenting, as carotid–subclavian bypass surgery can be technically difficult.

16.59 Clinical features of chronic lower limb ischaemia

- Pulses: diminished or absent
- Bruits: denote turbulent flow but bear no relationship to the severity of the underlying disease
- Reduced skin temperature
- Pallor on elevation and rubor on dependency (Buerger's sign)
- Superficial veins that fill sluggishly and empty ('gutter') on minimal elevation
- Muscle-wasting
- Skin and nails: dry, thin and brittle
- Loss of hair

Box 16.60 Medical therapy for peripheral arterial disease

- Smoking cessation
- Regular exercise (30 mins of walking, three times per week)
- Antiplatelet agent (aspirin 75 mg or clopidogrel 75 mg daily)
- Consider low-dose factor Xa inhibitor (rivaroxaban 2.5 mg twice daily)
- Reduction of cholesterol: statins
- Diet and weight loss
- Diagnosis and treatment of diabetes mellitus
- Diagnosis and treatment of associated conditions:
  - Hypertension
  - Anaemia
  - Heart failure

Buerger’s disease

- Buerger’s disease or thromboangiitis obliterans is an inflammatory disease of the arteries that is distinct from atherosclerosis and usually presents in young (20–30 years) male smokers. It is most common in those from the Mediterranean and North Africa. It characteristically affects distal arteries, giving rise to claudication in the feet or rest pain in the fingers or toes. Wrist and ankle pulses are absent but brachial and popliteal pulses are present.

- It may also affect the veins, giving rise to superficial thrombophlebitis. It often remits if the patient stops smoking. Symptomatic therapy with vasodilators such as prostacyclin and calcium antagonists or sympathectomy may also be helpful. Major limb amputation is the most frequent outcome if patients continue to smoke.

Raynaud’s syndrome

- This common disorder affects 5%–10% of young women aged 15–30 years in temperate climates. It does not progress to ulceration or infarction, and significant pain is unusual. The underlying cause is unclear and no investigation is necessary. The patient should be reassured and advised to avoid exposure to cold. Usually, no other treatment is required, although vasodilators such as nifedipine can may be helpful if symptoms are troublesome. More severe Raynaud’s syndrome can also occur in association with digital ulceration in patients with connective tissue disease

Diseases of the aorta

Aortic aneurysm

- Aortic aneurysm is as an abnormal dilatation of the aortic lumen.The most common site is the infrarenal abdominal aorta. The supra renal abdominal aorta and a variable length of the descending thoracic aorta may be affected in 10%–20% of patients but the ascending aorta is usually spared. Abdominal aortic aneurysms (AAAs) affect men threetimes more commonly than women

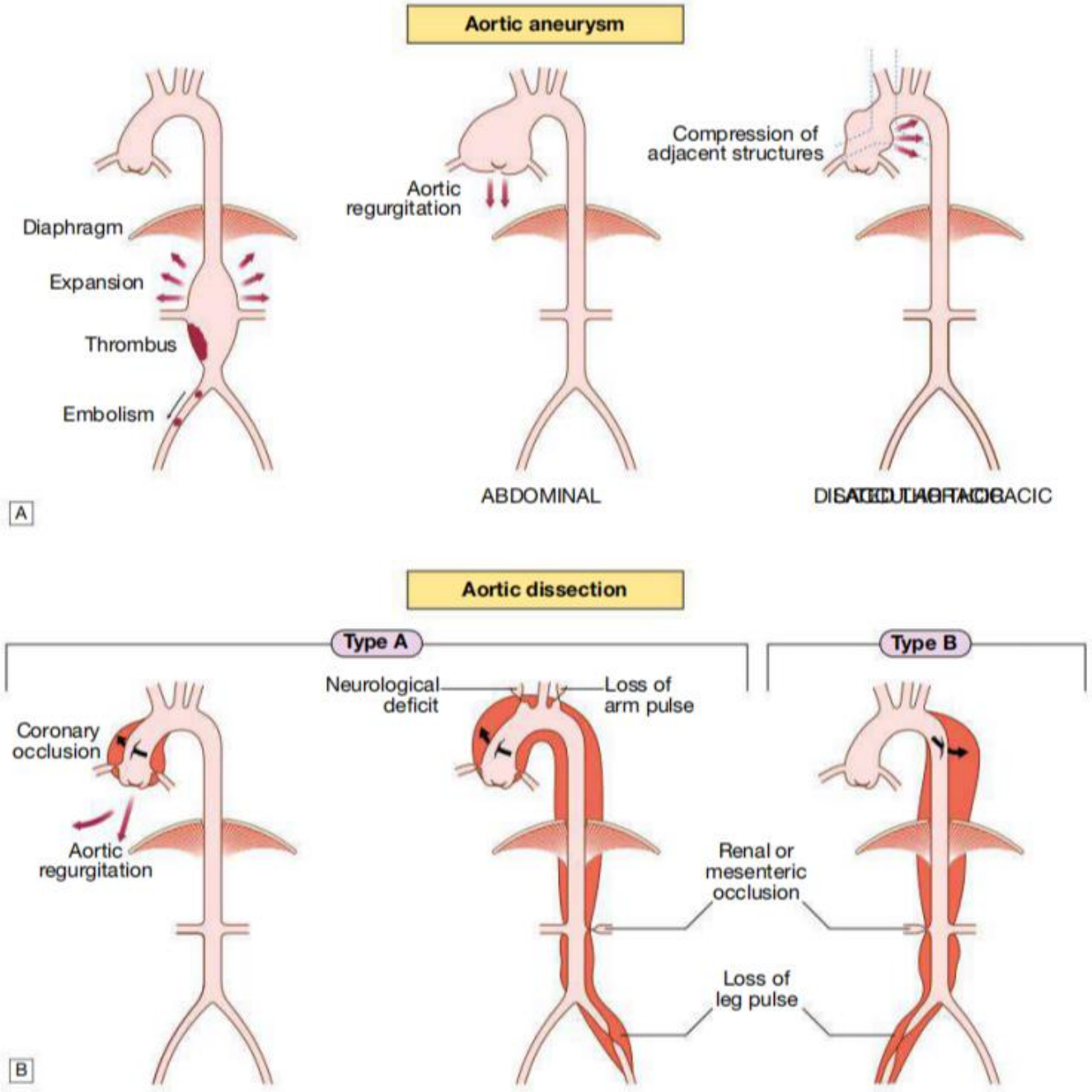

Fig. 16.71 **Types of aortic disease and their complications.** A Types of aortic aneurysm. B Types of aortic dissection.

Pathogenesis

- The most common cause of aortic aneurysm is atherosclerosis, the risk factors for which have previously been described. However, smoking
- and hypertension predominate with 90%–95% of patients having one or both of these risk factors. There also appears to be an additional and
- specifc genetic component since aortic aneurysm tends to run in families. This may explain in part why only some patients with risk factors for atheroma develop aneurysmal disease. Marfan syndrome is an inherited disorder of connective tissue that is associated with aortic aneurysm and
- aortic dissection

Clinical features

- The clinical presentation is dependent on the site of the aneurysm. Thoracic aneurysms may typically present with acute severe chest pain
- but other features, including aortic regurgitation, compressive symptoms such as stridor (trachea, bronchus), hoarseness (recurrent laryngeal
- nerve) and superior vena cava syndrome, may occur

- If the aneurysm erodes into an adjacent structure, such as the oesophagus or bronchus, the presentation may be with massive bleeding. AAAs affect the infrarenal segment of the aorta. They can present in a number of ways. The usual age at presentation is 65–75 years for elective presentations and 75–85 years for emergency presentations.

Investigations

- Ultrasound is the best way of establishing the diagnosis of an abdominal aneurysm and of following up patients with asymptomatic aneurysms that are not yet large enough to warrant surgical repair. CT provides more accurate information about the size and extent of the aneurysm, the surrounding structures and the presence of any other intra-abdominal pathology. It is the standard pre-operative investigation but is not suitable for surveillance because of the high cost and radiation dose.

- The risks of surgery generally outweigh the risks of rupture until an asymptomatic AAA has reached a maximum of 5.5 cm in diameter. All symptomatic AAAs should be considered for repair, not only to rid the patient of symptoms but also because pain often predates rupture.

- distal embolisation is a strong indication for repair, regardless of size, because otherwise limb loss is common. Most patients with a ruptured AAA do not survive to reach hospital, but if they do and surgery is thought to
- be appropriate, there must be no delay ingetting them to the operating theatre to clamp the aorta.

16.62 Abdominal aortic aneurysm (AAA): common presentations

Incidental

- On physical examination, plain X-ray or, most commonly, abdominal ultrasound
- Even large AAAs can be difficult to feel, so many remain undetected until they rupture
- Studies are currently under way to determine whether screening will reduce the number of deaths from rupture

Pain

- In the central abdomen, back, loin, iliac fossa or groin

Thromboembolic complications

- Thrombus within the aneurysm sac may be a source of emboli to the lower limbs
- Less commonly, the aorta may undergo thrombotic occlusion

Compression

- Surrounding structures such as the duodenum (obstruction and vomiting) and the inferior vena cava (oedema and deep vein thrombosis)

Rupture

- Into the retroperitoneum, the peritoneal cavity or surrounding structures (most commonly the inferior vena cava, leading to an aortocaval fistula)

- Open AAA repair has been the treatment of choice in both the elective and the emergency settings, and entails replacing the aneurysmal segment with a prosthetic (usually Dacron) graft. The 30-day mortality for this procedure is approximately 5%–8% for elective asymptomatic AAA, 10%–20% for emergency symptomatic AAA and 50% for ruptured AAA. However, patients who survive the operation to leave hospital have a long-term survival approaching that of the normal population. Increasingly, endovascular aneurysm repair (EVAR), using a stent graft introduced via the femoral arteries in the groin, is replacing open surgery. It is cost-effective and likely to become the treatment of choice for infrarenal AAA

Aortic dissection

- Aortic dissection occurs when a breach in the integrity of the aortic wall allows arterial blood to enter the media, which is then split into two layers, creating a false lumen alongside the existing or true lumen The aortic valve may be damaged and the branches of the aorta may be compromised. Typically, the false lumen eventually re-enters the true lumen, creating a double-barrelled aorta, but it may also rupture into the left pleural space or pericardium with fatal consequences.
-

- The peak incidence is in the sixth and seventh decades but dissection can occur in younger patients, usually in association with Marfan syndrome, pregnancy or trauma; men are affected twice as frequently as women.

Pathogenesis

- The primary event is often a spontaneous or iatrogenic tear in the intima of the aorta; multiple tears or entry points are common. Other dissections are triggered by primary haemorrhage in the media of the aorta, which then ruptures through the intima into the true lumen. This form of spontaneous bleeding from the vasa vasorum is sometimes conned to the aortic wall, when it may present as a painful intramural haematoma.

16.63 Risk factors for aortic dissection

- Hypertension (in 80%)
- Atherosclerosis
- Coarctation
- Genetic:
  - Marfan syndrome
  - Ehlers–Danlos syndrome
- Fibromuscular dysplasia
- Previous cardiac surgery:
  - CABG
  - Aortic valve replacement
- Pregnancy (usually third trimester)
- Trauma
- Iatrogenic:
  - Cardiac catheterisation
  - Intra-aortic balloon pumping

(CABG = coronary artery bypass grafting)

- Aortic disease and hypertension are the most important aetiological factors but other conditions may also be implicated .Chronic dissections may lead to aneurysmal dilatation of the aorta, and thoracic aneurysms may be complicated by dissection. It can therefore be difficult to identify the primary pathology.Aortic dissection is anatomically and for management purposes into type A and type B involving or sparing the ascending aorta, respectively. Type A dissections account for two-thirds of cases and frequently also extend into the descending aorta.

Clinical features

- Involvement of the ascending aorta typically gives rise to anterior chest pain, and involvement of the descending aorta to intrascapular back
- pain. The pain is typically described as ‘tearing’ and very abrupt in lonset; collapse is common. Unless there is major haemorrhage, the
- patient is invariably hypertensive. There may be asymmetry of the brachial, carotid or femoral pulses and signs of aortic regurgitation.

Investigations

- The investigations of choice are CT or MR angiography both of which are highly specices and sensitive. A chest X-ray should be performed. It characteristically shows broadening of the upper
- mediastinum and distortion of the aortic ‘knuckle’ but these findingm are absent in 10% of cases. A left-sided pleural effusion is common.

- ECG may show left ventricular hypertrophy in patients with hypertension or, rarely, changes of acute MI (usually inferior). Doppler echocardiography may show aortic regurgitation, a dilated aortic root and, occasionally,
- the of the dissection. TOE is particularly helpful because transthoracic echocardiography can provide images of the rst 3–4 cm of the ascending aorta only

- Management
- The early mortality of acute dissection is approximately 1%–5% per hour and so treatment is urgently required. Initial management comprises pain control and antihypertensive treatment. Type A dissections require emergency surgery to replace the ascending aorta.
- type B dissections are treated medically unless there is actual or impending external rupture, or vital organ (gut, kidneys) or limb ischaemia, as the morbidity and mortality associated with surgery are very high

- The aim of medical management is to maintain a mean arterial pressure (MAP) of 60–75 mmHg to reduce the force of the ejection of blood from the LV. First-line therapy is with β-blockers; the additional α-blocking properties of labetalol make it especially useful. Rate-limiting calcium channel blockers, such as verapamil or diltiazem, are used if β-blockers are contraindicated. Sodium nitroprusside may be considered if these fail to control BP adequately.

- Percutaneous or minimal access endoluminal repair is sometimes possible and involves either ‘fenestrating’ (perforating) the intimal ap so that blood can return from the false to the true lumen (so decompressing the former), or implanting a stent graft placed from the femoral artery

Aortitis

Syphilis is a rare cause of aortitis that characteristically produces saccular aneurysms of the ascending aorta containing calcification. Other conditions that may be associated with aortitis include Takayasu’s disease, giant cell arteritis and axial spondyloarthritis, all of which are discussed in more detail in

Coarctation of the aorta

- Coarctation of the aorta is the term used to describe a narrowing distal to the origin of the left subclavian artery. It is most commonly due to congenital heart disease, but narrowing of the aorta leading to similar symptoms can occur in other conditions such as Takayasu's arteritis and trauma. Diagnosis and management of coarctation are discussed later in this chapter in the section on congenital heart disease.