EMERGENCIES IN RHEUMATOLOGY

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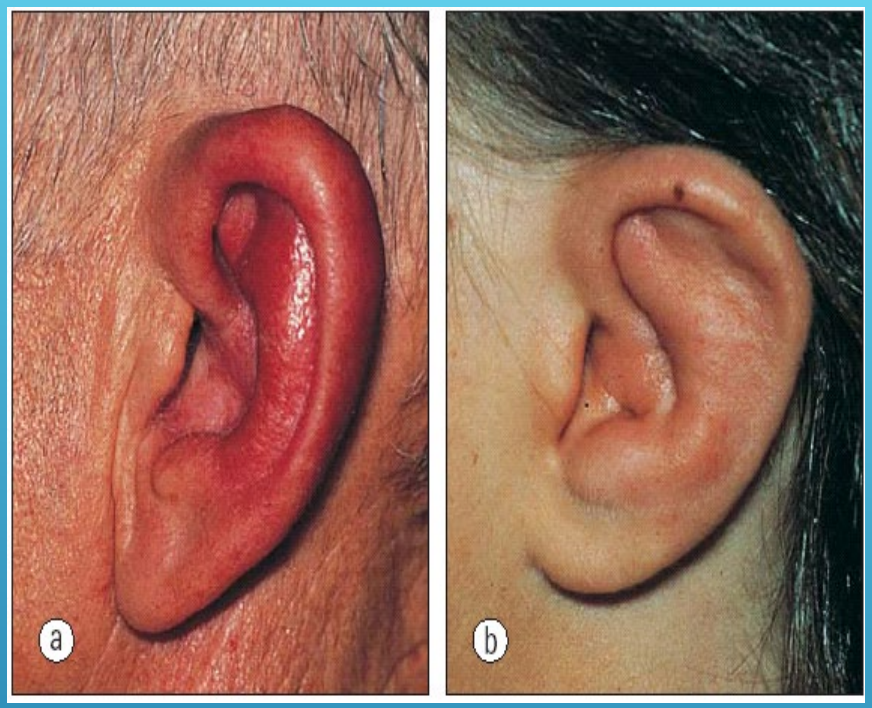
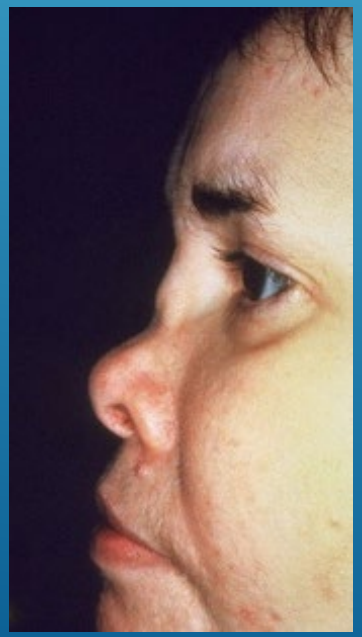
SECTION OF RHEUMATOLOGY

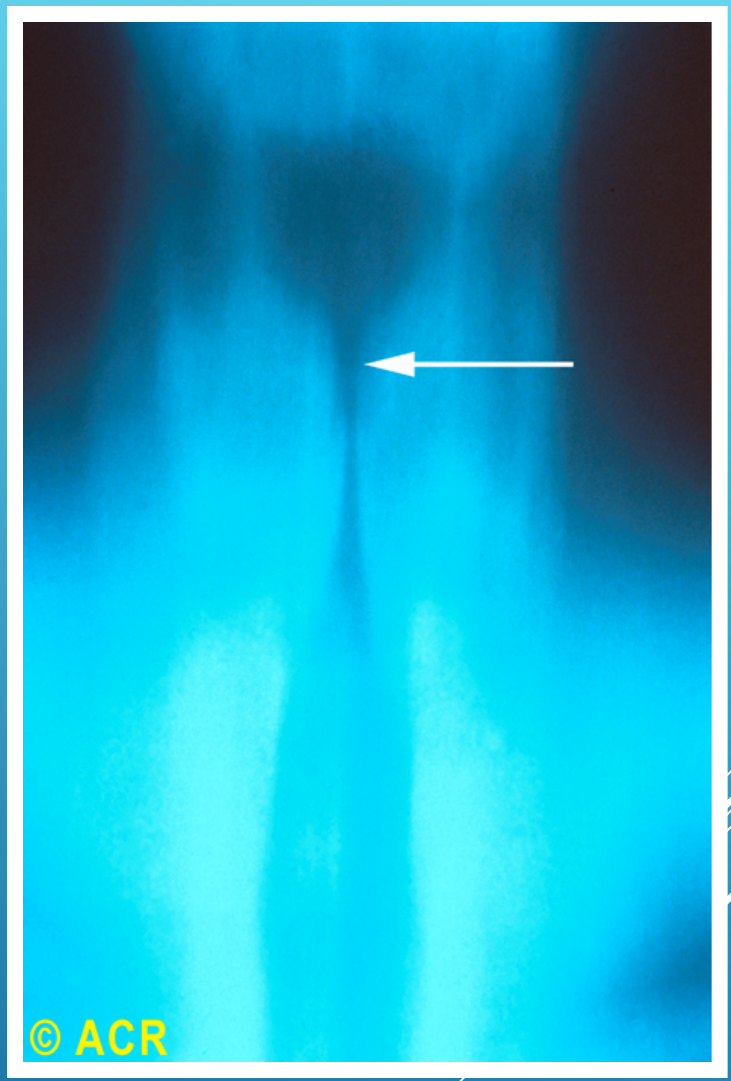
Difficulty Breathing

DIFFICULTY BREATHING – CASE 1

- A 45-year-old woman presents to the emergency room with glottic and subglottic inflammation and edema, requiring an urgent tracheostomy. She's treated with antibiotics, but cultures of the pharynx and larynx are thus far negative. Three days earlier, she developed pain and swelling of her nose. During the past year, she has had episodes of ear swelling and recurrent pain and swelling in the knees.
- On physical examination, a tracheostomy is in place, and she is afebrile. The joints show no swelling or limitation. There is swelling, redness, and warmth over the distal half of the nose. The remainder of the examination is normal.
- Laboratory studies
  - Leukocyte count - 11,000/μL Serum creatinine - 0.6 mg/dL
  - P-ANCA - 1:160 (positive) C-ANCA – Normal
  - Urinalysis – Normal Chest radiograph – Normal


a
b

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WHAT IS THE MOST LIKELY DIAGNOSIS?

A. Granulomatosis with polyangiitis
B. Systemic lupus erythematosus
C. Rheumatoid arthritis
D. Relapsing polychondritis
E. Polyarteritis nodosa

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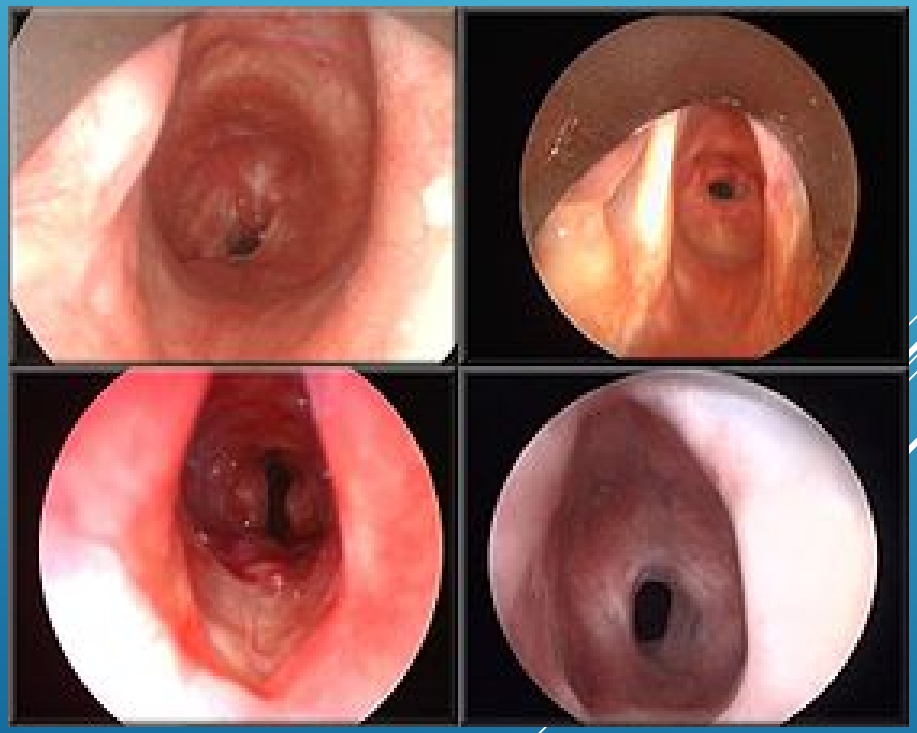
RELAPSING POLYCHONDRITIS

EPISODIC INFLAMMATION OF HYALINE CARTILAGE

- Ears and/or nose common
- Larynx and tracheal cartilage - life-threatening
- Non-erosive arthritis
- Eyes (scleritis)
- Aortic regurgitation
- Panniculitis of skin



Which of the conditions below is LEAST likely to cause stridor?

A. Rheumatoid arthritis
B. Complement mediated angioedema
C. Granulomatosis with polyangiitis
D. Inflammatory myopathy
E. Ankylosing spondylitis

Which of the conditions below is LEAST likely to cause stridor?

A. Rheumatoid arthritis
B. Complement mediated angioedema
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D. Inflammatory myopathy
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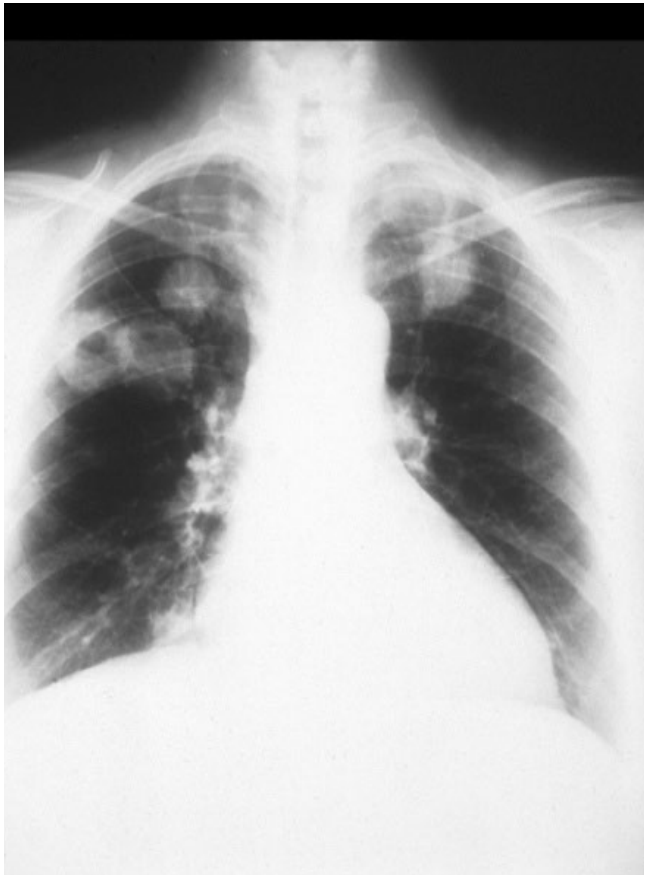
Rheumatologic causes of stridor

- Rheumatoid arthritis - crico-arytenoid synovitis
- Complement mediated angioedema - mucosal edema (C1s inh def, low C4)
- Granulomatosis with polyangiitis - laryngotracheitis, tracheomalacia
- Inflammatory myopathy - pharyngo/laryngeal muscle weakness

DIFFICULTY BREATHING – CASE 2

A 25-year old man presents with a one month history of fever, malaise and arthralgia, and recent cough, SOB and hemoptysis. Chest Xray shows multiple pulmonary infiltrates.



ESR 110,
Hct 25%,
WBC 10,000, normal diff,
Platelets 450,000.
Urinalysis 10-20 RBCs,
RBC casts, 3+ protein,
CRE 3.5 mg/dl, BUN 55
ANA 1:20, C3 170 (nl 75-150)

WHICH OF THE FOLLOWING IS TRUE ABOUT THIS MAN?

A. A positive p-ANCA (anti-myeloperoxidase) test would support a diagnosis of microscopic polyangiitis

B. Systemic lupus erythematosus is the most likely diagnosis

C. A renal biopsy would be diagnostic for granulomatosis with polyangiitis

D. Polyarteritis nodosa often presents with this clinical picture

E. Goodpasture's syndrome is an unlikely diagnosis

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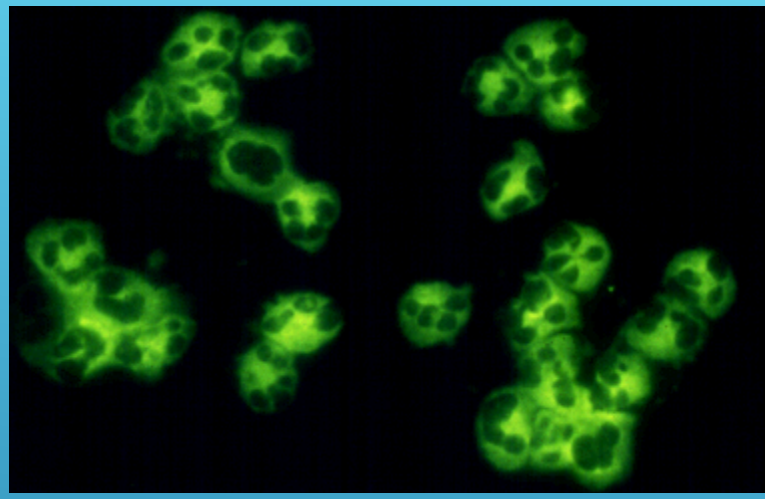
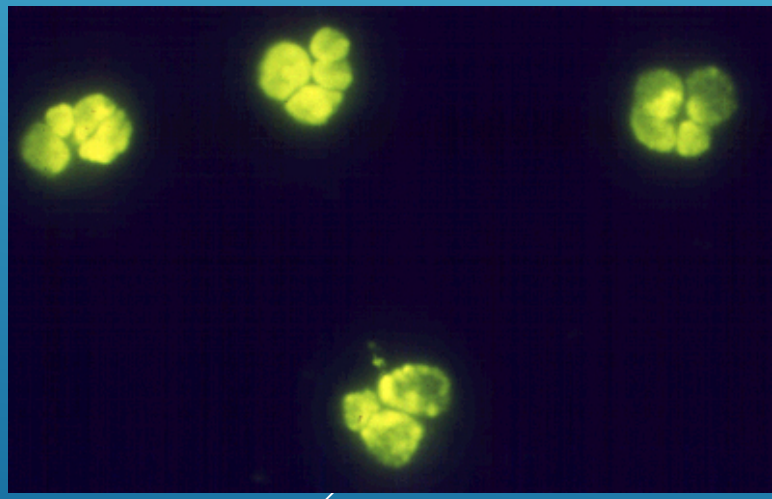
ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY



- *c-ANCA - anti-proteinase 3 (PR-3)
  - GPA, pauci-immune GN
- *p-ANCA - anti-myeloperoxidase (MPO)
  - microscopic polyangiitis (MPA)
  - pauci-immune GN (RPGN)
  - EGPA, (CS)
- * *rarely occur together*



PULMONARY/RENAL "VASCULITIC" SYNDROMES

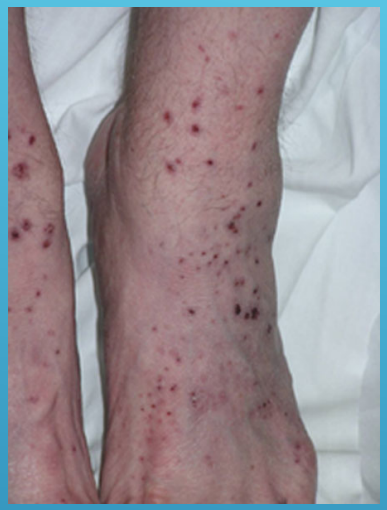
Diffuse Alveolar Hemorrhage (pulmonary capillaritis) + Renal disease

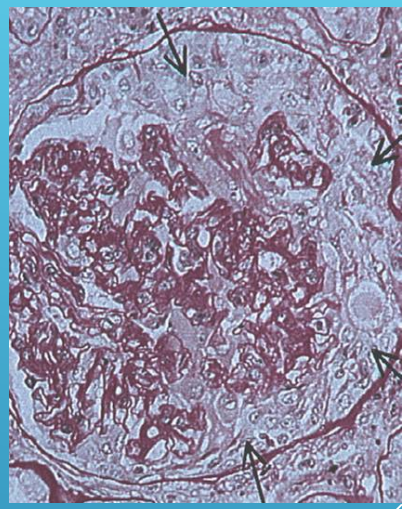
- MPA, EGPA: p-ANCA (anti-MPO) – pauci-immune GN
- GPA: c-ANCA (anti-Pr3) –pauci-immune GN
- GOODPASTURE'S: anti-GBM Ab – Ab-mediated GN
- CTD (SLE): ANA – immune complex GN
- CAPS: Antiphospholipid antibody – microangiopathy/ischemic glomerulopathy

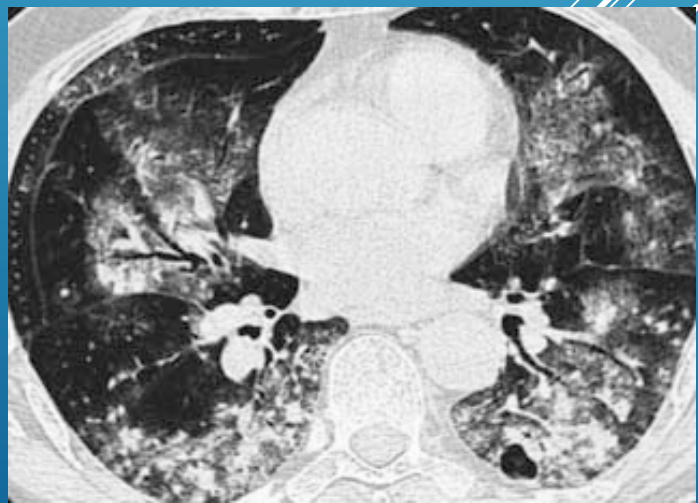
plasmapheresis + immunosuppressive Rx

MICROSCOPIC POLYANGIITIS (MPA)
CLINICAL FEATURES

Constitutional symptoms	76-79%
Fever	50-72%
Renal disease	99%
(pauci-immune crescentic GN)	
Arthralgias	28-65%
Purpura	40-44%
Pulmonary disease	50%
(hemorrhage, infiltrates, effusion)	
Neurologic disease	28%
(central, peripheral)	
Ear, nose, throat	30%



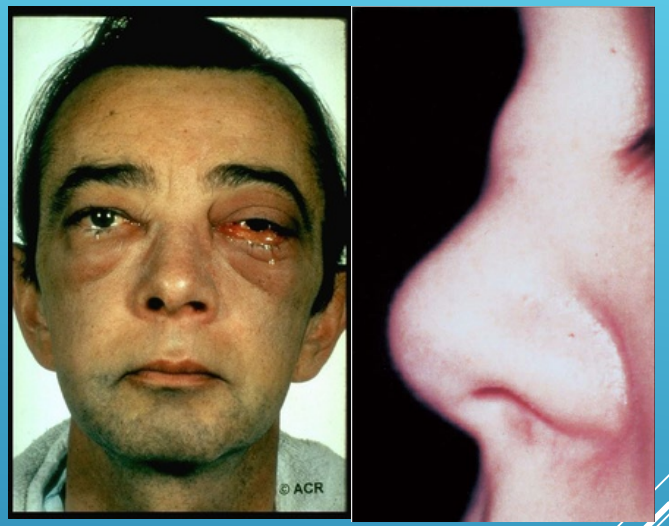


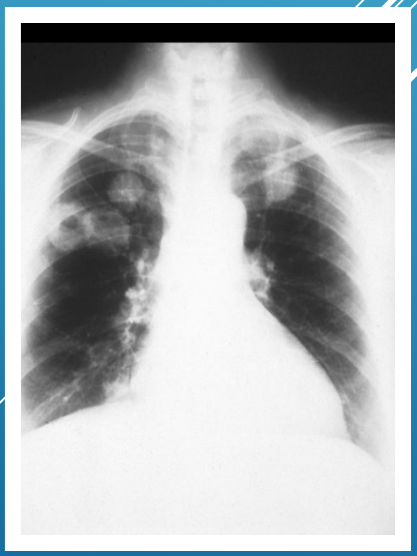


GRANULOMATOSIS WITH POLYANGIITIS
CLINICAL FEATURES (85 PTS, 21YRS -NIH)

Lung - nodules, infiltrates, cavitary lesions, hemorrhage	>90%
Upper airway - sinuses, nasopharynx, otitis, subglottic stenosis	>90%
Renal - focal to diffuse necrotizing GN, RPGN* - pauci-immune GN	85%
Joints - arthralgia/arthritis	67%
Eye - episcleritis, uveitis, vasculitis, pseudotumor	58%
Skin - HSV, nodules, ulcers	45%
Nervous system -mononeuritis multiplex, cranial neuropathies	22%

* resp + renal = generalized GPA





ARDS IN RHEUMATIC DISEASES

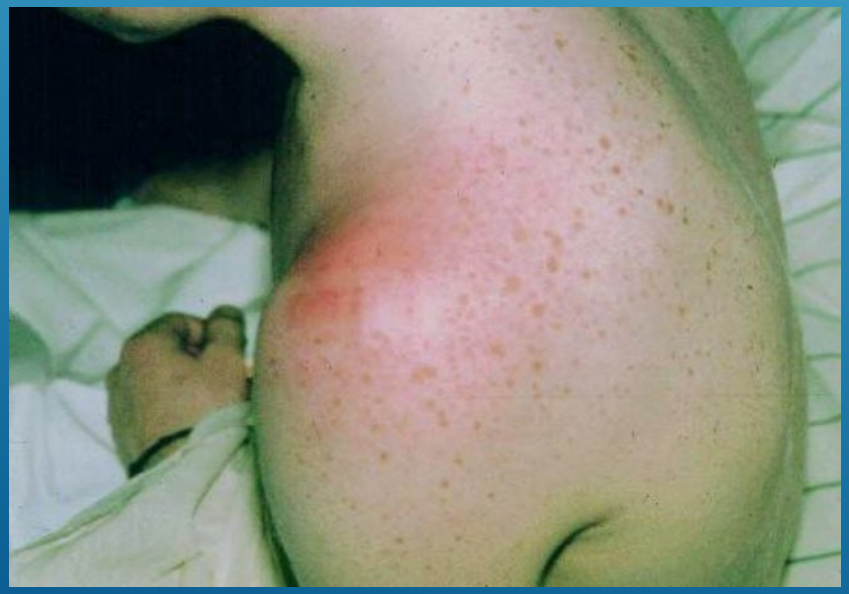
- Scleroderma (diffuse systemic)
- UCTDs (incl Sjogren's syndrome)
- DM/PM (antisynthetase syndrome – Jo-1)
- SLE (pulmonary hemmorhage)
- GPA
- MPA, EGPA
- Rheumatoid arthritis
- Medications (MTX lung)

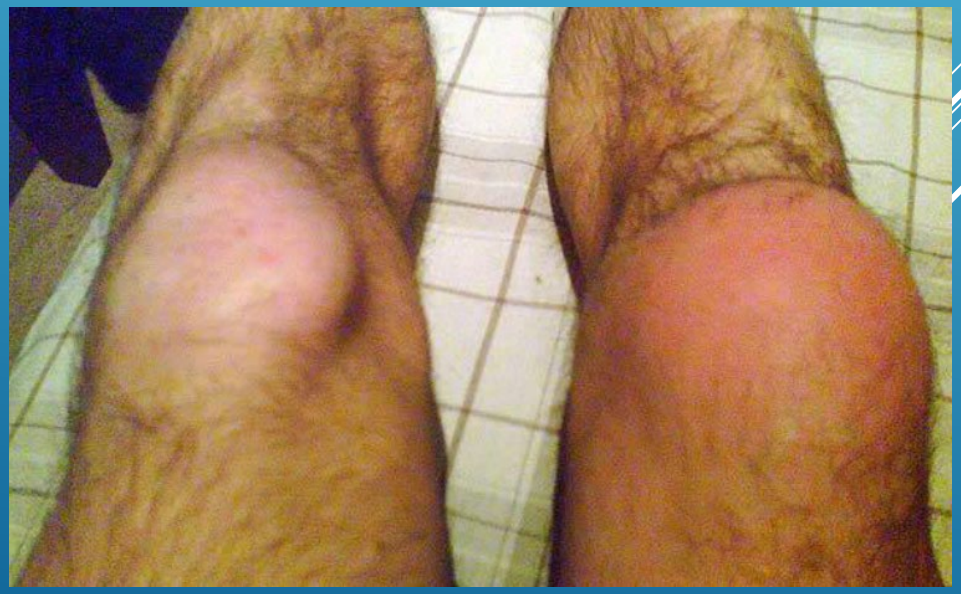
ACUTE JOINT PAIN

ACUTE JOINT PAIN – CASE 3

A 26 years old male with a history of IVDU for 4 years is sent in by GP acutely unwell and confused. He's been also complaining of knee and shoulder pain and swelling for the past 4 days.

Febrile –101F
CRP 35.1
WBC 29K





What is the most likely cause of this patients joint pain?

A. Rheumatoid arthritis
B. Septic arthritis
C. Acute gouty arthritis
D. Acute pseudogout
E. Traumatic arthritis

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Septic Arthritis

- A medical emergency
- 2-10 per 100 000 / year
- 10-22% mortality rate
- Pre-disposing factors:
  - Age >60
  - Diabetes/ Sickle Cell/ Immunosuppression
  - IVDU/ indwelling vascular lines/ invasive procedures
  - Pre-existing joint disease
  - Prosthetic joints
  - Post-intra-articular injection

Septic Arthritis

- Polyarticular in 20%
- Joint problem may not be the 1st presentation
- Some patients may not show 'typical' appearance
- The knee is the commonest joint in adults
- Causative organisms:
  - *Staphylococcus*
  - *Streptococcus*
  - Gram (–) Bacilli
  - *Haemophilus*
  - *N.gonorrhoeae*
  - Anaerobes
  - TB
  - Lyme

Septic Arthritis

- If ever in doubt about the cause of a joint effusion (which should be for EVERY case of MONOarthritis and potentially MANY cases of OLIGO or POLYarthritis) – Aspirate the joint!
- Septic arthritis is an ORTHOPEDOC emergency and needs urgent surgical drainage (with some exceptions).
- Followed by up to 6 weeks of IV antibiotics (depending on causative organism)

PAIN IN THE NECK

PAIN IN THE NECK – CASE 4

- A 68 y/o woman with long standing sero-positive, erosive rheumatoid arthritis presents to your office with complaints of progressive neck pain for the past several months. She has been recently started on anti-TNF therapy for poorly controlled disease and has noted some improvement in her peripheral joint pain, but not the neck.

- On exam, she is afebrile, but ROM in the neck elicits significant discomfort. She denies photophobia or subjective fevers. She manifests weakness of handgrip (3/5), hyperreflexia, and hypertonia. There are multiple subcutaneous nodules on extensor surfaces.

WHICH OF THE FOLLOWING IS THE MOST LIKELY CAUSE OF HER CURRENT CLINICAL PICTURE?

A. Degenerative arthritis of the c-spine
B. Atlantoaxial subluxation
C. Viral meningitis
D. Muscle spasm of the cervical spinal muscles
E. Transverse myelitis

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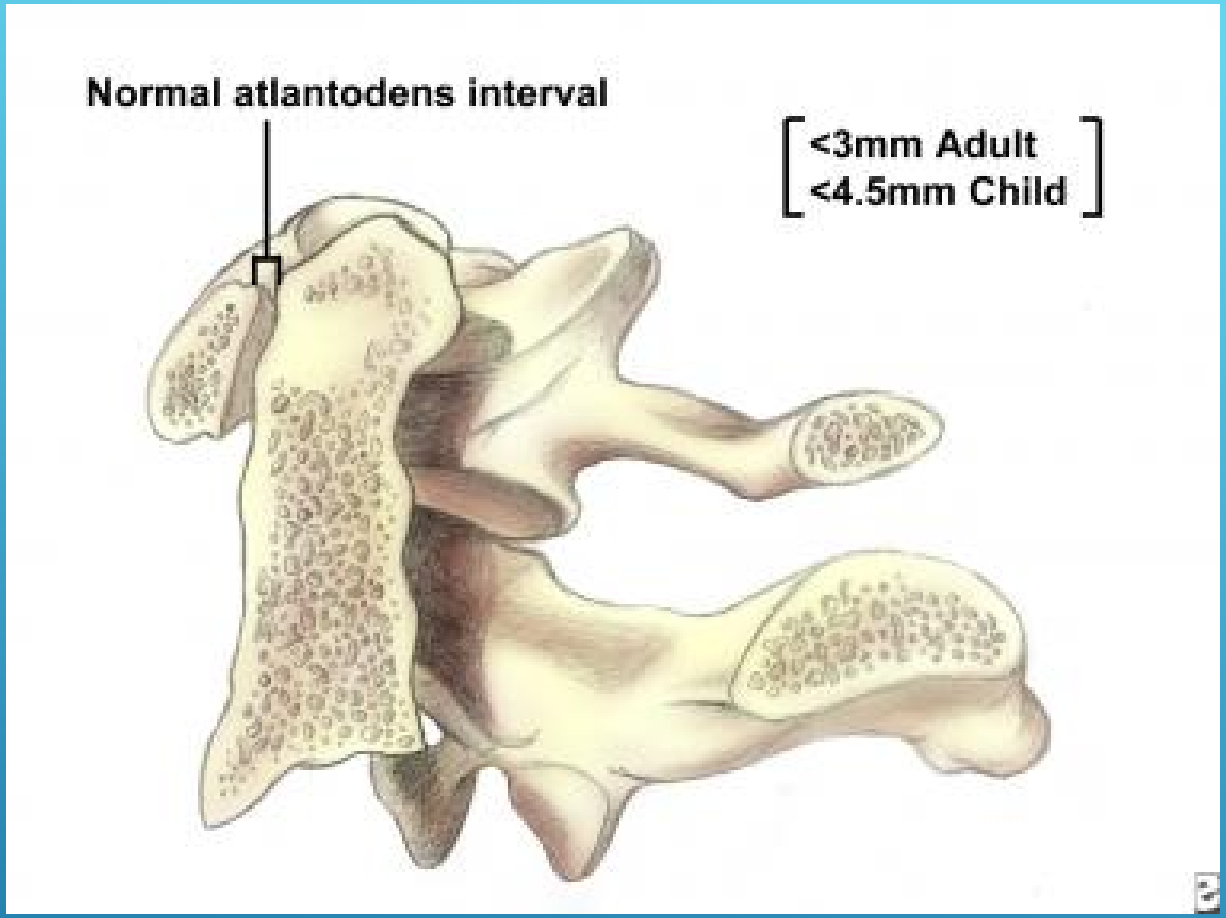
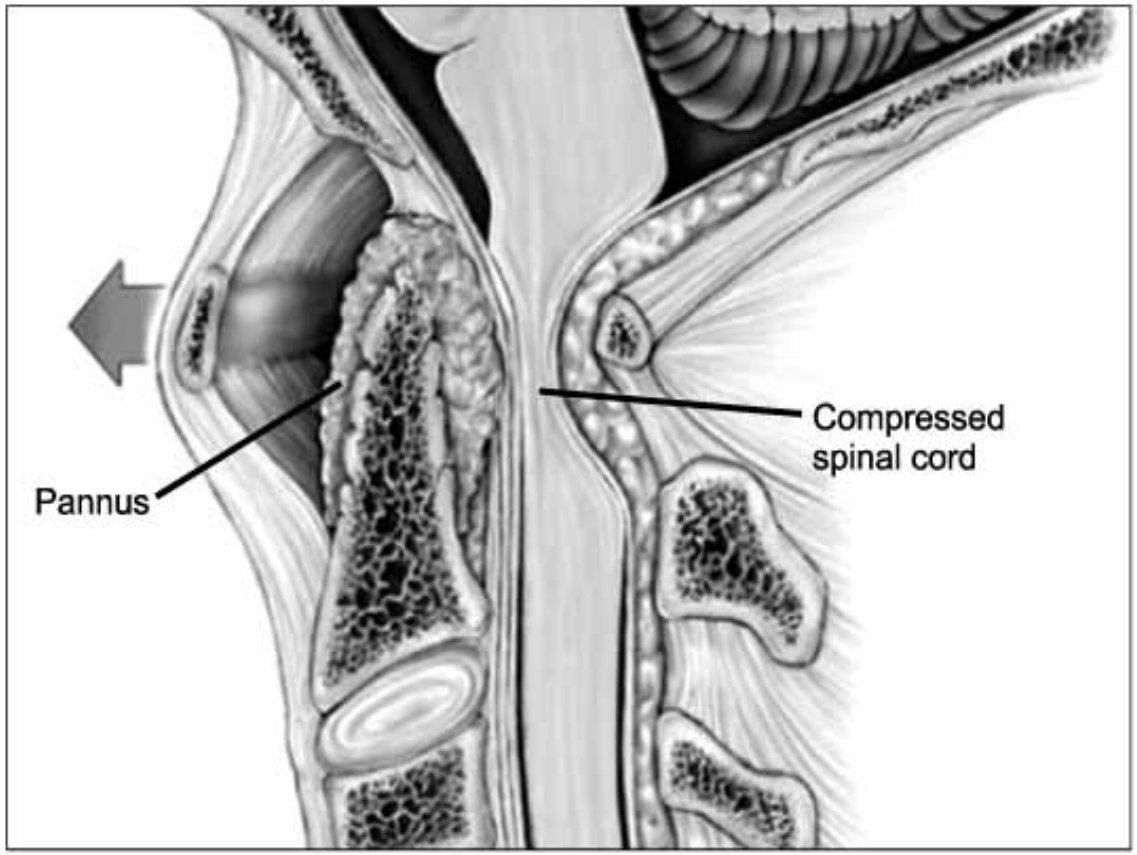
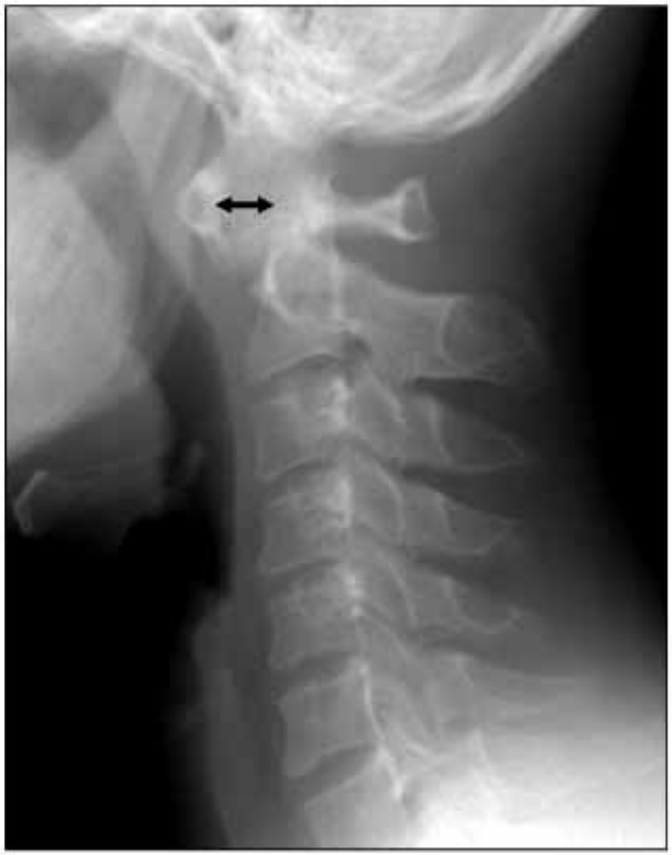


ATLANTOAXIAL DISLOCATION


Compressed
spinal cord
Pannus



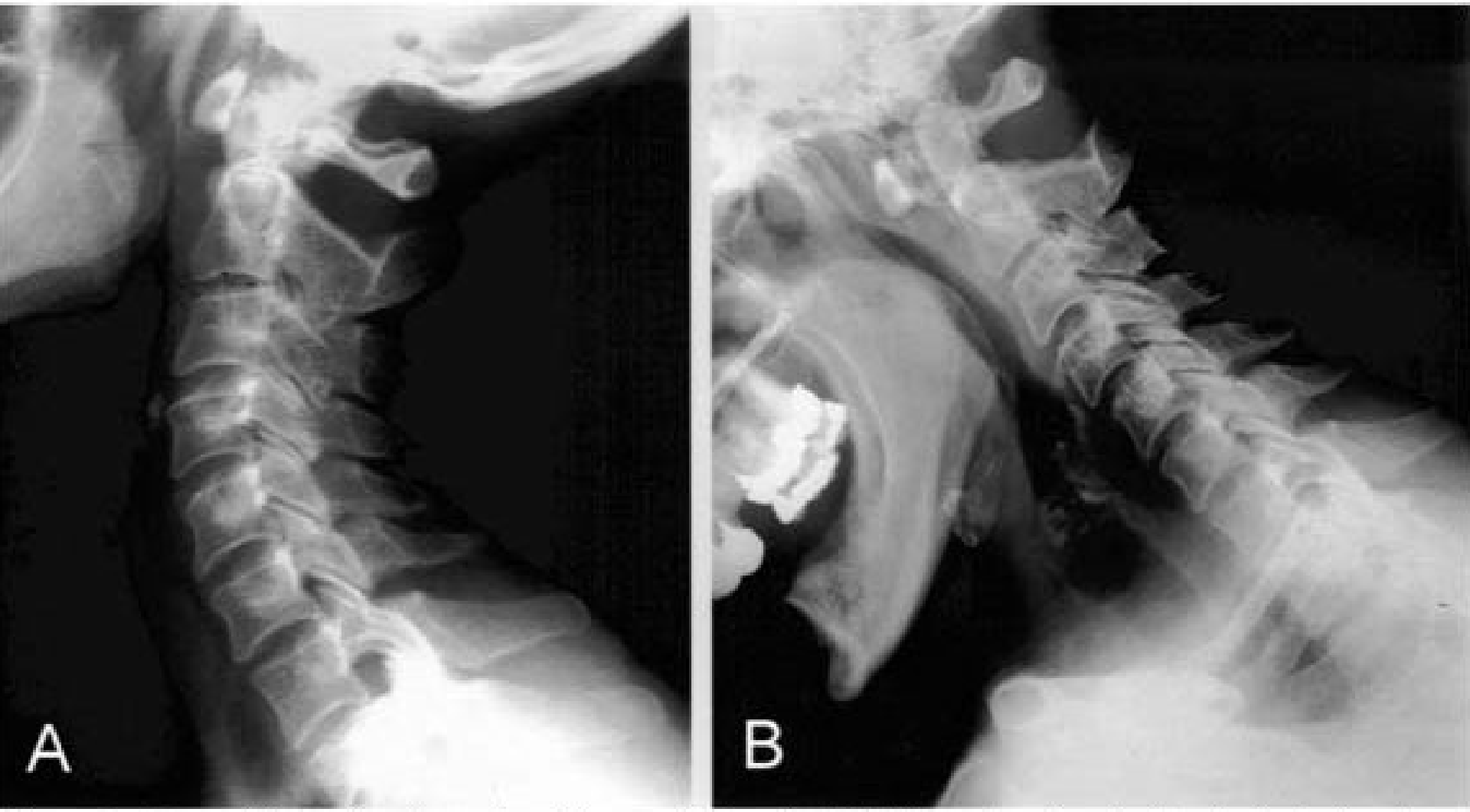


Figure 3 *- Dynamic lateral radiographs of the cervical spine (A- hiperextension; B- hiperflexion), showing atlantoaxial instability*

CERVICAL SPINE IN RA

- The frequency of involvement of the cervical area is 43-86%.
- Symptoms and signs develop in approximately 60-80% of patients with RA at some time during their illness.
  - Pain is the most common
  - Weakness and abnormal mobility can also be evident.
  - Neurologic manifestations occur in 11-58% of patients with RA and include paresthesias, paresis, muscle wasting, quadriplegia, and even sudden death.

CERVICAL SPINE INVOLVEMENT IN RA CORRELATES WITH DISEASE ACTIVITY

Table 2: Comparison between patients with and without cervical spine involvement

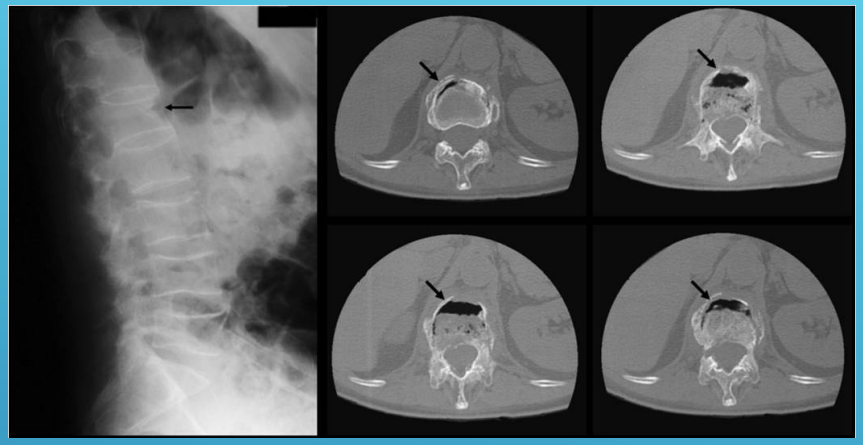
Parameter	Cervical spine involved (N = 32)	Cervical spine not involved (N = 43)	P value
Mean duration of disease (mo.)	105	20.9	<0.0001
Mean tender joint count	19.53	12.46	<0.0001
Mean swollen joint count	7.4	3.0	<0.0001
Rheumatoid nodules	9	3	<0.05
Joint deformities	12	7	<0.05
Extra-articular features	4	0	<0.0001
Rheumatoid factor	32	23	<0.0001
Erosion on Hand X-ray	32	11	<0.0001

ALL PATIENTS WITH RA NEEDING PRE-OP CLEARANCE NEED C-SPINE RADIOGRAPHS WITH FLEXION AND EXTENSION VIEWS!!!!!

OTHER IMPORTANT CAUSES OF NECK/BACK PAIN WITH NEUROLOGICAL FINDINGS

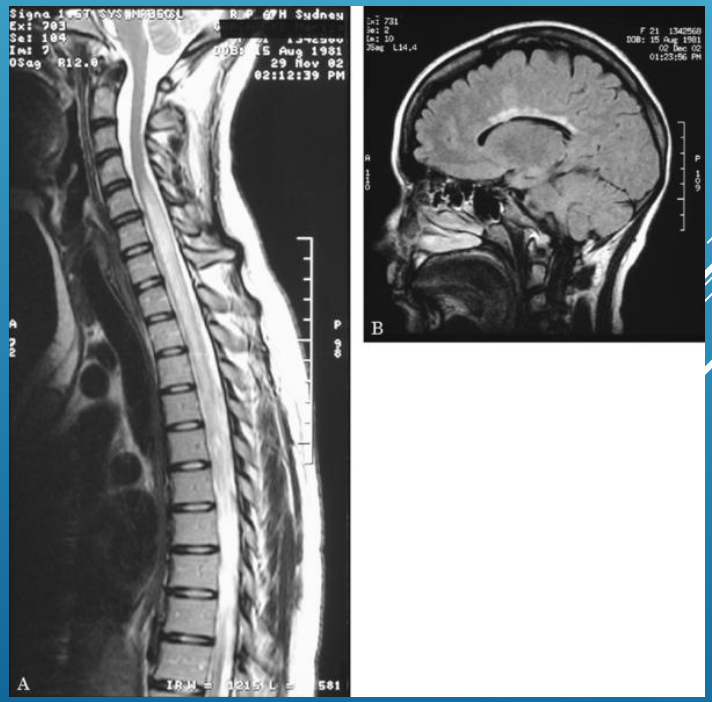
- Ankylosing spondylitis

  - vertebral fracture



- SLE

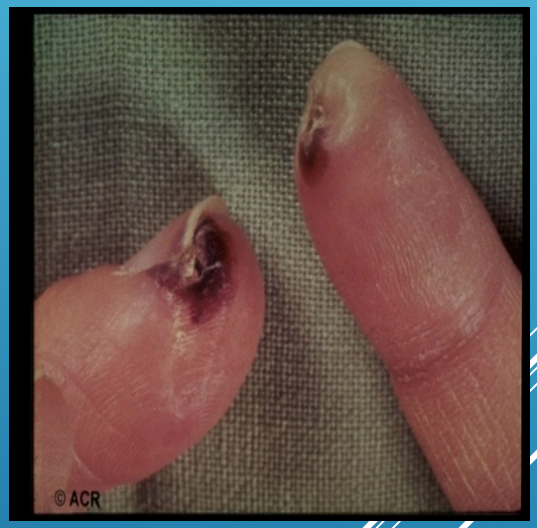
  - transverse myelopathy



Acute Abdominal Pain

ABDOMINAL PAIN – CASE 5

A 55 year man has a 2 year history of intermittent fatigue and joint pains with high acute phase reactants. He has been diagnosed as "atypical polymyagia rheumatica or rheumatoid arthritis". For the past 6 months he has had numbness in the R foot pain and discoloration in some fingers of both hands. For the past 1 month, he has developed weakness of the L foot and ischemic lesions of the fingertips. He presents to the emergency room with severe abdominal pain/tenderness of 1 week duration.



PE: He looks ill. T=99.5. BP 160/100

Tender, guarding mid-abdomen. Guaiac pos stool.

Hands as shown. No active synovitis. L foot drop.

Labs: ESR 90, Hbg 9.5, WBC 12, 500, platelet count 650,000. UA trace protein. BUN 35/creatinine 1.6. ALT 75, AST 55. ANA neg. RF (latex test) 1:4. C3/C4 normal. ANCA neg. Flat plate - some bowel loop dilation. CXR normal. Abdominal ultrasound neg.

THE MOST LIKELY DIAGNOSIS IS?

A. Crohn's disease with vasculitis
B. Polyarteritis nodosa
C. Giant cell arteritis
D. SLE
E. Rheumatoid vasculitis

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THE EMERGENCY TREATMENT OF CHOICE IS?

A. Pulse IV Medrol
B. Pulse IV Medrol plus IV Cytoxan
C. Pulse IV Medrol plus IV Cytoxan plus plasma exchange
D. Pulse IV Medrol plus surgical intervention
E. Pulse IV Medrol plus IVIg

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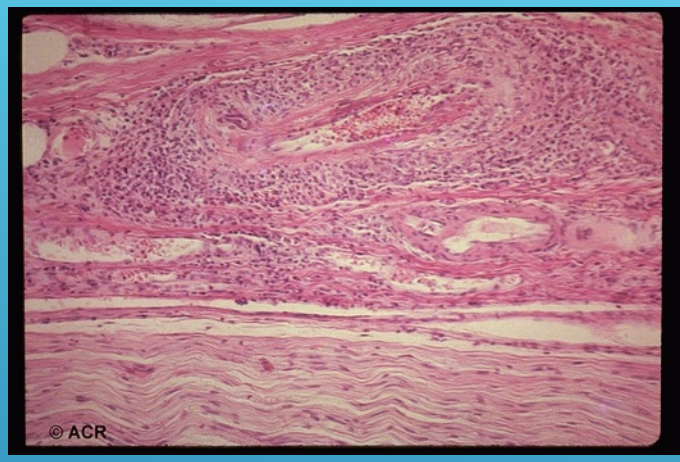
POLYARTERITIS NODOSA
CLINICAL FEATURES

- Peripheral nerve – Mononeuritis multiplex (>50%)
- Skin – Infarcts, ulcers, livedo (25-50%)
- Kidney – Focal necrotizing GN (70%), Renovascular hypertension (35%)
- Joint, muscle – Arthralgias (50%), arthritis (20%), myalgias (50-60%)
- Gastrointestinal – Abdominal pain (ischemic bowel), transaminitis (25-70%)
- Other – Testicular pain (uncommon)
  – Hepatitis B positive (15%)
  – ANCA negative

POLYARTERITIS NODOSA
DIAGNOSIS

- Laboratory clues
  - Inflammation (↑ ESR, ↑ CRP, anemia, ↓ albumin)
  - With Hep B assoc PAN: also should have HBeAg and HBV DNA positive
  - ANCA negative
- Tissue – biopsy accessible and symptomatic tissue (kidney will not be helpful)
- Imaging – mesenteric or renal angiogram



MONONEURITIS MULTIPLEX

- Systemic vasculitis (small, medium vessel)
- CTD (SLE, Sjogren's), cryoglobulinemia with vasculitis
- RA with vasculitis
- Diabetes
- Multiple compression neuropathies
- Sarcoidosis
- Infection - HIV, Lyme disease
- Paraneoplastic

PAN - TREATMENT

- untreated > 80% mortality
- prednisone + cyclophosphamide < 50%

Acute crisis:

pulse (IV) corticosteroids

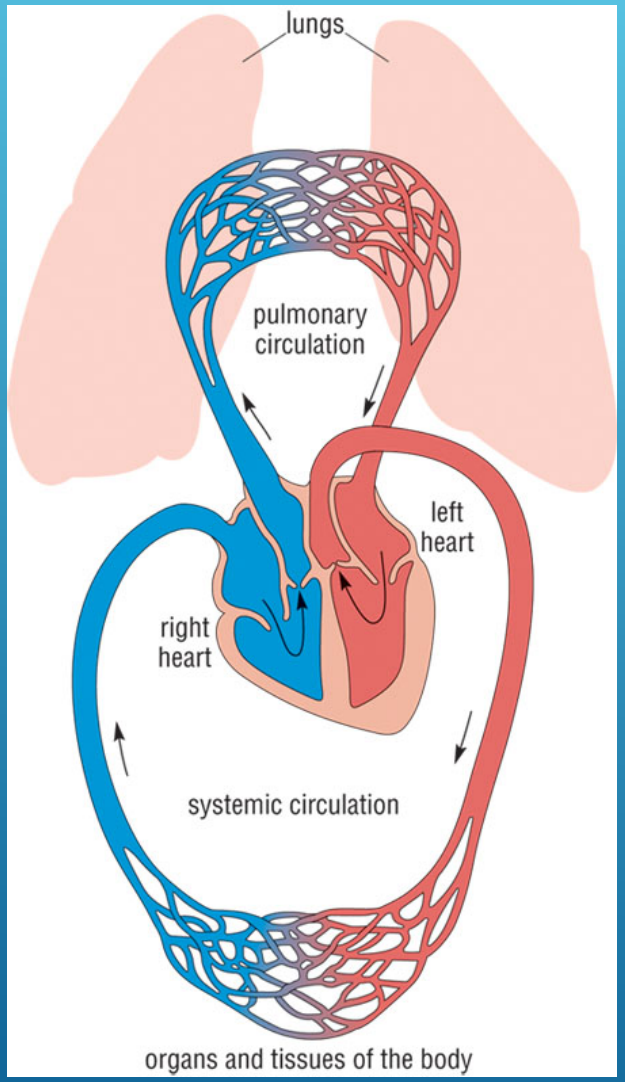
emergency bowel resection

daily IV cyclophosphamide

OTHER CAUSES ACUTE ABDOMINAL PAIN WITH SYSTEMIC RHEUMATIC DISEASES

- SLE – bowel vasculitis/perforation (colon), pancreatitis
- Adult Henoch-Schonlein purpura – vasculitis
- Systemic necrotizing vasculitis – pancreatitis
- Behcet's – mucosal ulceration

Circulatory Issues

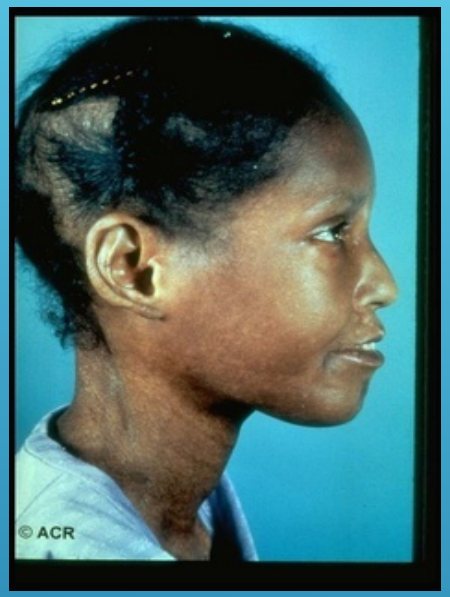


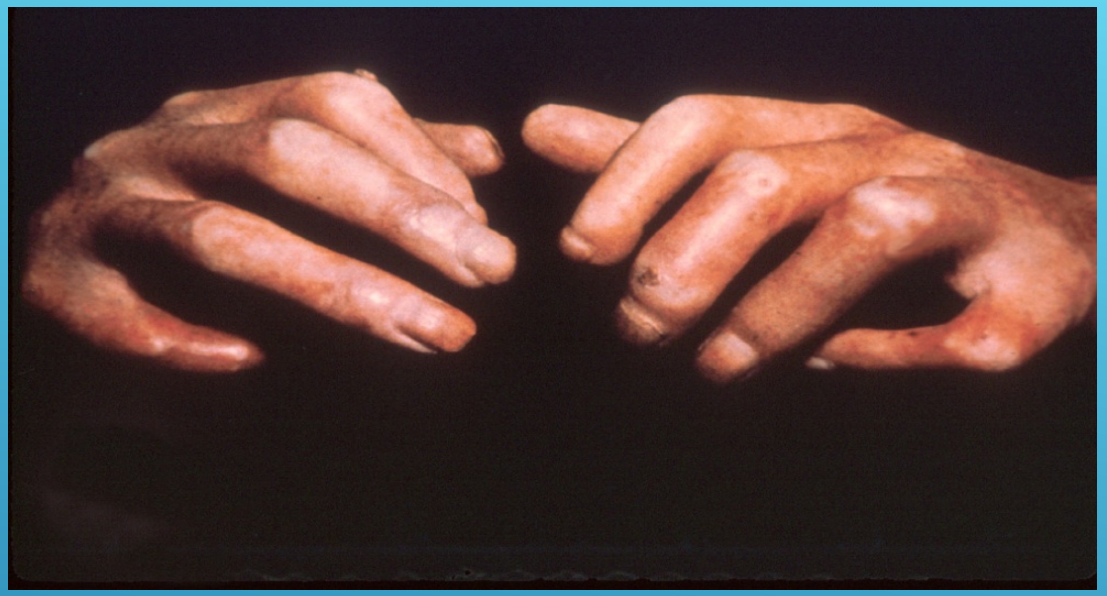
CIRCULATORY ISSUES– CASE 6

- A 28 y/o female medical student with diffuse scleroderma presents to your office for a follow-up visit. She was diagnosed with scleroderma 1 year ago when she presented with sclerodermatous skin changes on her fingers and face. At her last visit 1 month ago, she said her Raynaud's phenomenon was worse, and her sclerodermatous skin changes were progressing. She also has a 2-month history of chest pain and SOB. She has lost 10 pounds over the year.

- On exam she has acrosclerosis with flexion contractures of her hands. There is skin thickening of arms, legs and abdomen. BP is **160/105.** There are a few fine inspiratory crackles at both lung bases. There is a pericardial friction rub.

CIRCULATORY ISSUES– CASE 6





Labs: ESR 85, Hct 25%, WBC 5500, **platelets 80,000,** a **few fragmented RBCs**, Urinalysis **2+ protein, 5-10 RBCs**, no casts

Creatinine 1.8 mg/dl, BUN 35

ANA 1:2560, anti-Scl-70 positive, anti-DNA negative, C3 125 (nl 90-180)
Echocardiogram – moderate pericardial effusion

The treatment of choice for this patient is:

A. **Discontinue the nifedipine and PPI**
B. **Start plasma exchange, high dose glucocorticoids and cyclophosphamide**
C. **Start an ACE inhibitor**
D. **Treat with high dose glucocorticoids**
E. **Treat with a TNF antagonist (eg infliximab)**

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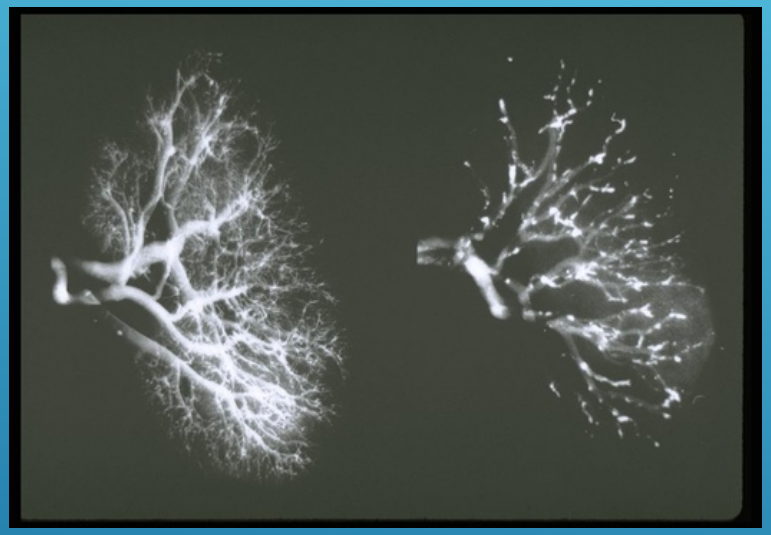
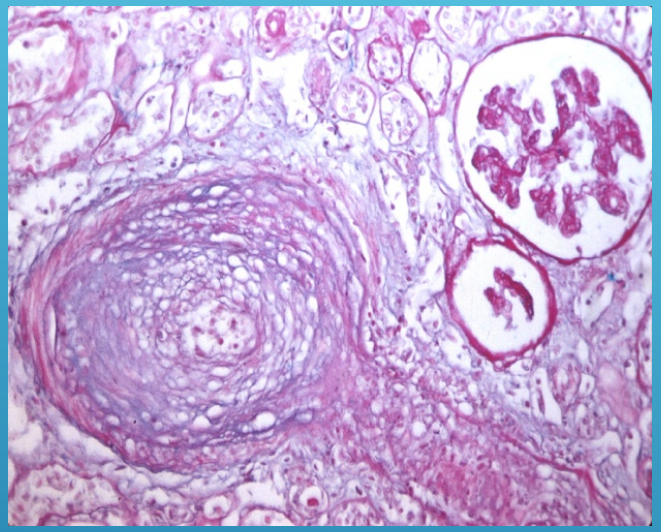
SCLERODERMA RENAL CRISIS

Malignant hypertension, oliguric renal failure, microangiopathy and thrombocytopenia





- diffuse scleroderma < 5 yrs
- recent rapid increase in skin thickening
- pericarditis/pericardial effusion
- treat with ACE inhibition, dialysis

Circulatory Issues

- **Large vessel vasculitis**
  - giant cell arteritis, Takayasu's arteritis
- **Medium vessel vasculitis**
  - polyarteritis nodosa, vasculitis with RA, CTDs
- **Non-inflammatory vasculopathy**
  - scleroderma
- **Thrombotic coagulopathy**
  - Antiphospholipid syndrome – medium and small vessel thrombosis
  - TTP

CIRCULATORY ISSUES– CASE 7

- A 75-year-old woman is evaluated for fever, fatigue, malaise, a severe headache in both temples, and discomfort in her jaw when chewing food. Last week, she also had an isolated episode of transient diplopia.

- On physical examination, temperature is 37.8 °C (100.1 °F). Except for scalp tenderness, the remainder of the examination is normal. Laboratory studies are normal except for an erythrocyte sedimentation rate of 30 mm/h. Temporal artery biopsy will be performed in 4 days.

Which of the following is the most appropriate management until temporal artery biopsy is performed?

A. Prednisone
B. Heparin
C. Acetaminophen with codeine
D. Combination therapy with methotrexate and sulfasalazine
E. No therapy until biopsy results are available

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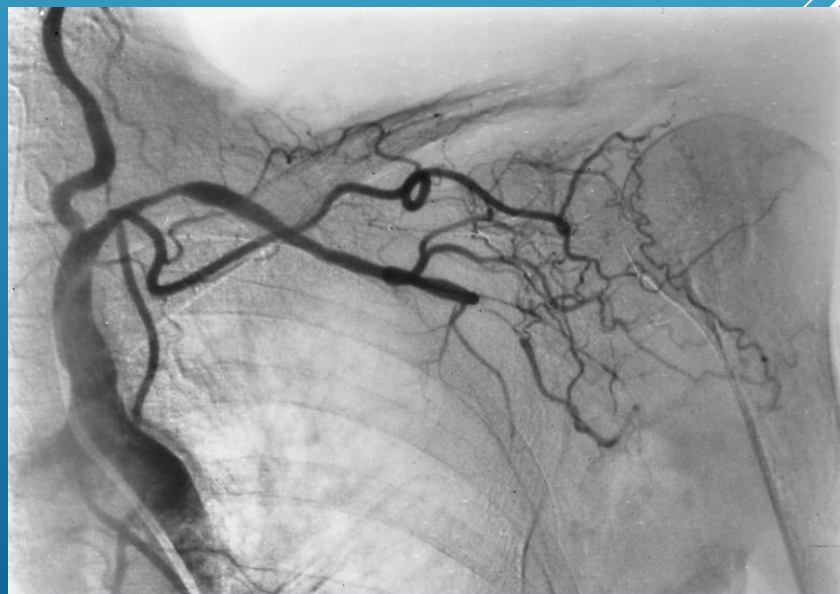
GCA – ARTERITIC FEATURES

- Temporal Headaches - tenderness, scalp necrosis
- Jaw Claudication - >50%
- Acute Ischemic Optic Neuropathy (AION)
  - ophthalmic, posterior ciliary aa
  - blurring
  - amaurosis fugax
  - blindness
- Large Artery Disease
  - aorta 10-15% with aneurysm +/- AI, dissection
  - carotid, subclavian, axillary artery
  - arm claudication,
  - subclavian steal
  - 50% negative TA biopsies]



CIRCULATORY ISSUES– CASE 8

- A 35-year-old man is referred to you by the emergency department for new onset hemiplegia. He was diagnosed with SLE 10 years ago but has had quiescent disease for the past several years. Skin examination shows livedo reticularis. He has a mitral regurgitation murmur. His leg examination is normal, without a Homan's sign. He is afebrile and BP is within normal limits. A CT scan done in the emergency department shows an infarct in the middle cerebral artery distribution, with no hemorrhage.

- Laboratory studies
  - Hematocrit - 45%
  - Platelet count - 110,000/μL
  - ANA 1:1280
  - C3/C4 normal
  - aPTT elevated

THE MOST LIKELY UNDERLYING CAUSE OF HIS STROKE IS:

A. Lupus mediated CNS vasculitis
B. Lupus cerebritis
C. Antiphospholipid antibody syndrome
D. Thrombotic thrombocytopenic purpura
E. Bacterial endocarditis

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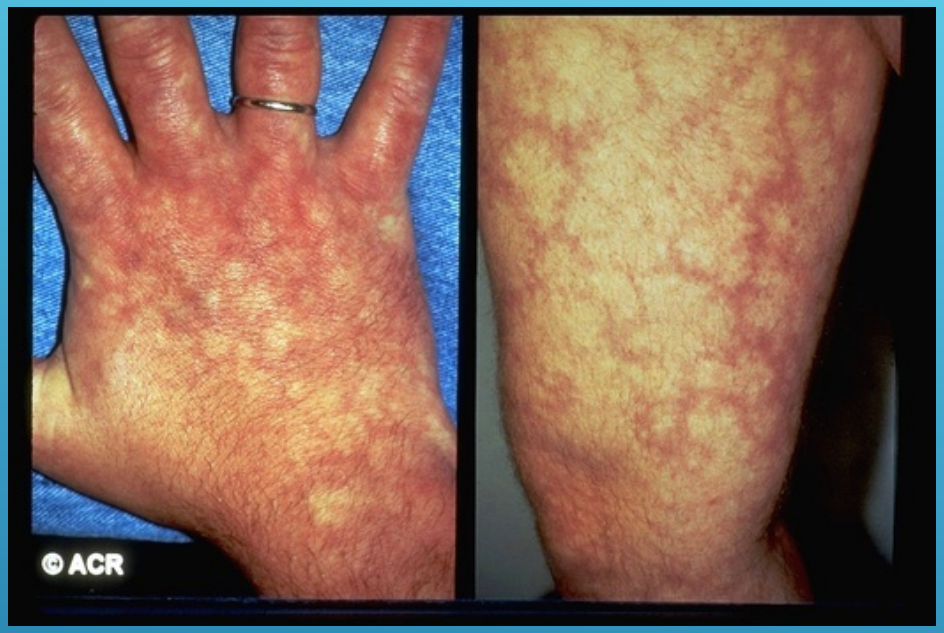
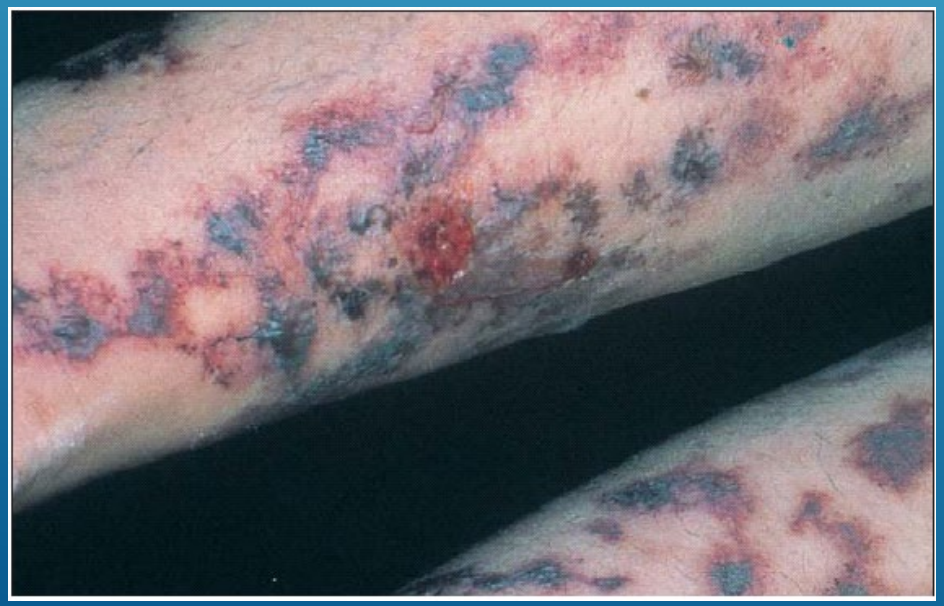
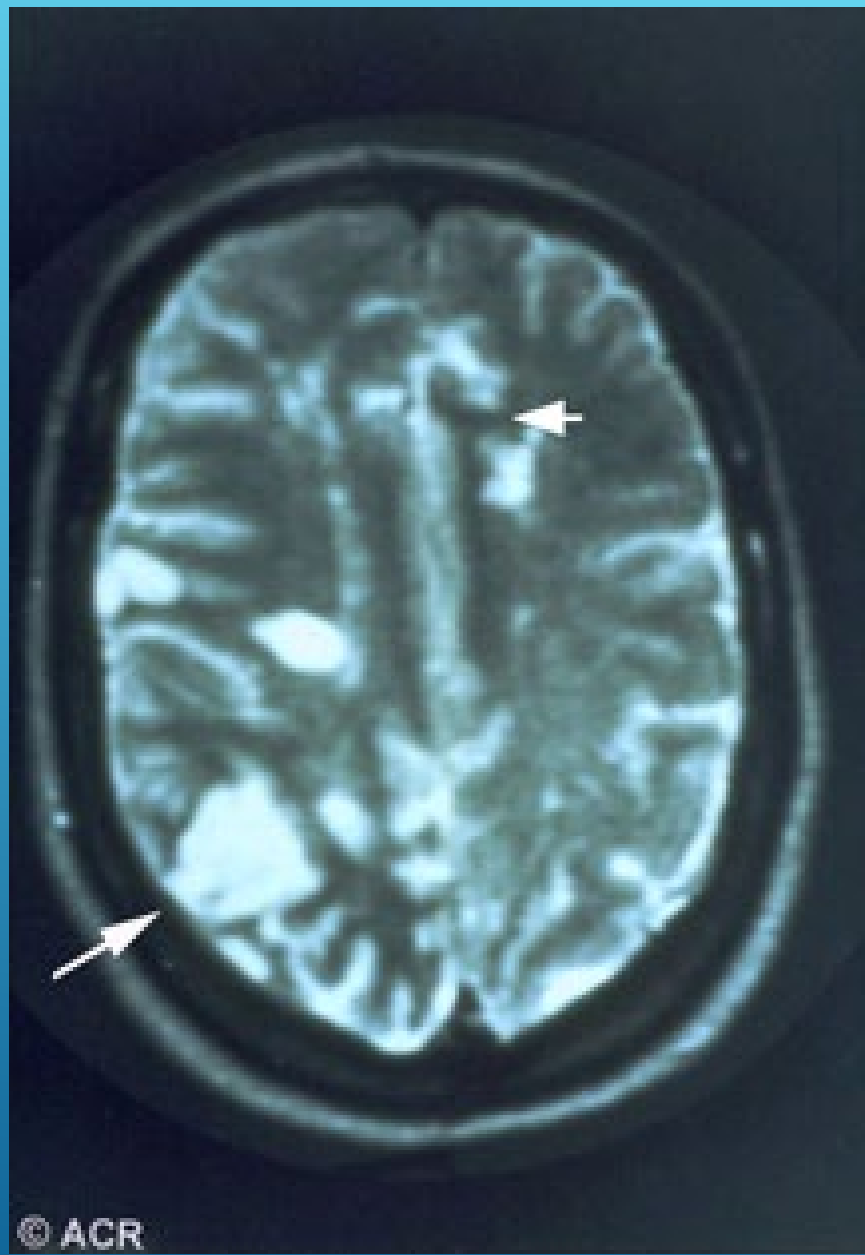
Antiphospholipid Antibody Syndrome







ANTIPHOSPHOLIPID ANTIBODIES

- Clinical Sequelae and Autoantibodies make the designation of aPL syndrome
- Clinical sequelae
  - **C**NS and cardiac manifestations
  - **L**ivedo reticularis
  - **O**bstetric loss – 3 spontaneous/1- 2nd trimester
  - **T**hrombosis – arterial and/or venous
- Laboratory abnormalities
  - aPTT, dRVVT- platelet depedency (confirmatory)
  - ACL antibodies (IgG, IgM, IgA), [false +RPR]
  - beta-2 glycoprotein -1 antibodies

CATASTROPHIC APL SYNDROME

1. Evidence of involvement of > or = 3 organs, systems, and/or tissues
2. Development of manifestations simultaneously or in < 1 week
3. Confirmation by histopathology of small vessel occlusion in at least 1 organ/tissue
4. Laboratory confirmation of the presence of aPL (LAC and/or aCL and/or anti-beta -2-GPI antibodies)

CATASTROPHIC APL SYNDROME

- Malignant hypertension
- Acute respiratory distress syndrome
- Disseminated intravascular coagulation
- Microangiopathic hemolytic anemia
- +/- schistocytes
- Thrombocytopenia

First line	Second line	Third line	Experimental
Anticoagulation Corticosteroids	IVIG Plasma exchange with or without FFP	Fibrinolytics Cyclophosphamide Prostacyclin Ancrod Defibrotide	Anticytokines Other

[b] IVIG = intravenous immunoglobulin; FFP = fresh frozen plasma.

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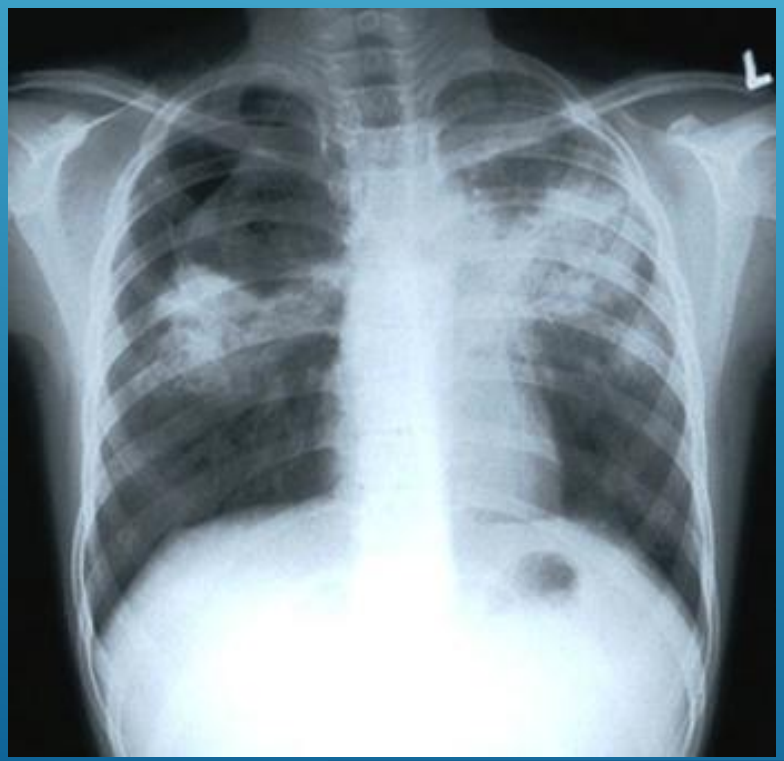
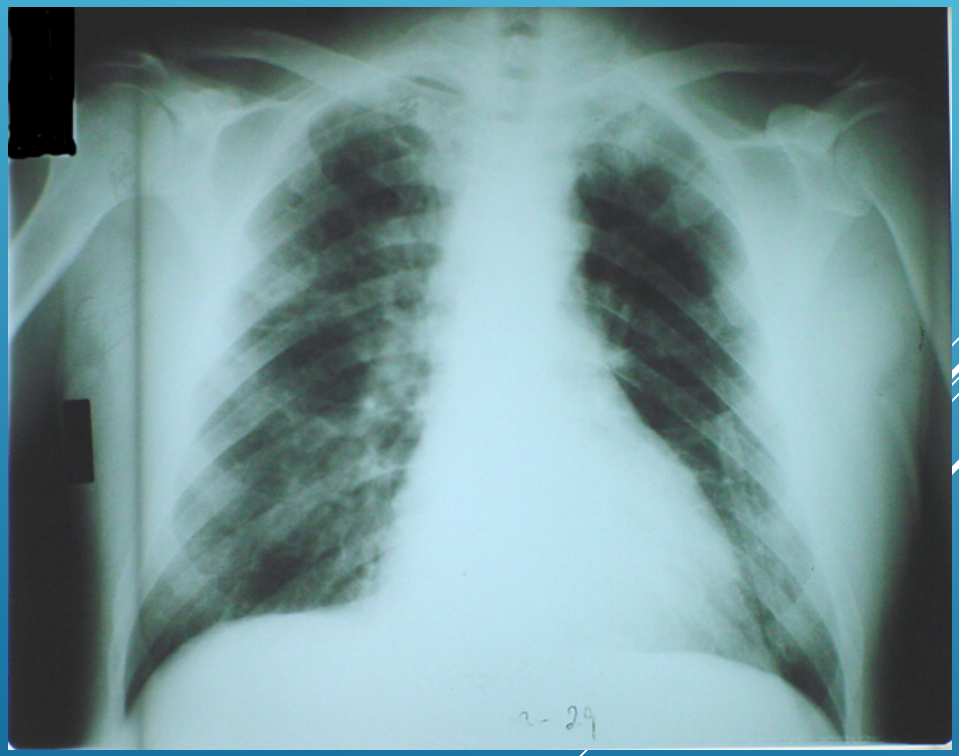
ACUTE MULTIORGAN THROMBOSIS

	TTP	DIC	CAPS	SLE (vasculitis)
MAHA	+	+	-/+	-/+
schistocytes	+	+	-/+	-/+
Fibn/FDP	N/N-↑	↓/↑	N-↓*/↑	N/N
PT/PTT	N/N	↑/↑	N-↓*/↑**	N/N-↑**
C3, C4	N -↓***	n	n	↓
*May have DIC **LAC ***SLE & TTP				

SOME FINAL THOUGHTS…

- Does the patient have a flare of their underlying autoimmune disease or an infectious complication?
- Patient presents with severe hemoptysis and is emergently intubated. The following CXRs represent 2 possible causes: one is acute GPA, the other active pulmonary TB.
- Can you tell the difference?





When in doubt, treat for both!

- No one should die in the ICU without a trial of steroids.
- TTP happens in our diseases (especially SLE). Don't miss it!
- Plasma exchange is an effective means of stabilizing an acutely ill patient with pathologic autoantibodies (ie ANCAs, ADAMTS13)
- Don't forget about CAPS – needs anticoagulation

QUESTIONS?