Vasospastic Syndromes

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Nomenclature

Raynaud's phenomena (RP)

a blanket term used to describe all vasospastic disorders.

Primary Raynaud's disease (RD)

vasospastic symptoms manifested on their own without any underlying systemic disease process.

Secondary Raynaud's syndrome (RS)

vasospasm associated with another known

disease entity.

Raynaud's phenomenon

- A clinical state characterised by episodic vasospasm
- Usually involving the distal small arteries of the upper limb although sometimes toes and feet
- Characterized by inflammatory changes in the arterial wall (Vasculitis)
- Maurice Raynaud first described this clinical picture in 1862.

The classical presentation

A sequence of colour changes in the following order:

Pallor, reflecting initial vasospasm.

Cyanosis, as a result of deoxygenation of stagnant blood during maximum vasospasm

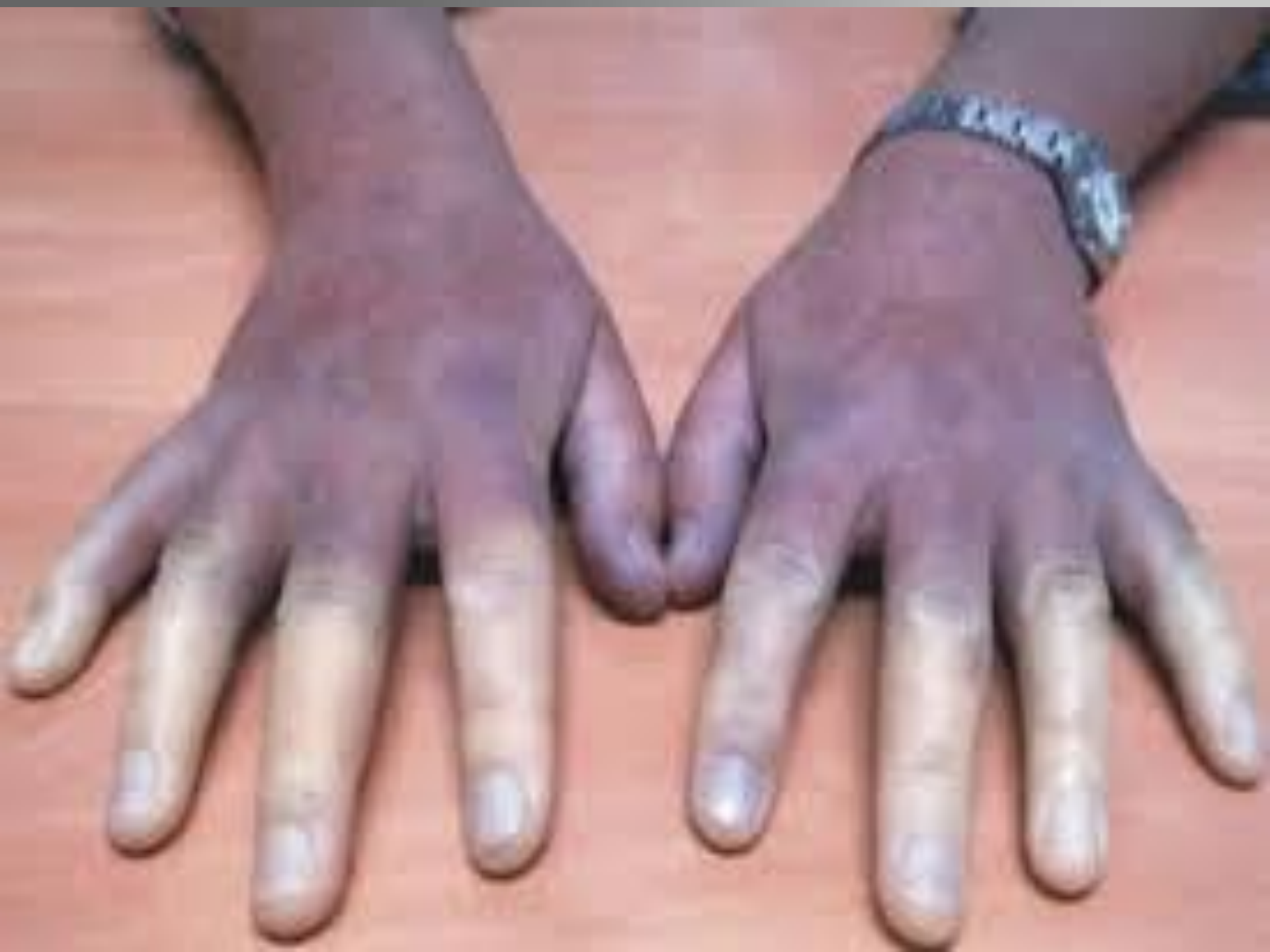
Rubor, representing inflow of oxygenated blood and reactive hyperaemia as the vasospasm subsides.

last for 30–60 min.

Some patients present with only cold hands and do not exhibit the classical triple colour response although they demonstrate a similar blood flow pattern to classical vasospasm

Epidemiology

- **11.8% of population**
- **women** affected nine times more often than men.
- A **familial** predisposition
- Over 50% of people using these tools may ultimately show symptoms of the disease.



White color of the finger in Raynaud's Disease.

The factors triggering

Factors provoking a vasospastic episode

- Cold exposure
- Emotional stress
- Vibration – hand arm vibration syndrome (HAVS)
- Industrial chemicals
- Tobacco smoke
- Trauma
- Drugs

Parts of the body affected by vasospasm

- Fingers (commonest)
- Toes
- Nose
- Ear lobes
- Tongue
- Nipples

Pathophysiology

Although the exact mechanism of RP is not completely understood, a number of key factors are implicated in its aetiology and pathogenesis. These include: ***a complex interaction of:***

1. ***Neurogenic alterations***
2. ***Haemodynamic changes***
3. ***Inflammatory and immune regulation***
4. ***Mechanical***
5. ***Genetic predisposition***

Neurogenic alterations

Patients with RP have an increased sensitivity to cold and show increased vasospastic tone in response to cold exposure and other triggering factors.

This vascular neurogenic response can occur in The absence of an obstructive arterial lesion.

The vasospastic response is explained on the basis of enhanced sensitivity of both alpha and beta adrenergic receptors in the peripheral sympathetic nervous system controlling the arterial tone.

Haemo-dynamic changes

Changes in blood and blood components:

- Platelet activation and aggregation leads to formation of platelet plugs
- Causing obstruction to the blood flow and release of thromboxane A2 resulting in vasospasm.
- Activated leukocytes release free radicals causing further vasoconstriction.
- Red cells become stiff and obstruct the vessel lumen resulting in further obstruction to microcirculation.
- Plasma viscosity is increased as a result of an increase in plasma proteins.

Changes in endothelial function:

- Patients with RP show signs of endothelial dysfunction, such as activation of von Willebrand factor (VWF), which promotes clotting and activates platelets.
- Tissue plasminogen activator (tPA) activity is reduced, resulting in less effective fibrinolysis and a prothrombotic state in patients with RP.

Clinical presentation

- Episodic with each episode lasting from a few minutes to an hour.
- Triggered by exposure to cold or emotional upset.
- Usually fingers and sometimes toes are affected.
- The distribution of involved digits
- Could be asymmetrical with one or more digits affected at one time although all digits can be affected in one particular patient.
- Involvement of one limb only suggests a possible local cause such as a cervical rib.
- Patients either show a biphasic or triphasic response of colour changes or associated symptoms.

Disorders associated with secondary Raynaud's syndrome

Connective tissue diseases (CTD)

- Systemic sclerosis
- Systemic lupus erythematosis
- Henoch–Schönlein purpura
- Scleroderma (CREST* syndrome)
- Sjögren's syndrome
- Rheumatoid arthritis
- Mixed connective tissue disease

Obstructive

- Atherosclerosis
- B uerger's disease (thromboangitis obliterans)
- Microemboli
- Thoracic outlet syndrome (cervical rib/band)

Myeloproliferative disorders

- Leukaemia
- Myeloid metaplasia
- Polycythemia rubra vera

Drugs

- β-blockers
- Cytotoxic drugs
- Anti-migraine drugs including ergotamine

Industrial

- Hand arm vibration syndrome
- Vinyl chloride
- Frozen food workers

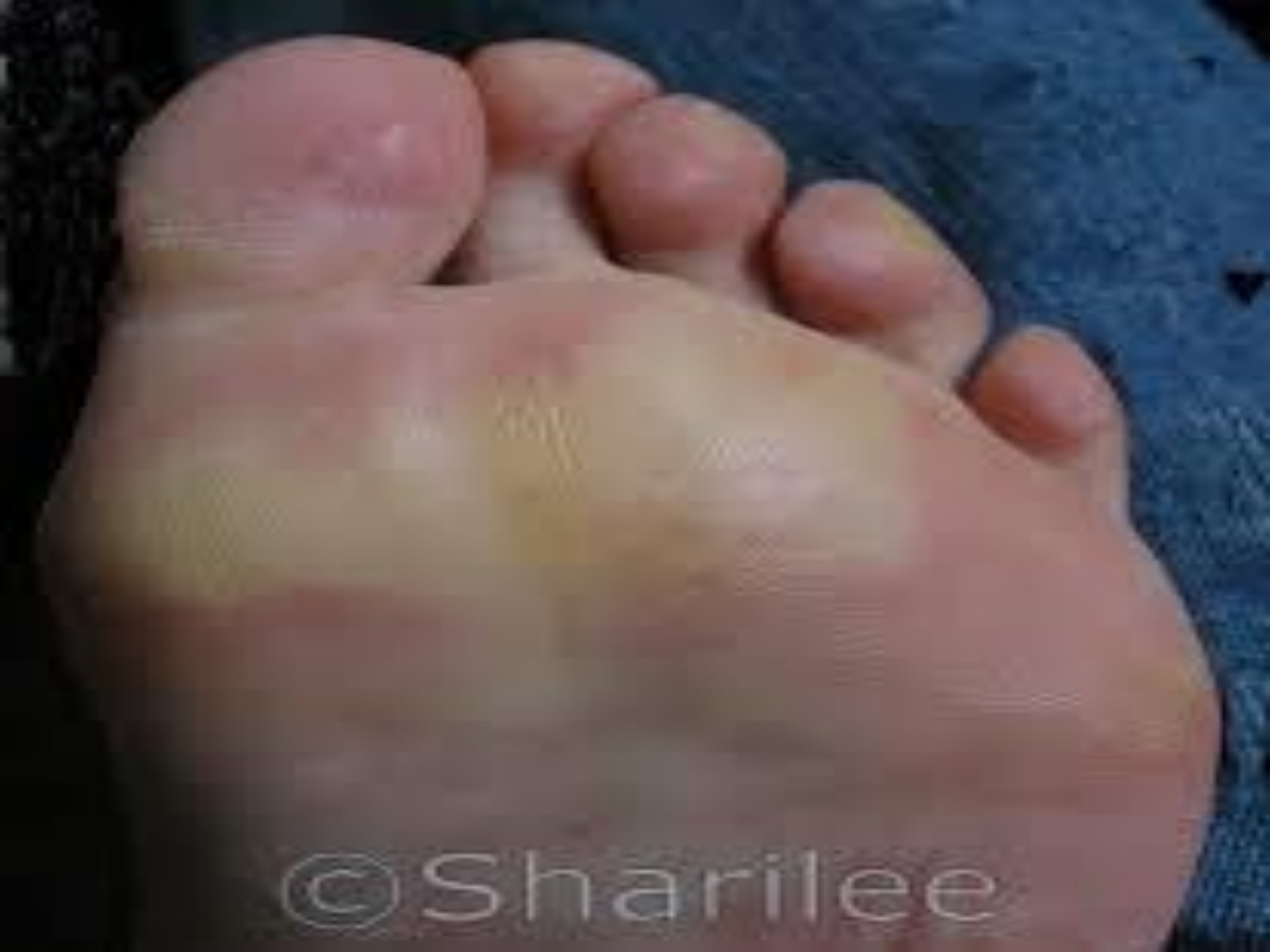
Circulating globulins

- Malignancy
- Multiple myeloma
- Cryoglobulinaemia

Miscellaneous

- Chronic renal failure
- Reflex sympathetic dystrophy
- Hypothyroidism

- The first phase is observed after initial exposure to the triggering factor and is associated with vasospasm characterized by clinical feature of pallor.
- Some patients would experience cold hands and numbness at this stage as a result of reduced blood flow to the digital arteries.
- The initial phase is followed by cyanosis and/or rubor because of reperfusion and is sometimes associated with pain and paraesthesias.
- Other parts of the body can be affected as described earlier, including ear lobes, nose and nipples.
- A cyanotic episode without preceding pallor is not usually because of RP.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Laboratory investigations

- The diagnosis of RP is mainly clinical, based on a history of biphasic/triphasic colour changes in response to cold exposure or emotional upset along with physical examination if the presentation is during an acute episode.
- Laboratory investigations are mainly aimed at differentiating primary RD from secondary RS by identifying any underlying systemic disease.
- Digital blood flow measurement is usually not required to make a diagnosis of RP unless the clinical assessment is inconclusive. The methods used for assessing digital blood flow include strain gauge plethysmography and computerized thermography, Nail fold capilloroscopy has been established as a corner stone in the diagnosis of connective tissue disease (CTD) in patients with RP

The relevant blood tests include the following:

- Full blood count, urea and electrolytes, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and urinalysis to detect renal dysfunction and anaemia of chronic illness.
- An autoantibody screen, which should include rheumatoid factor and antinuclear antibodies.
- Cryoglobulins and cold agglutinins are required only if there is a clinical suspicion of a prothrombotic state.
- Thyroid function test if suspecting hypothyroidism as an underlying cause of RP.

- Abnormal nail fold capilloroscopy combined with an abnormal autoantibody test

predicts CTD in 90%.

- A baseline upper extremity arterial Duplex scan should be carried out to exclude an underlying occlusive arterial disease.
- A plain chest radiograph can demonstrate basal pulmonary fibrosis seen in CTD and

cervical rib if present

Investigation	Technique	Interpretation
Digital systolic blood pressure measurement (measurements taken before and after cooling hands at 15°C)	Two techniques used for measuring blood pressure, strain gauge plethysmography and photoplethysmography	>30 mmHg drop in systolic pressure on cooling is considered significant Avoid testing for 2–3 hours after an acute episode, as the fingers would still be in a state of reactive hyperaemia
Nail-fold capilloroscopy	Microscopic examination of the nail bed for abnormal blood vessels.	Abnormal enlarged, dilated and tortuous blood vessels indicate possibility of CTD Beware that similar changes can occur in diabetes and nail fold trauma
Computerized thermography	Skin temperature is assessed as a marker of blood flow during different phases of RP.	Caution is required in interpreting the results as both the arterial as well as venous flow can affect the skin temperature

Management

Patients with primary RD usually have mild or moderate symptoms and do not require specific drug treatment.

Any causative drug, such as β-blockers, should be replaced with alternatives and any underlying disease such as hypothyroidism should be treated.

Good symptomatic control is possible with these measures, despite the non-availability of a definite cure.

General supportive measures

- RD showing mild to moderate symptoms without an underlying disease process.
- Reassurance, explanation and information leaflets.

Stop smoking.

Electric gloves and stockings.

Special shoes with broad and padded fitting (Abel shoes). Meticulous attention to areas of skin breakdown, ulcers and infection.

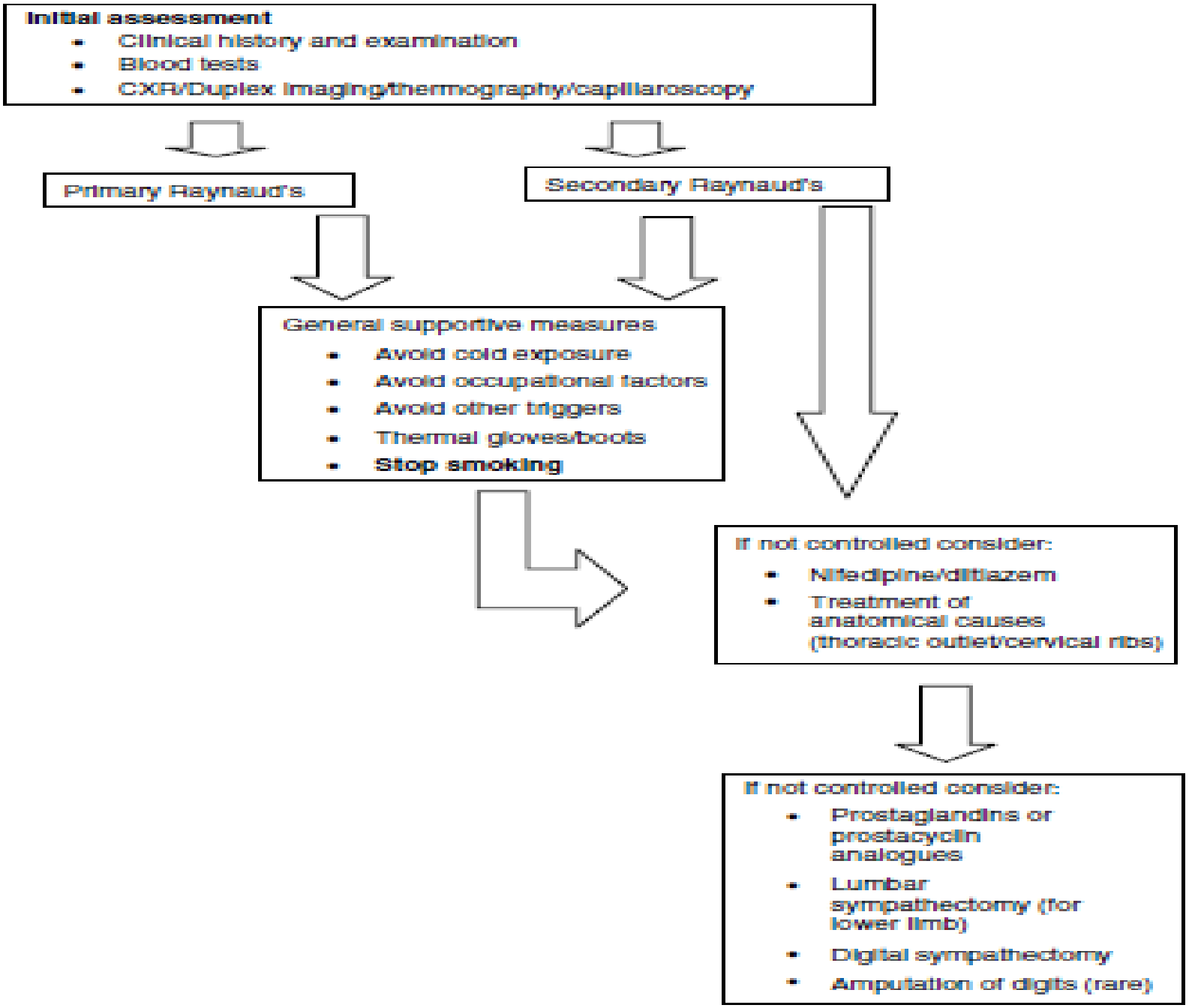


Figure 22.1 Algorithm for the management of Raynaud's phenomenon.

Peripheral vasodilators

These include naftidrofuryl, inositol nicotinate, pentoxifylline and moxisylyte.

Patients with primary RD benefit more from these agents than those with secondary RS.

A combination of low dose nifedipine and one of the peripheral vasodilators may avoid the adverse effects of both while achieving maximum symptomatic relief.

Prostaglandins (PGI2 and PGE1)

These are powerful vasodilatory agents with additional **antiplatelet activity** and **cytoprotective effects**.

Iloprost is a synthetic analogue with a longer half-life and is commonly used as an intravenous infusion over a period of 6 hours for 5 days during the course of one treatment.

The dose is titrated against the individual response and the maximum dose is adjusted at a rate lower than the dose, causing headache, hypotension and flushing (maximum permissible daily dose is 2 ng kg–1 min–1).

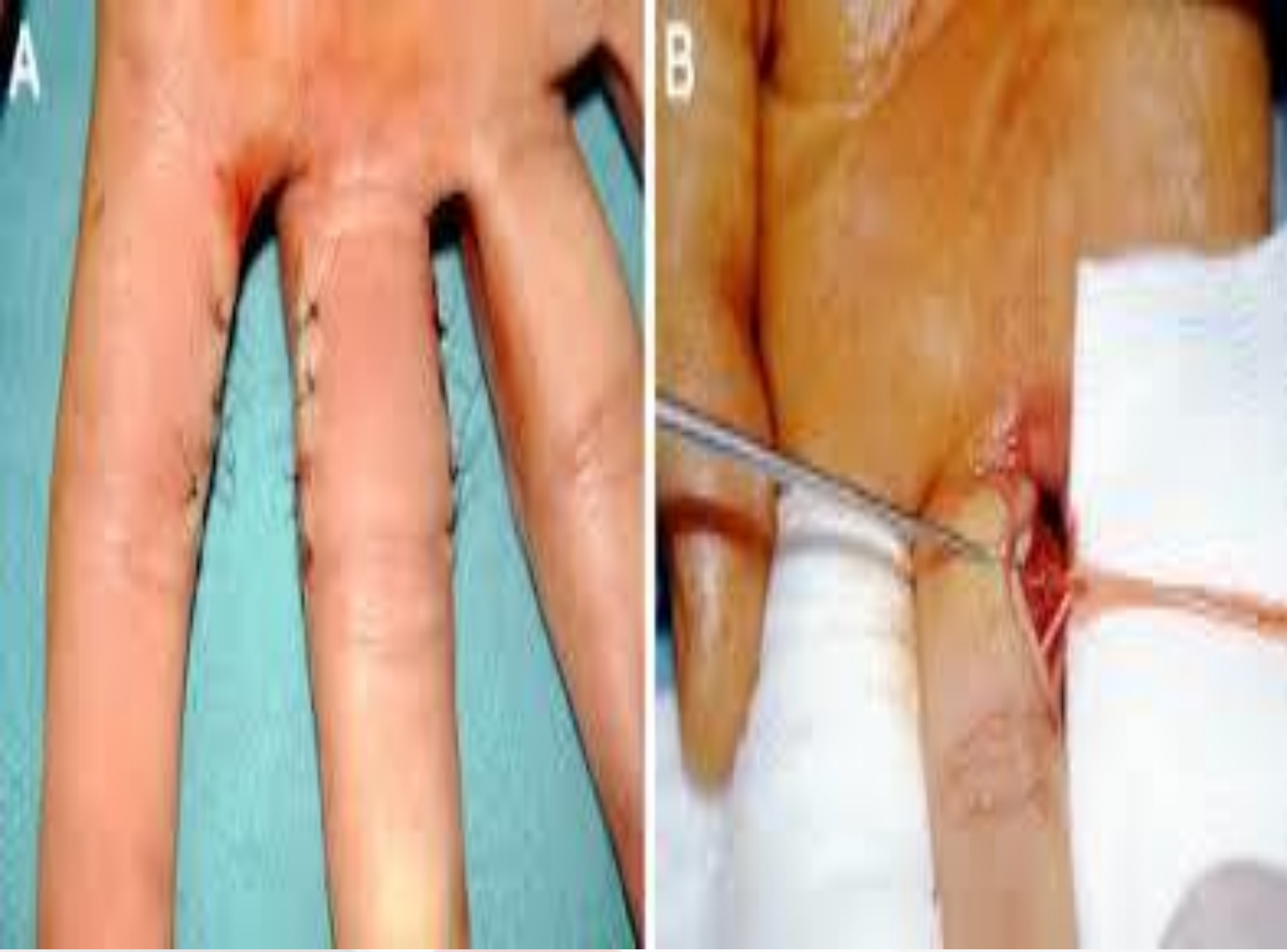
A single course of treatment may provide relief for several months.

Sympathectomy

Cervical and lumbar sympathectomy using phenol injection can sometimes relieve symptoms of upper and lower extremity RP,respectively. However, it should be reserved only as a last option for those with severe symptoms who do not respond to other methods of treatment.

The results of sympathectomy are not always predictable. Thoracoscopic cervical sympathectomy, in particular, is less effective and is associated with a higher rate of relapsing symptoms with only one-third achieving a long-term benefit.

In addition, there are frequent side effects and for this reason it is not recommended as routine. Digital sympathectomy can be helpful in alleviating the symptoms associated with chronic digital ischaemia in patients with severe RP.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