Vasculitis
by Paul Sutej, M.D.

A “bored” review ?!!!

Vasculitis

- Common problem
- ALWAYS asked on “boards”
- Easy to confuse
- Let’s look at the different kinds

Objectives of Lecture

- Provide definition
- Outline the different kinds of vasculitis
- Different clinical presentations of the vasculitic syndromes
- An approach to the treatment of the vasculitides

VASCULITIS

- A heterogenous group of clinical syndromes characterized by inflammation of blood vessels
- The clinical picture is essentially dependent on the size and extent of vessel involvement

Vasculitis

- Ambiguity of clinical presentations
- Limited diagnostic tests
- Difficulty in obtaining diagnostic tissue
- Therefore, difficult to diagnose
- AND classify

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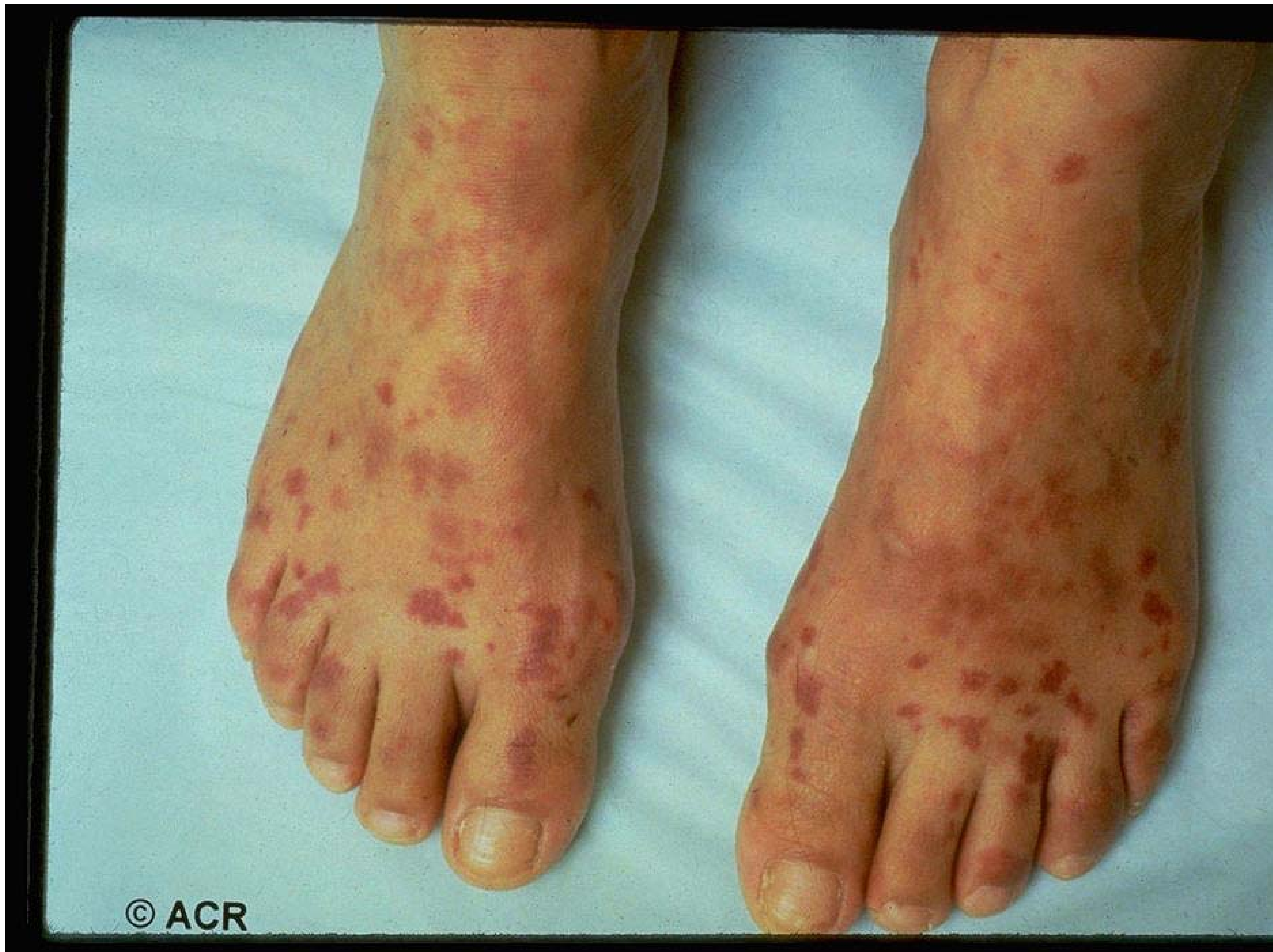
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Incidence of Vasculitis

- Variable because of definitions
- Kawasaki seen almost exclusively in pediatric population
- Most other vasculitides in the fifth decade of life

Pathology of Vasculitis

- Considerable overlap in patterns of pathological involvement
- Pathologic findings not diagnostic for a specific syndrome
- Can be focal and segmental
- Not all the vessel may be involved
- Occasionally, the vasculitis might be necrotizing

Blood Vessel Injury

- (Limited Response)
- Increased permeability
- Weakening (Aneurysm +/- hemorrhage)
- Intimal proliferation and thrombosis obstruction and local ischemia

Diseases that Mimic Vasculitis

- Infective endocarditis
- Strep. Infections
- D.I.C.
- Atrial Myxomas
- Amyloidosis
- Cholesterol emboli
- Drug abuse

Classification of Vasculitis Based on Vessel Size

- Large vessel: Example - GCA or Takayasu's
- Medium vessel: Example - polyarteritis nodosa , Kawasaki's disease
- Medium-to-small: Wegener's, Churg-Strauss,microscopic polyangiitis, ?Behcet,s
- Small vessel: Example – cutaneous leukocytoclastic vasculitis, HSP, cryoglobulinemic vasculitis

Takayasu's Arthritis

- Chronic vasculitis of aorta and branches
- Less common…pulmonary and coronary
- Common in young WOMEN of Asian descent
- Seldom after the age of 40

ACR Classification Criteria: Takayasu's Arteritis*

1. Age <40 Years at Disease Onset
2. Claudication of Extremities
3. Decreased Brachial Artery Pulse
4. BP Difference >10 mmHg Between Arms
5. Bruit Over Subclavian Arteries or Aorta
6. Arteriogram Abnormality:
   Occlusion or Narrowing in Aorta or Main Branches

*Must Have 3/6 Criteria.

Pre-pulseless Phase

- Malaise and arthralgia
- Mild synovitis
- Weakness
- Fever

Pulseless Phase

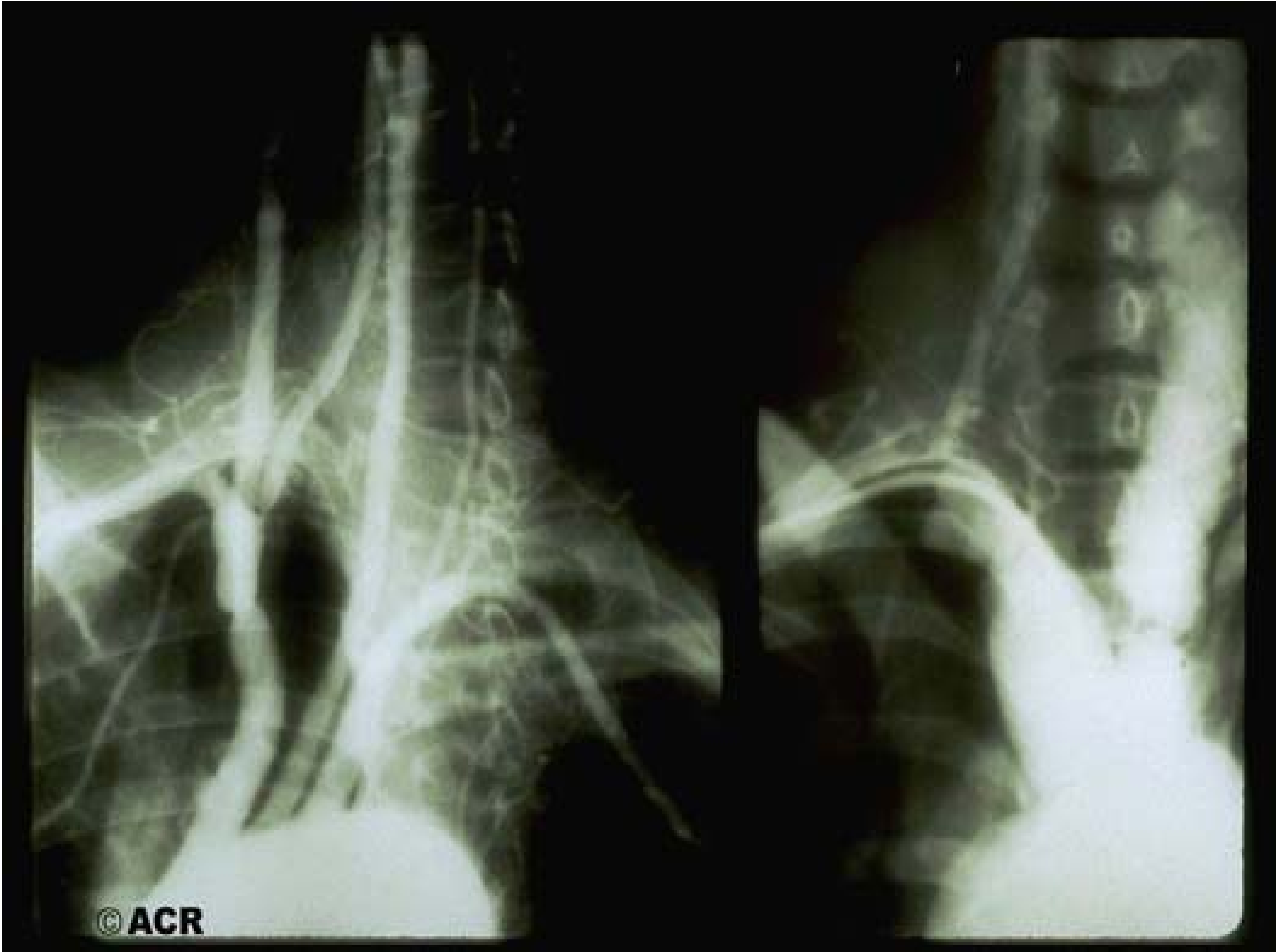
- Claudication
- Headaches, dizziness, and amaurosis or diplopia…difficulty in looking up
- Renovascular hypertension
- Cardiac….chest pain , palpitation
- Pulmonay…dyspnea, hemoptysis and pleurisy
- GI….anorexia,nausea
- Skin ….rare..E.Nodosum,ulcers

Takayasu’s and vessel

- Common carotid…visual defects, strokes, TIA
- Vertebral…dizziness,visual
- Subclavian…arm claudication
- Aorta…AI, CHF
- Pulmonary,cardiac,celiac axis
- Renal….HT
- Iliac ….claudication

Laboratory Findings

- Elevated sedimentation rate (ESR)
- Arteriogram…narrowing ,irregularity and obliteration
- NO SPECIFIC LAB TEST
- Tissue rarely available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Treatment

- Cortico- steroids if caught early
- Methotrexate as steroid-sparing agent
- Manage hypertension
- Percutaneous transluminal angioplasty
- Surgery

Giant Cell Arteritis and Polymyalgia Rheumatica

- Possibly opposite ends of clinical spectrum
- PMR….may be forme fruste of giant cell arteritis…in a subset

Giant cell arteritis

- Age always>50
- Women>men
- Prevalence high in Scandinavian countries
- VERY rare in Blacks and Hispanics

Cranial GCA

- Headaches…….severe
- Scalp tenderness +/- thickened vessels
- Ischemic optic neuropathy
- Jaw claudication in 50%
- CNS ischemia
- PMR

Fever/wasting syndrome

- Fever and chills
- Anorexia, weight loss
- Night sweats
- Weakness
- Depression
- Abnormal laboratory values in 90%
- Biopsy = procedure of choice

Temporal arteritis

- Females 70%
- Gradual onset 64%
- Weight Loss 50%
- Malaise 40%
- Fever 42%
- PMR 39%
- Headache 68%
- Art. Tenderness 66%
- Synovitis 15%
- Sore throat 9%

Large-vessel GCA/aortitis 10-15%

- Arm claudication…femoral is rare
- Pulselessness
- Raynaud’s phenomenon
- Aortic aneurysm
- Aortic insufficiency
- PMR
- Often lack cranial involvement

Giant Cell (Temporal) Arteritis: Local Manifestations

- Temporal headache
- Blindness
- Scalp necrosis
- Tongue gangrene
- Jaw claudication
- Cranial and peripheral neuropathies
- Aortic arch syndrome
- Rare, isolated organ involvement

ACR classification criteria: giant cell arteritis

ACR Classification Criteria: Giant Cell (Temporal) Arteritis*

1. Age >50 Years at Disease Onset
2. New Headache
3. Temporal Artery Abnormality (Tender or Decreased Pulse)
4. Elevated Westergren ESR ≥50 mm/Hr
5. Abnormal Artery Biopsy With Mononuclear Cell Infiltrate, Granulomatous Inflammation, Usually With Multinucleated Giant Cells)

*Must Have 3/5 Criteria.

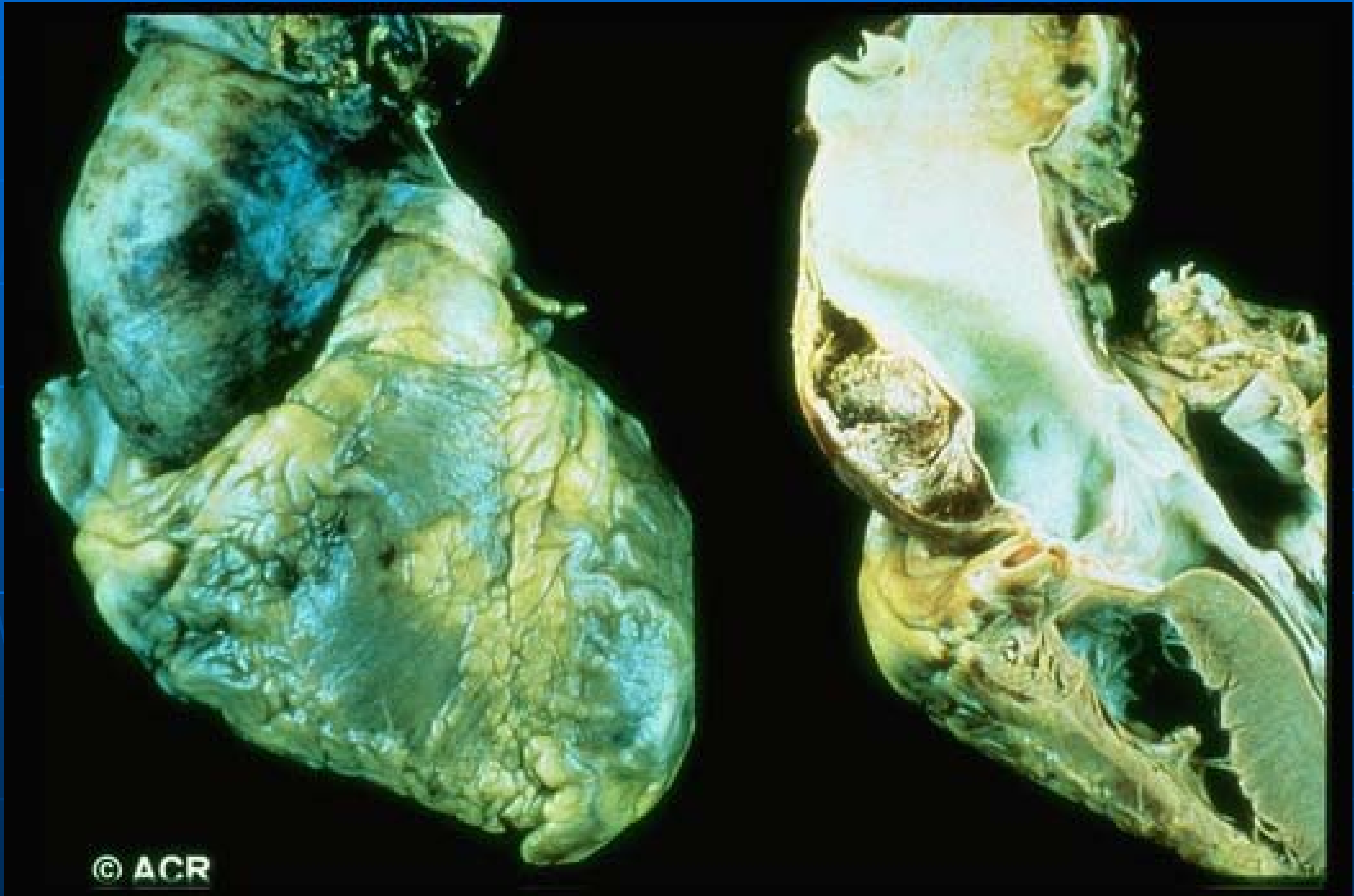
Giant cell arteritis

Giant Cell (Temporal) Arteritis

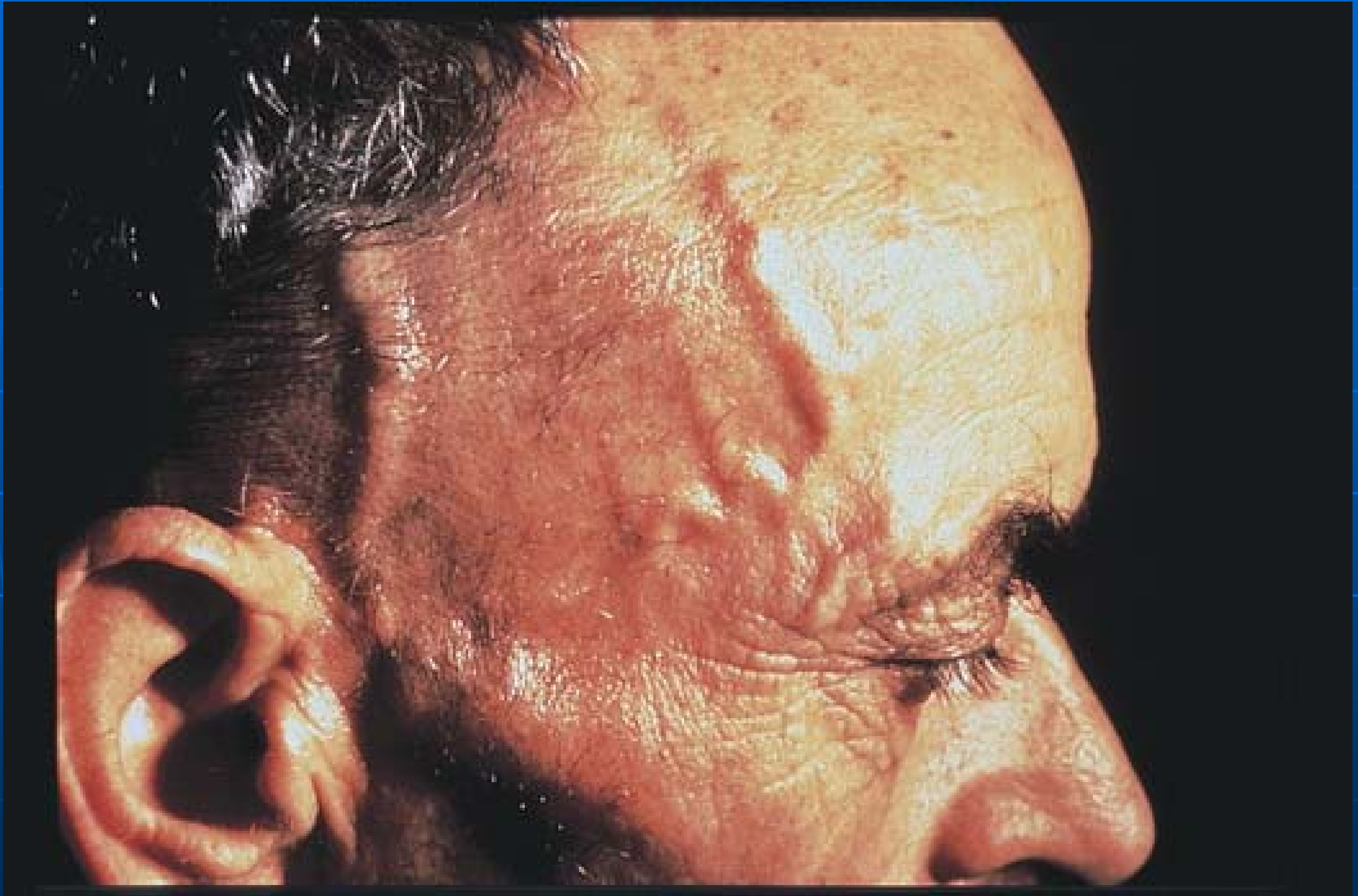
Systemic Features	Local Manifestations
Polymyalgia Rheumatica	Temporal Headache
Fever	Blindness
Anorexia	Scalp Necrosis
Malaise	Jaw Claudication
Weight Loss	Cranial and Peripheral Neuropathies
Elevated ESR	Rare Organ Involvement
Abnormal Liver Function	
Anemia	

Giant cell arteritis: retinal ischemia

Giant cell arteritis: aortic dissection



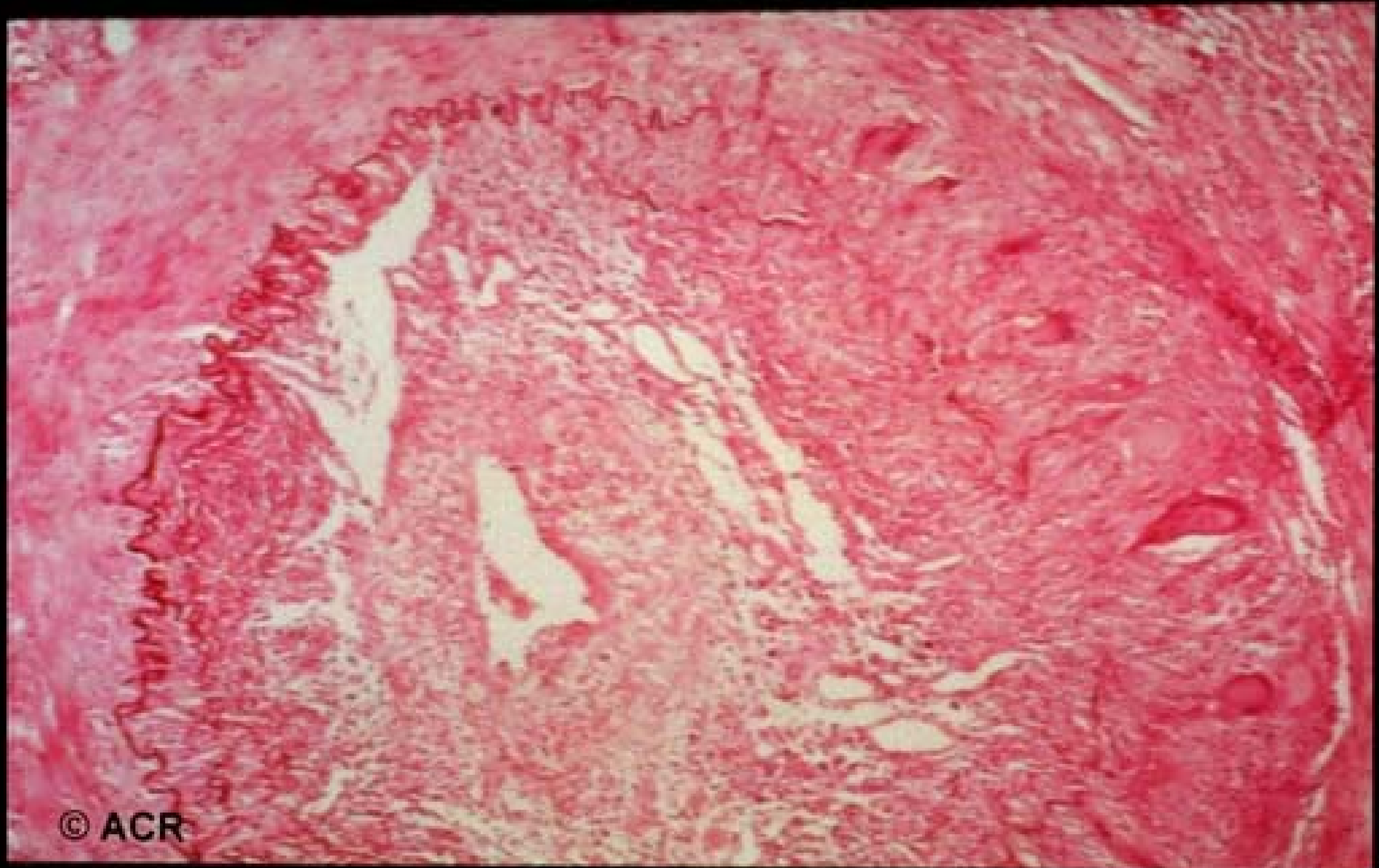
Giant cell arteritis: forehead



Biopsy in Temporal arteritis

- Biopsy abnormal site
- Occipital or facial
- 4-6 cm. if not obviously abnormal
- If strong suspicion and normal biopsy, then biopsy opposite side.
- Doppler guidance?

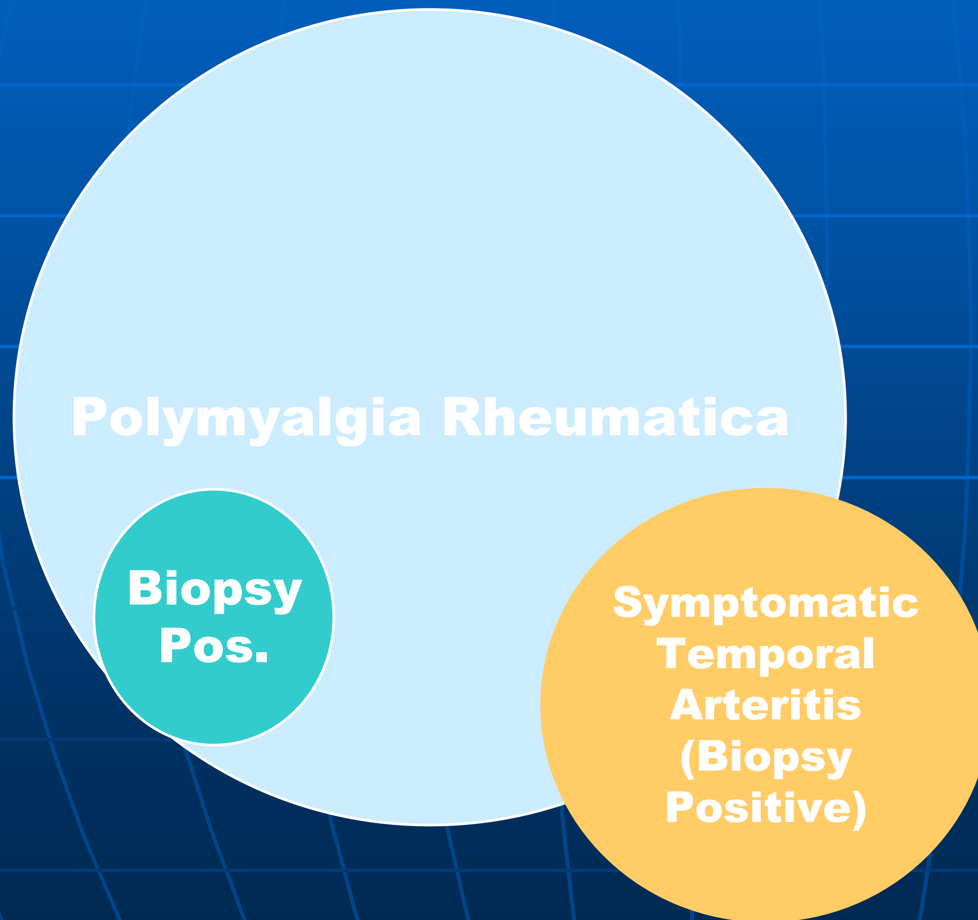
Giant cell arteritis (photomicrograph)



Treatment of GCA

- CORTICOSTEROIDS
- Incidence of blindness has declined
- 60 mg per day…relief DRAMATIC
- Taper by 10% per 2 weeks
- SELF–LIMITED…….maybe NOT
- Bisphosphonates…..remember

Relation of Polymyalgia Rheumatica to Temporal Arteritis



Polymyalgia rheumatica: differential diagnostic possibilities

Polymyalgia Rheumatica: Differential Diagnostic Possibilities

- Temporal Arteritis
- Viral Myalgia
- Rheumatoid Arthritis
- Polymyositis
- Multiple Myeloma
- Osteoarthritis
- Fibrositis
- Depression
- Occult Infection
- Occult Malignancy
- Endocrinopathy

PMR and TA

- PMR may be seen in 40-60% of TA
- PMR: 0-80% incidence of TA
- NO CONSENSUS in incidence and prevalence

Treatment of PMR

- Prednisone 15 mg
- Slow taper over 12 to 18 months
- Possible mtx use as 2nd line agent
- GIOP prophylaxis
- Look for temporal arteritis
- Concept of benign outcome challengeable

Polymyalgia rheumatica: characteristics

Polymyalgia Rheumatica: Characteristics

Patients Affected

- At Least 50 Years Old
- Usually Caucasian

Muscle Pain Persisting for at Least 1 Month

- Shoulders
- Pelvic Girdle

Severe Morning Stiffness and Gelling

PMR

- 4-weeks of PAIN and STIFFNESS
- In NECK, SHOULDER AND PELVIC GIRDLE…abrupt onset
- MALAISE, NIGHT SWEATS AND LOW-GRADE FEVER
- Increased ESR AND CRP
- NO pathognomonic test
- No myopathy
- Concept of normal ESR debatable

Medium vessel vasculitis

- Kawasaki's disease
- Polyarteritis nodosa
- Hepatitis B –related
- Familial Mediterranean fever
- Cutaneous PAN

Kawasaki's Syndrome

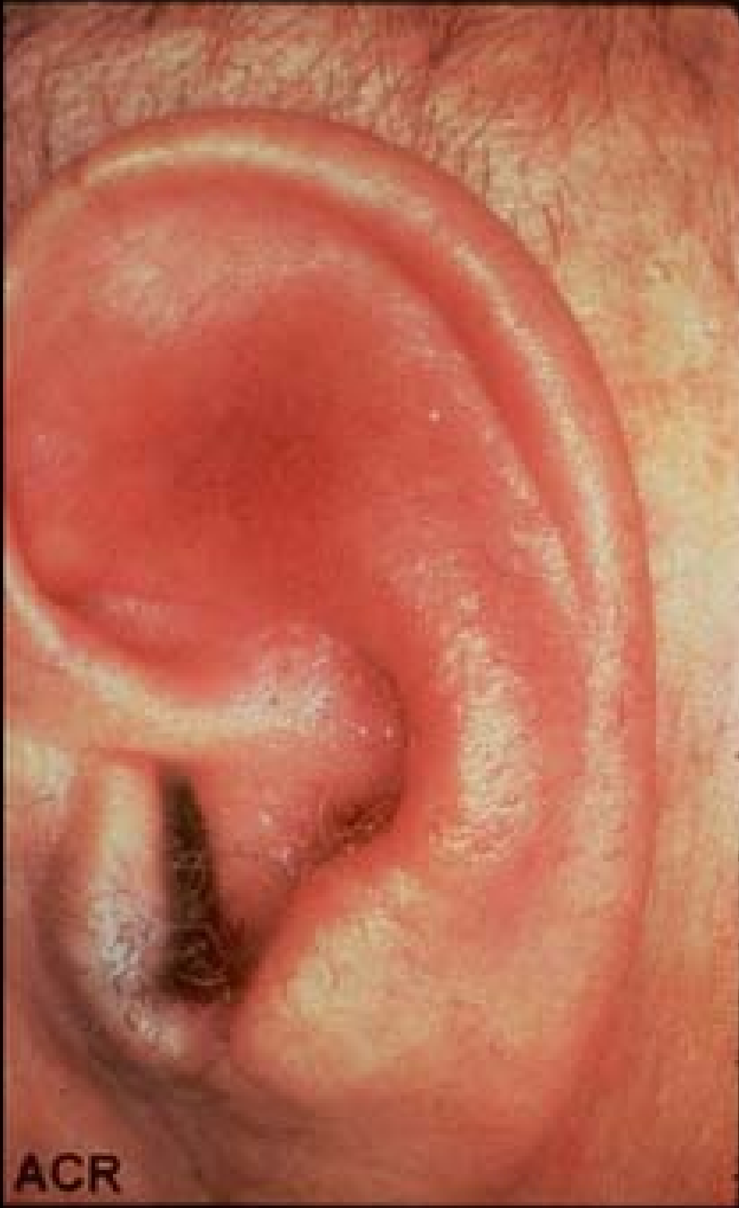
- Infants and young children
- Seasonal variation
- Well-defined epidemics
- Acute ,self-limited illness

Kawasaki Disease:

- Polymorphous rash
- Bilateral conjunctival injection
- Mucous membrane changes…injection,erythema or strawberry tongue
- Cevical lymphadenopathy
- Erythema of palm+/- sole …..edema,desquamation, Beau’s
- Exclusion of other illness
- RX…..IVIG…..reduce the incidence of coronary artery aneurysms

Relapsing polychondritis

- Uncommon, cartilage inflammation
- Episodic
- Auricular and nasal chondritis
- Saddle-nose deformity
- Arthritis,hearing loss,vertigo,LTB symptoms and vasculitis
- Associated disorders
- Prednisone..+?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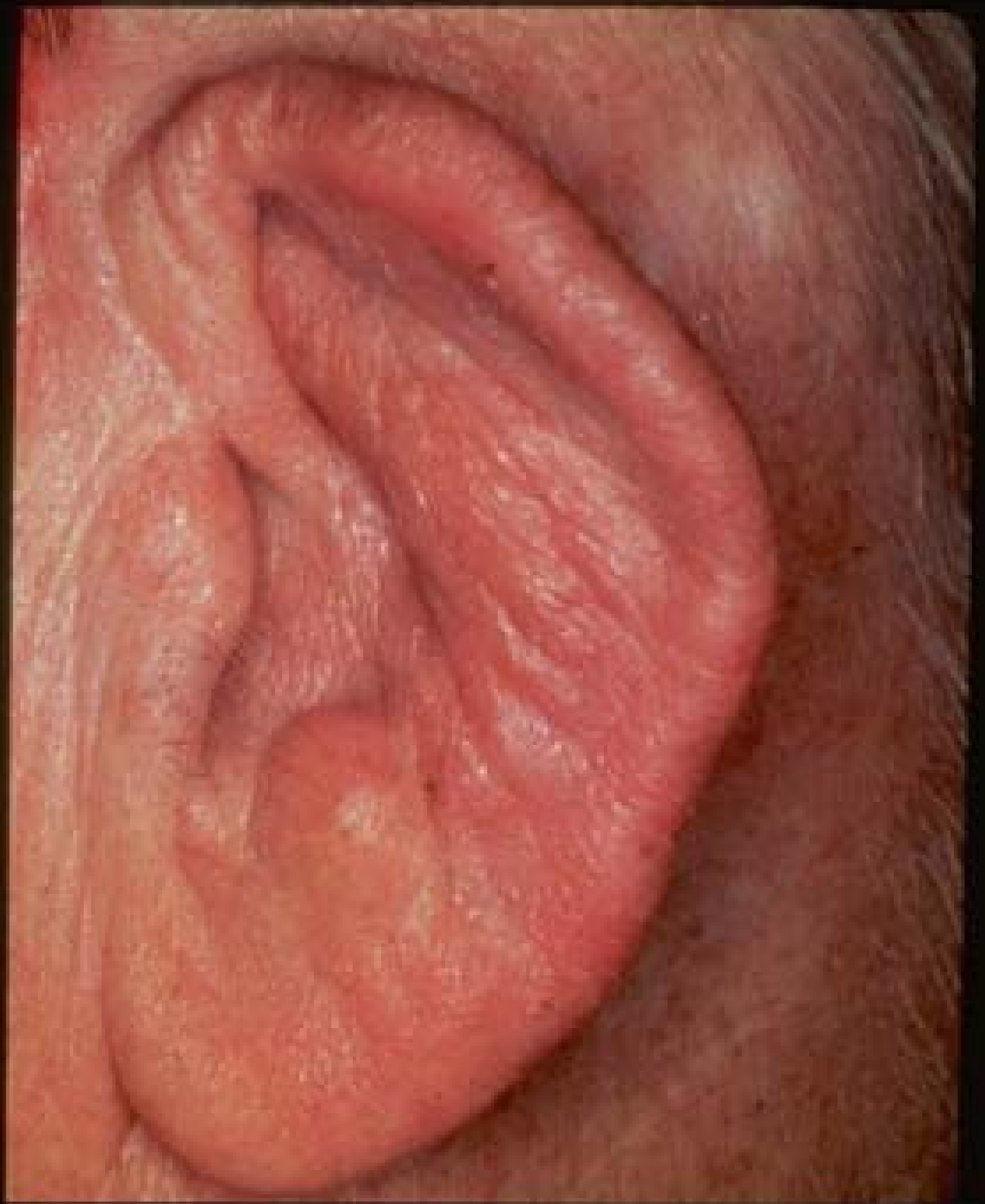

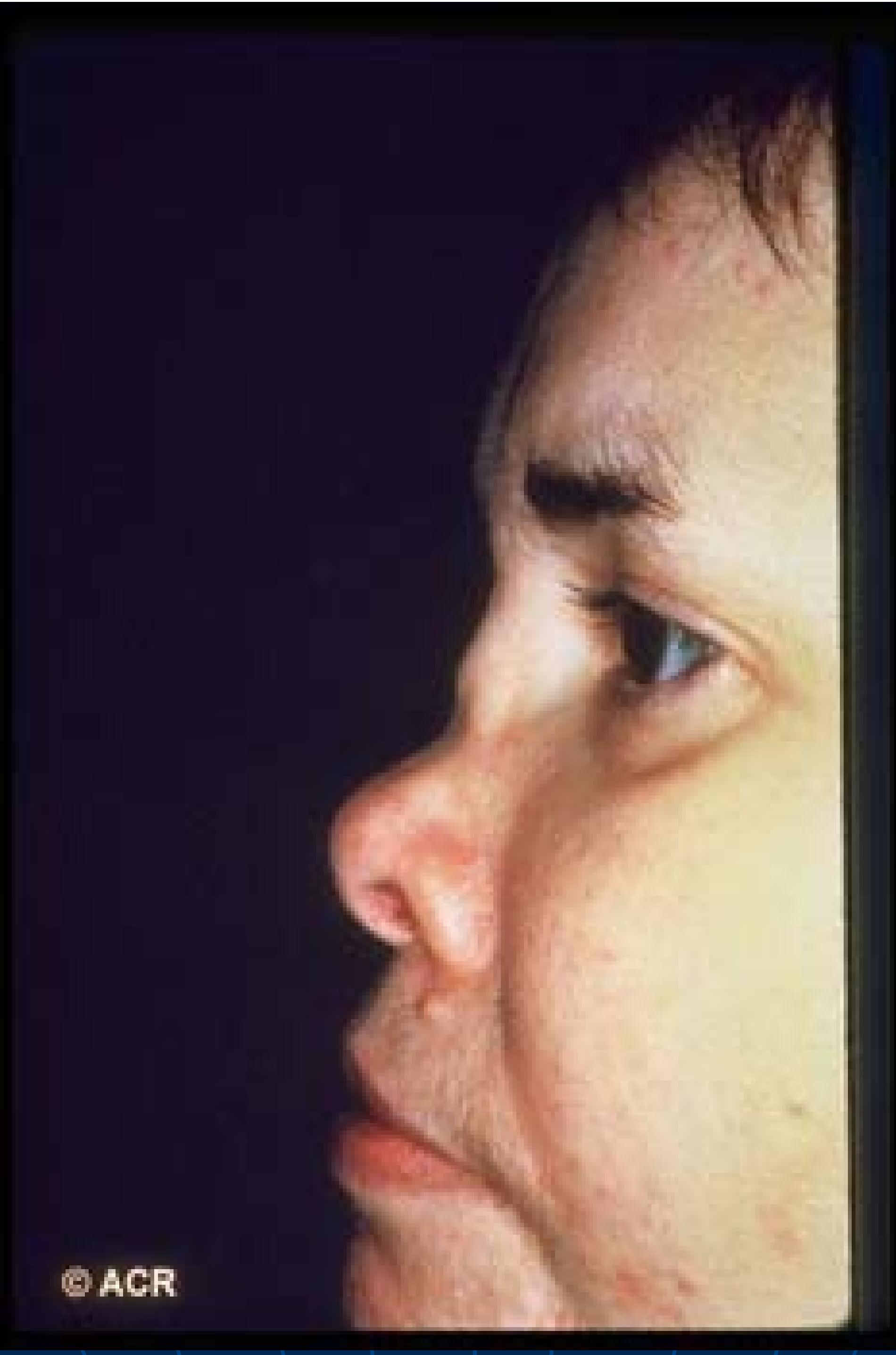
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Polyarteritis nodosa

- 1866…fever, weight loss, abd. Pain and polyneuropathy
- Nodular aneurysms along muscular arteries
- Fibrinoid necrosis
- “Necrotizing vasculitis”
- Rare association with Hep B
- AND hairy-cell leukemia

ACR Classification Criteria: Polyarteritis Nodosa*

1. Weight Loss >4 kg
2. Livedo Reticularis
3. Testicular Pain or Tenderness
4. Myalgias, Weakness, or Leg Tenderness
5. Mononeuropathy or Polyneuropathy

*Must Have 3/10 Criteria. An Association Between Polyarteritis Nodosa and Hepatitis C Has Been Noted.

ACR Classification Criteria: Polyarteritis Nodosa*

6. Diastolic BP >90 mmHg
7. Elevated BUN or Creatinine
8. Hepatitis B Virus
9. Arteriographic Abnormality
10. Biopsy of Small or Medium Artery Containing PAN

*Must Have 3/10 Criteria. An Association Between Polyarteritis Nodosa and Hepatitis C Has Been Noted.

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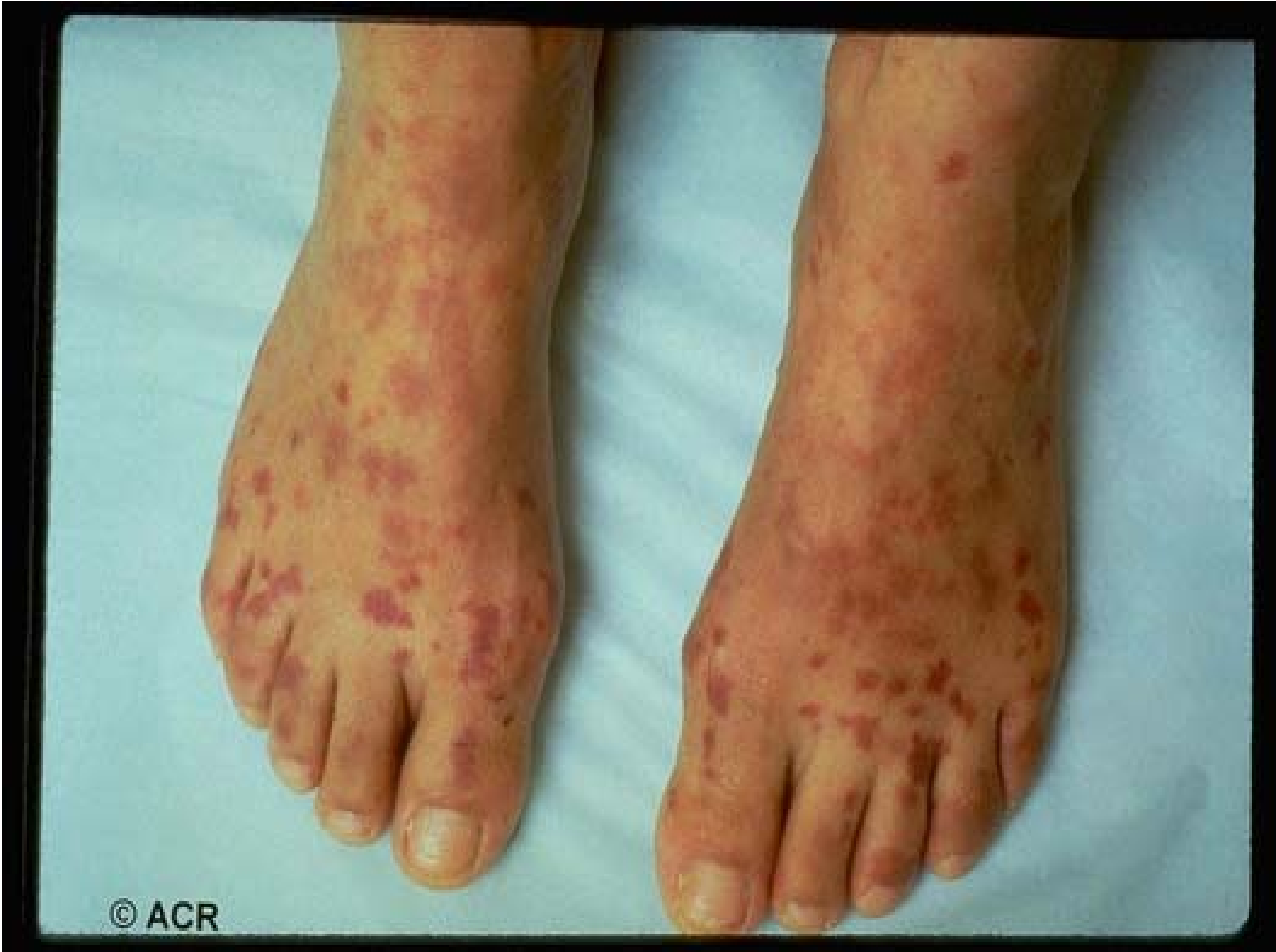
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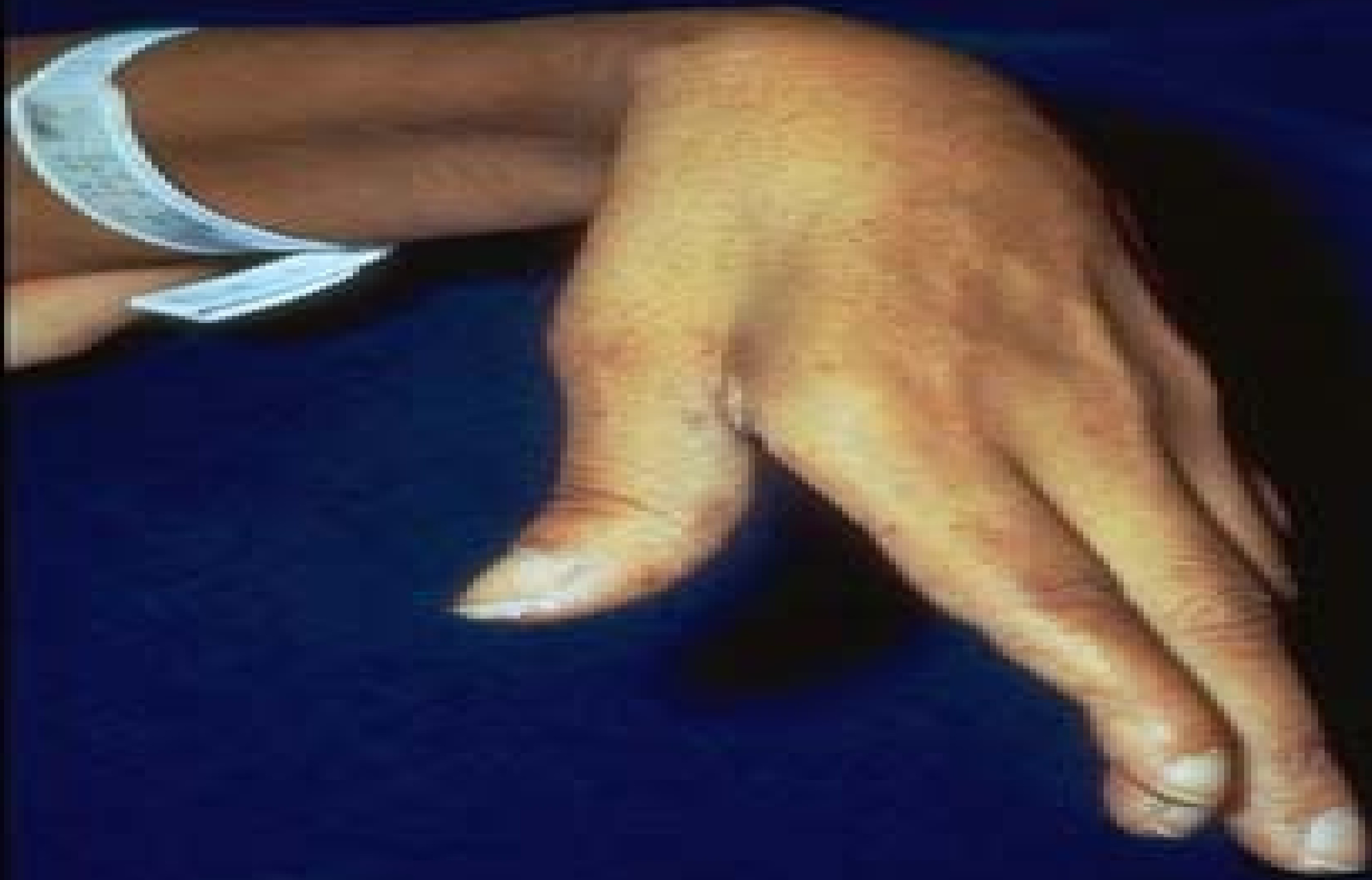
Common Clinical Manifestations

- Malaise, fever and arthralgias initially
- SKIN, GI TRACT, PERIPHERAL NERVES AND KIDNEYS
- MONONEURITIS in 80%
- CNS = rare
- Lungs are spared
- Vascular nephropathy
- Orchitis
- Cardiac ……tachycardia and MI
- GI tract ….transaminitis and infarction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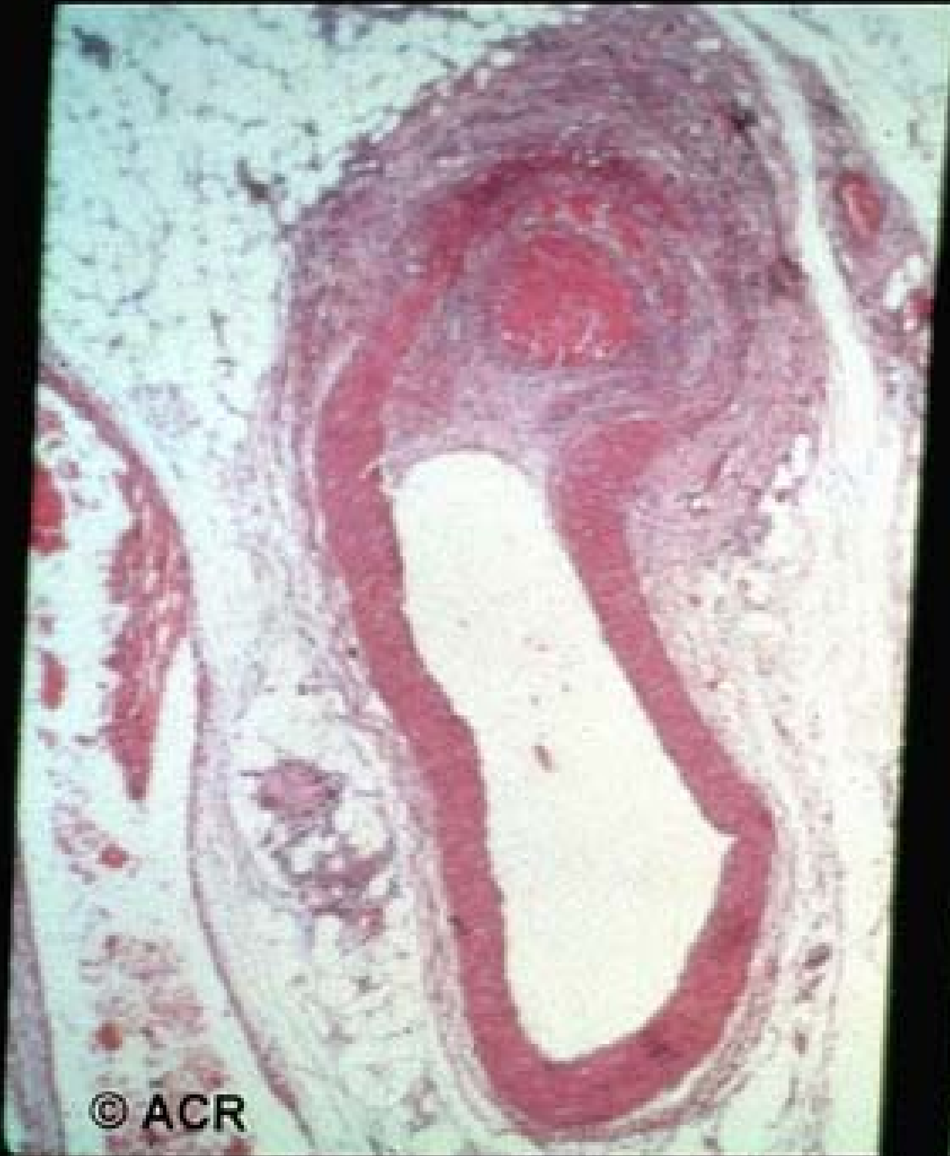
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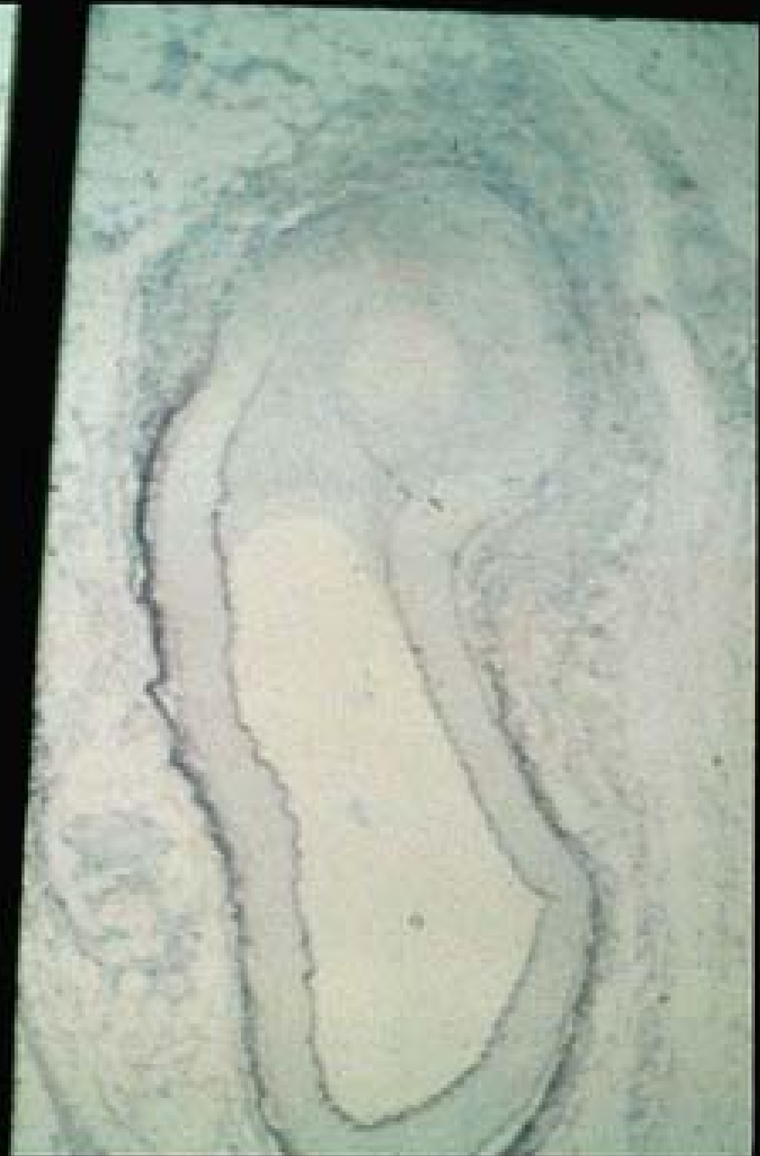

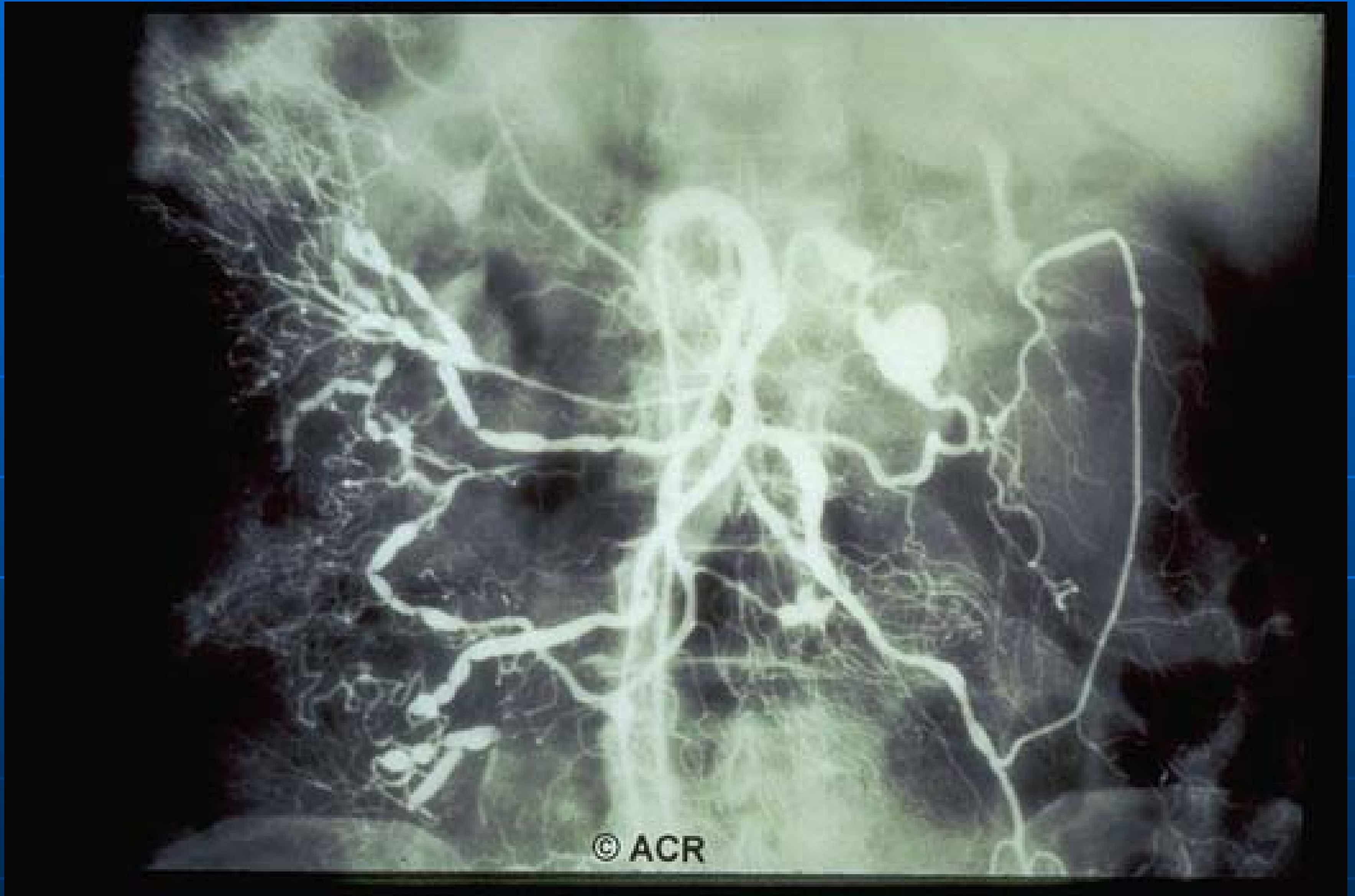
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Microscopic polyangiitis

- Systemic necrotizing vasculitis
- Small-sized vessels
- Focal segmental necrotizing GN
- P-anca association
- NO granuloma
- Renal….RPGN

Microscopic polyangiitis vs PAN

- GN AND LUNG INVOLVEMENT
- BOTH HAVE MONONEURITIS
- Aneurysms in PAN
- Veins may be involved in MP
- Cytoxan inevitable in MP

Treatment of P.A.N.

- Untreated: <20% 5- year survival
- Corticosteroids dramatically improve survival…..50% in remission
- Cytoxan for life-threatening internal organ involvement

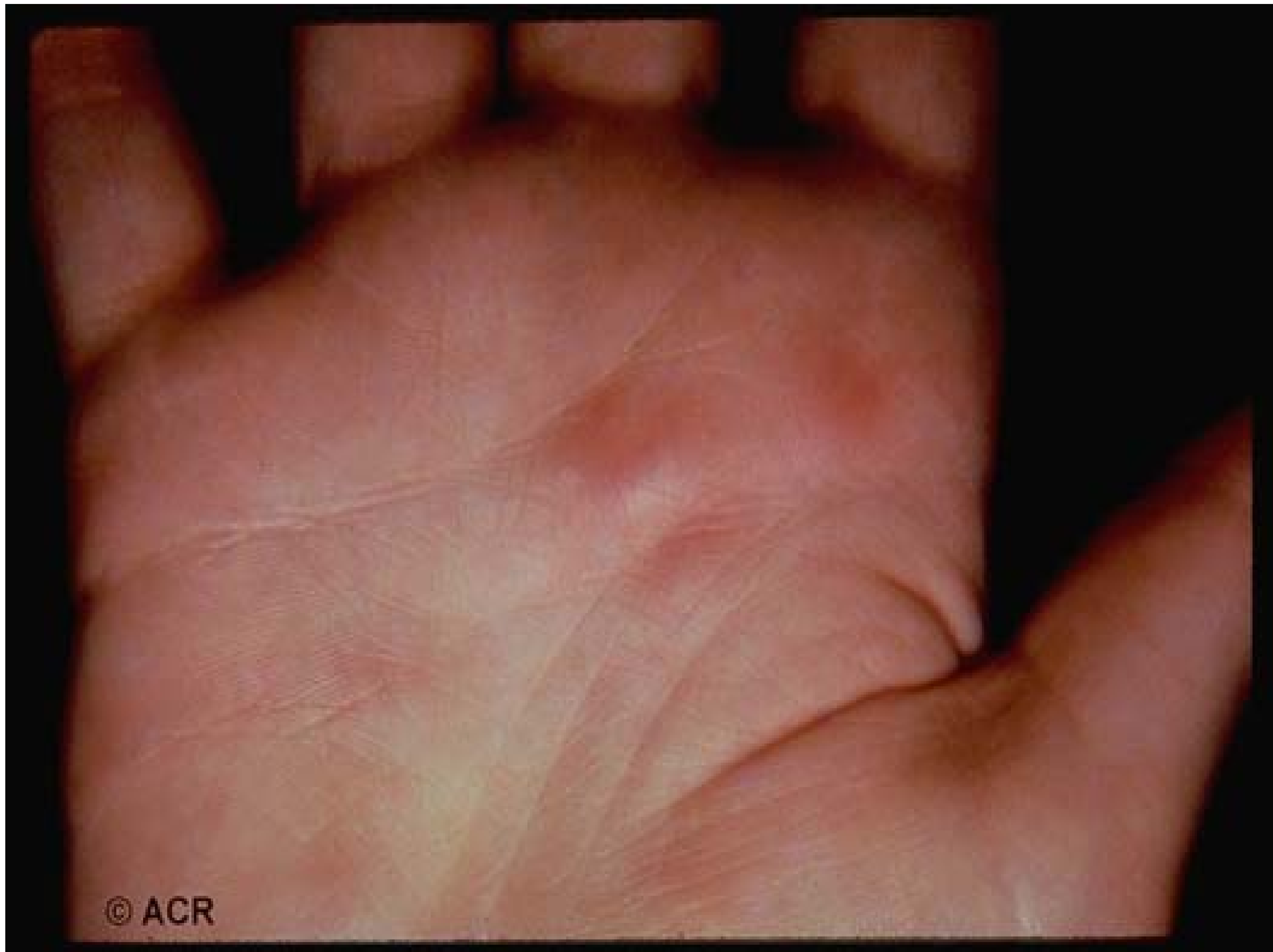
Treatment of MP

- Frequent relapses
- More prolonged treatment
- Prednisone AND cytoxan

Cutaneous PAN

- Chronic relapsing arteritis
- More in women
- 3 classes….
  - Mild…nodular ,livedo
  - Livedo more prominent and ulcers
  - Necrotizing livedo and acral gangrerne

  - RX=PRED+/- "SUPPRESSIVES"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ACR Classification Criteria: Churg-Strauss Syndrome* (Allergic Granulomatosis and Angiitis)

1. Asthma
2. Eosinophilia >10% WBC
3. Mononeuropathy or Polyneuropathy
4. Transitory Pulmonary Infiltrates
5. Paranasal Sinus Abnormality
6. Biopsy With Extravascular Eosinophils

*Must Have 4/6 Criteria.

ACR Classification Criteria: Wegener's Granulomatosis*

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)

*Must Have 2/4 Criteria.

Churg-Strauss Syndrome

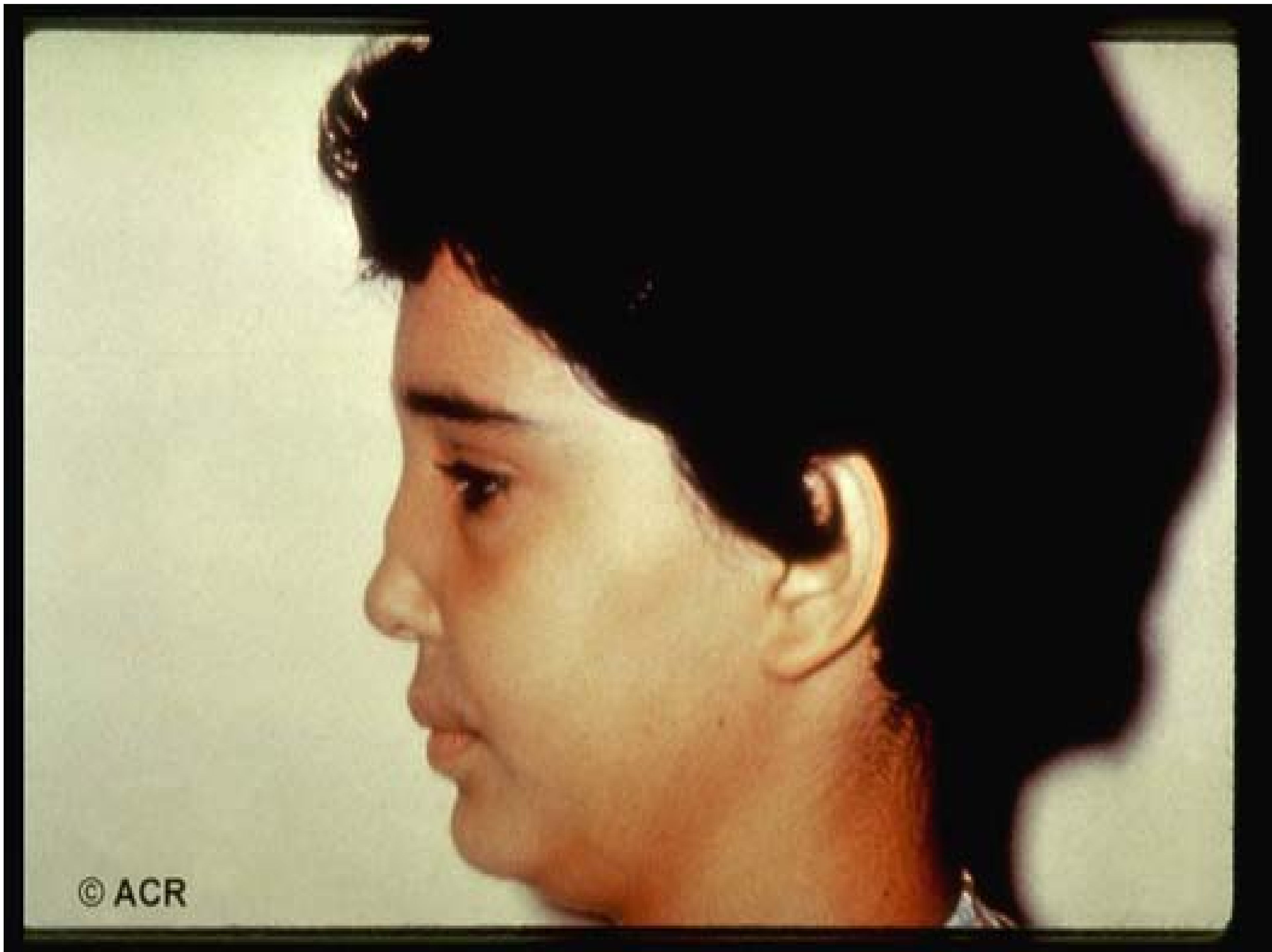
- Rare….but on the boards
- Asthma ,eosinophilia ,pulmonary infiltrates, allergic rhinitis
- Asthma usually precedes others
- RX…prednisone, cytoxan……interferon alpha

Wegener's

- Aseptic inflammation
- Granuloma and vasculitis
- Small and medium vessels involved
- Musculoskeletal features common but joint deformity is rare
- limited forms exist
- c-anca useful in diagnosis

Clinical features

- Neither renal nor lung involvement is common at presentation
- But will develop in 70-80%
- Presentation = upper or lower airway symptoms
- Epistaxis and mucosal ulceration
- Otolaryngeal symptoms
- Pulmonary infiltrates or nodules
- Pauci-immune GN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Prognosis of WG

- Initially lethal
- Prednisone ……one year survival
- Cytoxan per NIH protocol….91% marked improvement and 75% achieved remission
- 44% had >5year remissions

C-ANCA

- Indirect immunofluorescence
- c-Anca
- 90% sensitive for systemic in active stage of disease
- Antigen is proteinase 3
- Found in other vasculitides rarely

Treatment

- NIH protocol=gold standard
- Cytoxan and prednisone
- WCC>3.0
- One year remission= cytoxan cessation
- Increased awareness of cytoxan toxicity….bladder cystitis (50%)and cancer 5% at 10 year follow-up….hematuria= strong prognosticator
- Infections ….Pneumocystis in 6%

Alternatives to cytoxan

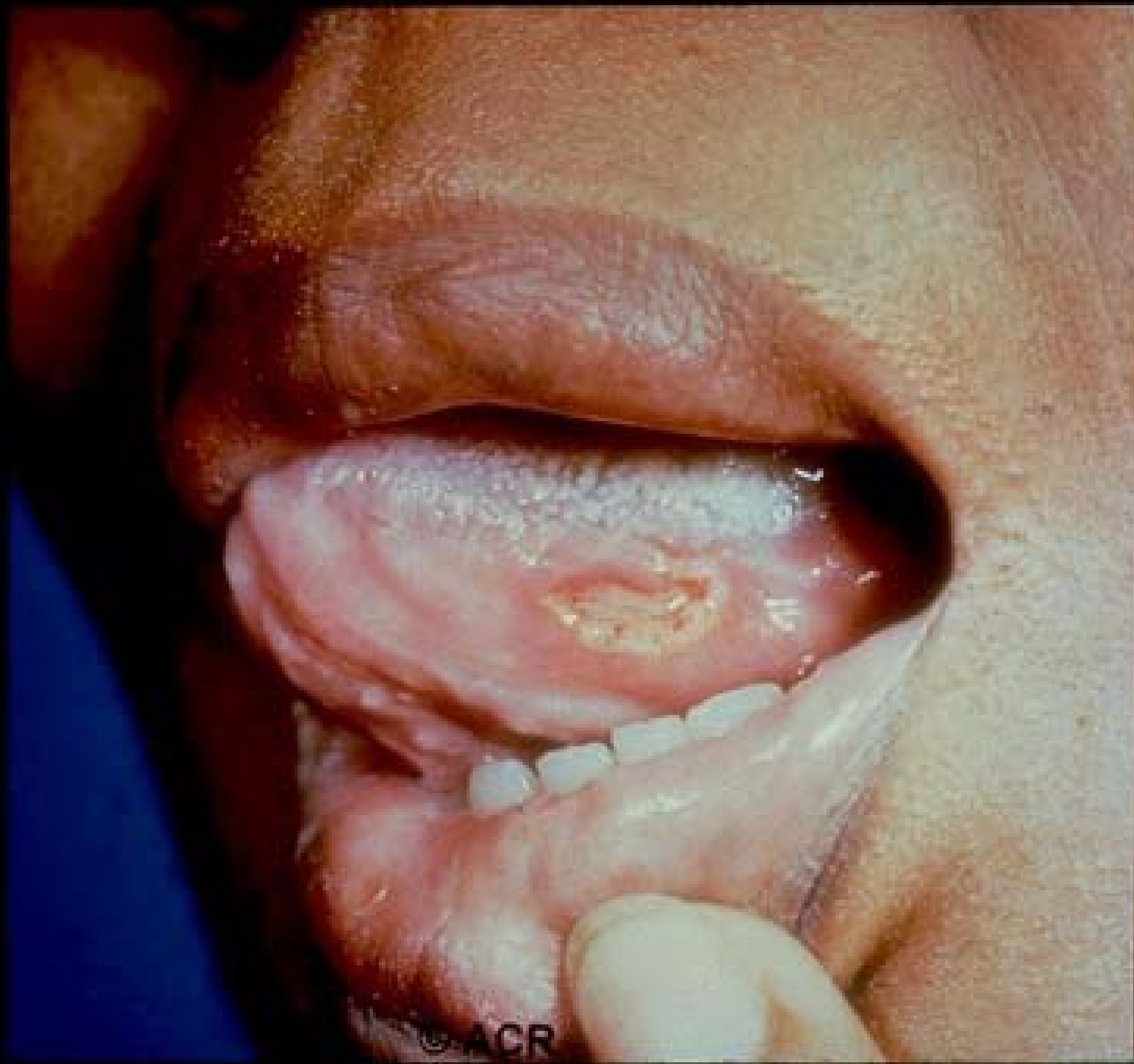
- IV- cytoxan
- Bactrim
- Methotrexate

Vasculitis associated with CTD's

- RA…..LCV in 10 -15% and rare medium –vessel involvement
- SLE
- Sjogrens …usually LCV
- Scleroderma = CASE REPORT

Behcet 's disease

- Recurrent oral ulcerations
- Recurrent genital ulceration
- Eye lesions….anterior and posterior uveitis, hypopyon
- Skin …..E.Nodosum, folliculitis
- Pathergy
- Large vessel….arterial and venous….pulmonary arterial bed
- GI abdominal pain…distal ilium
- GN and peripheral neuropathy= rare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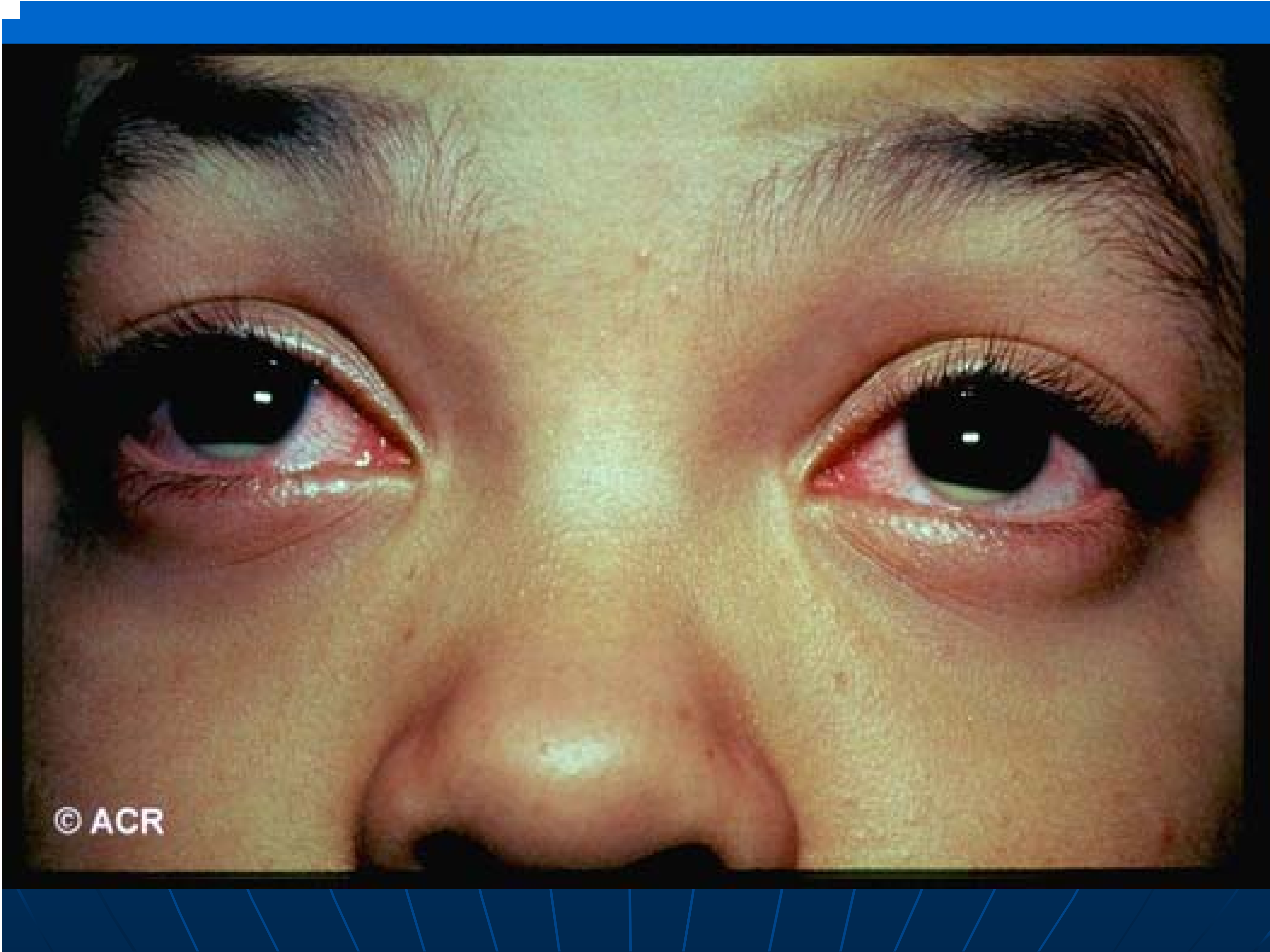
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Treatment

- Apthous lesions…colchicine, thalidomide
- Azathioprine for occular
- Cyclosporine

Cryoglobulins

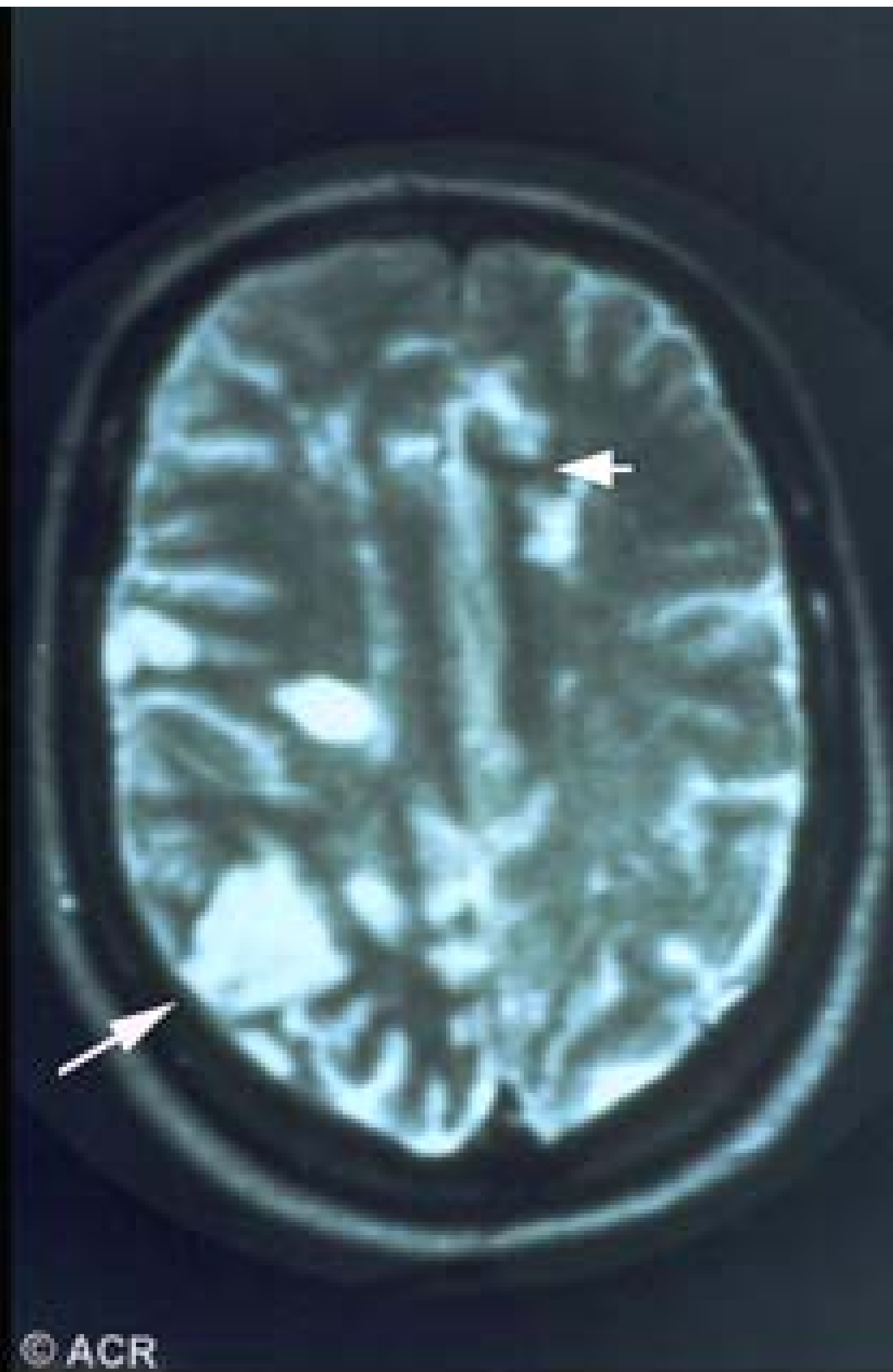
- Type 1 monoclonal myeloma
- Type 2 IgM is monclonal….neoplasm and hep C and connective tissue disease processes
- Type 3 IgM is polyclonal
- Hep C accounts for 80% of mixed cryoglobulins
- Palpable purpura, arthralgias, GN
- mononeuritis

Primary angiitis of the CNS

- Granulomatous 20%... Progressive focal and diffuse deficits with abnormal CSF….biopsy with high yield
- Benign angiopathy….young women..variable outcome..occasional vasoconstriction…30%
- 50% do not fit
- Look for a secondary cause… infections eg. Zoster and HIV…drugs that induce vasospasm…and CTD’s

Granulomatus Angiitis of the Central Nervous System

- Slowly progressive…prodrome of 6 months
- Additive focal and diffuse neurological deficits
- Abnormal CSF inevitable….mononuclear cell pleocytosis, increased protein and normal glucose
- Normal angiogram in 40%
- Normal CSF and normal MRI excludes the diagnosis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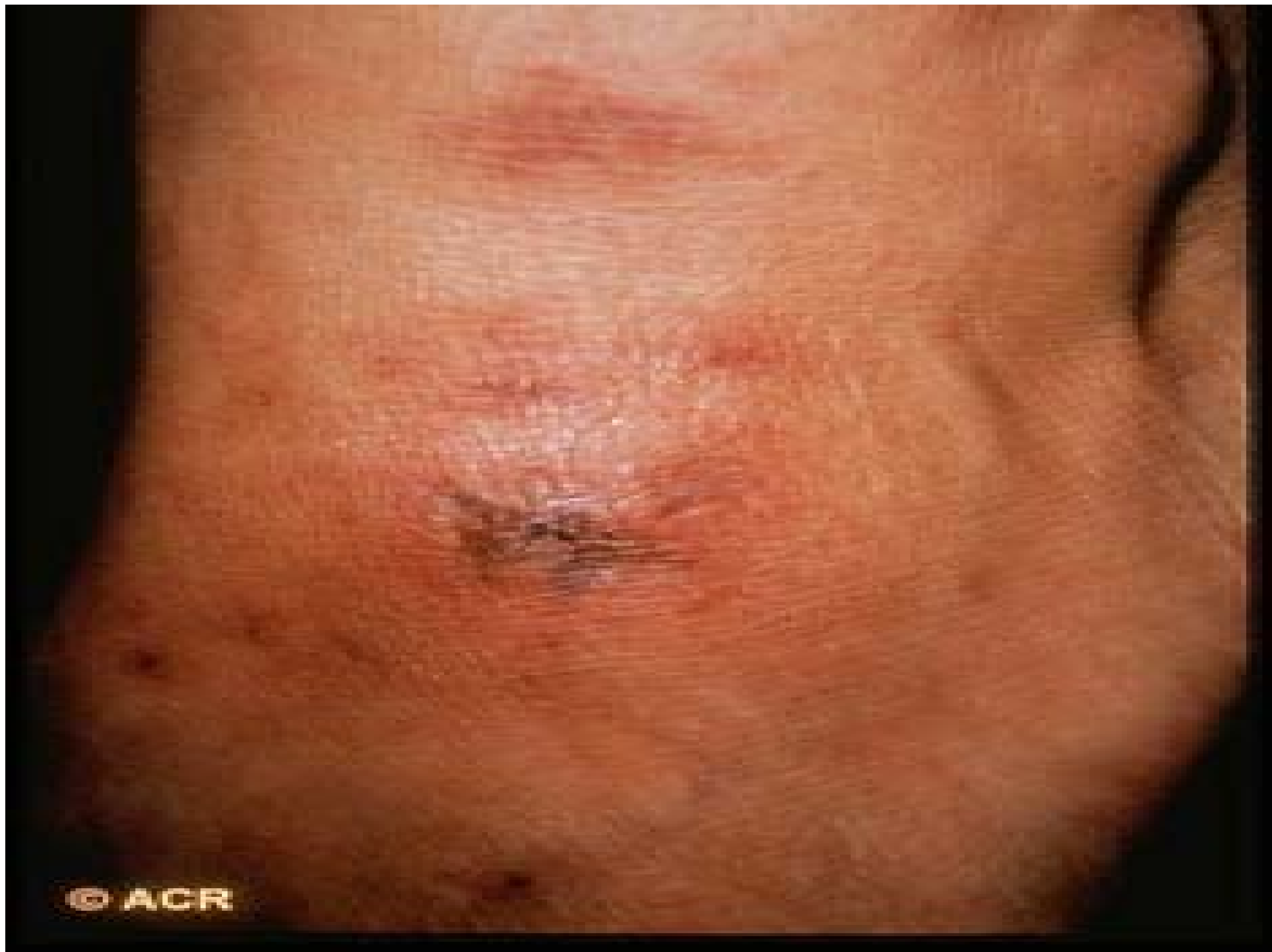
Thromboangiitis Obliterans

- Non necrotizing vasculitis
- Cause unknown
- Affects all populations…19-45 years
- Arms and legs…..claudication
- Amputation of limb but not lethal
- RX = alcohol abstinence

Small vessel vasculitis

- Cutaneous leukocytoclastic angiitis
- Henoch-Schonlein Purpura
- Cryoglobulinemic vasculitis
- Paraneoplastic
- Urticarial vasculitis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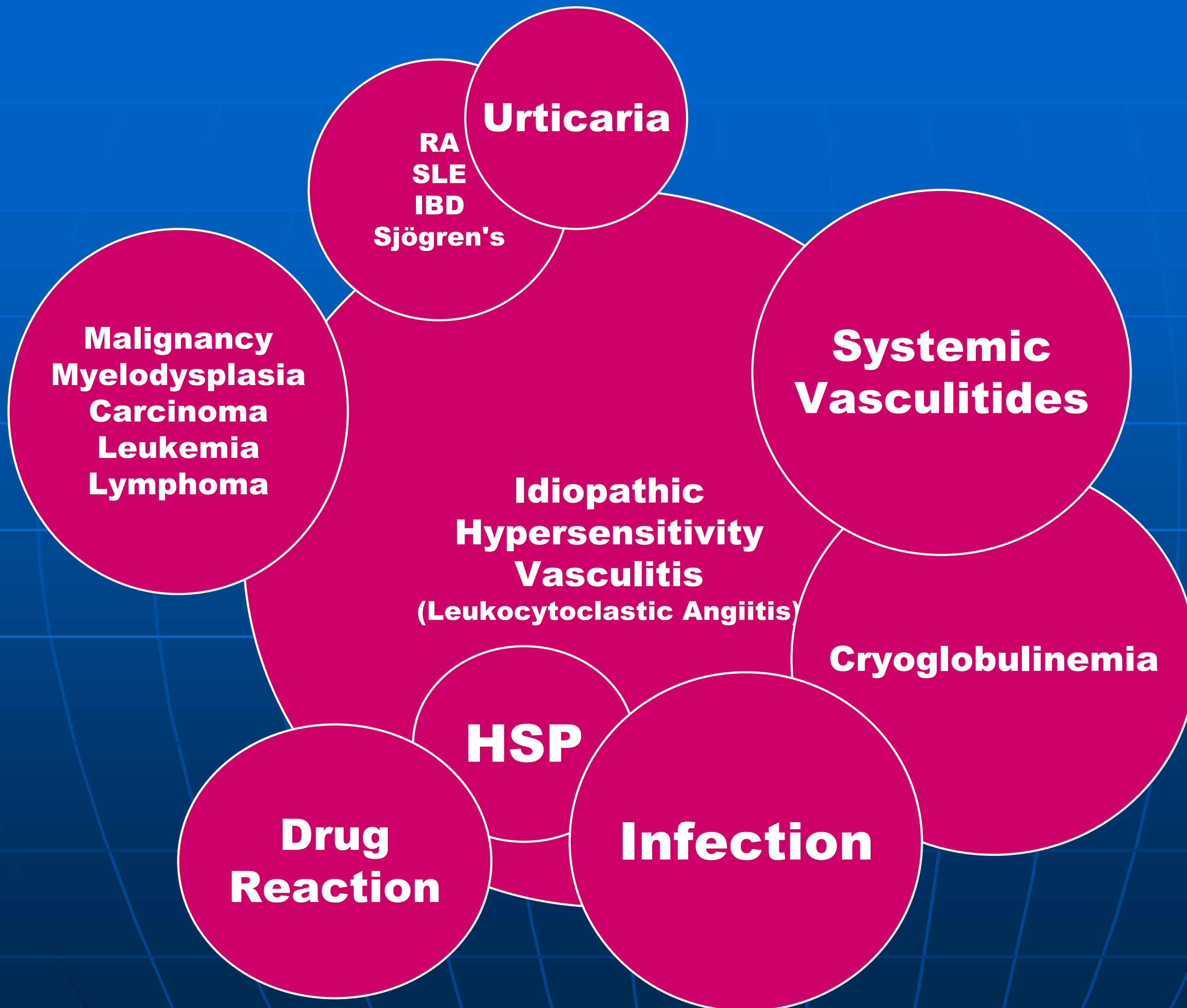
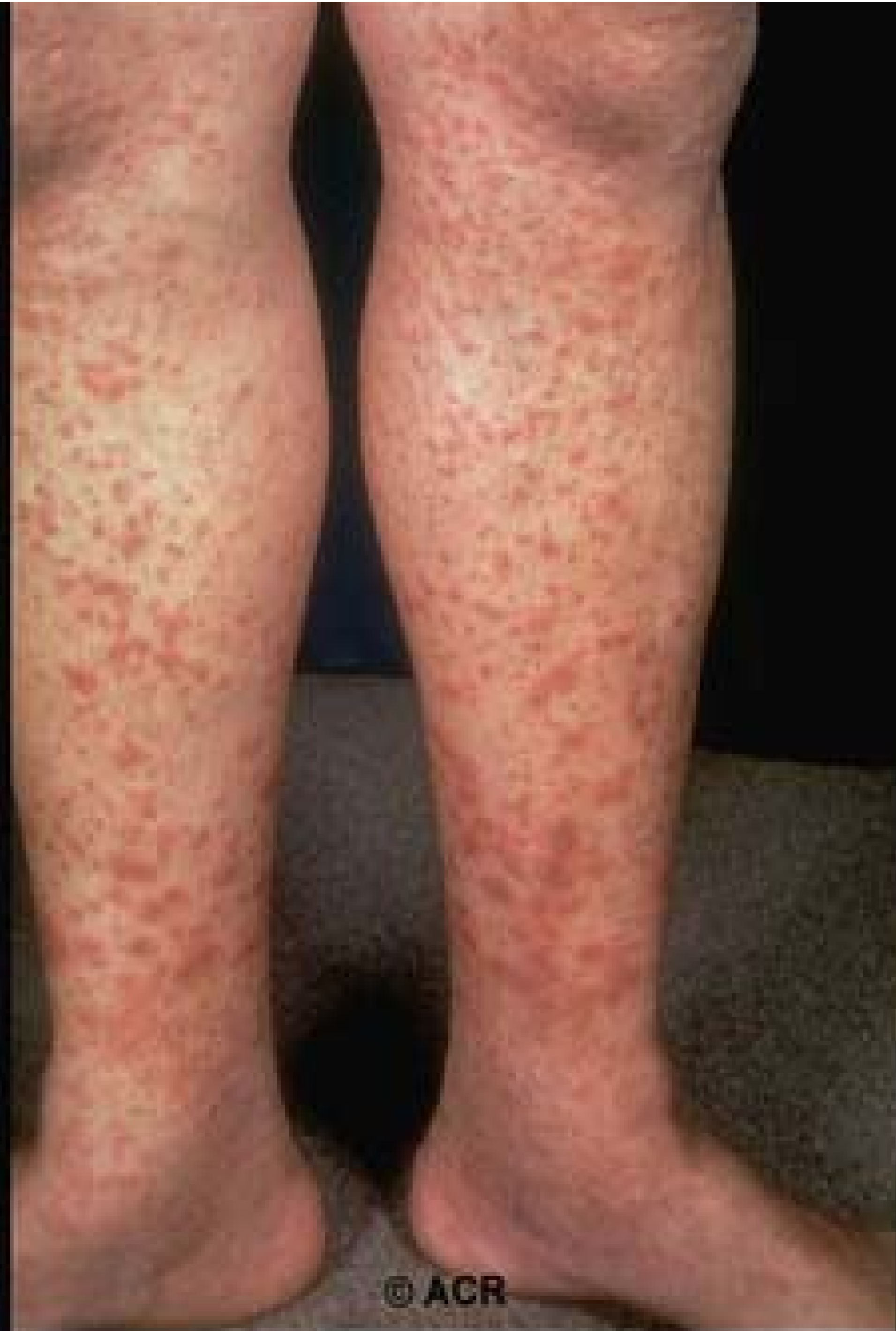

Urticaria
RA
SLE
IBD
Sjögren's
Malignancy
Myelodysplasia
Carcinoma
Leukemia
Lymphoma
Systemic Vasculitides
Idiopathic
Hypersensitivity
Vasculitis
(Leukocytoclastic Angiitis)
Cryoglobulinemia
HSP
Drug Reaction
Infection

ACR Classification Criteria: Hypersensitivity Vasculitis*

1. Age >16 Years at Disease Onset
2. Medication at Disease Onset
3. Palpable Purpura
4. Maculopapular Rash
5. Biopsy Including Arteriole and Venule With Granulocytes in Perivascular or Extravascular Location

*Must Have 3/5 Criteria.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Henoch-Schonlein Purpura

- Purpura, arthritis, abdominal pain and GN
- IgA deposition
- 90%=age<10
- Children=milder
- Adults with GN…13% renal failure

Cryoglobulinemic Vasculitis

- Type 1……monoclonal and lack RF….myeloma
- Type 2…..mixed because contain IgG and IgM=RF…monoclonal…hep C, neoplastic and connective tissue diseases
- Type 3…IgM=polyclonal…circulating immune complexes

Clinical features

- Purpura
- Weakness
- Arthralgias
- Raynaud's
- Neuropathy
- GN

Treatment

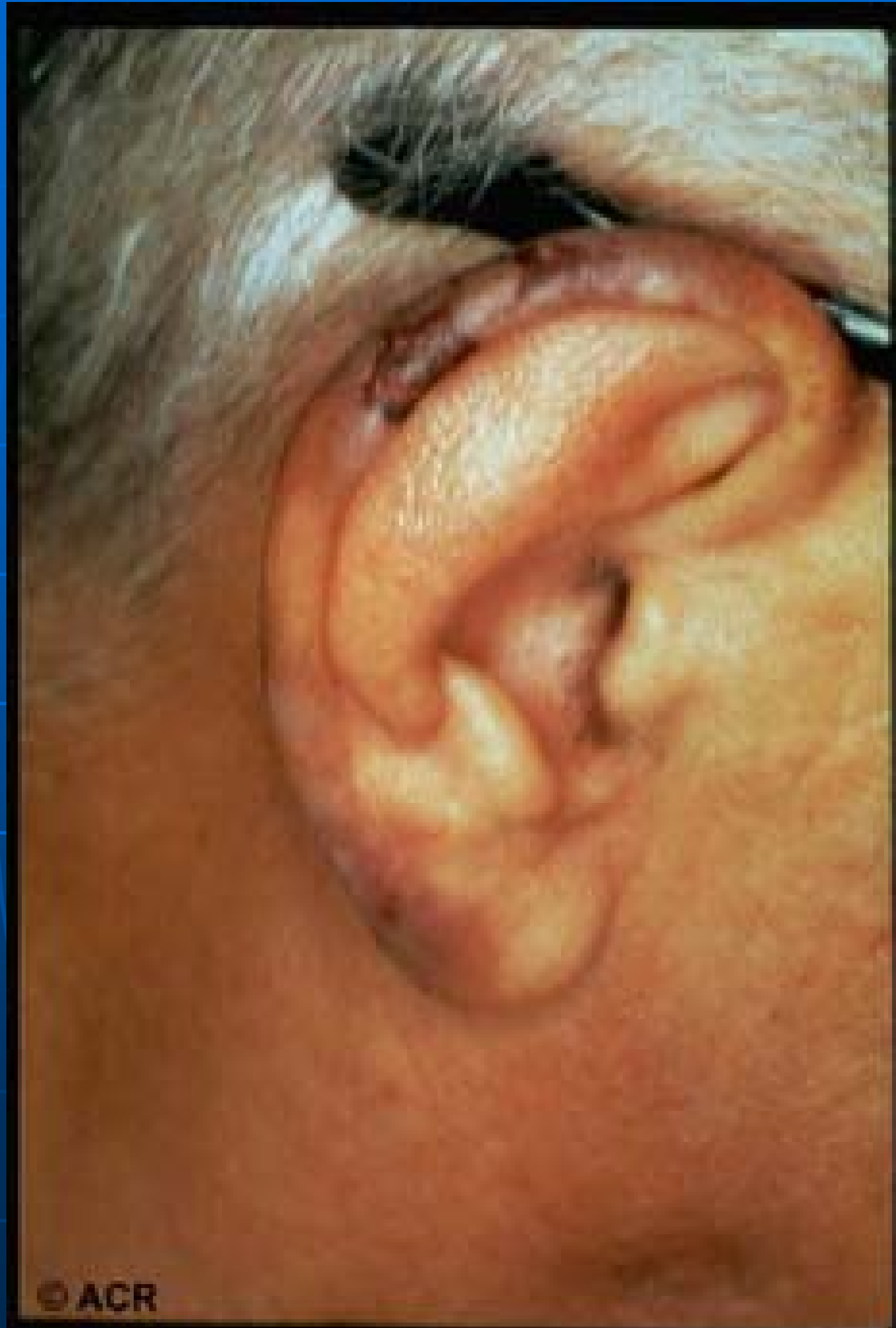
- Treat Hep C
- Prednisone and/ or cytoxan

Paraneoplastic

- T–cell lymphomas
- Rare

Urticarial vasculitis

- Lupus, sjogren’s and mixed cryoglobulinemia
- Biopsy reveals C1q
- Angioedema
- Arthritis
- GN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Good luck

- You will need it!???