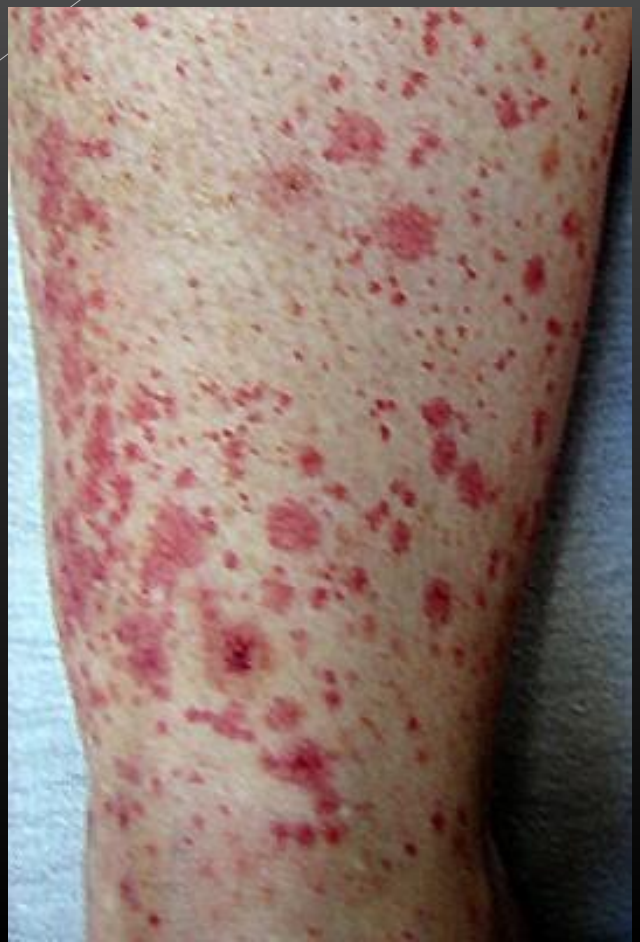
VASCULITIS

Clinical Approach



Basic Facts

- **Affects all ages**, *although some types are restricted to certain age groups*
- **Tends to affect Caucasians**, *although many African-Americans are affected*
- **Has a genetic component**, *but is not heritable*
- **It is a chronic relapsing disease**, *although some patients experience prolonged remission*

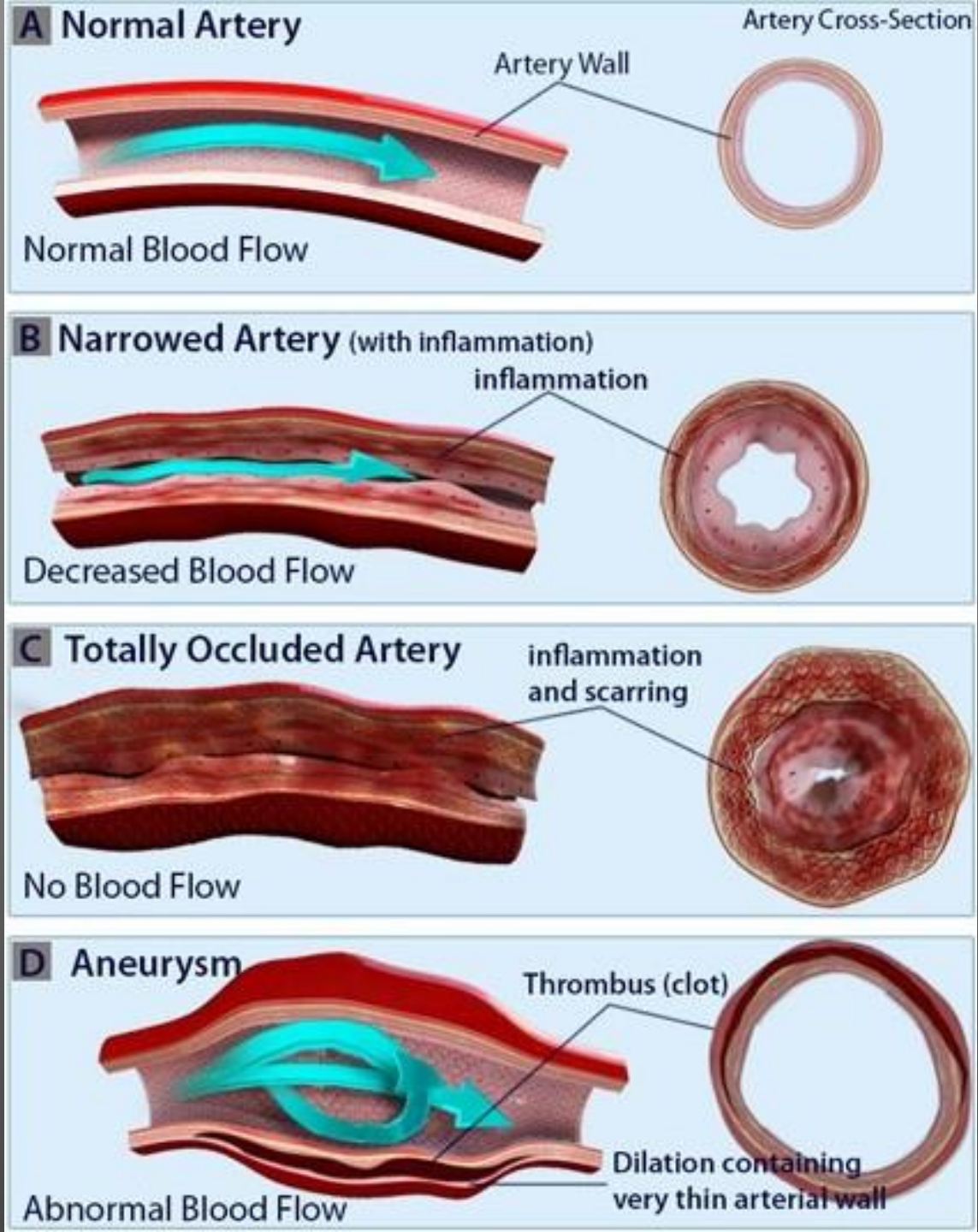
Definition

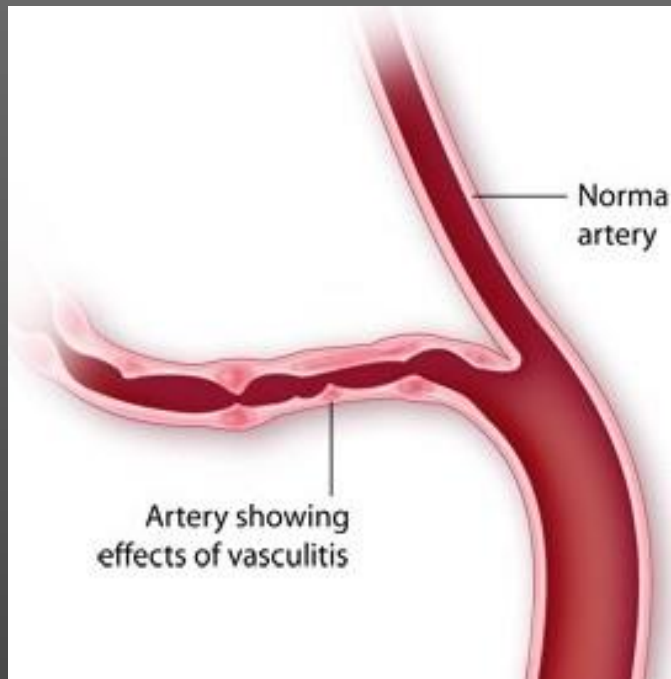
Inflammatory destruction of blood vessels

- **Infiltration** *of vessel wall with inflammatory cells*
  - *Leukocytoclasis*
  - *Elastic membrane disruption*
- **Fibrinoid necrosis** *of the vessel wall*
- **Ischemia**, *occlusion, thrombosis*
- **Aneurysm** *formation*
- *Rupture, hemorrhage*

A clinicopathologic process characterized by inflammatory destruction of blood vessels that results in occlusion or destruction of the vessel and ischemia of the tissues supplied by that vessel.

"Systemic vasculitides"


A Normal Artery
Artery Cross-Section
Artery Wall
Normal Blood Flow
B Narrowed Artery (with inflammation)
inflammation
Decreased Blood Flow
C Totally Occluded Artery
inflammation
and scarring
No Blood Flow
D Aneurysm
Thrombus (clot)
Dilation containing
very thin arterial wall
Abnormal Blood Flow


Norma
artery
Artery showing
effects of vasculitis

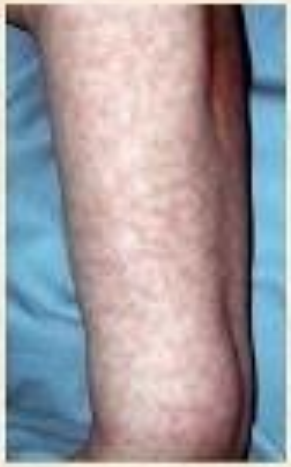
You Should Suspect Vasculitis

1. *Unexplained signs and symptoms*
2. *Multisystem involvement*
3. *Unexplained elevated ESR/CRP*
4. *Skin lesions (palpable purpura)*
5. *Ischemic vascular changes (Raynaud's, gangrene, livedo, claudication)*
6. *Glomerulonephritis*
7. *Mononeuritis multiplex*
8. *Intestinal angina*
9. *Inflammatory ocular disease*
10. *Arthralgia's/arthritis, myalgia's*
11. *Sudden visual loss/headache*

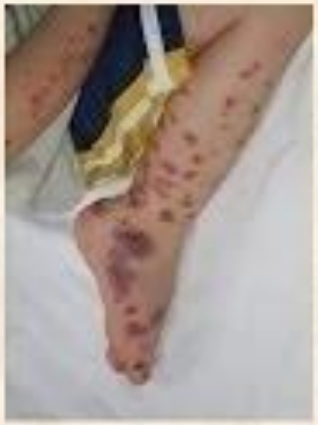
Clinical Features Highly Suggestive of Vasculitis

Mononeuritis Multiplex

Pulmonary-Renal Pattern



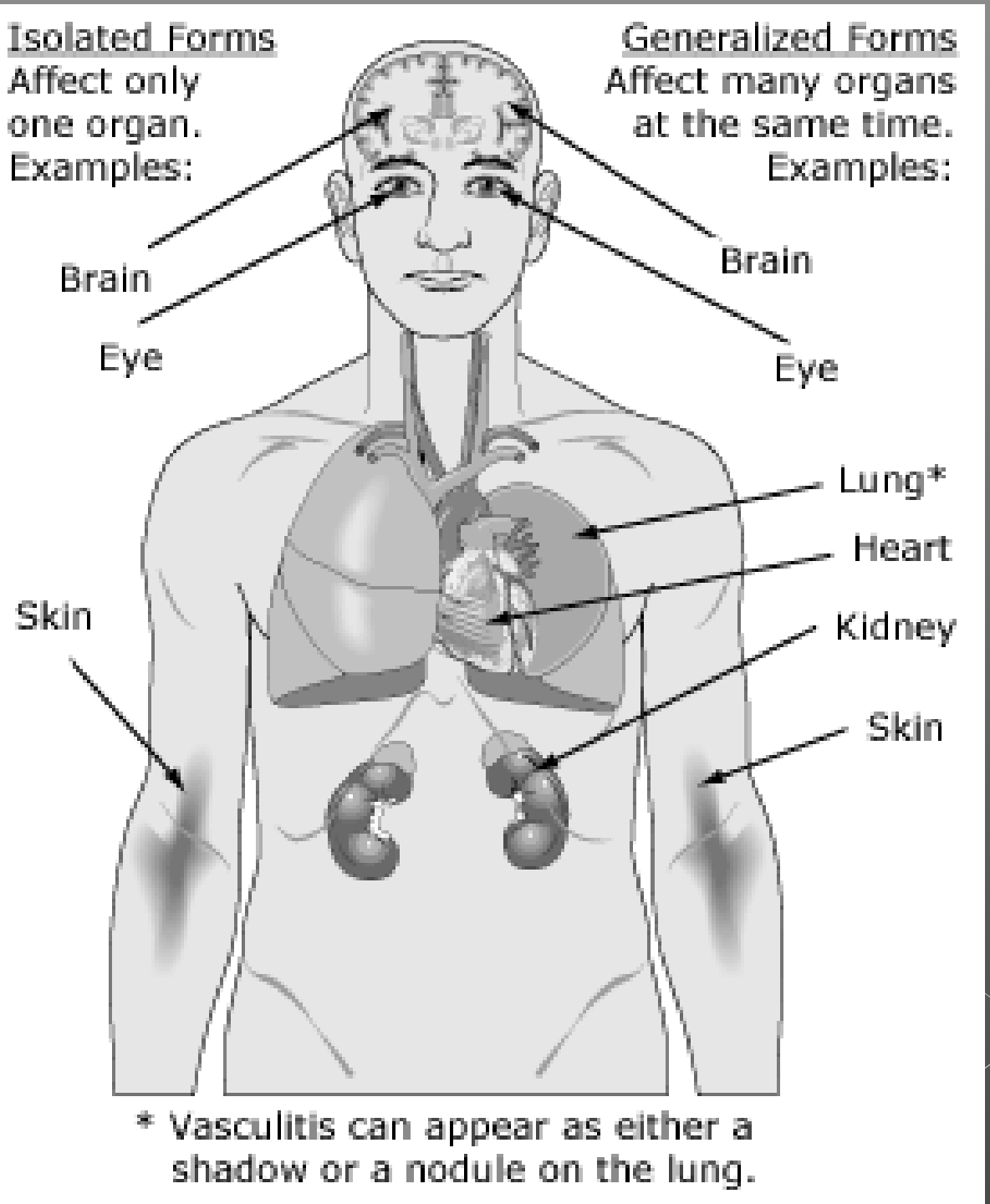
Livedo Reticularis



Palpable Purpura

Symptoms of vasculitis

1. *Fatigue*
2. *Weakness*
3. *Fever*
4. *Abdominal pain*
5. *Proteinuria , hematuria , casts*
6. *Nerve problems (numbness , weakness)*
7. *Skin rash*


Isolated Forms
Affect only one organ.
Examples:
Brain
Eye
Skin
Generalized Forms
Affect many organs at the same time.
Examples:
Brain
Eye
Lung*
Heart
Kidney
Skin
* Vasculitis can appear as either a shadow or a nodule on the lung.

CLASSIFICATION

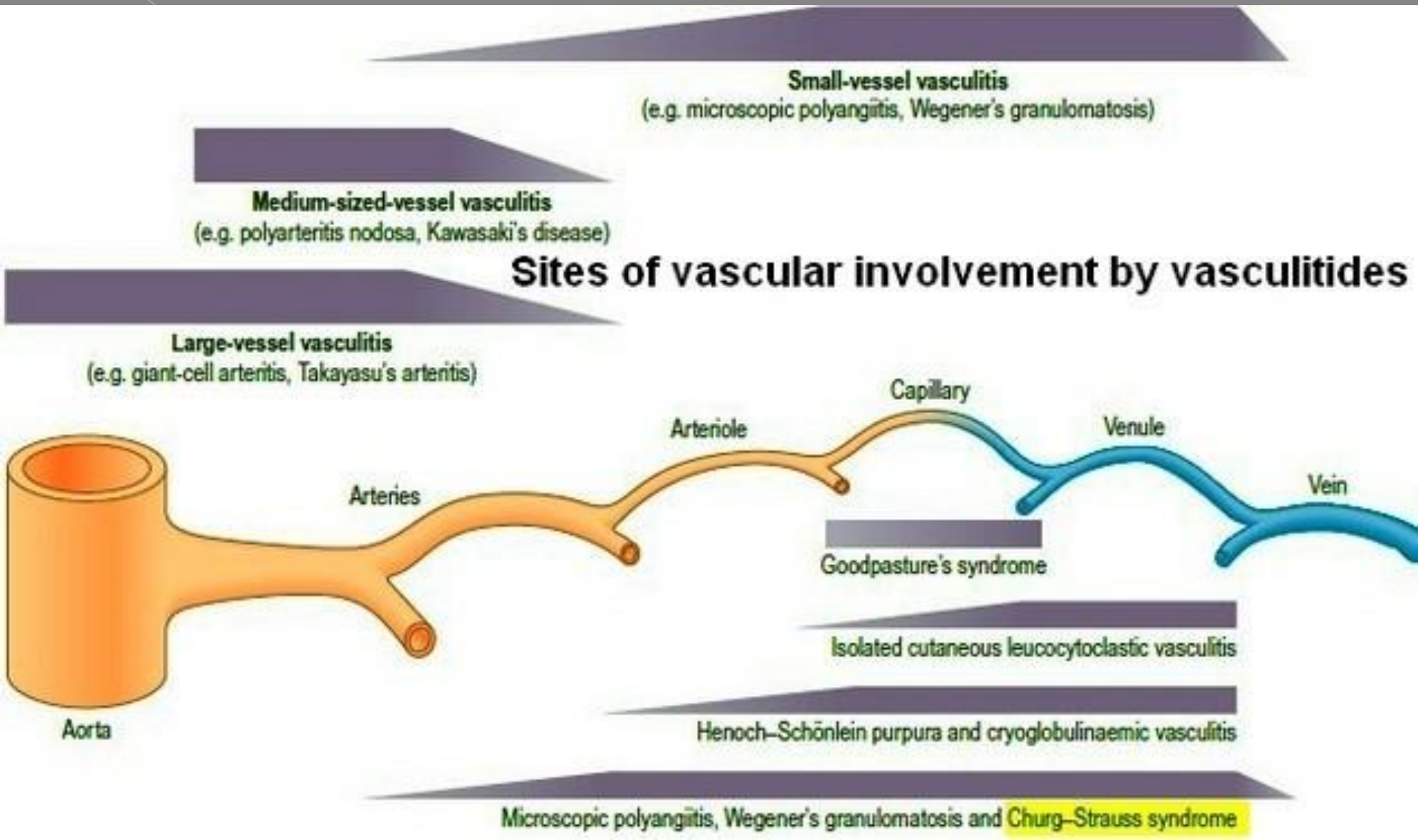
Based on

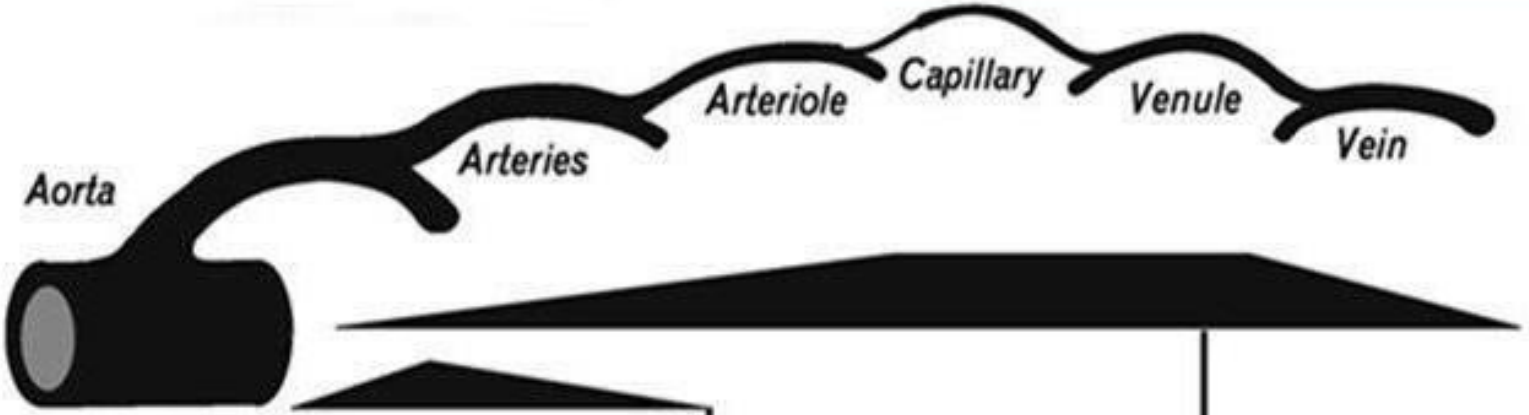
- Size of Vessels involved
- Site of involvement
- Characteristic Features

Vasculitis is a group of diseases of the blood vessels.

The diseases differ according to:

- the blood vessels involved
- the organs involved
- the main cause, if known


Small-vessel vasculitis
(e.g. microscopic polyangiitis, Wegener's granulomatosis)
Medium-sized-vessel vasculitis
(e.g. polyarteritis nodosa, Kawasaki's disease)
Sites of vascular involvement by vasculitides
Large-vessel vasculitis
(e.g. giant-cell arteritis, Takayasu's arteritis)
Capillary
Arteriole
Venule
Arteries
Vein
Goodpasture's syndrome
Isolated cutaneous leucocytoclastic vasculitis
Aorta
Henoch–Schönlein purpura and cryoglobulinaemic vasculitis
Microscopic polyangiitis, Wegener's granulomatosis and Churg–Strauss syndrome



Large vessel vasculitis

- Granulomatous arteritis in a patient >50 y → **Giant cell arteritis**
- Granulomatous arteritis in a patient <50 y → **Takayasu arteritis**

Medium vessel vasculitis

- Necrotizing arteritis without MCLN syndrome → **Polyarteritis nodosa**
- Necrotizing arteritis with MCLN syndrome → **Kawasaki disease**

Small vessel vasculitis

- Immune complexes in vessels
  - Other sources for immune complexes → **Other Im Cx vasculitis**
  - Cryoglobulins in blood and vessels → **Cryoglobulin vasculitis**
  - IgA-dominant vessel wall deposits → **H-S purpura**
  - SLE or rheumatoid arthritis → **SLE/rheumatoid vasculitis**
- Paucity of vascular Ig (often with ANCA)
  - Vasculitis with no asthma or granulomas → **Microscopic polyangiitis**
  - Granulomas and no asthma → **Wegener's granulomatosis**
  - Eosinophilia, asthma, and granulomas → **Churg-Strauss syndrome**

- **Large-vessel vasculitis**
  - *Giant cell arteritis, Takayasu's arteritis*
  - *Behcet's disease, Cogan's syndrome*
- **Medium-vessel vasculitis**
  - *Polyarteritis nodosa*
  - *Buerger's disease, Central nervous system vasculitis, Kawasaki's disease, Rheumatoid vasculitis*
- **Small-vessel vasculitis**
  - *Wegener's Granulomatosis , microscopic polyangiitis, Churg-Strauss* **(ANCA associated)**
  - *Cryoglobulinemic vasculitis, Henoch-Schönlein purpura* **(Non ANCA associated)**

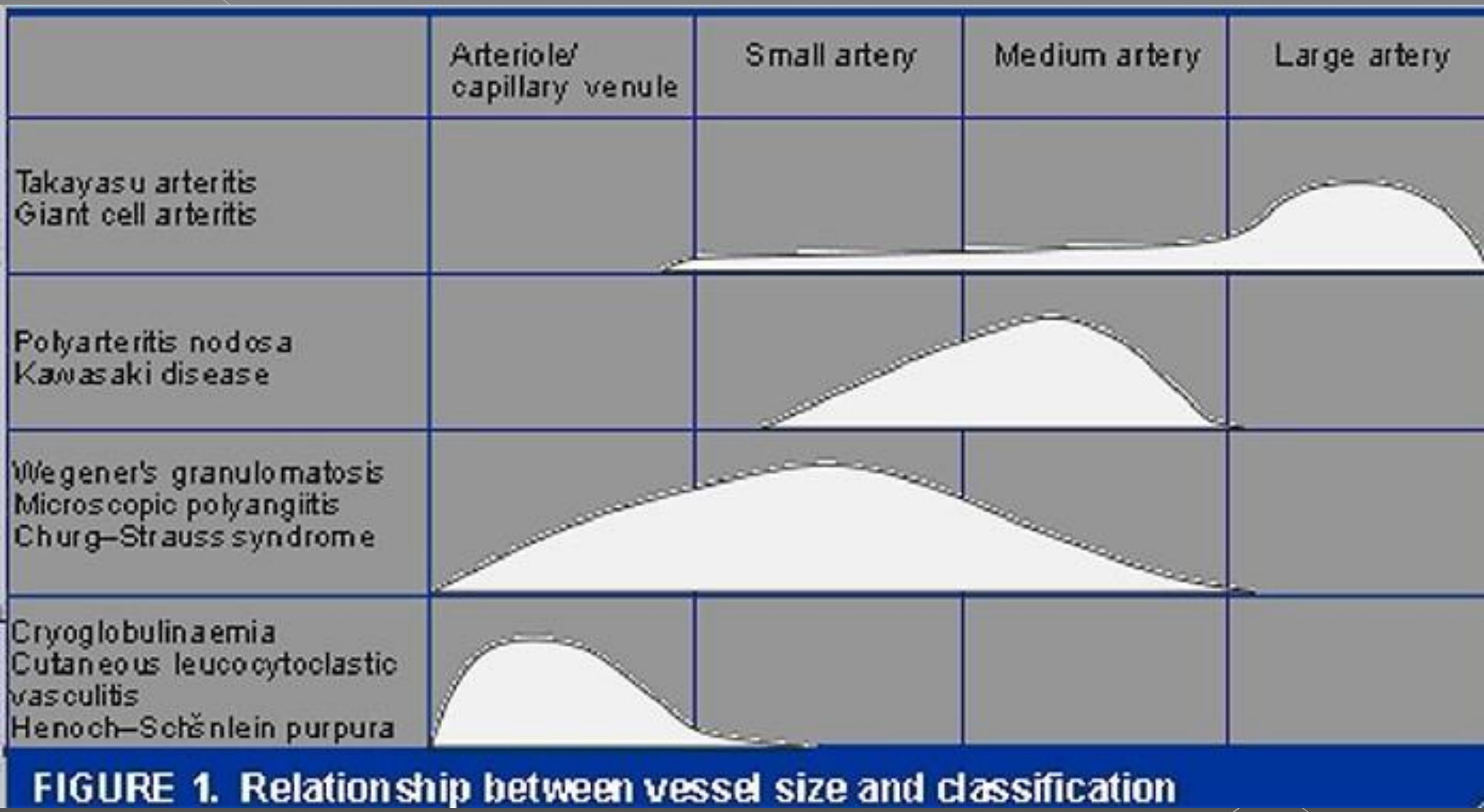
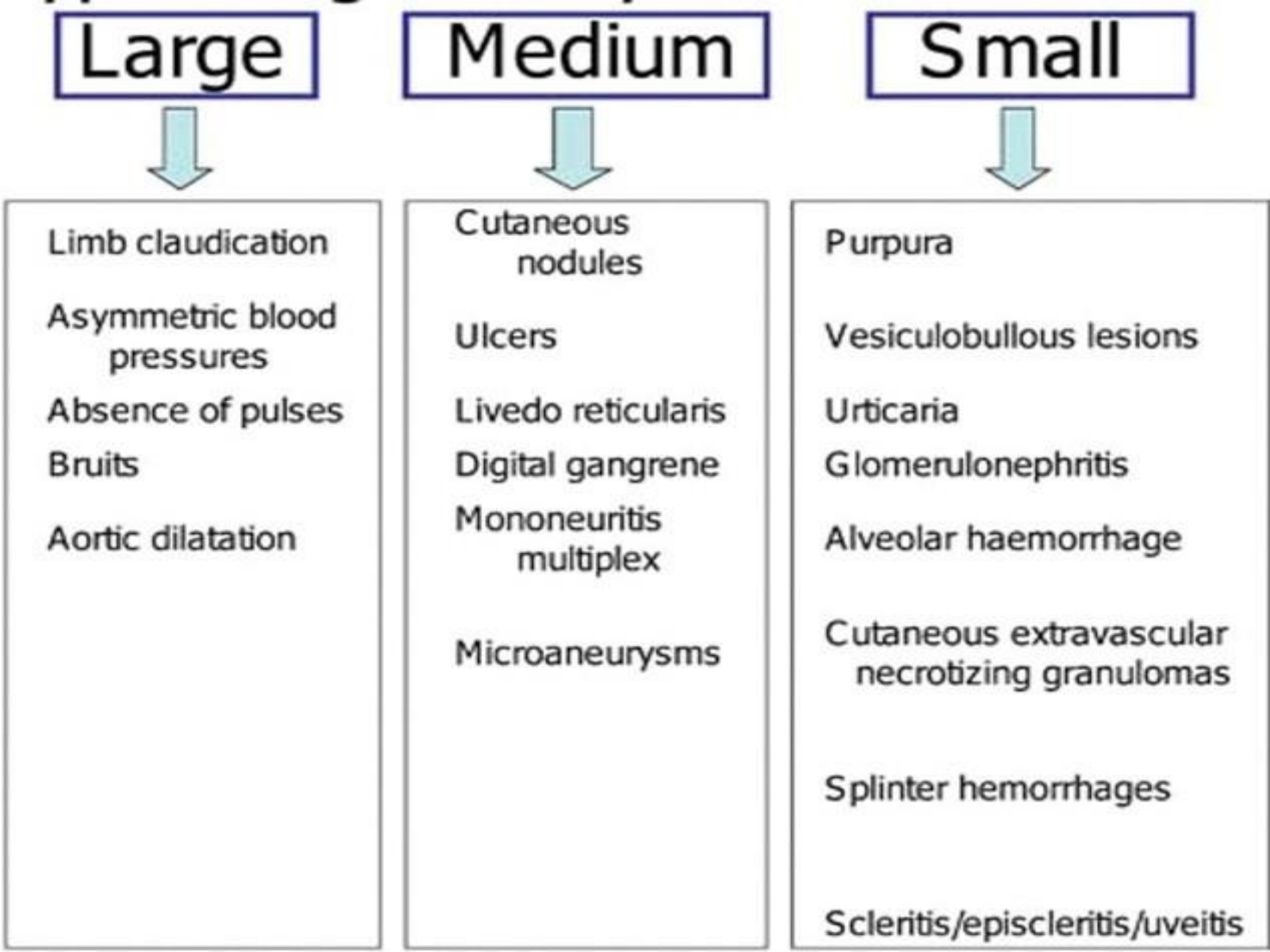


FIGURE 1. Relationship between vessel size and classification


Large
Limb claudication
Asymmetric blood pressures
Absence of pulses
Bruits
Aortic dilatation
Medium
Cutaneous nodules
Ulcers
Livedo reticularis
Digital gangrene
Mononeuritis multiplex
Microaneurysms
Small
Purpura
Vesiculobullous lesions
Urticaria
Glomerulonephritis
Alveolar haemorrhage
Cutaneous extravascular necrotizing granulomas
Splinter hemorrhages
Scleritis/episcleritis/uveitis

LARGE VESSEL ARTERITIS

Giant Cell Arteritis

Can occur exclusively but often seen with PMR

Rare: 15/100,000

Age >50

Cause unknown

Involves the medium/large blood vessels of the head and neck including the blood vessels that supply the optic nerve

Pathophysiology

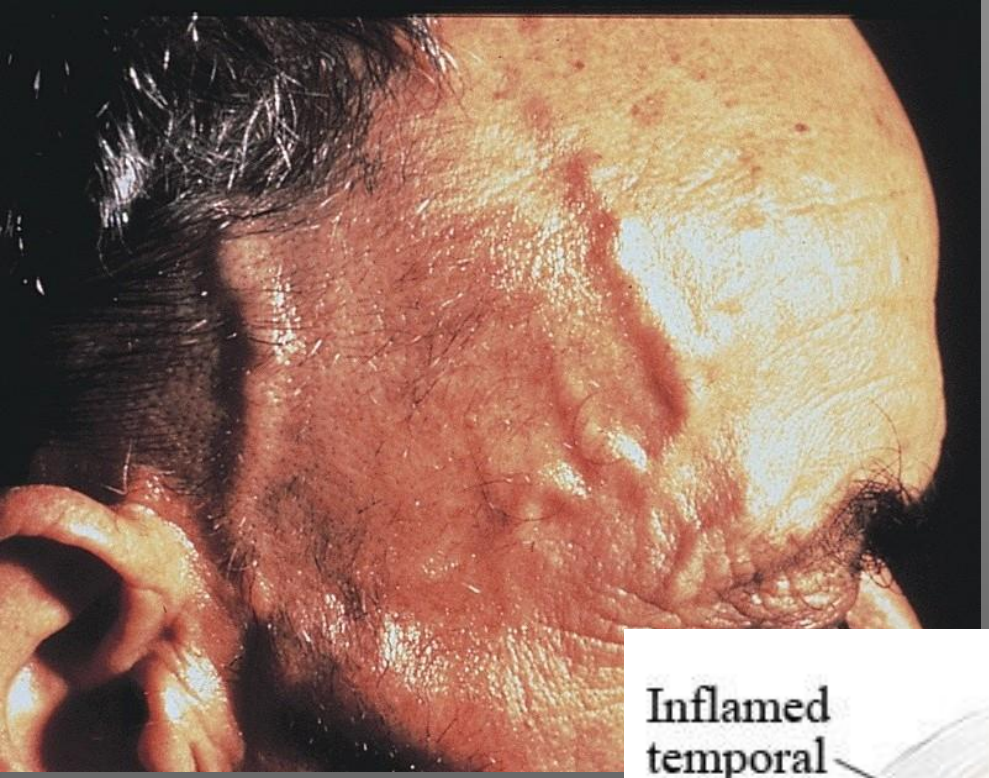
Unknown trigger causes inflammatory response with the release of IL-1 and IL-6.

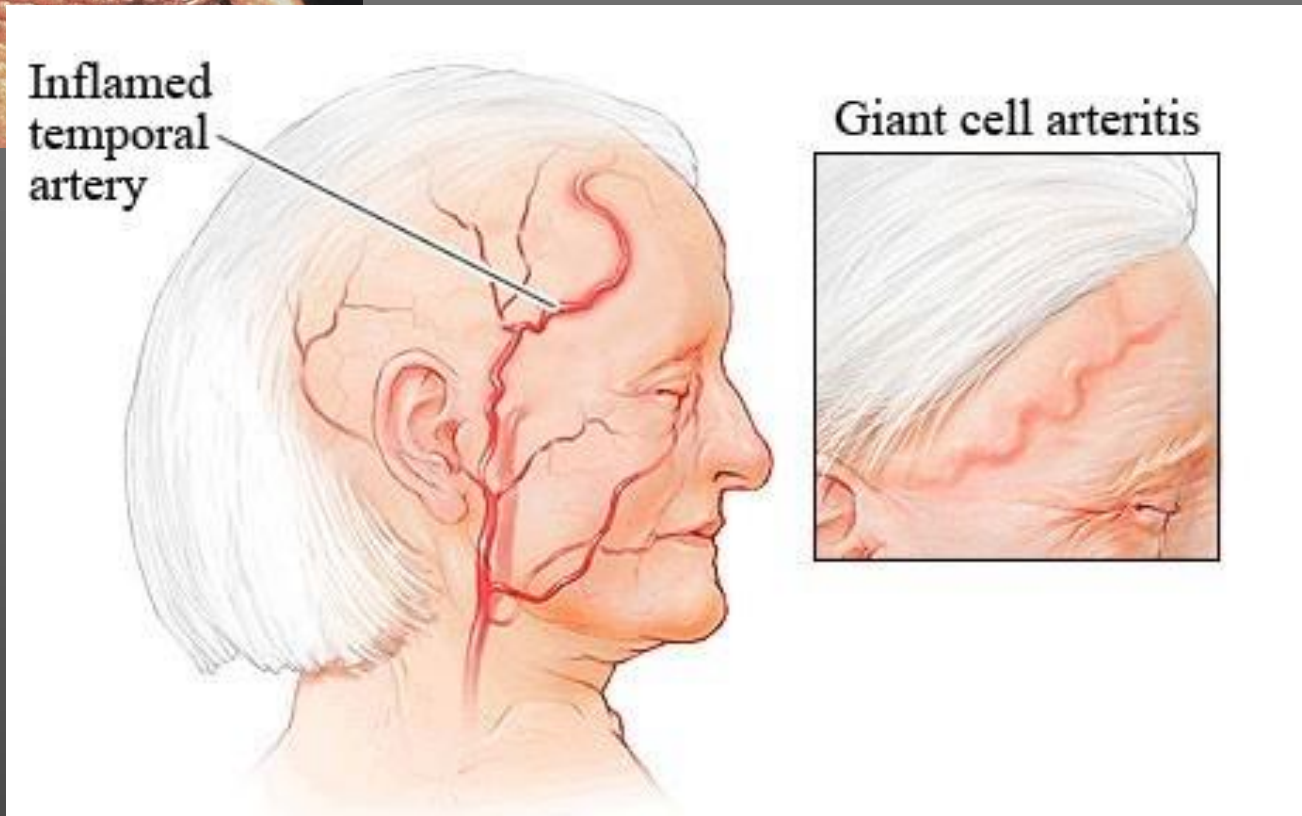
This leads to systemic symptoms and the infiltration of inflammatory cells into the adventitia of the temporal and other involved arteries

Typical histologic pattern: **Giant Cells**

Symptoms in giant cell arteritis*

Category	Symptoms
Symptoms due to involvement of cranial vessels	Headache Jaw claudication (pain on chewing) Scalp tenderness Loss of vision Abnormalities of the temporal artery (pain, nodules, absence of pulse)
Symptoms due to involvement of great vessels (aorta and branches of aorta)	Claudication of extremities (especially arm)
Symptoms due to systemic inflammation	Fever, night sweats, weight loss
Polymyalgia rheumatica	Mainly proximal myalgia and stiffness of the neck and shoulder and pelvic girdles




Inflamed
temporal
artery
Giant cell arteritis

Diagnostic Studies

- *Temporal Artery Biopsy is the gold standard*
- *Elevated ESR and CRP, usually levels higher than in PMR*
- *Anemia*
- *Elevated LFTs not uncommon*

Treatment

High dose Steroids (60 mg/day) is the only drug that works

Slow taper over time usually 1-2 years. Some patients require low dose (<10 mg/day) chronically

Complications

Blindness

Scalp Necrosis

Lingual Infarction

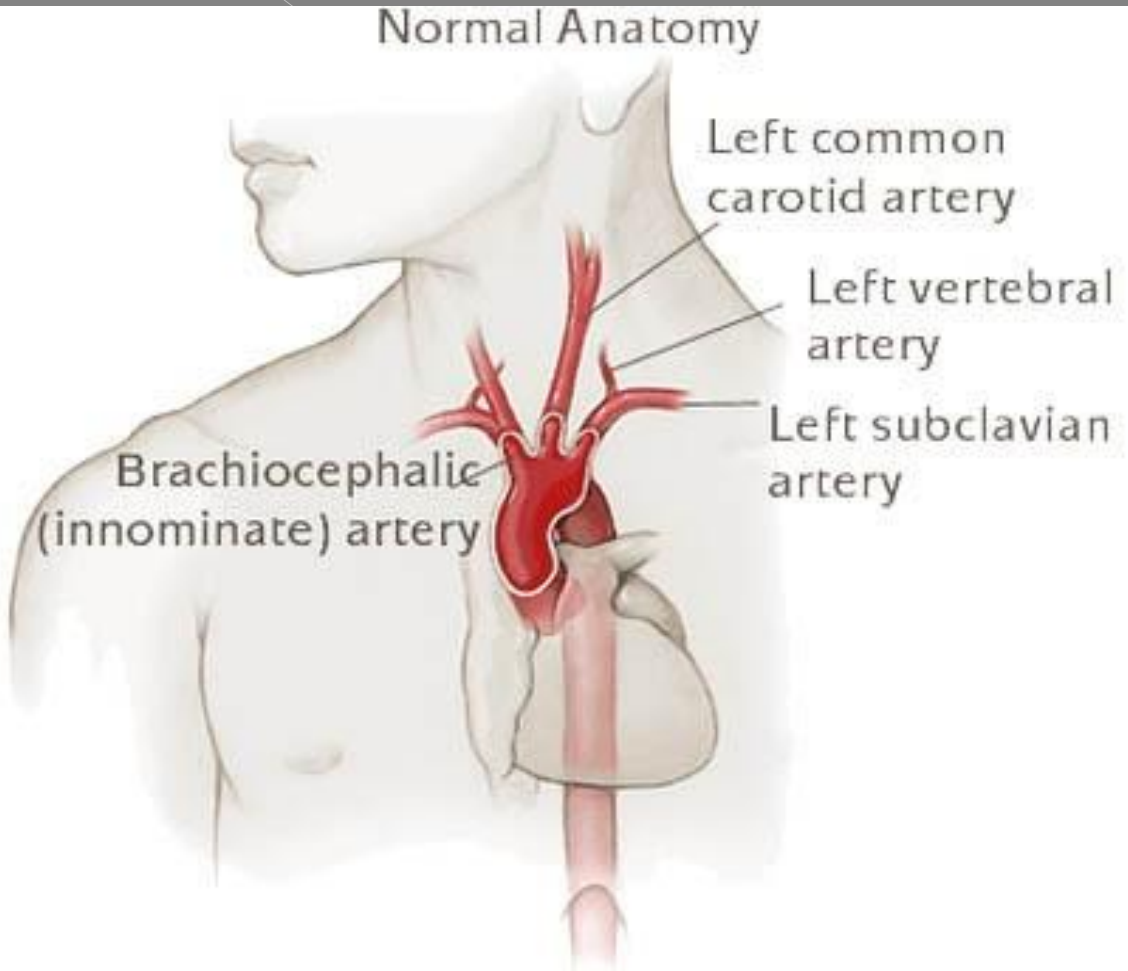
Aortic Dissection/Aneurysm

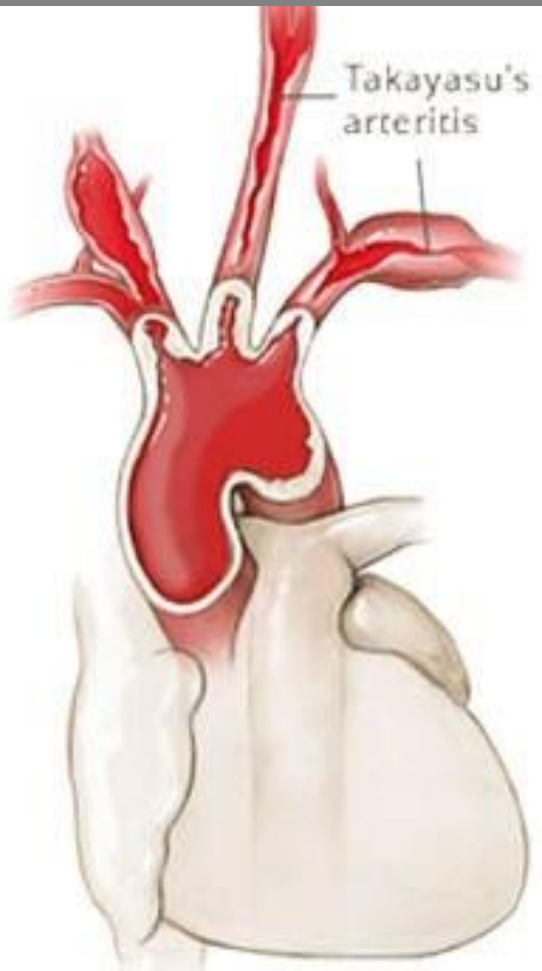
Complications from high dose steroids: osteoporosis, cataracts, elevated blood sugars, wt. gain etc.

Takayasu's arteritis is a rare disease that is most common in young women and teenage girls.

Clinical features

- Most common in females < 40 years
- Ocular changes: visual disturbances, retinal hemorrhages, blindness
- Progressive diminution of upper limb pulses with coldness or numbness of fingers - Pulseless disease
- Low BP in upper limb
- Neurologic defects – dizziness, focal weakness or complete hemiparesis


Normal Anatomy
Left common carotid artery
Left vertebral artery
Left subclavian artery
Brachiocephalic (innominate) artery

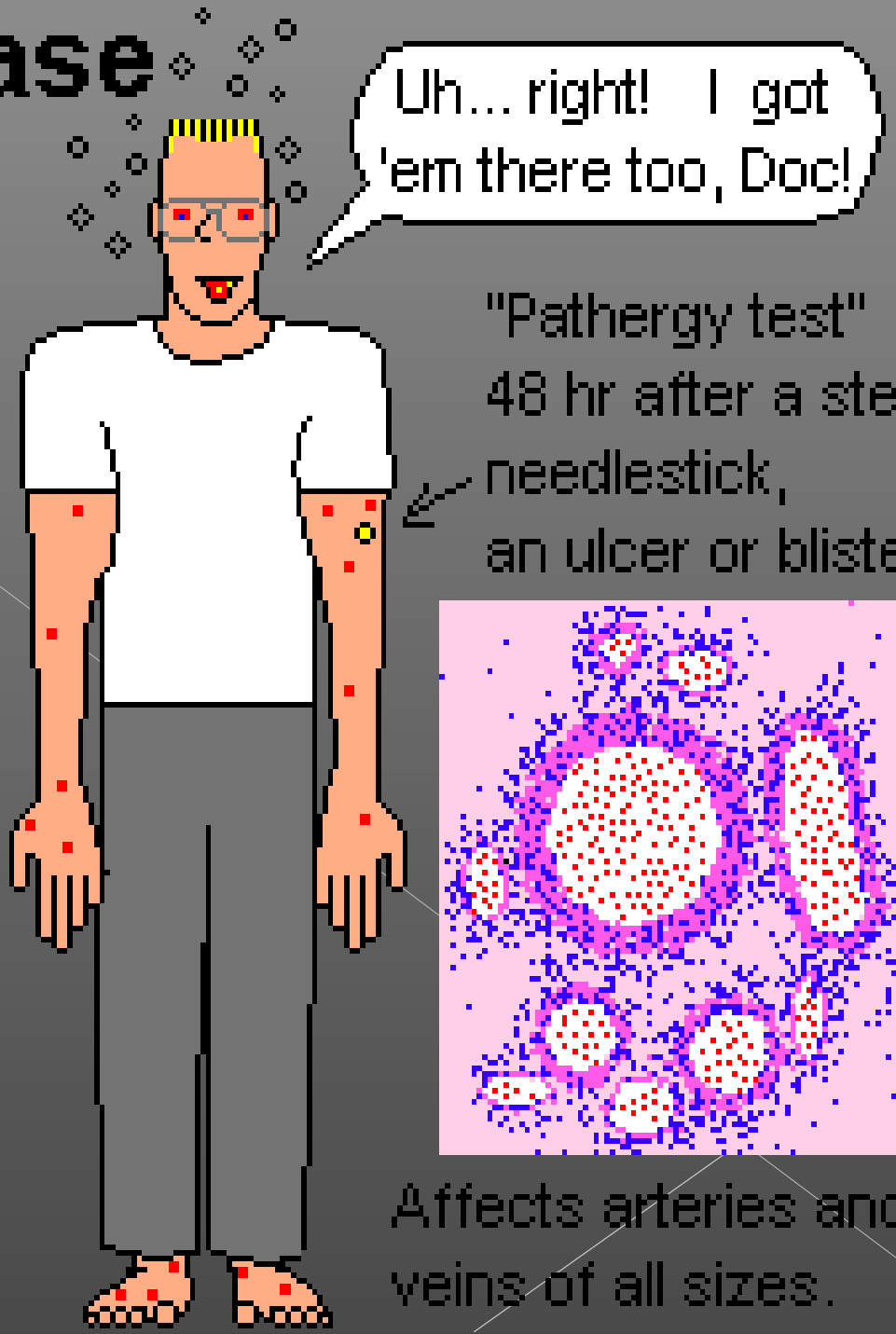

Takayasu's arteritis

Behçet's Disease

Easy to diagnose and treat -- if you think of it.

Autoimmunity against heat shock proteins (?) produces one of the truly great mimics.

Mouth ulcers (always)
Eye lesions
Genital ulcers
Skin lesions
Neurologic syndrome(s)
Infarcts of anything
Thrombosis of anything
Amyloidosis



"Pathergy test"
48 hr after a sterile needlestick,
an ulcer or blister.

Affects arteries and veins of all sizes.

Major

- Recurrent oral aphthous ulcers **70 %**
- Skin lesions
  - Erythema nodosum-like lesions
  - Folliculit, acneiform lesions
  - Thrombophlebitis
  - Cutaneous hypersensitivity
- Genital ulcers
- Ocular disease
  - Iridocyclitis
  - Posterior uveitis

Minor

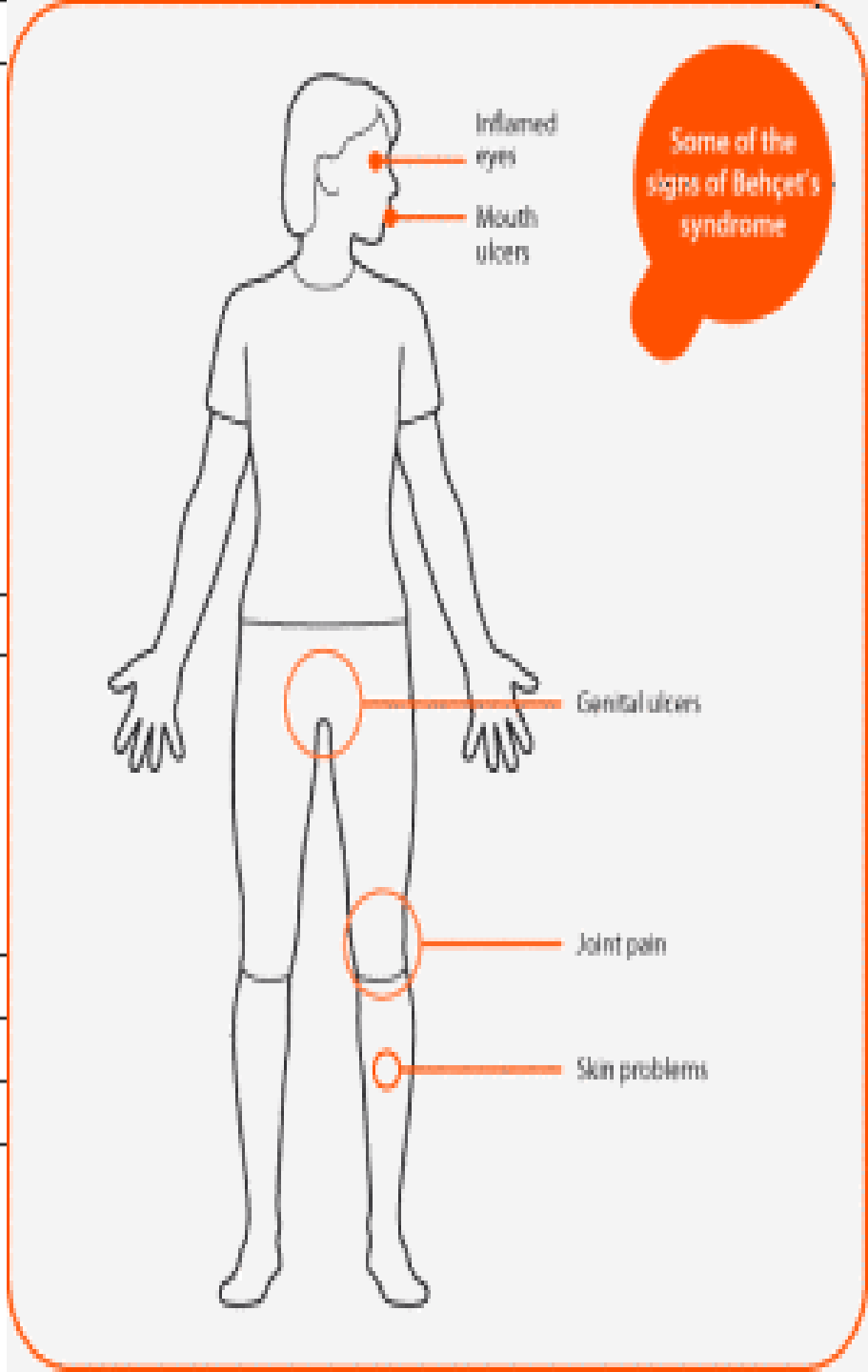
- Arthritis
- Epididymitis
- Intestinal symptoms attributed to ileocecal ulcerations
- Vascular symptoms
- Neurologic symptoms attributed to nervous system involvement

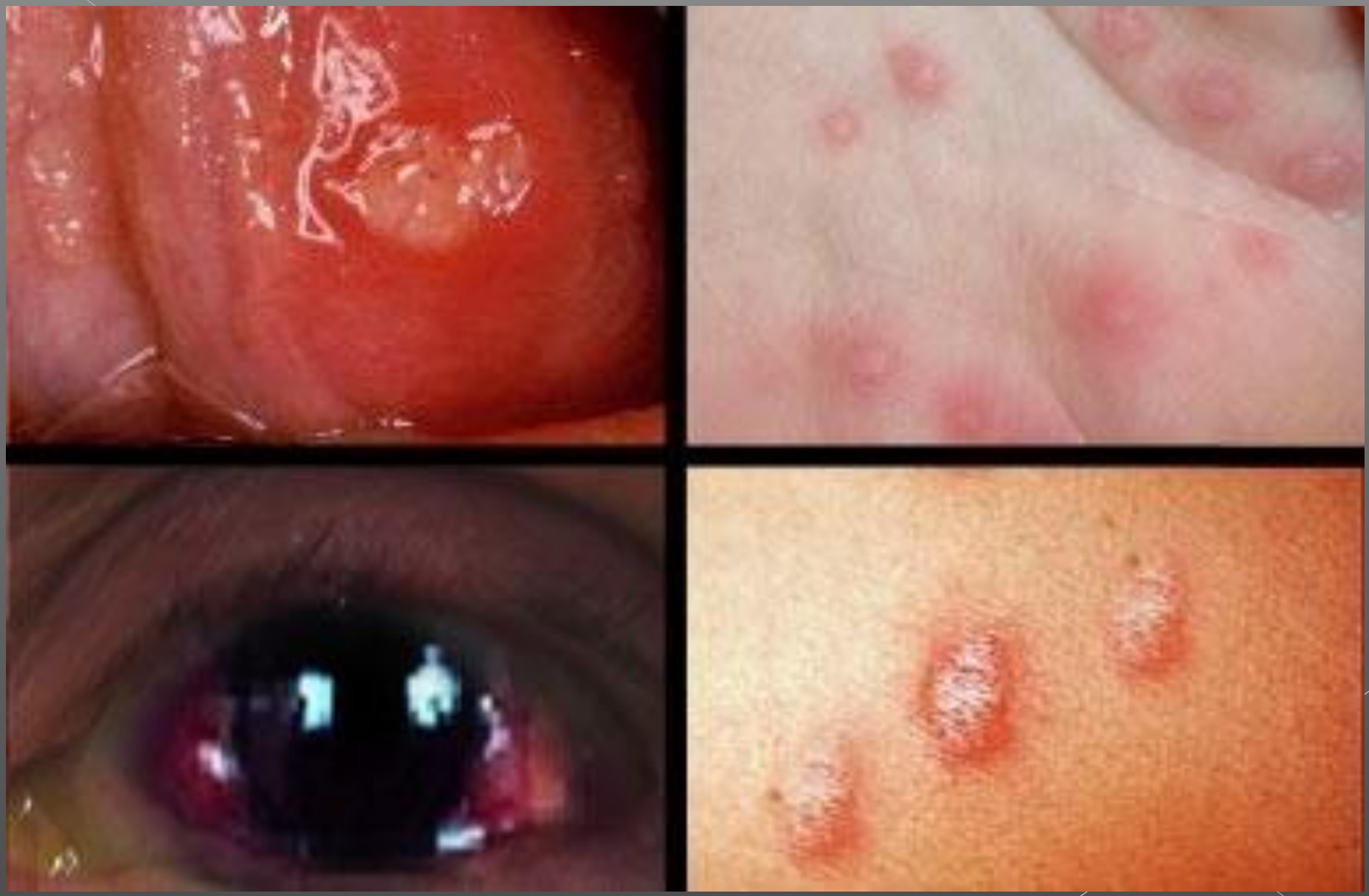
Complete type

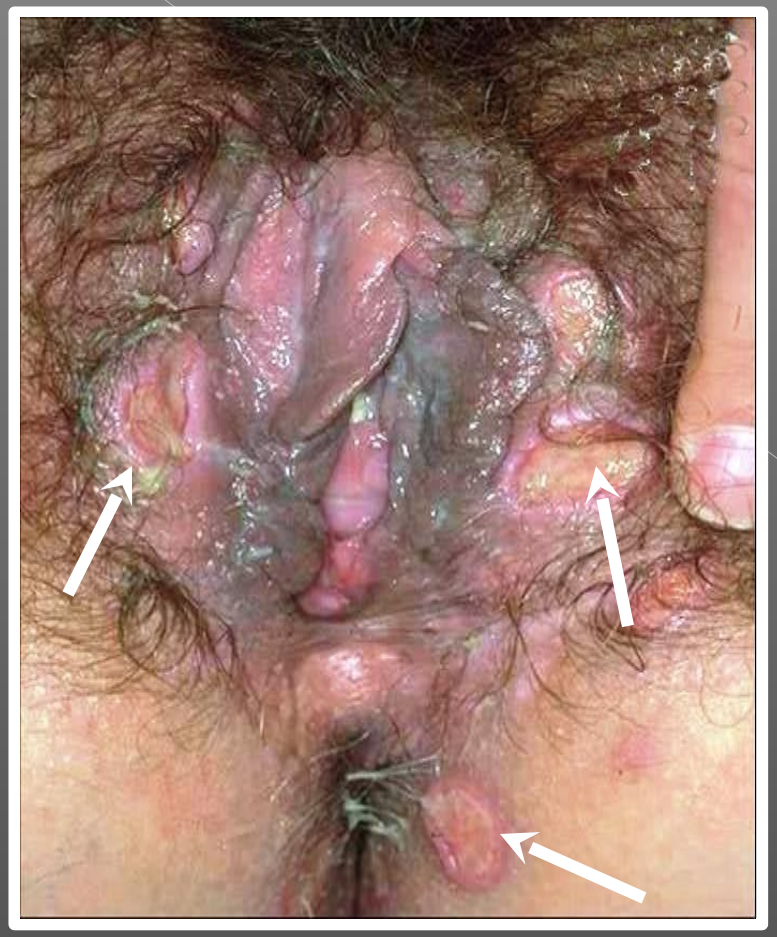
- The presence of all four major criteria

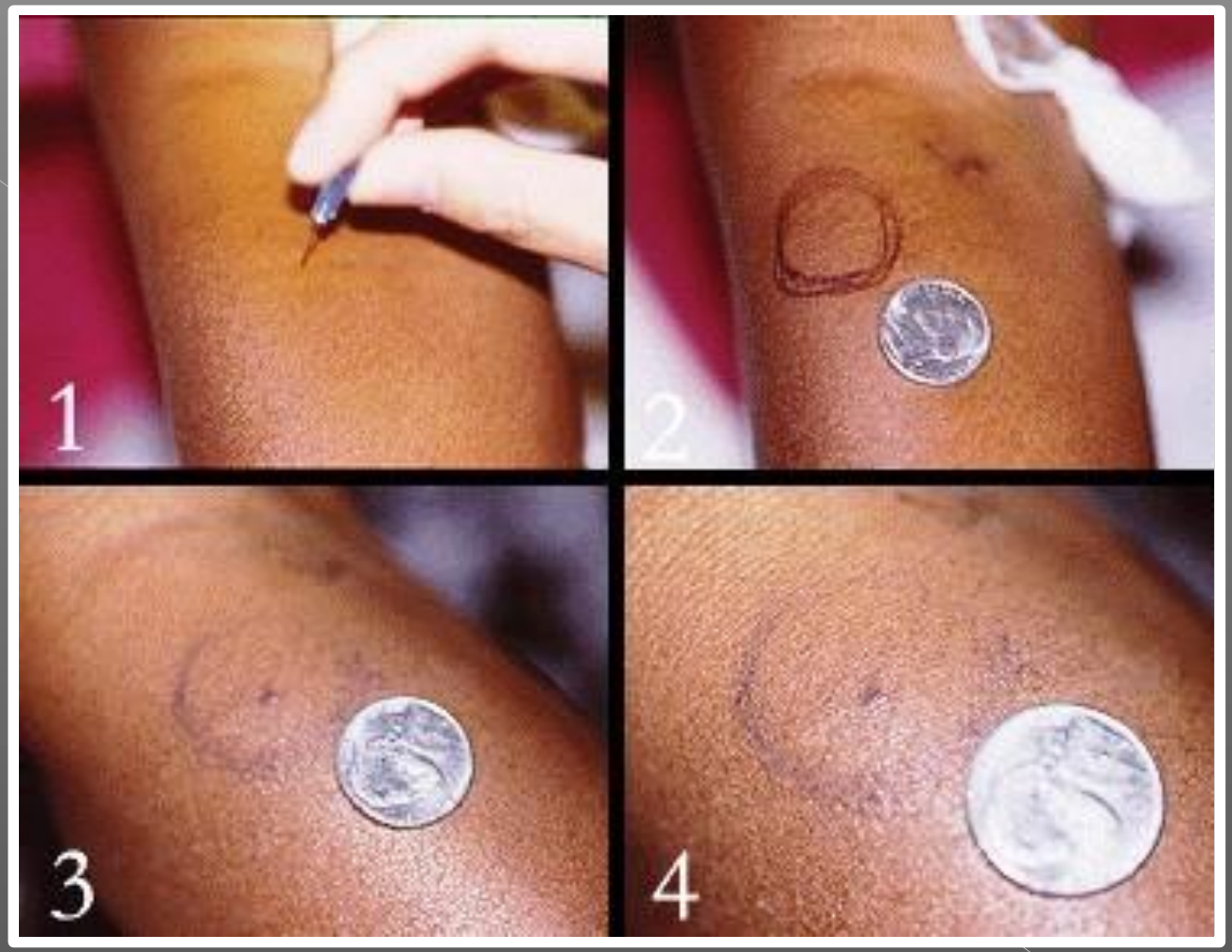
Incomplete type

- The presence of three major criteria
- Two major and two minor criteria
- Ocular disease plus one major criteria
- Ocular disease plus two minor criteria









Pathergy- An erythematous papule larger than 2 mm at the prick site 48 hours after the application of a 20- to 22-gauge sterile needle, which obliquely penetrated avascular skin to a depth of 5 mm as read by a physician at 48 hours

Polyarteritis Nodosa (PAN)

Medium vessel vasculitis

Can be caused by Hep B

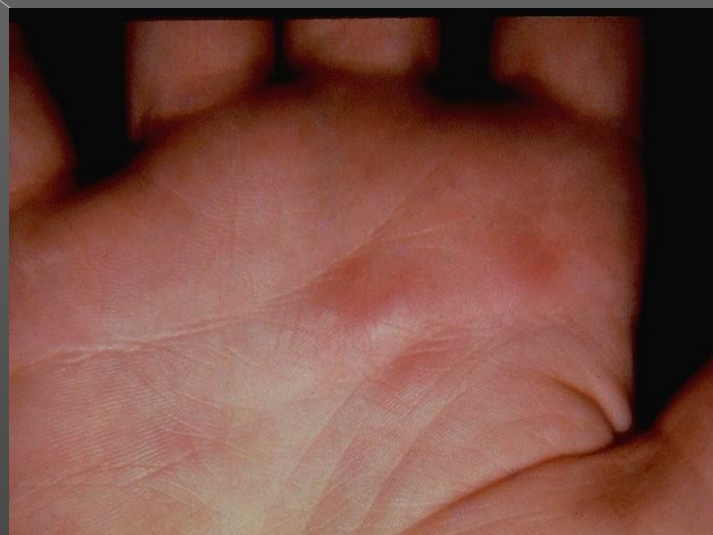
5/million cases

Peak incidence 50's & 60's, slightly more common inmales

Pathophysiology

In Hep B assoc cases immune complexes play significant role

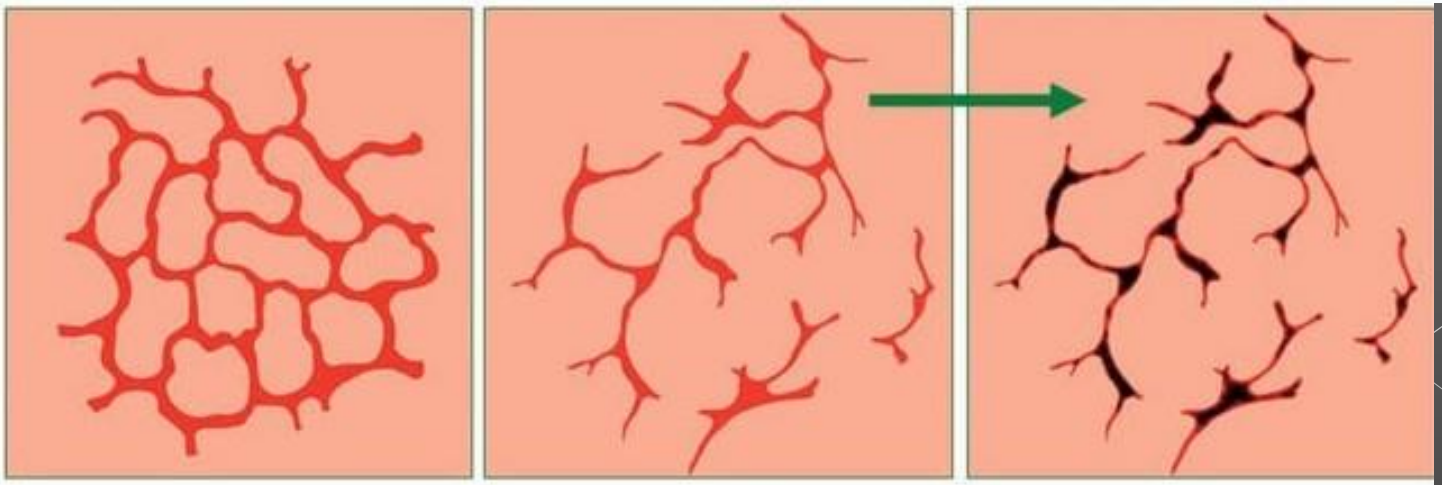
In non Hep B cases, the pathophysiology is less understood



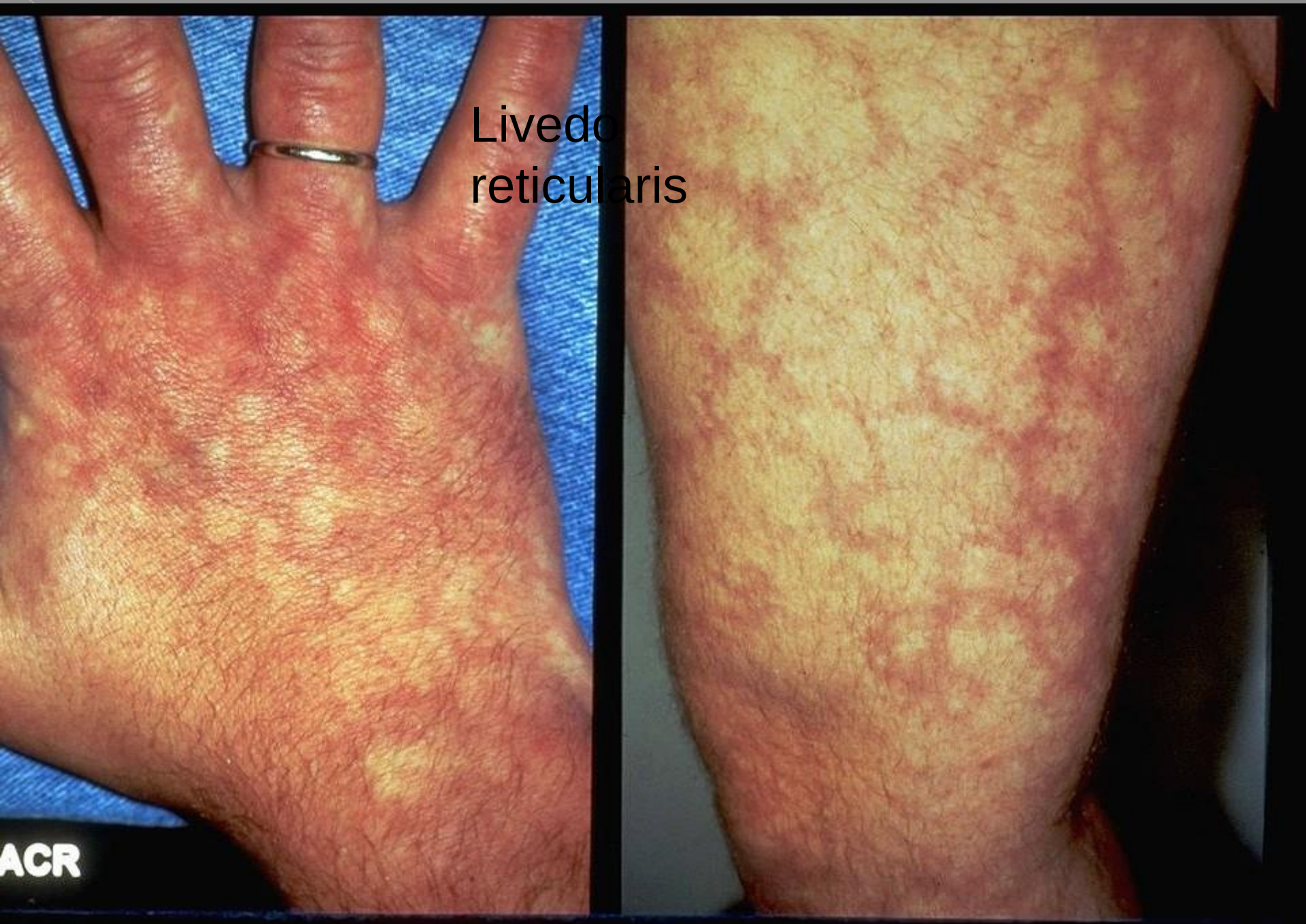
Clinical Presentation

- **Systemic:** *fever, fatigue, wt loss*
- **Abdominal pain** *due to mesenteric angina/ischemia*
- **Mononeuritis multiplex**
- **Myalgias/arthalgias/mild arthritis**
- **Renal:** *uremia, Hypertension*
- **Skin:** *livedo reticularis, palpable purpura, fingertip ulceration, subcutaneous nodules*
- **Testicular** *pain or tenderness*

Livedo reticularis	Livedo racemosa
Tight net-like pattern without any breaks	Breaks in the net-like pattern, resulting in larger irregular branching lesions
Symmetrical	Asymmetrical
Indicative of generalized impairment of blood flow (e.g., cutis marmorata)	Indicative of localized impairment of blood flow (e.g., vasculitis)
Varies with temperature changes	Does not vary appreciably with temperature changes



Livedo reticularis *Livedo racemosa* **Púrpura retiforme**


Livedo
reticularis
ACR

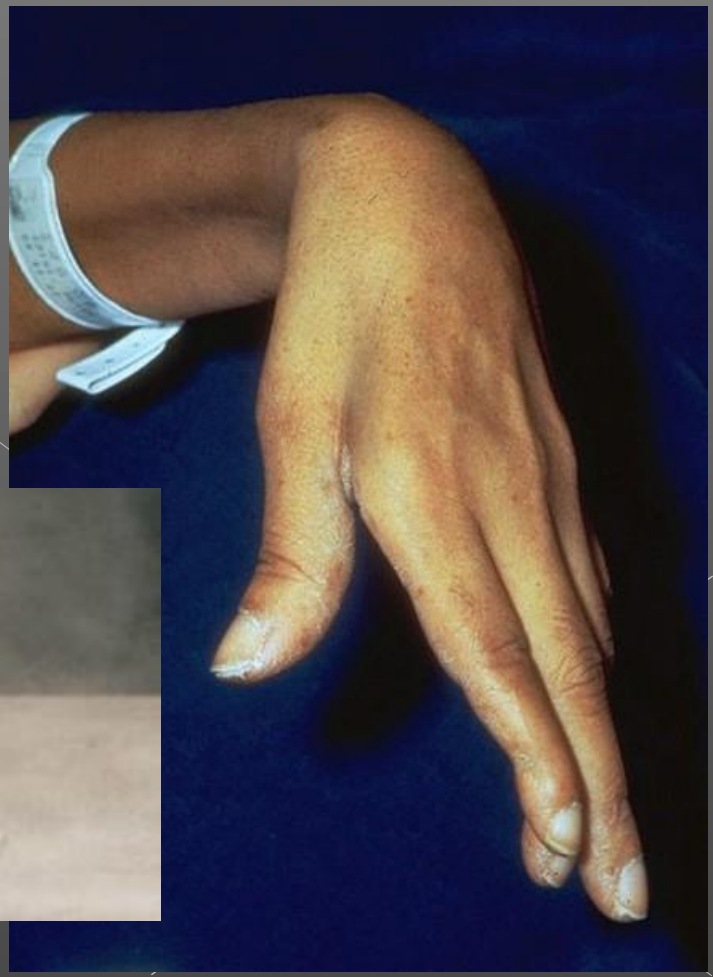
Complications

Chronic renal failure

Bowel perforation

Stroke/cerebral hemorrhage due to HTN

Foot/wrist drop



Investigations

Elevation of acute phase reactants (ESR, CRP etc)

Absence of ANCA

Elevated transaminases, decreased albumin

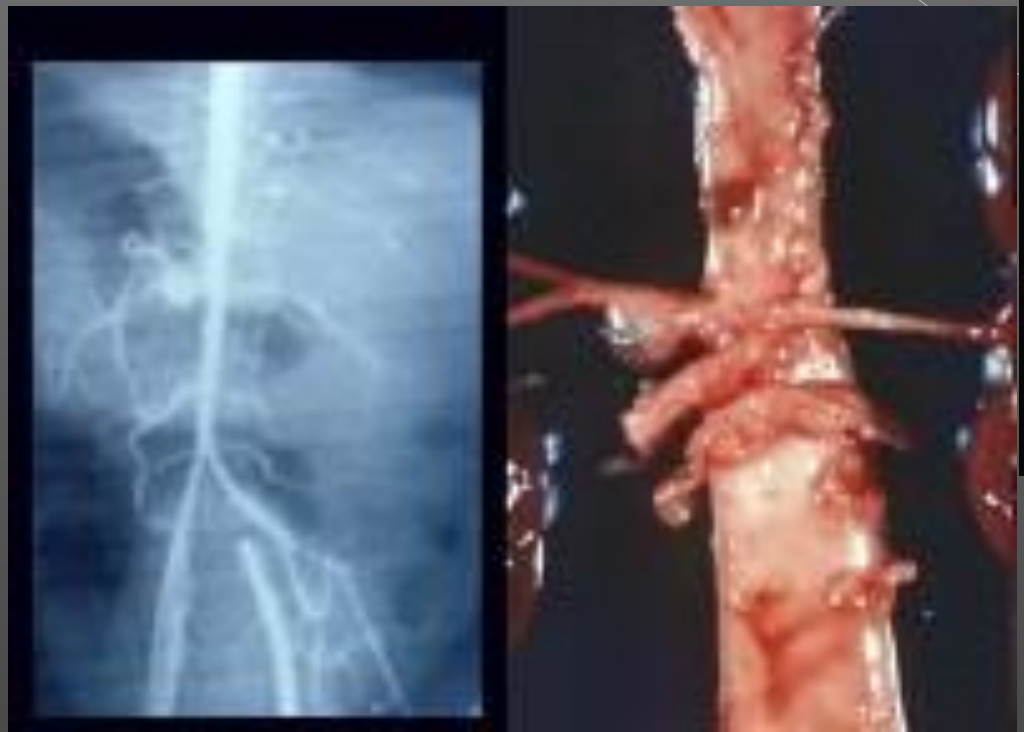
+/- Hep B

Urine: proteinuria and hematuria without casts

Imaging Studies

Mesenteric and/or renal angiography is the test of choice

Biopsies seldom done



STRING OF PEARLS

Treatment

High dose steroids and Cyclophosphamide

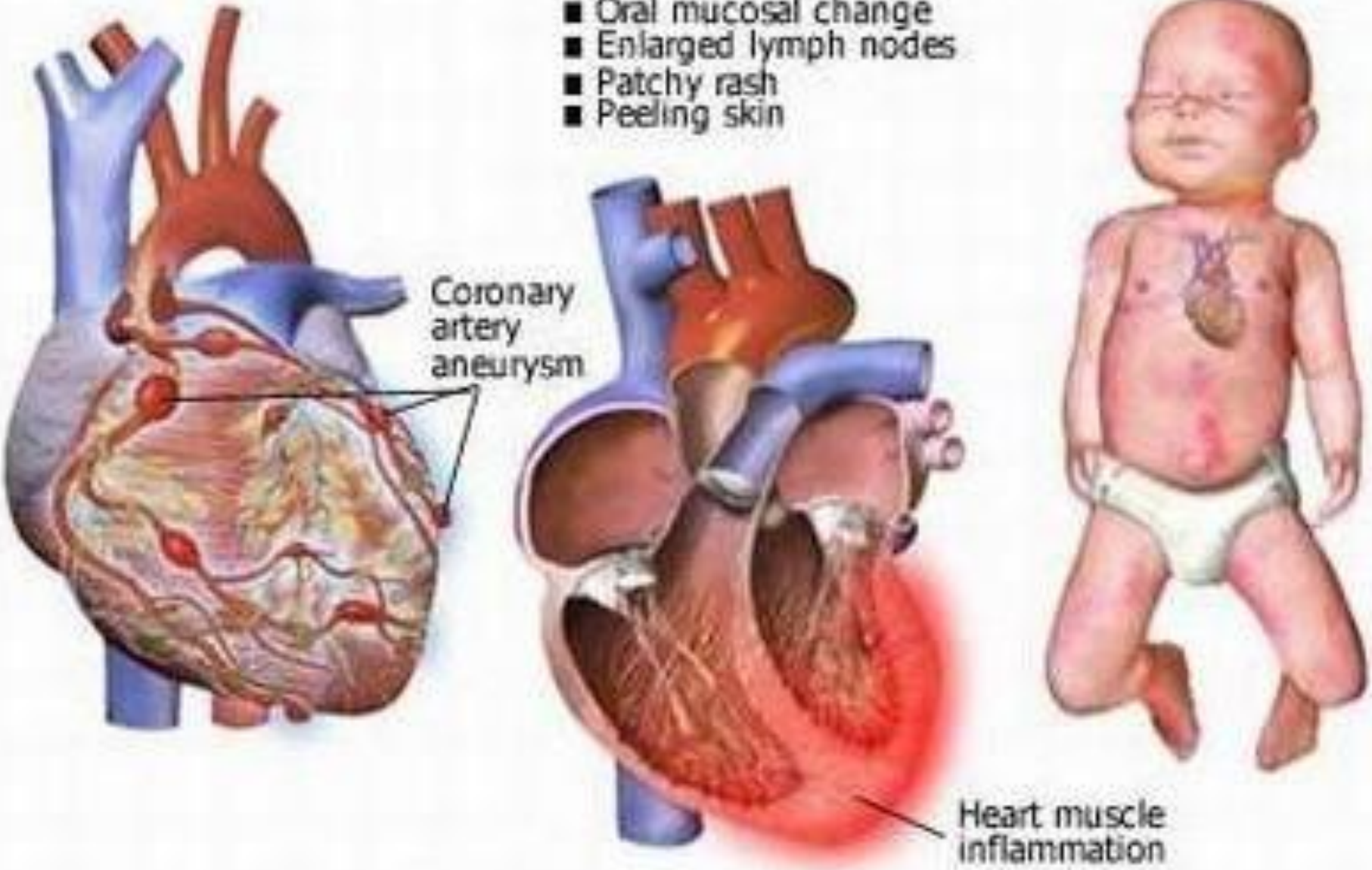
Methotrexate or Azathioprine is used as steroid sparing agents later once the disease is controlled

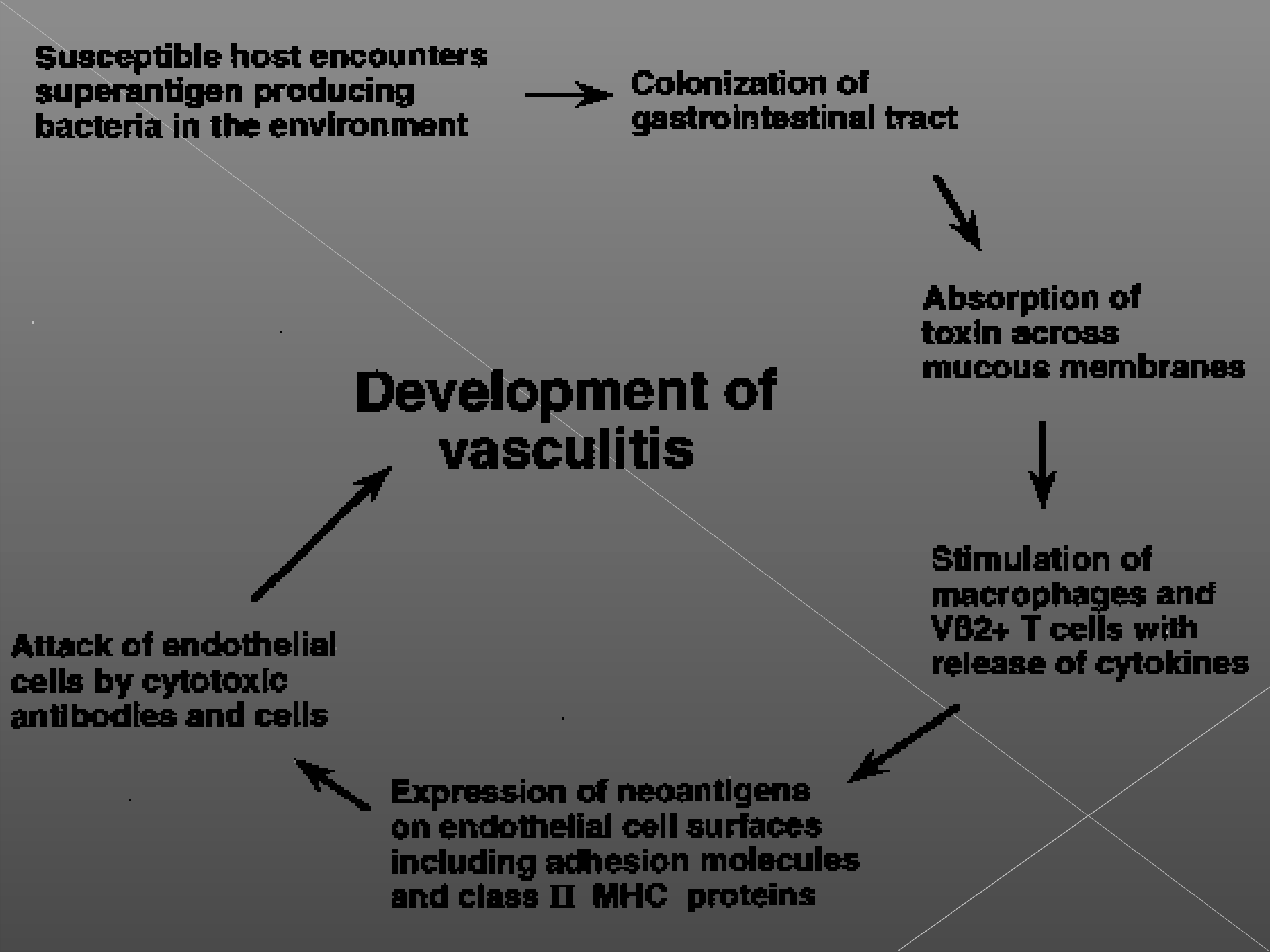
Treatment for Hep B with antivirals. Sometimes plasma exchange is used to remove immune complexes

Kawasaki Disease

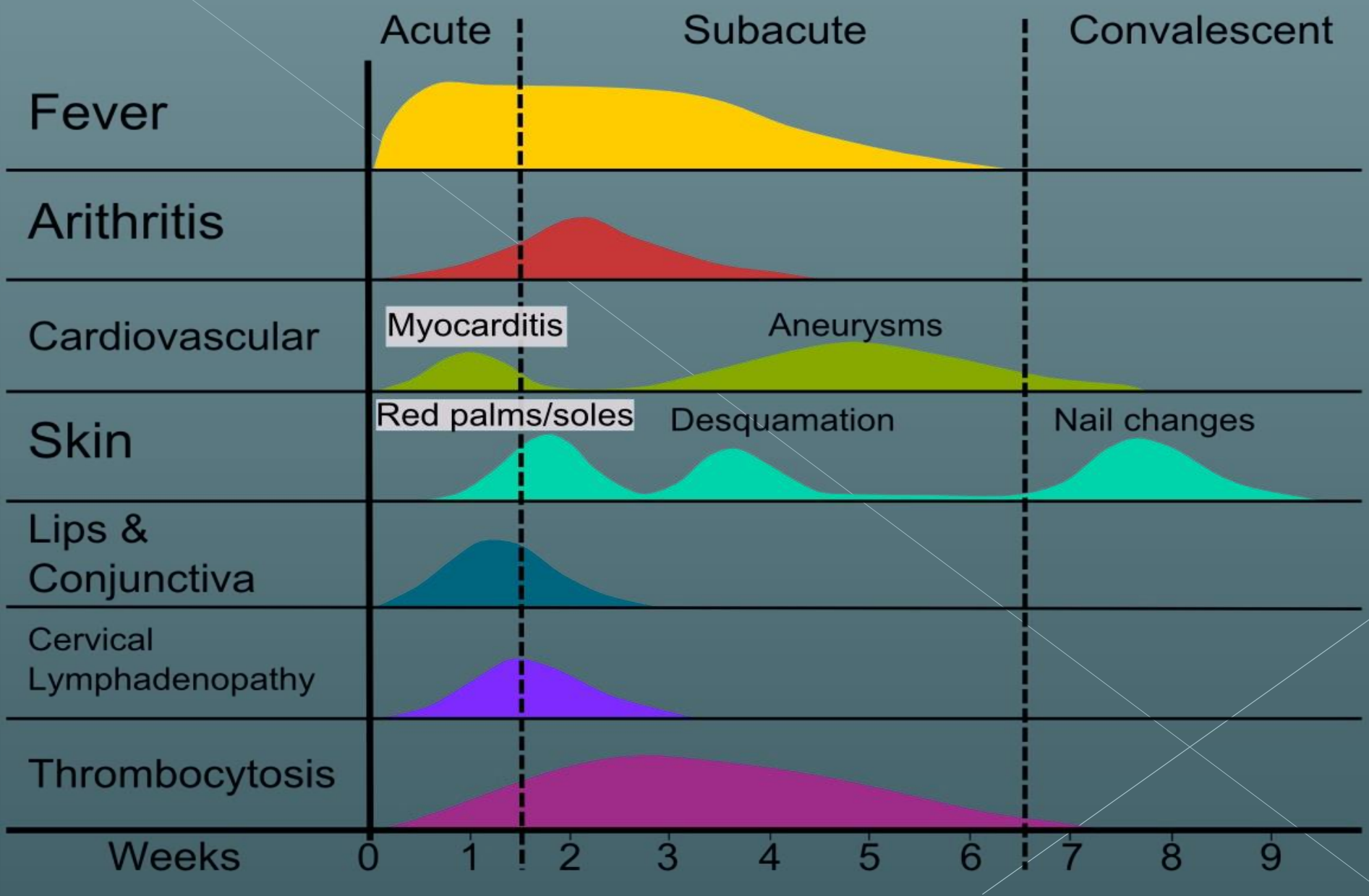
A type of disease that primarily affects young children and believed to be caused by a non-contagious infection. Symptoms include:

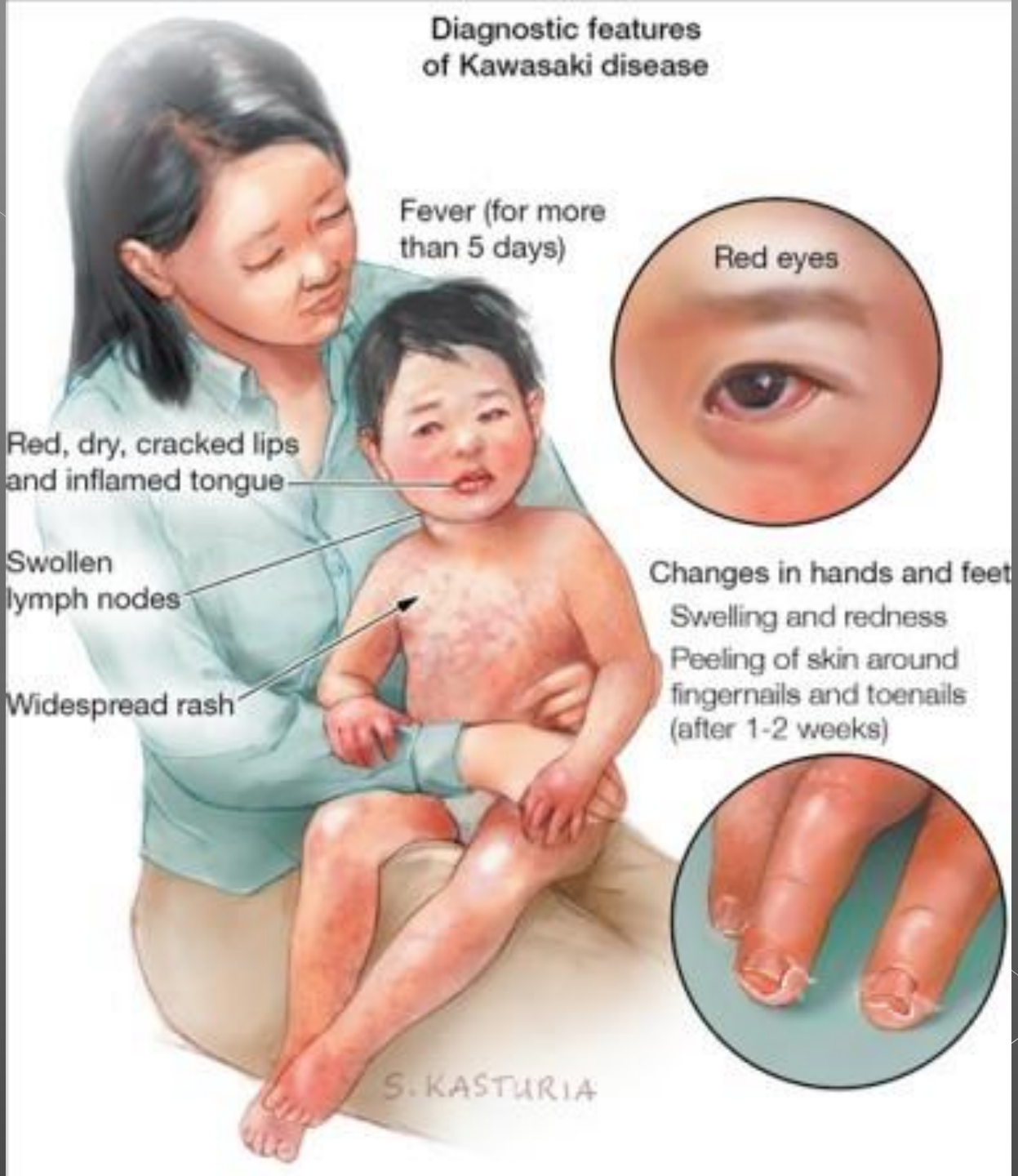
- Pink eye
- Oral mucosal change
- Enlarged lymph nodes
- Patchy rash
- Peeling skin




Susceptible host encounters superantigen producing bacteria in the environment
Colonization of gastrointestinal tract
Absorption of toxin across mucous membranes
Stimulation of macrophages and Vβ2+ T cells with release of cytokines
Expression of neoantigens on endothelial cell surfaces including adhesion molecules and class II MHC proteins
Attack of endothelial cells by cytotoxic antibodies and cells
Development of vasculitis

Clinical manifestations of Kawasaki Disease




Diagnostic features
of Kawasaki disease
Fever (for more
than 5 days)
Red eyes
Red, dry, cracked lips
and inflamed tongue
Swollen
lymph nodes
Widespread rash
Changes in hands and feet
Swelling and redness
Peeling of skin around
fingernails and toenails
(after 1-2 weeks)
S. KASTURIA

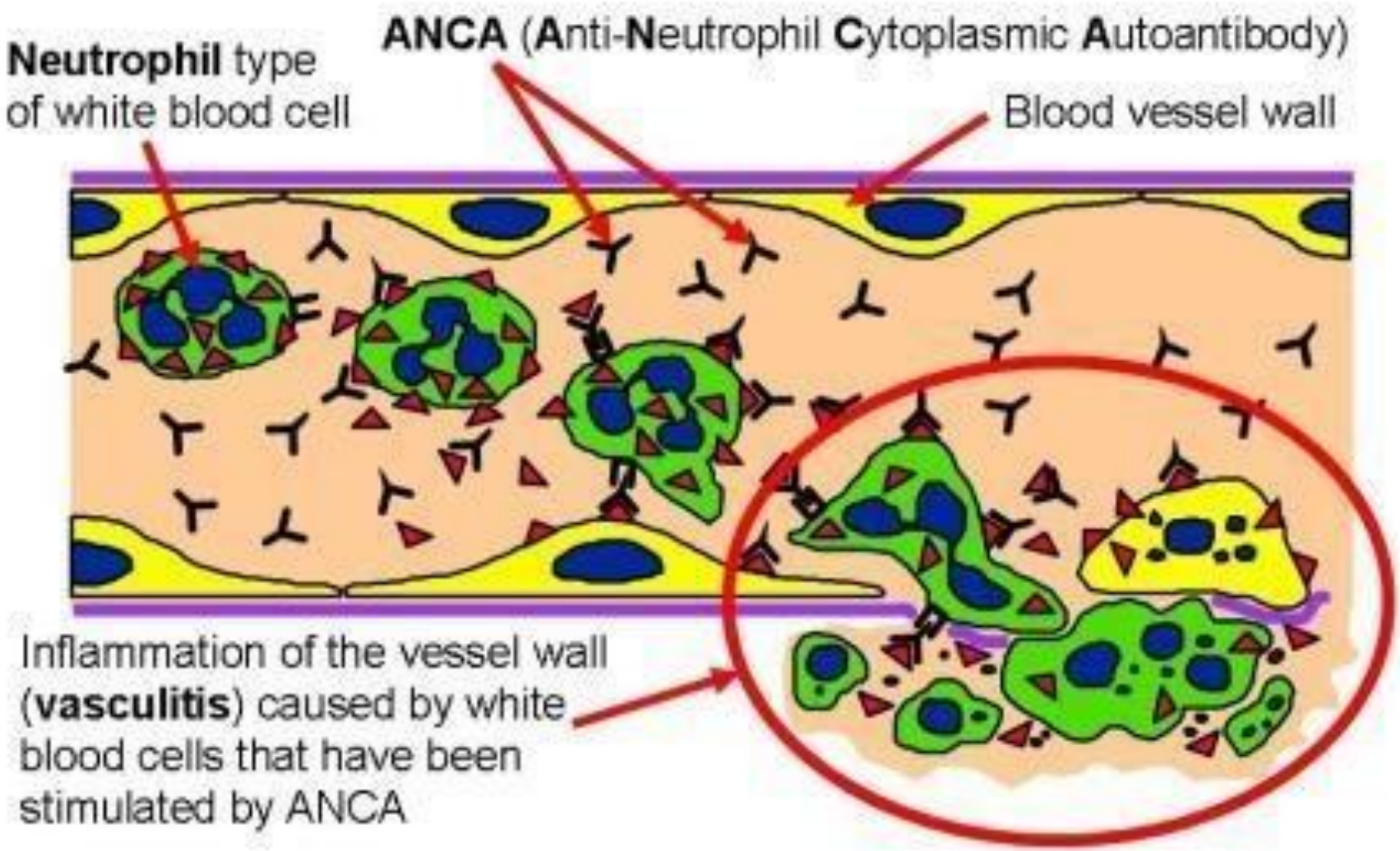
Small Vessel Vasculitides

ANCA +

- Churg-Strauss syndrome
- Microscopic Polyangiitis
- Wegener Granulomatosis

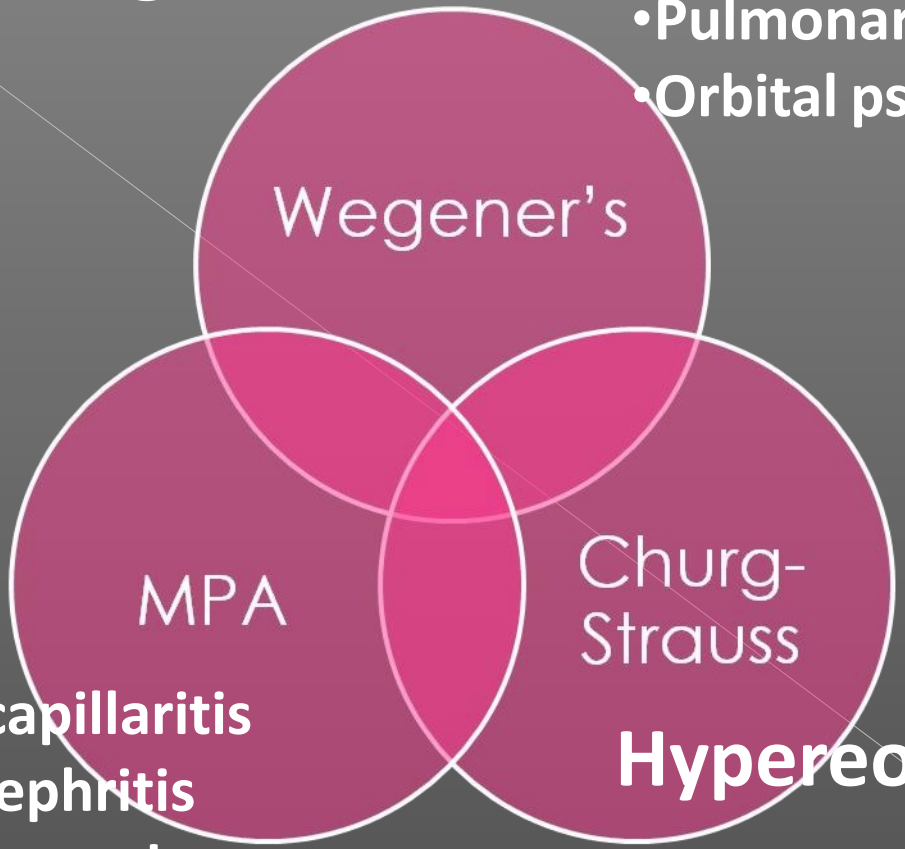
ANCA – Immune complex deposition

- Henoch-Schonlein Purpura
- Cryoglobulinemic Vasculitis
- Cutaneous Leukoclastic Vasculitis


Neutrophil type of white blood cell
ANCA (**A**nti-**N**eutrophil **C**ytoplasmic **A**utoantibody)
Blood vessel wall
Inflammation of the vessel wall (**vasculitis**) caused by white blood cells that have been stimulated by ANCA

Necrotizing Granuloma

- Sinusitis
- Subglottic stenosis
- Pulmonary nodules
- Orbital pseudotumor



- Pulmonary capillaritis
- Glomerulonephritis
- Sensory neuropathy
- Mononeuritis multiplex

Hypereosinophilia

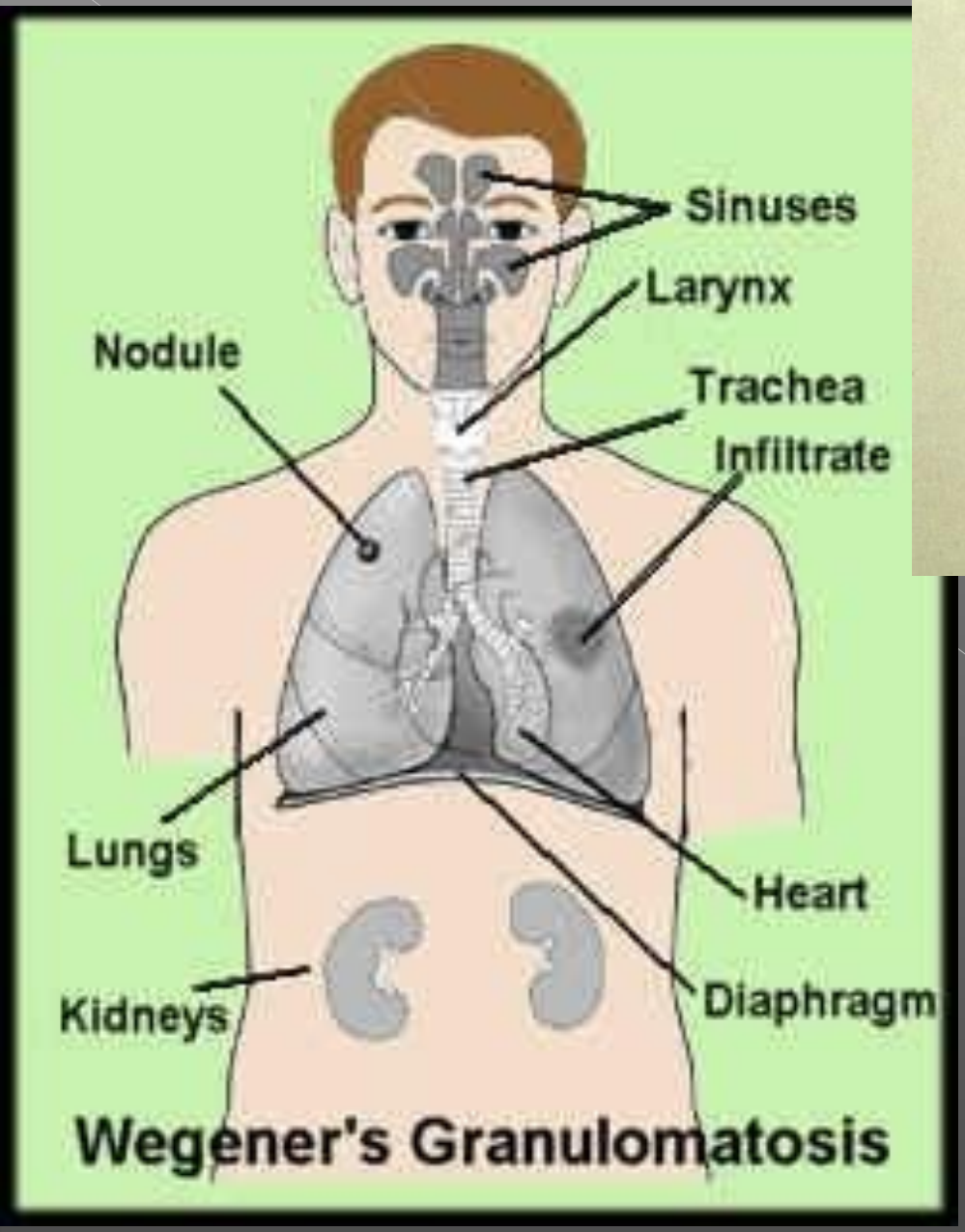
- Asthma
- Pulmonary infiltrates
- Myocarditis

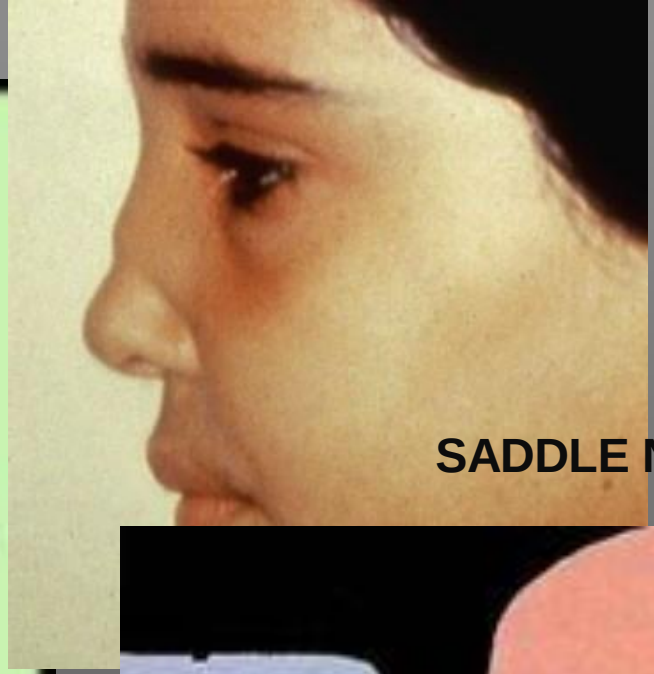
Wegener's Granulomatosis

Potentially fatal vasculitis involving small vessels

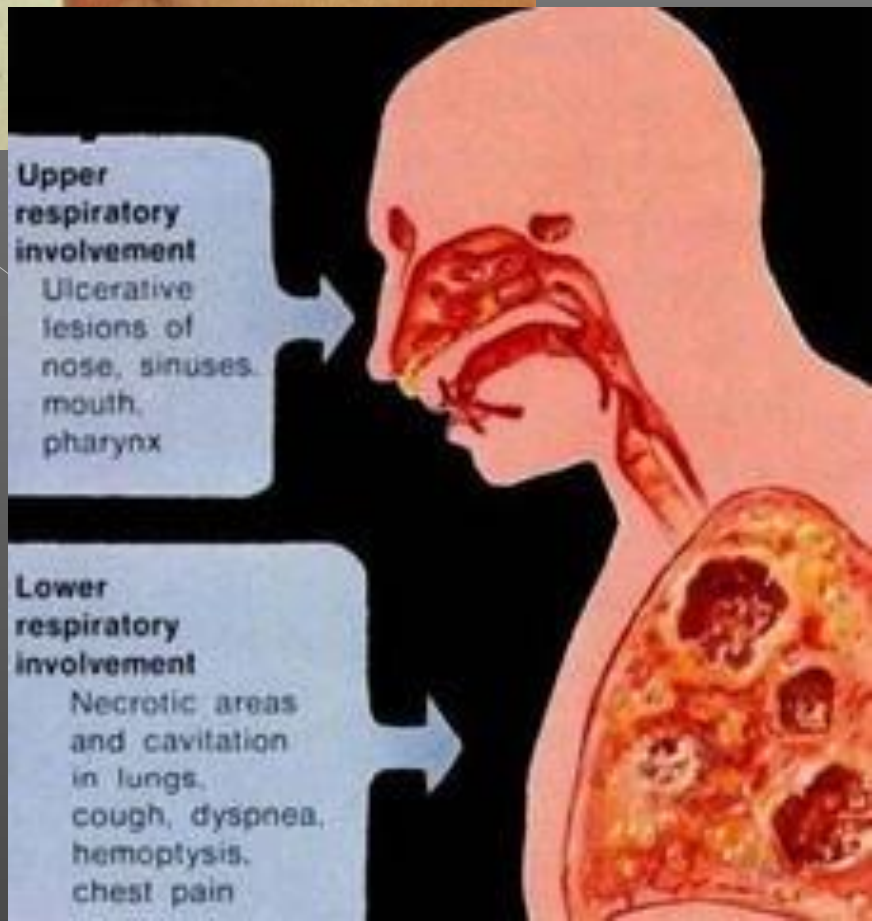
Rare: 3-14/million, more common in whites, any age but rare in children

Pathology shows necrotizing granulomas usually in upper airways, lungs and kidneys


Sinuses
Larynx
Nodule
Trachea
Infiltrate
Lungs
Heart
Kidneys
Diaphragm
Wegener's Granulomatosis

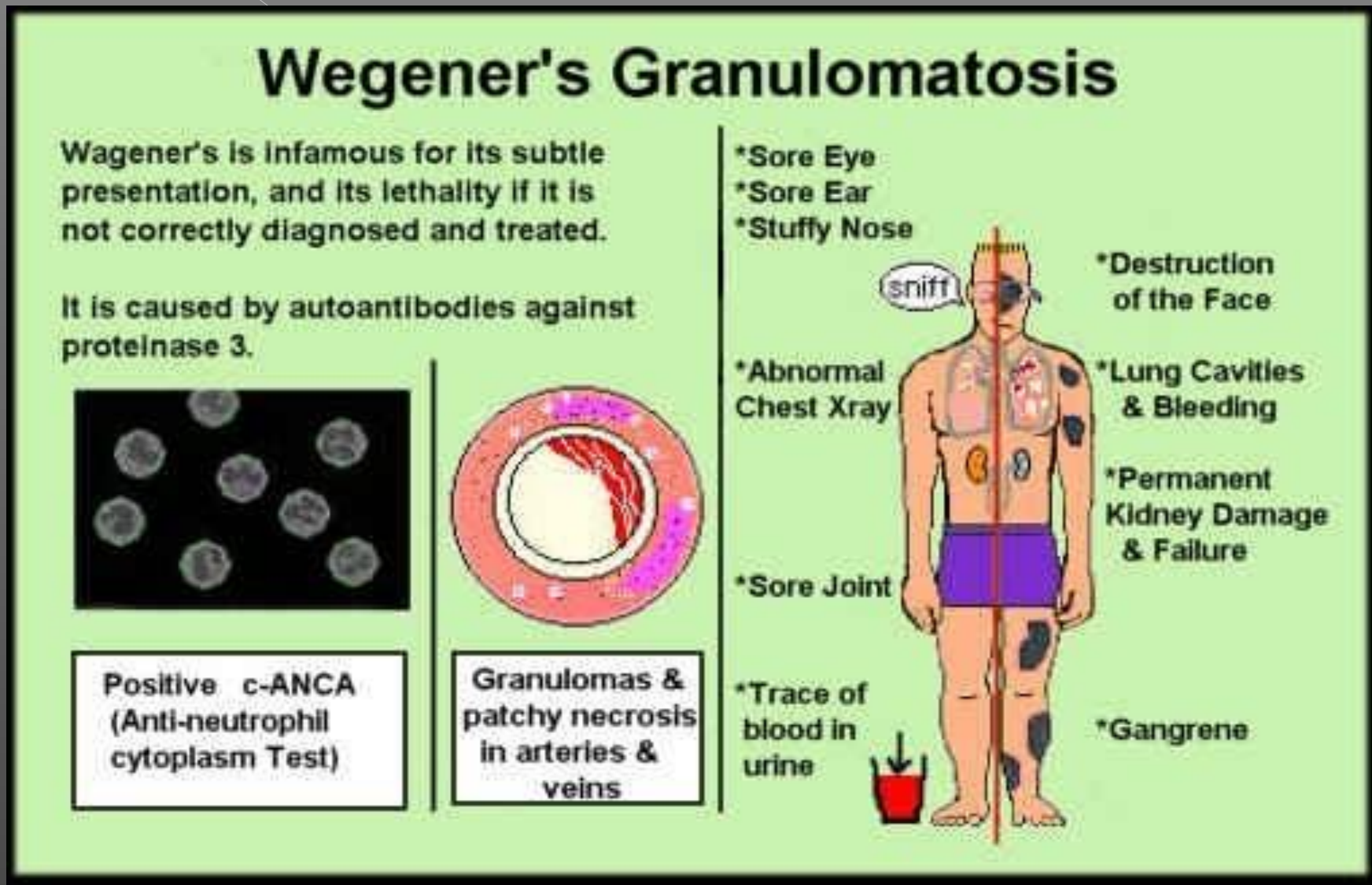


SADDLE NOSE

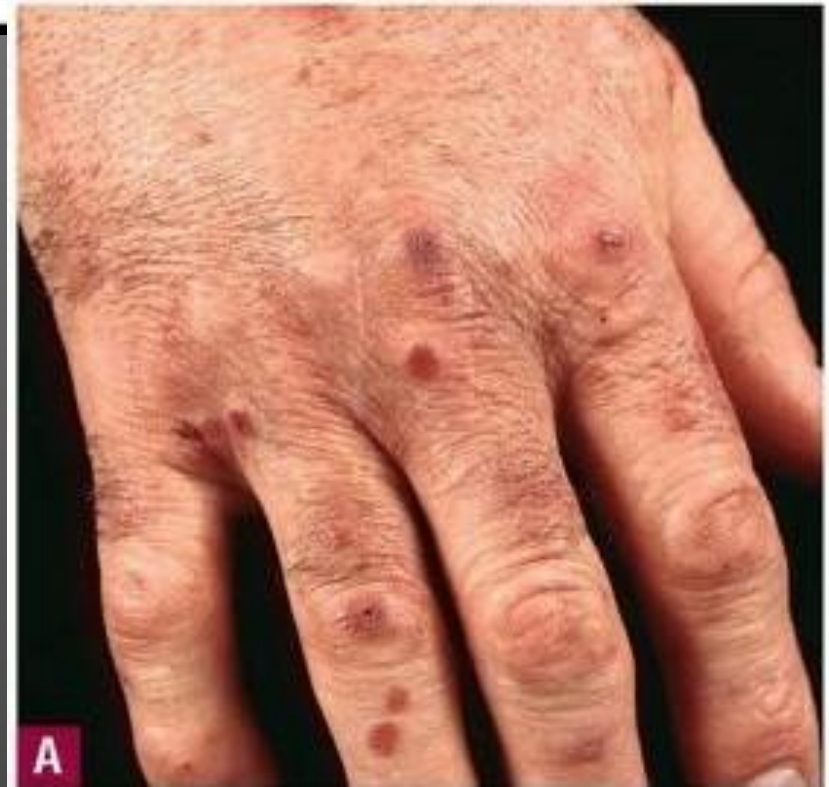

Upper respiratory involvement
Ulcerative lesions of nose, sinuses, mouth, pharynx
Lower respiratory involvement
Necrotic areas and cavitation in lungs, cough, dyspnea, hemoptysis, chest pain

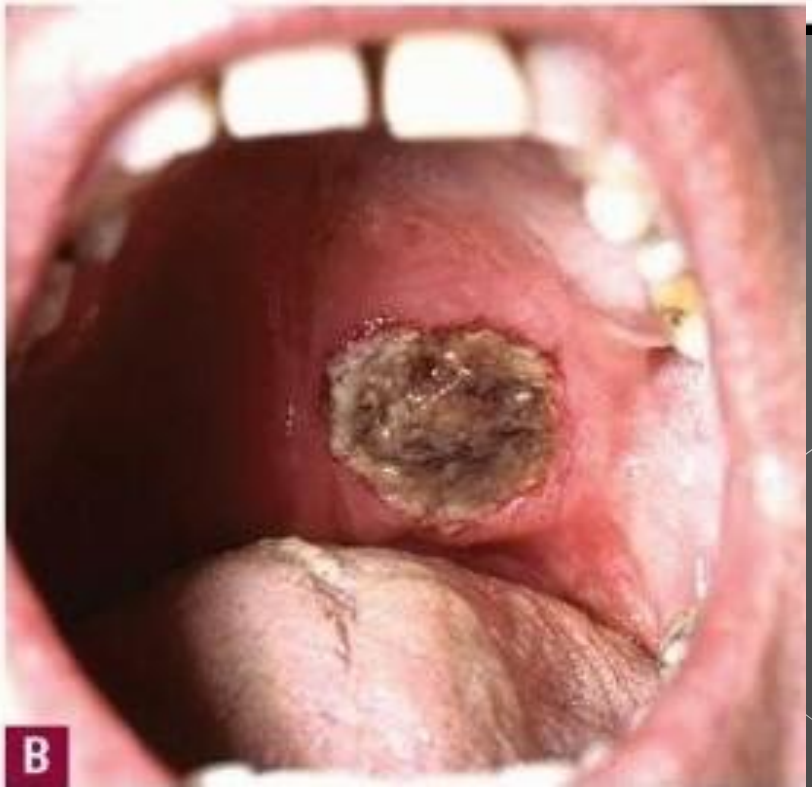
Clinical Presentation

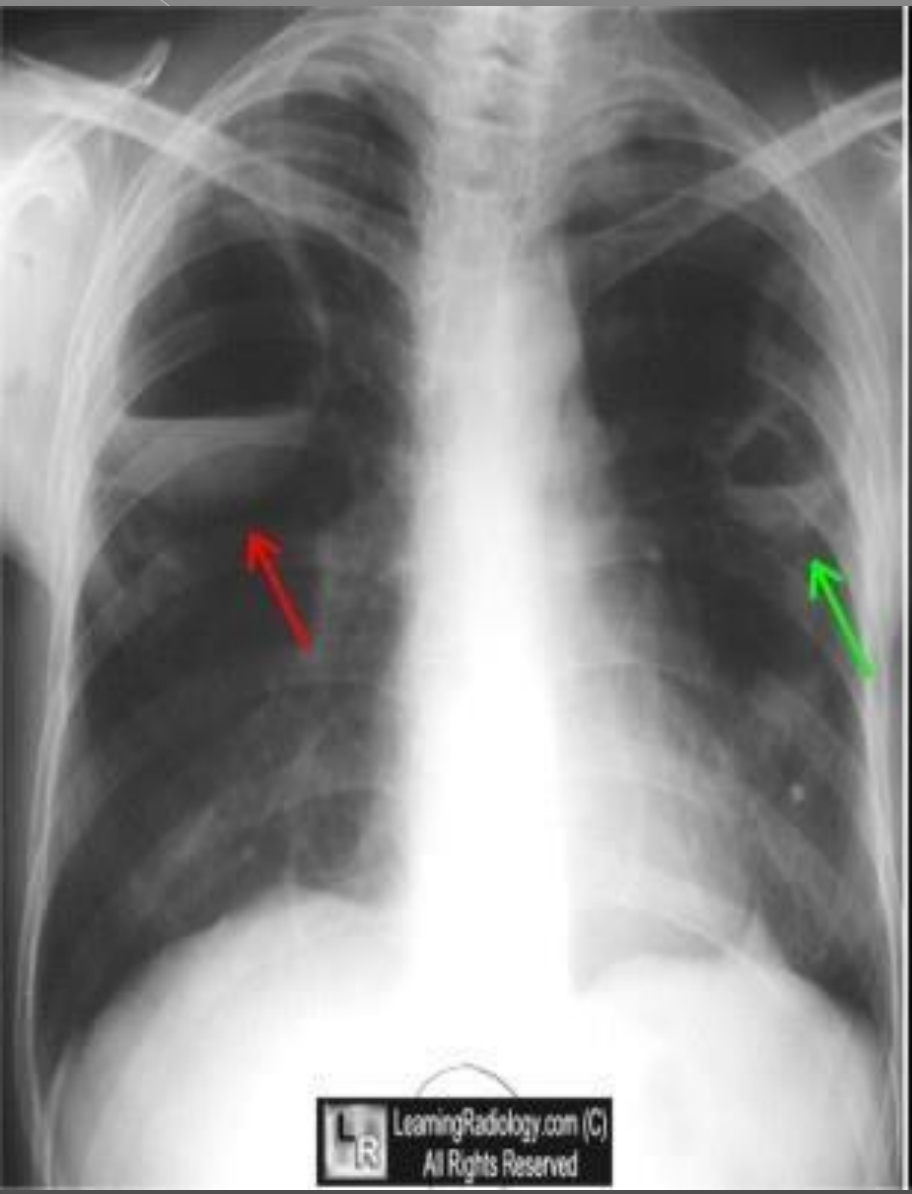
- *Variable, multisystem involvement*



Criterion	Characteristics
Nasal or oral inflammation	Painful or painless oral ulcers, purulent or bloody nasal discharge
Abnormal chest radiograph	Nodules, fixed infiltrates, cavities
Urinary sediment	Microhematuria (>5 red blood cells per high-power field), red cell casts
Granulomatous inflammation at biopsy	Involvement of the wall of an artery/arteriole, involvement of the perivascular/extravascular space



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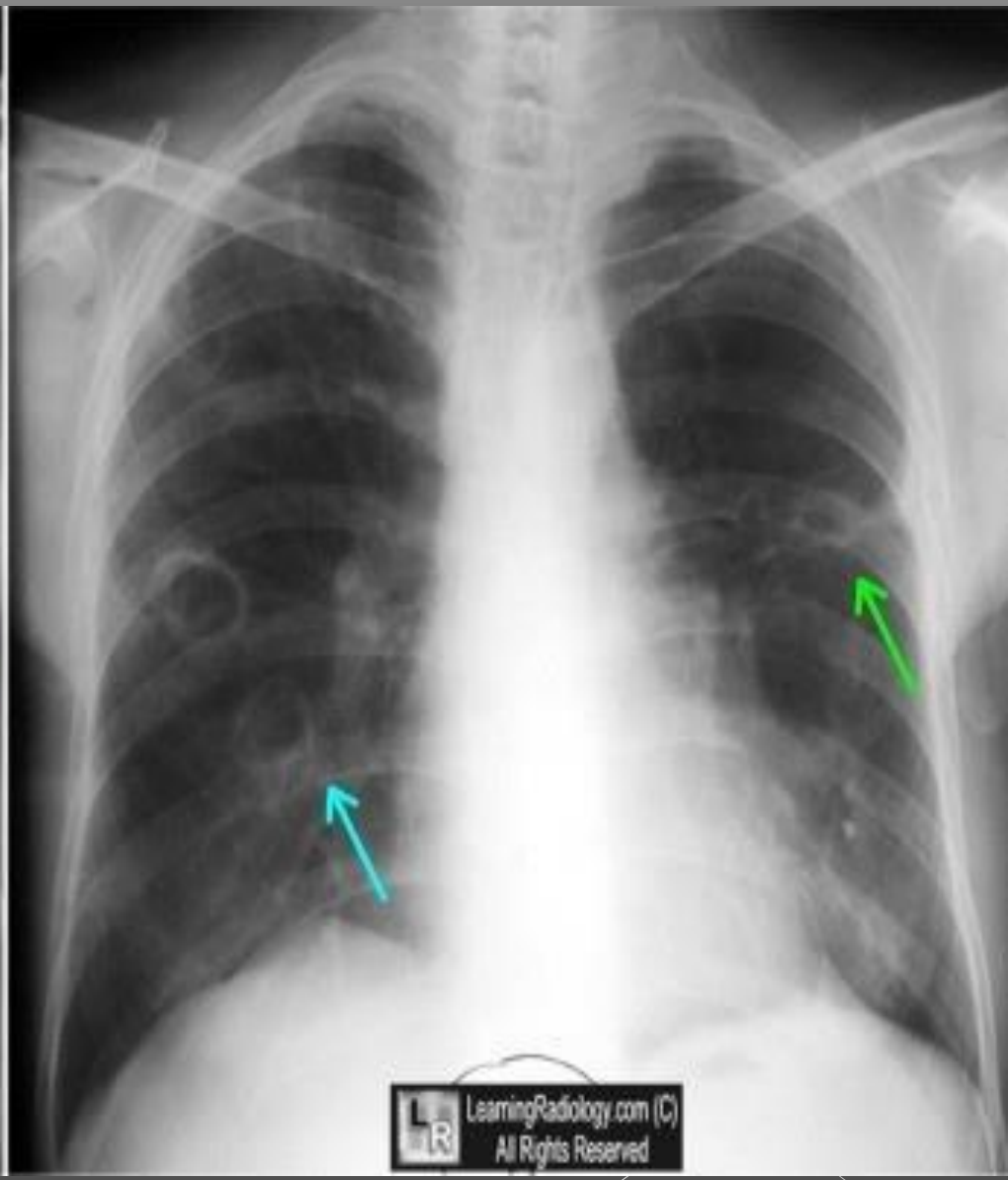
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Investigations

Presence of c-ANCA (cytoplasmic staining pattern antineutrophil cytoplasmic antibodies +clinical picture is often enough to make the diagnosis. It is + 80-90% of generalized WG.

Tissue biopsy of lung or kidney

Elevated CRP and ESR

Anemia, leukocytosis, & thrombocytosis

Elevated Cr

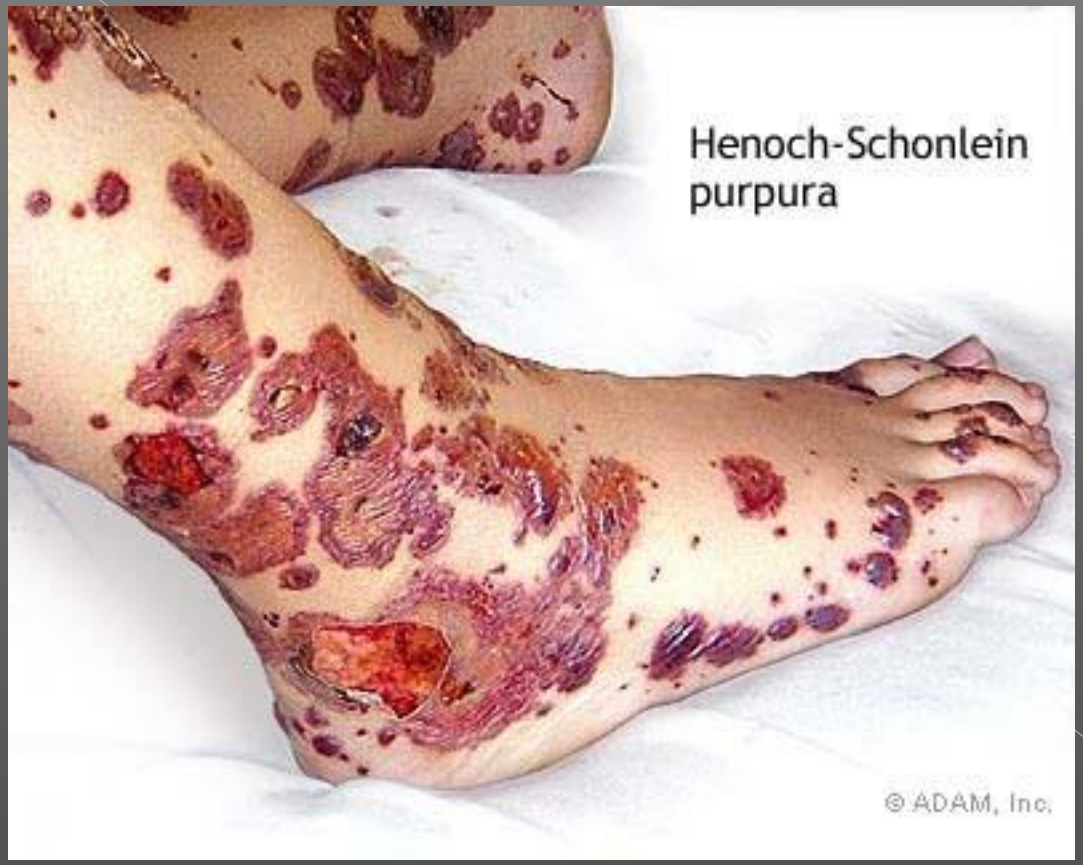
Active urine sediment with red cell casts, hematuria and proteinuria

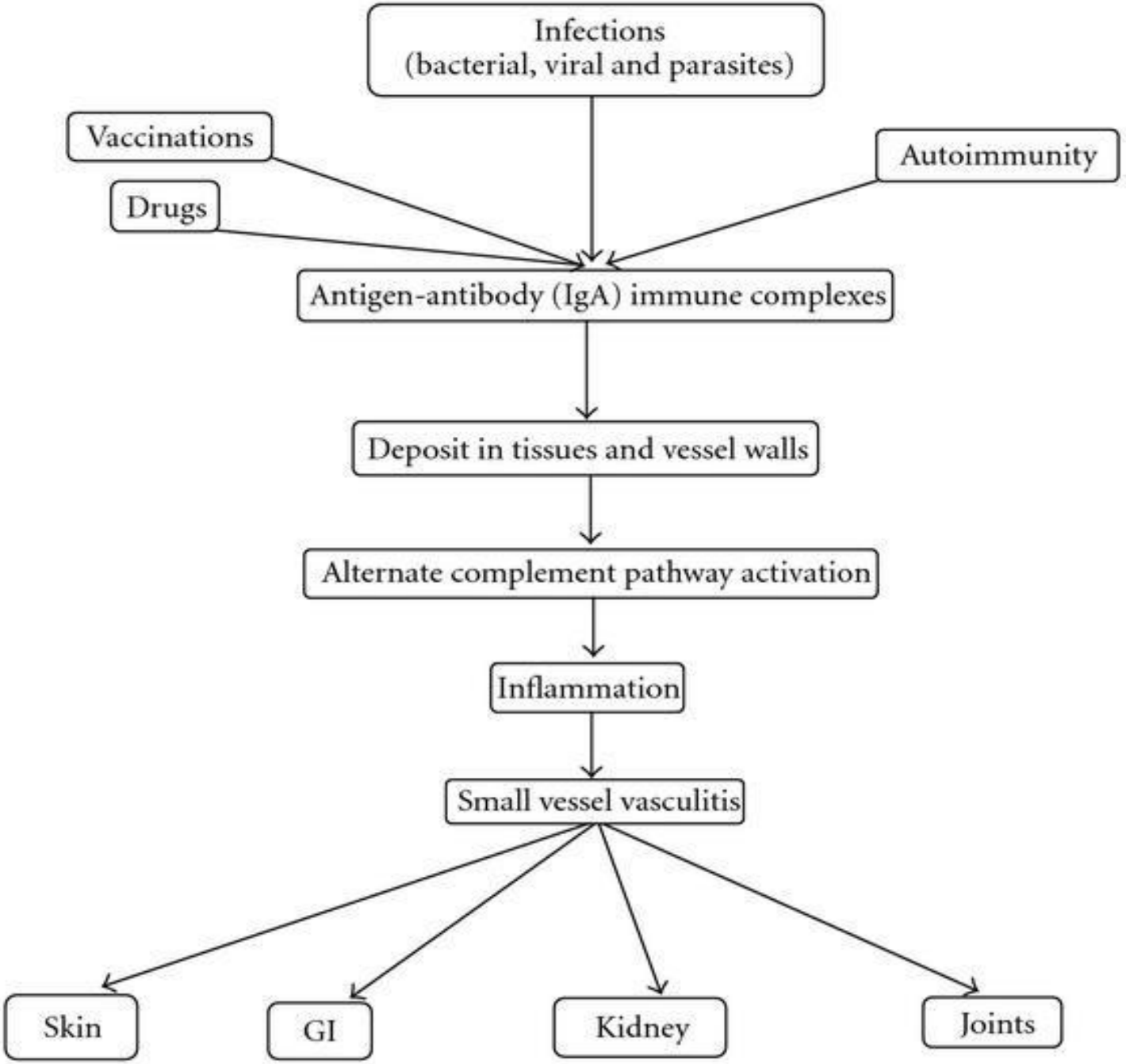
Clinical Course / Progression

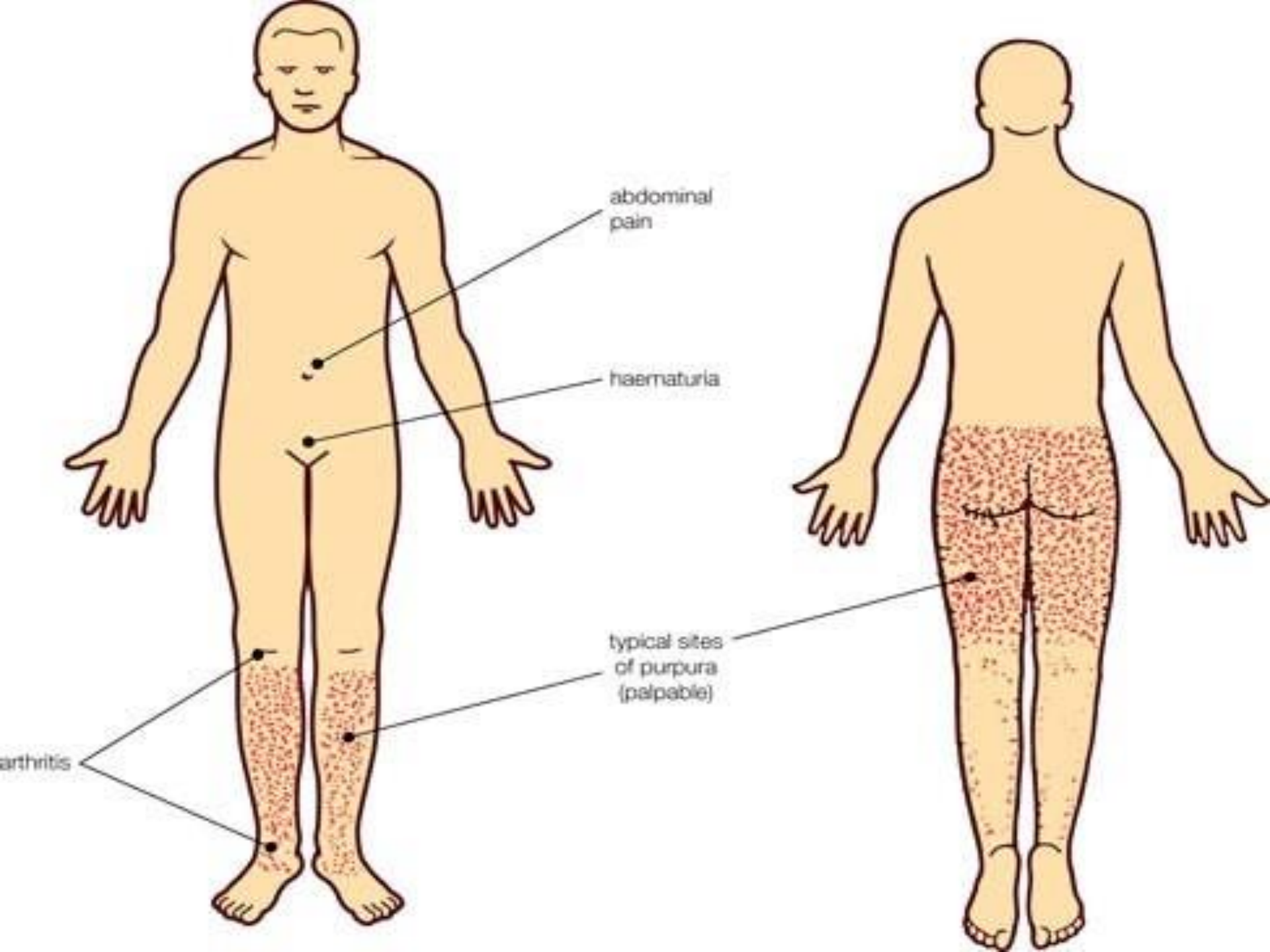
Prior to immunosuppression therapies, WG was uniformly fatal. Now survival rates almost 90% with aggressive treatment.

High dose steroids and Cyclophosphamide are cornerstone of therapy. Methotrexate or Azathioprine sometimes used as steroid sparing agents.

Henoch-Schonlein Purpura




Infections
(bacterial, viral and parasites)
Vaccinations
Drugs
Autoimmunity
Antigen-antibody (IgA) immune complexes
Deposit in tissues and vessel walls
Alternate complement pathway activation
Inflammation
Small vessel vasculitis
Skin
GI
Kidney
Joints


abdominal pain
haematuria
typical sites of purpura (palpable)
arthritis

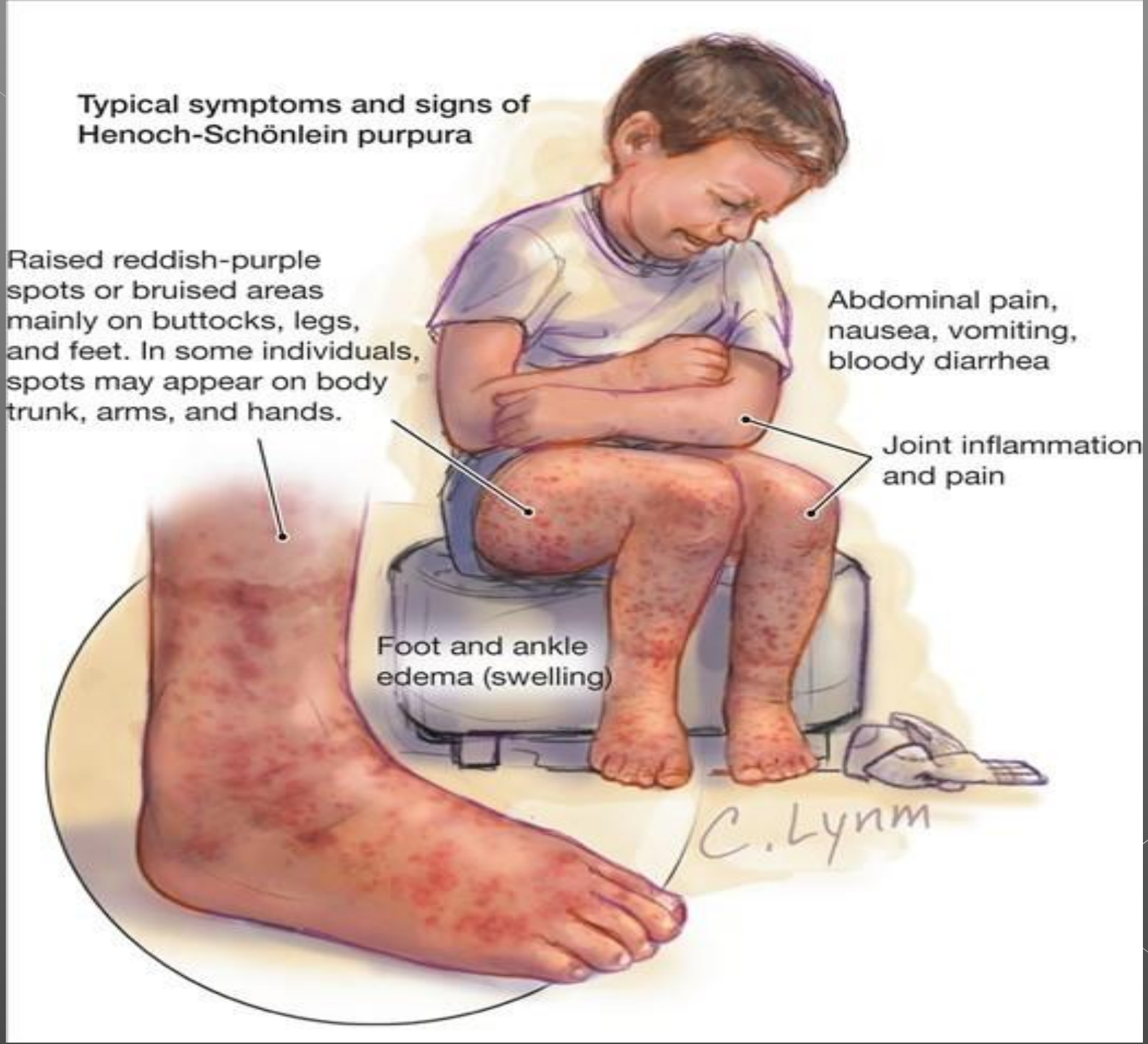

Typical symptoms and signs of Henoch-Schönlein purpura
Raised reddish-purple spots or bruised areas mainly on buttocks, legs, and feet. In some individuals, spots may appear on body trunk, arms, and hands.
Abdominal pain, nausea, vomiting, bloody diarrhea
Joint inflammation and pain
Foot and ankle edema (swelling)
C. Lynm

Table 2 : According to various studies following are the differences between children and adults with HSP

Features	Children	Adults
Gender distribution	Equal	Male> female
Seasonal	fall and winter	summer and winter
Peviousn URTI	Common	Less common
Diarrhoea	Less common	common
Abdominal pain	common	Less common
Fever	common	Less common
Joint pain	Less common	common
Leucocytosis,	Less common	common
Thrombocytosis	common	Less common
Renal involvement	Less common	Frequent & severe
Hospital stay	Shorter (4.3 days)	Longer (10 days)
Outcome	Very good (93.9% recovery)	Good (89.2% recovery)

Investigations

No specific diagnostic laboratory markers exist

The plasma coagulation factor XIII is reduced in about 50% of patients

Urinalysis reveals hematuria. Proteinuria may also be found

CBC can show leukocytosis with eosinophilia and a left shift. Thrombocytosis is present in 67% of cases

Serum IgA levels are increased in about 50% of patients during the acute phase of illness

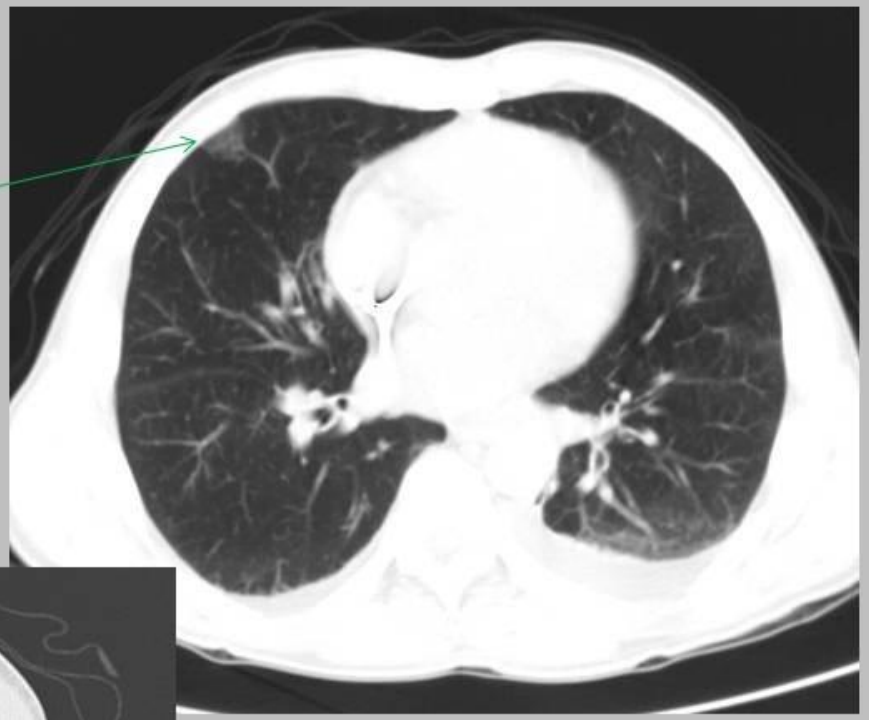
The antistreptolysin O (ASO) titer is elevated in 30% of cases

Treatment

- **Remission induction**:
  - *Cyclophosphamide 2mg/kg po qd x 3-6 months*
    [or 15 mg/kg IV q 2 wk x3 then q 3 weeks x 6-12 months]
  - *Prednisone 1mg/kg po qd x 1 month, then taper*
  - *[Bactrim, Calcium, Vitamin D]*
- **Remission maintenance** *(minimum 2 years)*
  - *Methotrexate 20-25 mg po q week + folate*
  - *Azathioprine 2mg/kg po qd*
  - *Mycophenolate mofetil 1.5 g po BID*
  - *Leflunomide 20-30 mg po BID*

Churg-Strauss Syndrome

Multifocal peripheral ground glass opacities that wax and wane … in a patient with asthma… is one of the most common presentations of Churg-Strauss Syndrome, although a very nonspecific one.



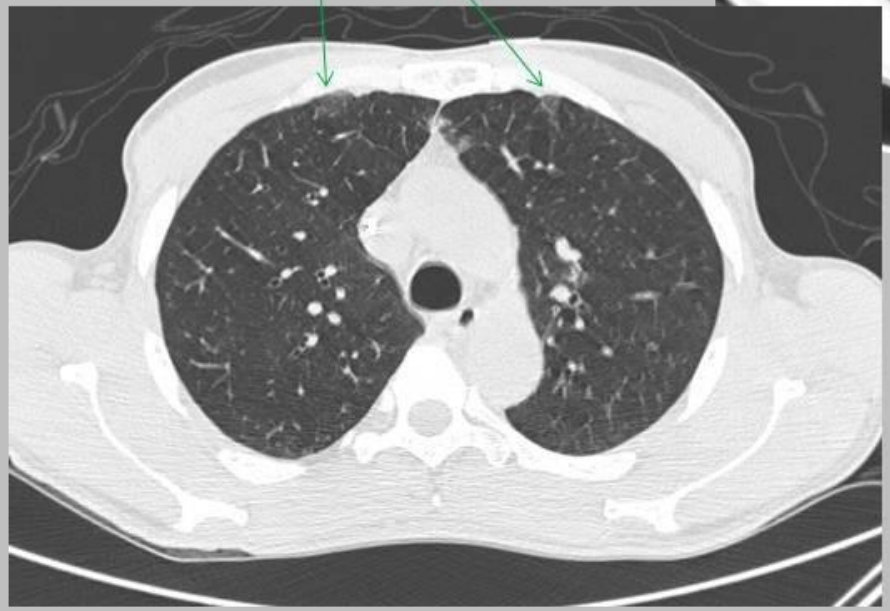


Table 3: Clinical phases of Churg-Strauss Syndrome

Prodromal phase

"Late-onset" allergic disease, early twenties
See evidence of asthma (cough, wheezing, dyspnea)
Allergic rhinitis, (nasal obstruction, chronic rhinitis, nasal polyposis)

Eosinophilic phase

Marked peripheral eosinophilia, eosinophilic tissue inflammation
Typical organs involved include lungs, GI tract, and skin

Vasculitic phase

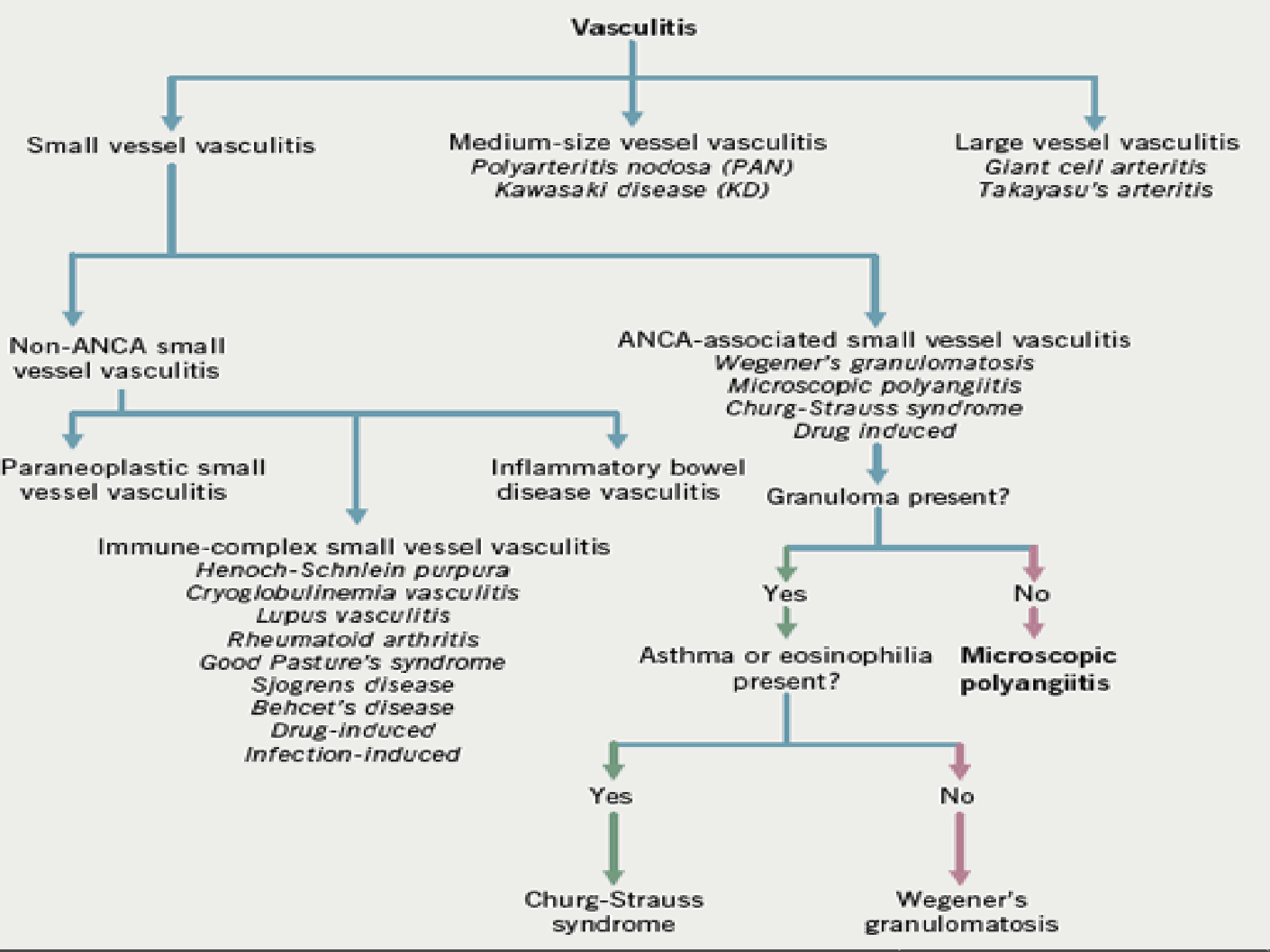
Constitutional symptoms (fever, myalgias, weight loss)
Cardiac symptoms: principle cause of death (coronary vasculitis, congestive heart failure, endocarditis, pericarditis)
Neurological symptoms (mononeutis multiplex)
Skin symptoms (subcutaneous skin nodules)
Kidney disease

- Asthma
- Eosinophilia >10%
- Neuropathy
- Pulmonary infiltrates
- Paranasal sinus abnormality
- Extravascular eosinophil infiltration on biopsy

[a]The presence of at least four of the six criteria indicates that Churg–Strauss syndrome is very likely to be the correct diagnosis.

Monitoring

- **Large-vessel vasculitis**
  - **MRI/MRA** *chest/abdomen/pelvis every 6-12 months*
- **Medium-vessel vasculitis**
  - **Mesenteric angiogram** *to assess disease activity*
  - **EMG/NCV** *to monitor nerve damage*
  - **Wound care** *for cutaneous ulcers*
- **Small-vessel vasculitis**
  - **Chest CT** *every 6-12 months*
  - **Blood and urine tests** *every 1-4 weeks*


Vasculitis
Small vessel vasculitis
Medium-size vessel vasculitis
Polyarteritis nodosa (PAN)
Kawasaki disease (KD)
Large vessel vasculitis
Giant cell arteritis
Takayasu's arteritis
Non-ANCA small vessel vasculitis
ANCA-associated small vessel vasculitis
Wegener's granulomatosis
Microscopic polyangiitis
Churg-Strauss syndrome
Drug induced
Paraneoplastic small vessel vasculitis
Inflammatory bowel disease vasculitis
Granuloma present?
Immune-complex small vessel vasculitis
Henoch-Schnlein purpura
Cryoglobulinemia vasculitis
Lupus vasculitis
Rheumatoid arthritis
Good Pasture's syndrome
Sjogrens disease
Behcet's disease
Drug-induced
Infection-induced
Yes
No
Asthma or eosinophilia present?
Microscopic polyangiitis
Yes
No
Churg-Strauss syndrome
Wegener's granulomatosis

Long-term Damage

- **Large-vessel vasculitis**
  - **Blindness, Stroke**
  - **Claudication:** *"Angina" of the arms*
- **Medium-vessel vasculitis**
  - **Foot drop:** *inability to lift a foot*
  - **Wrist drop:** *inability to lift a hand*
  - **Cutaneous ulcerations**
- **Small-vessel vasculitis**
  - **Oxygen dependence**
  - **Renal insufficiency/failure**