Raynaud's syndrome: Pathophysiology, Symptoms and Treatment

Raynaud's syndrome is a condition characterized by episodic vasospasm of the small arteries, typically in the fingers and toes, in response to cold or emotional stress. It leads to reversible skin color changes (pallor, cyanosis, erythema) and sensory symptoms such as pain or tingling.

Classification

- **Primary Raynaud's (Raynaud's disease):**
  - Idiopathic, more common (>80% of cases)
  - No underlying disease
  - Typically mild and symmetrical
  - Usually begins in women <30 years
  - No digital ulcers or tissue necrosis
- **Secondary Raynaud's (Raynaud’s phenomenon):**
  - Associated with underlying conditions such as:
    - Systemic sclerosis (most common)
    - SLE, Sjögren’s syndrome, dermatomyositis, RA
    - Atherosclerosis, thoracic outlet syndrome
    - Drugs (e.g., beta-blockers, ergotamines, chemotherapeutics)
    - Occupational (vibration injury)
  - Often severe, may be asymmetric, can lead to ulcers/gangrene

Pathophysiology

- **Vasospasm** ? ? blood flow ? **ischemia** (white phase)
- Accumulated deoxygenated blood ? **cyanosis** (blue phase)
- Reperfusion ? **reactive hyperemia** (red phase)

Mechanisms Involved:

- Hyperactivation of **alpha-2 adrenergic receptors**
- ? Platelet ?2-receptors in affected individuals
- Estrogen, serotonin, endothelin-1, and nitric oxide may play roles
- Genetic predisposition: familial clustering reported
- **Sympathetic overactivity** or **vascular dysfunction** likely contributes

Epidemiology

- More common in **females** (especially of childbearing age)
- Often resolves after **menopause**
- Occurs in up to 5-10% of the population

Clinical Features

Triggering factors:

- Cold exposure
- Emotional stress
- Vibrations

Phases:

1. **Pallor** (white): due to vasospasm and ischemia
2. **Cyanosis** (blue): due to desaturation of blood
3. **Erythema** (red): due to reactive hyperemia

Other features:

- Burning, tingling, numbness
- Symmetrical involvement in primary
- Typically spares the thumb
- Most commonly affects the index, middle, and ring fingers
- Attacks last minutes to hours

Diagnosis

- **Clinical diagnosis** based on symptoms and history
- Rule out **acrocyanosis** (persistent cyanosis without ischemia or pain)

Workup for Secondary Raynaud's:

- **ANA, ESR, RF**
- **Anti-centromere antibody** (CREST)
- **Anti-Scl-70 (anti-topoisomerase I)** (systemic sclerosis)
- Nailfold capillaroscopy
- Digital artery Doppler ultrasound

Management

General Measures:

- Avoid cold exposure
- Wear warm gloves
- Smoking cessation
- Stress management

Pharmacologic Therapy:

- **Calcium Channel Blockers (CCBs)** : First-line
  - *Nifedipine* , Amlodipine, Felodipine
- **Alpha-blockers** : e.g., *Prazosin*
- **Topical nitroglycerin** (for digital ulcers)
- **PDE inhibitors** : Sildenafil

- **Pentoxifylline** : improves microcirculation

Advanced/Severe Disease (usually secondary):

- **Iloprost** (IV prostaglandin analog) – for critical ischemia
- **Bosentan** (Endothelin receptor antagonist) – for digital ulcers in scleroderma
- **Surgical sympathectomy** : Reserved for refractory cases
- **Analgesics and antibiotics** for ulcer management

Contraindicated Drugs:

- **Beta-blockers** (except cardioselective ones like nebivolol)
- **Clonidine**
- **Ergot derivatives**
- **Sudafed and stimulants**

Key Differentiating Points:

Feature	Primary Raynaud's	Secondary Raynaud's
Age	<30 years	>30 years
Severity	Mild, symmetric	Severe, may be asymmetric
Ulcers/Gangrene	No	Common
Associated disease	None	Yes (e.g., SLE, scleroderma)
Nailfold capillaries	Normal	Abnormal (e.g., dilated, dropout)

High-Yield Notes:

- **Raynaud's can precede systemic sclerosis by years** – monitor closely.
- **Triphasic color change is classic** but not always present.
- Patients with **anti-centromere antibodies** are at risk of CREST syndrome.
- Avoid cold, caffeine, and sympathomimetic drugs in all patients.