VASCULITIS

Alexandra Balbir-Gurman

Definition

- **Blood vessels inflammation and damage**
- **Tissue ischemia**

Primary vasculitis

Secondary vasculitis

(infections, viruses, tumors, collagen diseases: RA, Sjögren's syndrome, SLE, SSc, Myositis)

VASCULITIS
CLASSIFICATION

LARGE-MEDIUM-SIZED VESSELS

- **Takayasu's arteritis**
- **Temporal arteritis**

MEDIUM-SMALL-SIZED VESSELS

- **Polyarteritis nodosa**
- **Kawasaki's disease**
- **Churg-Strauss syndrome**
- **Wegener's granulematosis**

SMALL-SIZED VESSELS

- **Schonlein-Henoch syndrome**
- **Cryoglobulinemia**
- **Goodpasture's (anti-GBM) disease**
- **Immune complex vasculitis (SLE, Serum sickness)**
- **Microscopic polyangiitis**

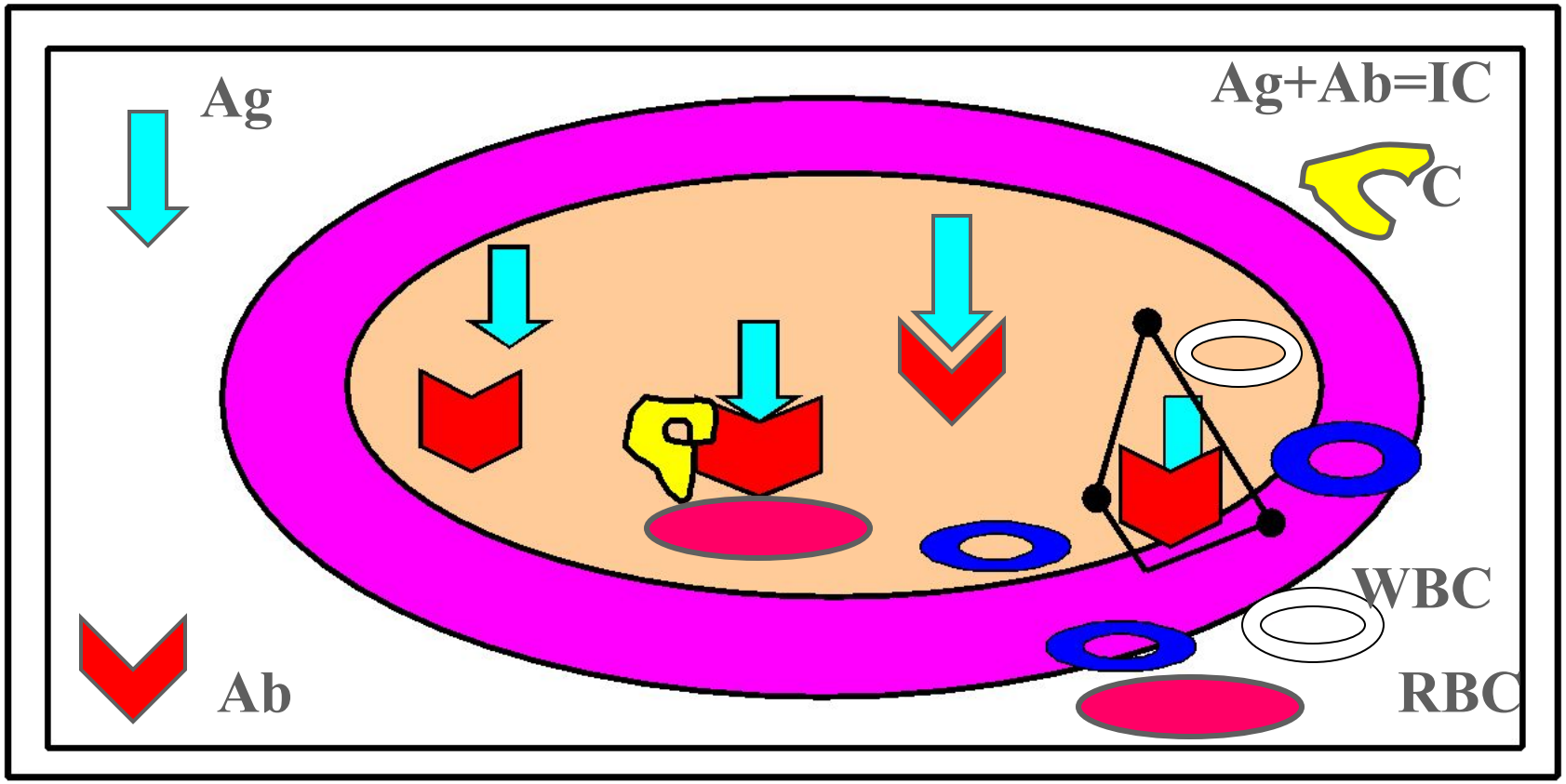
VASCULITIS
CLASSIFICATION

MISCELLANEOUS SYNDROMES

- **Behcet's syndrome**
- **Pyoderma gangrenosum**

VASCULITIS

Pathogenesis - Immune complexes formation



B-cell activation

Vasculitis with IC

- Serum sickness
- CTD
  - SLE
- PAN
  - Virus hepatitis B in IC
- Cryoglobulinemic vasculitis
  - Hepatitis C related IC in cryoprecipitates

Vasculitis with IC

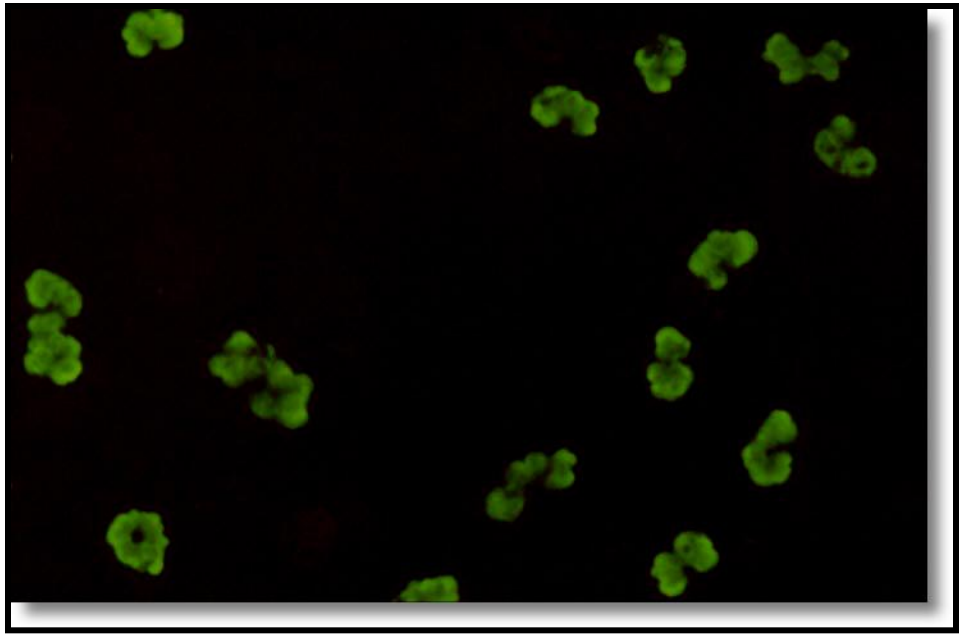
- Antigen excess
- IC formation
- Increased permeability of blood vessels
  - PLT & MC: histamine, bradykinin, leukotriens
- Activation of complement
  - C5a – chemotaxis of PMNC
  - Degranulation of PMNC
- Compromised blood flow
  - Tissue ischemia

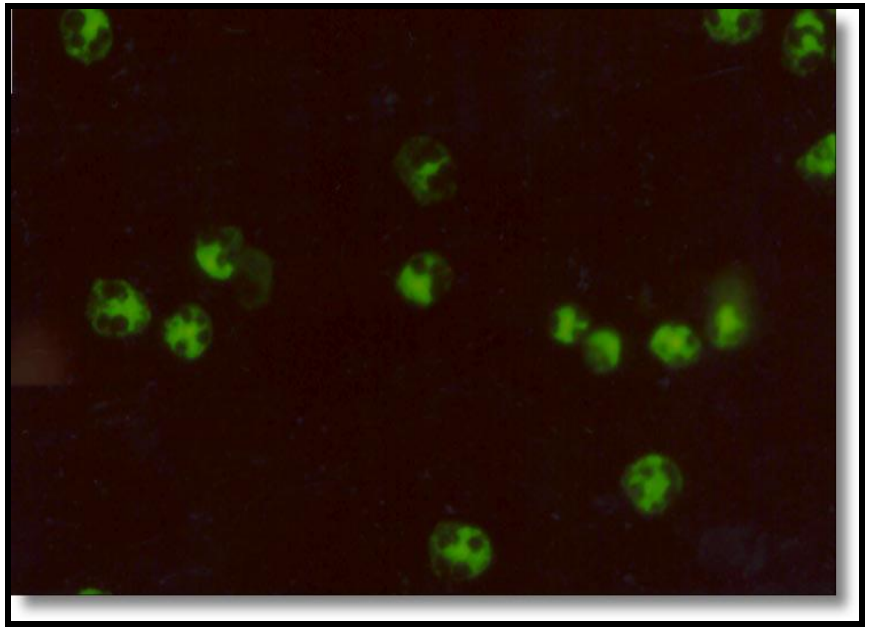
Vasculitis with IC depositions

- Henoch-Schonlein purpura
- CVD
- Serum sickness
- HCV related mixed cryoglobulinemia
- HBV related PAN

VASCULITIS

Pathogenesis - Anti-neutrophilic cytoplasmic Ab





pANCA – myeloperoxidase

cANCA-proteinase 3

ANCA related

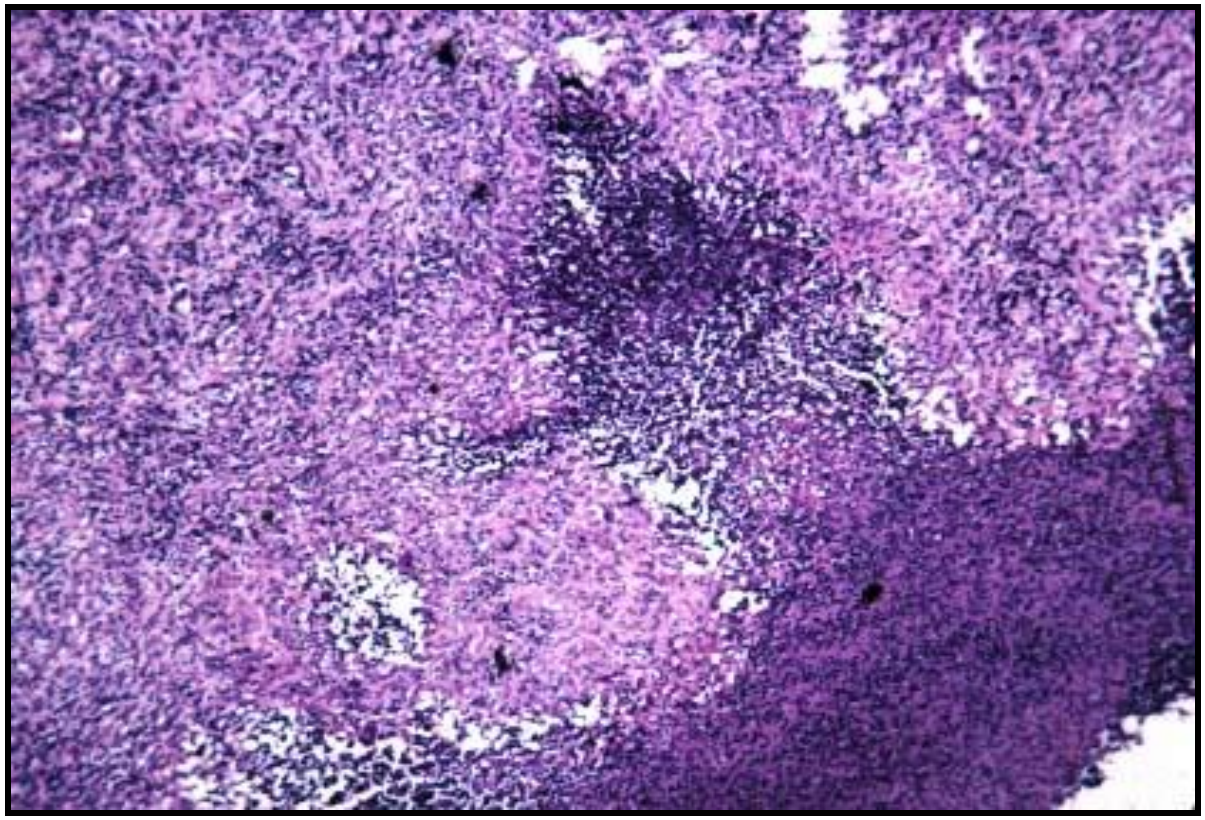
- Wegener’s granulomatosis
- Churg-Strauss syndrome
- Microscopic polyangiitis
- Necrotizing & crescentic GN
- Goodpasture’s syndrome
- Crohn’s disease , others IBD

ANCA associated vasculitis

- TNFα, IL-1 induce translocation of azurophilic granules to membrane of monocytes and PMNC
- Myeloperoxidase or proteinase 3 interact with extracellular ANCA
- Monocytes and PMNC degranulate and release ROS, IL-1, IL-8
- Tissue damage
- *No correlation between cANCA and WG activity*

VASCULITIS

with granuloma formation



T lymphocyte accumulation

VASCULITIS

with granuloma formation

- Ag or IC induce delayed hypersensitivity and cell mediated injury
- EC activation
  - INF, IL-1
  - T-ly activation
    - TNF
    - IL-1
      - Adhesion molecules formation
        - » ELAM-1
        - » VCAM-1

T-ly response and granuloma formation

- GCA
- Takayasu-s
- Wegener’s granulomatosis
- Churg-Strauss syndrome

Suspicion of vasculitis

- Systemic ilness
- Purpura
- Pulmonary infiltrates
- Microhematuria
- Chronic sinusitis
- Mononeuritis multiplex
- Unexplaned ischemia
- GN

DD vasculitis

- Infection
- Neoplasia
- Lymphoma
- Coagulopathy
- Drugs/toxins
- Others

Takayasu's Arteritis
Pulse-less disease

Incidence: 1-3/1 000 000/year.

Epidemiology: girls+young women

Japan, India, Africa, Asia, South America, Europe, US.

F:M=7:1. Age 10-50years (90% <30y)

Pathology: Involves aortic arch, descending aorta and its branches + AV involvement, coronary and pulmonary arteries

Panarteritis with *granuloma (mononuclears)* narrowed vessels and *thrombus* formation

Takayasu's Arteritis

General: malaise, fever, night sweats, weight loss, arthralgia/arthritis

Vascular:

- Arm claudication/numbness
- Pulses changes/discrepancy
- Hypertension
- Renal failure
- Aortic regurgitation (AR)
- Pulmonary hypertension

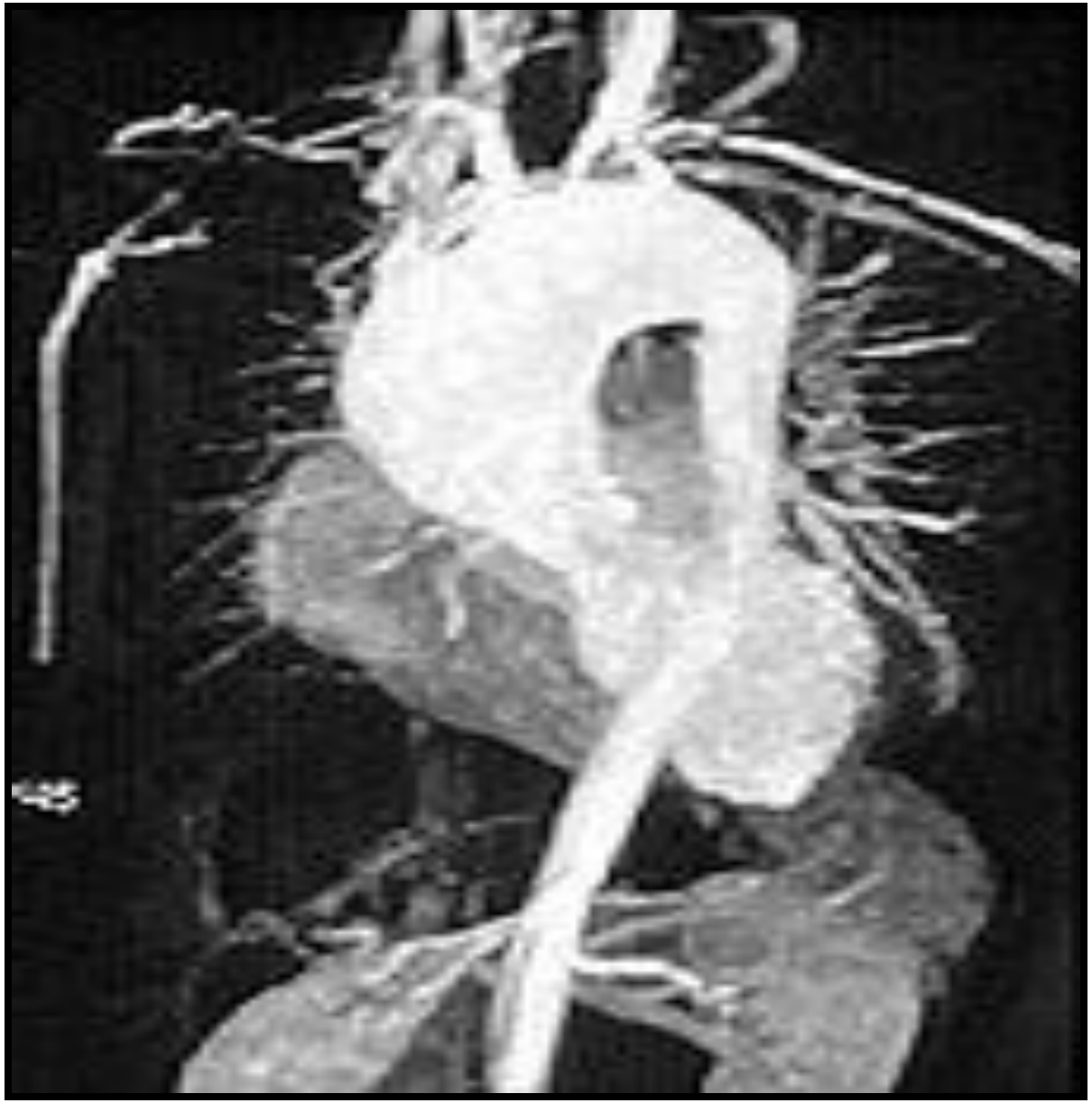
Laboratory: anemia, ESR/CRP elevation

Diagnosis: angiography, MRI angiography

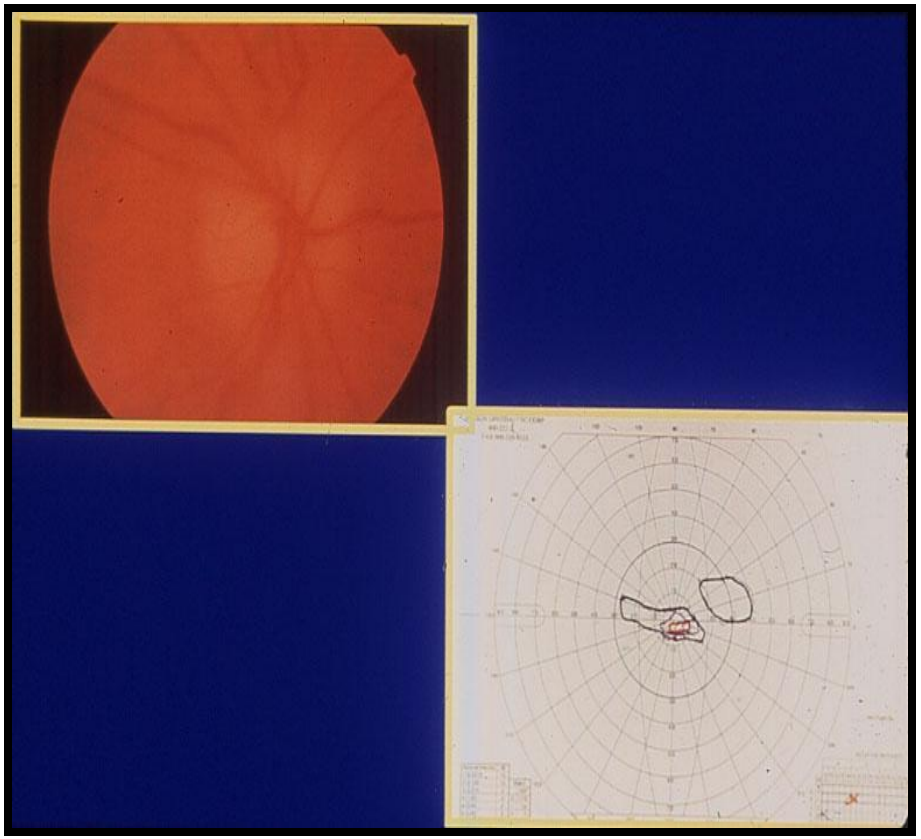
Treatment: steroids, cytotoxic drugs, control of hypertension, arterial reconstruction, AVR

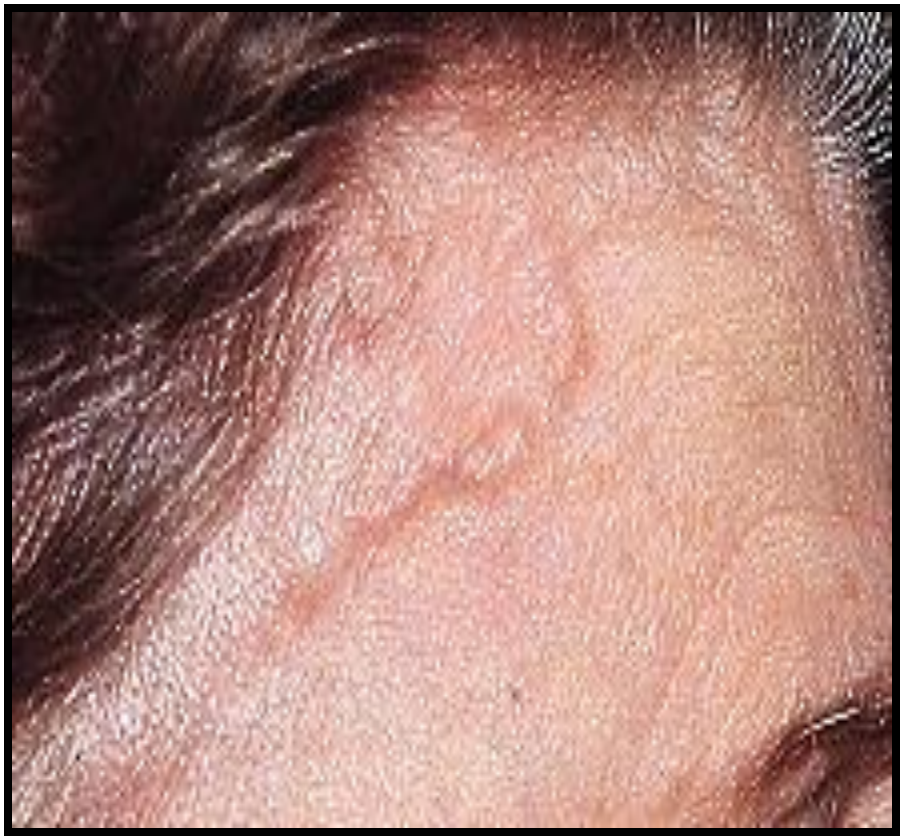
Prognosis: 15 year survival 90%

Takayasu's Arteritis



Giant Cell Arteritis/ Temporal arteritis





GCA

- Medial and large vessels vasculitis
  - Branches of carotid artery
  - Temporal arteries
- Strong association with PMR (50%)
  - Morning stiffness
  - Shoulder's and pelvic pain
- Isolated PMR is associated with GCA in 20%

GCA/PMR

- Age >50
- F>>M
- Rare in blacks
- 6-30/100000
- HLA DR4, HLA DRB1
- IL-2, INF
- CD4+
- Panarteritis with mononuclear cells accumulation and giant cells, intimal proliferation
- Ischemia of tissues

GCA

- **Fever**
- **Headache**
- **General signs**
- **PMR**
- **Scalp tenderness**
- **Jaw claudication**
- **Ischemic optic neuropathy, visual loss**
- **Visceral ischemia, strokes**
- **Aortic aneurisms, dissection**
- **Anemia**
- **High ESR**
- **Liver enzymes elevation**

GCA

- Diagnosis
  - US Doppler
  - TA biopsy
    - 14 days
- Treatment
  - Cs (40-60 mg/d ~1 months)
  - Aspirin
  - MTX
- Follow up: ESR

PMR

- Diagnosis
  - Shoulder and hip pain
  - Stiffness
  - High ESR
  - Absence of signs GCA
- Treatment
  - Cs (20mg/d)

Polyarteritis Nodosa (PAN)

Incidence: 5-9 to 80/1 000 000

Epidemiology: M:F=2-3:1, young patients

Pathology: *fibrinoid necrosis medium/small arteries*, *aneurysms formation*, mononuclear cells and PMNC infiltration, lumen thrombosis, obliteration of the lumen, sparing of pulmonary arteries. Segmental lesions

In kidney – arteritis without GN

Primary or secondary (RA, Sjogren's syndrome, SLE, *Hepatitis B, Hepatitis C, HIV, FMF, hairy cell leukemia*)

Polyarteritis Nodosa

Clinical features:

General: severe disease, weight loss, mild to high fever, malaise

Musculo-skeletal (64%): arthralgia, asymmetric polyarthritis, myalgia

Skin (43|%): palpable purpura, ulceration, ischemic necrosis

Neural (50%): peripheral neuropathy, mononeuritis multiplex, CVA

Polyarteritis Nodosa

GIT: abdominal pain, mesenteric thrombosis, peritonitis, bleeding

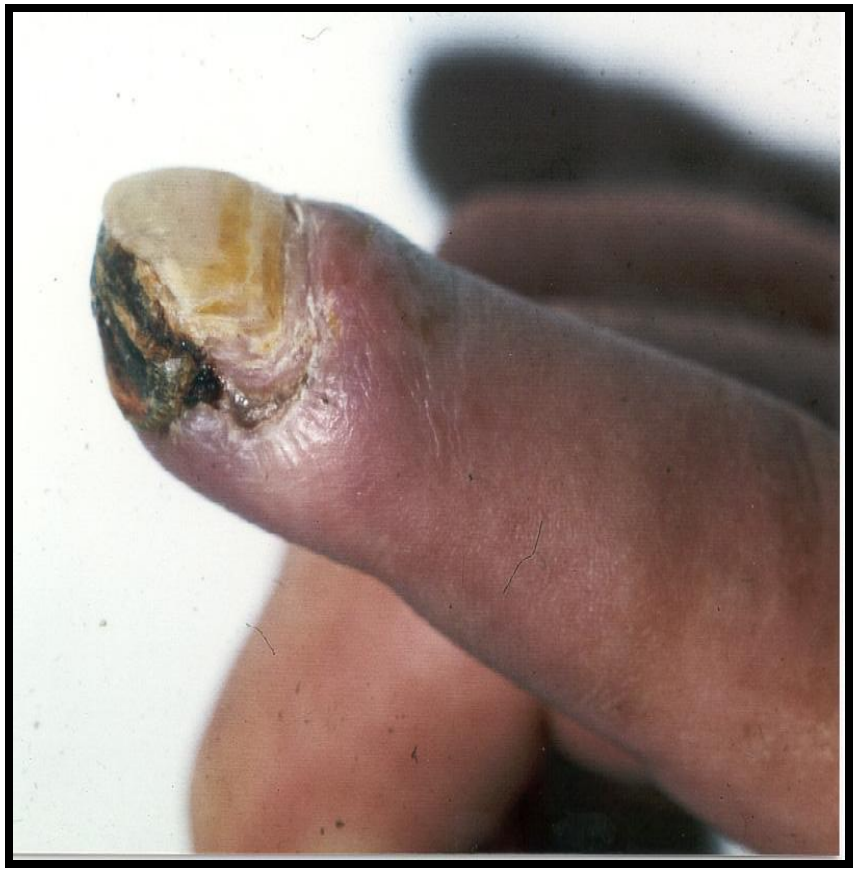
Kidney (60%): hypertension, renal failure, proteinuria, hematuria – not glomerulonephritis, hemorrhage from microaneurisms

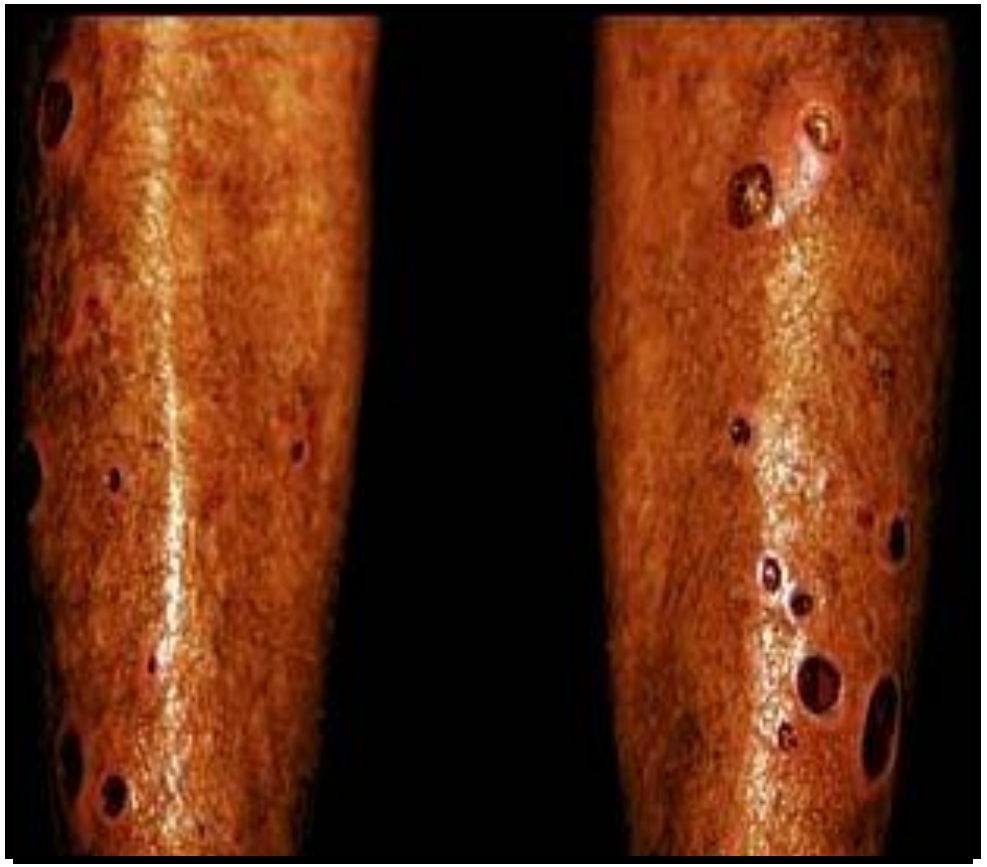
Cardiac (36%): CHF, MI

Eyes: retinal detachment, scleritis

Genito-urinary (25%): testicular, ovarian pain

PAN





Ischemic ulcers

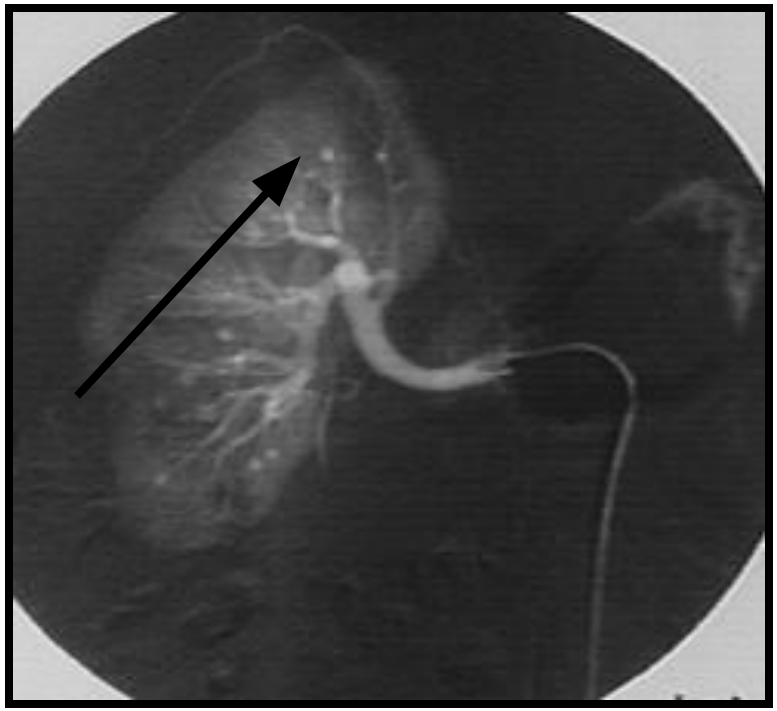
PAN

Laboratory data: ESR↑, anemia, globulins↑,

***30% HBS Ag+, aHCV+,* 20-30% pANCA+ ,**
abnormal urine

Diagnosis:

biopsy, angiography



Aneurysms formation

PAN

Prognosis: 5 year survival 15%-80%

Treatment:

***Hepatitis neg*: Steroids, Cyclophosphamide, Imuran, Methotrexate**

***Hepatitis pos*: Antiviral treatment (Interferon, plasmapheresis, Ribaverin), Cs, plasma exchange**

Relapse in 10%

Microscopic polyangiitis

- Necrotizing vasculitis of small vessels
- M>F, >55y
- GN (80%)
- Pulmonary capillaritis (12%) – hemorrhage
- Cardiac and GIT involvement
- Vascular lesions are similar to PAN, but in kidney – typical GN
- ESR, anemia, leukocytosis, thrombocytosis, abnormal urine, pANCA pos+++
- Diagnosis: kidney biopsy (pauci-immune GN)
- Treatment: Cs, CYC
- Relapse in 34%

Churg-Strauss Syndrome

Incidence: 1-2/1 000 000

Epidemiology: M:F=2:1

Pathology:

- ***allergic necrotizing angiitis*, *eosinophils infiltration*, extra-vascular *granuloma* formation**
- **Small and medium sized vessels**

Churg-Strauss Syndrome

Prodromal period: bronchial asthma

Second phase:

- **eosinophilia**
- **Lóffler s-me - eosinophilic pneumonia**
- **eosinophilic gastroenteritis**

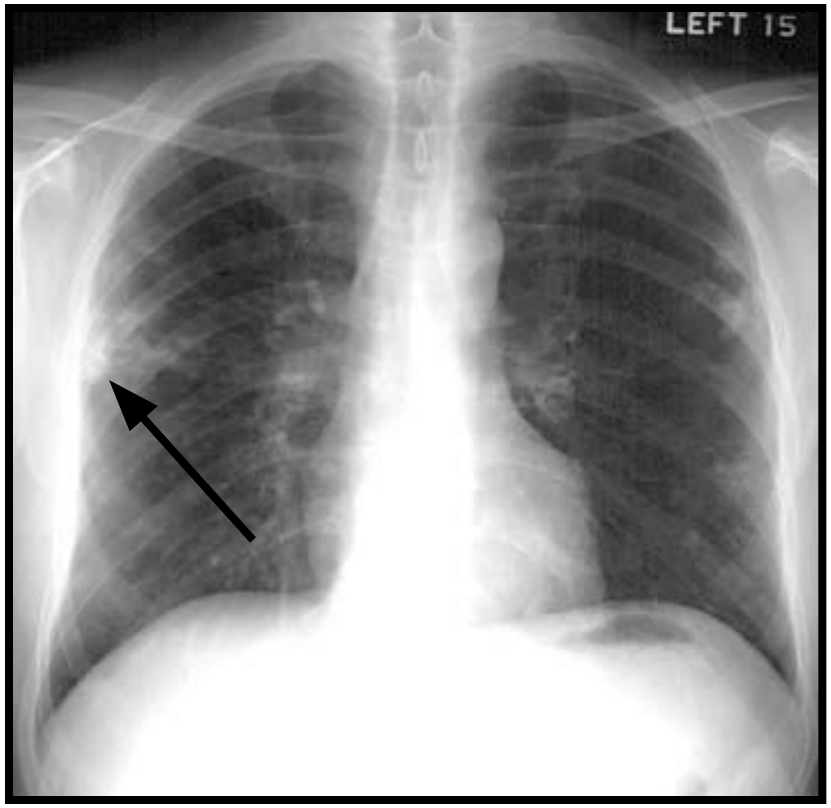
Third phase: systemic vasculitis

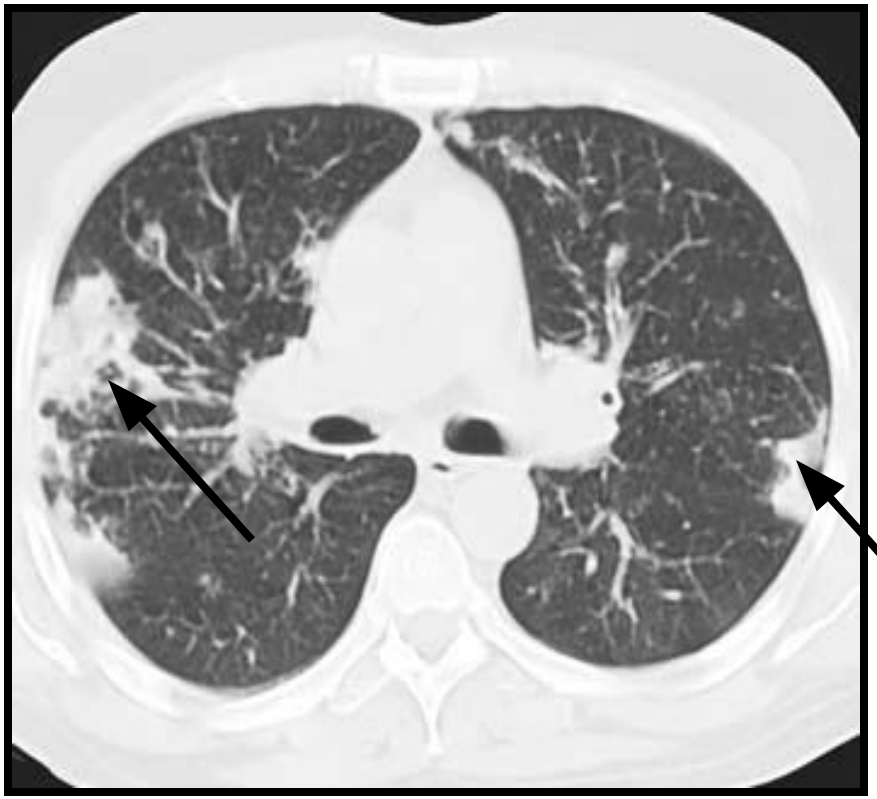
Churg-Strauss Syndrome

Clinical features:

- **General signs: fever, malaise, weight loss**
- **Lung involvement: asthma, lung infiltrates, allergic rhinitis and sinusitis**
- **GIT involvement: abdominal pain, diarrhea, bleeding**
- **NS involvement: mononeuritis multiplex**
- **Heart disease**
- **Kidney involvement: GN**
- **Skin: purpura**
- **Arthritis**

Churg-Strauss Syndrome





Peripheral lung infiltrates

Churg-Strauss Syndrome

Laboratory data: anemia, ESR ↑,

5 000-10 000 eosinophils/mm^3, IgE ↑, pANCA + (70%)

Diagnosis: biopsy

Prognosis: 5 years survival-65%

Treatment: Steroids, Cyclophosphamide, Imuran

Wegener's Granulomatosis

Incidence: 3/1 000 000

Epidemiology: M:F=1,2:1

Rare in blacks

Age >40 y

Pathology: ***necrotizing vasculitis of small arteies and veins, neutrophils accumulation and granuloma: upper airways (sinuses and nasopharyngs), lungs, kidney (pauci-immune GN no granuloma)***

INF, TNF, CD4+ ***(Th1 type)***

cANCA

Wegener's Granulomatosis

- **General signs: fever, malaise, weight loss**
- **Upper Respiratory Tract (95%): sinusitis, otitis media, nasal ulceration, septal perforation, subglottic stenosis**

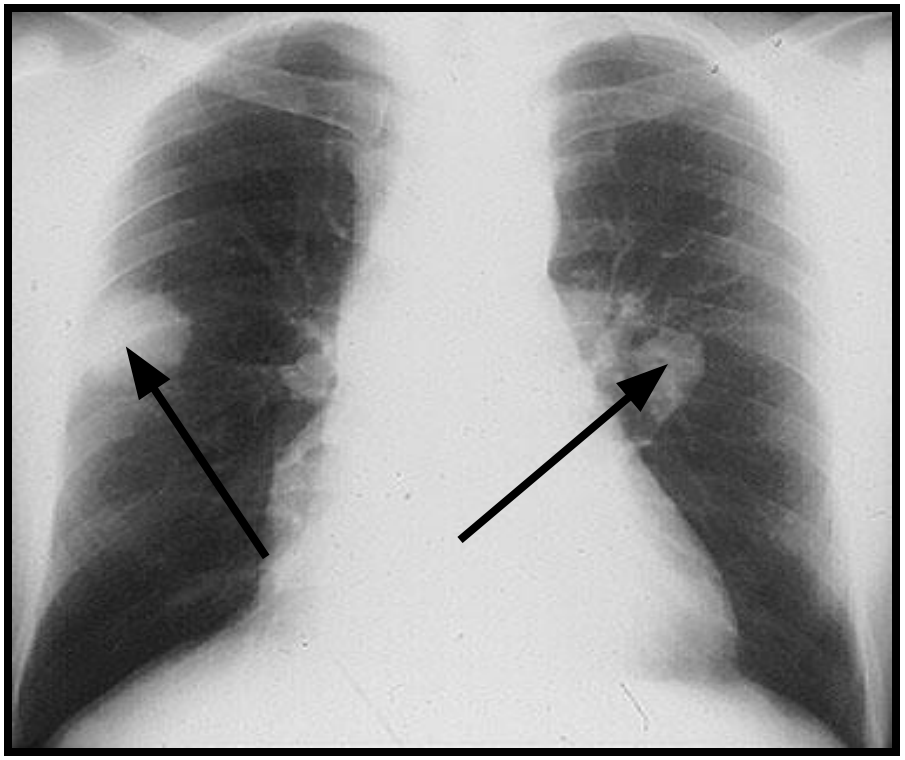
Often Staph aureus

- **Low Respiratory Tract (80%): Pulmonary infiltrates, nodules, cavities (cough, dyspnea, hemopthysis), bronchiectasia**
- **Kidney (75%): Glomerulonephritis, hypertension, renal failure**

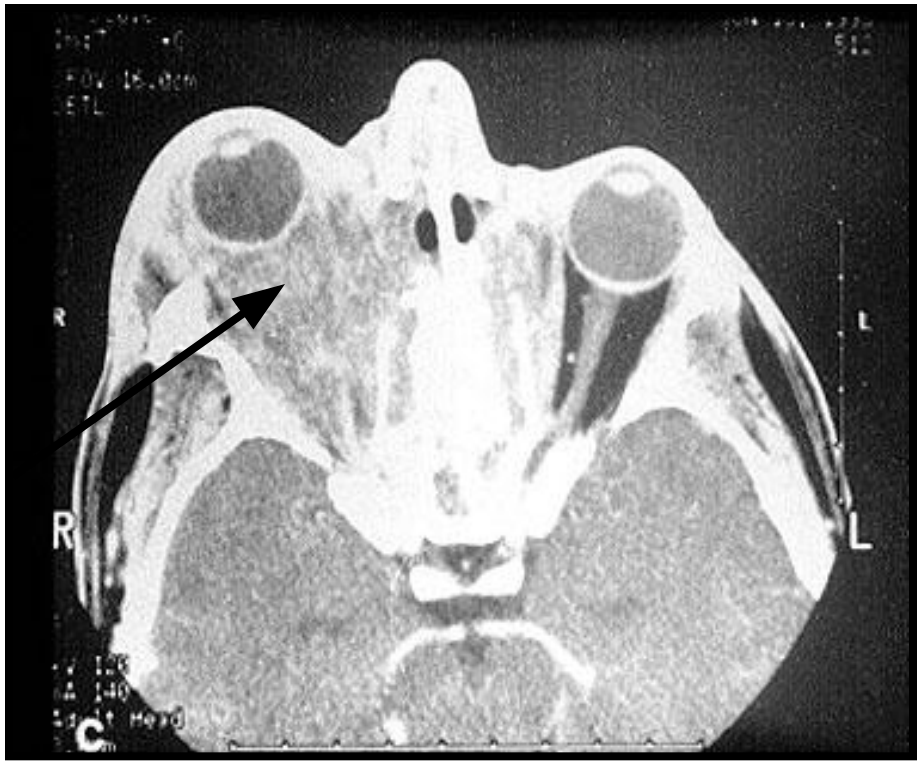
Wegener's Granulomatosis

- **Purpura (45%)→Necrotic ulcers**
- **Arthritis (50-70%)**
- **Eyes (52%): orbital/periorbital mass and damage, scleritis, vasculitis,**
- **NS: peripheral neuropathy, central (33%)**
- **Heart (8%): pericarditis, CHF, MI, arrhythmias**
- **DVT and PE more then in healthy**

Wegener's Granulomatosis



Pulmonary nodes
And cavitation



Orbital and nasal granuloma

Wegener's Granulomatosis

Laboratory data: leukocytosis, anemia, ESR↑, cANCA + (90%), abnormal urine, RF+, thrombocytosis

Diagnosis: nasal biopsy (granuloma), open lung biopsy (granuloma and vasculitis)

Renal biopsy is not specific

Wegener's Granulomatosis

Prognosis: 5 years survival - 50-75%

- **Progressive renal failure**
- **Late organ damage**
- **Co-morbidities**
- **Cancer (bladder)**

Follow up: clinically, ANCA???

Treatment: CYC (oral/IV) and Cs, Imuran, MTX, MMF, Trimethoprim Sulfamethoxazole (Resprim)

Biological (RTX+, ETN-)

Henoch-Schőnlein Purpura

Incidence: 4-10/100 000

Epidemiology: M:F=1,2:1, age 4-14 years

Pathogenesis: IC vasculitis (Drugs? Infections?)

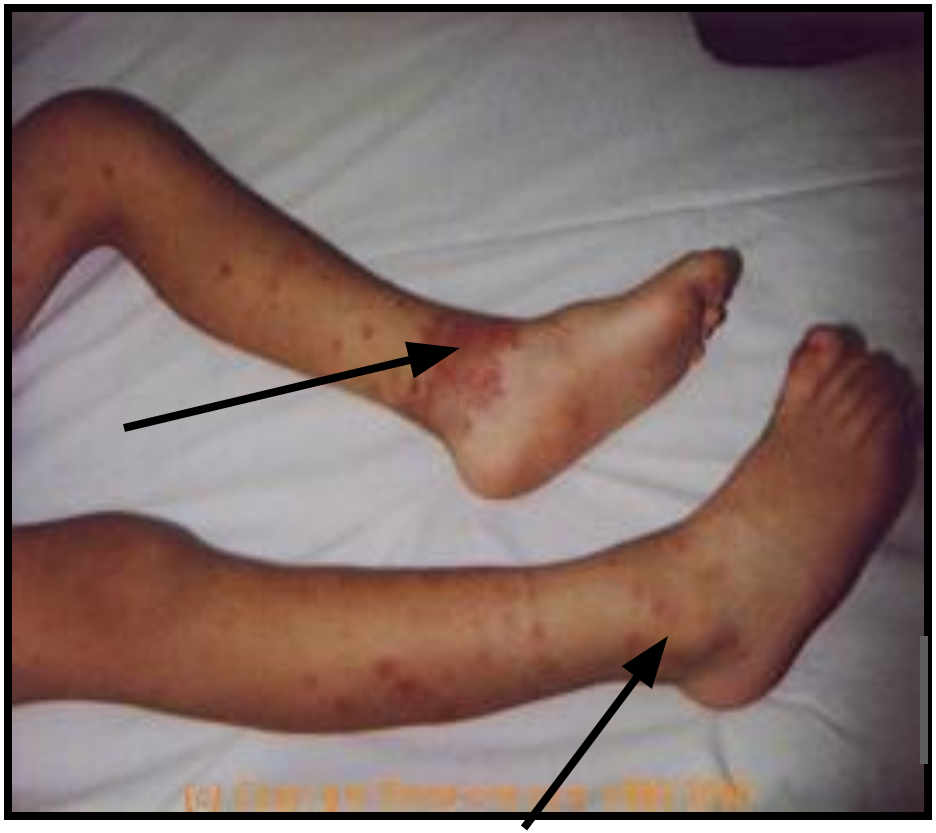
Pathology: small vessels *necrotizing leukocytoclastic vasculitis, fibrinoid necrosis, IC, IgA and C3 deposition (*skin, gut, kidney [glomerrular& tubular]), MNC infiltration

Henoch-Schőnlein Purpura

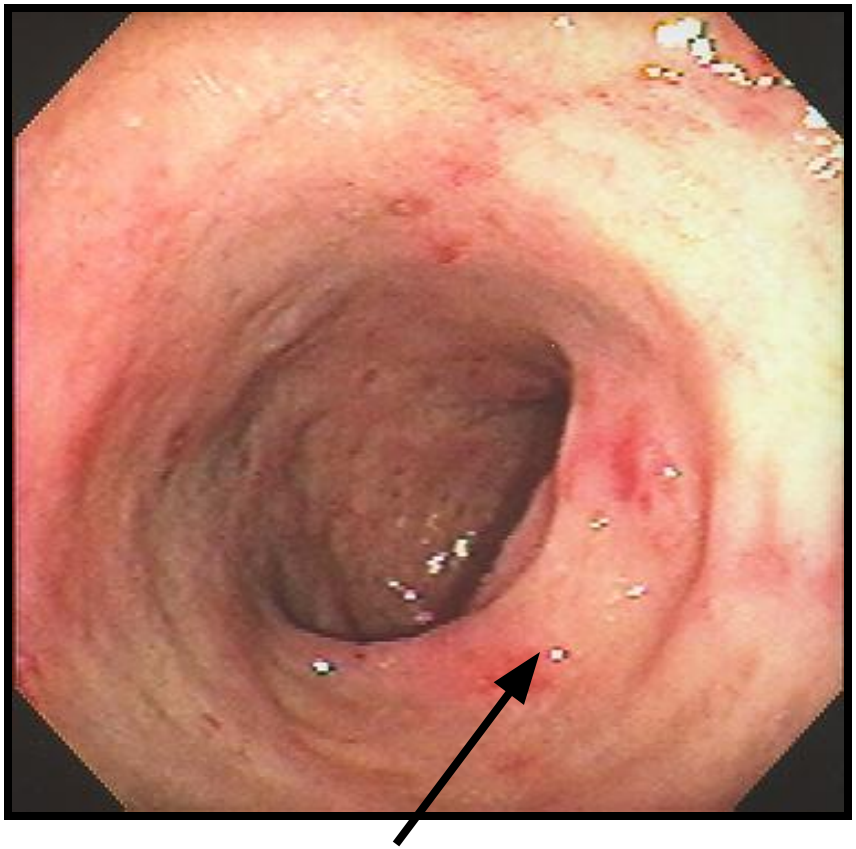
Clinical features:

- **General signs**
- **Skin: palpable purpura (100%), ulceration (rare)**
- **Arthritis, arthralgia (60%)**
- **GIT vasculitis (85%) abd. pain, diarrhea, bleeding**
- **Renal (IgA nephropathy) disease (10-40%) – segmental proliferative GN +/- crescents, IgA + C_3 deposition (Berger's disease) – hematuria, proteinuria**

Henoch-Schőnlein Purpura



Purpura, Arthritis



Ischemic colitis

Henoch-Schőnlein Purpura

<u>Laboratory data:</u> elevated ESR/CRP, leukocytosis, mild anemia, hematuria, high IgA

<u>Diagnosis</u>: clinical +/- biopsy

<u>Prognosis:</u> good *(except severe GIT vasculitis and IgA nephropathy)*

<u>Treatment</u>: rest, tratement of underlying disease, NSAID, Cs, CYC – only in severe internal organ involvement

Essential Mixed Cryoglobulinemia

- Cryo – cold-precipitable Ig (mono/polyclonal)
- Systemic signs
- Primary - rare
- Secondary in most cases

Cryoglobulinemic Vasculitis

Myeloma **Waldenström d-se** **Lymphoma**	**:Collagen disease** ***RA, SLE, SS, DM*** **Infections** ***SBE, Strept GN***	**<u>Hepatitis C</u>**

:<u>Biopsy</u>

<u>Skin:</u> Inflammatory infiltrate involving small blood vessels, fibrinoid necrosis, EC hyperplasia, hemorrhage, Ig and IC deposition

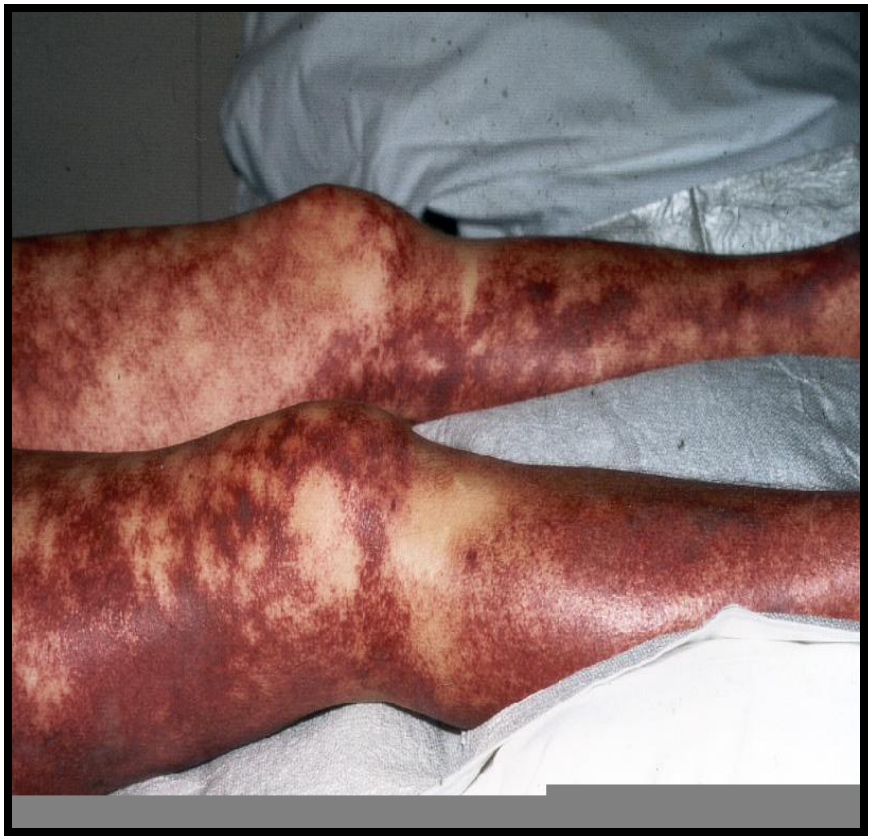
<u>Kidney</u>: Membranous GN

++<u>Hepatitis C</u> specific Ig, monoclonal IgM RF

ESR++, anemia, CRF, low C3/C4, HCV RNA+++, high IgM

Cryoglobulinemic Vasculitis

- **Hyperviscosity problems:**
  - **visual problems**
  - **TIA**
  - **neuropathy**
- **Vasculitis:**
  - **purpura**
  - **arthritis**
  - **kidney involvement**
    - **glomerulonephritis**
    - **progressive renal failure**
    - **nephrotic syndrome**



Cryoglobulinemic Vasculitis

<u>Prognosis:</u> poor, depends on viremia

<u>Treatment</u>:

plasmapheresis,

antiviral therapy (Ribaverin + Interferon α)

Cs = CYC

Behcet's Disease

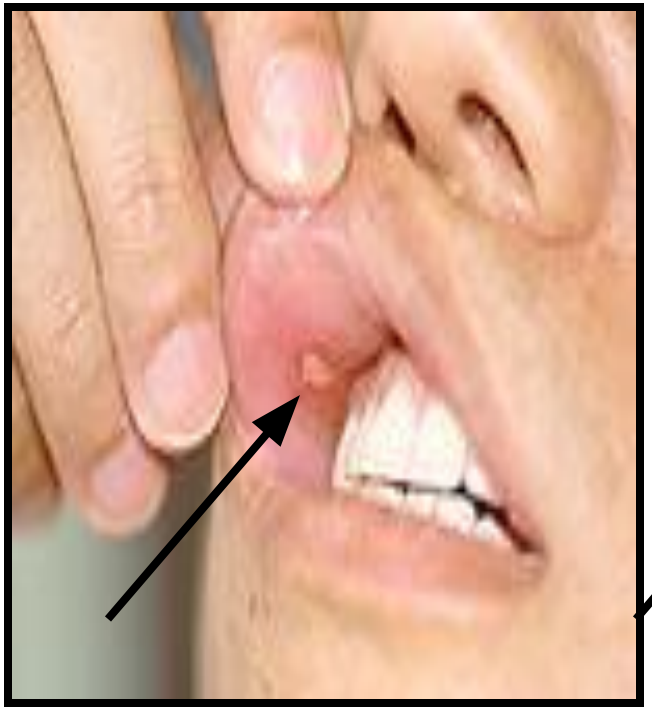
Epidemiology: Japan, Meddle East (Silk rood)

Family penetration

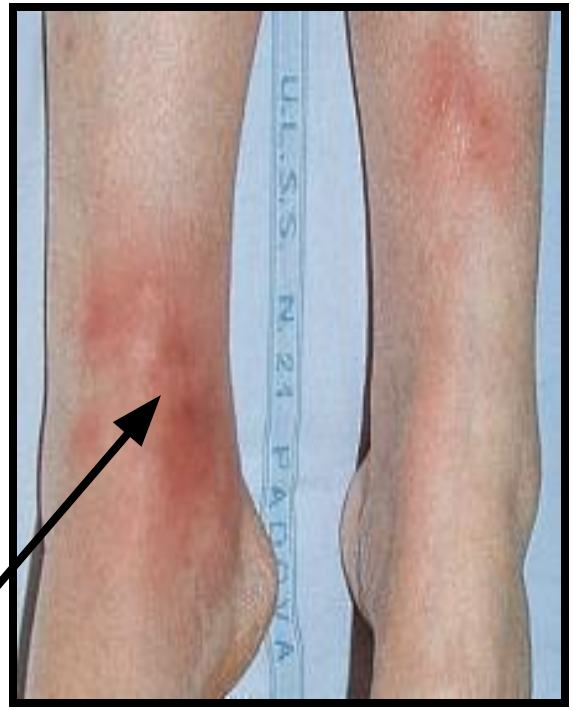
:Clinical feature

- **Oral aphthous ulcers (100%) – 3/year**
- **Genital ulcerations (80%)**
- **Eye inflammation (65%)-anterior/posterior uveitis, retinal vasculitis**
- **Skin inflammation (70%)-(folliculitis-like, acne-like, erythema nodosum-like)**
- **Vasculitis (arterial-CNS, venous – thrombosis superficial and deep)**

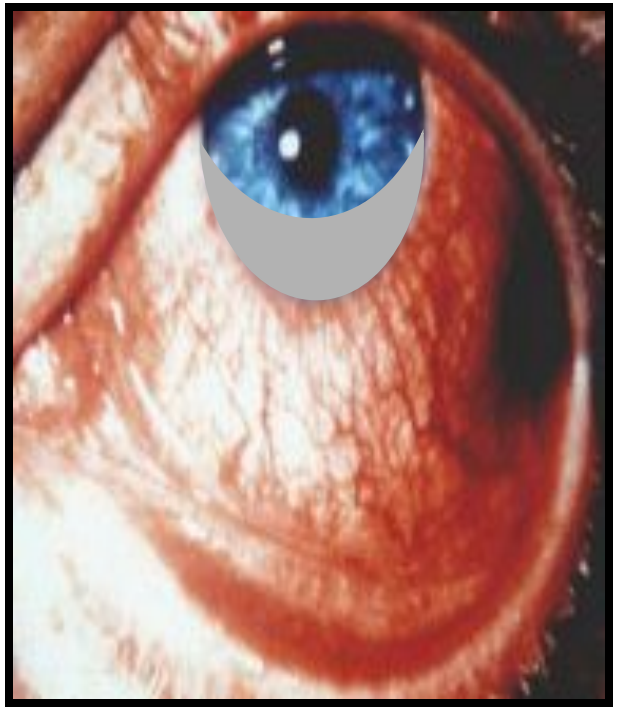
Behcet's Disease



Aphtha



Erythema nodosum



Hypopion

Behcet's Disease

.**Laboratory data: HLA B_{51} pos**

Pathergy skin test

Prognosis: serious in uveitis - blindness, CNS vasculitis, thrombosis

Treatment: Colchicine

CS +/- MTX, Imuran, Salazopyrine

CS +Neoral

Thalidomide

Anticoagulants

Pyoderma Gangrenosum
Neutrophilic Dermatosis

Inflammatory Bowel

:Diseases

Crohn's Disease

Ulcerative colitis

Myeloproliferative

:Diseases

Polycythemia Vera

Myeloma

Leukemias