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section 16 Cardiovascular disorders 3680 tend to be older than those with ascending aortic involvement and are more likely to have comorbidity. Diligent blood pressure man- agement is the usual initial treatment, as surgery on the descending thoracic aorta carries significant mortality and morbidity, including impaired blood supply to the spinal cord and paraplegia. However, some centres recommend elective surgery (after several weeks) in selected patients with Marfan syndrome, in younger patients with dissection associated with large aneurysms, and if thrombosis of the false lumen fails to occur. Surgery for type B dissection should be considered if there is evi- dence of proximal extension of the dissection, progressive aortic en- largement threatening external rupture, or ischaemic complications from involvement of major arteries. For example, the prognosis is extremely poor when ischaemia occurs in the territory of a major abdominal artery, in which case emergency surgical fenestration of the intimal flap can be life-saving. Endovascular stenting to obliterate flow in the false lumen by deploying a covered stent across the site of intimal tear can relieve branch ischaemia and prevent further aneurysmal dilation in pa- tients with complicated dissection starting distal to the left sub- clavian artery. Follow-up and prognosis Strenuous efforts to control blood pressure are indicated for all patients who have survived aortic dissection. β-Blockers are the agents of choice for most, with other agents added as required. Most patients will require a combination of antihypertensive agents to achieve satisfactory blood pressure control (systolic <120–130 mm Hg). Imaging at least once a year is recommended, using the modality with which there is most local expertise. Increased frequency of imaging is recommended following any acute event, for example severe chest pain, and for some patients with Marfan syndrome. The long-term survival of patients with type A aortic dissection who have surgery and survive to discharge is encouraging: 90% are still alive at 3 years. Although patients who are treated med- ically have extremely high in-hospital mortality (50%), two-thirds of patients who survive to hospital discharge are alive 3 years later. The mortality is often not related to

dissection but from other car- diovascular conditions. Patients with a history of atherosclerosis or prior cardiac surgery are at increased risk of death. In-hospital mortality for patients treated medically with type B dissection is 10%, and 3-year survival is approximately 70%. FURTHER READING Dake MD, et al. (1999). Endovascular stent graft placement for the treatment of acute aortic dissection. N Engl J Med, 340, 1546–52. Estrera AL, et al. (2006). Outcomes of medical management of acute type B aortic dissection. Circulation, 114, 384–9. Evangelista A, et al. (2005). Acute intramural hematoma of the aorta. A mystery in evolution. Circulation, 111, 1063–70. Klompas M (2002). Does this patient have an acute thoracic aortic dis- section? JAMA, 287, 2262–72. Kodolitsch Y, et al. (2004). Chest radiography for the diagnosis of acute aortic syndrome. Am J Med, 116, 73–7. Macura KJ, et al. (2003). Pathogenesis in acute aortic syndromes: aortic dissection, intramural hematoma, and penetrating atherosclerotic aortic ulcer. Am J Roentgenol, 181, 309–16. Nienaber CA, Eagle KA (2003). Aortic dissection: new frontiers in diagnosis and management. Part I: from etiology to diagnostic strat- egies. Circulation, 108, 628–35; part II: therapeutic management and followup. Circulation, 108, 772–8. Nienaber CA, et al. (1993). The diagnosis of thoracic aortic dissection by noninvasive imaging procedures. N Engl J Med, 328, 1–9. Silaschi M, et al. (2017). Aortic dissection: medical, interventional and surgical management. Heart, 103, 78–87. Trimarchi S, et al. (2006). Role and results of surgery in acute type B aortic dissection: insights from the international registry of acute aortic dissection (IRAD). Circulation, 114, 357–64. Tsai TT (2005). Acute aortic syndromes. Circulation, 112, 3802–13. Tsai TT, et al. (2006). Long-term survival in patients presenting with type A acute aortic dissection: insights from the international registry of acute aortic dissection (IRAD). Circulation, 114, 350–6. Vilacosta I, et al. (1998). Penetrating atherosclerotic ulcer: documen- tation by transoesophageal echocardiography. J Am Coll Cardiol, 32, 83–9. 16.14.2 Peripheral arterial disease Janet Powell and Alun Davies ESSENTIALS The most common presentations of peripheral arterial disease are intermittent claudication and abdominal aortic aneurysm. In patients under 50 years of age the cause of disease is most likely to be genetic, congenital, immunological, infectious, or traumatic; over 50 years of age the principal risk factor is smoking. Diagnosis—the main diagnostic method used to confirm the diag- nosis of peripheral arterial disease is Doppler ultrasonography, in particular to estimate the ratio of systolic blood pressure at the ankle and in the arm, the ankle–brachial pressure index (normal value 1.0– 1.4, <0.9 abnormal). Ultrasonography is the standard technique for demonstrating abdominal aortic aneurysms, usually defined as being when the maximum aortic diameter exceeds 3 cm. Critical leg ischaemia is defined as gangrenous change, ulceration, tissue loss, or rest pain lasting for 2 weeks, with an absolute ankle pressure of less than 50 mm Hg. Acute leg ischaemia Presents as a painful, pale, and pulseless limb, and is usually caused by thrombosis at the site of an atherosclerotic stenosis. Requires adminis- tration of analgesia and, if appropriate, rapid surgical intervention: (1) for irreversible ischaemia the options are amputation or palliative care; (2) for severe but potentially reversible ischaemia (white leg), sur- gery is usually the treatment of choice; and (3) for moderate limb is- chaemia (no paralysis and only mild sensory loss), arteriography with consideration of thrombolysis, endovascular angioplasty/stenting, or surgical embolectomy/endarterectomy/bypass.

16.14.2 Peripheral arterial disease 3681 Chronic leg ischaemia Most commonly presents with claudication affecting the calf and thigh. This is associated with high cardiovascular risk, but only 5% will go on to lose a limb, and surgical or endovascular intervention is not usually required. Key elements in management are smoking cessa- tion, aspirin, and statins. Abdominal aortic aneurysm Ruptured abdominal aortic aneurysm typically causes collapse and severe back or abdominal

pain: less than 20% reach hospital alive, and almost one-half of those undergoing emergency surgical die within 30 days. By standard definition, 2–3% of men older than 55 years have an abdominal aortic aneurysm, but most of these are small (3–5.5 cm). These should be managed by ultrasound surveillance, with attention to modification of cardiovascular risk factors. Repair is generally recommended for asymptomatic aneurysms larger than 5.5 cm in men (>5 cm in women), or symptomatic
aneurysms of any size. Minimally invasive endovascular aneurysm repair has an operative mortality of about 2%, which is only one- third of that associated with traditional open repair, but within 2 years the mortality advantage of endovascular repair has been lost and long-term outlook is unknown. Introduction Peripheral arterial disease, defined for the purpose of this chapter as diseases of the abdominal aorta and its branches, has risk fac- tors and features that overlap with, but can be distinguished from, those of coronary artery disease. The two conditions often coexist, but patients with coronary disease are almost always referred dir- ectly to physicians, whereas those with peripheral arterial disease are referred directly to vascular surgeons, particularly in regions where angiology is a poorly developed specialty, since medical therapies are limited. Vascular surgeons also manage patients with arterial disease in the carotid vessels and upper limbs. These aspects re- ceive only passing mention in this chapter: for discussion regarding the clinical features and management of carotid artery disease, see Chapter 24.10.1. The most common presentations of peripheral arterial disease are intermittent claudication and abdominal aortic aneurysm. Most peripheral arterial disease remains asymptomatic. It is not a new disease that results from a modern Westernized lifestyle. Atherosclerotic disease, partially occluding the peripheral ar- teries, has been described in the mummies of ancient Egypt. Life as a cavalry officer was associated with an increased risk of popliteal aneurysm, a condition treated by ligation by John Hunter, the pi- oneering 18th-century surgeon. Albert Einstein died of a ruptured abdominal aortic aneurysm. Techniques for repairing abdominal aortic aneurysms were not developed until the middle of the 20th century. This was the golden era for the development of vascular surgery as a specialty, with the increasing use of bypass surgery that reduced the need for amputa- tion. Today newer, less invasive approaches are being employed— angioplasty and endovascular stenting—but few specific medical therapies are on the horizon. Aetiology and epidemiology Peripheral arterial disease may occur in young people, but the prevalence increases sharply with age. Both young and old may suffer from occlusive (stenosing) disease of the peripheral arteries or dilating (aneurysmal) disease, while vasospastic disease is un- common. However, the underlying causes of peripheral arterial disease in those below and above 50 years of age tend to be very different. Peripheral arterial disease in patients less than 50 years old In younger patients, the cause of disease is most likely to be genetic, congenital, immunological, infectious, or traumatic. Patients with familial hypercholesterolaemia and related inherited disorders of lipid metabolism may present with peripheral limb ischaemia. There are also congenital causes of early-onset leg ischaemia. These in- clude aortic hypoplasia, which occurs during the embryonic fusion of the distal aortas, and popliteal entrapment, where the popliteal artery takes an unusual course through the head of the gastrocne- mius muscle, with exercise involving knee flexion causing intermit- tent occlusion of the artery and calf pain that resembles intermittent claudication. A fierce immunological inflammatory response to smoking causes Buerger’s syndrome, which involves the artery, vein, and associated nerves in both the legs and the arms. This disease, seen principally in men, is particularly prevalent in the Indian sub- continent, and may resolve if the patient stops smoking. Sudden thrombotic occlusion of the iliac and distal arteries may occur in those below 50 years of age, suggesting the presence of an inherited thrombotic disorder. Embolic occlusion from a proximal source is also possible.

Marfan syndrome may sometimes be confirmed only after a pa- tient has presented with a ruptured abdominal aortic aneurysm. In some variants of Ehlers–Danlos syndrome, patients with mutations in type III collagen present with visceral artery aneurysms. In South Africa (and elsewhere), aneurysms of the abdominal, femoral, or popliteal arteries in those under 50 years have been attributed to infectious causes, from HIV to tuberculosis. Syphilitic aneurysms, which used to affect principally the thoracic aorta, are now rare. Peripheral arterial disease in patients over 50 years old For patients over 50 years of age, the principal risk factor for per- ipheral arterial disease—stenosing, aneurysmal, or vasospastic—is smoking. The pathology is atherosclerotic change with superim- posed thrombosis. Of patients who present with peripheral arterial disease, less than 5% have never smoked. For this reason, more men than women presented with peripheral arterial disease in the past, but recently more women are affected, perhaps a reflection of the increasing number who smoke. Nevertheless, unlike Buerger's disease, cessation of smoking is not associated with an immediate dramatic improvement in symptoms and it may take several years without smoking to improve prognosis. Diabetes is another important risk factor for stenosing periph- eral arterial disease. Other risk factors include hypertension, raised levels of plasma fibrinogen, and hyperlipidaemia, with elevated plasma triglycerides being a common finding. The risk factors for dilating arterial disease are similar, with the exception of diabetes, which is rare.

section 16 Cardiovascular disorders 3682 For aortic aneurysms, strong familial clustering has been ob- served, and genome wide association studies have identified as- sociations with several genes not associated with coronary artery disease, including those modifying the protease MMP-9. White and northern European populations appear to be at higher risk of aneurysmal disease than black populations. Stenosing and aneur- ysmal disease are associated with degenerative changes of the artery wall, the prevalence of both diseases increasing sharply with age (Table 16.14.2.1). Epidemiological studies also indicate a difference between stenosing and aneurysmal disease, with death from aneur- ysmal disease (aortic aneurysm) being more common among those of higher social classes and in affluent geographical areas. Leg ischaemia Clinical features The terms acute and chronic relate purely to the length of time that symptoms have been present and must not be confused with terms related to severity, such as critical limb ischaemia. Critical leg ischaemia Critical leg ischaemia is defined as gangrenous change, ulceration, tissue loss, or rest pain lasting for 2 weeks, with an absolute ankle pressure of less than 50 mm Hg, although patients with diabetes are difficult to include in this classification because ankle pressures in such patients may be unreliable due to arterial calcification. Acute leg ischaemia The incidence of acute leg ischaemia, which presents as a painful, pale, and pulseless limb, is 1 in 12 000 patients per year. It can be due either to an embolic event or to thrombosis of an atherosclerotic stenosis. The commonest cause of a peripheral embolus used to be rheumatic heart disease in a patient with atrial fibrillation, but this is now uncommon, and other sources of emboli, such as an aortic aneurysm, must be considered. The development of a thrombosis at the site of an atherosclerotic stenosis, in either the superficial femoral artery or the popliteal artery, is undoubtedly now the com- monest cause of acute leg ischaemia. However, it should be stressed that, whatever the cause, there is no difference on clinical examin- ation of the acutely ischaemic limb. Arterial trauma due to road traffic accidents and knife or gunshot wounds is becoming commoner, as is iatrogenic trauma following the insertion of intra-arterial catheters for diagnosis or therapy. A rare but dramatic cause of acute leg ischaemia is phlegmasia cerulea dolens, in which massive thrombosis of all the major veins of the limb occurs with gross swelling that obstructs the arterial supply. Patients with a thrombosis of a popliteal aneurysm may present with classic symptoms of pain,

paralysis, loss of power, paraes- thesia, pallor, lack of pulse, and perishing cold. If the blood supply is not restored, fixed blue staining of the skin is a further sign of ir- reversible ischaemia, as is a tense calf with plantar flexion. However, most patients presenting with acute ischaemia have symptoms that are less severe. Chronic leg ischaemia Chronic leg ischaemia is much more common than acute ischaemia (Table 16.14.2.1), and its main cause is atherosclerosis. In the young patient, one should also consider cystic adventitial disease, entrap- ment of the popliteal artery, and occasionally fibromuscular hyper- plasia of the iliac arteries, particularly in women. Symptoms are pain on walking, claudication affecting the calf and thigh, rest pain, ulceration, and gangrenous change. Less com- monly, patients may present with buttock claudication and impo- tence (Leriche's syndrome). Although the differential diagnoses of the acutely ischaemic limb are few, in the chronically ischaemic limb pain may be due to spinal stenosis or nerve-root compression (spinal claudication) or arthritis of the hip or knee. Classically the patient with claudication will complain of cramp-like pain in the calf, appearing after walking a particular distance, relieved by a few minute's rest, and recurring again at the same distance if the pa- tient resumes walking. Failure of the pain to disappear on resting, or its reappearance after a shorter distance after each rest, suggests a possible musculoskeletal cause, particularly if distal pulses are pre- sent on examination. However, it should also be remembered that distal pulses may be felt at rest in the limbs of patients with claudi- cation due to peripheral vascular disease, but disappear on exercise to the point of pain. Investigations The main diagnostic method used to confirm the diagnosis of periph- eral arterial disease is Doppler ultrasonography (duplex scanning), Table 16.14.2.1 The increasing prevalence of peripheral arterial disease with age in the populations of northern Europe
Age (years) Population Asymptomatic peripheral
arterial disease (ABPI <0.9) (%) Intermittent claudication (%) Abdominal aortic aneurysm (>3 cm) (%) 55–64 Men 8 1.2 1 55–64 Women 7 0.8 0.2 65–74 Men 16 2.5 2.5 65–74 Women 11 1.2 0.4 75+ Men

> 30 4.0 6 75+ Women 30 1.5 1.5 ABPI, ankle–brachial pressure index. Most peripheral arterial disease, both stenosing and dilating, is asymptomatic. The data have been derived from several studies and geographical variation may occur.

 an example of which is shown in Fig. 16.14.2.1. The ratio of systolic blood pressure at the ankle and in the arm, the ankle–brachial pres- sure index (ABPI), provides a physiological measure of blood flow at the level of the ankle. At rest, in a normal leg, the ABPI lies be- tween 1.0 and 1.4. As the blood flow in the leg is compromised, the ABPI falls sharply, and values below 0.9 are considered abnormal and likely to confirm the diagnosis of peripheral vascular disease. To emphasize the important overlap between this condition and cor- onary artery disease, a reduction in ABPI nearly always signals the presence of coronary artery disease, which is the cause of death in most patients with peripheral arterial disease. Exercise testing provides an objective method of assessing walking distance and helps with the identification of disease processes, such as angina, that may be limiting. It only needs to be used in those people who have a history of claudication but have normal resting ABPI, and can be used as a way of eliminating or suggesting other diagnoses. In addition to establishing the diagnosis of peripheral arterial disease, duplex ultrasonography is able to determine the site of dis- ease and indicate the degree of

stenosis or length of an occlusion and hence aid in the planning of interventional treatment. Other imaging modalities such as CT scanning and magnetic resonance angiography can provide three-dimensional reconstructions of the diseased vessels and may be used for planning surgical treatment. Angiography is only required as an adjuvant to endovascular treat- ment, for surgical planning in some circumstances, or in the man- agement of the acutely ischaemic limb. Attention to risk factors, in particular smoking, blood pressure, and exercise, are important issues. Management Critical and acute leg ischaemia Critical limb ischaemia requires administration of analgesia and rapid surgical intervention. The severity of ischaemia will determine the treatment options considered. However, all patients with a se- verely ischaemic limb should be given adequate analgesia and 5000 units of heparin intravenously. Many will be old and frail, with sig- nificant medical comorbidities. These issues must be considered in deciding whether or not surgical intervention is appropriate for any individual case, with action taken to improve those aspects of the patient's medical condition that can be improved before surgery, or as part of continuing medical management. For a patient with irreversible ischaemia (fixed skin staining and tense muscles), the main decision is whether a primary amputation or palliative care should be offered. If severe but potentially reversible ischaemia is present (white leg), surgery is usually the treatment of choice. Delay while thrombolytic therapy is tried is not advisable in this group. For patients with moderate limb ischaemia, where there is no paralysis and only mild sensory loss, arteriography with con- sideration of the potential use of thrombolysis should be performed. However, it should be remembered that thrombolysis is associated with numerous potential complications, most notably gastrointes- tinal haemorrhage and stroke, and is contraindicated in the early postoperative period. If the limb is salvageable, it may be possible to offer the patient an endovascular procedure, such as an angio- plasty (with or without stenting). Surgical treatment can involve simple embolectomy, but may require a bypass procedure or end- arterectomy, and in the severely ischaemic limb fasciotomies may be needed to treat or prevent a compartment syndrome. For at least 10% of patients, it will not be possible to offer revascularization: a few of these may benefit from the use of a prostacyclin analogue (iloprost), which might diminish amputation rates and alleviate pain. Any benefits of gene therapy on avoidance of amputation, with vascular endothelial growth factor, fibroblast growth factor, or other molecular mediators, are far from established and the only large ran- domized trial was disappointing. Limb salvage rates for patients pre- senting with critical limb ischaemia are variable, probably 50–60% at 2 years, dependent on the severity of disease. In a patient presenting with acute leg ischaemia the outlook is poor, with only about 60% leaving hospital with an intact limb. The 30-day mortality for this group of patients can be as high as 30%, the main cause of death being cardiac disease. The strategy for manage- ment is described in Fig. 16.14.2.2. Controversial areas in the treat- ment of acute leg ischaemia include the role of arteriography, which technique of thrombolysis is the safest and most cost-effective, and whether initial treatment with thrombolysis is beneficial or harmful as compared to surgery. A recently updated Cochrane review, which included five randomized trials comparing thrombolysis and sur- gery for the initial treatment of acute limb ischaemia, found no overall difference in outcomes (limb salvage or death) at 1 year. Initial thrombolysis was associated with higher risk of major haem- orrhage, stroke, and distal embolization, but also less severe degree of intervention overall. In the patient who has had an embolic event, long-term anticoagulation should not be forgotten, and nor should a search for the source of embolus. If the patient is not in atrial fibrillation, and has normal cardiac enzymes and 12-lead electrocardiogram (ECG), Fig. 16.14.2.1 Occlusion of the superficial femoral artery demonstrated by colour-coded duplex ultrasonography. On the left, the common femoral artery (CFA) lies outside the colour box. In the colour box

antegrade flow through the profunda femoris artery (PFA) is shown in blue. The red flash represents rebound flow against the occluded origin of the superficial femoral artery (SFA).

section 16 Cardiovascular disorders 3684 then they should have an echocardiogram to exclude any valvular lesion, a 24-h electrocardiogram (ECG) to look for arrhythmia, an ultrasound scan to exclude abdominal aortic aneurysm, and a screen for thrombophilia. In many centres a CT scan of the thoracic and abdominal aorta will be performed. Chronic leg ischaemia In chronic limb ischaemia, management depends upon the severity of the disease. Most patients present with claudication, which is rela- tively benign: symptoms of intermittent claudication will progress to critical limb ischaemia in less than one in five patients and only about 5% will go on to lose a limb. However, claudication identifies patients with a threefold increased risk of death from either heart disease or cerebrovascular disease compared with age- and sex- matched controls. It is important when planning treatment that all the potential risk factors are covered. In the past surgical interven- tion was usually considered unnecessary: at least one-third will have improvement of symptoms with simple medical treatment and ex- ercise. However recent trials have suggested that either angioplasty with adjunct and stents or coated balloons or angioplasty combined with exercise therapy may offer early benefits (to 2 years) and longer- term results are awaited eagerly. The current treatment of patients with chronic lower leg pain is shown in Fig. 16.14.2.3. General management Careful attention must be paid to the cleanliness of ischaemic feet to avoid infection, and particular care should be given to the cutting of toenails. In many patients this is best done by a careful relative or chiropodist, since apparently minor lacerations can lead to ul- cers, infection, and gangrene. Patients are recommended to exercise. Walking to the point of claudication is not harmful and may improve collateral circulation with beneficial results. Supervised exercise therapy is more effective than merely providing advice to exercise more, but availability of such supervision is variable. Smoking is by far the most significant risk factor for occlusive ar- terial disease and every effort should be made to encourage smokers to stop. If patients undergo surgical treatment, then the long-term patency rate following arterial reconstruction is four times greater in smokers who stop than in those who persist. Pharmacological treatment Since coronary artery disease is the main cause of death in those with peripheral arterial disease, patients with the latter condi- tion should receive similar cardiovascular risk reduction therapy to patients with coronary heart disease. Low-dose aspirin therapy (75–325 mg/day) should be recommended for all. If aspirin cannot be tolerated, ADP receptor antagonists, such as clopidogrel, are equally effective in reducing the risk of cardiovascular events (stroke, myocardial infarction, and vascular deaths). Secondary prevention trials have demonstrated the benefits of statin therapy in reducing cardiovascular morbidity and mortality in those with stenosing atherosclerotic disease of the peripheral arteries. Statins also may improve operative cardiovascular mor- bidity and mortality, but neither fibrates nor chelation therapy offer benefits. The options for facilitating smoking cessation are increasing and nicotine replacement therapy or e-cigarettes can be used with either bupropion or varenicline if necessary, although many will not stop smoking until surgery threatens. Vasodilators may be used where supervised exercise does not bring symptomatic improvement and further endovascular or sur- gical intervention is decided against, or as a bridge to future angio- plasty or surgery. There is evidence that praxilene (naftidrofuryl oxalate) and cilostazol (a selective cAMP phosphodiesterase in- hibitor) improves walking distance in those with intermittent clau- dication, although the mechanism of action is not clear, side effects are frequent, and the drug is contraindicated in patients with con- gestive heart failure. Surgical treatment In general, surgeons are conservative with respect to interventional treatment for patients with claudication,

despite a possible early benefit for those having an endovascular procedure. However, in the patient who has severe claudication, with symptoms that signifi- cantly affect their quality of life, it is certainly possible and appro- priate to offer interventional treatment. Both endovascular techniques (angioplasty with or without stent) and bypass surgery are effective treatments, with little to choose between the two. For infrainguinal bypass, good-quality autolo- gous vein is the conduit of choice. However, reasonable results can be obtained with synthetic grafts, particularly where the distal • Pain relief • Intravenous heparin (5000 IU) • Assessment of patient prognosis and limb salvage with vascular surgical consultation
Irreversible Fixed skin staining Tense muscles Amputation or palliative care Severe White leg Surgery Moderate Dusky leg Mild sensory loss Duplex or arteriogram to evaluate treatment modaility Fig. 16.14.2.2 Management of the patient with an acutely ischaemic leg. ABPI ≥ 0.9 Nonvascular Orthopaedic opinion Possibly spinal claudication or arthropathy ABPI <0.9–0.6 Probably vascular Conservative therapy first Supervised exercise, risk factor modification e.g. aspirin, statins, smoking cessation, symptomatic relief consider angioplasty ABPI <0.5 Probably rest pain Intervention and secondary prevention Angioplasty, bypass or amputation if no other options available Fig. 16.14.2.3 Management of the patient with chronic lower leg pain, but no tissue loss, stratified by ankle–brachial pressure index (ABPI).

16.14.2 Peripheral arterial disease 3685 anastomosis is above the knee. Below the knee, an adjuvant vein interposition in the form of either a Miller cuff or Taylor patch is used. Stenting is used widely, but its use is contentious, and, at least in the infrainguinal arteries, it may not be of value. The role of ex- ercise therapy compared with angioplasty in the treatment of mild to moderate claudication continues to be debated, but it might be prudent to consider the conjoint treatment of angioplasty with ex- ercise therapy. Ischaemia of the arm Ischaemia of the arm is usually a result of embolism from the heart. Occasionally the subclavian artery is diseased or has suffered trau- matic injury or radiation damage following radiotherapy. The basic principles of investigation and management are the same as for the leg. However, it should be noted that the upper limb has multiple interconnection of collateral vessels, hence occlusion of the major arterial supply may still leave a viable limb. The other disease process that needs to be considered in differential diagnosis is the thoracic outlet syndrome, which gives rise to symptoms in the arm as a result of arterial, venous, or neurological compression caused by an add- itional cervical rib or by scalene bands. Management may require surgical intervention, either cervical rib excision or thoracic outlet decompression with the removal of the first rib. Mesenteric ischaemia Mesenteric ischaemia is uncommon. Over one-third of cases of acute mesenteric ischaemia are due to arterial embolism, with em- boli lodging at the ostium of the superior mesenteric artery in many cases. Patients with acute mesenteric artery thrombosis have often had symptoms of mesenteric ischaemia prior to the acute episode. Chronic mesenteric ischaemia typically presents with weight loss and abdominal pain on ingestion of food, the classic story being that the patient is constantly hungry, but frightened to eat. Other causes of acute mesenteric ischaemia include venous thrombosis and non- occlusive ischaemia secondary to hypoperfusion. Patients with acute mesenteric ischaemia will usually present with abdominal pain, but the abdominal physical signs may be much less dramatic than would be anticipated from the subsequent clinical course. Suspicion of the diagnosis should be heightened in the pres- ence of atrial fibrillation or widespread atheromatous vascular dis- ease. Patients may deteriorate suddenly and present in shock. The diagnosis of acute mesenteric ischaemia is difficult to make. In the acute situation, clues to look for include leucocytosis, hyperamylasaemia, and unexplained acidosis. Liver function tests are usually

normal. Radiological imaging is rarely able to make a positive diagnosis, although it can be very useful in excluding other possibilities. Angiography is not always accurate. CT scanning can be helpful in the diagnosis of mesenteric venous thrombosis. Intensive resuscitation to replace fluids is essential. Surgery is usually necessary for the patient to survive, and the possibility of acute mesenteric ischaemia remains one of the dwindling number of reasons for requiring an emergency diagnostic laparotomy. Depending on the findings, resection of small bowel may suffice, but formal arterial surgery may be necessary, and in some unfortunate instances the extent of irreversible ischaemia can preclude any at- tempt at resection or revascularization. In cases where the surgeon is unsure of the viability of bowel remaining after resection, a second laparotomy may be planned to assess the situation a few days later. Repeat laparotomy may also be required to examine, and if necessary resect, more bowel in the patient who is not 'doing well' postoperatively. The prognosis for patients who present with acute mesenteric ischaemia is poor. For patients who present with chronic mesenteric ischaemia, the aim of treatment is to improve blood flow and prevent the cata- strophic disaster of arterial occlusion. This is most commonly due to atherosclerosis, but in younger patients the median arcuate ligament syndrome needs to be considered (compression of the diaphrag- matic crura on the coeliac artery). The potential options, having identified the site of the disease process by duplex scanning and angiography, include angioplasty, endarterectomy, reimplantation, or a surgical bypass procedure. Abdominal aortic aneurysm Definition There is no fixed definition of an abdominal aortic aneurysm beyond agreement that it is a localized dilatation of the abdominal aorta, usually fusiform, with dilation starting distal to the renal arteries. Some would apply the term when the maximum aortic diameter is more than 1.5 times the diameter of the undilated proximal aorta. Manual palpation to detect abdominal aortic aneurysms is un- reliable, unless undertaken by a specialist on a nonobese patient. The most convenient method of screening for the presence of these aneurysms is ultrasonography, measuring the anterior–posterior diameter. Since the reproducibility of ultrasound measurements of the suprarenal aorta is poor, a convenient working definition of an abdominal aortic aneurysm is when the maximum diameter ex- ceeds 3 cm, which in most people is more than 1.5 times the diam- eter of the undilated proximal aorta. Epidemiology Population screening studies in northern Europe have shown that the disease is usually without symptoms, much more common in men than in women (Table 16.14.2.1), and strongly associated with smoking. The decline in prevalence observed this century has been associated with a parallel decline in smoking prevalence. The asso- ciations with hypertension and hyperlipidaemia are inconsistent. The prevalence of large aneurysms (>5 cm in diameter) detected by screening is <1% in men and the large majority of screen-detected aneurysms are 3 to 5 cm in diameter. The natural history of abdom- inal aortic aneurysms is progressive enlargement (with the diameter increasing by 2–5 mm each year) without symptoms, until the aortic wall is so weakened that it ruptures, which is a catastrophic event. The infrarenal aorta is by far the most common site of aneur- ysmal dilatation, and usually the abdominal aorta is the only site of dilatation. When patients present with aneurysms of the iliac, femoral, or popliteal arteries, abdominal aortic aneurysm is often present and screening for this is mandatory. This emphasizes the tendency of some patients to have a more generalized form of dilating arterial disease.

 Most patients (60%) with abdominal aortic aneurysm die from cardiovascular causes, and up to 25% of other male family members may develop occult aneurysms. Ruptured aneurysms The symptoms of a ruptured abdominal aortic aneurysm are col- lapse (shock) and severe back or abdominal pain. Rarely a rup- tured aneurysm will present with

gastrointestinal bleeding from an aortoduodenal fistula or high-output cardiac failure from an aortocaval fistula. Less than half of patients with a ruptured abdominal aortic an- eurysm reach hospital alive, and even among those that undergo emergency surgical repair almost one-third will die within 30 days. New evidence indicates that mortality may be reduced considerably if the rupture is repaired using endovascular repair under local an- aesthesia. With this bleak prognosis and the very significant costs associated with emergency repair following rupture, evidence has accumulated that screening of men over 65 years of age to detect those with the largest aneurysms, at highest risk of rupture, is cost- effective. Accordingly, national screening programmes for abdom- inal aortic aneurysm in men have been implemented in the United Kingdom, Sweden, and other countries. Management of ruptured aneurysms requires: • Access lines, cross-matched blood, and resuscitation—maintaining moderate hypotension at c.70 mm Hg may be beneficial. • Confirmation of diagnosis—ultrasound (to show aneurysm); CT scan (to confirm diagnosis of rupture). • Rapid assessment, by an experienced vascular surgeon, of whether patient would benefit from emergency repair—if yes, immediate endovascular or surgical repair, but remembering to respect any advance patient directives. Aneurysms detected before rupture Abdominal aortic aneurysms are commonly symptomless, but rupture—as just explained—is catastrophic. However, elective re- pair of an abdominal aortic aneurysm, a major surgical procedure, is not without risk. Traditionally, larger aneurysms have been repaired by cross-clamping of the aorta and insertion of a Dacron inlay graft at open surgery. This is a durable procedure and effectively ‘cures’ the patient. However, although some specialized surgical centres report an operative mortality of less than 2% associated with this elective procedure, on a population basis the mortality is more likely to be 5–6%, which is an important reason for avoiding surgery in those with small aneurysms. Minimally invasive endovascular aneurysm repair, via femoral access vessels, has developed rapidly. Only about two-thirds of pa- tients have an aneurysm that is anatomically suitable for this mode of repair with a standard commercial device but adjunct proced- ures widen the applicability to over three-quarters of patients. Randomized trials have shown that the operative mortality associ- ated with endovascular repair is less than 2%, which is only one-third of the mortality associated with traditional open repair. However, within 2 years the mortality advantage of endovascular repair has been lost and a significant proportion of patients with endovascular repair require further interventions to ensure continued exclusion of the aneurysm. Hence many patients with endovascular repair are likely to require lifelong surveillance. The long-term durability and cost-effectiveness for this newer technique have been less well established. In the United Kingdom endovascular repair has been considered cost-effective for elective procedures (http://www.nice. org.uk/TA167). However, new NICE guidelines are imminent and may be less favourable towards endovascular repair. However, most patients would prefer this approach, although some still prefer open repair principally because there is no requirement for long- term follow-up. For endovascular repair, late secondary rupture is a greater problem than for open repair. Although the endovascular approach was initially developed for patients not considered fit for open surgery because of numerous comorbidities, the operative mortality rises to 9% in this cohort and there is no evidence that endovascular aneurysm repair prolongs patient survival. Two large randomized trials have shown that for aneurysms of 4.0 to 5.5 cm in diameter a policy of early elective open surgery confers no long-term survival benefit, and hence early surgery should not be recommended. Later, two small trials comparing early endovascular repair versus surveillance also showed that early intervention con- ferred no survival benefit. The data of all four trials are summarized in a Cochrane review. For such patients’ surveillance, with measure- ment of ultrasound diameter every 6 months, is a safe policy that en-

genders little patient anxiety, and the risk of aneurysm rupture is very low—1% per year. By contrast, for patients with aneurysms greater than 6 cm in diameter the risk of rupture may be as high as 25% per year, and in most such cases elective repair is recommended. Over 90% of the patients enrolled in the trials were men, and in women recent guidelines recommend a diameter threshold of 5 cm. Repair is also recommended when symptoms are attributed to the aneurysm, whatever its size, the commonest being back or ab- dominal pain, or tenderness to palpation. It is assumed that such aneurysms are at high risk of rupture and need early repair. As the aneurysm dilates, onion-skin layers of laminated thrombus deposit in the lumen, to leave a blood-flow channel of approximately normal aortic diameter. These layers of thrombus are very stable and only in rare circumstances are the sources of emboli to the legs. The an- eurysms which most often provoke symptoms have very thick, inflamed, fibrotic walls, which entrap nerves and may become ad- herent to other tissues. These are known as inflammatory aneurysms and the thickened wall can often be detected by CT or MRI. They are technically demanding to repair. There is no convincing evidence that a course of preoperative corticosteroids is beneficial. In the Japanese population, inflammatory aneurysms have been associated with active cytomegalovirus infection. A strategy for the management of abdominal aortic aneurysms de- tected before rupture is shown in Fig. 16.14.2.4. Patients with small 3.0–3.9 cm Ultrasound surveillance at 1–2 yearly intervals Stop smoking Control hypertension Check lipids 4.0–5.5 cm Ultrasound surveillance at 6 monthly intervals Cardiovascular risk reduction With statin, smoking cessation, aspirin, etc. 5.6 + cm or symptomatic Consider intervention Cardiovascular risk reduction With statin, smoking cessation, aspirin, etc. Fig. 16.14.2.4 Management of men with asymptomatic, unruptured abdominal aortic aneurysm stratified by aneurysm diameter.

16.14.2 Peripheral arterial disease 3687 aneurysms should stop smoking and have their blood pressure con- trolled. Since screening detects mainly small aneurysms, it would clearly be beneficial if a treatment to limit aneurysm growth were available. Although β-blockers or losartan have proved effective in limiting the dilation of the proximal aorta in patients with Marfan syndrome, there is no evidence that they are effective for abdom- inal aortic aneurysms. Furthermore, many patients with abdom- inal aortic aneurysm have impaired lung function, perhaps through smoking, and β-blockers are often poorly tolerated. However, ef- fective control of blood pressure and cessation of smoking are both likely to minimize the rate of aneurysm growth and the risk of rup- ture, and statins may also be helpful. Intervention to exclude the an- eurysm remains the only available treatment for aneurysms larger than 5.5 cm in diameter. Medical management Just as for patients with limb ischaemia, patients with abdominal aortic aneurysm are at high risk of cardiovascular events. All patients with abdominal aortic aneurysm should be offered statin therapy to reduce the risk of morbidity and mortality from other forms of co- existent cardiovascular disease. Antiplatelet therapy should be con- sidered, and there is some evidence that, for hypertensive patients, angiotensin-converting enzyme inhibitors minimize the chance of aneurysm rupture. Conventional surgical management Preoperative evaluation requires CT or MRI to define the anatomy and extent of the aneurysm. Cardiac, pulmonary, and renal func- tion should always be assessed, and optimal treatment instituted be- fore surgery: poor renal and lung function are associated with an increased risk of postoperative morbidity and mortality. The most common surgical approach to an abdominal aortic aneurysm is through a transperitoneal incision under general an- aesthesia. The retroperitoneal approach, which avoids bowel ma- nipulation and permits a more rapid return to oral diet, has similar cross-clamp, operating, and recovery times. The transperitoneal approach offers the advantage of exploring the abdominal cavity for other pathology. In this approach, after the bowel has been removed from the operative field, the aorta is

exposed anteriorly from the left renal vein to the bifurcation. The infrarenal neck of the aneurysm is exposed anteriorly and laterally so that an occluding clamp may be applied. Both common iliac arteries are exposed for the placement of the distal occluding clamps. The an- eurysm is opened longitudinally on the anterior surface and the remainder of the procedure performed from inside the aneurysm cavity. Usually following a small dose of intravenous heparin, ar- terial clamps are applied. Clot and debris are evacuated and any back-bleeding lumbar or mesenteric arteries ligated. A Dacron prosthesis is then sutured, end-to-end, to the normal-diameter aorta above the aneurysm. This anastomosis is tested for leaks be- fore the graft is trimmed to appropriate length and sutured in place above the aortic bifurcation. The aneurysmal sac is closed over the prosthesis, before replacement of abdominal contents. Such tube grafts are the most common type, but when the iliac arteries are dilated or diseased a bifurcated prosthesis is used. The cross-clamp time should be less than 1 h and the whole procedure completed within 2 to 4 h. The longest procedures involve inflammatory an- eurysms and cases where the proximal aneurysm neck lies above the renal arteries. The patient should be ready to leave hospital 6 to 9 days after the operation, with a durable repair. Endovascular aneurysm repair The technique of endovascular repair was introduced in the early 1990s and the technology has now stabilized. The procedure may be performed under general, regional, or even local anaesthesia. This flexibility allows endovascular repair in patients where general an- aesthesia is risky, and the avoidance of aortic cross-clamping is an additional benefit for those with limited cardiac reserve. Preoperative investigation to evaluate the extent and size of the an- eurysm (spiral CT or MRI) is of critical importance. The length of the aneurysm neck below the renal arteries, angulation of the aorta, and tortuosity of the iliac arteries must be evaluated precisely so that the correct size of graft can be placed via the femoral artery, with modular component facilitating the placement of bifurcated endografts. The insertion of the graft is performed under fluoroscopic control. This requires the use of significant amounts of contrast material, which may underlie the unfavourable results reported in patients with pre- existing renal impairment. The proximal end of the graft is held in place by hooks and barbs, balloon, or self-expandable stents. The length of the procedure is similar to, or less than, that for open repair, but the transfusion requirements are less and the patient re- covers more rapidly and is ready to leave hospital within 2 to 5 days and some recent reports indicate that day-case procedures are feasible for some patients. The long-term success of the procedure depends on the successful exclusion of the aneurysmal sac and the security of the proximal attachment to prevent graft migration. Endoleaks may develop when the aneurysm is not completely excluded, the graft migrates or fatigues, or there is back-bleeding from lumbar vessels or the inferior mesenteric artery into the aneurysm sac. These are associated with an important risk of continued aneurysm expansion and rupture. Data from 15-year follow-up of the earlier random- ized trials has led physicians to re-evaluate the role of EVAR in the younger patient. These data have shown an early survival benefit of EVAR compared to open repair, but inferior late survival (beyond 8 years) mainly attributable to secondary aneurysm sac rupture. Lifelong annual surveillance with evaluation of the aneurysm with duplex or CT scanning is necessary, with reintervention if necessary. The endovascular revolution has affected the management of all categories of peripheral arterial disease, although in many instances the advantages and indications for the use of the (often more expen- sive) endovascular approach are not based on evidence from ran- domized trials. FURTHER READING ACC/AHA (2006). 2005 guidelines for the management of peripheral arterial disease. J Am Coll Cardiol, 47, 123–312. BASIL Trial Participants (2005). Bypass versus angioplasty in severe ischaemia of the leg (BASIL): multicentre, randomized controlled trial. Lancet, 366, 1925–34. Belch J, et al. (2011). Effect of fibroblast growth factor NV1FGF on am- putation and death: a randomised placebo-controlled trial of gene therapy in critical limb ischaemia. Lancet, 377, 1929–37. Berridge

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