Peripheral arterial disease (PAD) is a common circulatory disease in which arteries are narrowed due to atherosclerotic plaques, causing reduced blood flow (ischaemia) to muscles and other tissues of the legs or arms. Often the term PAD is used to describe symptoms occurring in the lower legs, as these are the most common. At times, however, the term lower limb peripheral arterial disease is used to distinguish occlusion of the lower limbs from wider peripheral arterial disease.

**Classification of PAD**
The Fontaine scheme classifies PAD into four stages depending on severity:

- **Stage I: asymptomatic disease** – patients will not have symptoms of PAD; however, the disease may be suspected after clinical examination and diagnostic tests
- **Stage II: intermittent claudication** – patients will have discomfort in the calf muscles with exertion that resolves after a few minutes of rest
- **Stage III: ischaemic rest pain** – patients will have progressive development of pain in the lower extremity at rest; additional symptoms outlined below may also be present
- **Stage IV: necrosis** – also referred to as ulceration and gangrene – patients may have constant pain in the lower extremity at rest; they can also have non-healing wounds on the foot or calf, which may include skin ulceration or tissue necrosis.

PAD can be defined as acute or chronic. If onset is rapid, it is often classified as acute limb ischaemia (ALI). ALI results in an abrupt decrease in arterial perfusion of a limb. There is a range of potential causes, including trauma, cardiac embolism or thrombosis. The treatment of ALI is classified as an emergency in order to save the limb. The time between the onset of symptoms to irretrievable damage to the leg is variable, but may be as little as six hours. ALI is classified according to the prognosis of the limb:

- **no immediate threat**
- **salvageable if promptly treated**
- **salvageable if promptly revascularised**
- **major tissue loss with permanent nerve damage.**

Chronic limb ischaemia can present as either intermittent (pain in the lower limbs in response to exercise) or critical (impaired circulation, meaning there is imminent risk of limb loss).

**Prevalence of PAD**
It has been estimated that 202 million people worldwide are affected by PAD, with approximately 40 million living in Europe. From 2000 to 2010 there was a 23% increase in incidence as a result of population increase, global ageing and increased incidence of diabetes and smoking in low- and middle-income countries. Although limited data is available, this increasing trend is likely to continue.

**Risk factors for PAD**
The risk factors for PAD are similar to those for other cardiovascular/atherosclerotic diseases, such as heart attack or stroke.

- **Smoking** – this is a strong risk factor for PAD, with risk increasing with smoking intensity. The risk persists even after smoking cessation; however, it falls after 10 smoke-free years
- **Hyperlipidaemia** – high low-density lipoprotein (LDL) and low high-density lipoprotein (HDL) cholesterol is associated with increased risk for PAD
- **Hypertension** – high blood pressure is a strong predictor of incidence and outcome of acute and chronic PAD
- **Diabetes** – this is strongly associated with PAD. Risk increases with diabetes duration, and is linked to higher mortality and amputation rates
- **Obesity** – poor dietary habits and a sedentary lifestyle may contribute to overall PAD risk
- **Male gender** – in high-income countries, PAD, especially symptomatic PAD, is more prevalent in men
- **Age** – PAD usually appears in people aged over 50 years, with an exponential increase
The patient's ankle brachial pressure index (ABPI) should be determined when diagnosing PAD, which disappears after a few minutes' rest (intermittent claudication). Both legs are often affected; however, the pain may be worse in one leg, progressing to foot pain at rest, which may be worse at night.

- numbness or weakness in the legs
- hair loss on the legs or feet
- brittle, slow-growing toenails
- non-healing ulcers on legs or feet
- abnormal skin colour (pale or bluish) or shiny skin
- muscle wasting
- erectile dysfunction, especially men with diabetes.

The signs and symptoms of PAD vary from patient to patient. It is possible to have severe disease without symptoms – some patients may not walk far enough to reveal symptoms (eg those with heart failure), while others may have reduced pain sensitivity (eg diabetic neuropathy).

Usually, patients with intermittent claudication who present in a pharmacy setting should be referred to their GP.

The symptoms of chronic limb ischaemia often develop slowly over time and may include:
- ache or cramp-like pain in the calf on walking,
- pain
- pale skin
- pulseless leg/foot
- extreme cold.

Diagnosis of PAD

Evaluation of a patient with suspected PAD should start with a clinical history, a review of their symptoms and a physical examination. This examination is fundamental, but the diagnosis must be confirmed by objective tests.

The patient's ankle brachial pressure index (ABPI) should be determined. This is a simple test that can be carried out in a doctor’s office. It involves measuring the blood pressure in both the ankle and upper arm (brachial), before calculating the ABPI for each leg by dividing the highest ankle pressure by the highest arm pressure. An ABPI <0.9 is abnormal and indicates PAD. An ABPI between 0.7 and 0.9 is considered mild disease, while 0.5 and 0.69 is moderate, and less than 0.5 is severe.

Additional hospital-based tests may be required, such as:
- ultrasound – this should be offered to all patients with PAD for whom revascularisation is being considered. It will identify the site and extent of any blockages
- angiography – when further imaging is required, contrast-enhanced magnetic resonance (MR) or a computed tomography (CT) angiography may be offered.

What other conditions could PAD be confused with?

Alternative diseases that present with similar symptoms include:
- Baker’s cyst – this presents with swelling and tenderness behind the knee and down the calf; symptoms are present at rest and while exercising
- venous claudication – symptoms include tight, bursting pain in the entire leg, which is worse in the calf; symptoms are worst after walking, and can subside slowly, with relief speeded by elevation of the leg
- arthritis – hip, foot or ankle arthritis may cause variable amounts of discomfort or pain after exercise; the pain is not relieved quickly on resting, but may be relieved by not bearing weight
- nerve root compression (sciatica) – nerve compression may cause sharp pain that radiates down the leg, which may be induced by sitting, standing or walking; pain can be present at rest and may be improved by repositioning
- diabetic neuropathy – nerve damage caused by high glucose levels can present as pain and numbness in the legs and feet.

Prognosis for PAD

Studies have shown that patients with PAD have increased mortality and morbidity.

In most people with intermittent claudication, the symptoms remain stable with treatment, but patients may develop increasingly severe symptoms, with 21% developing critical limb ischaemia, of whom up to 27% have amputations.

Additionally, patients with PAD symptoms have an approximately 3-fold risk of major cardiovascular events, such as heart attack or stroke.

Management of PAD

Mild symptoms are generally managed in primary care by the patient’s GP; however, referral to a multidisciplinary secondary care team for more extensive treatment may be necessary if symptoms do not resolve or deteriorate. PAD treatment has two main aims:

- reducing a patient’s symptoms and improving quality of life
- reducing a patient’s overall cardiovascular morbidity and mortality.

The treatments outlined below focus on improving limb symptoms and salvaging the limb. Additional pharmacological treatments (eg statins) to reduce general cardiovascular issues may also be indicated, but are not discussed here.
Management of intermittent claudication

Exercise
Structured exercise therapy is an important aspect of care for patients with PAD. Patients with intermittent claudication should be offered a place in a supervised exercise programme, which generally involves two hours of supervised exercise a week for a three-month period. Patients should be advised to exercise to the point of maximal pain.

Angioplasty and stenting
Angioplasty is the process of using a balloon to widen a narrowed or blocked artery. Often the angioplasty procedure also includes inserting a stent into the artery to allow blood to flow more freely. Angioplasty should be offered only when risk factor reduction has been reinforced, the supervised exercise programme has not improved symptoms and imaging tests have confirmed that angioplasty is suitable for the patient.

Bypass surgery
This involves attaching a blood vessel, taken from another part of the body, above and below the narrowed or blocked section of the artery. Bypass surgery should be offered only to patients with severe lifestyle-limiting intermittent claudication and when angioplasty has been unsuccessful or is unsuitable.

Naftidrofuryl oxalate
The drug is a powerful vasodilator with an antagonist effect on 5-HT2 receptors of the smooth muscle cells. It may be considered for patients when supervised exercise has not led to satisfactory improvement, and the patient prefers not to be referred for angioplasty or bypass surgery. For PAD, a dosage of 100-200mg three times a day is recommended. Caution should be taken regarding patients with renal or hepatic disorder, as the drug is metabolised by the liver and excreted mainly in urine. Progress should be reviewed after three to six months and naftidrofuryl oxalate discontinued if there has been no symptomatic benefit.

Management of critical limb ischaemia
There are a range of options available to help manage critical limb ischaemia:

Revascularisation
In a similar manner to the treatment of intermittent claudication, angioplasty or bypass surgery should be considered.

Pain relief
Paracetamol, and either weak or strong opioids (depending on the severity), may be offered to relieve critical limb ischaemic pain. Laxatives and antiemetics may also be necessary to manage the adverse effects of the pain relief medication. Referral to a pain management specialist may be required.

Amputation
This is the last treatment option and should not be offered unless all other options for revascularisation have been considered.

Management of acute limb ischaemia
The therapeutic strategy and the emergency level depend on the clinical presentation and the classification.

Pharmacological treatment
Unfractionated heparin should be given along with appropriate analgesia.

Revascularisation
Multiple options are available for urgent revascularisation, including percutaneous catheter-directed thrombolytic therapy, percutaneous mechanical thrombus extraction, thromboaspiration or surgical thrombectomy.

Amputation
This may be necessary to prevent further damage if the limb is unsalvageable.

Complications of PAD
Disease progression and treatment interventions can cause additional complications to arise such as:
- chronic non-healing wounds – treatment should aim to achieve complete wound healing by: managing infections; using advanced wound care therapies; providing offloading support; surgery; or a combination
- surgical complications – such as wound infection
- mental health issues – depending on disease severity, patients with PAD may have a decreased quality of life due to pain or immobility; this can cause a variety of mental health issues, including depression.

Self-care tips
There is a range of advice and support that pharmacists and members of their teams can give to patients with PAD.
- Invite patients who smoke to participate in the pharmacy smoking cessation scheme
- Provide overweight patients with advice on diet and exercise, and refer to local weight management programmes
- Emphasise the benefits of lowering cardiovascular risk beyond the management of PAD
- Give advice on foot care, including how to keep feet clean to avoid infection and to avoid injury even when cutting the toenails
- Explain the importance of good glycaemic control and regular foot and leg examination (for non-healing wounds) to diabetic patients
- Advise patients to have their annual influenza vaccine
- Refer patients to sources of further information about their disease.

Knowing the symptoms of PAD and
Peripheral arterial disease CPD – planned learning

What are you planning to learn?
I want to learn more about peripheral arterial disease (PAD), including what it is and its risk factors, symptoms and diagnosis. I also want to learn about how PAD is treated and the possible complications, and improve my knowledge of the advice and support that pharmacists and their teams can give to patients.

This learning will help me to improve my knowledge of PAD and to be able to confidently provide better, more effective advice to the patients I serve in my pharmacy.

How are you planning to learn it?
• I plan to read more about PAD on the Patient website at tinyurl.com/peripheral1.
• I plan to read more about angioplasty, stenting and bypass surgery on the Circulation Foundation website at tinyurl.com/peripheral2.
• I plan to find out about useful sources of information and support for patients with PAD, such as the British Heart Foundation website at tinyurl.com/peripheral3.

Give an example of how this learning has benefited the people using your services
A patient previously diagnosed with PAD asked to speak to me, as his leg pain was getting much worse despite being on medication and taking part in a regular exercise scheme twice a week. He was worried he would not be able to continue his exercise class and get out and about, and feared being stuck at home on his own. I was able to advise him there were other treatment options and that it was important for him to make an appointment with his GP as soon as possible, before the symptoms became even worse.

References

Take the 5-minute test online

1. Intermittent claudication is defined as discomfort in the calf muscles on exertion that resolves after a few minutes of rest.
   - True or false
2. Causes of acute limb ischaemia include trauma, cardiac embolism and thrombosis.
   - True or false
3. The worldwide incidence of PAD increased by 36% between 2000 and 2010.
   - True or false
4. In high-income countries, symptomatic PAD is more prevalent in women than in men.
   - True or false
5. PAD usually appears in people aged over 50 years, with an exponential increase after 65 years.
   - True or false
6. Symptoms of chronic limb ischaemia include continuous pain in the calf, cold pale skin, paralysis and lack of pulse in the ankle or calf.
   - True or false
7. An ankle brachial pressure index between 0.7 and 0.9 indicates severe PAD.
   - True or false
8. In patients with intermittent claudication, 21% will develop critical limb ischaemia.
   - True or false
9. Patients with PAD symptoms have an approximately 3-fold risk of major cardiovascular events, such as heart attack or stroke.
   - True or false
10. Naftidrofuryl oxalate is recommended by Nice as first-line treatment for PAD along with an exercise programme.
    - True or false