Rheumatology Presentation

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- Hyperuricemia
- Gout
- Raynaud’s

Hyperuricemia

- High serum urate without gout, or uric acid renal disease
- About two-thirds or more of such individuals remain asymptomatic
- Asymptomatic hyperuricemia has also been associated with other disorders that appear to be largely unrelated to crystal deposition, including hypertension, chronic kidney disease (CKD), cardiovascular disease, and the insulin resistance syndrome

Hyperuricemia

Caused by

- Impairment of renal and gut urate excretion
- Overproduction of urate

Hyperuricemia Is Not GOUT

- Most hyperuricemic individuals never experience a clinical event resulting from urate crystal deposition
- Hyperuricemia is necessary to develop gout

Hyperuricemia- Risk Factors for the development of Gout

- **Non-modifiable risk factors**

male gender, advanced age, and ethnicity

- **Modifiable risk factors**

Obesity
Alcohol-containing beverages (especially beer)
Sodas and fruit juices
Hypertension
Diuretics - thiazide or loop diuretic, Cyclosporine, Low dose Aspirin
Chronic kidney disease
Postmenopausal
Trauma, surgery
Initiation of urate-lowering therapy

- Smoking and coffee reduce the risk

Gout - Introduction

- Monosodium urate crystal deposition disease
- Extracellular fluid urate saturation

The clinical manifestations of gout may include:

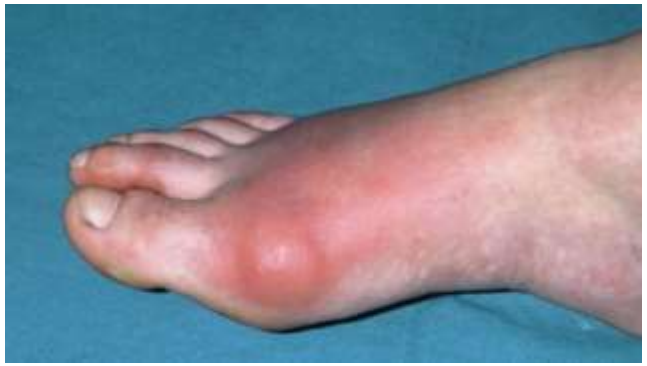
- Recurrent flares of inflammatory arthritis (gout flare)
- A chronic arthropathy
- Accumulation of urate crystals in the form of tophaceous deposits
- Uric acid nephrolithiasis
- Chronic nephropathy

Gout

- Higher levels of urate is associated with a greater risk for developing gout but not necessarily more severe gout
- Gout tends to occur earlier in life in men than women and is rare in childhood
- 3 percent of adults
- Incident peak in - Men 40-50 y
  - Women 60-70 y

all patients with gout have hyperuricemia at some point in their disease However

CLINICAL MANIFESTATIONS

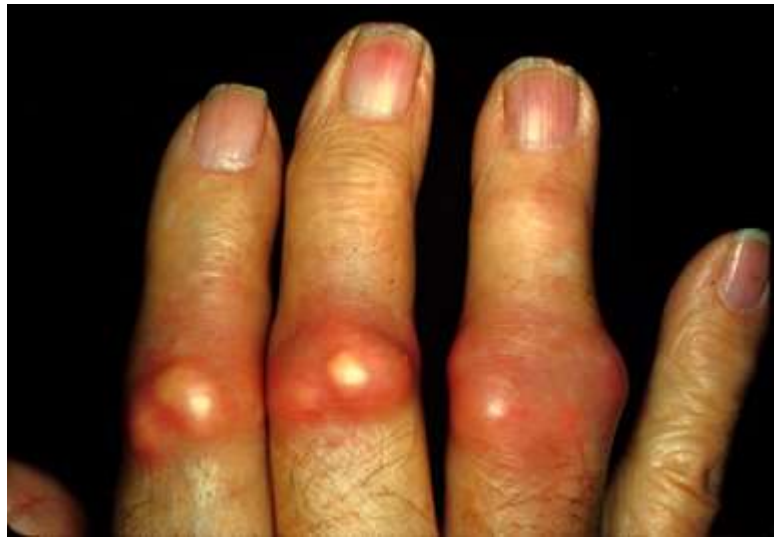


- Gout flares - mainly monoarticular , severe inflammation, lower extremities
- Maximal severity develop within 12 to 24 hours
- Onset more often at night
- Inflammation extend beyond the joint that is primarily involved – This feature may give the impression of dactylitis (sausage digit) or cellulitis or tenosynovitis.
- Complete resolution - almost always occurs within a few days even in untreated individuals
- Resolution of the gout flare is sometimes accompanied by desquamation of the skin overlying the affected joint
- Patients with gout who have sustained chronic hyperuricemia may develop poly articular flares

CLINICAL MANIFESTATIONS
Polyarticular gout

- Polyarticular gout flares - less than 20 percent of patients
- Polyarticular symptoms are particularly common late in the course of untreated gout
- Polyarticular flares are more frequent among hospitalized patients and can be accompanied by fever and mimic sepsis
- Polyarticular - more frequent in patients with myeloproliferative or lymphoproliferative disorder

CLINICAL MANIFESTATIONS
Tophaceous gout



- Tophaceous gout — collections of solid urate

- chronic inflammatory and often destructive changes

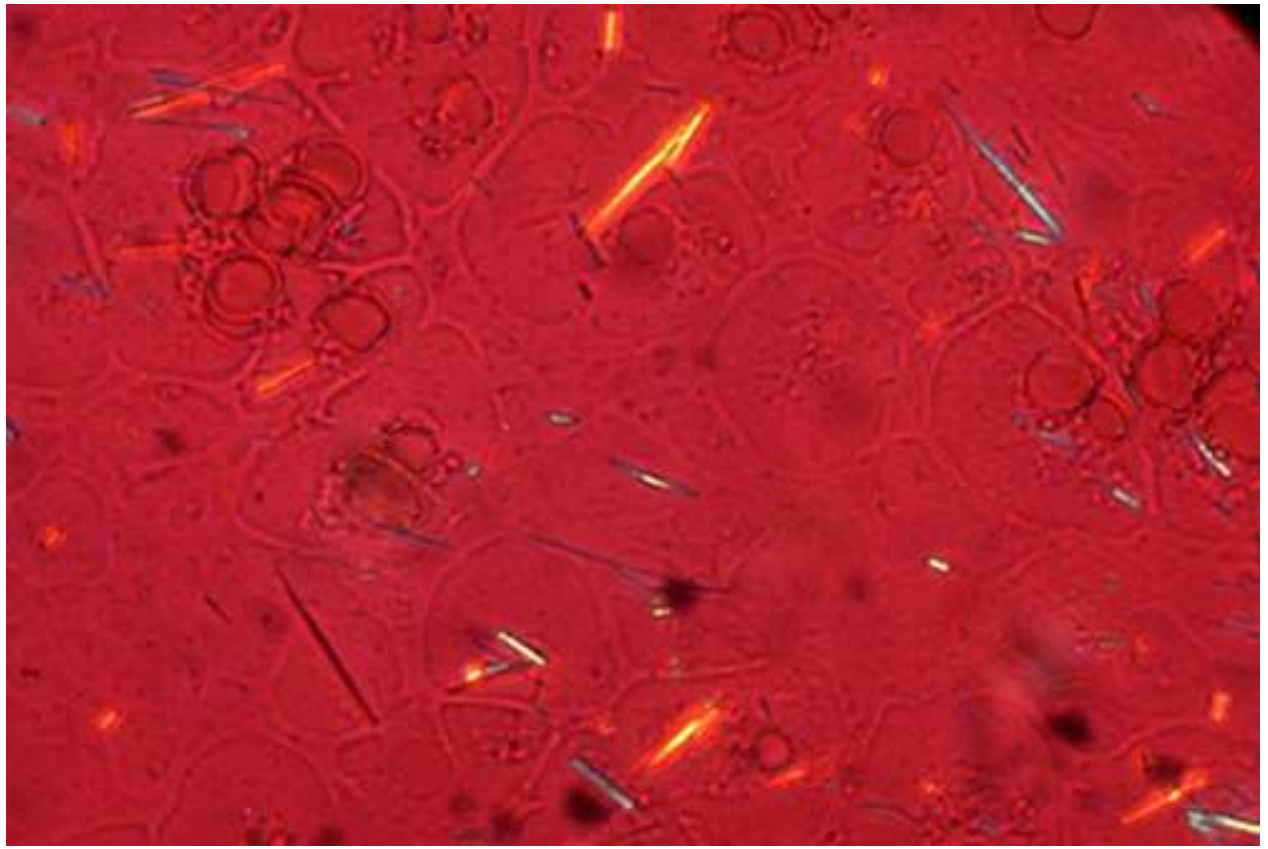
- tophi are often visible and/or palpable

- can be present on the ears or in the soft tissues, including articular structures, tendons, or bursas

- Tophi are typically not painful

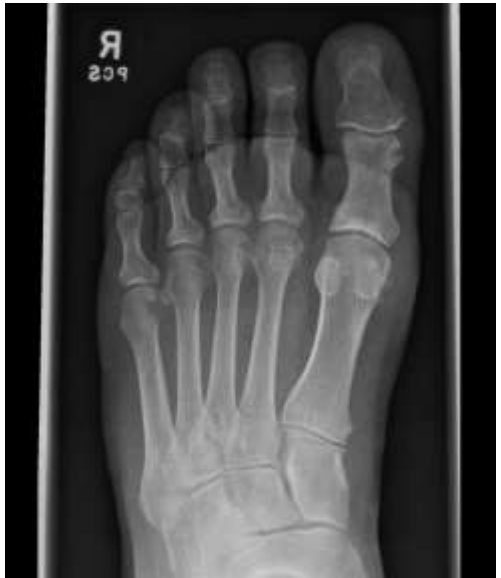
Investigations

- Synovial fluid analysis — monosodium urate crystals in synovial fluid obtained from joints or bursas



Investigations

- Blood tests — During a gout flare, blood tests may show nonspecific changes consistent with inflammation; the urate level may be high, normal, or low:
- Raised Neutrophils , ESR, CRP
- Serum urate levels can be difficult to interpret during a gout flare
- XR Normal in early stages, bone cysts and erosions
- **Ultrasonography**



Comparison of gout and CPPD disease

Characteristic	Gout	CPPD disease
Prevalence	17 to 20 per 1000 individuals, largely adult men and postmenopausal women	<1 per 1000 individuals experience acute CPP crystal arthritis (pseudogout); CPPD disease is common in osteoarthritis and increases with age
Crystal chemistry	Monosodium urate	CPP dehydrate
Crystal appearance	Negatively birefringent; needle-shaped or rods	Weakly positively birefringent; rods or rhomboidal
Articular involvement	Monoarticular > oligoarticular; polyarticular <30%	Monoarticular > oligoarticular
Most frequently affected joints	First MTP joint	Knee, wrist, other
	Initially 50%	
	Eventually 90%	
	Ankle, knees, other	
Predisposing conditions/risk factors	Hyperuricemia*, obesity, hypertension, hyperlipidemia, alcohol ingestion, lead ingestion, hereditary enzyme defect	Hemochromatosis, osteoarthritis, hypomagnesemia, hyperparathyroidism, hereditary (rare), and increased age
Therapeutic options	Acute gout attacks	Acute CPP crystal arthritis (pseudogout)
	NSAIDs, glucocorticoids, colchicine	NSAIDs, glucocorticoids, colchicine
	Chronic gout management	Chronic CPPD disease management
	Urate-lowering agents, colchicine	NSAIDs, colchicine
		DMARDs: hydroxychloroquine, methotrexate (no randomized trials showing clinical benefit)

CPPD: calcium pyrophosphate deposition; CPP: calcium pyrophosphate; Pseudogout: a

Treatment – Acute Flares

- Systemic and intraarticular glucocorticoids- use early, taper
- NSAIDs
- Colchicine
- Biologic agents that inhibit the action of interleukin (IL), Anakinra & Canakinumab

Urate Lowering Drugs

Indications :

- Frequent or disabling gout flares
- Clinical or radiographic signs of structural joint damage
- Tophaceous deposits in soft tissues or subchondral bone
- Gout with renal insufficiency (creatinine clearance <60 mL/minute/1.73 m^2)
- Recurrent uric acid nephrolithiasis

Urate Lowering Drugs

Xanthine oxidase inhibitors

- Allopurinol or
- Febuxostat
- Oxypurinol - an active metabolite of allopurinol for patients intolerant of allopurinol

Febuxostat

- Dose 40, 80, 120 mg/day
- Same or may be better than Allopurinol in lowering Urate level
- Better for Mild to moderate renal impairment
- Side effect: - Liver toxicity - Need to monitor Liver function
  - Thromboembolic CVD – MI, Angina, TIA
  - nausea, arthralgia, and rash
  - More incidents of Gout attaches after initiation

Uricosuric drugs

Indications

- Patients with relative renal underexcretion of uric acid (ie, low or normal values for urinary uric acid excretion in the presence of hyperuricemia) are potentially candidates for uricosuric drug therapy
- Uricosuric drug monotherapy should be avoided in those with a history of nephrolithiasis to avoid renal stone recurrence
- Probenecid and sulfinpyrazone are effective for most patients but may be ineffective in those with moderate to severe CKD
- Benzbromarone may be more effective for patients with mild to moderate renal insufficiency

Uricase

Uricase (urate oxidase) is the enzyme that catalyzes conversion of urate to a more soluble purine degradation product

Urate-lowering therapy for gout with uricase is aimed at supplying the absent enzyme activity safely and for a sufficient period of time to promote depletion of body urate pools, thus resulting in clinical benefits such as gout flare reduction and tophus resolution

Pegloticase, Rasburicase

Raynaud’s Phenominon

Introduction –Raynaud's

- Raynaud phenomenon is an exaggerated vascular response to cold temperature or emotional stress
- Sharp demarcated color changes of the skin of the digits
- There is an abnormal vasoconstriction of digital arteries and cutaneous arterioles due to a local defect
- Primary Raynaud's - occur alone
- Secondary Raynaudes – associated with an illness, such as systemic lupus erythematosus and systemic sclerosis

EPIDEMIOLOGY

- 3-20 % in women
- 3 -14 % in men
- More common among younger age groups
- The prevalence of Raynaud's in a given population is influenced by the climate of the region studied

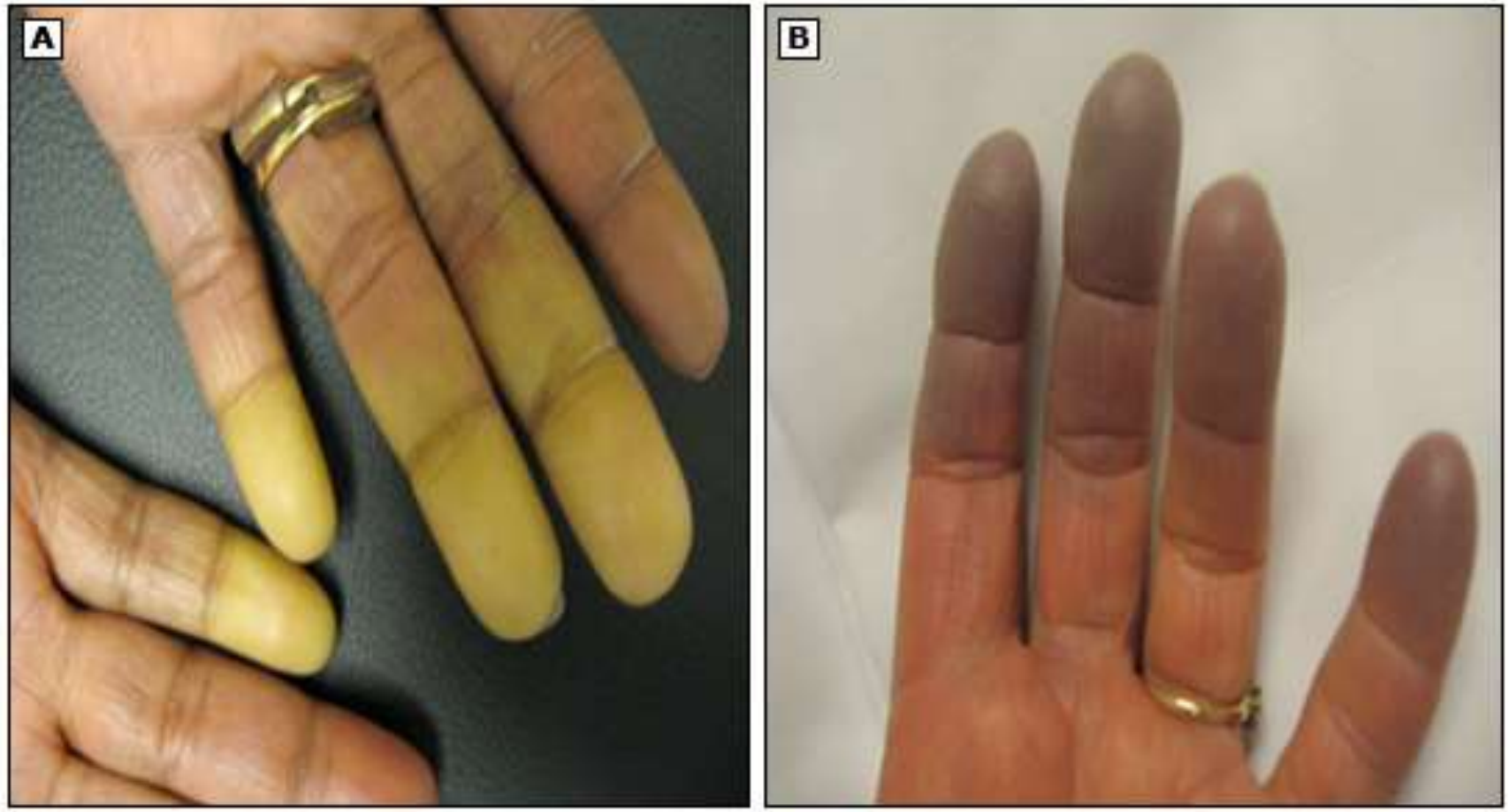
Primary Raynaud phenomenon

- Primary or idiopathic Raynaud disease are terms to describe those patients without a definable cause for their vascular events.
- Exaggeration of normal vasoconstriction to cold exposure therefore the term "disease" is inappropriate
- Onset 15 and 30 years of age
- More common in women
- May occur in multiple family members
- Careful assessment for secondary causes is most important
- Hypertension, atherosclerosis, cardiovascular disease, and diabetes mellitus can make symptoms worse
- Increase in prevalence among patients with fibromyalgia syndrome

One survey found no association between skin temperature and digital color changes in patients with fibromyalgia ? suggesting a unique cause for RP in fibromyalgia compared with patients with primary RP

Clinical Manifestation - Raynaud's

- Raynaud attack typically begins in a single finger and then spreads to other digits symmetrically in both hands
- The index, middle, and ring finger are the most frequently involved digits, while the thumb is often spared entirely
- Involvement of the thumb may indicate a secondary cause
- Cutaneous vasospasm - skin of the ears, nose, face, knees, and nipples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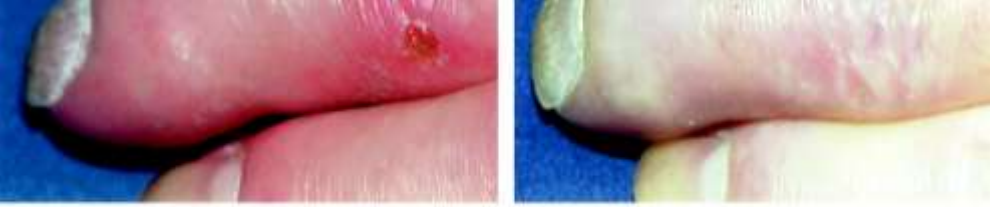
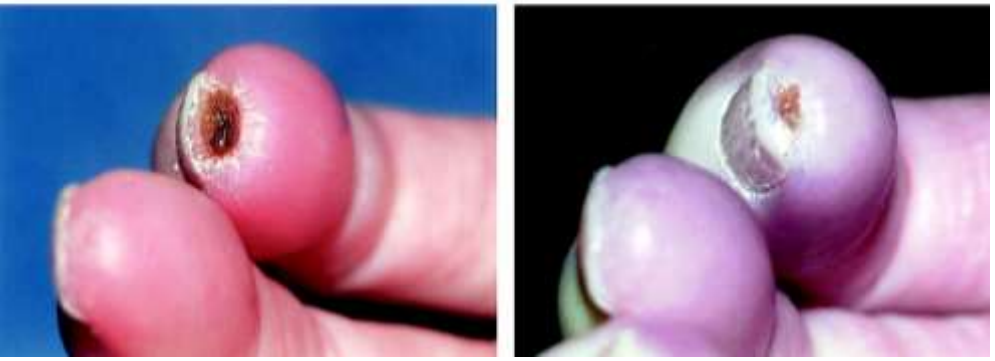
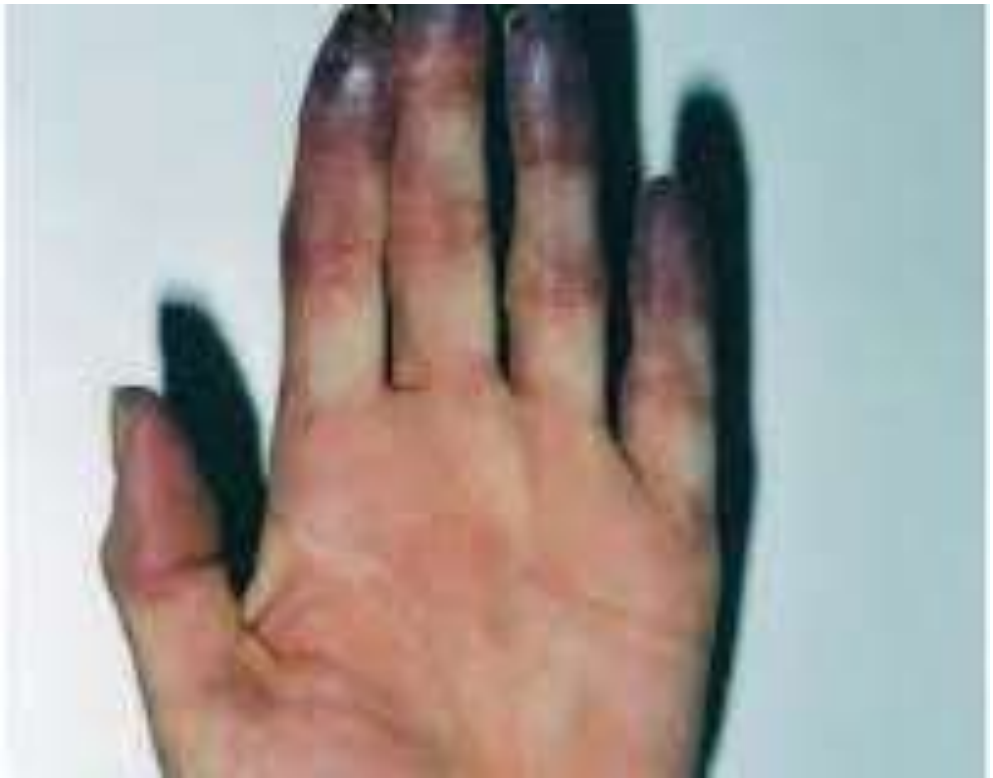


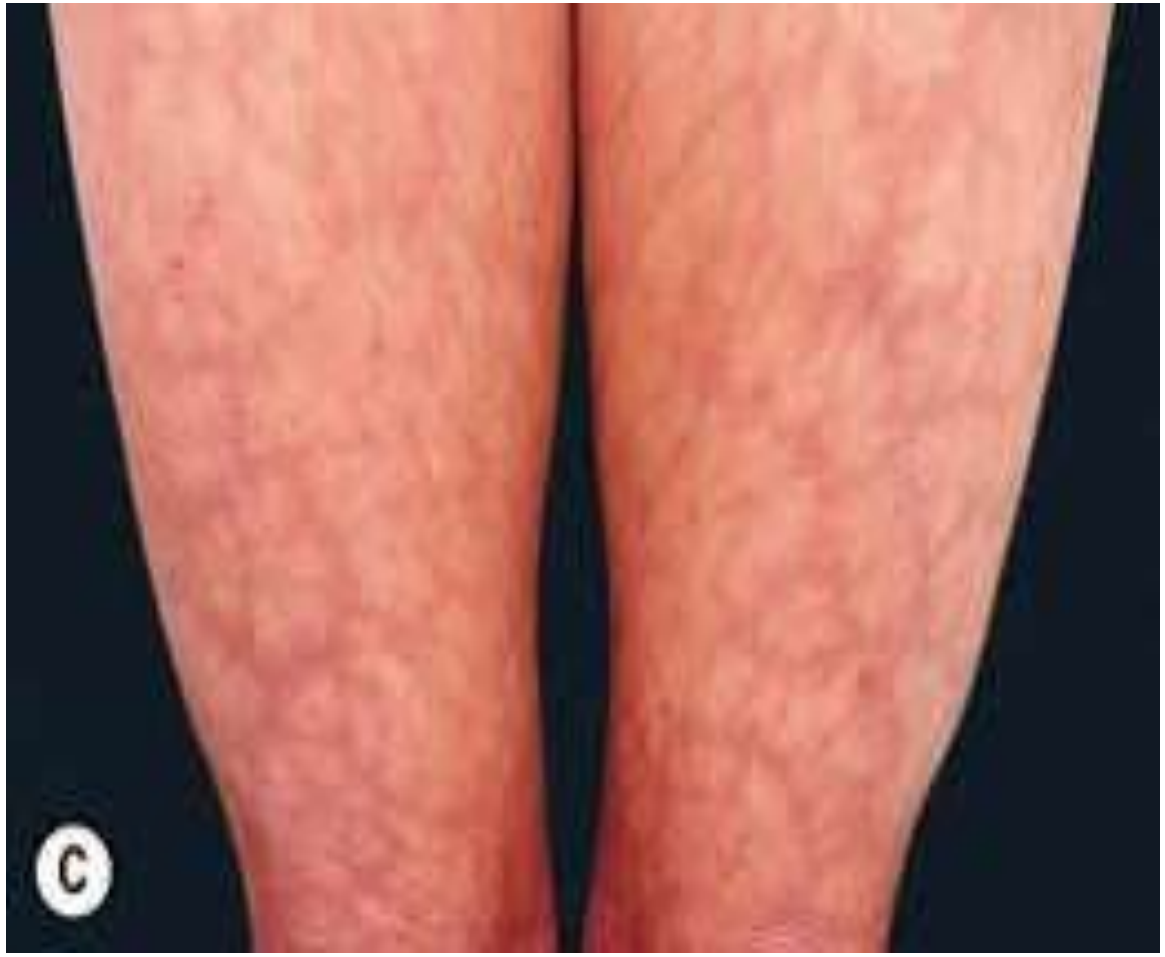




Clinical Manifestation - Raynaud's Symptoms of acute or chronic ischemia

- Ischemia can be transient or prolonged
- Acute ischemia may be mild and associated with sensations of pins and needles, numbness and/or clumsiness of the hand, and finger aching. Reversible
- More in Secondary Raynaud’s - ulceration of the skin (typically the tips of the fingers and toes)

Livedo reticularis



- Patients with Raynaud's may exhibit livedo reticularis
- Violaceous mottling or reticular pattern of the skin of the arms and legs
- Sometimes with regular unbroken circles
- This finding is benign and completely reversible with rewarming

Provoking factors

- Cold Exposure
- Protection – Whole body not only the hands
- Emotional Stress - sympathetic stimulation

It is not uncommon to witness a typical attack during the first consultation

Management - Aims

- Improve quality of life and to prevent tissue loss (ulceration, gangrene)
- Reduce the intensity of attacks
- Abolishing cold sensitivity and eliminating all Raynaud events is not possible particularly in secondary Raynaud’s

Initial Management
Non-pharmacologic measures

General measures

- **Avoidance of cold exposure**
- Avoidance of repeated trauma to the fingertips
- avoidance of vibrating tools
- Control or limitation of emotional stress
- Avoidance of vasoconstricting drugs B-Blockers, Sumatriptan
- Smoking cessation

Pharmacologic measures

- Calcium channel blocker -dihydropyridine There are no clear data to support the use of one dihydropyridine over another

- Amlodipine
- Nifedipine – has more data
- Better to use long acting

- Phosphodiesterase (type 5) inhibitor Sildenafil 25 -50 mg two to three times daily

Pharmacologic measures

- Angiotensin II receptor blocker

Patients receiving Losartan 50mg experienced greater reduction in the severity and frequency of attacks compared with Nifedipine 40mg/day

- Selective serotonin reuptake inhibitor

Fluoxetine 20mg – start 10mg then increase to 20mg

Treatment of Refractory Raynaud's

- Intravenous prostaglandins

For patients with acute or prolonged digital ischemia who have not responded to optimal therapy with oral or topical vasodilators

- Local or regional block

Thank You