

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 granulomatosis

SMALL-SIZED VESSELS

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

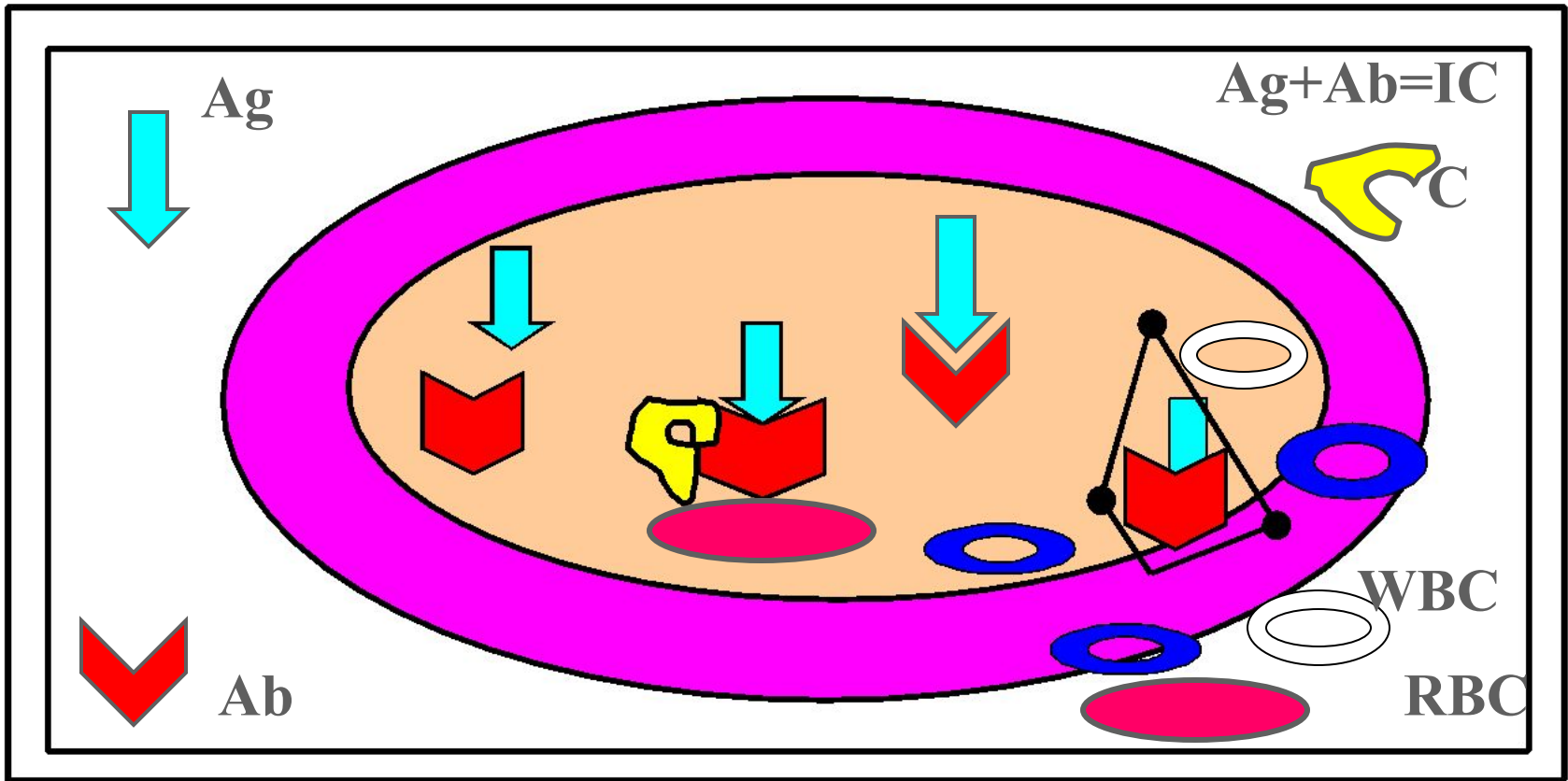
VASCULITIS CLASSIFICATION

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

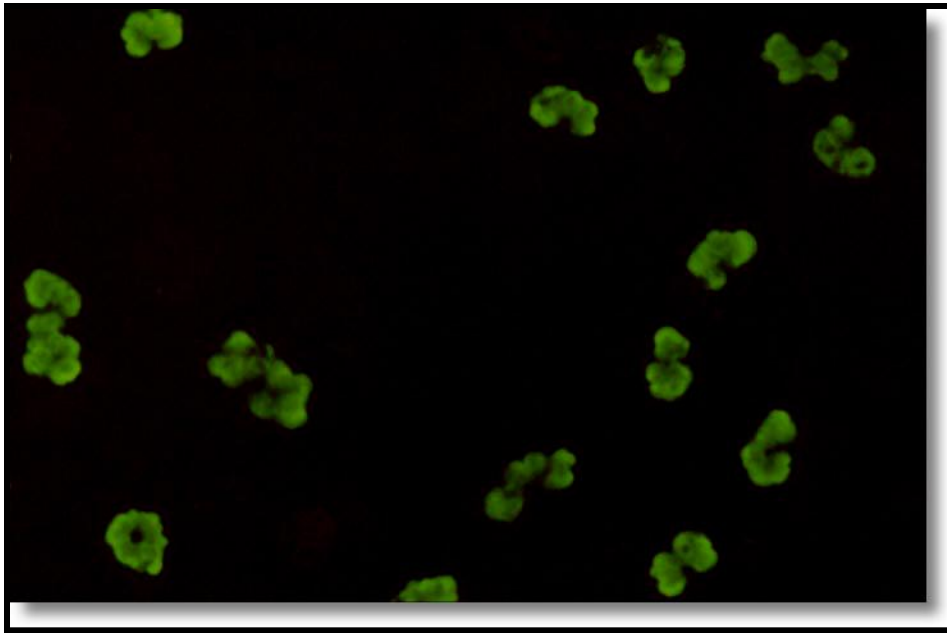
- Antigen excess
- IC formation
- Increased permeability of blood vessels
 - PLT & MC: histamine, bradykinin, leukotriens
- Activation of complement
 - C5a – chemotaxis of PMNC
 - Degranulation of PMNC
- Compromised blood flow
 - Tissue ischemia

Vasculitis with IC depositions

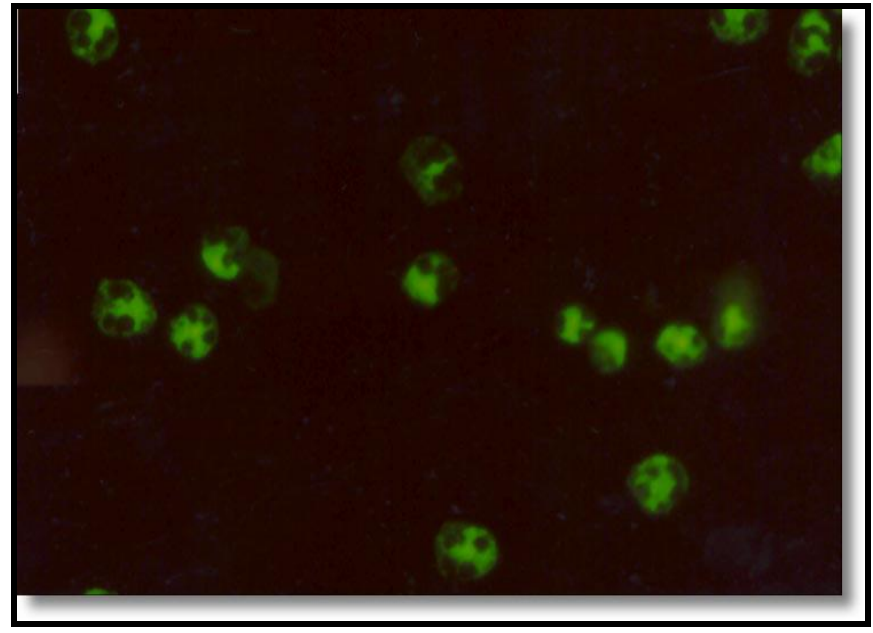
- Henoch-Schonlein purpura
- CVD
- Serum sickness
- HCV related mixed cryoglobulinemia
- HBV related PAN

VASCULITIS

Pathogenesis - Anti-neutrophilic cytoplasmic Ab



pANCA – myeloperoxidase



cANCA-proteinase 3

ANCA related

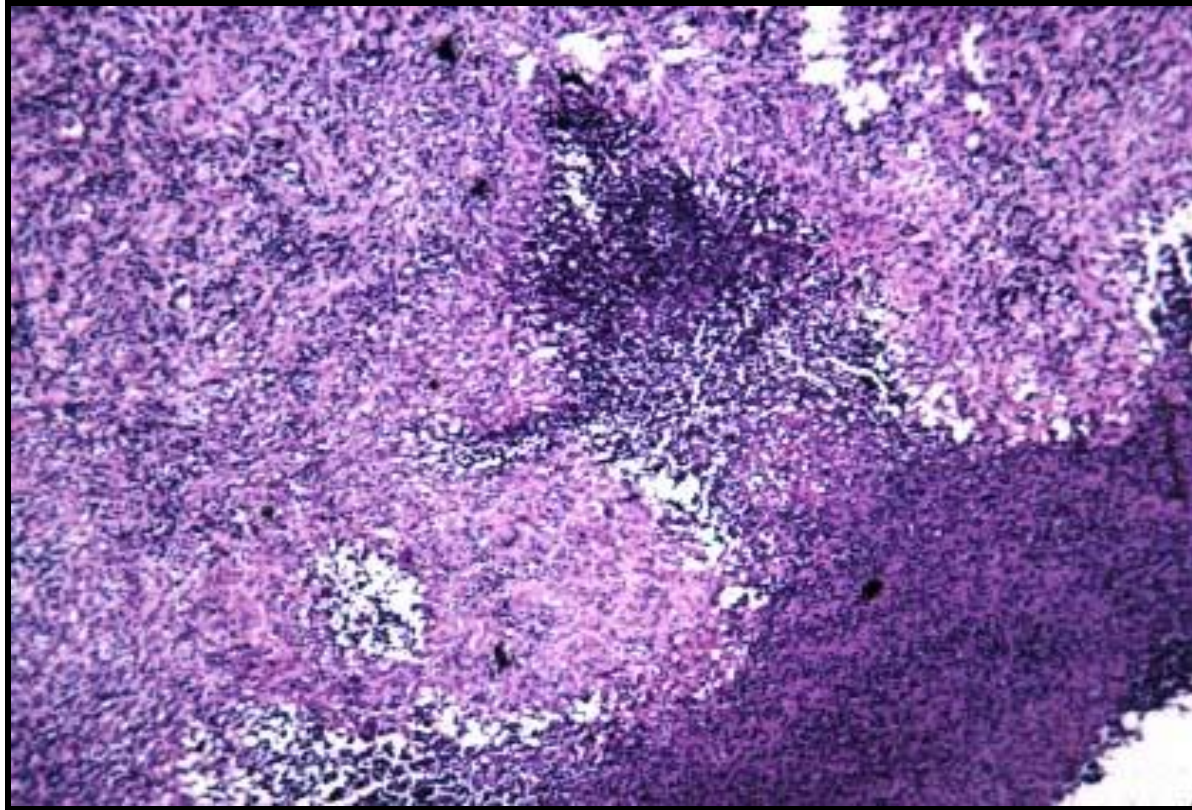
- Wegener's granulomatosis
- Churg-Strauss syndrome
- Microscopic polyangiitis
- Necrotizing & crescentic GN
- Goodpasture's syndrome
- Crohn's disease , others IBD

ANCA associated vasculitis

- $\text{TNF}\alpha$, 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 illness
- Purpura
- Pulmonary infiltrates
- Microhematuria
- Chronic sinusitis
- Mononeuritis multiplex
- Unexplained 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

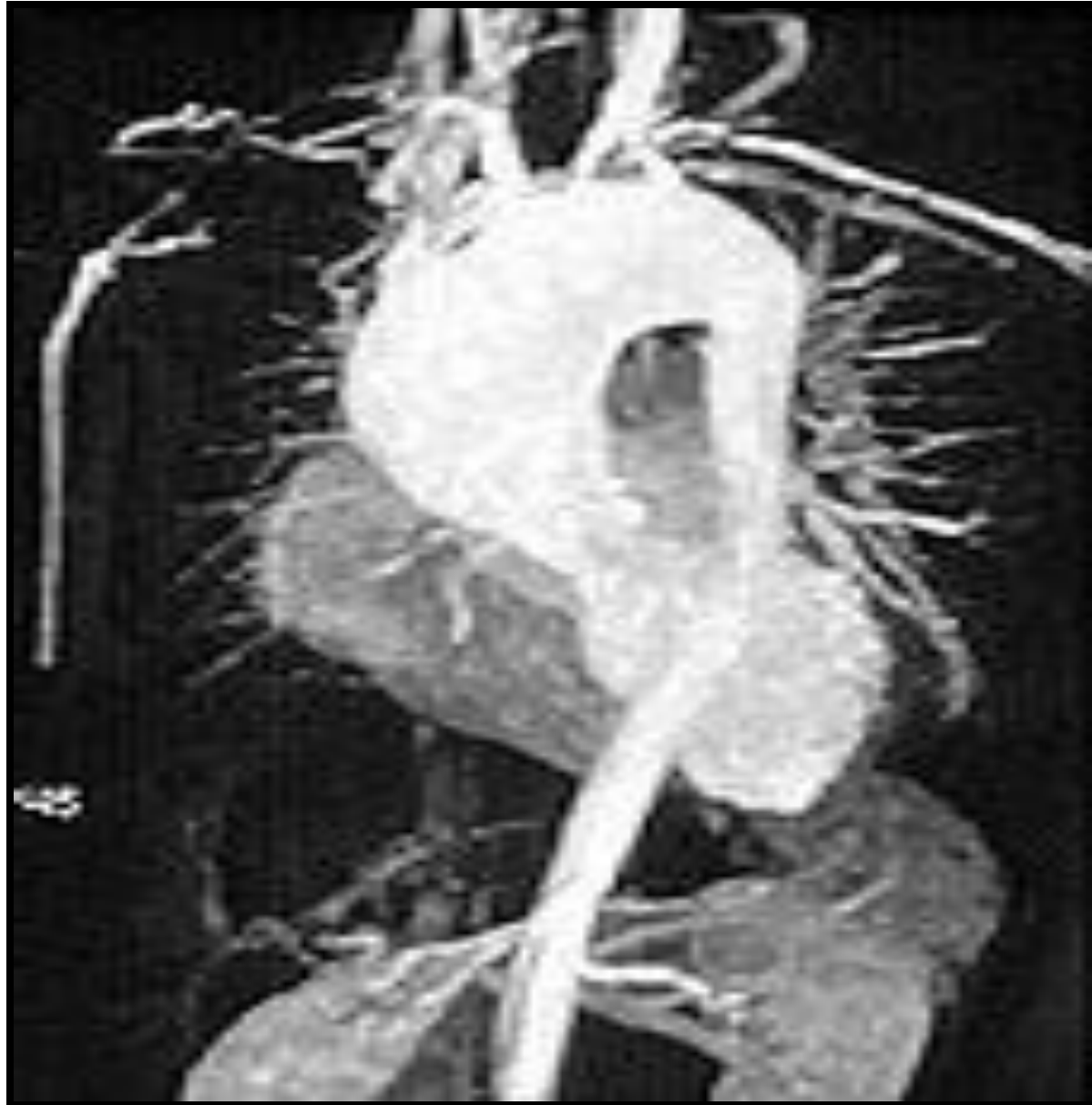
Laboratory: anemia, ESR/CRP elevation

Diagnosis: angiography, MRI angiography

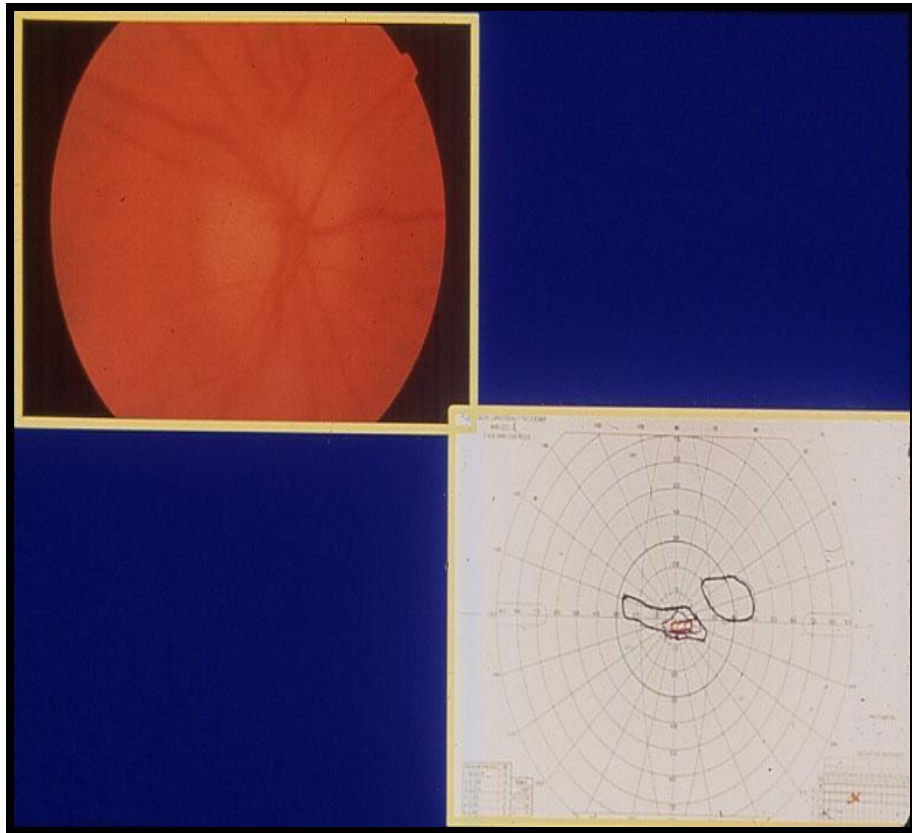
Treatment: steroids, cytotoxic drugs, control of hypertension, arterial reconstruction, AVR

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 polyarthritits, myalgia

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

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

Polyarteritis Nodosa

GIT: abdominal pain, mesenteric thrombosis, peritonitis, bleeding

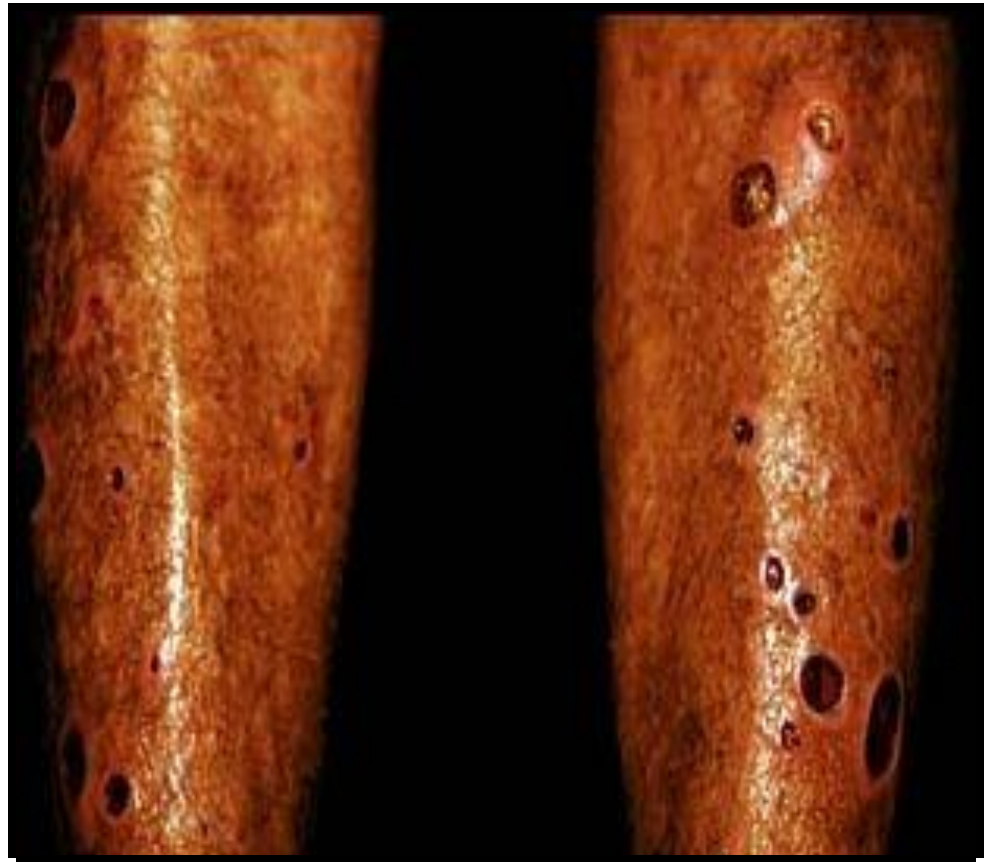
Kidney (60%): hypertension, renal failure, proteinuria, hematuria – not glomerulonephritis, hemorrhage from microaneurisms

Cardiac (36%): CHF, MI

Eyes: retinal detachment, scleritis

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

PAN



Ischemic ulcers

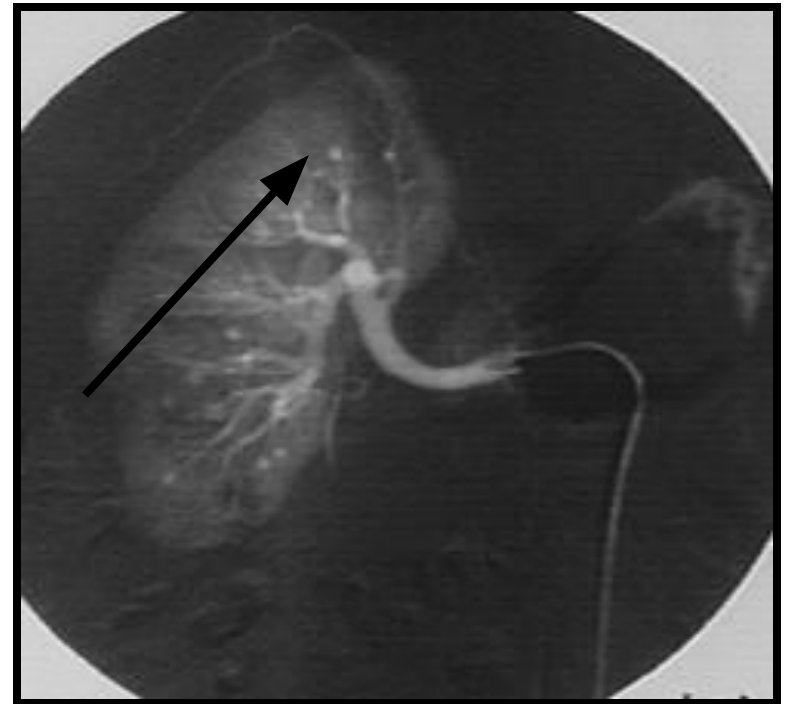
PAN

**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**
- **Löffler s-me - eosinophilic pneumonia**
- **eosinophilic gastroenteritis**

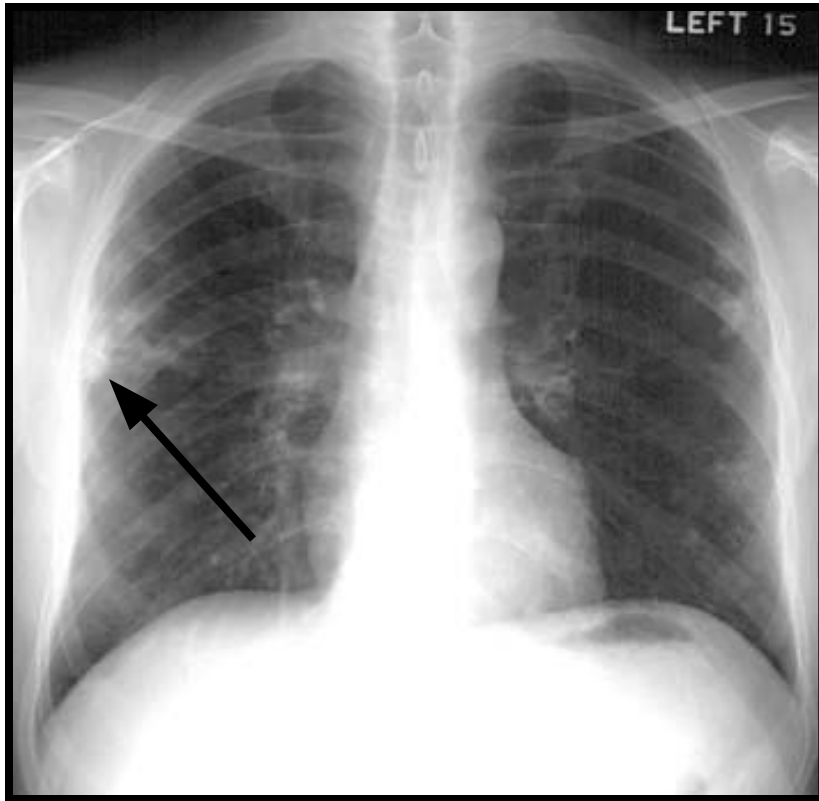
Third phase: systemic vasculitis

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/mm³, 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 arteries 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

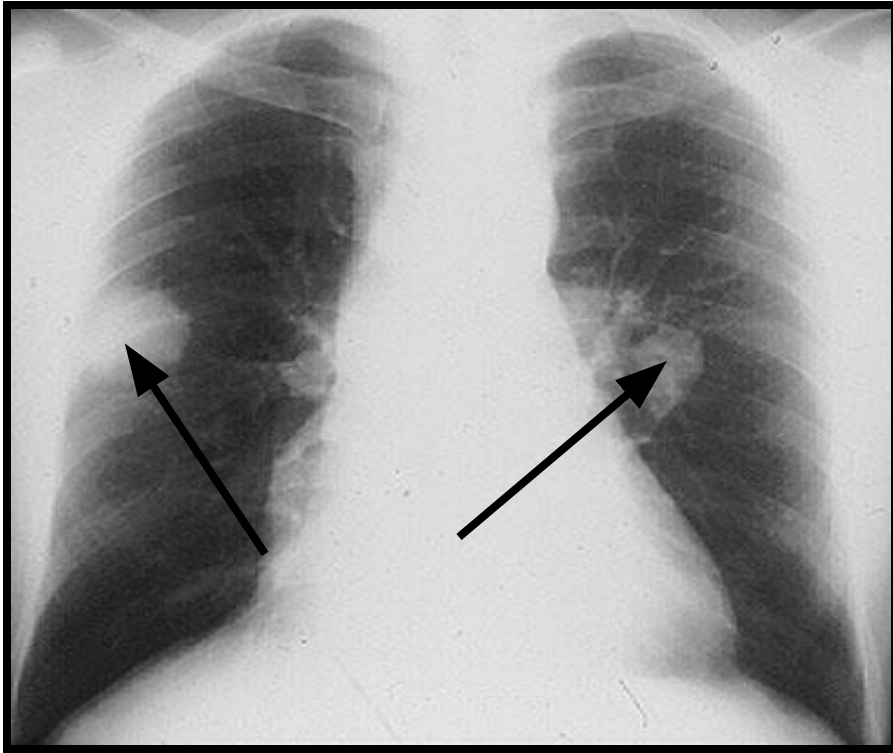
Often Staph aureus

- **Low Respiratory Tract (80%)**: Pulmonary infiltrates, nodules, cavities (cough, dyspnea, hemoptysis), 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 than 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-Schönlein 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 [glomerular & tubular]), MNC infiltration

Henoch-Schönlein Purpura

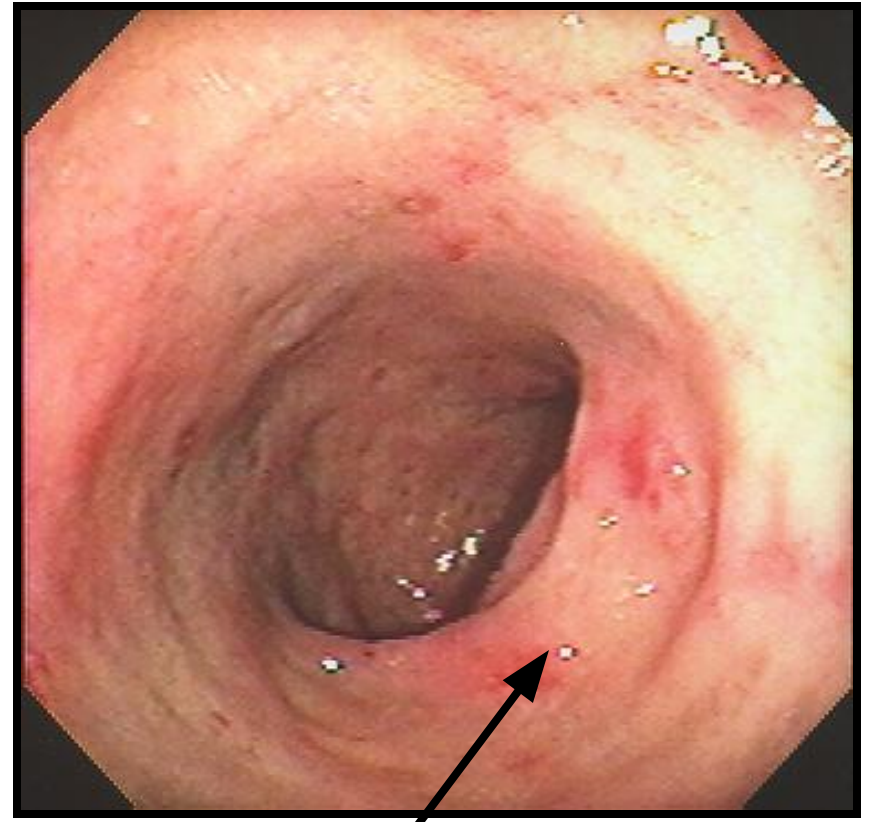
Clinical features:

- **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 + C₃ deposition (Berger's disease) – hematuria, proteinuria**

Henoch-Schönlein Purpura



Purpura, Arthritis



Ischemic colitis

Henoch-Schönlein Purpura

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

Diagnosis: clinical +/- biopsy

Prognosis: good (*except severe GIT vasculitis and IgA nephropathy*)

Treatment: rest, treatment 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 <i>RA, SLE, SS, DM</i> Infections <i>SBE, Strept GN</i>	<u>Hepatitis C</u>
--	--	---------------------------

:Biopsy

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

Kidney: Membranous GN

++Hepatitis C 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

Prognosis: poor, depends on viremia

Treatment:

plasmapheresis,

antiviral therapy (Ribavirin + Interferon α)

Cs = CYC

Behcet's Disease

Epidemiology: Japan, Meddle East (Silk road)

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)**

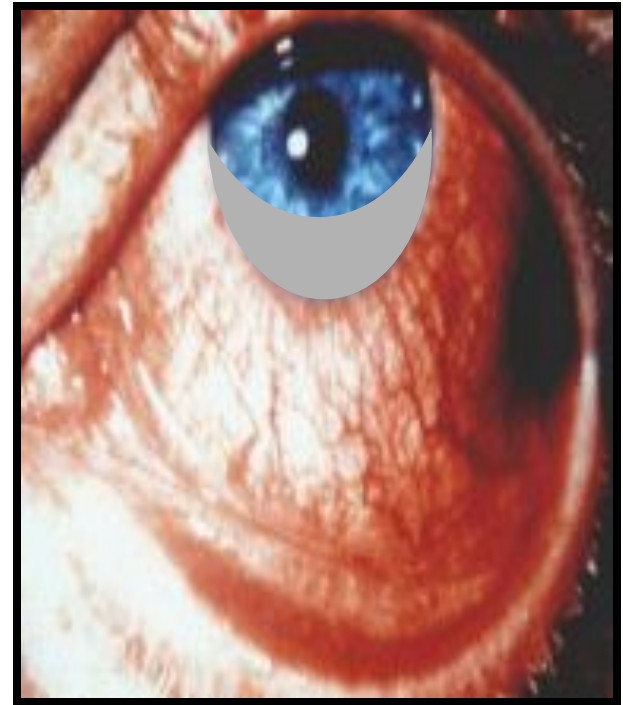
Behcet's Disease



Aphtha



Erythema nodosum



Hypopion

Behcet's Disease

Laboratory data: HLA B₅₁ 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 Dermatositis

Inflammatory Bowel

:Diseases

Crohn's Disease

Ulcerative colitis

Myeloproliferative

:Diseases

Polycythemia Vera

Myeloma

Leukemias

