overview of Acrosyndromes

Steven M. Dean, DO, FACP, RPVI
Associate Professor of Internal Medicine
Wexner Medical Center at The Ohio State University
A 35 year old male presents with a 5 year hx of recurrent cold associated discolored fingers.
differential Diagnosis of acroSyndromes:

1. Acrocyanosis
2. Pernio (Chilblains disease)
3. Raynaud phenomenon
4. Acrorygosis
5. Spontaneous venous hemorrhage/benign blue finger
6. Erythromelalgia/Erythermalgia
AcRocyanosis

“A painless condition characterized by discoloration of different shades of blue in the distal parts of the body (most commonly in the hands, feet, and face) that is marked by symmetry and persistence of color changes aggravated by cold exposure, and which is frequently associated with local hyperhidrosis of hands and feet.”

Acrocyanosis

- Acrocyanosis may extend to or even above the wrists and ankles
- Discoloration exacerbated by cold and improved with warmth yet persists
- Discoloration increased with limb dependency and improved with elevation
- Hyperhidrosis
“Crocq’s sign described in the earliest report of acrocyanosis is the slow and irregular return of blood from the periphery (but not from beneath) to the center in the area of blanching produced by pressure on the skin. It is characteristic of, but not specific for, acrocyanosis."
Crocq’s Sign aka “iris” sign
AcRocyanosis - “Different Hues”
Acrocyanosis

Primary

Or

Secondary??
Secondary Causes of Acrocyanosis

- Hypoxemia
- Stroke
- Myocardial infarction
- Buerger’s disease
- Lung diseases:
  - Pulmonary hypertension
  - Pulmonary embolism
  - Pulmonary alveolar proteinosis
  - Pulmonary arteriovenous malformations
- Acrocyanosis of infancy
- Atheromatous embolism
- Connective tissue / rheumatologic diseases:
  - Wegener’s granulomatosis
  - Overlap syndrome
  - Rheumatoid arthritis
  - Lupus erythematosus
- Eating disorders:
  - Anorexia nervosa
  - Chronic starvation
- Neoplasms
- Hematologic disorders:
  - Lymphoproliferative
  - Myeloproliferative disorders
  - Cold agglutinins
  - Cryofibrinogen
  - Antiphospholipid antibodies
Secondary Causes of Acrocyanosis

Drug exposure associations:
- Tricyclic antidepressants\(^{41,42}\)
- Interferon\(^{43-45}\)
- Vasopressors (terlipressin,\(^{46}\) dopamine\(^{47}\))
- Sirolimus\(^{48}\)
- Clonidine\(^{49}\)
- Amphotericin B\(^{50}\)
- Phenazopyridine\(^{3}\)
- Benzocaine\(^{51}\)
- Propoxyphene\(^{52}\)
- Bleomycin\(^{53}\)
- Intravenous immune globulin\(^{54,55}\)
- Butyl nitrite\(^{56}\)

Toxicities:
- Arsenic\(^{57}\)
- Blastcidin S\(^{58}\)
Secondary Causes of Acrocyanosis

Heritable diseases:
- Ethylmalonic aciduria
- Cytochrome C oxidase deficiency
- Mitochondrial disease (oxidative phosphorylation disorders)
- Spondyloenchondrodysplasia
- Palmoplantar keratoderma syndrome
- Fucosidosis
- **Down’s syndrome**
- Prader-Willi syndrome
- Sneddon’s syndrome
- Aicardi-Goutières syndrome
- **Marfan’s disease**
- Riley-Day syndrome (familial dysautonomia)
- Ehlers-Danlos syndrome

Psychiatric:
- Bipolar disorder
- Asperger’s syndrome
- Orthostatic intolerance and postural tachycardia syndrome (POTS)
Secondary Causes of Acrocyanosis

- Spinal cord injury
- Ozena
- Chronic hypertrophic and primary atrophic rhinitis
- Atopic dermatitis
- Hypersensitivity coronary syndrome (Kounis syndrome)

Infections:
- HIV
- Psittacosis
- Chikungunya infection
- Mononucleosis
- Hepatitis C
- ‘Puffy hand syndrome’
Pernio/
Chilblain’s
31 y.o Female with Recurrent Digital Ulcerations Every Winter...Burning, Itching

Pernio (Chilblain’s Disease)
Acroerygosis

Subjective acral coldness *without* color changes
This man Presents with Sudden Pain and Swelling of the Right Third Finger
Spontaneous Venous hemorrhage/benign blue finger

• Spontaneous benign blue finger develops without antecedent trauma or illness.
• Typically one finger becomes acutely blue and painful. The discoloration sometimes appears more violaceous than blue.
• Classically, the finger tip is spared (‘tip sparing‘). This is not mandatory, but when present is very distinctive.
• The resolution is usually rapid, within days; Discoloration tends to disappear, without going through the usual stages of hematoma resolution.
• No treatment is necessary.
Spontaneous Venous hemorrhage/benign blue finger

Photo Courtesy of Dr. Bruce Mintz
Erythromelalgia

"The antithesis of Raynaud phenomenon"

- Erythema
- Increased warmth
- Painful burning
- Aggravated by warmth
- Relief with cold
Erythromelalgia

Classification

Primary erythromelalgia

Secondary erythromelalgia

- Myeloproliferative syndrome [PCV, ET]
- Drug induced [nifedipine, bromocriptine, pergolide]
- Neurological [peripheral neuropathy, MS, spinal cord injury]
- Autoimmune disease
Raynaud’s attacks superimposed on acrocyanosis are not uncommon and may complicate the diagnosis.

Acrocyanosis and Raynaud phenomenon may coexist with and are more common in patients with pernio (chilblains disease).

Erythromelalgia can coexist with and/or Raynaud phenomenon.
Livedo Reticularis/Racemosa
A 35 year old male presents with a 5 year hx of recurrent cold associated discolored fingers
Does this Patient have Raynaud phenomenon?

Raynaud Disease?

Raynaud Phenomenon?

Raynaud Syndrome??
Nomenclature: Consensus Statement of the Royal Society of Medicine (vascular medicine division) 2011

- **Abandoned terms**: “Raynaud Disease” and “Raynaud Syndrome”
- **Preferred terms**: “Primary Raynaud Phenomenon” “Secondary Raynaud Phenomenon”
Consensus Statement of the Royal Society of Cardiovascular Medicine of FOMA District 2
Diagnosis of Raynaud phenomenon

**Diagnosis**: 

1. History of digital cold sensitivity 

   + 

3. Episodic pallor or cyanosis [or both] of the distal digits upon cold exposure 

*Wigley F. NEJM 2002;347:1001-1008*
Only a minority of patients display the classic triphasic color change! Thumb sparing
Does this Patient have Raynaud phenomenon?
What about “Cold Immersion” Testing?
“It is not necessary to perform a provocative test [immersion of the patient’s hand in ice water] to make a definitive diagnosis”

“A history alone must be accepted as diagnostic since no simple office test consistently triggers an attack”

“A cold water challenge is NOT

*Wigley F. NEJM 2002;347:1001-1008
Wigley F. Up to Date. March 2012
The diagnosis of Raynaud Phenomenon is a **clinical diagnosis** and should **not** be made on the basis of a non invasive vascular laboratory test!
Cold Stimulation Test

Do not let your doctor dunk your hands in ice water to test for Raynaud's! It is painful, unnecessary and possibly even dangerous!

Some doctors run a Cold Stimulation Test which involves taping a heat sensor to your hand, then submerging them in an ice-water bath to measure how long it takes to return to normal temperature. Needless to say, this test is not very popular with Raynaud's patients as it is both painful and unnecessary. It is also hazardous if you have gangrene or open, infected wounds on your hands. No tests are required to diagnose Raynaud's!

*Sclero.org
What do you achieve by performing ice water immersion test on these patients?
Does the patient have Primary or Secondary Raynaud phenomenon??
Primary Raynaud phenomenon

- Younger age (<30)
- Female
Secondary Raynaud phenomenon

- *Male* or female
- Later age of onset (> 40)
- Asymmetrical attacks
- Sclerodactyly, gangrene, or trophic changes (pitting, scarring, ulcers)
- Signs of secondary disease
- Occluded peripheral aa/ abnormal Allen’s test
- Abnormal nail fold capillaroscopy
- Abnormal laboratory parameters (ANA, ESR, specific autoantibodies)
Signs of secondary Disease
Signs of secondary disease
Signs of secondary disease
Signs of secondary disease

Livedo racemosa
Nail Fold CAPillaroscopy
Nail Fold Capillaroscopy

- An abnormal nailfold capillaroscopy is the best predictor of eventual disease transition

- “If capillaroscopy if normal, the likelihood of developing scleroderma is almost nil”

Ulcerations = Secondary cause
Secondary causes of Raynaud syndrome

1. Autoimmune disorders
2. Occupational
3. Drugs/chemicals
4. Hyperviscosity
5. Occlusive arterial disease
6. Miscellaneous
Evolution of Primary to Secondary Raynaud Phenomenon

- Occurs in minority of patients
- Overall: 12-20%
- 1% of patients with Primary RP transition to Secondary PR/year
- Most common secondary disease: scleroderma
Raynaud phenomenon: Investigation

If a thorough H & P that includes nail fold capillaroscopy is normal and suspicion for a secondary disease is low, there is no need for additional laboratory or non invasive arterial testing.
Patient summary

- Normal serology
- Normal nail fold capillaroscopy
- Normal non invasive arterial studies with reversible diffuse vasospasm

Diagnosis???
Steven.dean@osumc.edu