Vasculitis

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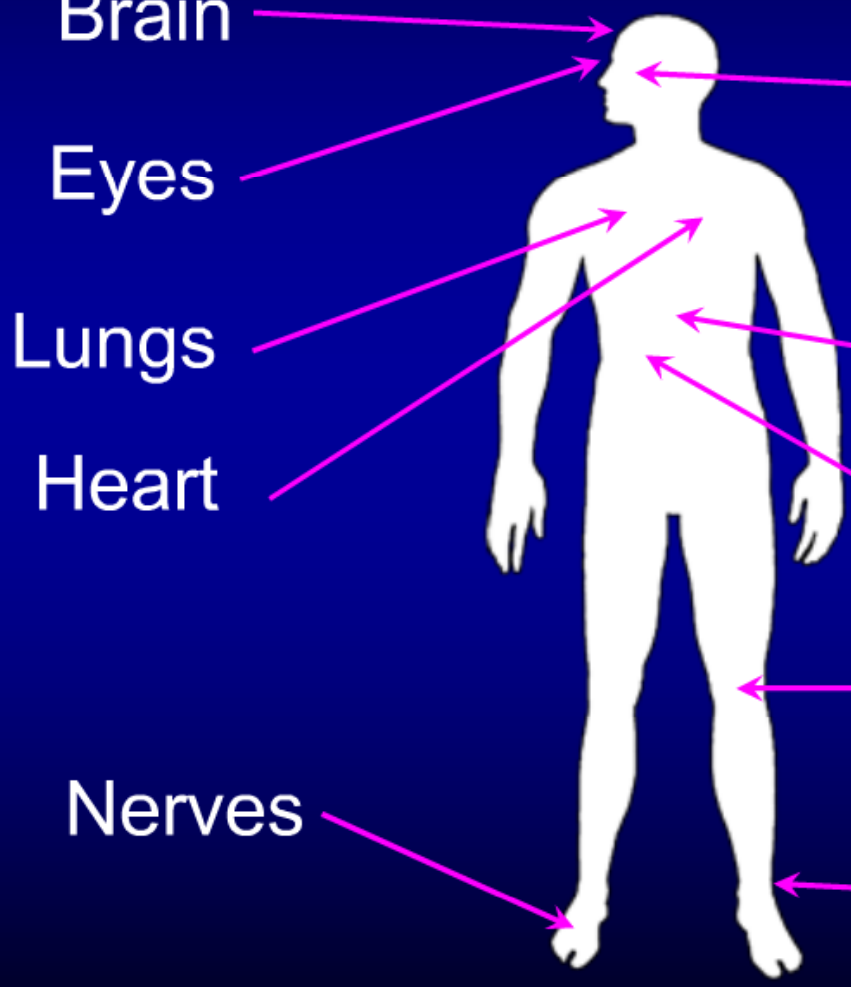
WAY TOO MUCH INFORMATION

- Vasculitis is a HUGE Topic
- Cannot be completely covered in a short period of time
- **Other References**: American Family Physician
  - **An Approach to Diagnosis and Initial Management of Systemic Vasculitis**
    - http://www.aafp.org/afp/991001ap/1421.html
  - **ANCA-Associated Small-Vessel Vasculitis**
    - http://www.aafp.org/afp/20020415/1615.html
  - **Johns Hopkins Vasculitis Center**
    - http://vasculitis.med.jhu.edu/index.html

Organ Systems Affected



Classification of Vasculitis

- Vasculitis may be classified by:
  - The size and type of vessel involvement
  - The histopathologic features (leukocytoclastic, granulomatous vasculitis, etc.)
  - The pattern of clinical features

CLASSIFICATION TREE

Vasculitis

Large Blood Vessel
- Temporal Arteritis
- Takayasu Arteritis

Small Blood Vessel

Medium Blood Vessel
- Polyarteritis Nodosa
- Kawasaki's Disease

ANCA Associated
- Wegener's Granulomatosis
- Churg-Strauss Vasculitis
- Microscopic Polyangiitis
- Drug Induced

Non-ANCA Associated

Immune Complex
- Hypersensitivity Vasculitis
- Cryoglobulinemic Vasculitis
- CTD related Vasculitis
- Henoch Schonlein Purpura
- Behcet's

Miscellaneous
- Paraneoplastic Vasculitis
- Inflammatory Bowel Disease

Vasculitis
History & Examination

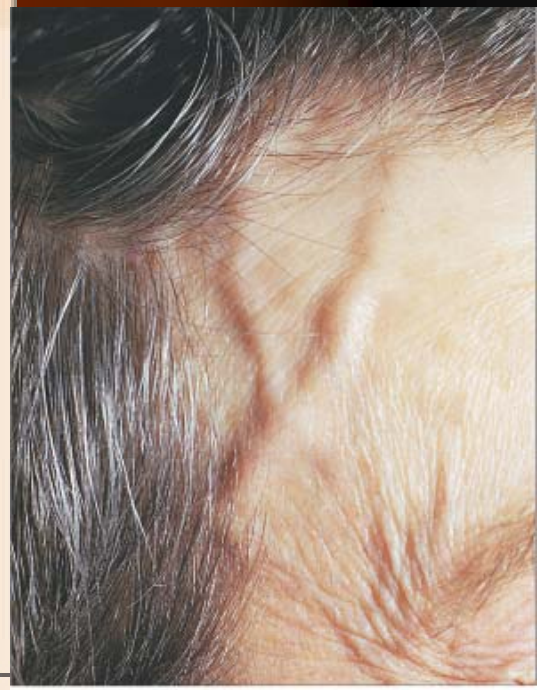
General clinical feature	*Signs or presenting disorder*	*Type of vasculitis*
Constitutional symptoms	Fever, fatigue, malaise, anorexia, weight loss	Any type of vasculitis
Polymyalgia rheumatica	Proximal muscle pain with morning stiffness	Giant cell arteritis; less commonly, other vasculitides
Nondestructive oligoarthritis	Joint swelling, warmth, painful range of motion	Polyarteritis, Wegener's granulomatosis, Churg-Strauss vasculitis
Skin lesions	Livedo reticularis, necrotic lesions, ulcers, nodules, digital tip infarcts	Polyarteritis, Churg-Strauss vasculitis, Wegener's granulomatosis, hypersensitivity vasculitis
	Palpable purpura	Any type of vasculitis except giant cell arteritis and Takayasu's arteritis
Multiple mononeuropathy (mononeuritis multiplex)	Injury to two or more separate peripheral nerves (e.g., patient presents with both right foot drop and left wrist drop)	Polyarteritis, Churg-Strauss vasculitis, Wegener's granulomatosis, cryoglobulinemia
Renal involvement	Ischemic renal failure related to arteritis	Polyarteritis, Takayasu's arteritis; less commonly, Churg-Strauss vasculitis and Wegener's granulomatosis
	Glomerulonephritis	Microscopic polyangiitis, Wegener's granulomatosis, cryoglobulinemia, Churg-Strauss vasculitis, Henoch-Schönlein purpura

GCA
ACR Criteria for Classification Of Temporal Arteritis

Criterion	Definition
1. Age at onset >50 years	Development of symptoms or findings beginning aged 50 years or older
2. New headache	New onset of, or new type of, localized pains in the head
3. Temporal artery abnormality	Temporal artery tenderness to palpation or decreased pulsation, unrelated to atherosclerosis of cervical arteries
4. Increased ESR	ESR >50mm/h by Westergren method
5. Abnormal artery biopsy	Biopsy specimen with artery showing vasculitis characterized by a predominance of mononuclear cell infiltration or granulomatous inflammation

A classification of giant cell arteritis requires three of the five criteria.

(From Hunder *et al.*[35])



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GCA
Differential Diagnosis

1. Polymyalgia Rheumatica
2. Rheumatoid Arthritis,CTD, Cervical OA
3. Neoplastic Disease, MM, Leukemia, Lymphoma
4. Inflammatory Muscle Disease: Polymyositis
5. Hypothyroidism

Physical Examination
Vitals –BP & pulse

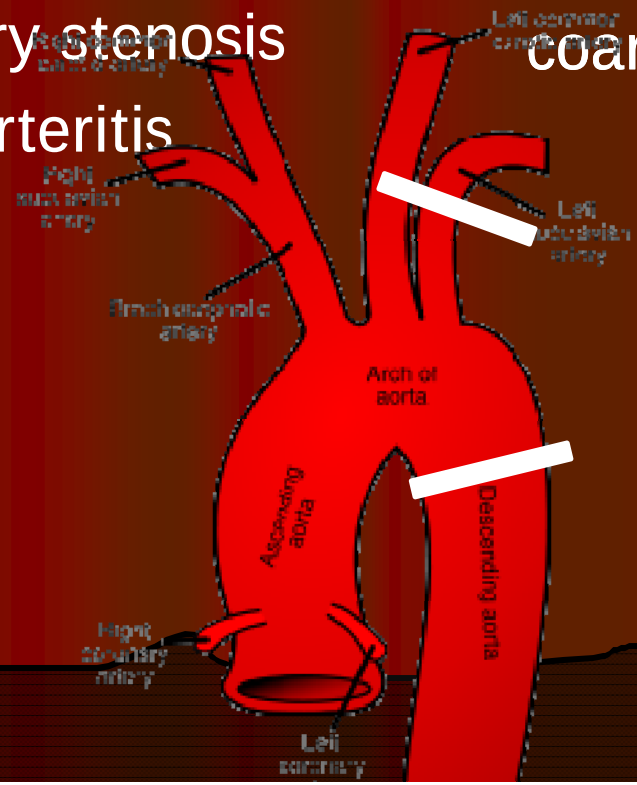
Difference both arms

Difference between arm and leg

subclavian artery stenosis

Takayasu arteritis

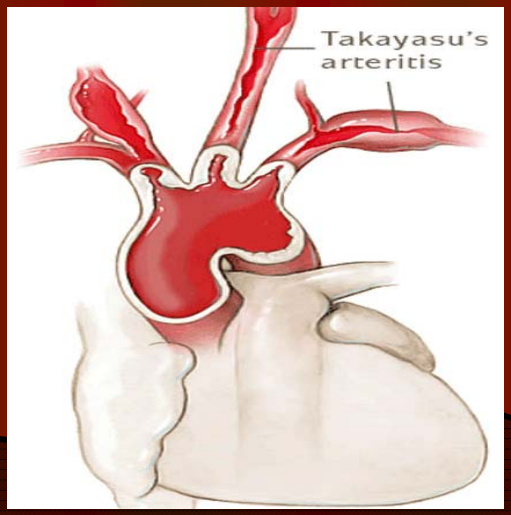
coarctation of the aorta

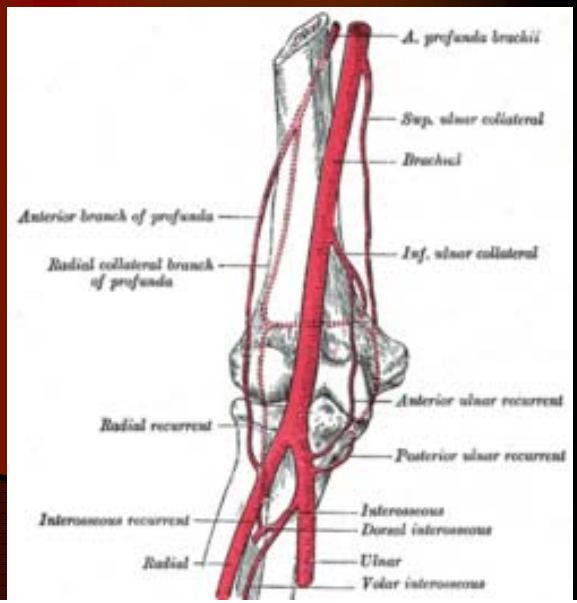


Takayasu's arteritis

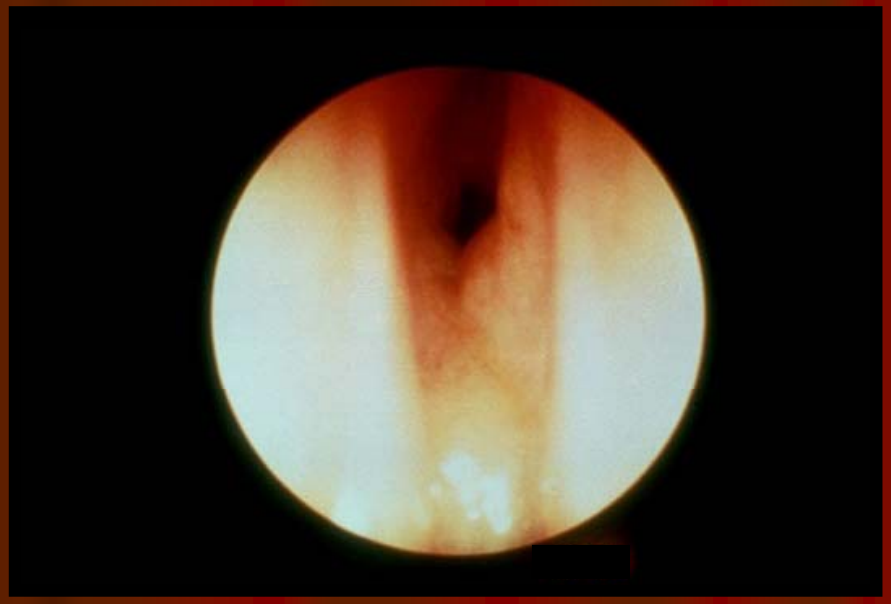
1. Age less than 40
2. Claudication of an extremity
3. Decrease Brachial artery pulse
4. BP difference between arms >10mmHg or bruit over subclavian artery or aorta or arteriogram abnormality

- 3 or >





Physical Examination
Head & Neck
Upper air way inflammation



ACR classification criteria: Wegener's Granulomatosis

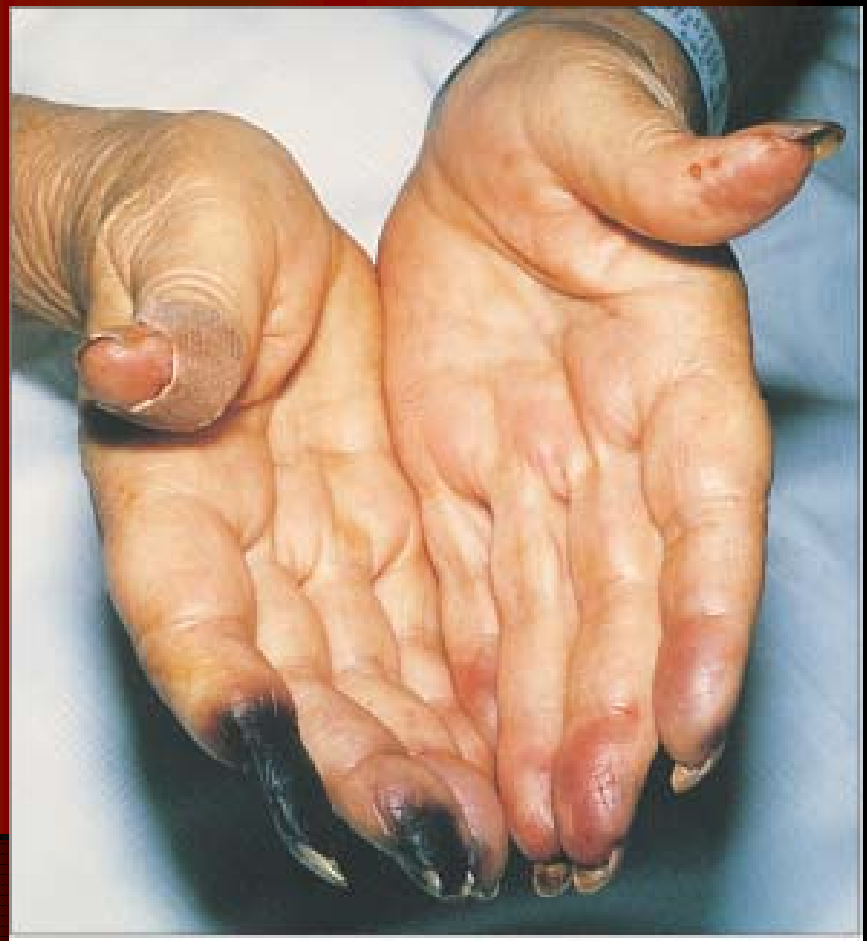
- Must have at least 2 / 4 criteria present

1. Nasal or oral inflammation (oral ulcers or bloody nasal drainage)
2. Abnormal chest radiograph (nodules, fixed infiltrates, cavities)
3. Urinary sediment (>5 RBC/hpf or RBC casts)
4. Granulomatous inflammation on biopsy (in wall of artery or arteriole, perivascular, or extravascular)

- Sensitivity 88.2% and specificity 92.0%

Physical Examination
Hands
Peripheral Gangrene

- Medium
  - PAN
- Small
  - CSS
  - WG
  - Burgers
  - Cryoglobulinemia
  - APA



CRYOGLOBULINAEMIA

Type I single homogeneous monolonal IG

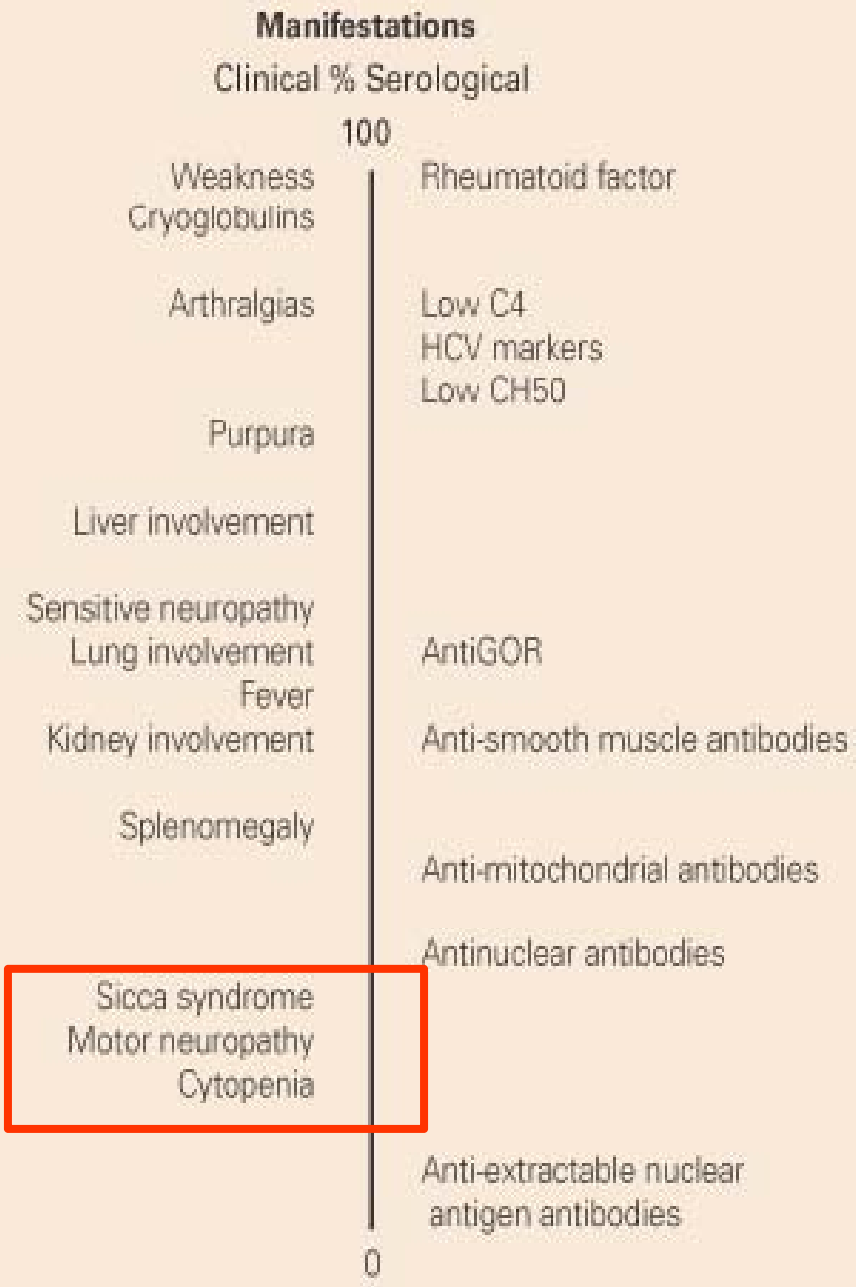
Type II mixed cryoglobulins with a monoclonal component against a polyclonal IgG

Type III mixed polyclonal

CRYOGLOBULINAEMIA

- Unmixed (I)L :
  - Myeloma, lymphoma, waldenstrom, essential
  - Raynauds, thrombosis, ulceration.
- Mixed (II & III):
  - CTD, infection, essential
  - Raynaud, Purpura, arthritis, renal, neuropathy

SPECTRUM OF CLINICAL MANIFESTATIONS IN MIXED CRYOGLOBULINEMIA



Physical Examination
Feet
Mononeuritis Multiplex

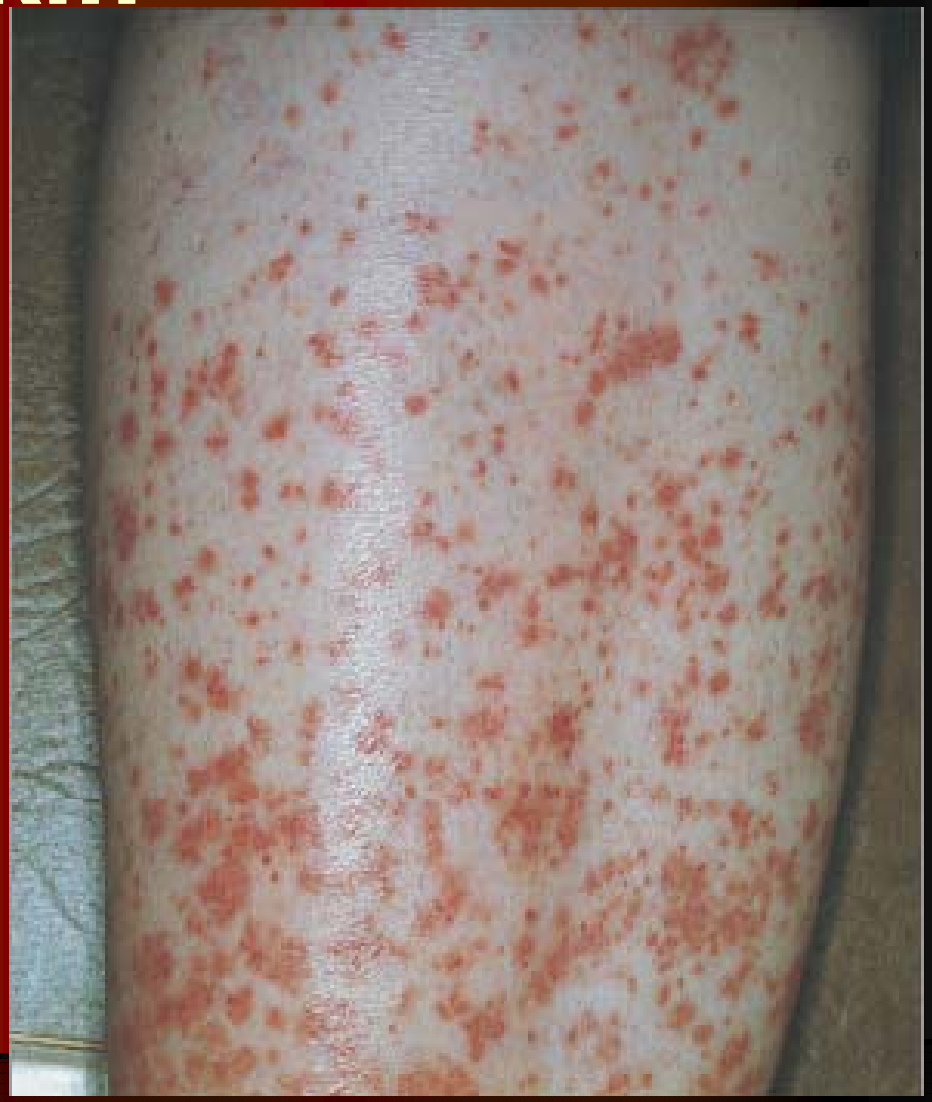
- **Wrist Drop**
- **Foot Drop**
  - **The gait**
    - As if toes stuck to ground
    - High step so toes can clear
- DDX:
  - PAN
  - CSS
  - WG
  - Cryoglobulinemia

TABLE 146.1 1990 CRITERIA FOR THE CLASSIFICATION OF POLYARTERITIS NODOSA

Criterion	Definition
1. Weight loss >4kg	Loss of 4kg or more body weight since illness began, not due to dieting or other factors
2. Livedo reticularis	Mottled reticular pattern over the skin of portions of the extremities or torso
3. Testicular pain or tenderness	Pain or tenderness of the testicles, not due to infection, trauma or other causes
4. Myalgias, weakness or polyneuropathy	Diffuse myalgias (excluding shoulder and hip girdle) or weakness of muscles or tenderness of leg muscles
5. Mononeuropathy or polyneuropathy	Development of mononeuropathy, multiple mononeuropathies or polyneuropathy
6. Diastolic BP >90mmHg	Development of hypertension with diastolic BP higher than 90mmHg
7. Increased BUN or creatinine	Increase in BUN >40mg/dl (14.3μmol/l) or creatinine >1.5mg/dl (132μmol/l), not due to dehydration or obstruction
8. Hepatitis B virus	Presence of hepatitis B surface antigen or antibody in serum
9. Arteriographic abnormality	Arteriogram showing aneurysms or occlusions of the visceral arteries, not due to arteriosclerosis, fibromuscular dysplasia or other non-inflammatory causes
10. Biopsy of small or medium-sized artery containing PMN	Histologic changes showing the presence of granulocytes or granulocytes and mononuclear leukocytes in the artery wall

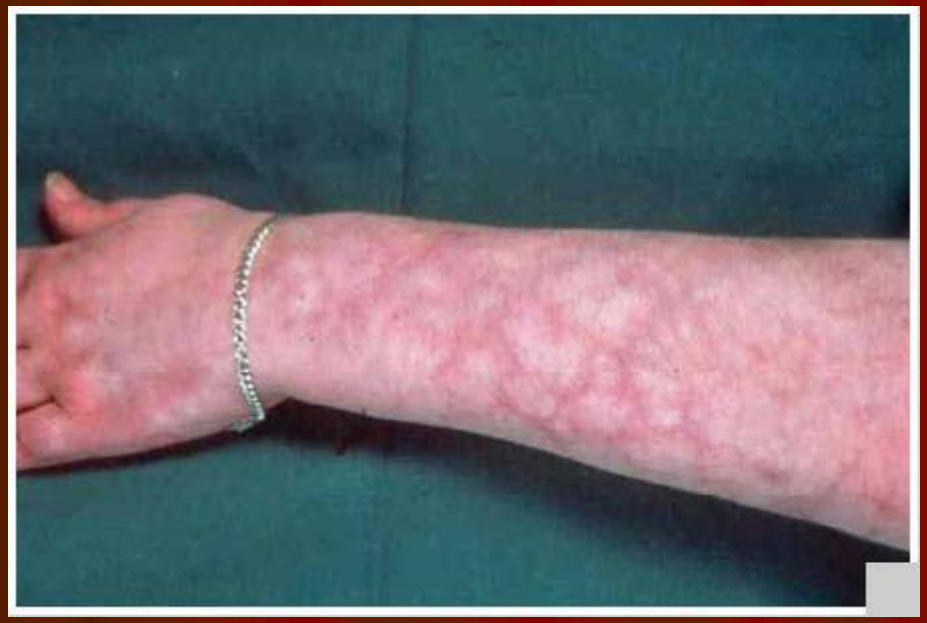
Physical Examination
Skin

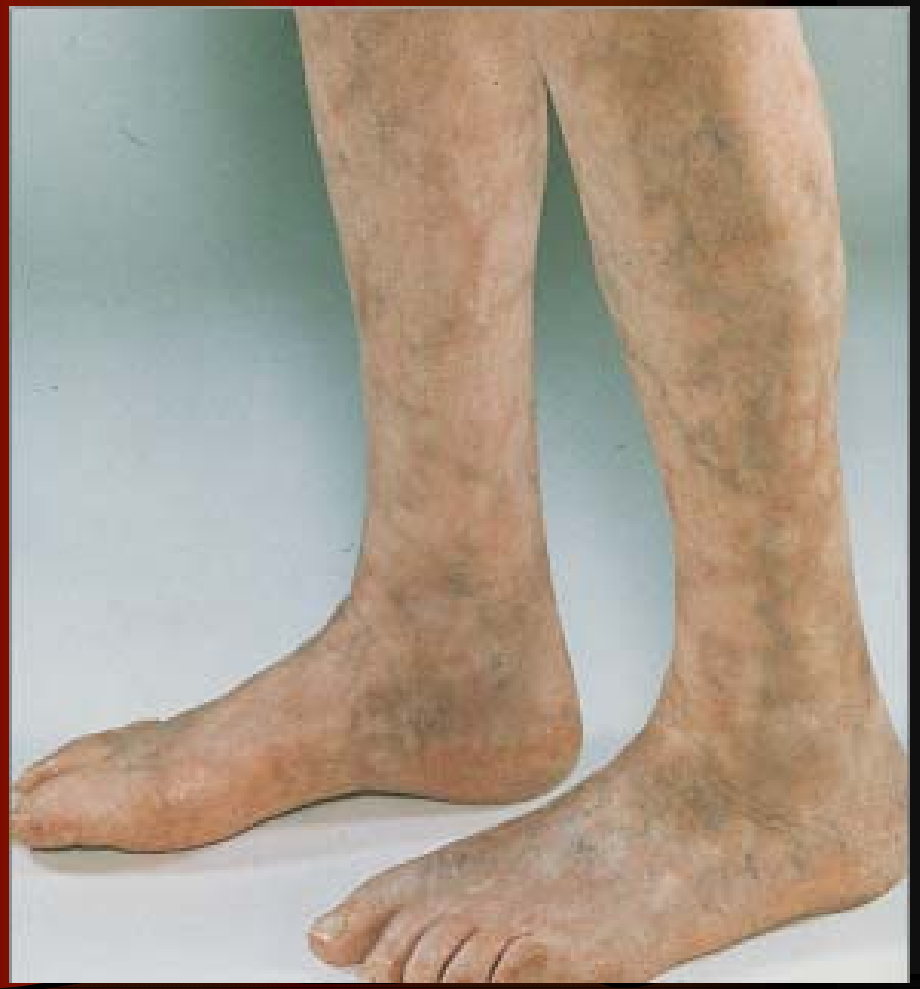
- **Purpura**
  - Drugs
  - Infections
  - Malignancy
  - HSP
  - Autoimmune
  - Cryoglobulinemia
  - Urticarial vasculitis



Physical Examination
Skin

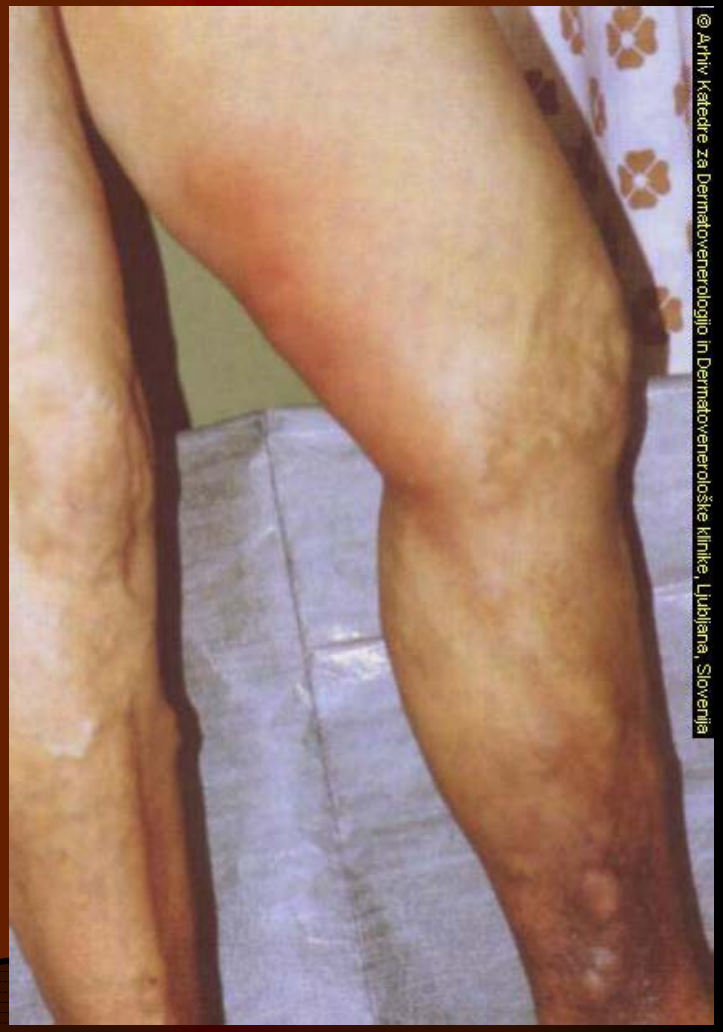
- **Livedo Reticularis**





Physical Examination
Skin

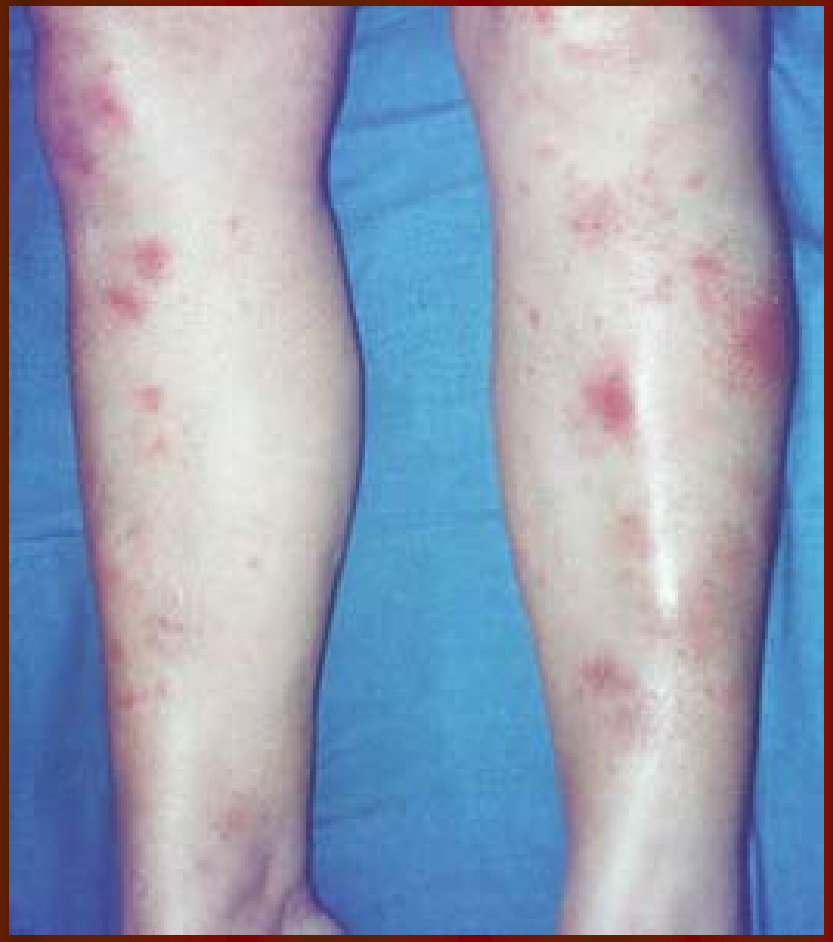
- **Thrombophlebitisis**

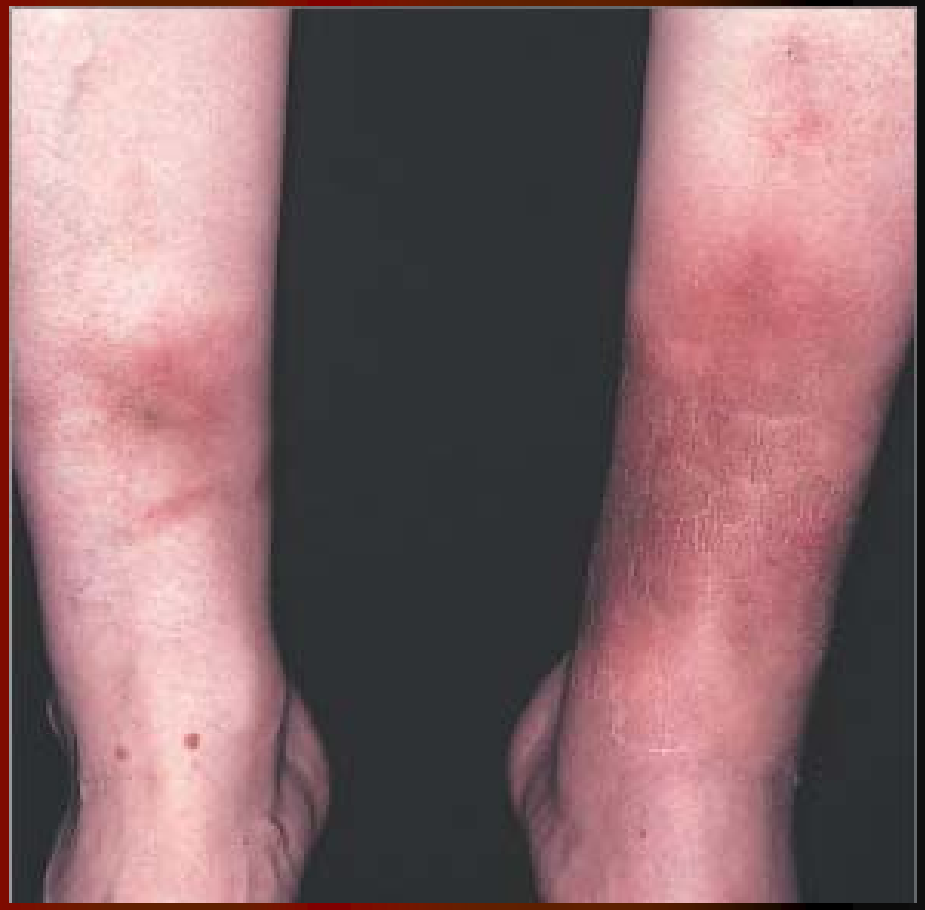


Antiphospholipid syndrome Classification criteria

- **Clinical Criteria**
  - Vascular thrombosis
    - > 1 arterial, venous, o small-vessel thrombosis and
    - Thrombosis confirmed by imaging or Doppler or histopathology and
    - Without evidence of inflammation in vessel wall on histpathologic confirmation
  - Pregnancy morbidity
    - 3 consecutive spontaneous abortions or
    - > 1 fetal death > 10th week gestation or
    - > 1 premature birth > 34th week with preeclampsia or placental insufficiency
- **Laboratory criteria**
  - Anticardiolipin antibody IgG or IgM present medium or high titers > 2 times at least 6 weeks apart or
  - Lupus anticoagulant present > 2 times at least 6 weeks apart

Physical Examination
Skin





Erythema nodosum

Criteria for Behçet's Syndrome

- Recurrent oral ulceration (3 x /12 months)
  - Aphthous or herpetiform

Plus 2 of:

- Recurrent genital ulceration
- Eye lesions
  - Anterior/posterior uveitis, cells in vitreous, or retinal vasculitis observed by an opthamologist
- Skin lesions
  - Erythema nodosum pseudofolliculitis, papulopustular lesions, or acneiform nodules
- Positive pathergy test

Investigation-General

- Assess Organ invovlement:
  - CBC
  - Urea and cr
  - LFT
  - Urine Analysis
  - Chest-Xray
- Assess inflammation: ESR, CRP
- Serological : ANCA, RF, ANA, Anti-GBM, Cryoglobulin, APA, C3 & C4
- HBsAg, HepCAb, HIV

Investigation-Specific

- Blood culture
- Eco-cardiology
- Angiogram
- Tissue Biopsy

Diagnosis of Vasculitis

- Organ Involvement
  - CBC: Look for Inflammation
  - Cr & Urinalysis: Look for renal involvement
  - CXR: Infiltrates
- Infection Screening
  - Liver Enzymes: Look for evidence of hepatitis
  - Hepatitis B & C Serology
  - HIV

Investigation

Assessment of inflammation

Blood count and differential (total white cell count, eosinophils)
Acute-phase response (ESR and CRP)
Liver function

Assessment of organ involvement

Urine analysis (proteinuria, hematuria, casts)
Renal function (creatinine clearance, 24-hour protein excretion, biopsy)
Chest radiograph
Liver function
Nervous system (nerve conduction studies, biopsy)
Muscle (EMG, creatine kinase, biopsy)
Cardiac function (ECG, echocardiography)
Gut (angiography)
Skin (biopsy)

Serological tests

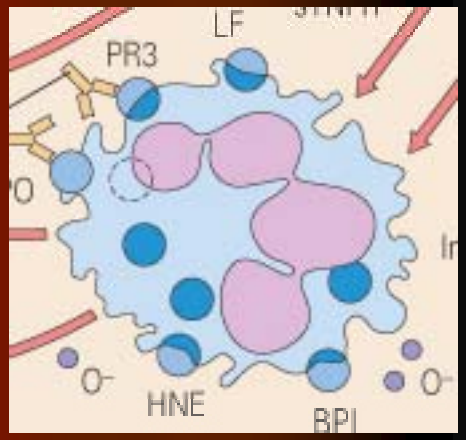
ANCA (including proteinase 3 and myeloperoxidase)
Antinuclear antibodies
Rheumatoid factor
Anticardiolipin antibodies
Complement
Cryoglobulins

Differential diagnosis

Blood cultures
Viral serology (HBV, HCV, HIV, CMV)
Echocardiography (two-dimensional, transesophageal, or both)

Investigation
ANCA
Anti-Neutrophil Cytoplasmic Antibody

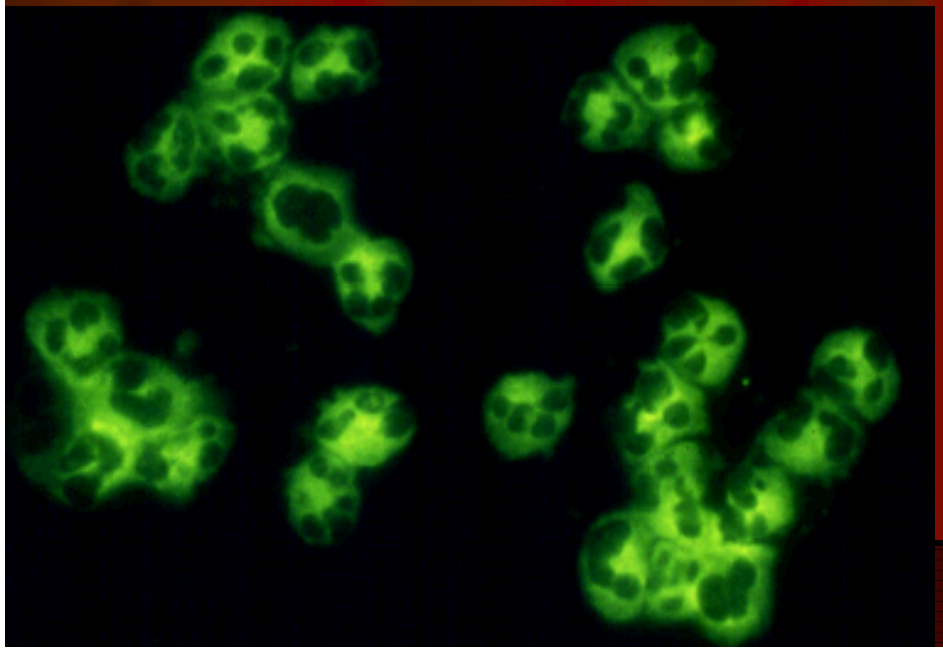
- Antibodies directed to certain antigen found in the cytoplasm of the neutrophils
  1. MPO: Myeloperoxidase.
  2. PR3: Serine Proteinase.
  3. Lactoferrin
  4. Elastase
  5. Lysozyme
  6. Catalase



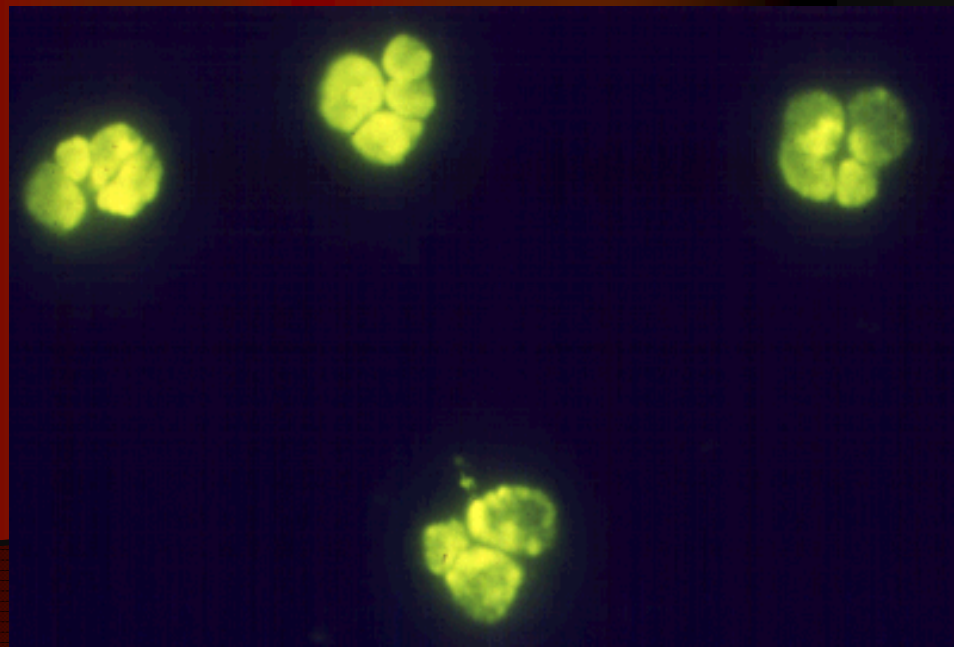
Investigation
ANCA
Anti-Neutrophil Cytoplasmic Antibody

1- Immunoflourecent essay

C-ANCA
Cytoplasmic



P-ANCA
Perinuclear



Investigation
ANCA
(Anti-Neutrophil Cytoplasmic Antibody)

2-ELISA

C-ANCA

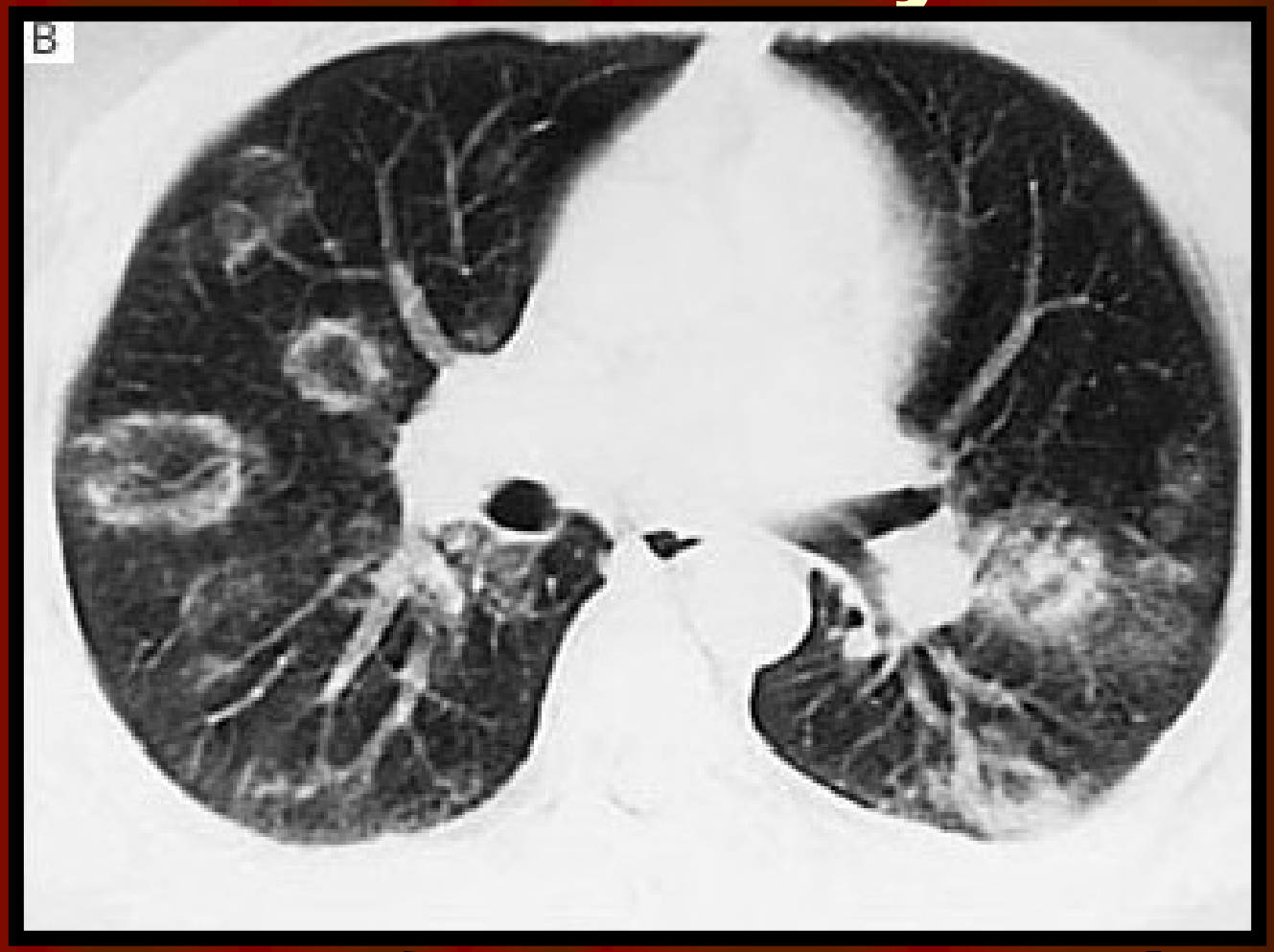
Anti PR3

1. WG 90%
2. MPA 50%
3. CSS 10%

P-ANCA

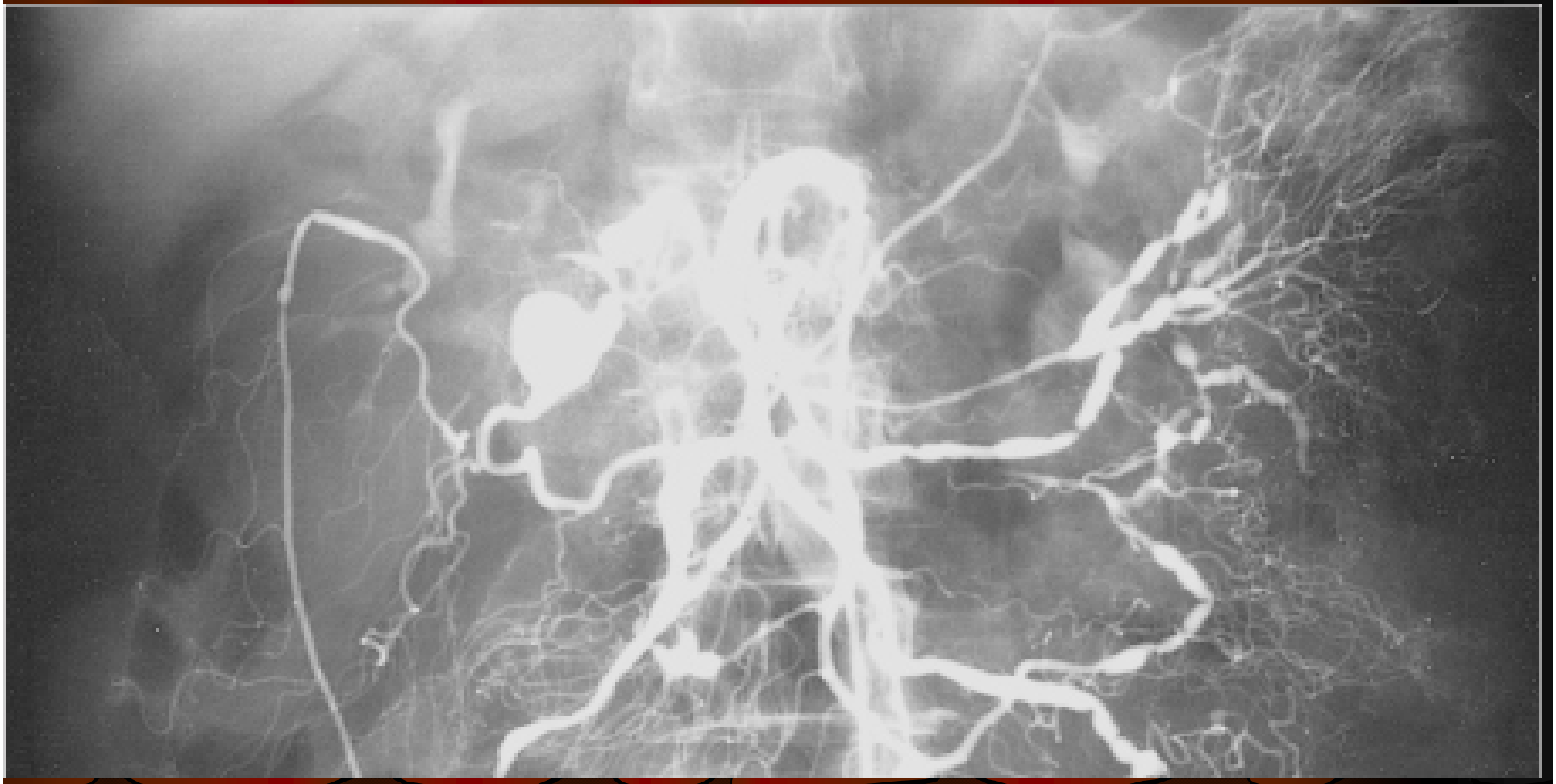
- Anti-MPO
  - CSS 70-85%
  - Pauci-immune GN 50-85%
  - MPA 60-70%
  - Drug induced syndromes
- Non-MPO: **Lactoferrin,Elastase**
  - Ulcerative Colitis
  - Autoimmune disease: liver,RA,SLE
  - HIV infection
  - Certain chronic infections & neoplastic diseases,as cystic fibrosis

Investigation
Chest X-Ray

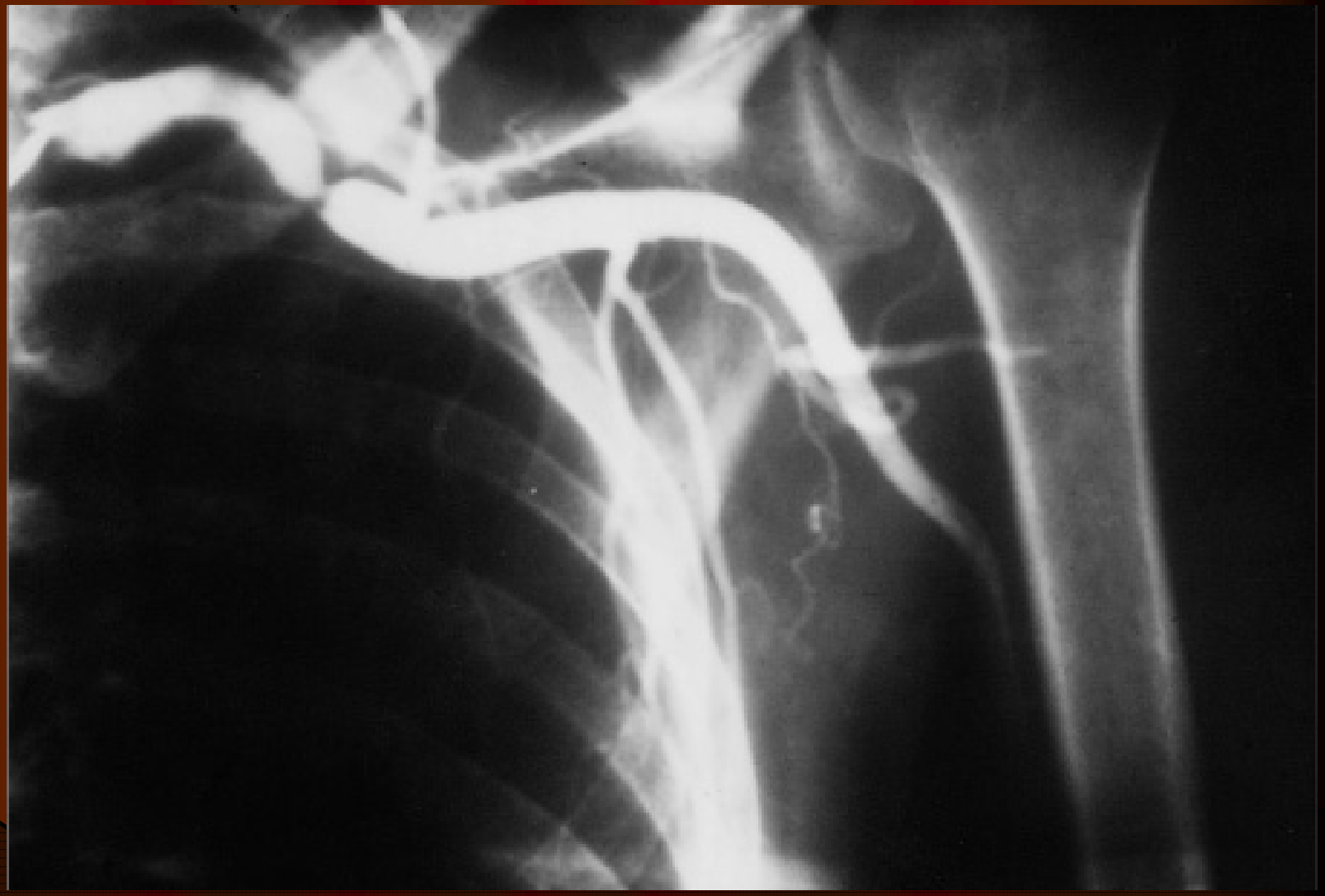


Pulmonary-Renal Syndrome

Investigation
Angiogram



Investigation
Angiogram



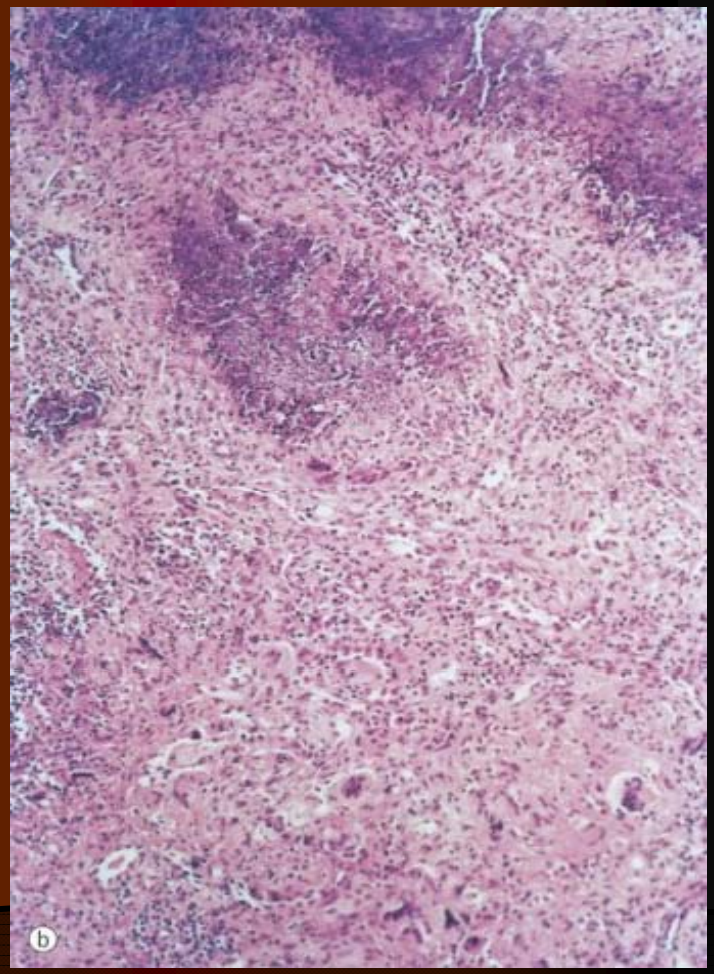
Investigation
Tissue Biopsy

- Skin
- Lung
- Kidney
- Nerve

Investigation
Tissue Biopsy

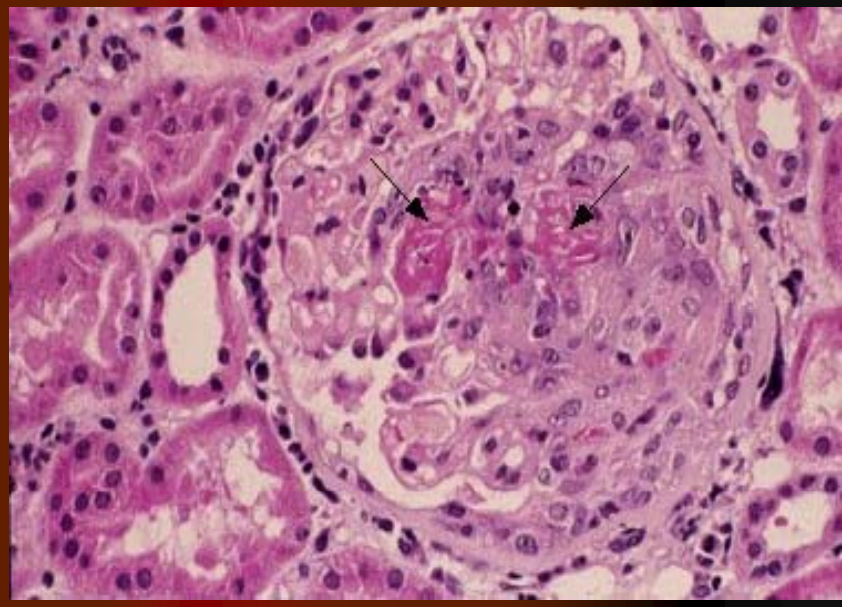
- Upper airways,Lungs
  - Necrotizing granulomatous inflammation (Not caseating)

- Vasculitis of small to medium vessels
  - WG



Investigation
Tissue Biopsy

- Kidney biopsy : focal segmental necrotizing GN which is not specific

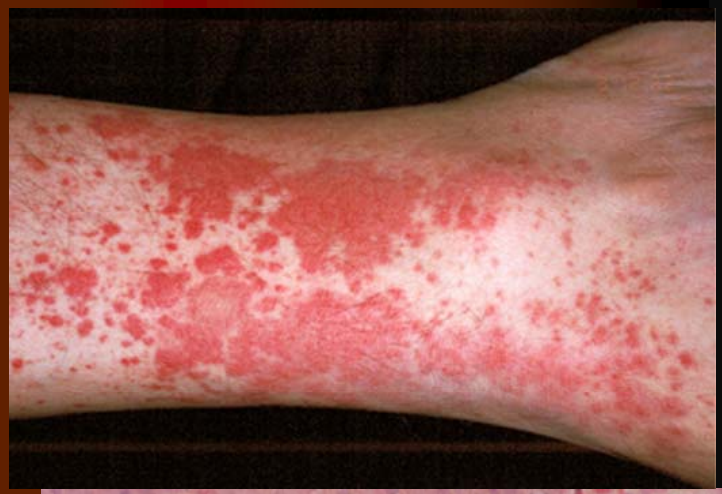


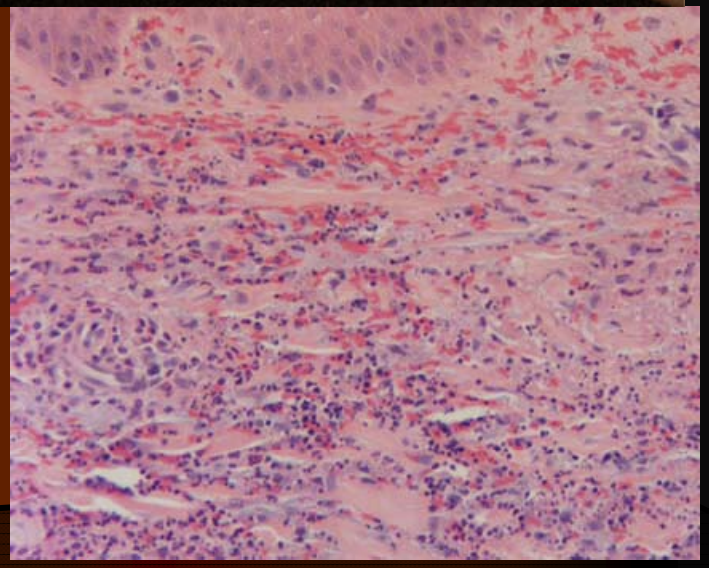
DDx :

- Wegener's
- Microscopic polyangiitis
- Churg-Strauss
- Idiopathic necrotizing GN

Investigation
Tissue Biopsy

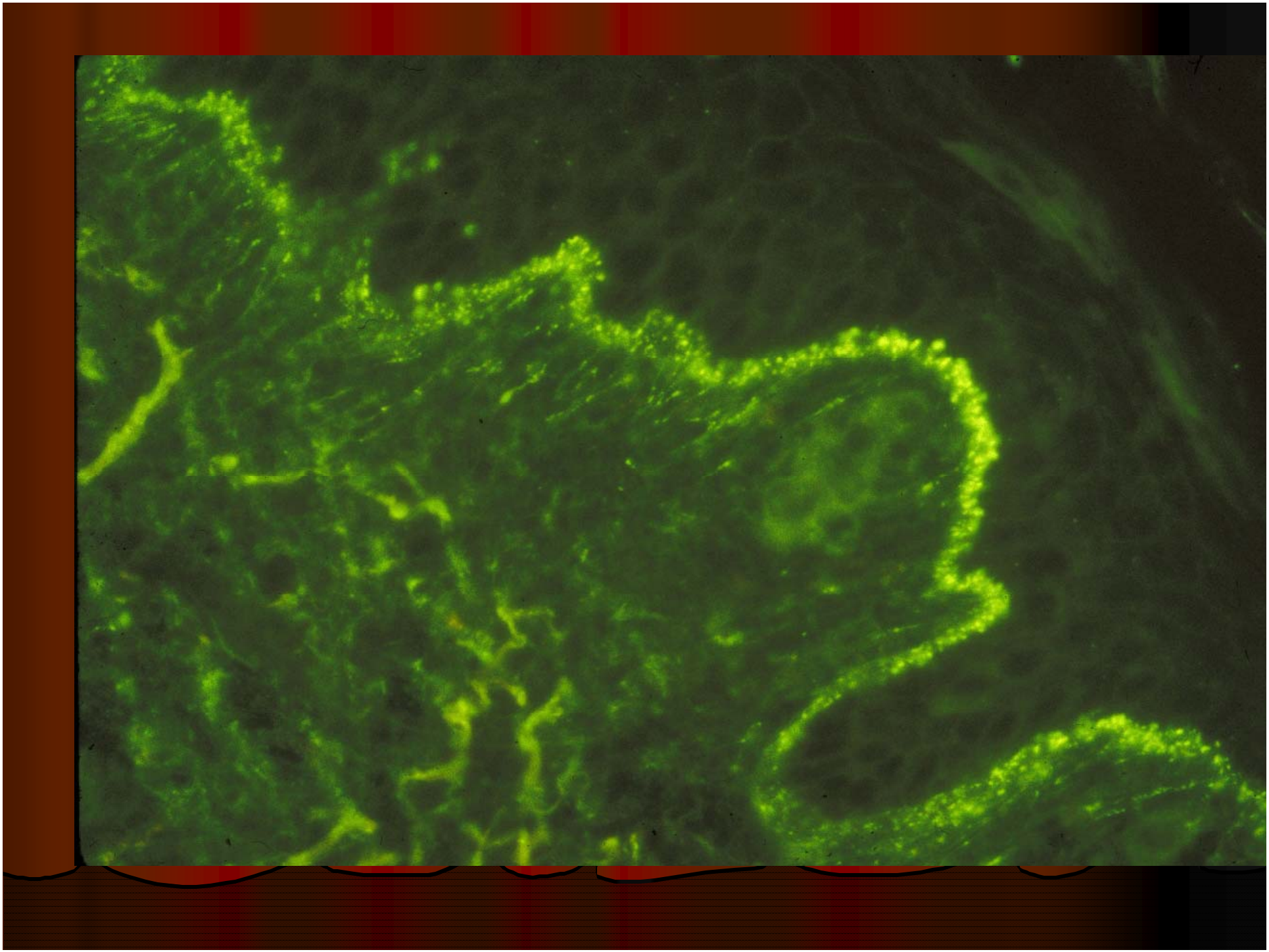
- Leucocytoclastic vasculitis





Investigation
Tissue Biopsy

	HSP	Hypersensitivity vasculitis
Age	**1-Less than 20**	**1-More than 16**
Clinically	2-Bowl angina	2-Medication at the disease onset
Rash	**3-Palpable purpura**	**3-Palpable purpura** **4-Maculopapular rash**
Biopsy	4-Leucocytoclastic vasculitis IgA deposition	**5-Leucocytoclastic vasculitis**
ACR	2/4	3/5 UTD



Treatment

Self Limited

- Treatment of underlying cause
- Conservative

Life Threatening

Acute

- Prednisone
  - Pulse IV 1000mg
  - 1mg/kg oral
- IVIG
- Plasmapharesis

Chronic

- Immunosuppressive
  - Induction Cyclophosphamide
  - Maintenance Methotrexate
    Azathioprine

Conclusion

- It is difficult and big subject
- Early recognition and treatment is warranted for better prognosis