Managing Raynaud’s phenomenon

As temperatures lower, pharmacists are more likely to encounter people with Raynaud’s phenomenon. Susan Allen explains...

Raynaud’s phenomenon was first described in 1862 by Maurice Raynaud. It is characterised by episodic spasming of the small blood vessels of the extremities. The fingers are most commonly affected, but vasospasm can also occur in the toes, nose, ears and, occasionally, the tongue and lips.

The vasospasm cuts off the blood supply in the affected fingers, resulting in whitening and pain. This is sometimes followed by cyanosis (the affected fingers turn blue) due to pooling of deoxygenated blood. An episode ends with vasodilation and reperfusion and the finger(s) turns red. This white-blue-red colour change is characteristic of the reversible local ischaemia but is not observed in all patients.

The ischaemic pain during an attack can be considerable and has been compared to plunging your hands into a bucket of icy water and holding them there. As blood flow returns, in the final stage, there is often tingling, throbbing, numbness and further pain. During an attack, hand function is limited. The vasospasm is thought to be an exaggerated response to cold or some other form of stress. Attacks are usually mild and last for a few minutes, but some people experience multiple and prolonged episodes, lasting hours.

When Raynaud’s symptoms first present, one or two fingers may be affected but, with time, all fingers tend to become involved. Episodes tend to be symmetrical, affecting each hand equally. Complications of the phenomenon include ulceration, scarring and pitting, and gangrene, but these are rare.

In over 90 per cent of cases there is no identifiable cause for the condition and this is termed primary Raynaud’s phenomenon (also sometimes referred to as Raynaud’s disease). If, however, the condition is due to an underlying disease (see Panel 1, p648, for examples), it is described as secondary Raynaud’s phenomenon. It has been estimated that scleroderma accounts for 65 per cent of secondary Raynaud’s phenomenon (see Panel 2, p648).

Raynaud’s symptoms can also be caused by exposure to vibration, known as “vibration white finger” (eg, in occupations that involve using pneumatic drills or chainsaws), prolonged cold (eg, in meat packers), or chemicals (eg, in the polyvinylchloride industry).

Raynaud’s phenomenon has been linked to some autoimmune diseases. Up to 5 per cent of patients with rheumatoid arthritis have Raynaud’s symptoms as do up to 30 per cent of people with systemic lupus erythematosus.

Drugs that can cause (or exacerbate) Raynaud’s phenomenon include some angiotensin-converting enzyme inhibitors (eg, enalapril and lisinopril) beta-blockers, some cytotoxics (eg, bleomycin, cisplatin)...

Identify knowledge gaps

1. What can cause Raynaud’s symptoms?
2. What practical advice can be offered someone with Raynaud’s phenomenon?
3. What drugs are used to manage Raynaud’s phenomenon?

Before reading on, think about how this article may help you to do your job better. The Royal Pharmaceutical Society’s areas of competence for pharmacists are listed in “Plan and record”, (available at: www.rpsgb.org/education). This article relates to “common disease states” and (see appendix 4 of “Plan and record”).

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www.pjonline.com
Connective tissue disease (eg, scleroderma, Sjögren’s syndrome, systemic lupus erythematosus, systemic vasculitis)

Autoimmune disease (eg, rheumatoid arthritis)

Obstructive arterial disease (eg, atherosclerosis, thromboembolism)

Neurological disorders (eg, carpal tunnel syndrome, multiple sclerosis)

Hyperviscosity disorders (eg, polycythaemia)

Miscellaneous (eg, neoplasms, primary pulmonary hypertension, hypothyroidism)

Infections (eg, bacterial endocarditis, viral hepatitis)

bromocriptine, clonidine, ergotamines, lisuride, methysergide, pergolide and sumatriptan. Other drugs that have been linked with Raynaud’s phenomenon include amphetamines, interferon-alpha, lithium and combined oral contraceptives.

The overall incidence of Raynaud’s phenomenon is 3–20 per cent of the adult population worldwide, with more women (over 90 per cent) affected than men. In the UK, around 10 per cent of women experience Raynaud’s phenomenon to some degree. Surveys of Scandinavian women aged 18 to 60 years suggest that higher numbers are affected — up to 22 per cent.

Typical age of onset is usually quoted as being in the teenage years or early twenties. However, a recent Bandolier look at 10 studies including 639 patients found the average age of onset of primary Raynaud’s phenomenon was 34 years.

Diagnosis

Diagnosis of primary Raynaud’s phenomenon in women under the age of 30 years following a detailed medical history is usually straightforward. However, if symptoms present in someone over the age of 30 (secondary Raynaud’s phenomenon tends to present later in life), especially in the presence of other factors, further investigations may be warranted to distinguish between primary and secondary disease. Other factors are:

- Abrupt onset with rapid progression
- Unilateral or asymmetrical vasospasm
- Symptoms of arthralgia or arthritis
- Skin rashes or photosensitivity
- Symptoms of palmar erythema
- Skin ulcers
- Muscle weakness or pain
- Swallowing difficulties
- Breathlessness
- MOUTH ULCERS

Investigations that can be undertaken to screen for underlying disease include:

- Nailfold capillary microscopy to look for any capillary abnormalities
- Erythrocyte sedimentation rate (ESR) to measure the degree of inflammation
- Antinuclear antibody test (ANA) to screen for the presence of antibodies found in connective tissue or other autoimmune disorders

Patients with primary Raynaud’s experience periodic vasospastic attacks precipitated by cold or stress. Their halffold capillaries are normal, as are their ESR and ANA results. Complications (eg, tissue death) are less likely in people with primary disease.

Since it is unlikely for symptoms to be evident at the point of consultation, it can be useful for patients to ask someone to photograph their hands (or other affected area) during an attack. Other conditions, such as chilblains (see Panel 3) can be confused with Raynaud’s phenomenon. People with continued episodes of suspected chilblains should be referred to their GP.

Management

Disease severity is assessed by enquiring about the frequency of episodes, the severity of ischaemia, the sites affected and impact on daily life. For most patients with primary Raynaud’s phenomenon, symptoms are mild and do not interfere with day-to-day living. And for two thirds of patients, symptoms are likely to resolve spontaneously.

A study following 1,358 patients with primary Raynaud’s phenomenon over seven years found that in 64 per cent of people, symptoms had remitted by the end of the study. However, 10 per cent of patients will develop some form of connective tissue disease within about 10 years of the onset of Raynaud’s phenomenon.

For all patients with Raynaud’s, non-pharmacological measures should be recommended and are sufficient to manage most cases. These are listed in Panel 4 (p650).

Drug treatment

When non-pharmacological strategies are insufficient and symptoms interfere with daily life, drug treatment should be considered. Treatment is usually more successful in people with primary disease.

Several drugs have been investigated for use in Raynaud’s phenomenon, but interpre-
**Panel 3: Chilblains**

Raynaud’s phenomenon can be confused with chilblains. Also called pernio or perniosis, these are small painful itchy swellings on the skin of the extremities that develop in response to cold and are most commonly seen on the fingers, toes, nose and earlobes, but particularly on the small toes. It is thought that around 10 per cent of the people in the UK suffer from chilblains at some stage in their life.

Chilblains occur as a result of an abnormal vascular reaction to cold and humidity, which limits blood supply to areas of skin. In predisposed individuals, they tend to appear several hours after the exposure to the cold — as the skin warms following cold exposure, there is some leakage of fluid into the tissues which causes local inflammation and swelling. This is more likely if the cold skin is warmed too quickly.

Some drugs (e.g., beta-blockers) cause peripheral vasoconstriction and so may predispose to chilblains.

**Symptoms**

Symptoms include:
- Small swellings, although they may be close together and merge into a larger swelling
- Itching
- Redness, but may become purple as time progresses
- Pain and tenderness
- Blistering and occasionally tissue break down to form an ulcer, which delays healing

**Treatment**

A chilblain usually disappears after one or two weeks. Some patients find lotions and creams containing, for example, witch hazel or calamine, soothing. According to the British National Formulary, topical circulatory preparations (e.g., Hirudoid) are of little value. Sometimes a steroid cream, such as betamethasone, is used to reduce inflammation.

**Prevention**

Keep extremities warm in cold weather — wear warm gloves and socks or insoles. Consider heated gloves if necessary, and ideally exercise before going into the cold to dilate blood vessels. Do not rapidly warm up hands and feet by putting them next to a direct heat source when coming in from the cold.

**Drug treatment is usually more successful in people with primary disease**

have shown some benefits in small studies. Verapamil and diltiazem are not recommended because their main site of action is on myocardial tissue and they have a lesser effect on the peripheral vasculature.

**Licensed drugs**

Other peripheral vasodilators such as naftidrofuryl and inositol nicotinate are sometimes used but are of uncertain value. They may have application in those who are intolerant to calcium antagonists. Pentoxifylline, prazosin and moxisylyte are also licensed for use in Raynaud’s, but are not established as being effective.

**Unlicensed drugs**

ACE inhibitors (despite the fact that some cause Raynaud’s symptoms) and angiotensin-II receptor antagonists may provide some small benefits in Raynaud’s phenomenon. There is no evidence to suggest that they are more effective than calcium channel blockers. In trials investigating its short-term use, losartan has shown benefits in Raynaud’s symptoms in patients with scleroderma. Long-term use is yet to be investigated.

The effect of the serotonin reuptake inhibitor fluoxetine, has been investigated. Serotonin causes vasoconstriction so by reducing serotonin levels, some vasodilation is achieved. Results to date have been promising but more evidence is needed.

Prostaglandin E1 and prostacyclin are potent vasodilators and inhibit platelet aggregation. The prostacyclin analogue iloprost (with a half-life 10 times that of prostacyclin) has been used on a named-patient basis to manage severe Raynaud’s symptoms, particularly in patients with scleroderma. It has been shown to reduce both frequency and severity of symptoms.
Stop smoking. Nicotine causes vasoconstriction and smoking can make symptoms worse (smoking a cigarette can cause a reduction in fingertip temperature of 2–3°C). Caffeine can trigger symptoms. Avoid beverages containing caffeine for a few weeks to see if symptoms improve.

Keep warm in cool and cold conditions. (Wear gloves, socks and shoes when outside in cold weather. Make sure gloves are put on before going out. It may help to keep gloves and socks on a radiator so they are warm when they are put on. Hairdryers can be a quick and easy way to warm gloves and socks before going out. Wear several layers of clothing—thermal fabrics can help—and a hat to maintain the body’s core temperature.)

After a bath, leave the water in the tub in while dressing—it will give off enough heat to keep you warm.

For people with severe symptoms, portable heat packs, battery powered heated or micro- and macrovascular dilating properties of sildenafil have shown promising results in accelerating digital ulcer healing rates in scleroderma patients with Raynaud’s symptoms. In a trial, 50mg bd of sildenafil, given for four weeks, gave clear improvement of symptoms.

Food supplements A number of food supplements have been proposed as being beneficial in Raynaud’s phenomenon, including antioxidants and fish oils. The World Health Organization has recommended the use of Ginkgo biloba in the treatment of Raynaud’s. Ginkgo biloba 120mg tds, was effective in reducing the number of attacks of Raynaud’s compared with placebo. The supplement was well tolerated by patients.

Surgery For patients with severe symptoms and who do not respond to other treatments, a sympathectomy — cutting the nerves that supply the affected part — may be performed.

Crisis in the event of an acute ischaemic crisis (ie, where there is danger of the loss of tissue), the person should be directed to hospital immediately. Treatment includes vasodilatation (eg, intravenous infusion of iloprost, oral nitidipine), pain relief (eg, lidocaine or bupivacaine), surgery and anticoagulation (eg, low-dose aspirin or short-term heparin if there is persistent critical ischaemia or occlusive disease of large arteries). Ischaemic crises are rare and most likely in patients with scleroderma.

Conclusion For most people, primary Raynaud’s phenomenon is more an annoyance than a serious illness. It can usually be managed with lifestyle changes although some people need pharmacological intervention. Secondary Raynaud’s phenomenon can be more difficult to manage and has a poorer prognosis, but drug treatment may help reduce the frequency or severity of attacks. Pharmacists can play a role by:

- Recognising symptoms and referring where appropriate
- Ensuring people (serious circulatory problems are uncommon)
- Being aware of drugs that can cause or worsen symptoms
- Giving advice on non-pharmacological strategies

**References**


**Resources**

- The Raynaud’s and Scleroderma Association (www.raynauds.org.uk) provides support for patients and publications for health professionals.
CORRECTION
(17 December 2007)

On p650, top left hand corner, after "It is usually given as a six-hour intravenous infusion at a dose of 2ng/kg on three consecutive days".

The note should say:

This should read 2ng/kg/min and not 2ng/kg. Schering Health advises that the dose is adjusted according to individual tolerability within the range of 0.5 to 2.0 ng/kg/min over six hours daily. Treatment periods of three to five days are often sufficient in Raynaud's phenomenon to achieve improvement over several weeks.