EARN CPD POINTS Complete How to Treat quizzes online (www.australiandoctor.com.au/cpd) or in every issue – see page 38.

Peripheral arterial disease

Background

PERIPHERAL arterial disease (PAD) is a common problem facing GPs and cardiovascular physicians. Atherosclerosis, the most common cause of symptomatic obstruction in the peripheral arterial tree, remains a leading cause of morbidity and mortality in the world.

The prevalence of PAD increases with age — 2-3% at age 60, increasing to 20-25% in people over 70. PAD occurs most often in elderly men (mean age 66; ratio of men to women 2:1). Although less common in younger people, it is prevalent in patients over 50 with common atherosclerotic risk factors.

Other disease states affecting the peripheral circulation include atheroembolic syndromes, thromboangiitis obliterans (Buerger's disease), the vasculitides, vasospastic disorders, popliteal entrapment syndrome, fibromuscular dysplasia and hypercoagulable states.

Atherosclerotic PAD typically involves the superficial femoral and popliteal arteries, occurs in older patients and has a close association with coronary artery disease.

Patients with diabetes develop extensive and rapidly progressive disease at a younger age, typically multi-segmental in distribution, with frequent involvement of the popliteal trifurcation and tibio-peroneal arteries, as well as sequential lesions within one arterial segment.

They also demonstrate an increased prevalence of occlusive disease in distal small vessels, and potential collateral pathways such as the profunda femoris are more frequently involved than in people without diabetes. Aorto-iliac disease tends to occur predominantly in younger patients.

The clinical presentation of patients with PAD is highly variable and depends on the involved vascular territory. Symptoms range from mild lower extremity discomfort during intense exercise, to the presence of constant rest discomfort, painful ulceration, or frank gangrene (chronic critical limb ischaemia).

For the purposes of management, PAD can be classified into the following three major groups:

- Intermittent claudication and asymptomatic PAD.
- Chronic critical limb ischaemia.
- Acute limb ischaemia.

inside

the author

DR PETER R VALE, interventional cardiovascular physician, department of vascular medicine, St Vincent's Clinic, Darlinghurst, and department of cardiology, Mater Misericordiae Hospital, Crows Nest, NSW.

Intermittent claudication

CLAUDICATION is variably described as pain, tightness, aching, soreness, hardness, heaviness, cramping or discomfort of the muscles of the lower limb, typically in the calf, thigh, buttocks, or arch of the foot.

It occurs with exercise and resolves promptly with rest. It is consistently reproducible and the severity is measured in terms of the claudication distance (the distance travelled before the onset of symptoms), which is usually constant.

The sudden onset of severe limb symptoms or conversion of stable claudication to rest pain implies superimposed thrombosis, which invariably accompanies severe atherosclerotic PAD.

Calf claudication alone suggests superficial femoral artery and/or popliteal disease. Calf, thigh and buttock claudication suggests aorto-iliac disease. Isolated foot pain with ambulation may suggest infrapopliteal disease or Buerger's disease.

Neurospinous conditions may be the cause of symptoms (pseudoclaudication [table 1]) if the severity of the pain varies widely, the pain does not subside quickly with rest or if it is accompanied by numbness and paraesthesiae.

Claudication is experienced by only 10-20% of patients with PAD, whereas 50% have atypical symptoms, such as aching or tiredness after walking, or foot or ankle pain while walking.

Symptoms related to PAD rarely occur until the atherosclerotic process has narrowed the vessel diameter by at least 50%. However, the presence of one or more lesions causing 50% stenosis does not imply that the patient will be symptomatic — patients with complete occlusion of the major blood supply to a limb or organ may have few symptoms if an ample collateral supply is present.

Also, subjective description of claudication may not be recognised because of lack of exercise — sedentary individuals with moderate-to-severe PAD may not experience claudication.

Table 1: Differentiation of claudication from neurospinous disease (pseudoclaudication)

	Claudication	Pseudoclaudication
Character of pain	Cramping, tightness	Weakness or clumsiness
Location	Buttock, thigh, calf, foot	Back, buttock, hip, thigh, calf, foot
Exercise induced	Yes	Yes or no
Distance to onset of pain	Same each time	Variable
Occurs with standing	No	Yes
Relief	Stop walking	Sit or change body position

Table 2: Effects of smoking and diabetes on the natural history of claudication in patients with PAD

	Smoking (ongoing)	Smoking (ceased)	Diabetes	No diabetes
10-year all cause mortality	27%	12%	49%	23%
Major amputation	11%	0%	21%	3%
Surgery	31%	8%	35%	19%
Claudication stable or improved	40%	56%	—	—

Physical findings

The most important sign is the diminution or absence of lower extremity pulses. For example, a normal common femoral pulse but absent popliteal and ankle pulses indicate occlusion of the superficial femoral or popliteal artery. In the absence of a popliteal pulse there may be an increase in skin temperature in the region of the knee, indicating an expanded genicular collateral circulation.

Examination should include auscultation for bruits over the abdominal aorta, the common femoral arteries at the groin, the adductor canal and at the popliteal fossa, especially in patients with diabetes. The feet should always be inspected for skin integrity and wounds.

Palpation of the arterial pulses and auscultation for bruits can provide an indication of the degree of stenosis. A reduced pulse with a loud bruit over that vessel indicates at least a 70% stenosis. A barely palpable pulse associated with a soft bruit indicates ≥ 90% stenosis. With complete occlusion, no pulsations or bruits are detectable, except for bruits in collateral vessels.

In patients with occlusive arterial disease, elevation of the legs at an angle >60° and repeated flexing of the calf muscles (Buerger's test) produces pallor of the soles of the feet, followed by a rubor of reactive hyperaemia when the legs are placed in a dependent position.

Risk factors

All patients with vascular disease should be assessed for risk factors, including smoking, diabetes, dyslipidaemia, hypertension and obesity; 60-70% of patients will have more than two risk factors and only 1% will have none.

Tobacco smoking is the single most powerful risk factor for PAD; smokers have a sixfold increase in PAD incidence and 75-90% of patients are, or have been, smokers.

PAD is five times more common among patients with diabetes.

Dyslipidaemia increases the risk and the rate of progression of PAD. The incidence of PAD is twice that of coronary artery disease in patients with hypertension, and hypertension is present in 30-40% of patients with occlusive PAD.

Systolic blood pressure appears to be a better predictor of PAD than diastolic blood pressure. Other recently recognised influencing factors include hyper-homocysteinaemia, infection and inflammation, genetics and hypercoagulable states.

Natural history and prognosis

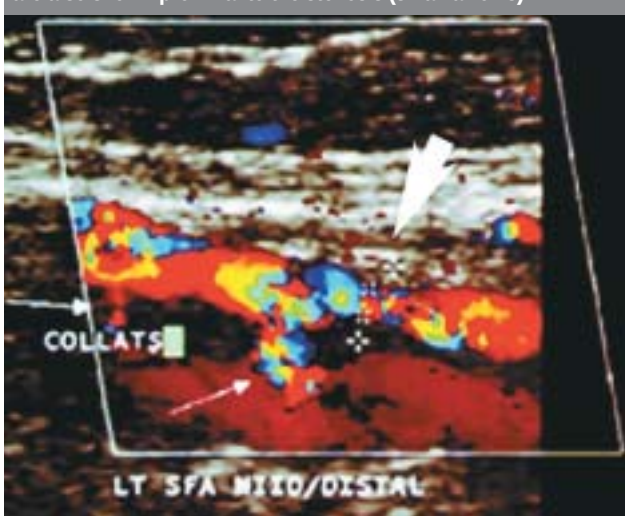
PAD is usually considered an indolent, slowly progressive disease. About 70-80% of patients with intermittent claudication will have stable symptoms or become less symptomatic after 5-10 years because of collateral vessel development.

Progressive deterioration of claudication to rest pain or gangrene occurs in 3-5% of patients annually and in 15-20% patients over a period of 5-10 years. Amputation is required in 1% annually and in 5-10% over 5-10 years.

Patients with diabetes are a unique subgroup — they have a high likelihood of developing critical limb ischaemia, with an amputation rate seven times greater than for patients with PAD but no diabetes.

The natural history of patients with occlusive PAD is influenced by the extent of coexistent coronary artery and cerebrovascular disease. Fifty per cent of patients presenting with symptomatic PAD also have severe coronary artery disease, with an overall reduction in life expectancy of 10 years; 10-20% will have non-fatal MI or stroke and the mortality rate approaches 30%.

Figure 1: Duplex ultrasound of the left superficial femoral artery in a patient with intermittent claudication, showing a critical stenosis (arrowhead) in the adductor canal. Collateral vessels are also shown proximal to the stenosis (small arrows).



The choice of appropriate footwear is important because most limb-threatening complications in patients with occlusive arterial disease arise from some type of trauma.

Investigations and diagnosis

PAD is assessed by non-invasive techniques to:

- Establish the diagnosis of PAD objectively.
- Assess the severity of the disease.
- Select appropriate management strategies.
- Provide a prognostic guide and monitor natural progression.

The ankle-brachial pressure index (ABI), calculated from the ratio of ankle systolic pressure to brachial systolic pressure, gives a sensitive estimate of the degree of arterial insufficiency and usually correlates with functional symptoms.

For example, an ABI of 0.7-0.9 would be consistent with mild intermittent claudication. In the presence of rest pain, the ABI is usually <0.3. ABI alone does not indicate the level of disease and cannot differentiate stenosis from occlusion.

Doppler flow velocity waveform analysis is useful when pressure measurements may be invalid, for example, in patients with diabetes and calcified non-compressible arteries (ankle pressure >240mmHg). A monophasic waveform indicates moderate-to-severe arterial insufficiency, whereas a multi-phasic waveform excludes significant obstructive PAD.

ABI measurement has prognostic value in PAD. Ten-year survival rates for all-cause mortality are 83% for ABI >0.85, 62% for ABI 0.4-0.85 and 44% for ABI <0.40. A patient with an ankle pressure index of ≤ 0.85 should be referred to a vascular medicine unit for evaluation and consideration of revascularisation.

Treadmill exercise testing allows objective assessment of functional limitations and can differentiate PAD from other causes of exercise-induced lower-limb symptoms (eg, neurospinous disease). If symptoms are reproduced without a drop in ABI, significant PAD is effectively excluded.

Duplex ultrasound scanning using dual imaging and Doppler waveform analysis to assess anatomy and perfusion (figure 1) provides an accurate anatomical description of arterial disease.

Diagnostic angiography remains the time-honoured approach for diagnosing and assessing obstructive PAD and is an essential component of percutaneous revascularisation.

Magnetic resonance angiography (MRA) has been increasingly used for assessing the lower-limb vasculature.

Management

The goals of therapy are to maintain functional status, reduce or eliminate ischaemic symptoms and prevent progression of disease. A secondary goal is to reduce the incidence of coronary and cerebrovascular events.

Conservative measures

Ischaemic tissues tolerate infection poorly. Maintaining skin integrity is therefore important in patients with arterial insufficiency, so meticulous foot, skin and nail care and good footwear are essential.

Patients should examine their feet on a daily basis, looking for blisters, dryness, trauma, ulcers, tinea and areas of unusual skin discolouration. Dryness and fissuring of the skin around the heel predisposes to infection.

The choice of appropriate footwear is important because most limb-threatening complications in patients with occlusive arterial disease arise from some type of trauma — mechanical, chemical or thermal. In moderate arterial insufficiency, elastic compression stockings are to be avoided because they reduce skin blood flow.

Any infection needs to be treated early with appropriate antimicrobial therapy. Chronic fungal infection is a major problem because it commonly leads to secondary bacterial infection.

Risk factor modification. The importance of smoking cessation and aggressive control of hyperlipidaemia, hypertension and diabetes remain fundamental to the medical management of PAD. The GP must assume a major role in lifestyle modification because modifying risk factors decrease the rate of cardiac and vascular ischaemic events.

Patients who stop smoking have significantly better outcomes (table 2), and cessation of smoking contributes to reducing re-occlusion rates after revascularisation.

Meticulous control of diabetes is paramount in reducing progression of atherosclerosis, reducing vascular thrombosis and limiting infected ischaemic lesions, which are typically resistant to treatment and troubling for patients. Aggressive lipid-lowering therapy is indicated in patients with PAD.

Exercise. Regular exercise can double the claudication-free walking distance in patients with mild or moderate symptoms and stimulate development of collateral arterial circulation. Patients should be reassured that claudication pain does not represent damage to the limb, and encouraged to exercise for at least 30-60 minutes a day and to progressively increase levels.

Pharmacotherapy

In patients with PAD, drug treatment is most often used for:

- Treating coexisting disease (eg, hypertension).
- Modifying risk factors (eg, hyperlipidaemia).

cont'd page 34

from page 32

- Prophylaxis against thrombotic events associated with atherosclerosis (eg, with antiplatelet drugs).

In contrast to the medical treatment for coronary artery disease, no pharmacological agent has proved efficacious enough in significantly improving symptoms of PAD to gain widespread acceptance or use.

While antiplatelet agents have been reported to decrease progression of atherosclerosis in occlusive PAD, no improvement in exercise capacity has been demonstrated. Clopidogrel has been shown to reduce the overall risk of ischaemic vascular events in PAD patients.

All patients with PAD should receive antiplatelet therapy with at least aspirin. Neither anticoagulant agents nor thrombolytic agents have been shown to be effective in chronic occlusive arterial disease.

Several vasodilators (eg, calcium-channel blockers, alpha-adrenergic antagonists) and metabolic agents (L-carnitine, L-arginine) have been studied but none has been conclusively demonstrated to improve symptoms related to PAD.

Oxpentifylline (Trental), a rheolytic agent, has been shown to increase walking distance by up to 21% over placebo. Patients most likely to benefit were those with moderately severe occlusive arterial disease (ABI <0.80) who have been symptomatic for more than one year. However, most investigators agree that oxpentifylline should not be considered as a substitute for exercise and risk factor modification in symptomatic PAD.

Management of associated disorders

All patients being considered for revascularisation and with a history of past vascular events, symptoms of ischaemia or multiple risk factors for atherosclerosis should be assessed for myocardial ischaemia using sestamibi, left ventricular function with echocardiography, and carotid artery disease using extracranial carotid artery duplex ultrasound.

Interventional therapy

Invasive therapy to restore pulsatile flow is the most effective treatment for the immediate relief of symptoms of PAD. Revascularisation is usually reserved for:

- Patients with progressive disease (increasing symptoms for longer than six months).
- Severe or disabling symptoms that interfere with employment or lifestyle (claudication distance usually <100m).
- Acute limb ischaemia.
- Chronic critical limb ischaemia.

When the indications for invasive therapy are clear and the anatomical substrate has been defined, the choice will be between conventional surgery and catheter-based techniques.

Figure 2: A: Digital subtraction angiography (DSA) image of the aorta and iliac vessels in a patient with disabling buttock and thigh claudication, showing focal stenotic disease of the aortic bifurcation and ostia of the common iliac arteries. B: DSA image of the same patient after percutaneous revascularisation using bilateral simultaneous angioplasty and deployment of balloon-expandable stents.

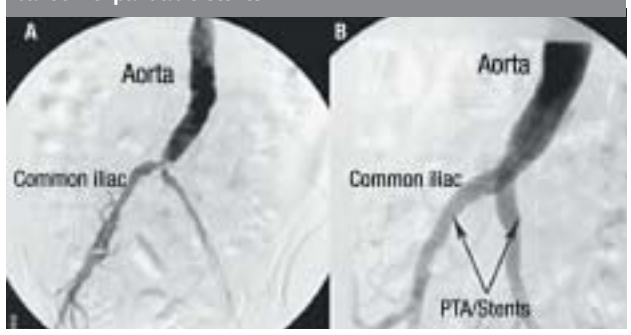


Figure 3: A: Iliac occlusion: DSA image showing chronically occluded left iliac system. Previously this patient would be referred for surgical revascularisation. B: Percutaneous transluminal angioplasty (PTA) and stent. DSA image after percutaneous revascularisation using hydrophilic glide-wire and a combination of balloon-expandable and self-expanding stents.

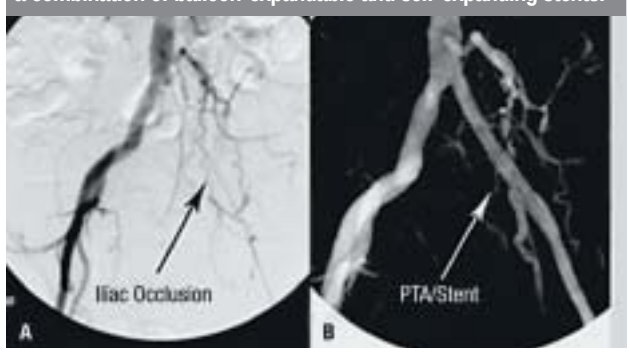
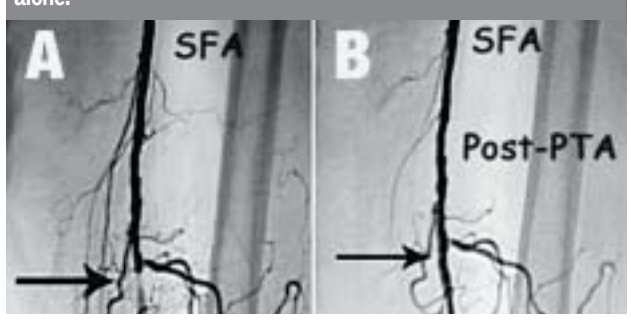


Figure 4: A: DSA image of a patient with disabling claudication, showing a critical stenosis of the left superficial femoral artery (SFA) in the adductor canal, with numerous collateral vessels. B: Post-PTA DSA image from the same patient after balloon angioplasty, showing restoration of patency using angioplasty alone.



All patients with PAD should receive antiplatelet therapy with at least aspirin.

Surgery

Surgery typically involves placement of saphenous-vein or prosthetic materials to bypass or substitute for the diseased native artery. Patency rates for surgical procedures at five years are 80-90% for aorto-bifemoral bypass, 60-80% for above-knee vein grafts, and 50-70% for below-knee vein grafts.

The choice of surgical procedure is influenced by the distribution of disease, the adequacy of distal run-off vessels, and by comorbidities. In some situations (aortic occlusion, common femoral artery bifurcation disease, popliteal aneurysm), surgery remains the gold standard for revascularisation.

Usually, these operations require general anaesthesia. They involve significant blood loss and fluid shifts in patients who may have profound involvement of the blood supply to other critical organs, thereby increasing operative morbidity and mortality. When possible, use of catheter-based (endovascular) treatments provides a similar level of correction and durability and substantially minimises risk and disability.

Figure 5: A: DSA images after PTA to the left SFA (large arrowhead) of a patient with disabling claudication. A flow-limiting dissection is evident (small arrows). B: Post-stent DSA images from the same patient after stent deployment (small arrows) across the area of dissection and covering the area of initial obstructive disease (large arrowhead).

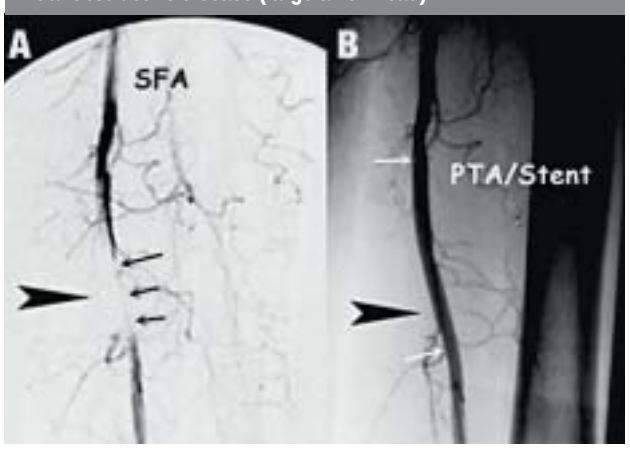
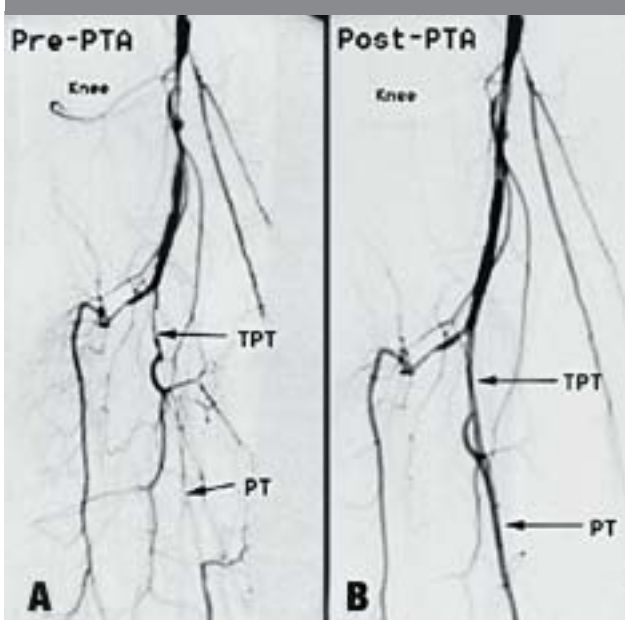


Figure 6: A: Pre-PTA DSA image of the popliteal and infrapopliteal vessels in a patient with diabetes and a non-healing ulcer of the right foot, showing a tight stenosis in the popliteal artery at the level of the knee joint, an occluded anterior tibial artery, subtotal occlusion of the tibio-peroneal trunk (TPT), and occlusion of the proximal posterior tibial (PT) artery. (The peroneal artery [not visualised] was also occluded.) B: Post-PTA DSA images from the same patient after angioplasty of the popliteal artery, TPT and peroneal artery. Restoration of flow facilitated healing of the ulcer.



Lumbar sympathectomy

Lumbar sympathectomy is used alone in patients not fit for surgery or as an adjunct to aorto-femoral reconstruction. There is no good clinical evidence that lumbar sympathectomy increases graft patency or improves limb survival.

Endovascular therapy and anatomical regions of interest

Percutaneous revascularisation has become increasingly popular as first-line therapy for PAD. Intervention is indicated in selected patients with disabling intermittent claudication in whom exercise treatment has failed, except in two unique subgroups:

- Patients with diabetes (increased rates of chronic critical limb ischaemia and sevenfold amputation rates), who need a more aggressive approach on signs of deterioration.
- Patients who develop acute limb ischaemia (see page 35).

Aorto-iliac disease. Considerable controversy exists concerning the optimal treatment in this situation. Percutaneous transluminal angioplasty is generally used for more focal disease of the distal aorta, common iliac arteries and external iliac arteries (figure 2). However, the availability of hydrophilic guide-wires has led to an increased ability to revascularise even lengthy, chronic iliac occlusions percutaneously (figure 3).

Endovascular stents (and stent grafts) have dramatically changed the short-term (90-100% technical success) and long-term results (75-90% five-year patency) of percutaneous transluminal angioplasty. This compares favourably with results of surgical recanalisation for aortoiliac disease (primary patency at five years 75-80%) but at the cost of 2-3% mortality.

Superficial femoral and popliteal artery disease. The role of percutaneous therapy versus surgery is controversial in this group. In superficial femoral artery or popliteal stenotic disease, angioplasty has a high technical success rate and reasonable long-term patency rates (up to70% [figure 4]) and now must be considered as first-line therapy.

Percutaneous revascularisation even of lengthy occluded segments may facilitate healing in patients with non-healing lesions and/or threatened limb loss when the risks of surgery are considered prohibitive or when veins are unavailable for distal bypass.

In patients with rest pain or severe claudication, percutaneous transluminal angioplasty may be less risky than conventional surgical reconstruction.

An important caveat in the management of patients with symptomatic superficial femoral artery or popliteal disease is the issue of restenosis, which affects up to 50% of patients.

At present, stents are deployed for acute treatment of a flow-limiting dissection and for failed balloon angioplasty (figure 5), usually in the setting of eccentric stenoses, long-segment stenoses (and occlusion), and stenoses due to intimal hyperplasia at graft anastomosis. Clopidogrel should be used for six months after stent deployment.

For patients with claudication severe enough to warrant intervention, percutaneous transluminal angioplasty is the preferred initial treatment. The role of laser angioplasty in superficial femoral artery or popliteal revascularisation remains controversial and unproven.

Infrapopliteal disease. In the rare subset of patients who have claudication due solely to infra-popliteal disease, percutaneous therapy is becoming more popular. In patients with rest pain or ischaemic ulceration, restoration of uninterrupted patency of at least one of the three major branches is generally required to obviate symptoms and/or heal a distal ischaemic lesion (figure 6).

The long-term clinical outcome of percutaneous therapy may ultimately equal that of distal bypass grafting, particularly for critical limb ischaemia (as opposed to claudication) and for patients at too high risk or otherwise unqualified for bypass surgery. This is because patency rates of distal surgical bypass are inferior to those of more proximal reconstruction, regardless of the conduit.

Studies of percutaneous transluminal angioplasty have demonstrated technical and clinical success rates of 80-95%. The incidence of restenosis, which remains high, should not be a factor in deciding whether to use a percutaneous approach for what is, in many of these patients, a short-term problem One patent artery typically results in healing of ulceration, a common reason for revascularisation, even if it only stays open for 3-6 months.

Endovascular stents are not recommended for infrapopliteal vessels.

Chronic critical limb ischaemia

THIS clinical entity describes patients with advanced chronic occlusive PAD compounded by permanent microcirculatory changes, disturbed flow regulation, loss of normal vasomotion, and inappropriate activation of the microvascular defence system, resulting in microthrombosis, inhibition of fibrinolysis and local tissue damage.

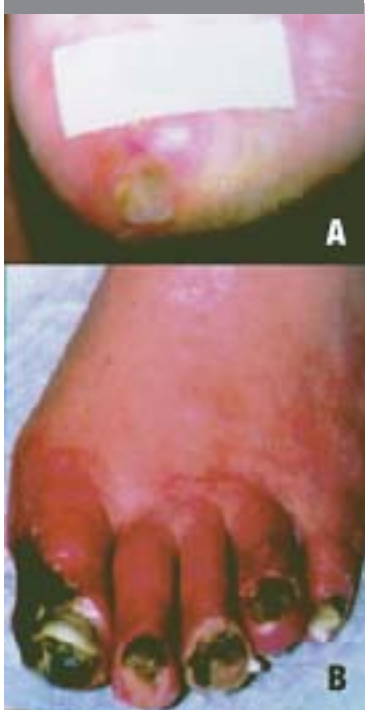
The natural history and prognosis is similar to that of malignancy. Within 12 months, 25% of patients with this condition will have had a major amputation and 20% will have died, leaving only 55% alive with both legs intact. Patients with diabetes are several times more likely to develop it than those without diabetes.

Clinical features

Chronic critical limb ischaemia is characterised by rest pain, ulceration and skin necrosis or superficial gangrene. Rest pain is usually more severe at night and can only be relieved by placing the legs in a dependent position. However, prolonged dependency may cause oedema, further compromising the microcirculation, with delayed healing of ulceration.

An ischaemic neuropathy, characterised by a severe lancinating or burning sensation in the leg and foot, may be superimposed and persist for many months even after correction of the ischaemia.

Figure 7: Clinical features of severe arterial insufficiency in a patient with critical limb ischaemia, showing necrotic ulceration of the heel (A) and toes (B).



Clinical signs include skin atrophy accompanied by rubor and reduced skin temperature, hair loss, thickened nails with chronic fungal infection and poor nail growth. The ulcers occur mostly over areas subject to friction (toes, malleoli, heels) and are typically necrotic, dry and extremely painful, with ill-defined and cyanotic borders. They are often covered with a black eschar (figure 7).

Most progress to gangrene and amputation if the circulation cannot be improved. Infection is typically polymicrobial (including anaerobes) but the classic signs of infection are often masked by poor circulation.

Investigations

Non-invasive criteria for diagnosis are an ankle systolic pressure <50mmHg and/or a toe systolic pressure <30mmHg. Duplex ultrasound usually confirms the presence of multi-segmental disease including involvement of the distal arteries.

Management

All patients with chronic critical limb ischaemia should be referred for urgent vascular medicine consultation and assessment of other critical circulations. If possible, admission to hospital is ideal.

General measures include analgesia, limb protection, treatment of infection, cessation of smoking and strict control of risk factors. The limb must be placed in an arterial position with the foot dependent, usually at 30° below the horizontal.

Topical nitrates improve skin circulation. Substitution of beta blockers is recommended because of their potential to increase peripheral vascular resistance.

Provided there is no ulceration or necrosis, ambulation is beneficial because it encourages development of the collateral circulation. In patients with ulceration, exercise is restricted until ulceration has healed.

Strict control of diabetes is crucial because uncontrolled diabetes is a hypercoagulable state that also encourages infection. Patients with diabetes also suffer from various neuropathies (sensory, motor, autonomic) that contribute to callous formation, shearing stresses, sub-callous haemorrhage and infection and, ultimately, ulceration. Therefore even minor foot lesions in these patients should be treated vigorously.

Antibiotics (including anaerobic cover) should be given in the presence of clinical evidence of cellulitis. In severe infections IV antibiotics are indicated. Topical antibiotics are of no value and should be avoided.

Heparin should be started to prevent arterial thrombosis and to decrease the risk of venous thromboembolism that accompanies immobility and reduced limb perfusion. Thrombolysis may be indicated in selected patients. Compression stockings and calf-thigh compression devices cannot be used for DVT prophylaxis in the presence of severe occlusive PAD.

Long-term treatment with antiplatelet agents reduces the risk of cardiovascular death from concurrent MI or cerebrovascular disease in patients with PAD and maintains patency after revascularisation.

Prostaglandins by infusion have benefit in patients with chronic critical limb ischaemia and intractable ulceration, frank gangrene before surgery (to accelerate demarcation) and for rapidly progressive ischaemia. Some ulcers heal quickly or demonstrate a marked reduction in size with this treatment. The circulatory benefits, especially relief of rest pain, may continue for 6-8 weeks.

A revascularisation procedure should be attempted if there is at least a 25% chance of saving a useful limb for at least one year. Surgery or angioplasty are essentially limb-salvage procedures. However, an artery that remains open for only a few months may allow ulceration or necrotic lesions to heal.

When a revascularisation procedure is not possible, primary amputation may be the only option to control spreading infection or gangrene, toxaemia or rest pain. Sympathectomy is of limited benefit but some patients experience pain relief, perhaps due to interruption of pain fibres in afferent pathways.

Acute limb ischaemia

ACUTE limb ischaemia is a medical emergency. Successful management depends on early diagnosis and urgent intervention; the patient should be immediately transferred to an institution with facilities for angiography and revascularisation.

Aetiology

This condition occurs most often after thrombotic occlusion of atherosclerotic native arteries or bypass graft in-situ thrombosis, with or without underlying impediment to flow. Thrombotic occlusion of a popliteal artery aneurysm is almost always a serious limb-threatening complication.

Embolic occlusion accounts for about 40% of cases. The source is cardiac (AF, post MI, valvular heart disease) in >75% of cases. Emboli may also originate from aneurysmal disease and atherosclerotic lesions of the thoracic or abdominal aorta.

Rarer causes include Buerger's disease, arterial trauma, arteritis, drugs (eg, ergot alkaloids), arterial dissection and popliteal artery entrapment. When spontaneous thrombosis occurs in the absence of an underlying high-grade stenosis, the possibilities extend to a previously unrecognised hypercoagulable state or to a myeloproliferative disorder.

Table 3: Classification of acute limb ischaemia by clinical features

Category	Description	Capillary return	Muscle weakness	Sensory loss	Arterial doppler	Venous doppler
Viable	Not threatened	Intact	None	None	Audible (AP >40mmHg)	Audible
Threatened	Salvageable if promptly treated	Intact, slow	Mild, partial	Mild, incomplete	Not audible (AP <40mmHg)	Audible
Irreversible	Major tissue loss, amputation	Absent (marbling)	Paralysis	Anaesthesia	Not audible (AP <40mmHg)	Not audible

AP = ankle pressure

Clinical features

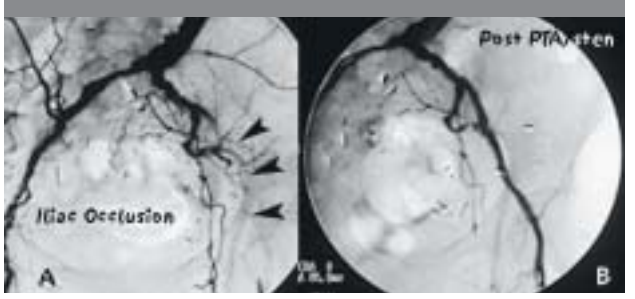
The clinical presentation is typically dramatic, with acute onset of severe pain, paraesthesiae, numbness and coldness, muscle tenderness and paresis. The extremity is cool, pale and pulseless.

Presentation depends on the duration and level of occlusion, the status of the underlying vessels, and general factors (blood pressure, cardiac output, presence or absence of diabetes, O_2 saturation).

A preceding history of stable claudication, abrupt shortening of the claudication distance and the finding of arterial bruits elsewhere suggest thrombotic occlusion of a pre-existing arterial narrowing. Embolic events may have a subtle presentation with a cold or blue digit.

A series of clinical categories with well-defined diagnostic criteria help determine whether the affected limb is viable, threatened or already irreversibly damaged (table 3).

Figure 8: A: DSA image of the aorta and iliac vessels in a patent with acute on chronic limb ischaemia as a result of occlusion of the external iliac artery (arrow heads). Pre-existing obstructive disease is evident, as seen in the right iliac system and by the presence of collateral vessels on the left side. B: Successful revascularisation of the left external iliac artery using angioplasty and stent deployment, with restoration of flow to the left lower limb.



The clinical status of the limb is a more reliable guide to viability than the time between event and presentation. Paradoxically, the patient with less underlying PAD often develops the most severe ischaemia; for example, the patient with AF and normal peripheral vessels and embolism to the common femoral or popliteal arteries. The presence of better developed collaterals in a patient with pre-existing PAD can be protective.

Investigations

An ankle pressure of >40mmHg indicates viability of the limb. If the pressure is <40mmHg, the limb is threatened with loss of viability in less than six hours.

Management

When the diagnosis is made on clinical grounds, with or without non-invasive confirmation, the patient should be immediately anticoagulated with heparin to prevent propagation of the thrombus, recurrent embolism and loss of valuable collaterals.

Urgent angiography is indicated to determine the therapeutic options, including surgical or catheter-based thrombectomy, bypass, thrombolytic therapy or direct percutaneous recanalisation. Urgent investigations include FBC, INR, activated partial thromboplastin time, electrolytes and renal function, creatine kinase, ECG and CXR.

If the limb recovers spontaneously because of clot dissolution or fragmentation and anticoagulation, a conservative approach including anticoagulation and close observation for progression of ischaemia may be implemented initially. The limb, and especially the heel, should be protected against pressure injury and NOT elevated. Vasodilators are of no benefit and may be deleterious if accompanied by hypotension.

Immediate surgical revascularisation is indicated in the profoundly or irreversibly ischaemic limb. Procedures include direct or suction embolectomy, endarterectomy or bypass grafting. Even with a favourable post-embolectomy limb-salvage rate of 75-85%, the 30-day mortality rate is about 20-30%, emphasising the coexistence of cardiac and other major arterial diseases in these patients.

Trials comparing intra-arterial thrombolysis to surgical intervention suggest percutaneous, catheter-based thrombolytic therapy may be an appropriate initial treatment, provided the limb is not immediately or irreversibly threatened. Ideal situations include thrombus in an atherosclerotic vessel or arterial bypass graft, embolism to a non-atherosclerotic limb, or when surgical intervention is contraindicated.

In contrast to coronary thrombolysis, thrombolytic agents are infused directly at the site of occlusion to achieve dissolution of the large peripheral arterial thrombo-emboli. Using this approach the underlying lesions can be further defined by angiography and definitive percutaneous revascularisation can be performed immediately (figure 8).

In selected patients, long-term management will include warfarin anticoagulation.

Other selected disease states of the peripheral arteries

Atheroembolism

ATHEROEMBOLISM is caused by macro-embolisation of friable or ulcerated atherosclerotic plaque debris, or micro-embolisation of cholesterol crystals liberated from the proximal arterial tree, either spontaneously or after provocation (direct surgical or catheter manipulation, thrombolysis or anticoagulation). It is more common in elderly men with advanced atherosclerosis.

Clinical presentation depends on the region affected, the embolic load and the status of the underlying vasculature. Atheroembolism to the lower extremities may be focal, affecting one or more toes (so-called blue toe syndrome) or diffuse, causing bilateral livedo reticularis, cyanosis and ischaemic pain, with progression to painful ulceration and gangrene.

Involvement of the renovascular bed may result in deteriorating renal function and/or renal failure. There may be non-specific symptoms and signs suggesting a systemic illness, with fever, malaise, anorexia, weight loss, headache and myalgia, or it may provoke acute catastrophic multi-organ failure.

Atheroembolism should be considered when a patient presents with new limb ischaemia, renal failure, transient cerebral ischaemia or angina not explained by local large artery occlusive disease. Suggestive laboratory findings include an elevated ESR, leucocytosis with eosinophilia, hypocomplementaemia, anaemia, elevated transaminases and azotaemia.

Atheroembolism may be confirmed by fundoscopy or tissue biopsy, showing pathognomonic cholesterol crystals in retinal branch arteries or small vessels of affected tissues.

Treatment strategies include conservative local measures for the affected tissue and, importantly, appropriate steps to prevent future embolic events, including antiplatelet therapy and avoidance of surgical and catheter manipulation near the presumed source of embolisation.

Occasionally, especially in the case of recurrent atheroembolism, exclusion of the embolic source (aortic aneurysm, ulcerated aorto-iliac plaque) by either percutaneous or surgical means may be necessary. Renal failure often requires dialysis support. These patients have a high rate of cardiovascular death in subsequent years.

Buerger's disease

Buerger's disease (thromboangiitis obliterans) is an aggressive form of obliterative arteritis affecting predominantly the small- and medium-sized arteries and veins of the upper and lower extremities. It is associated with a segmental, inflammatory thrombotic vasculitis and mostly affects younger men (<50) and smokers.

Patients typically present with ischaemic ulceration of one or more digits, which may progress to gangrene. They may have associated arch, foot or calf claudication, cold sensitivity, and/or episodic superficial thrombophlebitis. The disease almost always involves two or more limbs; an abnormal Allen test is present in two-thirds of patients.

Buerger's disease must be distinguished from premature atherosclerosis: angiography demonstrates normal proximal vessels, with abrupt segmental occlusion of small distal branches. Survival is similar to that of age-matched controls.

Therapy consists primarily of absolute cessation of smoking. Additional therapy includes treatment of ulcers (including amputation if needed), palliation of symptoms with judicious use of vasodilators, anticoagulants in early disease stages, and antiplatelet therapy for long-term treatment.

Prostaglandins and sympathectomy may be appropriate in certain cases to facilitate wound healing. Invasive treatment, both surgical and percutaneous, has little or no role.

Vasculitis

The vasculitic syndromes are quite heterogeneous in their pathophysiology, clinical presentation, and consequences. The systemic necrotising vasculitides (eg, polyarteritis nodosa, Wegener's granulomatosis) and the hypersensitivity vasculitides can occasionally cause symptoms of claudication, but more often they are associated with cutaneous manifestations or signs and symptoms of systemic involvement.

Vasospastic diseases

Vasospastic diseases can produce transient ischaemic symptoms in the extremities, particularly involving digits. Most of these abnormalities are related to, or exacerbated by, cold exposure. Raynaud's syndrome may be idiopathic or occur in a range of collagen, vascular, hypercoagulable, malignant, ischaemic, drug-related or metabolic syndromes.

Although most 'attacks' are mild, patients with severe Raynaud's occasionally present with ulceration or gangrene due to prolonged vasospasm. Treatment of Raynaud's and other vasospastic disorders is aimed at local (warming the extremity) and pharmacological measures that facilitate vasodilation.

Popliteal artery entrapment syndrome

This syndrome is caused by a congenital abnormality in the relationship between the popliteal artery and the medial head of gastrocnemius muscle. It may be present without symptoms or cause either acute or chronic lower limb ischaemia. The diagnosis should be considered in active people who present with exercise-induced calf claudication.

Normal ankle pulses are present with the ankle in extension but become decreased or absent when the ankle is flexed. Angiography demonstrates segmental occlusion of the medial segment of popliteal artery, medial deviation, post-stenotic dilation or popliteal aneurysm formation.

Treatment consists of operative release of the entrapped artery, thrombolysis of occluded segments and/or vein bypass grafts for symptomatic individuals as well as asymptomatic patients at risk for severe limb-threatening ischaemia.

Fibromuscular dysplasia

Fibromuscular dysplasia is a congenital hyperplastic disease that affects medium and small arteries (usually the renal, carotid, subclavian and iliac arteries), causing serial eccentric stenoses and dilation of the diseased arteries. Coronary and mesenteric arteries are infrequently involved. It is more prevalent in young adults aged 20-40, especially women.

Presenting features depend on the region involved. Classic angiographic appearance is a 'string of beads', with focal stenoses and post-stenotic dilation. Treatment is angioplasty of the affected vessel in symptomatic patients.

Hypercoagulable states

Hypercoagulable states may present with clinical features of arterial insufficiency. Some (eg, hyperhomocysteinaemia) are associated with premature onset of peripheral atherosclerosis and, secondarily, predisposition to thrombosis.

Others, including the primary hypercoagulable states (eg, antithrombin III deficiency, protein C or S deficiency) and antiphospholipid antibody syndrome, predispose patients to early thrombosis of arterial grafts and veins.

The therapeutic approach to these patients includes early recognition of the abnormality and judicious use of anticoagulants and/or antiplatelet agents.

The future

In the future, invasive therapy for PAD will continue to shift toward a predominantly percutaneous, as opposed to surgical, approach. As interventions become more effective and safe, the threshold for treatment will be lowered and the number of percutaneous interventions will rise.

For patients who have had to opt for amputation in the absence of viable options for conventional revascularisation, the possibility of encouraging the formation of new vascular conduits by introducing angiogenic factors or stem cells may offer new hope for limb salvage.

Author's case study

Early revascularisation is essential for limb salvage

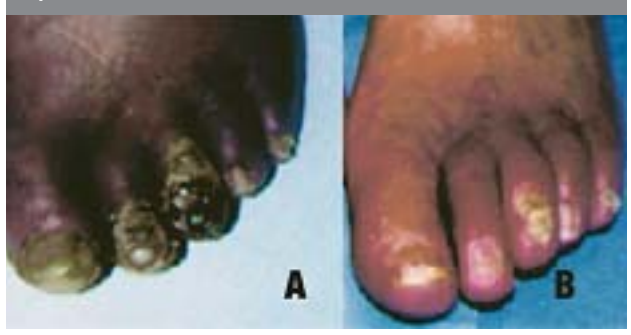
MR JW, 76, has a background of diabetes, dyslipidaemia, hypertension, coronary artery disease with stable angina, asymptomatic carotid artery disease, hyperuricaemia and essential thrombocythaemia. He was referred by his GP for vascular assessment of gangrenous toes.

He had a 3-6-month history of pain in the left foot at rest, with progression to severe nocturnal pain requiring narcotic analgesics over the last month. He developed traumatic pressure-related ulcers of the toes, which became infected and necrotic (figure 9A). He was unable to walk. Glycaemic and hypertension control were poor.

Immediate management consisted of urgent admission to hospital for strict bed rest, IV antibiotics and SC low-molecular-weight heparin.

Platelet count was 578 × 10^9/L. There was a neutrophil leucocytosis and mild normochromic normocytic anaemia. Lower-limb arterial Doppler ultrasound revealed ABIs of 0.33 and 0.76 on the left and right, respectively, at rest.

Figure 9: A: Mr JW's left foot, with necrotic ulceration of three toes, ischaemic rubor, atrophic skin and loss of hair. B: The left foot of the same patient three months after percutaneous revascularisation. Note the healing of necrotic ulceration and improved skin colour.



Duplex ultrasound of the left leg showed patent common femoral and superficial femoral arteries and a 50% lesion in the popliteal artery. The tibio-peroneal trunk was patent. The anterior tibial artery was not continuous and the peroneal and posterior tibial arteries were not visualised.

Left lower-limb diagnostic angiography showed diffuse plaque throughout the superficial femoral artery, 50% stenosis of the popliteal artery, 50% stenoses of the tibio-peroneal trunk, occluded posterior tibial artery, occluded peroneal artery and subtotal occlusion of the anterior tibial artery (figure 10A).

Immediate revascularisation of the popliteal artery and infrapopliteal vessels was performed percutaneously. Full anticoagulation with IV heparin was continued. Angioplasty was performed, restoring luminal patency to the three infra-popliteal vessels, and additional angioplasty was performed to the above-knee popliteal segment (figure 10B).

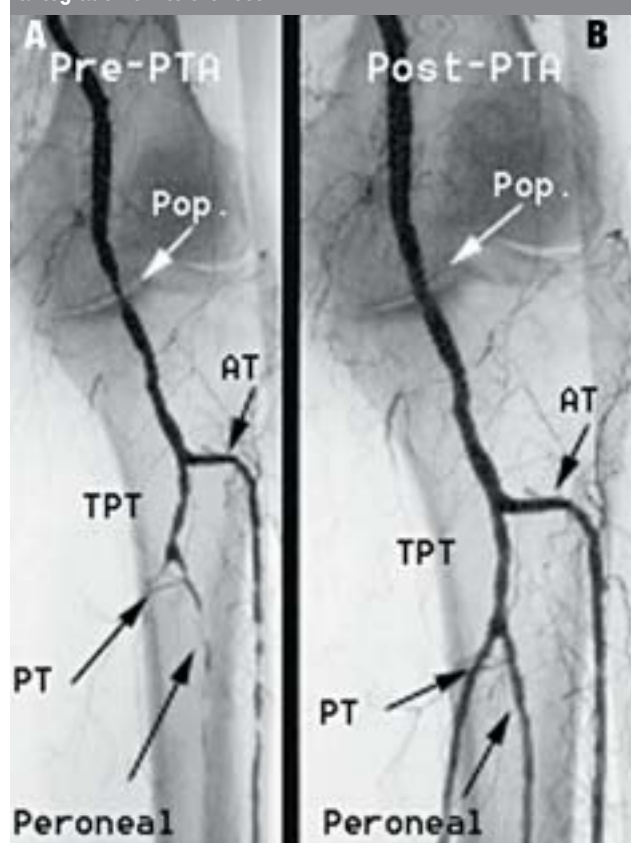
Post-procedure ABI was 1.06 and both posterior tibial and dorsalis pedis pulses were palpable. Anticoagulation was continued for 72 hours and antiplatelet therapy was started. Oral antibiotics were continued after discharge from hospital.

After three months there was healing of the necrotic toes and resolution of ischaemic rest pain (figure 9B). At 12 months' follow-up, ankle pulses were palpable and the resting ABI was 0.96. Duplex ultrasound confirmed patency of all three infra-popliteal vessels, with minor restenosis of the popliteal artery.

Comment

This case highlights critical limb ischaemia, a common complication of PAD in the setting of diabetes. Prompt management with antibiotics, anticoagulation and restoration of pulsatile flow by percutaneous methods allows healing of necrotic tissue and avoids amputation.

Figure 10: A: Pre-PTA DSA image of Mr JW's left lower leg, showing 50% stenosis of the popliteal artery, 50% stenoses of the tibio-peroneal trunk, occluded posterior tibial artery, occluded peroneal artery and subtotal occlusion of the anterior tibial artery. B: Post-PTA DSA after percutaneous revascularisation of the popliteal artery, tibio-peroneal trunk and all three infrapopliteal run-off vessels, with restoration of antegrade flow to the foot.



GP's contribution

DR DAMIEN BRAY
Cronulla, NSW

Case study

GEOFFREY is a 58-year-old heavy smoker, and in the course of attending for a (rare) annual checkup, mentions some recent episodes of "terrible pain" in his left foot while golfing. He asks if he might have gout, like his golfing partner, and whether he should have his foot X-rayed.

On closer questioning, the only time Geoffrey has experienced this pain is on the golf course — he does no other exercise. The pain is described as a "severe ache in the middle of the foot" and only occurs on the longer holes. "I'm fine on the par 3s," he says. The pain resolves quickly with rest. New golf shoes made no difference.

Geoffrey's blood pressure is 150/90mmHg, his BMI is 32, and a lipid profile two years ago revealed total cholesterol 6.5mmol/L, HDL 1.1mmol/L, and LDL 4.5mmol/L. Fasting glucose was 5.9mmol/L. All peripheral pulses were palpable except for the left pedal pulses.

Questions for the author

What further history would be useful in Geoffrey's case?

Does the pain occur on walking in day-to-day activities? Are the symptoms worse on hills? Has there been any rest pain of a similar but less intense nature? Is there a history of trauma or chronic back problems, sciatica or generalised arthritis? Is the pain on the dorsum or plantar aspect of the foot? Are there associated paraesthesiae?

What is the differential diagnosis?

Atherosclerotic PAD should be considered strongly, given the absence of pedal pulses and the multiple atherosclerotic risk factors, particularly smoking, hypertension and dyslipidaemia.

The absence of pedal pulses suggests infrapopliteal disease alone (although this would be unusual in the absence of diabetes) but the pedal pulses may also be absent in multi-segmental disease involving the iliac vessels or femoral vessels. The presence of a palpable pulse does not indicate that it is normal and it may be reduced compared with the same pulse on the other leg.

The differential diagnoses should also include Buerger's disease, given the history of heavy smoking, although this would be an unusual presentation. You should also consider a musculoskeletal problem related to the ankle or forefoot, or possibly plantar fasciitis as well as neurospinous disease.

The ankle-brachial pressure index (ABI) is a useful gauge to the degree of arterial insufficiency. Can a GP record this in the surgery using a standard sphygmomanometer? What type of BP cuff should be used and at what site on the leg? How should the patient be positioned? Can the auscultatory method be used and, if so, at which artery?

The ABI can be recorded in the GP's office using a standard sphygmomanometer, with the patient lying horizontal and a standard cuff placed around the lower calf, leaving about 2-3cm above the medial malleolus.

However, the auscultatory method with a stethoscope is not suitable. The arterial pulse is best detected with either a 5MHz or 8MHz Doppler probe over either the dorsalis pedis or posterior tibial artery, but I recommend obtaining ankle pressures at both arteries.

What investigations does Geoffrey need, and over what time frame?

To evaluate the presence of PAD, the patient should have resting and exercise ABIs as well as a duplex ultrasound of the femoropopliteal and infrapopliteal arteries on the symptomatic leg. There is no rest pain so there is no urgency. However, if the patient has significant infrapopliteal disease, earlier revascularisation would be indicated.

Geoffrey has multiple atherosclerotic risk factors and should therefore also undergo complete cardiovascular assessment including coronary, renal and carotid circulations, as well as assessment of the effects of hypertension and smoking.

He should also have X-rays of the foot and ankle to exclude any mechanical pathology, routine blood testing and testing specifically for acute inflammatory markers, uric acid and rheumatoid factor.

General questions for the author

Rest pain in chronic critical limb ischaemia is usually worse at night. How can this be clinically differentiated from pain of neurospinous origin?

Ischaemic rest pain is often relieved with the limb placed in a dependent position (ie, downwards). Therefore, the patient may gain relief if the foot of the bed is lowered or if they hang their foot over the side of the bed. Also, patients often cannot tolerate contact of the bedclothes with their feet. In contrast, neurospinous pain will not change with this type of manoeuvering.

Furthermore, patients with critical limb ischaemia will have the other hallmarks of severe arterial insufficiency, namely, absent or reduced pulses, rubor, atrophic skin and nail changes.

In what cases of PAD would magnetic resonance angiography be a useful investigation?

MRA is accurate for assessing all lower extremity arteries, specifically for detecting stenoses of >50%; three-dimensional gadolinium enhancement improves the diagnostic performance.

Advancement in techniques have resulted in accuracy of MRA comparable to that of conventional arteriography or digital subtraction angiography for assessing lower-extremity arteries, particularly the infrapopliteal vessels. However, revascularisation outcomes based on MRA versus conventional angiography will determine the best diagnostic method.

How To Treat Quiz

Peripheral arterial disease — 13 May 2005

INSTRUCTIONS

Complete this quiz to earn 2 CPD points and/or 2 PDP points by marking the correct answer(s) with an X on this form. Fill in your contact details and return to us by fax or free post.

FAX BACK	FREE POST	ONLINE
Photocopy form and fax to (02) 9422 2844	Australian Doctor Education Reply Paid 60416 Chatswood DC NSW 2067	www.australiandoctor.au/cpd for immediate feedback

1. Which TWO statements about PAD are correct?
- ❑ a) Diastolic hypertension is a better predictor of PAD than systolic hypertension
- ❑ b) PAD is twice as common in people with diabetes
- ❑ c) Dyslipidaemia increases the rate of progression of PAD
- ❑ d) Tobacco smoking is the single most significant risk factor in PAD

2. Trevor, 75, has exercise-induced thigh and calf pain. Which ONE feature would alert you to the possibility that the claudication is a result of PAD and not secondary to neurospinous disease?
- ❑ a) Leg clumsiness and weakness
- ❑ b) Pain with standing
- ❑ c) Pain relieved rapidly by rest
- ❑ d) Variation in the distance walked before pain begins

3. Trevor has absent ankle pulses and a right femoral bruit. His ABI is 0.8 bilaterally. Which THREE statements about the information provided by an ABI are correct?
- ❑ a) An ABI has a prognostic value in determining both limb survival and survival for all-cause mortality
- ❑ b) It can differentiate stenosis from occlusion
- ❑ c) It is a sensitive indicator of the degree of arterial insufficiency
- ❑ d) It is useful for functional assessment in conjunction with treadmill exercise testing

4. Which TWO treatments may increase Trevor's exercise capacity?
- ❑ a) Oxpentifylline (Trental)
- ❑ b) Regular exercise
- ❑ c) Antiplatelet therapy
- ❑ d) Vasodilators such as calcium-channel blockers

5. George, 82 with a past history of cerebrovascular disease and smoking, has chronic critical limb ischaemia. He has developed rest pain and a punched-out ulcer on the dorsum of his foot. Superficial femoral artery stenosis is identified on angiography. Which ONE procedure may improve limb survival with minimal risk to the patient?
- ❑ a) Lumbar sympathectomy
- ❑ b) Endovascular therapy
- ❑ c) Surgical recanalisation
- ❑ d) Laser angioplasty

6. George is concerned about the incidence of re-stenosis after endovascular therapy. Which THREE statements about re-stenosis are correct?
- ❑ a) Clopidogrel is used for six months after stent insertion to reduce the risk of re-stenosis
- ❑ b) Healing of the ulcer will typically occur if the artery remains patent for 3-6 months
- ❑ c) If re-stenosis occurs, amputation is the only solution
- ❑ d) Risk factors for PAD should be strictly controlled

7. In which TWO ways should George's leg be managed?
- ❑ a) Meticulous care is necessary to prevent pressure sores
- ❑ b) Topical antibiotics should be applied to any ulcerated areas
- ❑ c) Compression stockings should be used to reduce the risk of DVT
- ❑ d) Topical nitrates may be helpful

8. Vince, 72, has atherosclerosis and presents with an acutely ischaemic lower leg. The ankle pressure is <40mmHg and there is evidence of slow capillary return and mild sensory and motor loss. However, there is an audible venous Doppler and the limb is not considered to be irreversibly threatened. What is the most important part of the initial management (choose ONE)?
- ❑ a) Angiography
- ❑ b) Surgical revascularisation
- ❑ c) Anticoagulation
- ❑ d) Elevate the limb

9. Vince has percutaneous catheter-based thrombolytic therapy. Which ONE statement about this therapy is correct?
- ❑ a) If restenosis occurs after percutaneous therapy, repeat percutaneous intervention can be considered
- ❑ b) Thrombolytic agents are given IV
- ❑ c) The procedure needs to be done within 24 hours
- ❑ d) This is the treatment of choice for an irreversibly threatened limb

10. Which TWO statements about thromboangiitis obliterans (Buerger's Disease) are correct?
- ❑ a) Antiplatelet therapy is useful in management
- ❑ b) It mostly affects men >50 who smoke
- ❑ c) Angiography demonstrates normal proximal blood vessels
- ❑ d) Invasive treatment (surgical or percutaneous) is very important in the management

CONTACT DETAILS

Dr: ..... **Phone:** ..... **E-mail:** .....

RACGP QA & CPD No: .....**and /or ACRRM membership No:** .....

Address: ..... **Postcode:** .....

Australian Doctor Education.

HOW TO TREAT Editor: **Dr Lynn Buglar**
Co-ordinator: **Julian McAllan** Quiz: **Dr Marg Tait**

The mark required to obtain points is 80%. Please note that some questions have more than one correct answer. Your CPD activity will be updated on your RACGP records every January, April, July and October.

NEXT WEEK The next How to Treat is on the aetiology, diagnosis and management of bronchiectasis. The authors are **Dr Paul King**, respiratory physician, Monash Medical Centre, Clayton, and Dandenong Hospital, Dandenong, and senior lecturer, Monash University, Vic; and **Associate Professor Peter Holmes**, respiratory physician and deputy director, respiratory medicine, Monash Medical Centre, Clayton, Vic.