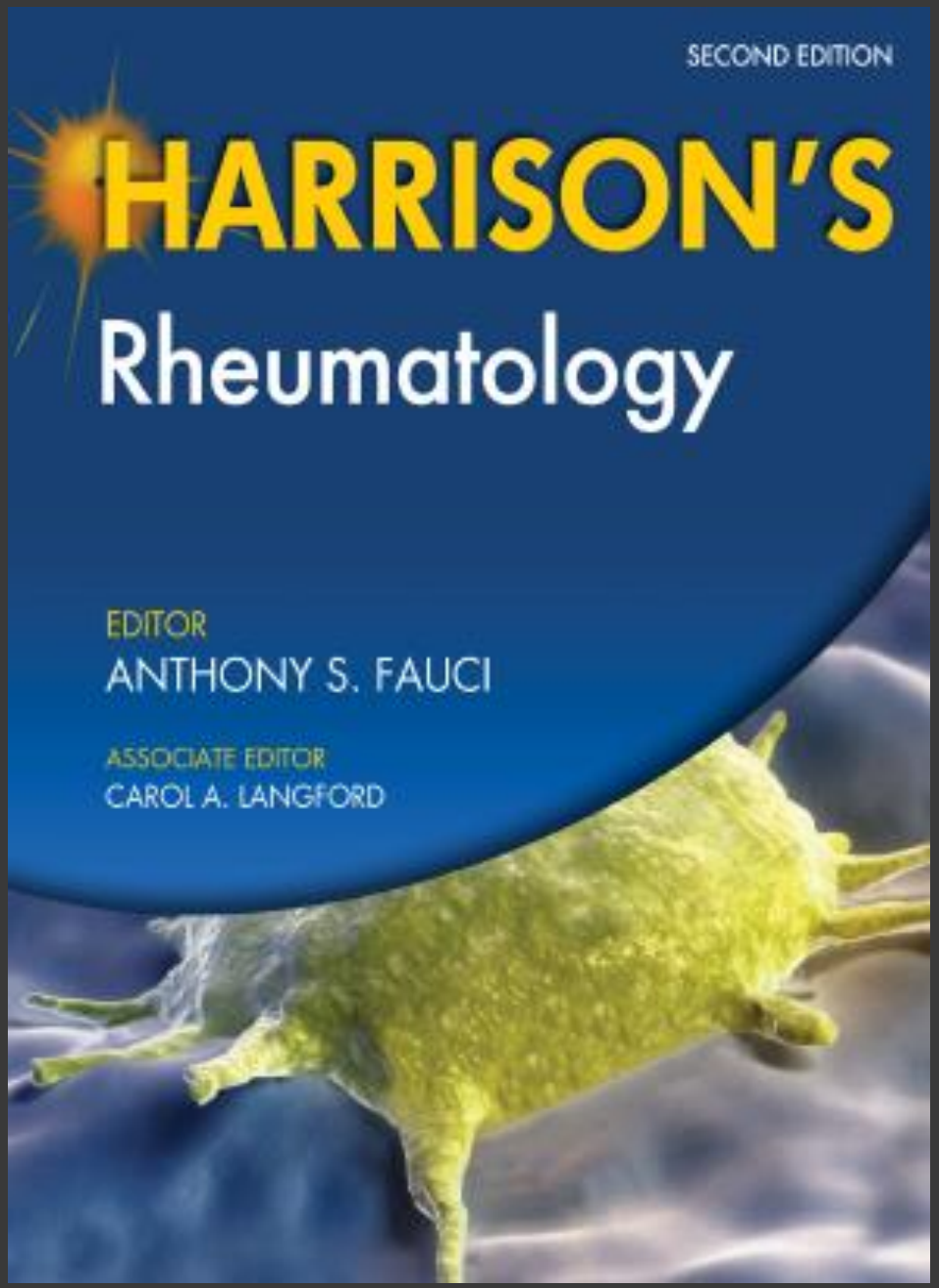
# Vasculitis

4th year MBBS

Marwan Adwan *MBChB, MRCPI, MSc, MRCP(rheum)*

*Consultant Rheumatologist*


SECOND EDITION
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# Case 1

- A 45 man presents with 3 wk hx of fever, fatigue, malaise, abdo pain and polyarthralgia. He noticed a rash on both legs & pain & weakness of L foot.
- O/E: temp 39, abdo tender diffusely. Livedo reticularis & palpable purpura on legs, L foot drop

# Investigations

- Hb↓, platelets↑, ESR 95 ↑ ↑
- ANA, ANCA, hep B&C negative
- Abdo x ray normal
- Skin biopsy: non granulomatous necrotising vasculitis
- NCS: L common peroneal nerve lesion
- Abdo angio: microaneryms & stenoses in mesenteric arteries.

# Diagnosis??

# Objectives

- Definition & Classification
- Epidemiology
- Manifestations & differential diagnosis
- Large vessel vasculitis
- ANCA asscociated vasculitis
- Medium vessel vasculitis
- Small vessel vasculitis
- Other

# Vasculitis

- A heterogeneous group of disorders linked by the primary finding of inflammation within blood vessel walls.
- At least 20 forms of systemic vasculitis are recognized
- Uncommon
- Cause significant morbidity and mortality

# Classified by the size of blood vessel involved:

- **Small vessel**
  - (capillaries and postcapillary venules)
- **Medium vessel**
  - (muscular arteries and arterioles)
- **Large vessel**
  - (the aorta and its major branches).

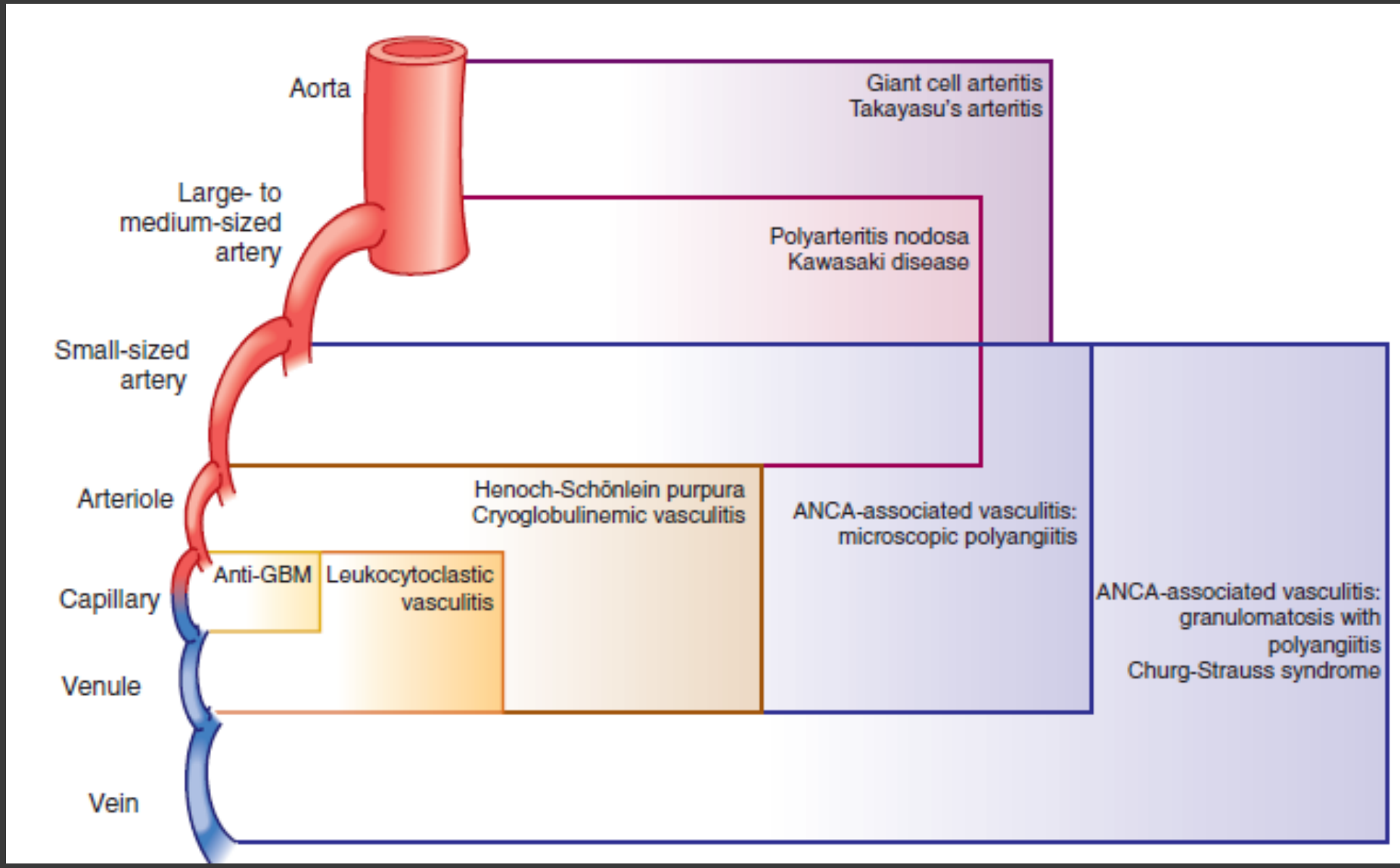
# Vasculitis

- May be:
  - primary or
  - secondary

| Dominant vessel involved | Primary | Secondary |
|---|---|---|
| Large arteries | Giant cell arteritis (GCA)<br>Takayasu arteritis (TA) | Aortitis associated with RA<br>Infection (e.g., syphilis, tuberculosis) |
| Medium arteries | Classical PAN<br>Kawasaki disease | Hepatitis B virus associated PAN |
| Small vessels and medium arteries | Wegener's granulomatosis (WG)[a]<br>Churg–Strauss syndrome (CSS)[a]<br>Microscopic polyangiitis[a] | Vasculitis secondary to RA, SLE<br>Sjögren's syndrome<br>Drugs[b]<br>Infection (e.g., HIV) |
| Small vessels (leukocytoclastic) | Henoch–Schönlein purpura (HSP)<br>Cutaneous leukocytoclastic angiitis | Drugs[c]<br>Infection<br>Hepatitis C virus induced cryoglobulinemia |

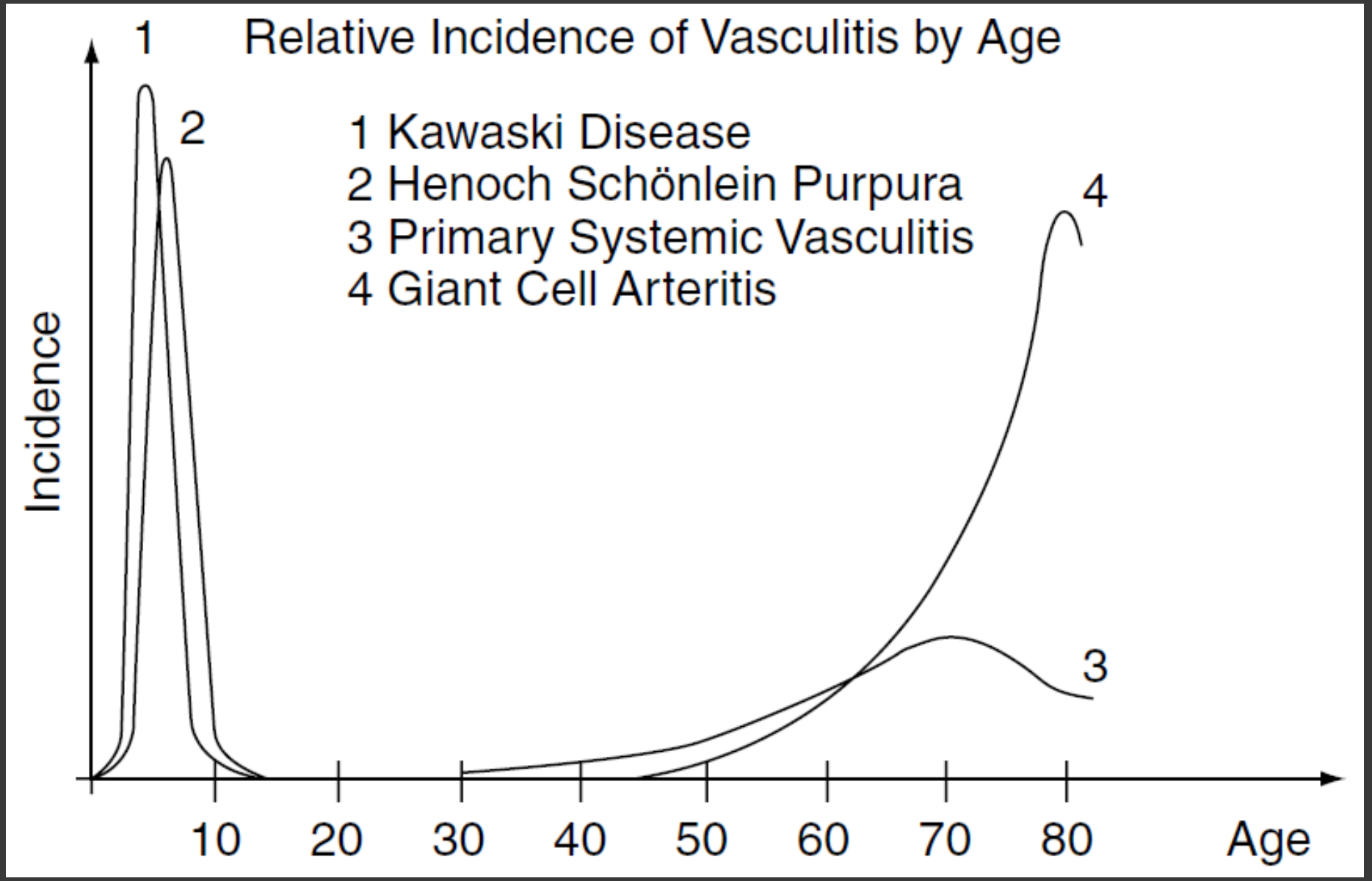
# Drugs that may cause vasculitis:

- **Prescribed**
  - Propylthiouracil
  - Hydralazine
  - Allopurinol
- **Abused**
  - Cocaine
  - Heroin
  - Amphetamine


Aorta
Large- to medium-sized artery
Small-sized artery
Arteriole
Capillary
Venule
Vein
Giant cell arteritis
Takayasu's arteritis
Polyarteritis nodosa
Kawasaki disease
Henoch-Schönlein purpura
Cryoglobulinemic vasculitis
ANCA-associated vasculitis: microscopic polyangiitis
Anti-GBM
Leukocytoclastic vasculitis
ANCA-associated vasculitis: granulomatosis with polyangiitis
Churg-Strauss syndrome

# Epidemiology

- Diseases of childhood or old age
- GCA most common Scandinavia and relatively uncommon in Africans and Japanese
- Takayasu more common in Japan
- AAV overall incidence (20/millon/year)
- Cause unknown
- ? Environmental agent (unknown) in a genetically predisposed host


Relative Incidence of Vasculitis by Age
1 Kawaski Disease
2 Henoch Schönlein Purpura
3 Primary Systemic Vasculitis
4 Giant Cell Arteritis
1
2
4
3
Incidence
10
20
30
40
50
60
70
80
Age

# Typical clinical manifestations of large-, medium- and small-vessel involvement by vasculitis

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

**Constitutional symptoms: fever, weight loss, malaise, arthralgias/arthritis (common to vasculitides of all vessel sizes)**

# Clinical Features Suggesting Vasculitis

- Multisystem inflammatory disease
- Rapidly progressive major organ dysfunction
- Constitutional symptoms (fever, weight loss)
- Unexplained infarction in multiple vascular territories
- High ESR, severe anemia, thrombocytosis
- Evidence of small-vessel inflammation:
  - In the kidneys = active urinary sediment (RPGN)
  - In the lungs = hemoptysis, dyspnea(Diffuse alveolar hemorrhage )
  - In the skin = palpable purpura/hemorrhage
- Acute neurologic changes
  - Foot drop
  - Altered mental status

# Differential diagnosis of vasculitis

## Infection

- Bacterial endocarditis.
- Hepatitis B
- Hepatitis C
- HIV
- Occult abscess
- Syphilis

## Malignancy

- Lymphoma
- Hypernephroma
- Metastatic carcinoma
- Multiple myeloma Macroglobulinemia

## Autoimmune disease

- Rheumatoid arthritis .
- Systemic lupus
- **Multiple emboli/cholesterol emboli.**
- **Drug allergy**

# Case 2

- A 48 year old man, IVDU, presented with a 4 week history of generally feeling unwell and purpuric rash over both legs. He looked ill, and there were several nail fold infarcts and vasculitic lesions over his fingers. Blood picture was in keeping with systemic inflammatory response. CXR showed cavitating lesions. Skin biopsy showed leucocytoclastic vasculitis. His illness was attributed to systemic vasculitis and specialist opinion was sought.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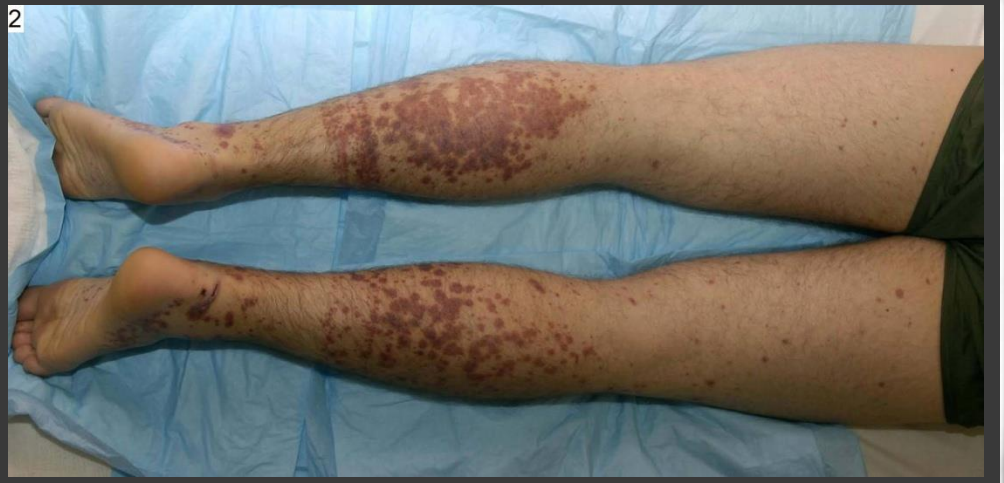
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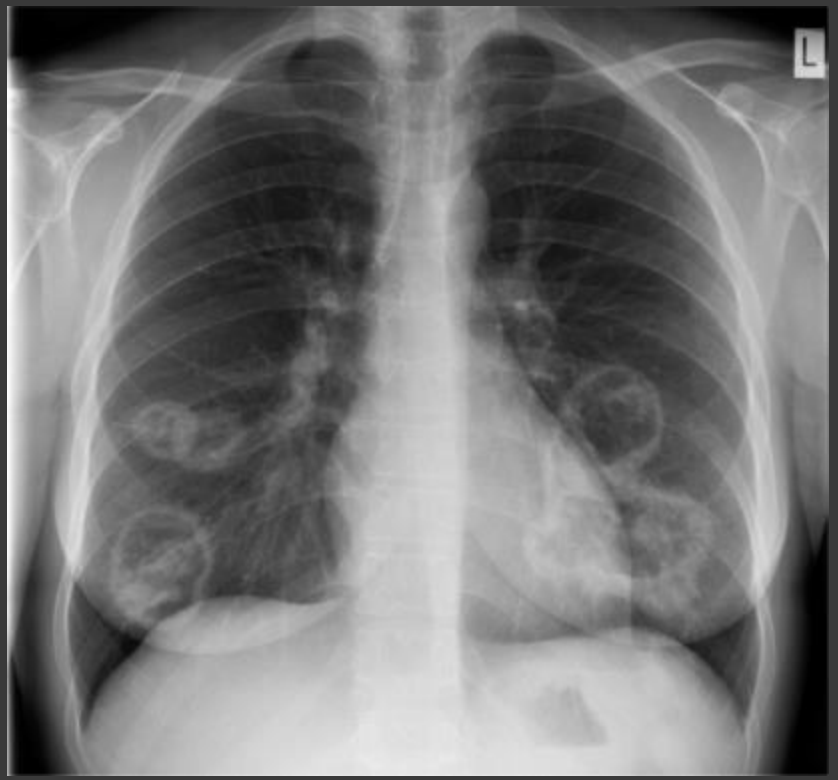
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- Several days after admission serial blood cultures and echocardiogram were arranged. Blood cultures grew Staphylococcus aureus and TTE showed vegetations around the tricuspid valve consistent with right heart endocarditis. The cavitating lesions were lung abscesses secondary to septic emboli.


Because treatment of vasculitis entails the use of immunosuppressive drugs, the consequences of not recognising infection would be disastrous.

Thus, it is mandatory to perform a full infection screen in all patients with suspected vasculitis

# Large vessel vasculitis

# Giant cell arteritis (GCA)

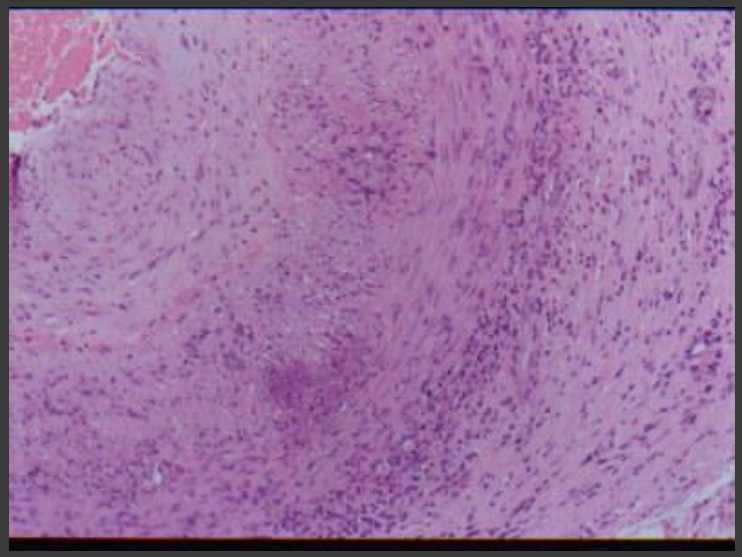
- Rare under age 50
- Headache: temporal / occipital
- Scalp tenderness
- ? Thickened, nodular, tender TA
- ? ↓ / absent TA pulse
- Jaw claudication: internal maxillary artery
- Tingling tongue: lingual artery
- Amaurosis fugax
- Unilateral permanent loss of vision ➔ other eye affected within 1-2 wks (ophthalmic & posterior ciliary arteries)

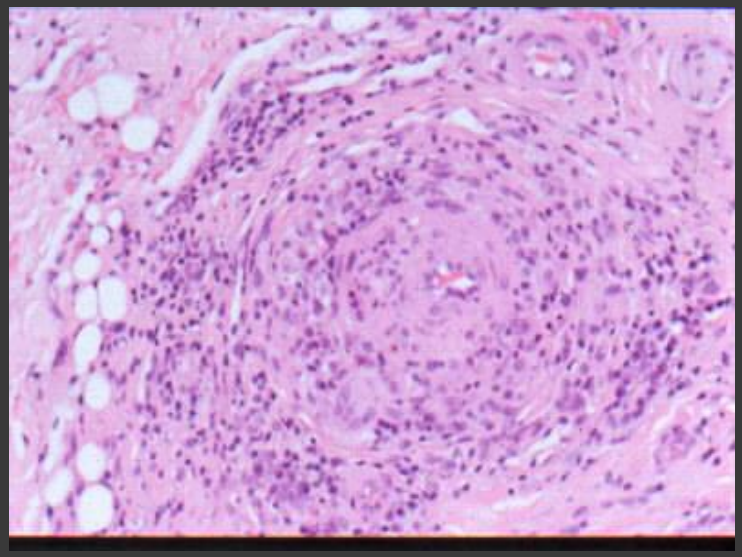
# GCA

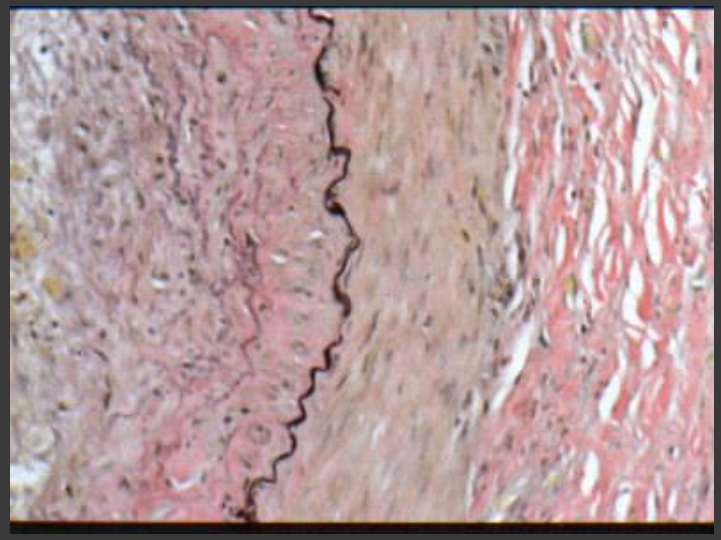
- **Diagnosis**
  - 1. Normocytic anaemia
  - 2. High ESR & CRP
  - 3. Temporal artery biopsy: skip lesions common
  - Doppler US

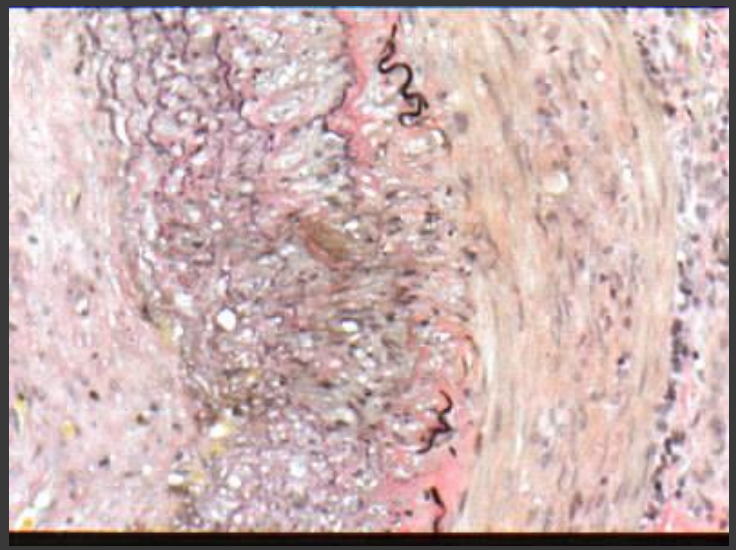
- **Complication**: sudden loss of vision if untreated
- **Treatment**: Steroids (good response)

# GCA









# Doppler US

# Polymyalgia Rheumatica (PMR)

- Closely associated with GCA
- May be seen in 40–50% of patients With GCA
- Pain and stiffness in shoulder and pelvic girdles worse in morning
- Good response to steroids

# Takayasu's Arteritis

- Affects young people <40
- Characterized by stenosis, occlusion, and sometimes aneurysm formation of large arteries
- Commonest in Asia, the Middle East and South America
- F:M = 9:1
- No autoantibodies

# Takayasu's Arteritis Clinical Features

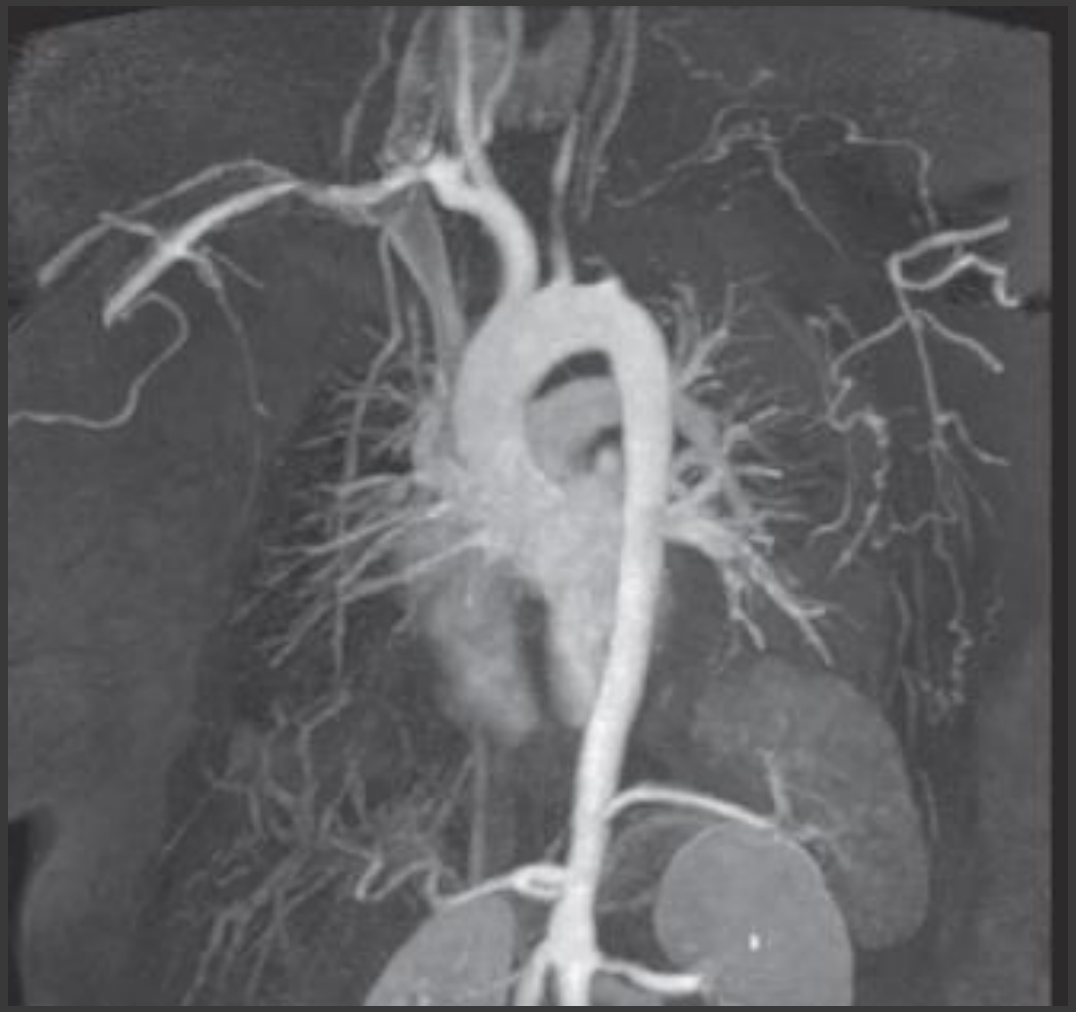
- **3 phases:**

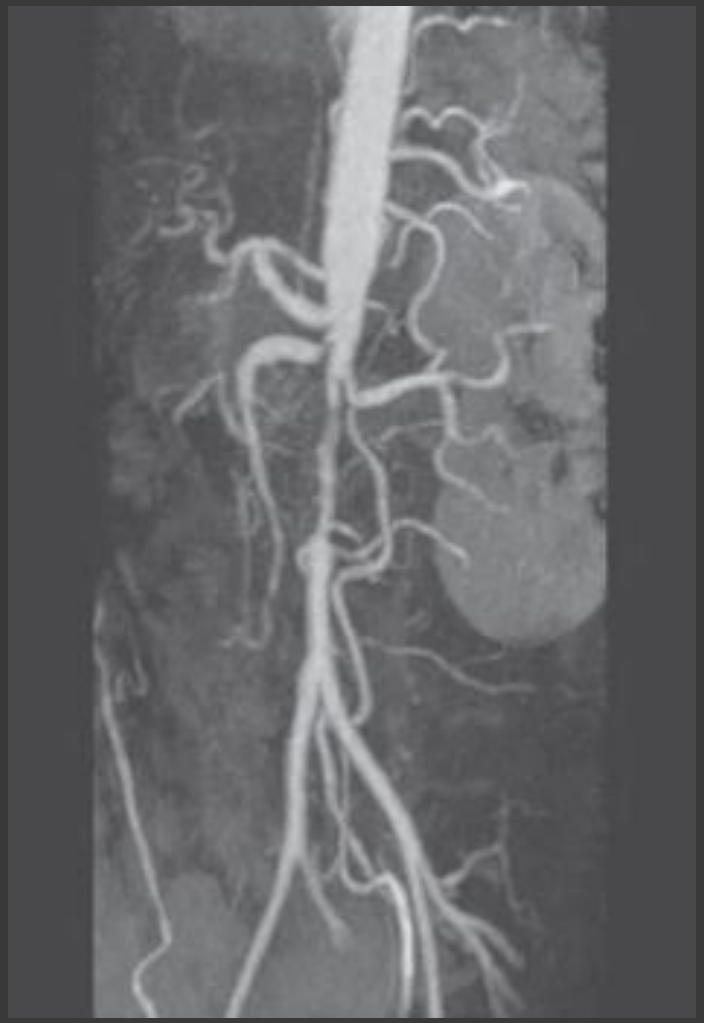
1. **Systemic phase:**
   - Fatigue, weight loss, night sweats, fever, arthralgia, and myalgia
2. **Vascular phase:**
   - asymmetry of peripheral pulses
   - claudication of arm or legs
   - Difference in BP between R & L arm
   - transient visual disturbance, scotoma, blurring, or diplopia
3. **Burnt-out pulseless phase**

# Takayasu's Arteritis: Examination

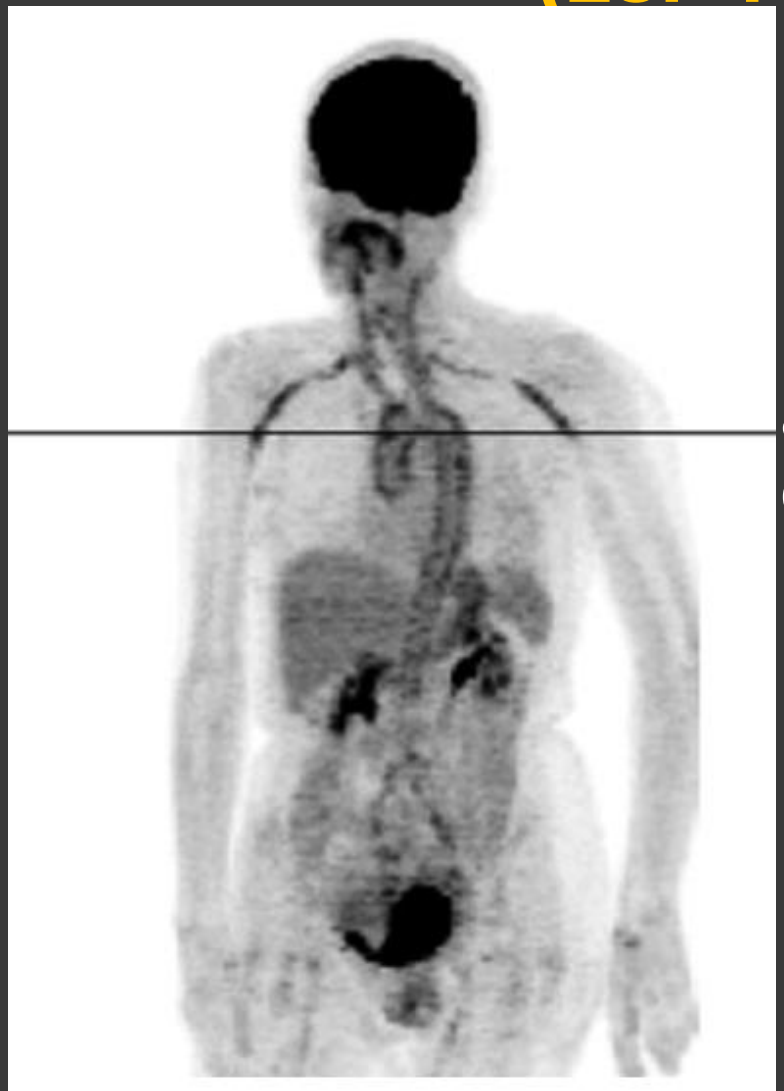
- Diminished or absent pulses
- Bruits
- Asymmetric blood pressure between extremities
- Carotidynia
- Hypertension

# Takayasu's Arteritis: radaiology

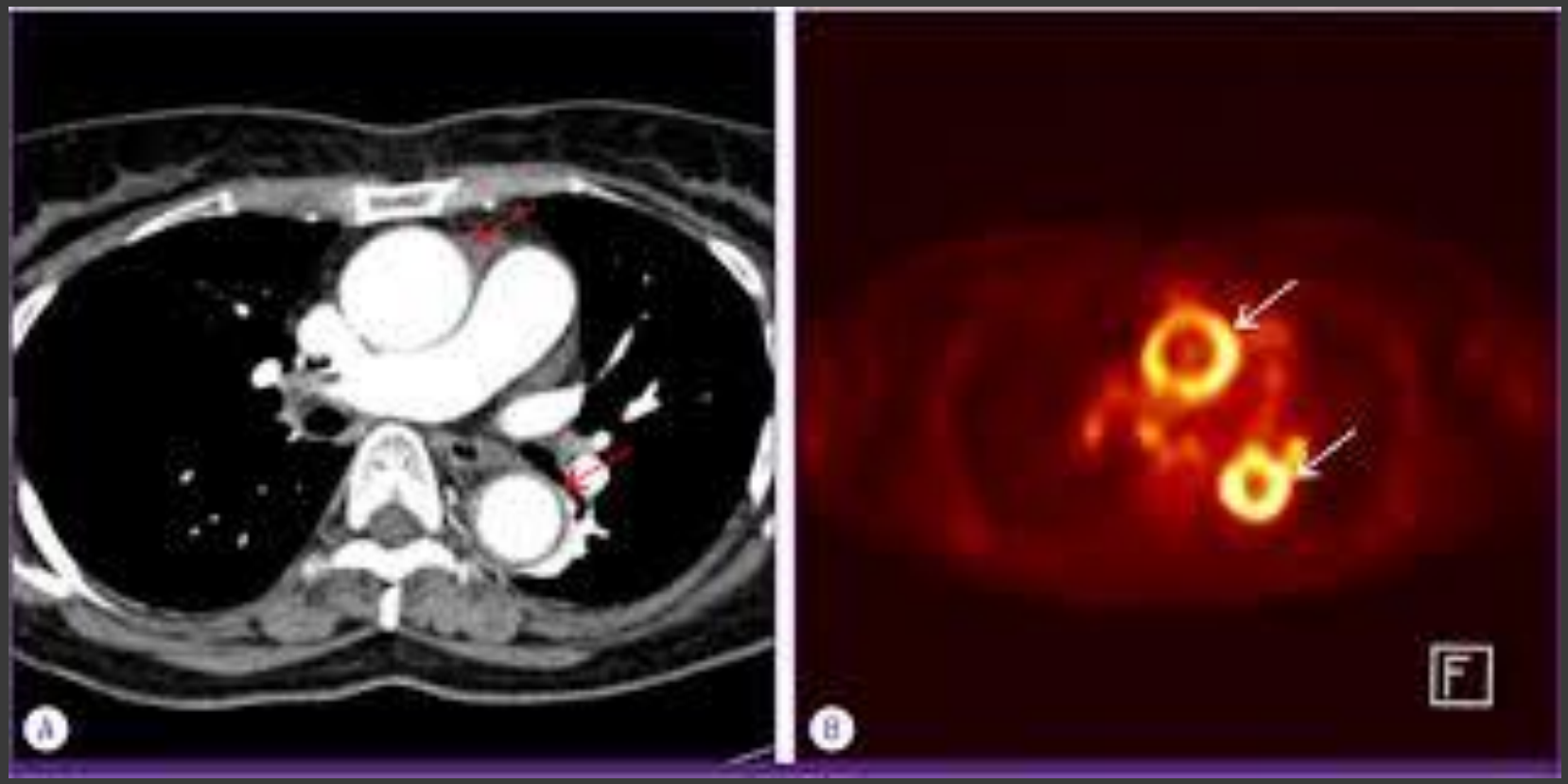




# 18F-fluorodeoxyglucose positron emission tomography (18F-FDG-PET)



18F-FDG is taken up by metabolically active cells including at sites of inflammation. Uptake can be visualized in the walls of inflamed large vessels


A
B
F

# Takayasu's Arteritis: Treatment

- High-dose oral prednisolone at 0.5–1 mg/kg
- Steroid-sparing agents: Azathioprine, methotrexate
- Surgery

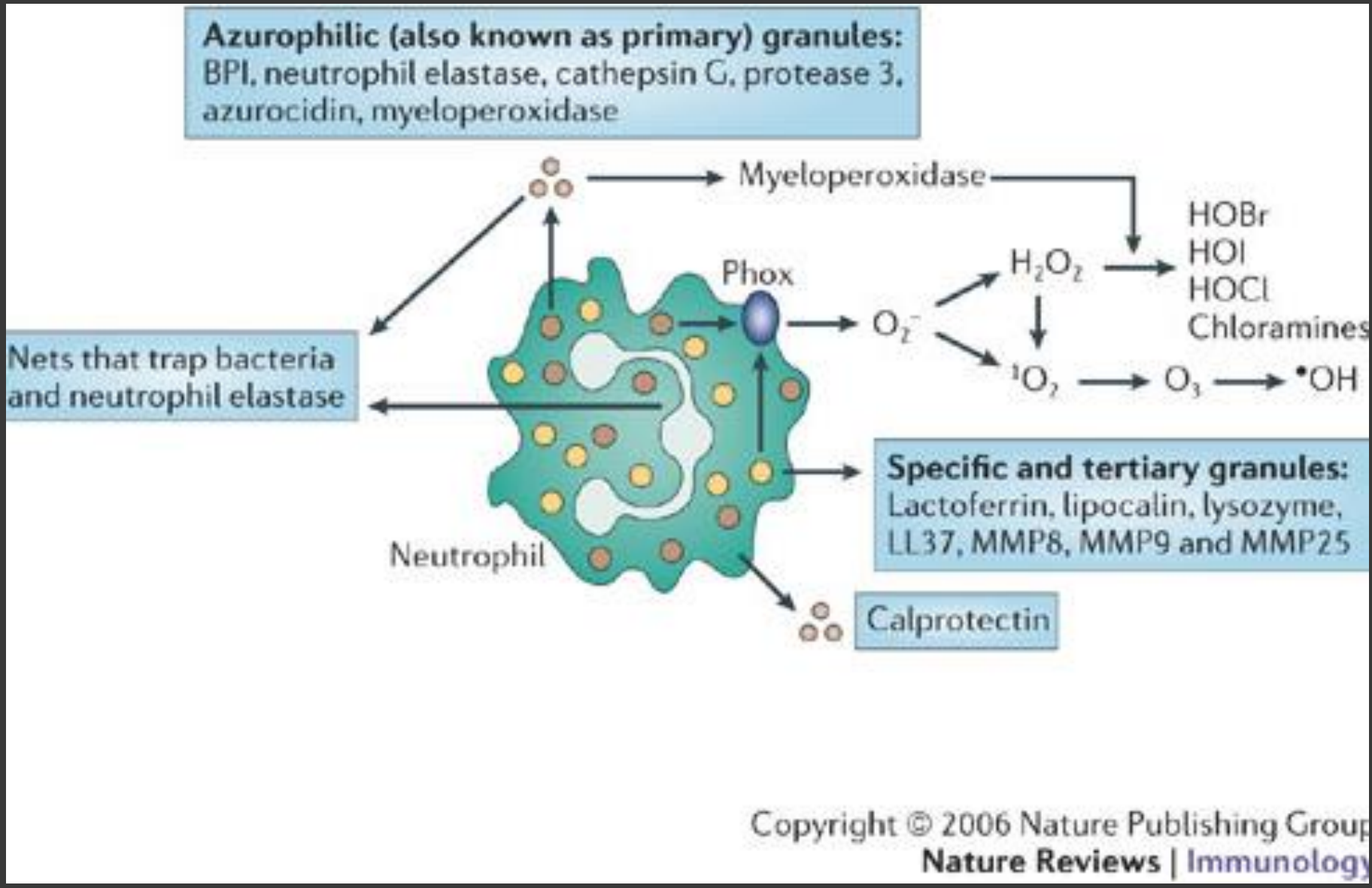
# ANCA associated vasculitides

# ANCA Associated Vasculitides (AAV)

1. Microscopic polyangiitis (MPA)
2. Granulomatosis with polyangiitis (GPA, formerly Wegener's)
3. Eosinophilic granulomatosis with polyangiitis (EGPA, formerly Churg-Strauss)

# Antineutrophil Cytoplasmic Antibodies (ANCA)

- Antibodies against azurophilic granules in neutrophils
- 2 types:
  - Cytoplasmic (cANCA): against proteinase 3. specific for Wegener's
  - Perinuclear (pANCA): against myeloperoxidase. Occur in CSS & MPA
- pANCA in diseases other than primary vasculitis is directed against other antigens (elastase, lactoferrin, cathepsin G)





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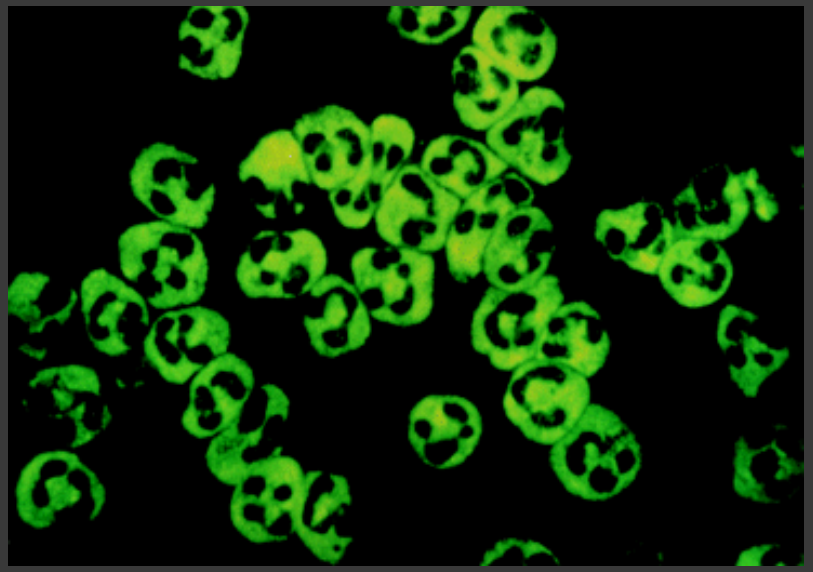
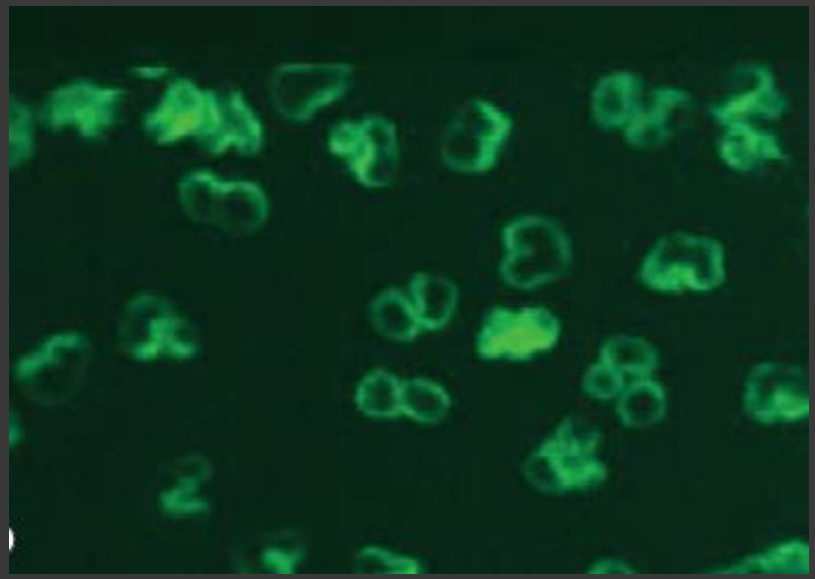
# ANCA

cANCA



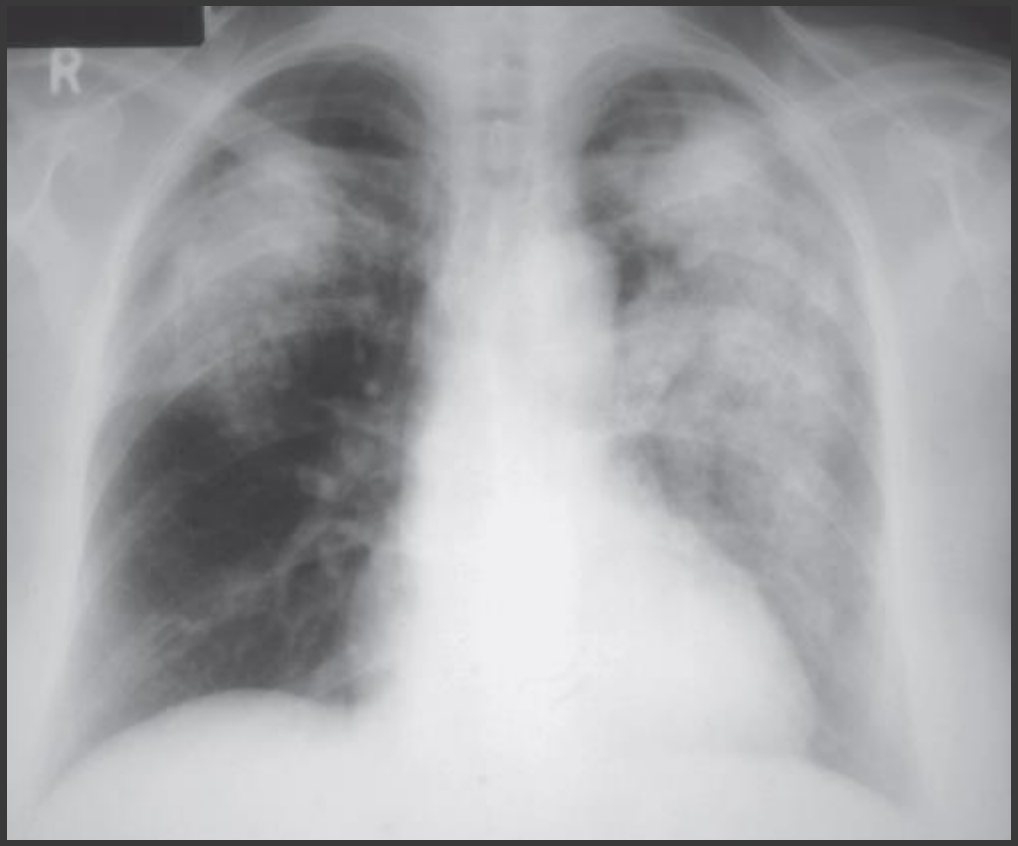
pANCA



# Microscopic Polyangiitis (MPA)

- **Presents:**
  - acutely with renal disease ➔ RPGN, or
  - Pulmonary-renal syndrome
- Affect small vessels (arterioles, venules, capillaries)
- pANCA directed against MPO

# Pulmonary haemorrhage in MPA



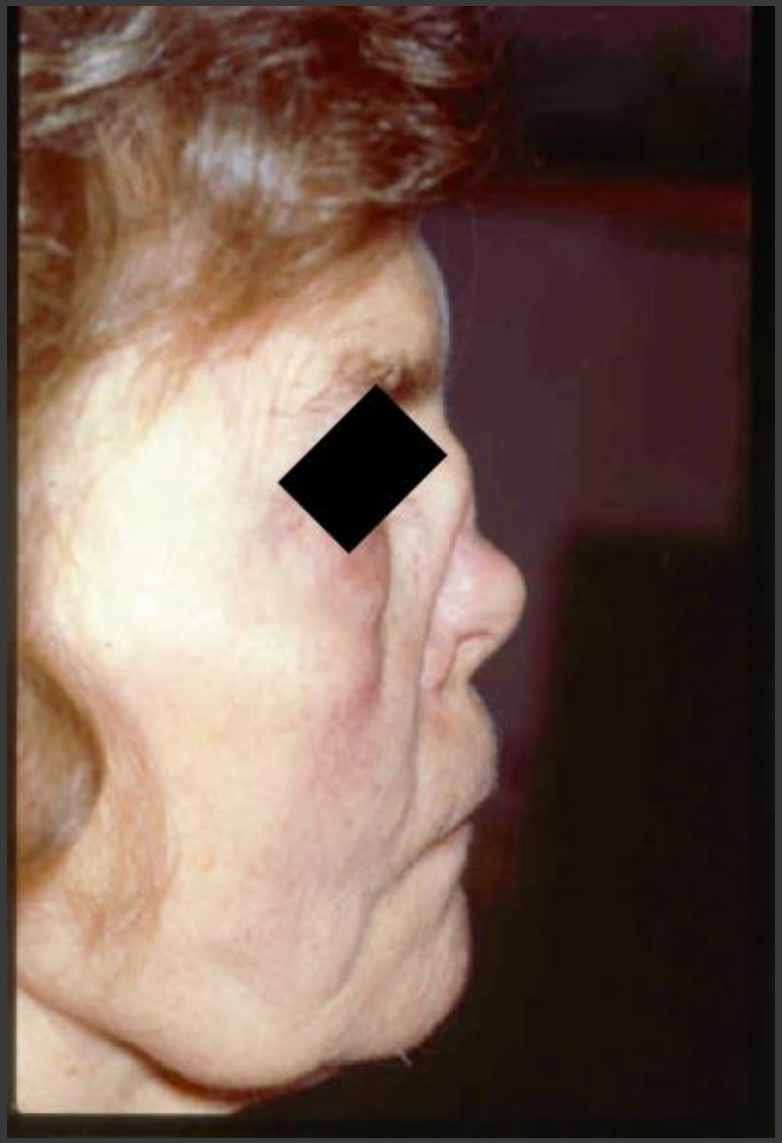
# Granulomatosis with polyangiitis (GPA, formerly Wegener's)

- Granulomatous necrotising vasculitis affecting small to medium vessels
- Affects ENT, kidney & lung
- ANCA in >90% (mostly cANCA)
- 10/million/year
- Aetiology unknown

# GPA features

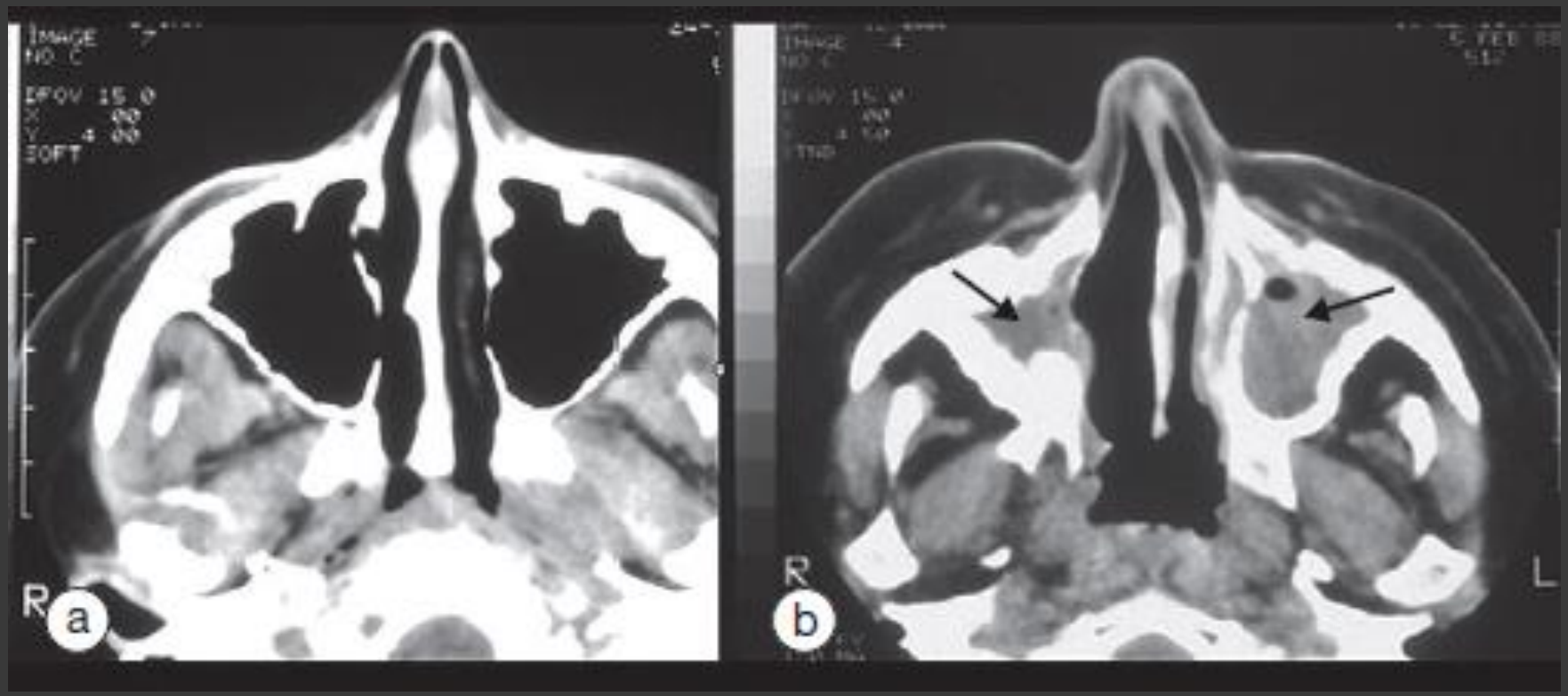
- **Systemic**: Fever, weight loss, myalgia, and arthralgia
- **Lung**: haemoptysis, dysponea
- **Skin**: purpura
- **ENT**: epistaxis, nasal crusting, sinusitis. nasal collapse
- **GI**: vasculitis
- **Neuro**: neuropathy
- **Renal**: RGPN (Paucimmune, crescentic)
- **Eye**: scleritis, proptosis due to retro-orbital mass

# Saddle-nose in WG

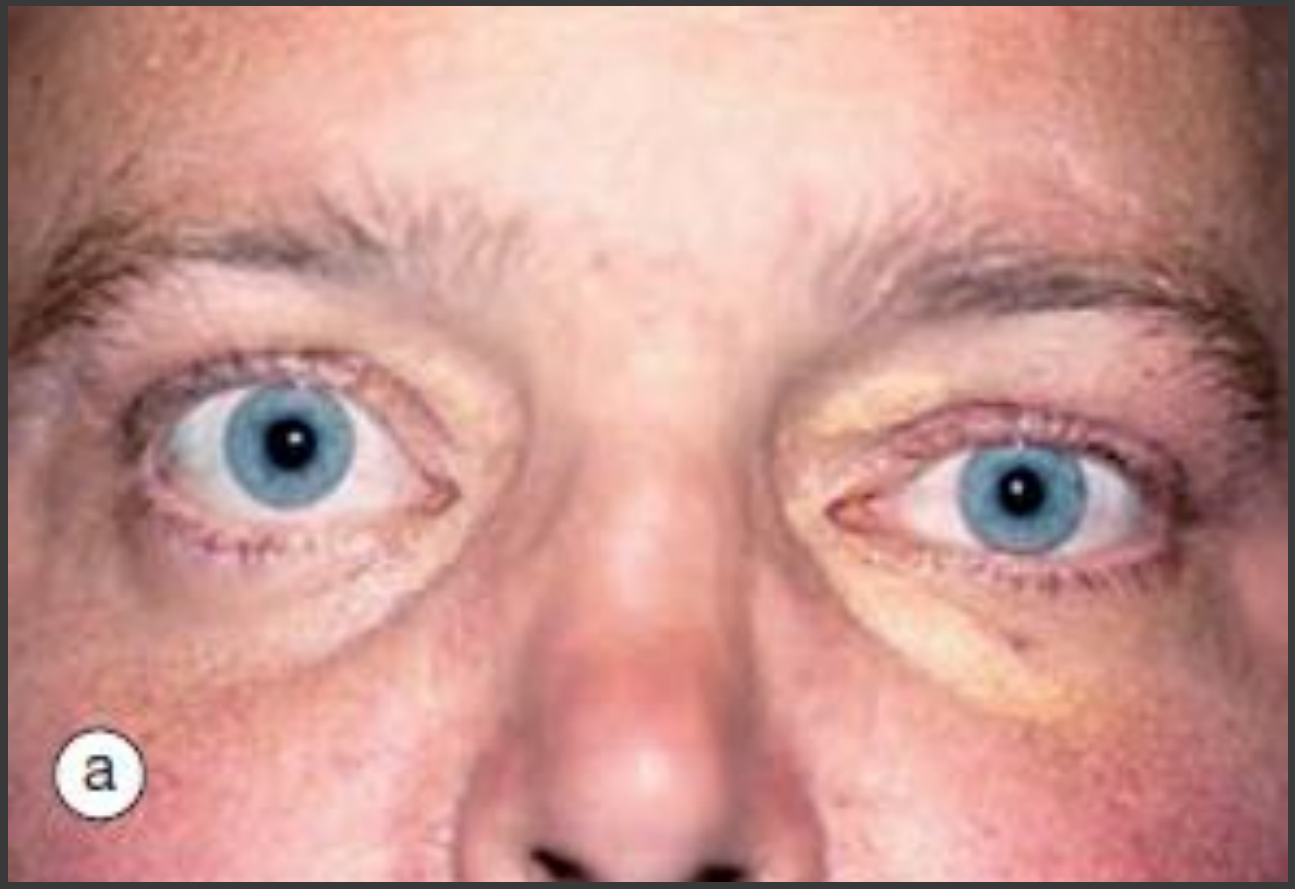


Normal

GPA/Wegener's

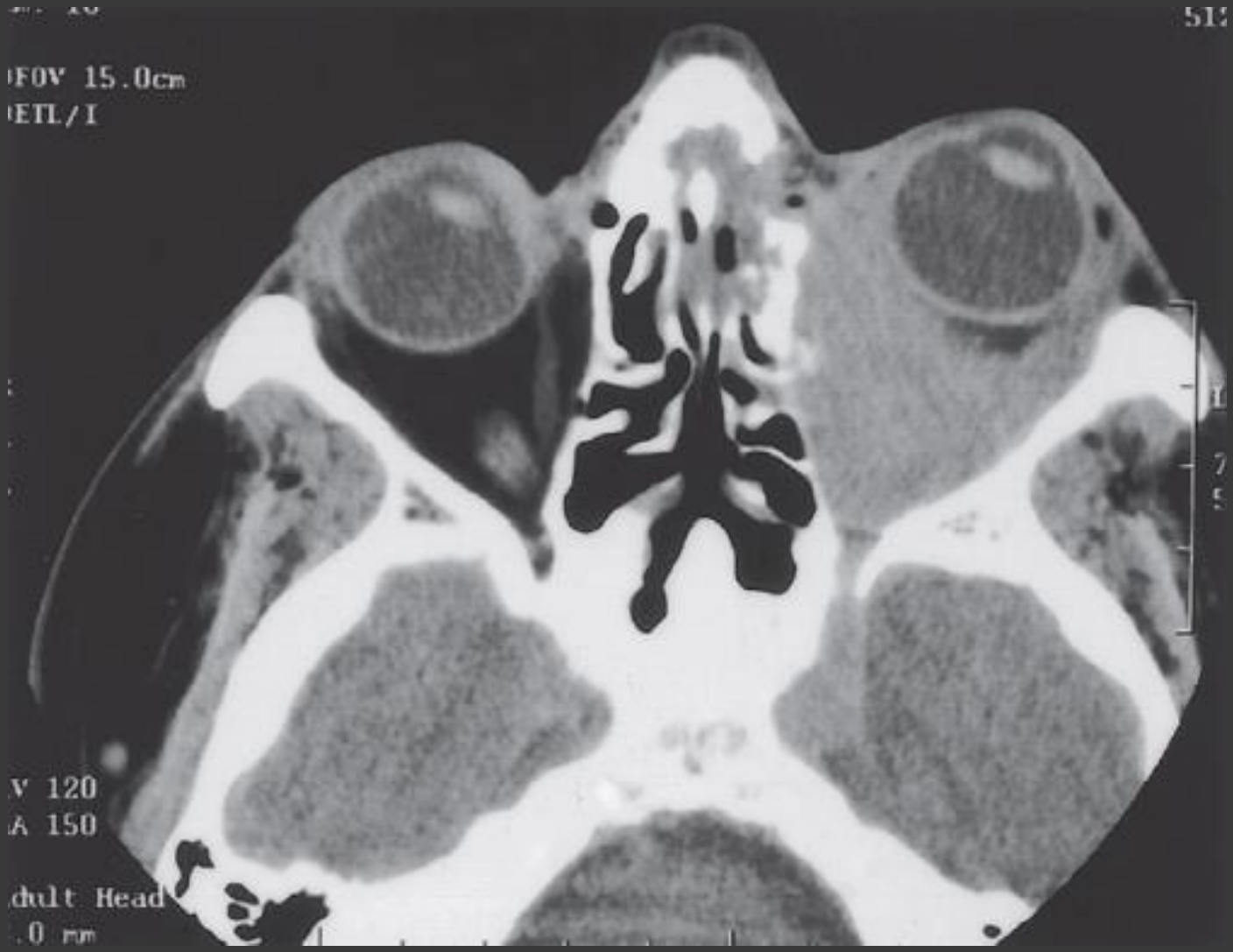


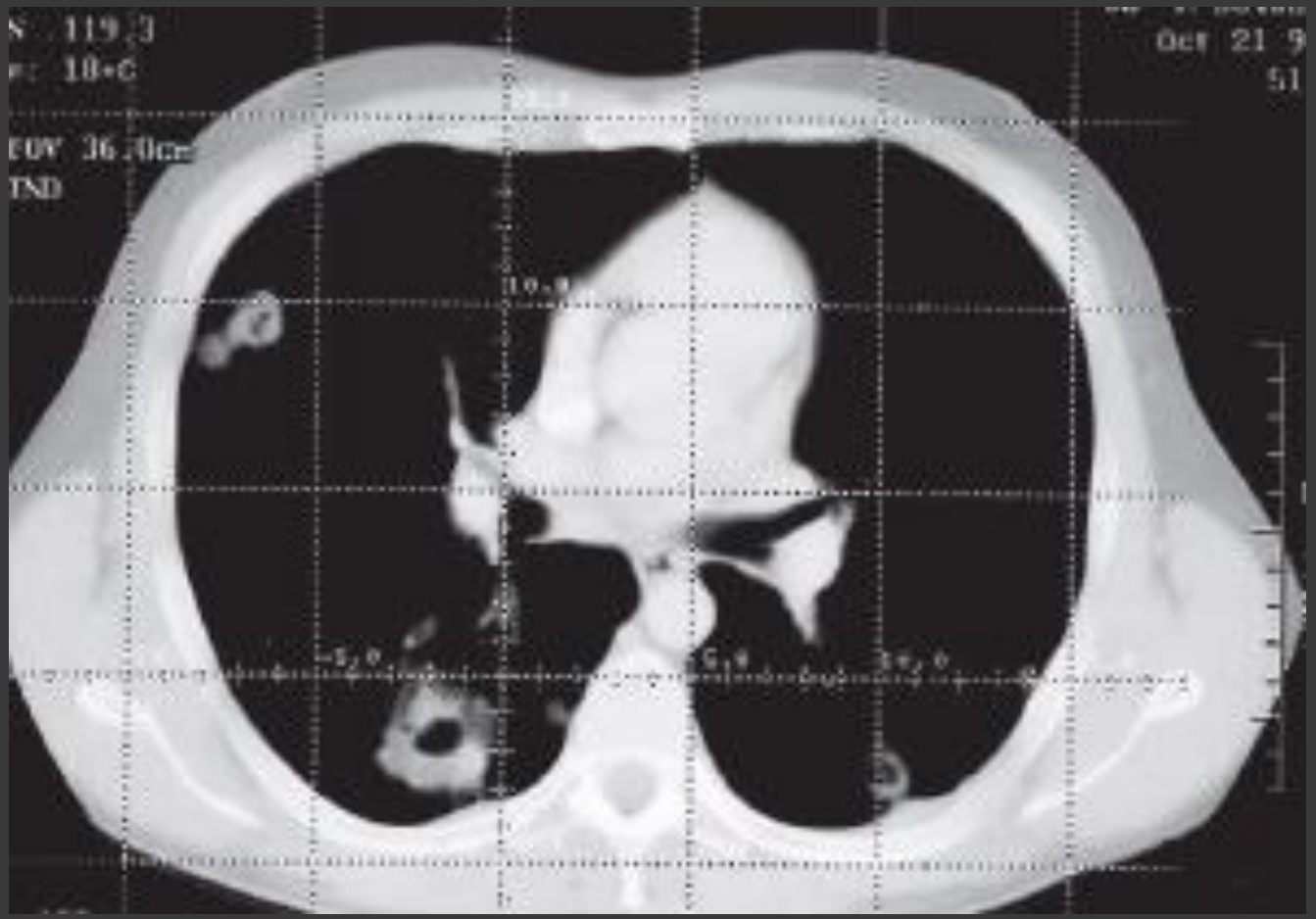
# Exophthalmos due to orbital pseudotumors




Intractable pain and loss of vision
Refractory to therapy

WG: Left orbital mass causing proptosis and visual loss through compression of the optic nerve





**Multiple bilateral pulmonary nodules, many of which have cavitated.**

# Eosinophilic granulomatosis with polyangiitis (EGPA, formerly Churg-Strauss)

- Eosinophil-rich granulomatous inflammation involving the respiratory tract, & necrotizing vasculitis affecting small to medium-sized vessels, associated with asthma & eosinophilia
- Cardiac involvement common: The principal cause of morbidity and mortality and accounts for 50% of deaths
- pANCA
- eosinophil count is useful in monitoring dis activity

# EGPA: 3 phases

1. **Prodromal phase**
   - may last for years: asthma, atopic features (e.g., allergic rhinitis, nasal polyposis).
2. **Eosinophilic phase**
   - Peripheral blood eosinophilia and eosinophilic tissue infiltration of lung and GI tract.
3. **Vasculitic phase**
   - The most severe phase: may only become apparent several years after prodromal phase.
   - Malaise, lethargy, weight loss, fevers & vasculitis

# Treatment of ANCA associated vasculitis

- Induction:
  - IV steroids +
  - IV cyclophosphamide OR rituximab
- Maintenance :
  - Oral steroids +
  - Oral MTX or azathioprine

# Medium Vessel Vasculitis

# Polyarteritis nodosa (PAN)

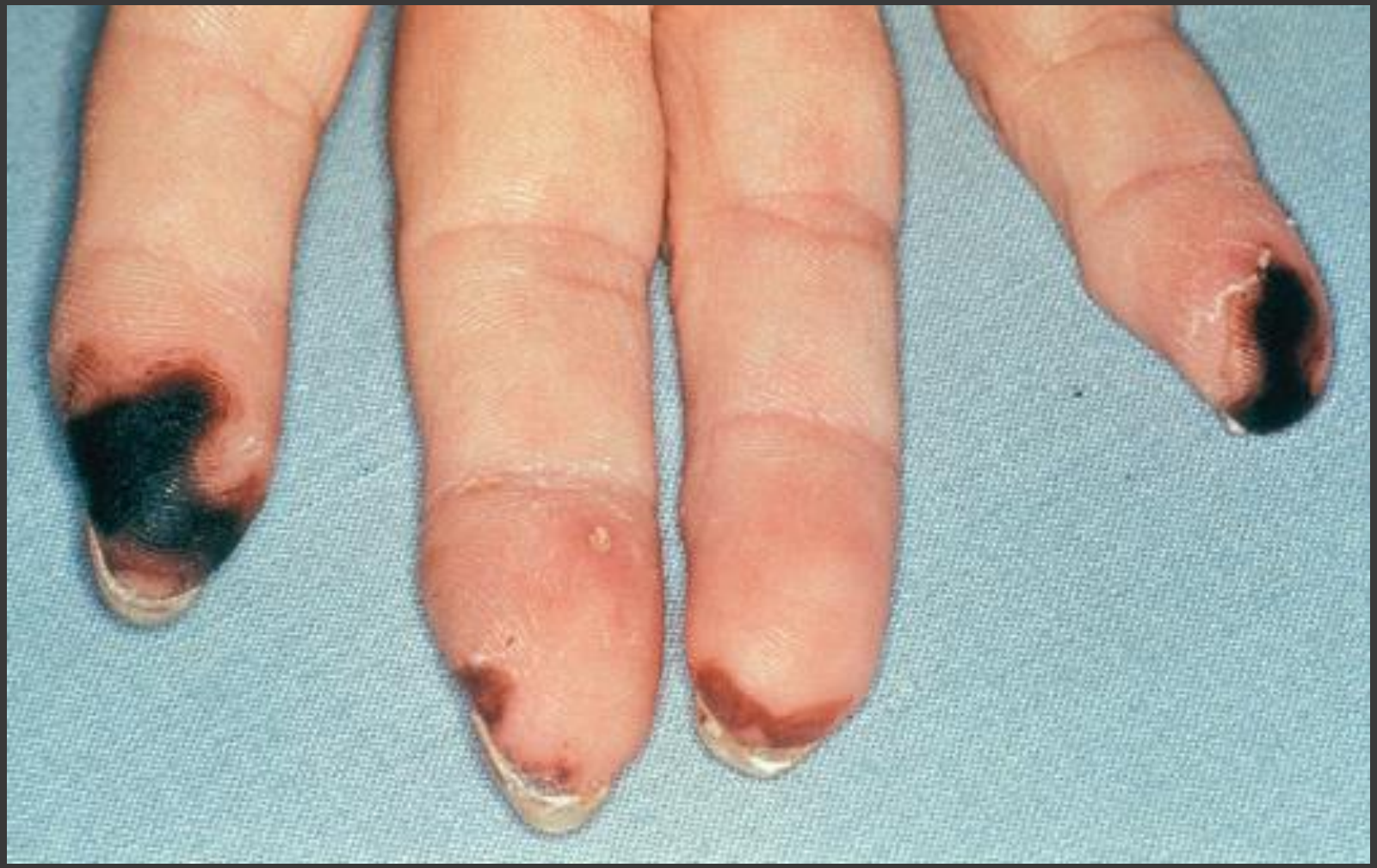
- A multisystem, necrotizing vasculitis of small- and medium-sized muscular arteries
- Involvement of the renal and visceral arteries is characteristic.
- *PAN does not involve lungs*
- No ANCA association
- Hepatitis B in 10-30%

# PAN

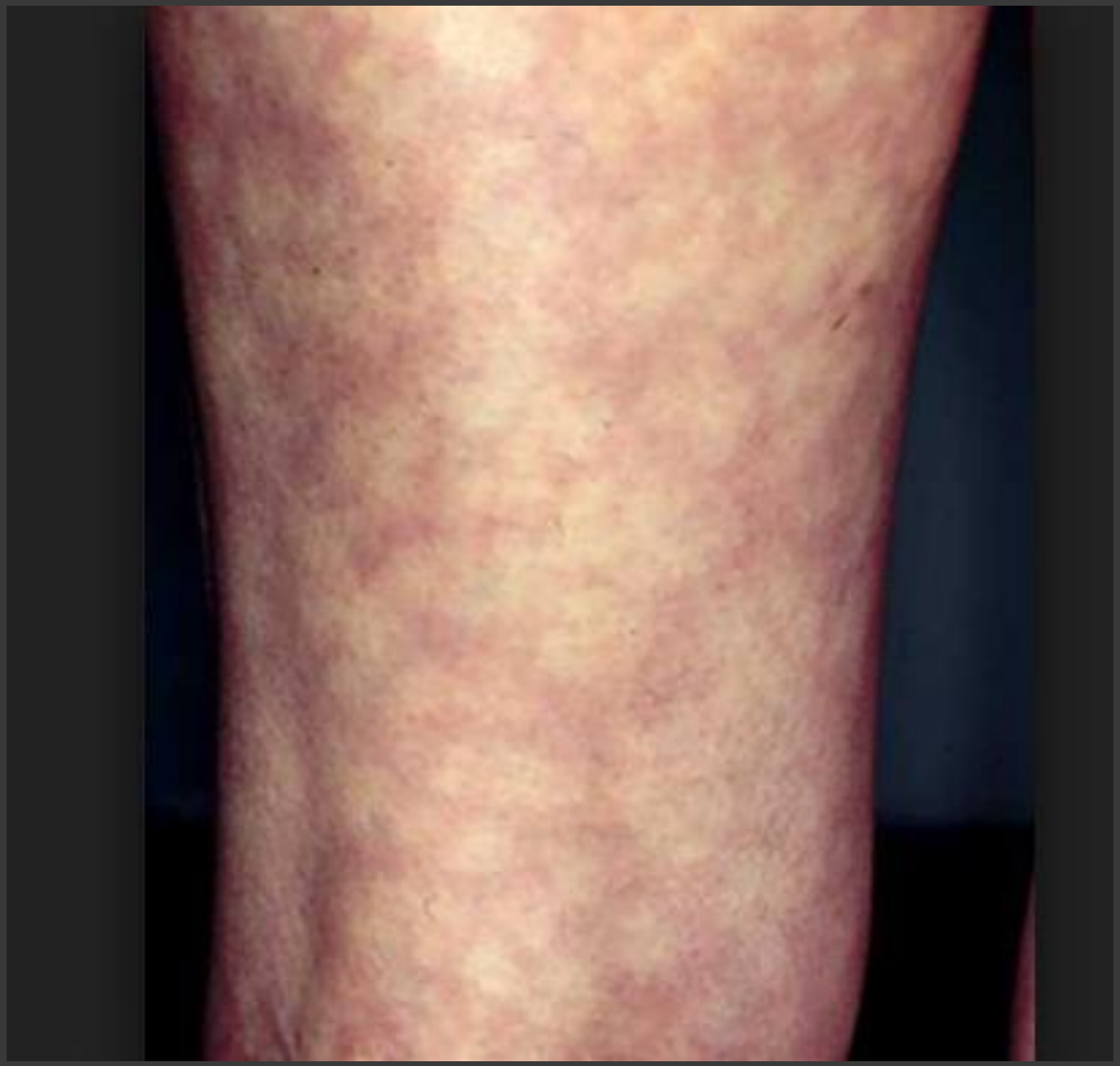
**CLINICAL MANIFESTATIONS RELATED TO ORGAN SYSTEM INVOLVEMENT IN CLASSIC POLYARTERITIS NODOSA**

| ORGAN SYSTEM | PERCENT INCIDENCE | CLINICAL MANIFESTATIONS |
|---|---|---|
| Renal | 60 | Renal failure, hypertension |
| Musculoskeletal | 64 | Arthritis, arthralgia, myalgia |
| Peripheral nervous system | 51 | Peripheral neuropathy, mononeuritis multiplex |
| Gastrointestinal tract | 44 | Abdominal pain, nausea and vomiting, bleeding, bowel infarction and perforation, cholecystitis, hepatic infarction, pancreatic infarction |
| Skin | 43 | Rash, purpura, nodules, cutaneous infarcts, livedo reticularis, Raynaud's phenomenon |
| Cardiac | 36 | Congestive heart failure, myocardial infarction, pericarditis |
| Genitourinary | 25 | Testicular, ovarian, or epididymal pain |
| Central nervous system | 23 | Cerebral vascular accident, altered mental status, seizure |

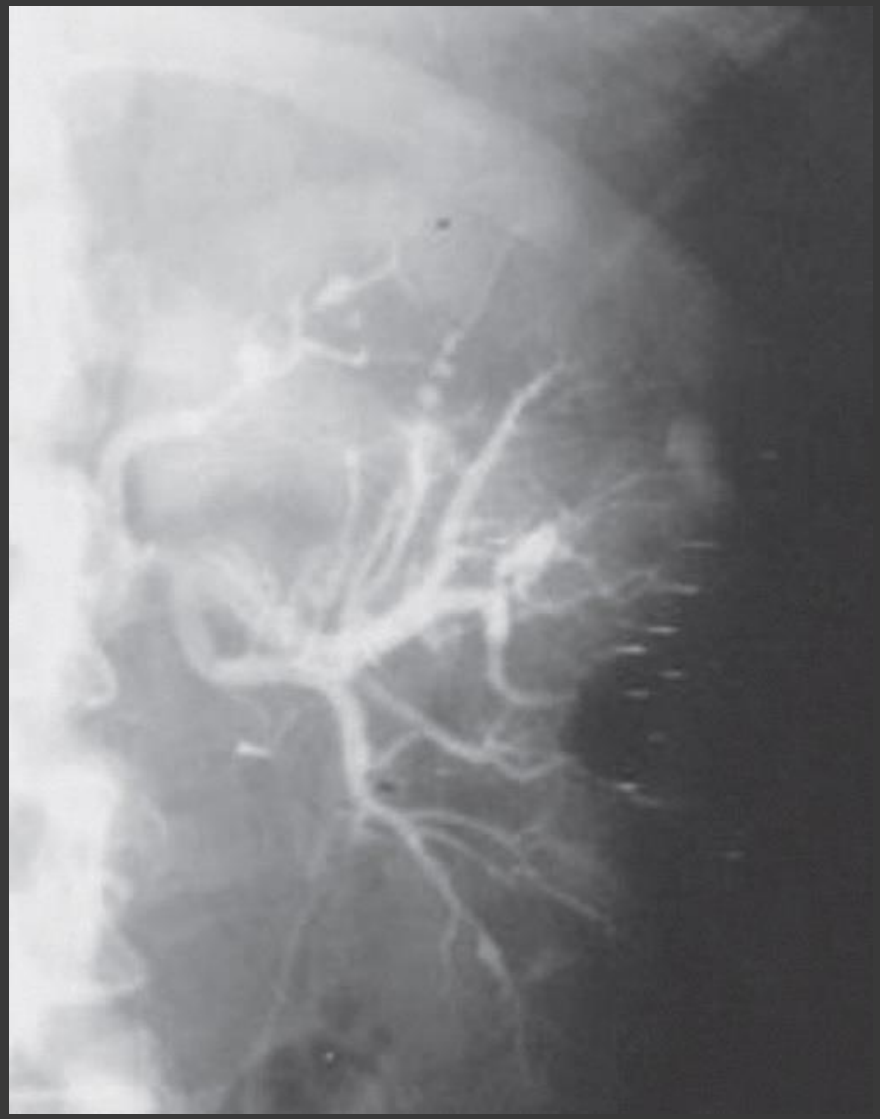
# Digital tip infarction in polyarteritis nodosa

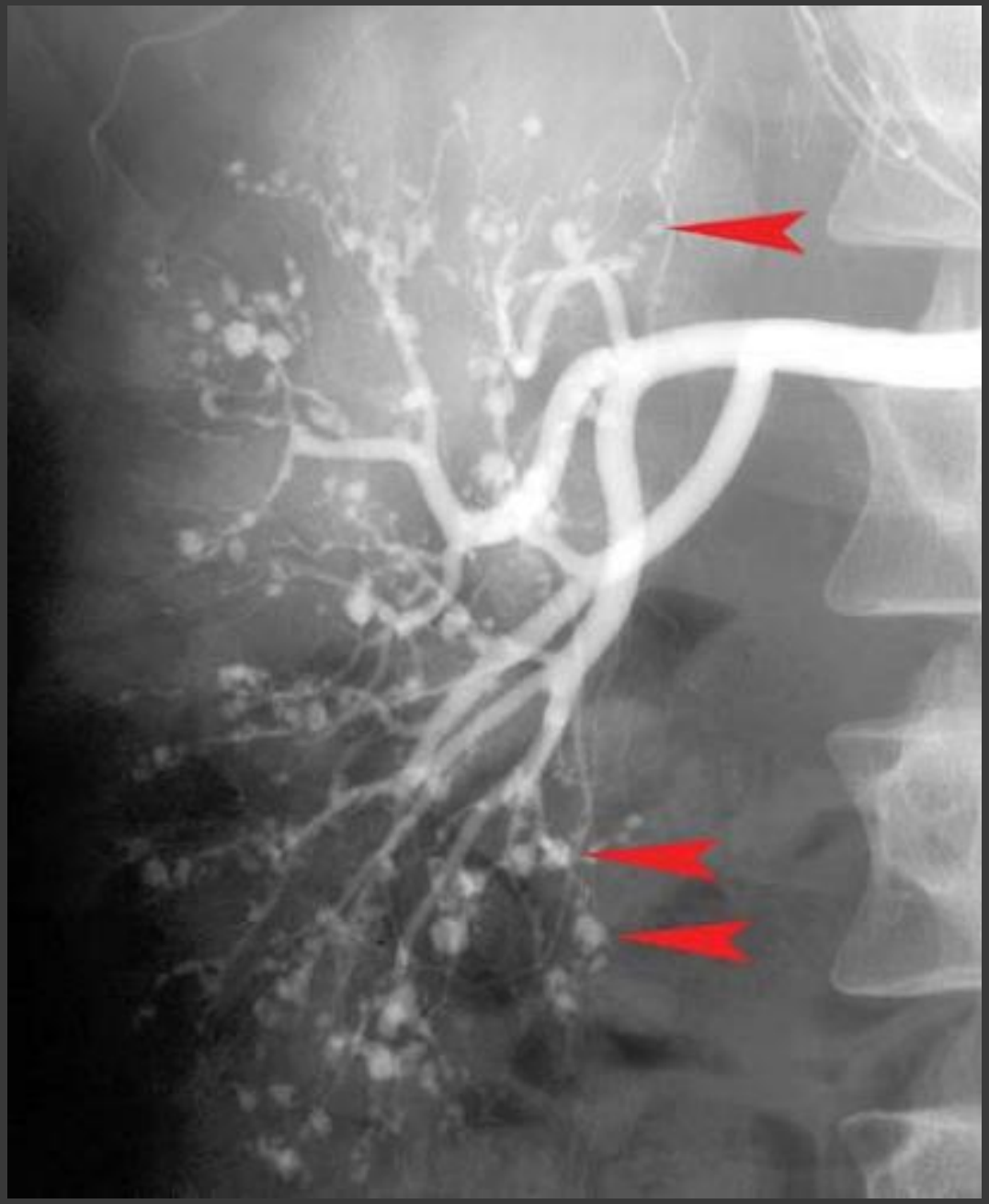


# Livedo reticularis in polyarteritis nodosa

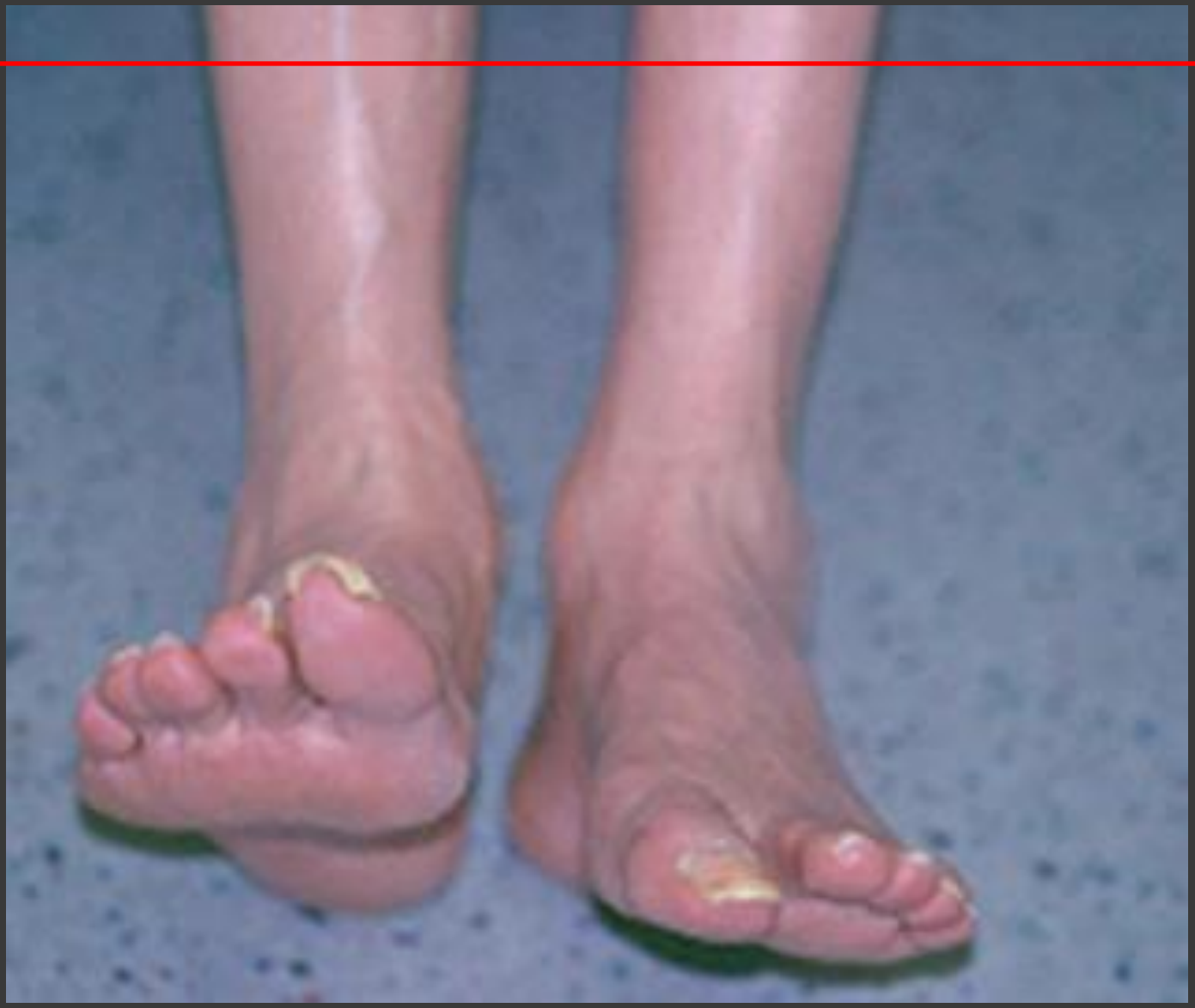


# Angiogram showing microaneurysms in polyarteritis nodosa

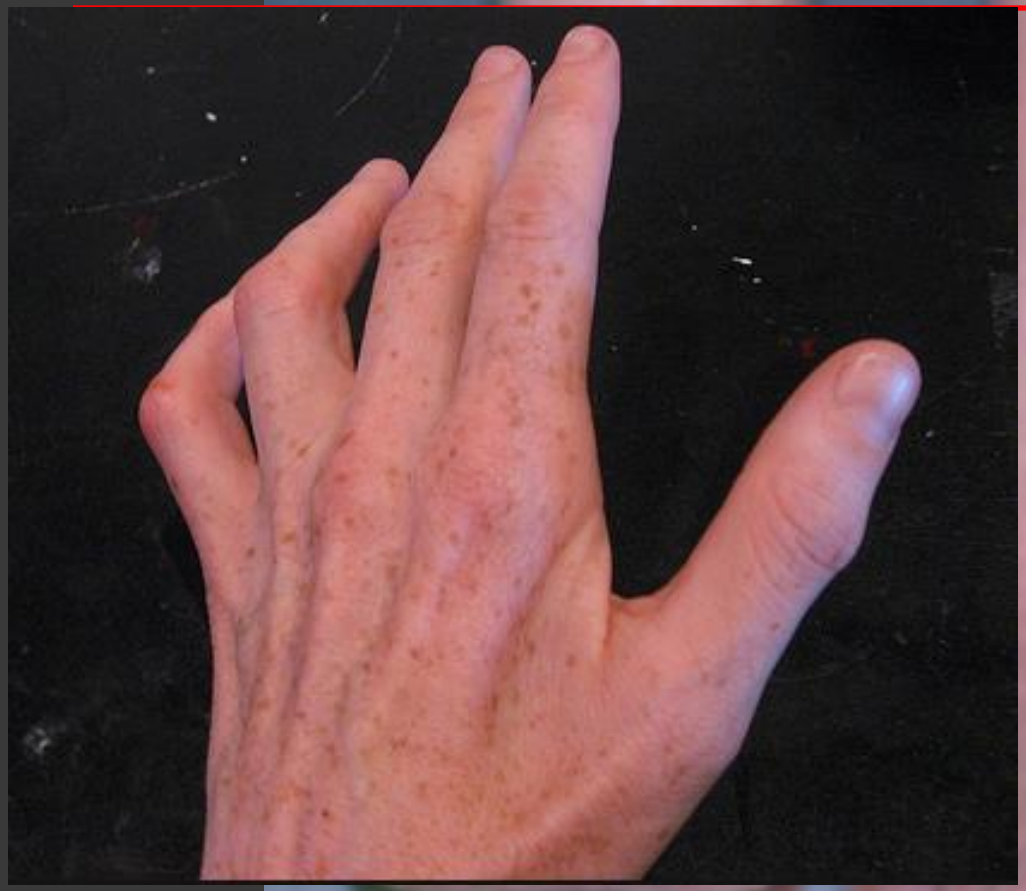




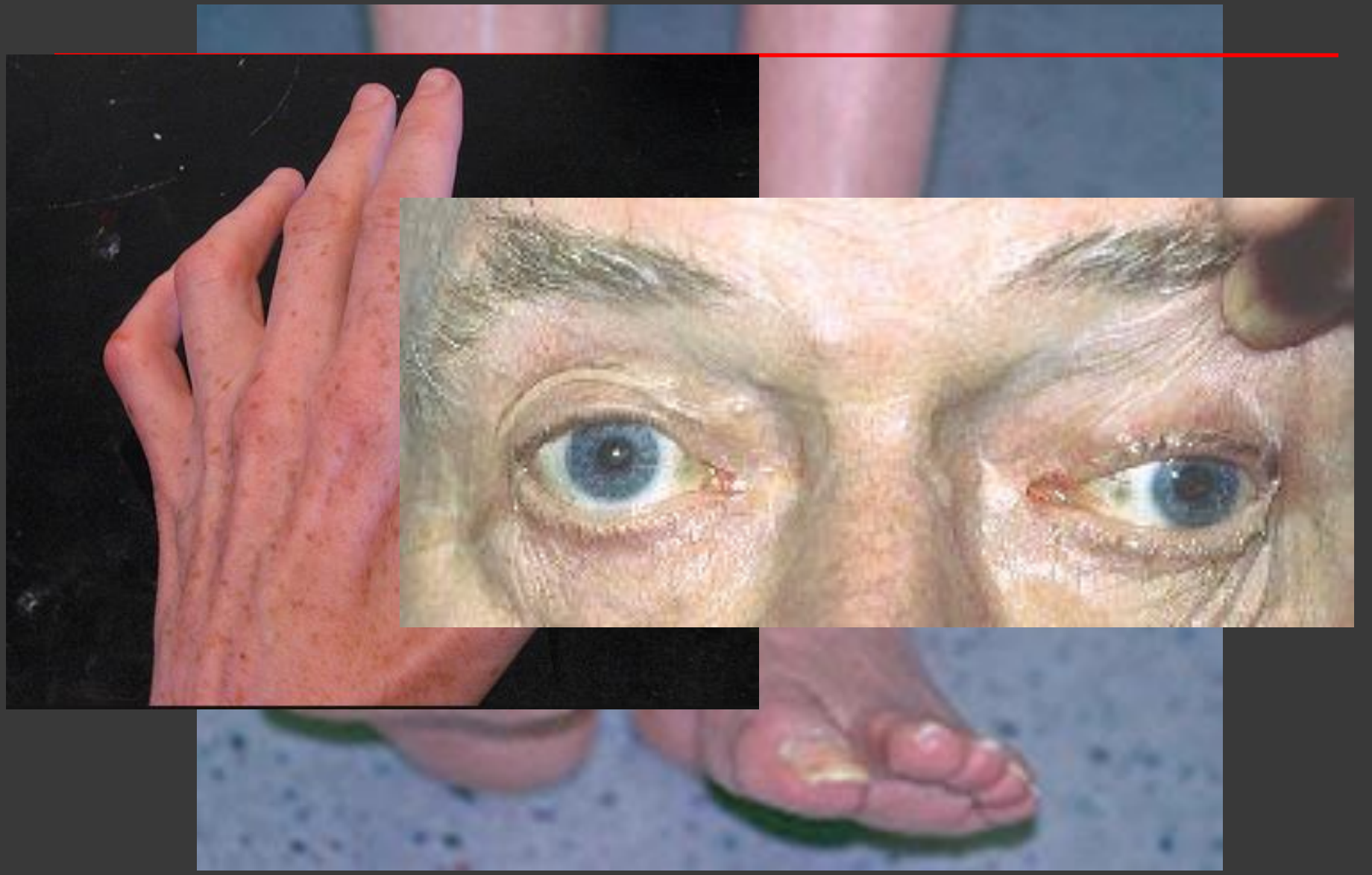
# Mononuritis multiplex



# Mononuritis multiplex



# Mononuritis multiplex



# Small Vessel Vasculitis

# Hypersensitivity Vasculitis

## Primary or secondary

**Immune complex**

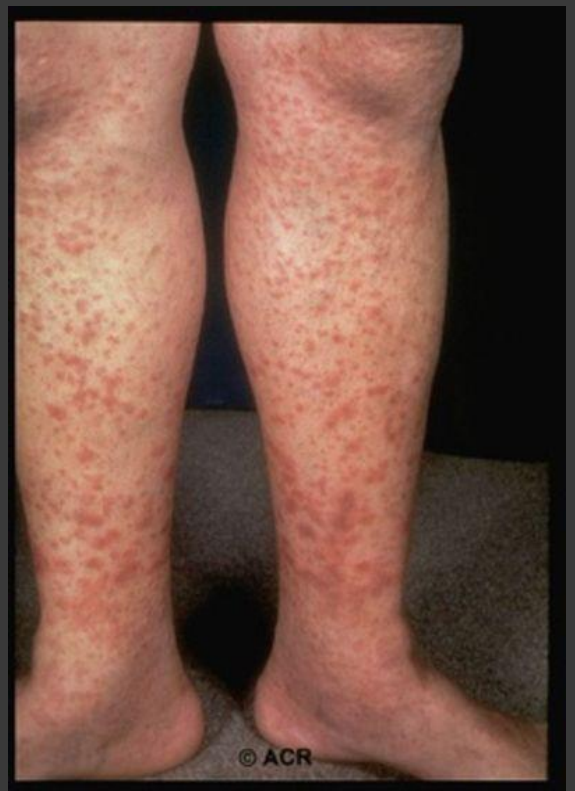
**Most common form of vasculitis.**

**Histology- leukocytoclastic vasculitis.**

**Almost invariably involves skin:-**palpable purpura

**Visceral involvement is infrequent , mild**

- **Alveolar hemorrhage**
- **Intestinal ischemia or hemorrhage**
- **Glomerulonephritis.**




## Secondary:-

- **Autoimmune disease**
- **Drugs.**
- **Infection.**
- **Allergy**
- **Hematologic**

# Hypersensitivity vasculitis/Henoch-Schönlein purpura (HSP)

- Vasculitis with IgA-dominant immune deposits affecting small vessels
- Age at onset <20 years (majority <10)
- The most common vasculitis in children
- Follows upper respiratory infection
- involves alternate complement pathway & therefore C3 & C4 are normal

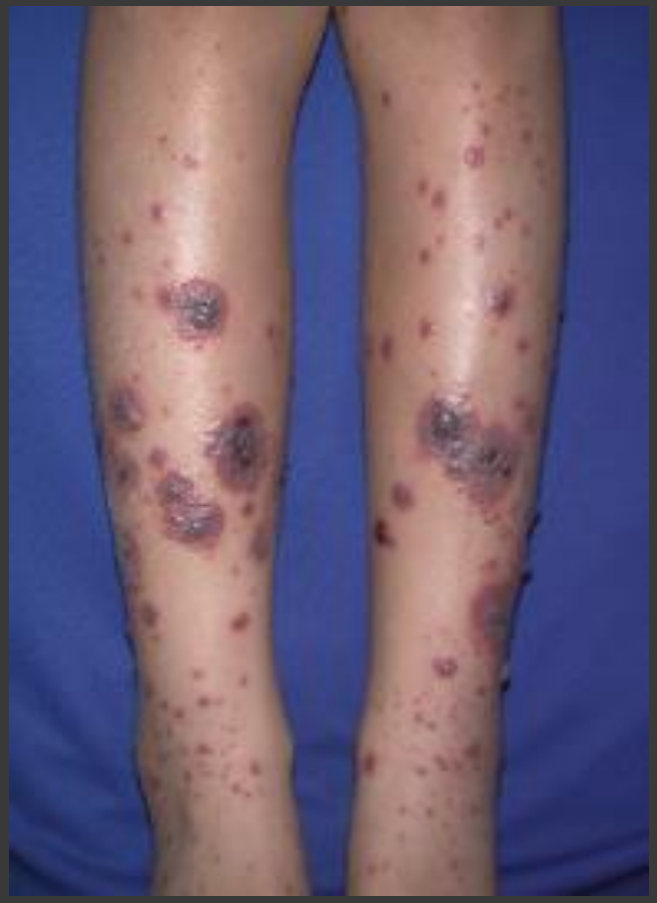
# HSP: Clinical features

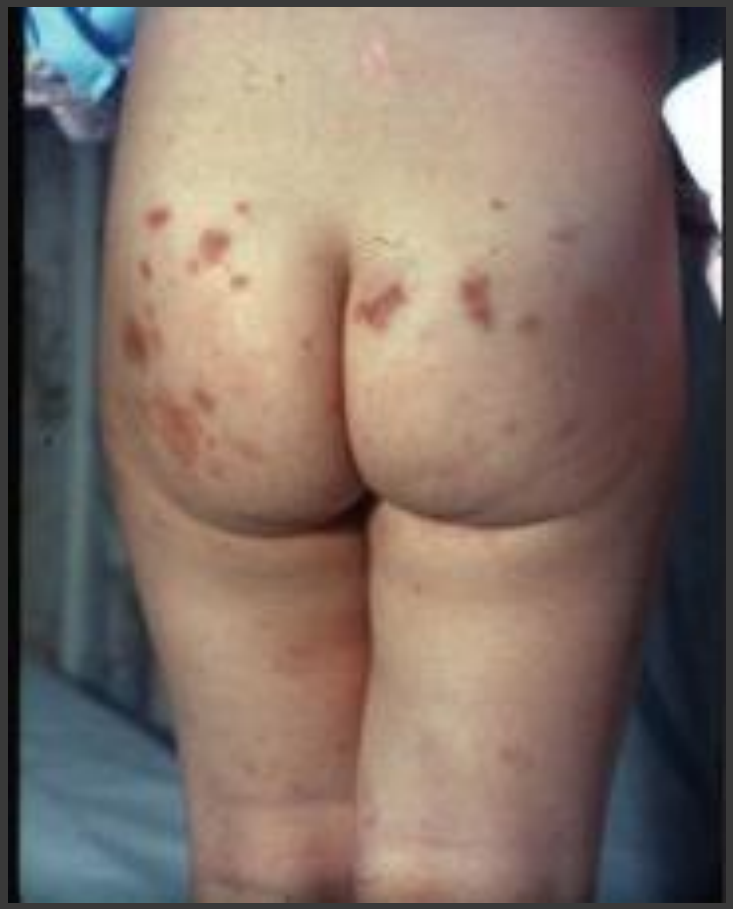
- Purpuric rash on legs & buttocks
- Colicky abdo pain
- Melaena
- Arthralgia: transient and self-limiting
- Haematuria & proteinuria
- Sometimes focal or diffuse proliferative glomerulonephritis develops
- Sometimes intussusseption develops

# HSP

- **Diagnosis**:
  - Skin biopsy: leucocytoclastic vasculitis
  - Immunoflorescence: IgA deposits
- **Treatment**: none
- Most have a self-limiting disease & settle within 2–3 weeks
- <5% of children develop chronic renal failure
- Renal failure is more common in adults

# Henoch-Schönlein purpura (HSP)





# Cryoglobulinaemia

- Cryoglobulins: immunoglobulins that precipitate at temperatures <37° C and redissolve on rewarming
- Associated with Hepatitis C virus infection
- Affects skin, kidneys & nerves
- Immune complex mediated
- Investigations:
  - Cryoglobulins
  - High RF
  - Low C4
  - Hep C serology

# Cryoglobulinaemia: Clinical features

- Purpura
- Joint pain
- Raynaud’s
- Neuropathy
- Renal: membranoproliferative GN

# Cryoglobulinaemia: Treatment

- Interferon alpha + ribavirin + rituximab
- Plasma exchange for severe cases to remove cryoglobulins

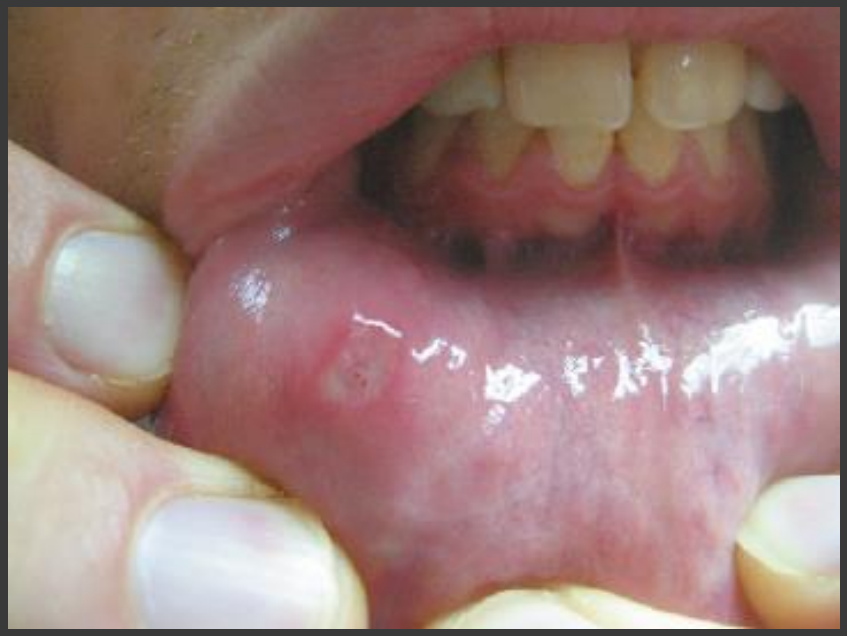
# Other

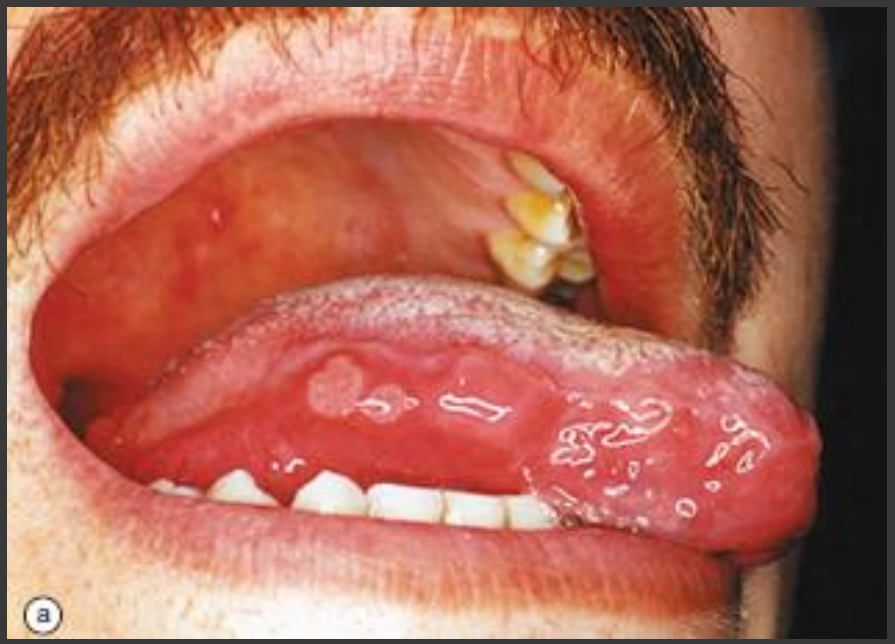
# Behcet's disease

- Common along the silk route
- HLA-B51 association
- **Recurrent oral ulceration plus two of the following:**
  - Recurrent genital ulceration
  - Eye lesions
  - Skin lesions
  - Pathergy test
- Oral ulcers heal without scarring
- Genital ulcers leave scars
- No confirmatory blood or histological test, diagnosis clinical

# Behcet

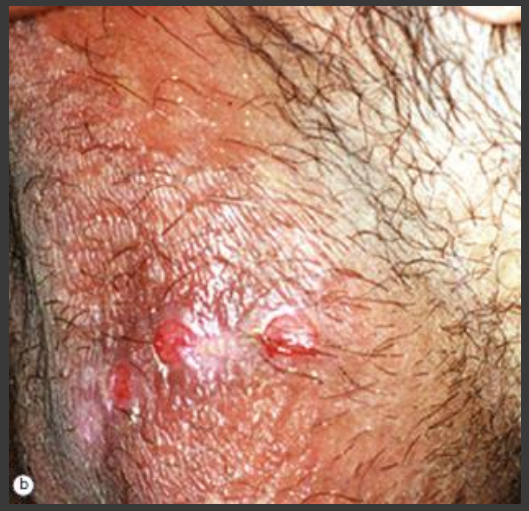
## Oral ulcers



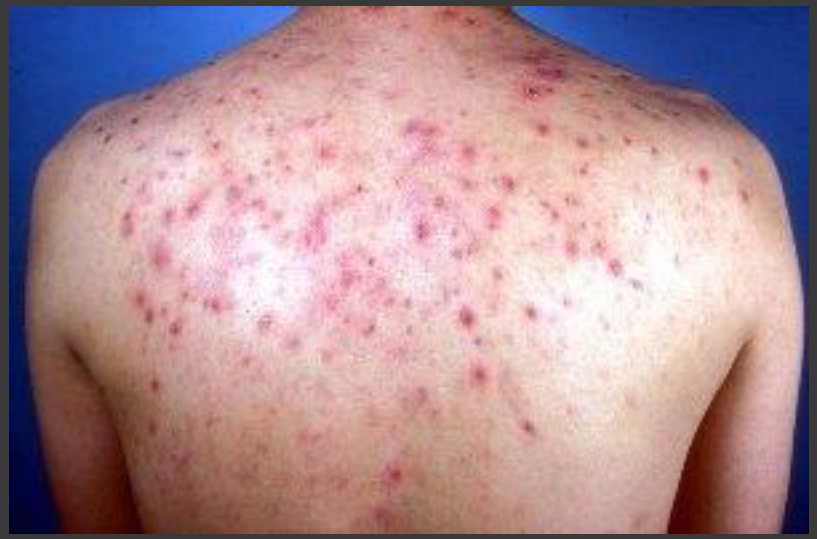


# Behcet
## skin lesions

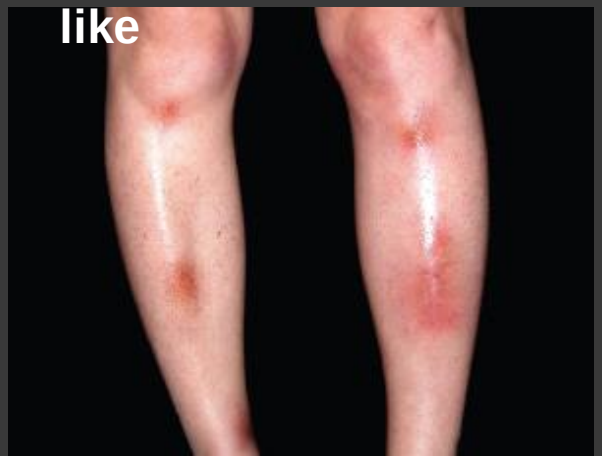
**Genital ulcers**



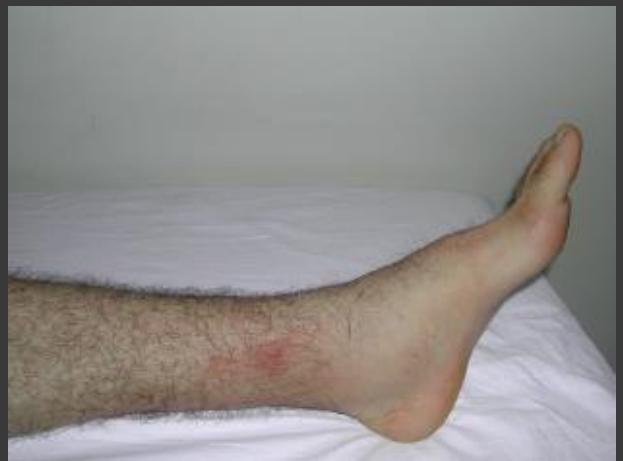
**Acneiform lesions**



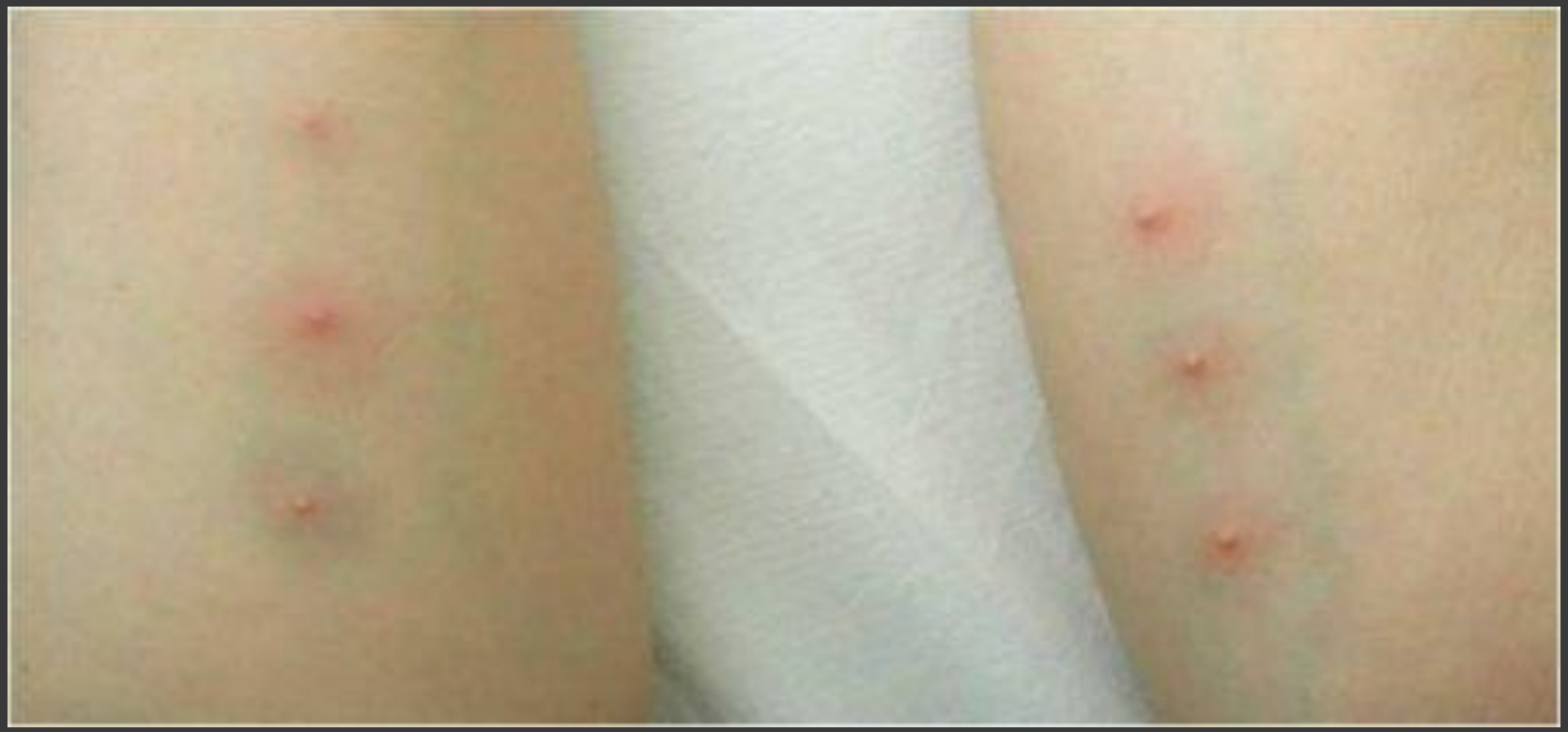
**Erythema nodosum-like**



**Superficial thrombophlebitis**

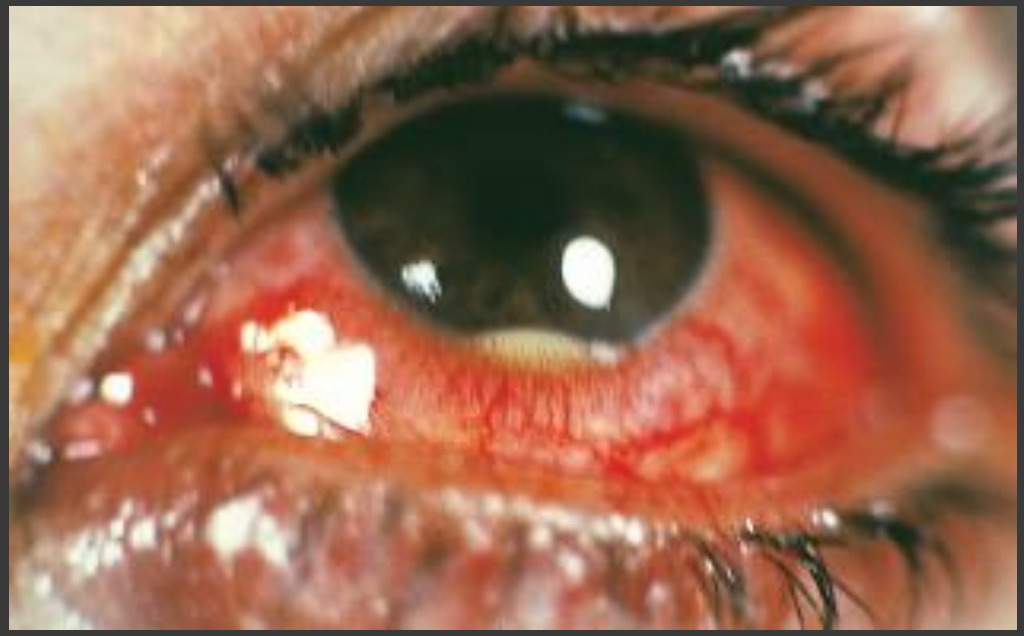


# Pathergy



# Behcet

## Eye lesions

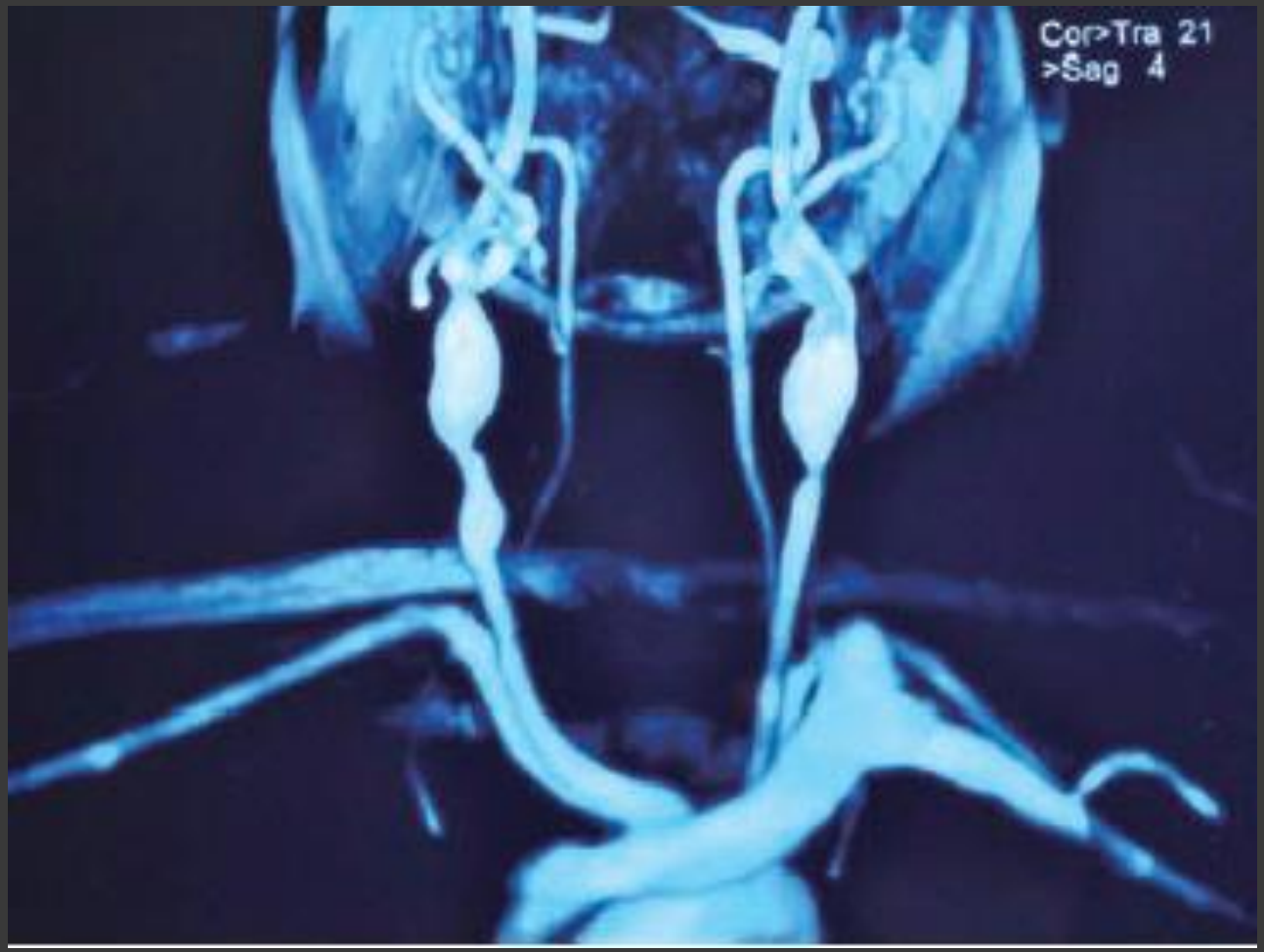


Anterior uveitis & hypopyon

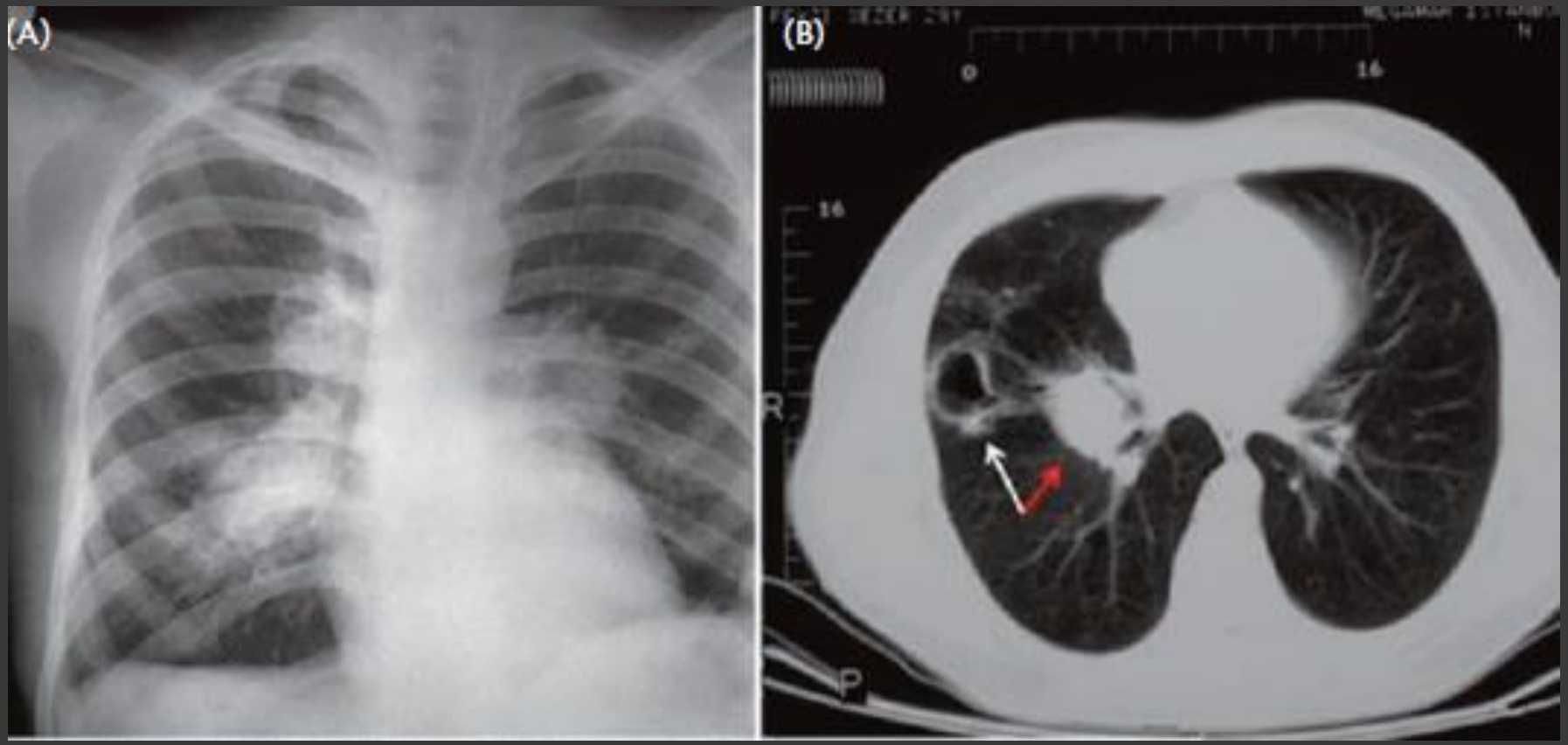
# Vascular manifestations of Behcet's

- **Arterial**
  - Aortic aneyrysm
  - Carotid anerysm
  - Pulmonary anerysm
- **Venous**
  - superficial venous thrombosis
  - DVT
  - Vena cava thrombosis
  - Cerebral venous thrombosis
  - Budd-Chiari syndrome
  - Portal vein thrombosis

# Carotid aneurysm



# Pulmonary artery aneurysm



# Behcet: Nervous system invovement

1. Brainstem or corticospinal tract syndromes (neuro-Behçet's syndrome)
2. Venous sinus thrombosis
3. Aseptic meningitis
4. Isolated behavioral symptoms, or isolated headache
5. Cranial and Peripheral neuropathy
6. Optic neuritis
7. Vestibular involvement

- Poor prognosis is associated with a progressive course, parenchymal or brainstem involvement, and cerebrospinal fluid abnormalities

# Behcet's Treatment

**Depends on manifestations**

- **Oral lesions:**
  - Colchicine
  - Azathioprine
  - Thalidomide
- **Arthritis**:
  - Colchicine
- **Eye**:
  - Steroids
  - Azathioprine
  - Interferon alpha
  - MMF
  - Infliximab
  - Rituximab
- **Vasculopathy**:
  - Steroids & cyclophosphamide
- **Neurological**:
  - Steroids
  - Interferon alpha
  - Anti-TNF

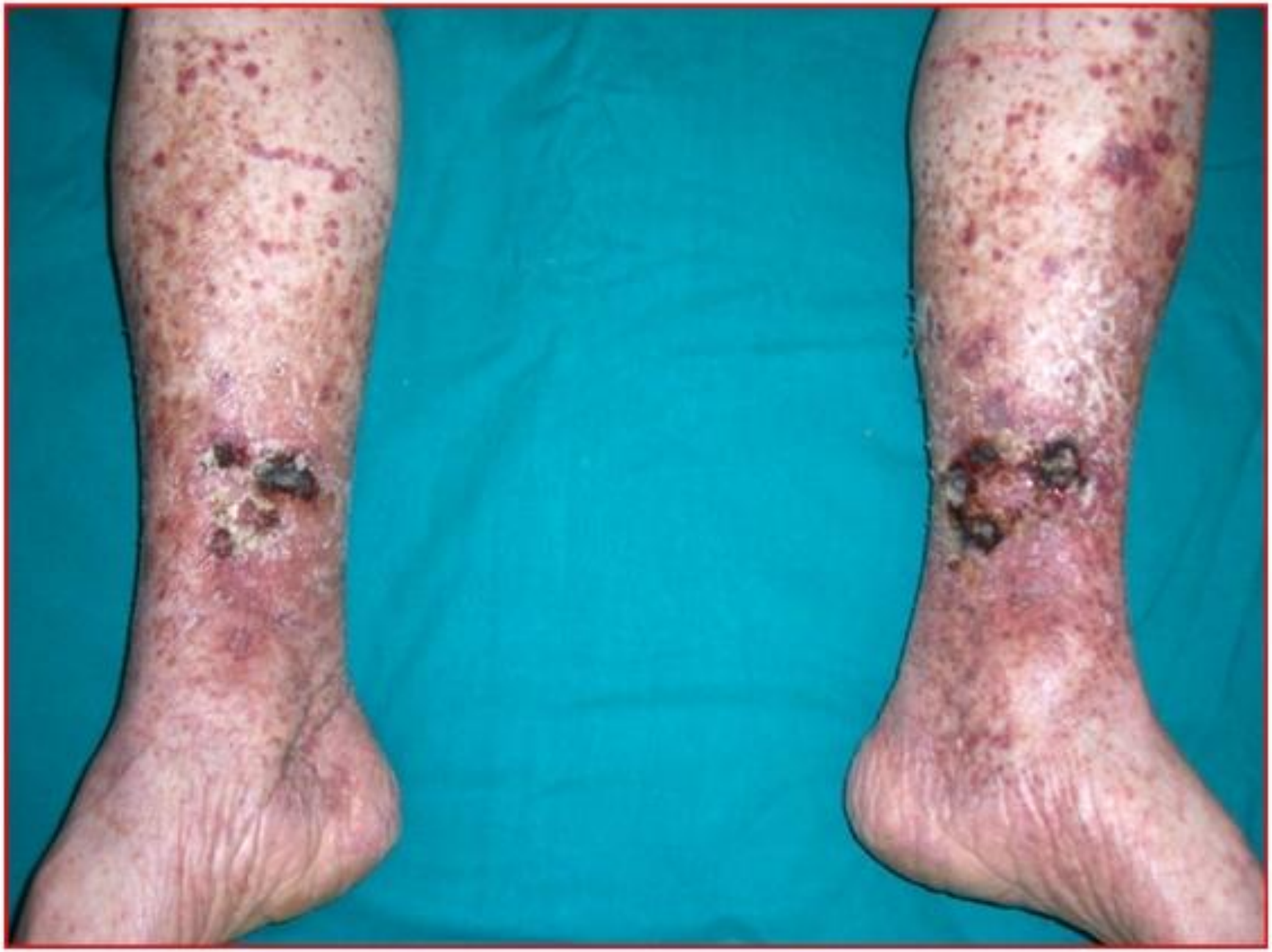
# Vasculitis pearls

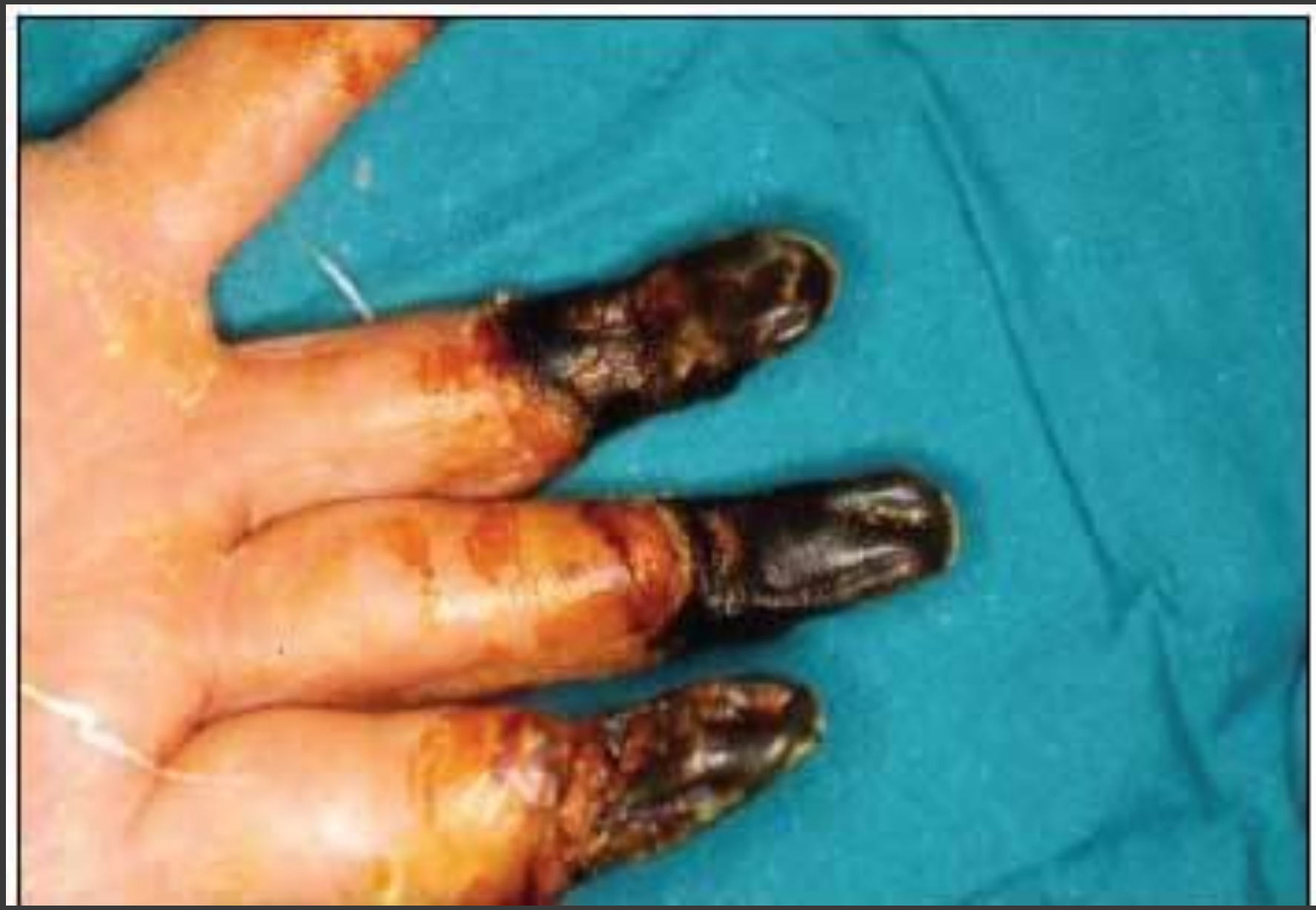
1. GCA is the most common vasculitis
2. Secondary vasculitis is more common than primary vasulitis
3. In GPA, the lung infiltrates are fixed, in EGPA, they are not fixed
4. renal and lung involvement is a negative prognostic factors in GPA & MPA
5. in EGPA most deaths occur from cardiac involvement.

6. Medium to small vessel respond to steroids + immunosuppressives
7. Large vessel respond to high dose steroids
8. Small vessel respond to low dose steroids
9. The appearance of active urinary sedement or rise in serum Cr in vasculitis is an indication for prompt aggressive treatment
10. Urinalysis is the most important investigation as prognosis is determined by the extent of renal involvement

# Last Case

- A 52-year-old woman has had arthralgias and occasional purple spots on her legs for several years. She now presents with florid small, nonblanchable, palpable lesions on her legs and black fingers and obvious synovitis of multiple small joints. Some of the skin lesions have centers of necrosis. Radiographs of the hands and wrists show no erosions. In the past, she has been diagnosed at different times with RA and SLE, because of markedly positive RF, ANA, low C4, but normal C3 and Raynaud's. 30 years ago , she had a complicated but safe delivery of her only pregnancy, a breech presentation, which necessitated the transfusion of multiple units of blood.





- What further investigations
- What s the diagnosis?

# Questions?