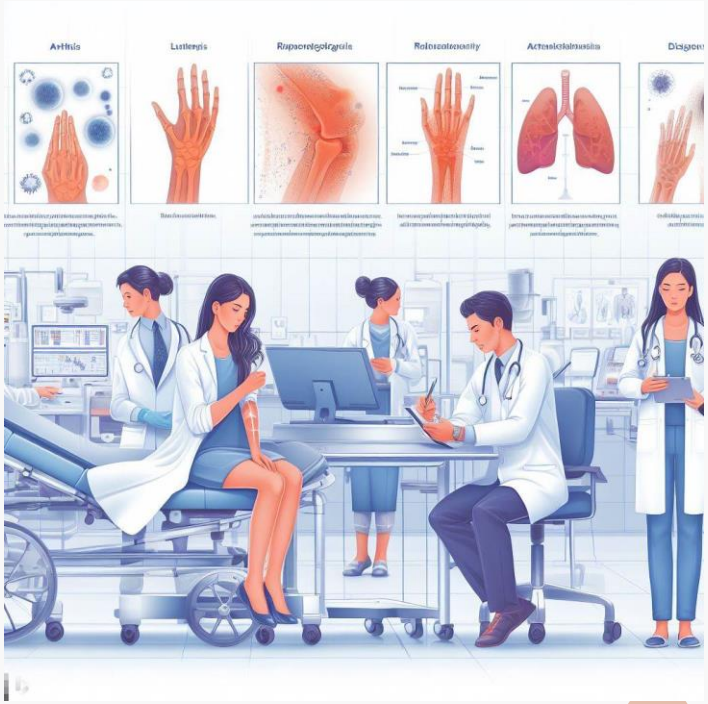
• Rheumatological emergencies



Zaid Abu-Hamour
Rawan Hmamreh
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Raynaud’s phenomenon

Defenition

- Raynaud's phenomenon (RP) is an exaggerated vasoconstrictive response of distal arteries and arterioles (most commonly in the fingers and toes) to cold or emotional stress.
- Vasospastic attack triggered by **cold** or **emotional stress**
- More common in female individuals
- It's classified into 2 types : **Primary** and **Secondary**

1-Primary Raynaud's phenomenon (previously called Raynaud's disease) :

- Idiopathic (no identifiable vascular changes); possible genetic susceptibility.

- Vasospasms of the digital arteries and arterioles.

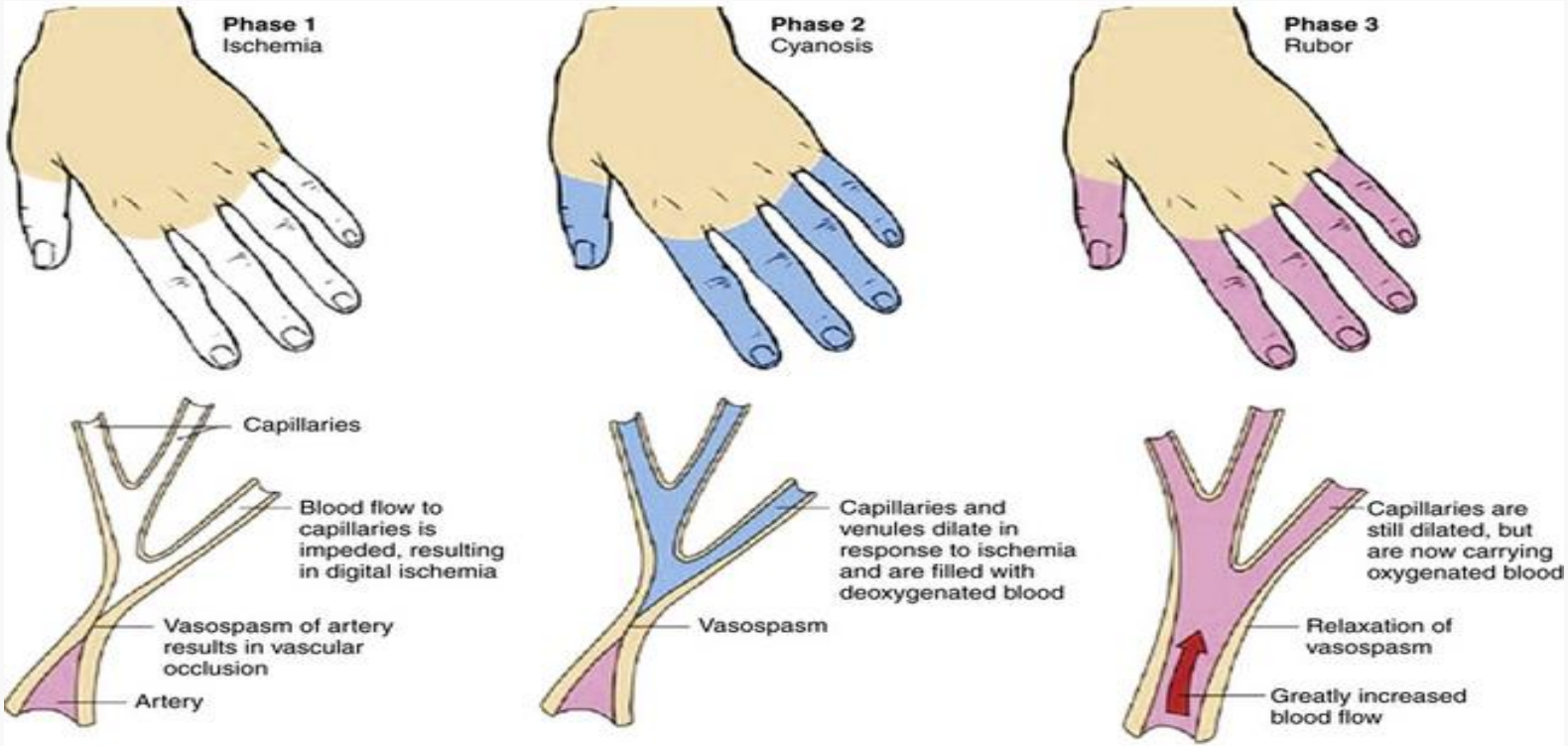
- **Onset usually < 30 years of age.**

- **Secondary Raynaud's phenomenon (previously called Raynaud's syndrome):**
- Vasospasms due to arteriolar changes in the fingers (and/or toes), which may be precipitated by the following:
  - Drugs**:** beta blockers, ergotamine, bleomycin
  - Smoking
  - Occupational trauma: from handling vibrating tools, typing
  - Hyperviscocity: polycythemia, paraproteinemias (plasmacytoma, **Waldenstrom macroglobulinemia**), **cryoglobulinemia**, cold agglutinin disease
  - Vasculitides: e.g., Buerger disease

- Connective tissue diseases (CTDs): e.g., **scleroderma** (CREST syndrome), systemic lupus erythematosus, mixed CTDs, Sjogren syndrome
- Arterial disease: e.g., peripheral artery disease
- Frostbite
- Neurological disease: e.g., carpal tunnel syndrome, intervertebral disc disease

- **Onset usually ≥ 30 years of age**

Pathophysiology



Clinical features

- Most commonly affects the **fingers** and toes bilaterally (may be asynchronous and asymmetric)

- The **thumb is typically spared** in primary RP.

- Can also affect ears, nose, areolar tissue, tongue (uncommon)

- Classic **triphasic presentation**
  - Ischemic phase (white): exposure to trigger → vasoconstriction of digital arteries and arterioles → ischemia and pallor
  - Hypoxic phase (blue): deoxygenation of residual blood → cyanosis
  - Hyperemic phase (red): restoration of reduced blood flow → reactive hyperemia

- Livedo reticularis may occur during episodes.

- Rewarming is associated with transient numbness, pain, and/or paraesthesias in the affected areas.

- **Duration:**

- Vasospastic episodes are usually **reversible**.

- Symptoms normally subside within an hour (typically **15–20 minutes** after cessation of trigger exposure).

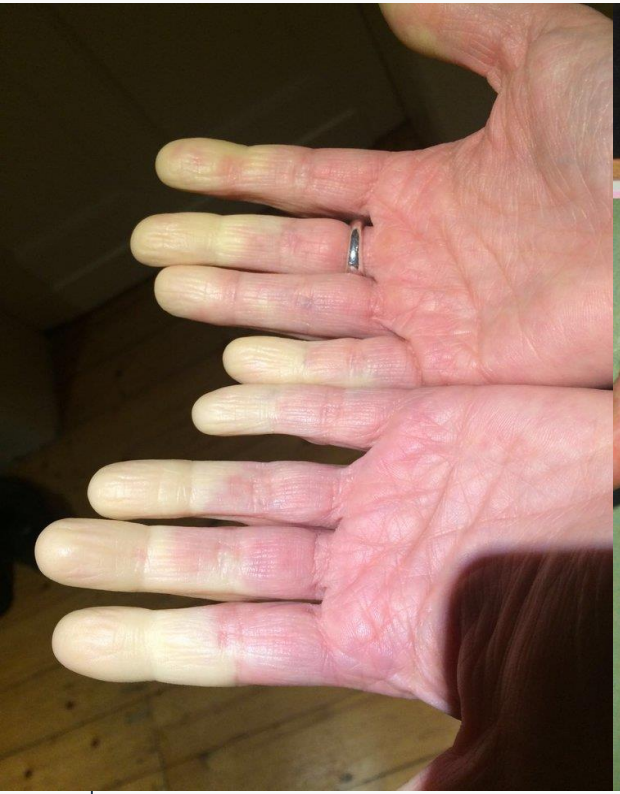
- Can potentially last for several hours

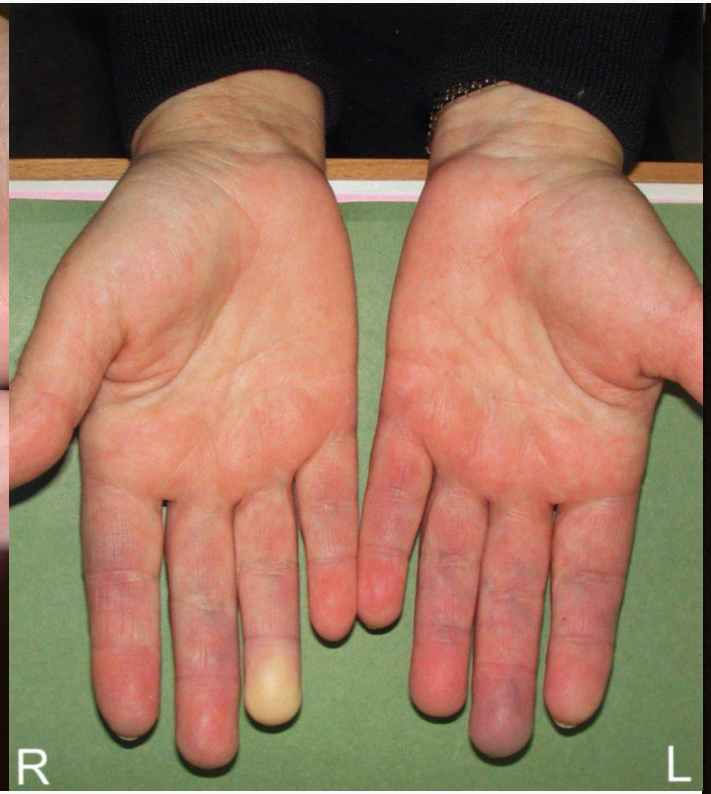
- **Associated findings:**

- In primary RP: symptoms of systemic vasospasm (e.g., migraine, irritable bowel syndrome)

- In secondary RP:
  - Severe pain and **ulcerations/necrosis** due to critical ischemia
  - Signs of associated systemic disease (e.g., telangiectases, skin fibrosis, sclerodactyly, calcinosis, photosensitivity, patchy alopecia)

- Clinical features of peripheral arterial disease are absent: Pulses, Allen test, and bilateral BP readings are normal in both primary and secondary RP.

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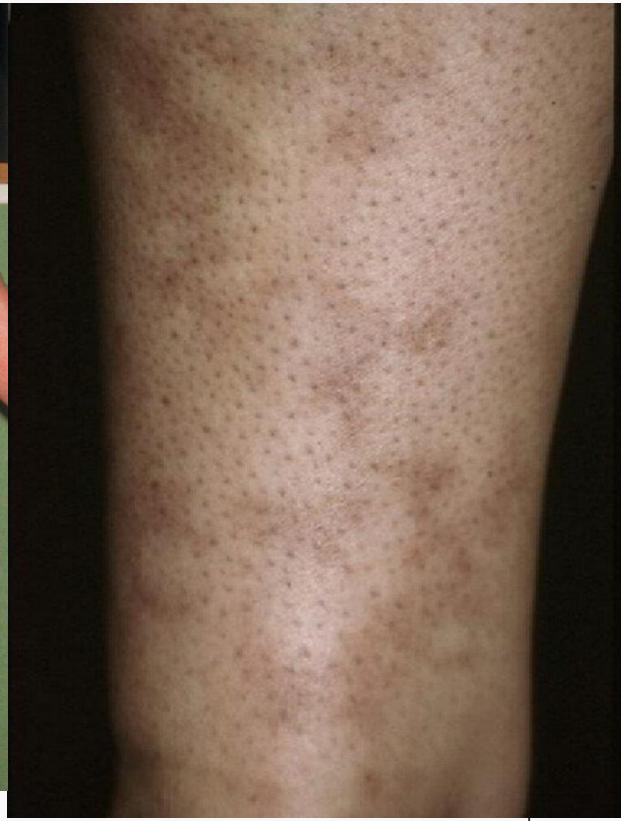


Diagnosis

- RP is primarily a clinical diagnosis.

- Distinguish between primary and secondary RP.

- **Diagnostic studies**

-Findings are described in the table below.

- **Laboratory studies**
  - CBC
  - Antinuclear antibodies (ANAs): if positive, send an ENA panel
  - Inflammatory markers (ESR or CRP)
- **Nailfold capillary microscopy**
  - An assessment of capillaries microvascular structure
  - One of the most sensitive methods of detecting early connective tissue diseases
- **Cervical spine and upper thoracic imaging**: Consider to evaluate for thoracic outlet syndrome caused by a bony cervical rib.

Primary vs. secondary Raynaud phenomenon [4][6]

	Primary RP	Secondary RP
Characteristic features	• Onset < 30 years of age • Episodes entirely reversible • Thumb is typically spared • No tissue loss • No signs of CTD	• Onset > 40 years of age • Irreversible ischemia • Episodes are severe and frequent • Evidence of digital ischemic injury (pitting, ulceration, gangrene) present • Signs of CTD
Laboratory studies	• Normal CBC • Negative or low (≤ 1:40) ANA titer [4] • ESR/CRP typically normal	• CBC may be abnormal. [10] • Positive ANA titer • Increased ESR/CRP

Nailfold capillaroscopy	• Normal pattern
	  ◦ Uniform and regularly distributed
	  ◦ Hairpin capillary morphology
		• Abnormal (scleroderma pattern)
		  ◦ Decreased capillary density (i.e., dropout)
		  ◦ Dilated "giant" capillaries (diameter ≥ 50 µm)
		  ◦ Abnormal architecture
		  ◦ Hemorrhages

Differential diagnoses:

1-**Perniosis (chilblains)**

2-**Acrocyanosis**

3-**Erythromelalgia**

4-**Peripheral artery disease (PAD)**

5-**Acute arterial occlusion of an extremity**

6-**Thoracic outlet syndrome**

Treatment

A-Trigger avoidance

- Avoidance of cold (e.g., wearing warm gloves or multiple layers of clothing)
- Stress management (e.g., anxiety attacks, episodes of irritability/anger)
- Minimize vibration exposure (e.g., occupational use of power hand tools such as jackhammers)
- Smoking cessation (smoking promotes vasoconstriction)
- Discontinuation of medications that may trigger attacks (e.g., β-blockers, ergotamine, oral contraceptives)
- **Cold avoidance and stress management are key aspects of managing RP.**

B-Pharmacotherapy

- **First-line**: **calcium channel blockers** monotherapy
  - Preferred: **nifedipine**
  - Alternative: amlodipine OR felodipine
- **Second-line**
  - ARBs, ACE inhibitors, PDE5 inhibitors (sildenafil), SSRIs, α-blockers, nitrates
  - Topical vasodilators: glyceryl trinitrate (GTN)

C-Interventional therapies and surgery :
-Indications: refractory or severe RP (e.g., critical digital ischemia, as evidenced by persistent ulceration or gangrene)

-Procedures:
1-Botulinum toxin injections
2-Selective digital sympathectomy
3-Amputation when necessary

Giant cell arteritis

(Temporal arteritis, Horton disease)

Definition and etiology

- Giant cell arteritis (GCA) is a type of autoimmune vasculitis that causes chronic inflammation of large and medium-sized arteries, in particular the carotid arteries, its major branches, and the aorta.

- Unknown cause; possible contributing factors include:
  - Genetic predisposition (e.g., human leukocyte antigen HLA-DR4)
  - Viral infections (e.g., parvovirus B19)

- Association with **polymyalgia rheumatica (PMR)**: up to 50% of patients with giant cell arteritis also have PMR.

Pathophysiology

- Giant cell arteritis is thought to be due to a cell-mediated immune response to endothelial injury. However, the initiating factors are not fully understood.

1-Inflammation:

  - Activation of dendritic cells in the adventitia of blood vessel walls → dendritic cells recruit Th1 cells, CD8+ T cells, and monocytes

  - Monocytes differentiate into macrophages and giant cells, which produce cytokines (e.g., **IL-6**, TNF-α) that augment the inflammatory response → focal granulomatous inflammation

2-Local vascular damage:

- Macrophages produce metalloproteinases → destruction of vessel wall structures (e.g., internal elastic lamina)
- Most commonly involves external carotid artery branches (especially temporal artery), as well as the aorta and vertebral arteries

3-Concentric intimal hyperplasia : macrophages and giant cells produce PDGF and VEGF → stimulate intimal proliferation →reduced blood flow and ischemia

Clinical features

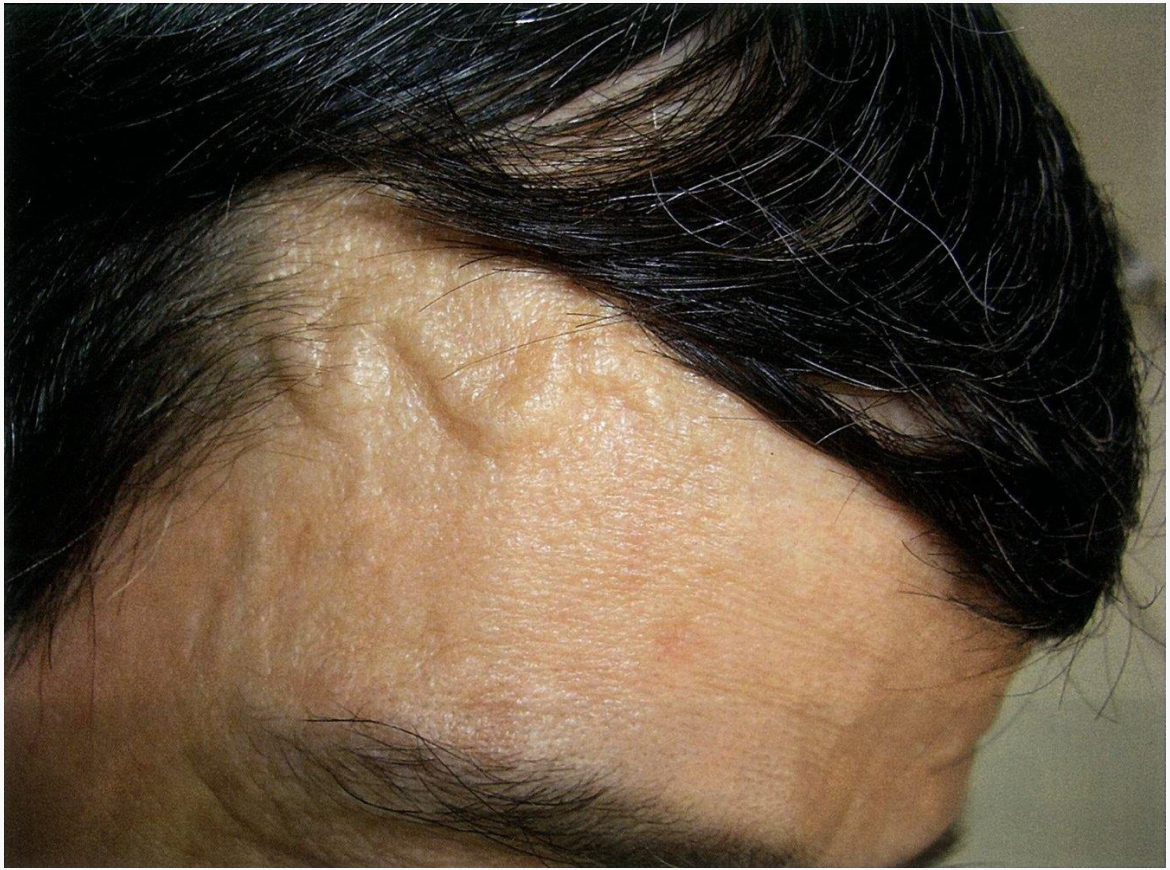
- Constitutional symptoms

- Clinical features of **arterial inflammation:**

Cranial giant cell arteritis: involves the **extracranial branches of the common carotid, internal carotid, and external carotid arteries** (the temporal artery is the most commonly affected vessel)

    - New-onset unilateral (or bilateral) **headache**
        - Can be pulse-synchronous, throbbing, dull

- Hardened and tender temporal artery
- Jaw claudication: jaw pain when chewing
- Vision loss: due to inflammation and occlusion of the ophthalmic artery and its branches
- Symptoms of polymyalgia rheumatica (if both diseases are present)
- About 50% of patients with giant cell arteritis also have polymyalgia rheumatica.



Diagnostics

- Demonstration of arterial inflammation on imaging and/or histopathology is required to make a diagnosis of GCA

Laboratory studies

- **Inflammatory markers**: initial laboratory test in suspected GCA
  - ↑ **ESR**,↑ CRP
- **Additional laboratory tests**
  - CBC: normal or mild thrombocytosis, leukocytosis, or normochromic anemia
  - Liver chemistries: normal or ↑ ALP, ↑ transaminases, or ↓ albumin
  - Coagulation studies: normal or ↑ fibrinogen

- **Confirmatory diagnostic studies**
- All patients require imaging and/or a temporal artery biopsy to confirm the diagnosis.

- **Temporal artery biopsy (gold standard) :**

-Indications

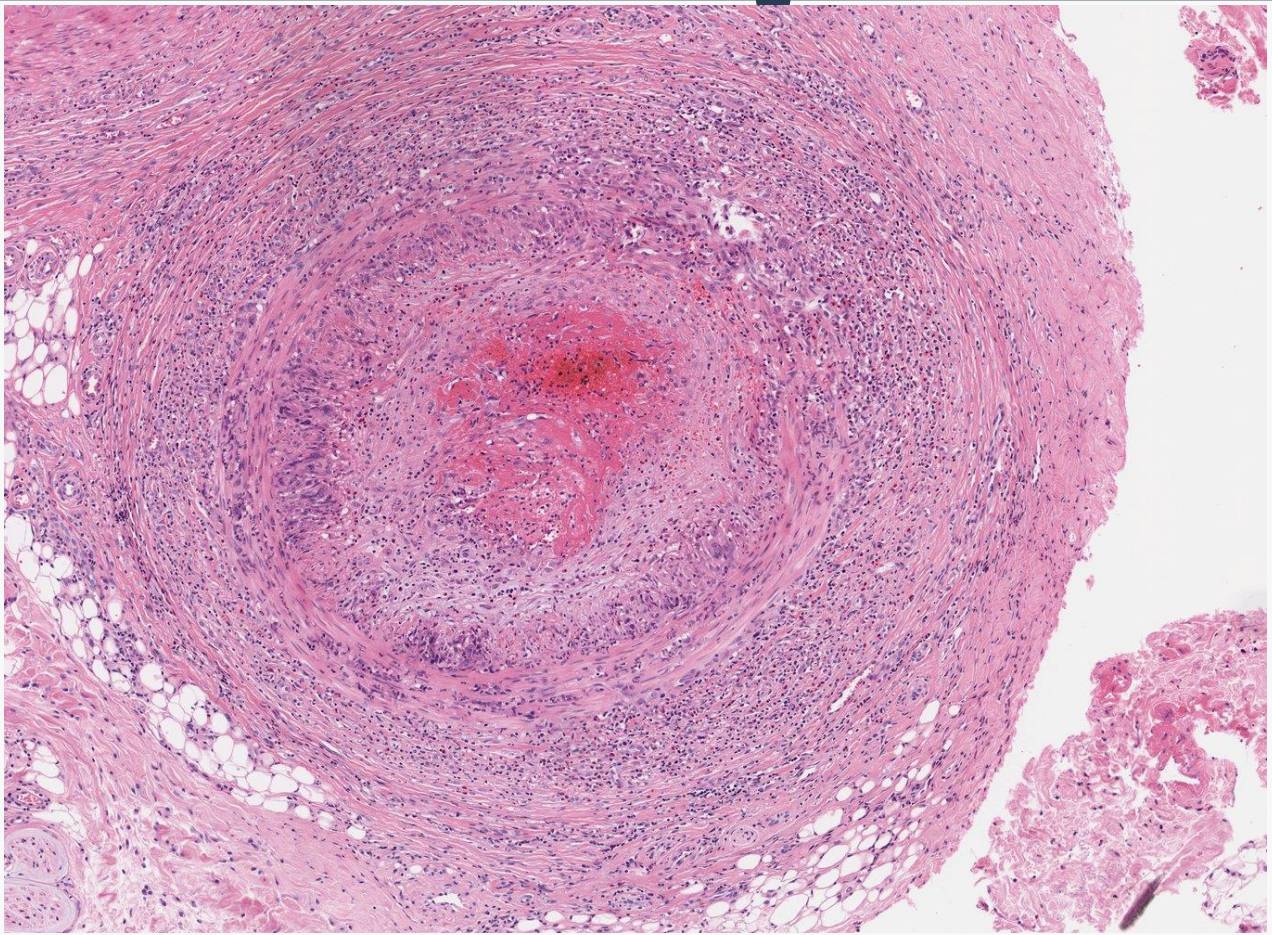
  - Consider in all patients with suspected GCA
  - High clinical suspicion for GCA despite inconclusive findings on imaging

- **-Findings**:
- Panarteritis of the large and medium-sized arteries
- Proliferation of the intima (and subsequent stenosis of the artery)
- Necrosis of the media
- Fragmentation of the internal elastic lamina
- Predominantly **mononuclear infiltration** of the vessel wall with formation of **giant cells**

-Important considerations

  - The minimum length of biopsy is 1.5 cm.
  - Histopathology may be falsely negative due to skip lesions

- **Duplex ultrasound (US)**
- **Indications:**
  - Duplex US of the temporal arteries: first-line imaging technique in suspected GCA
  - **Supportive findings** :
  - Edema and thickening of the vessel wall (halo sign)
  - Noncompressible artery (compression sign)
  - Stenosis and occlusion



Differential diagnoses of GCA

- **Polymyalgia rheumatic**

- **Other vasculitides**

- **Other causes of monocular vision loss**
  - Carotid artery disease
  - Thromboembolism
  - Retinal vein occlusion

Treatment

- **Glucocorticoid therapy:**

-This is the mainstay of treatment for patients with GCA.

-Initial high-dose therapy (induction therapy)

-Indication: all patients with new-onset or recurrent GCA

-Uncomplicated disease: **oral glucocorticoids**, e.g., prednisolone

-Ischemic organ damage (e.g., impaired vision): Consider initial pulse therapy with **IV glucocorticoids** before oral glucocorticoids

- **Maintenance therapy:**

-Slowly taper glucocorticoids to the lowest dose needed to control symptoms.

- **Adjunct therapy:**

1- Glucocorticoid-sparing therapy

2-Low-dose aspirin

Complications :

1-Permanent vision loss: ~ 20–30% if giant cell arteritis is left untreated

2-Cerebral ischemia

3-**Aortic aneurysm**

Scleroderma renal crisis

- **Scleroderma renal crisis (SRC)**: medical emergency, Presents in 10–15% of individuals with diffuse SSc and 1–2% of individuals with limited SSc

    - Clinical features of SRC
        - **Oliguric** acute kidney injury, proteinuria, hematuria
        - Hypertension with or without symptoms of hypertensive emergency
        - **Microangiopathic hemolytic anemia** (MAHA) and thrombocytopenia

    - Treatment: ACE inhibitors

-Management of SRC:

-Clinical suspicion:
There are no validated diagnostic criteria.

- Elevated blood pressure or an acute increase from baseline (e.g., SBP ↑ ≥ 30 mm Hg or DBP ↑ ≥ 20 mm Hg)
- Other clinical features of SRC (e.g., oliguric AKI, MAHA)

-Blood pressure management :

- First-line: Start or increase the dose of an ACEI (e.g., captopril).
  - Titrate to achieve a 10% reduction in blood pressure per day until normotensive.
  - Continue therapy indefinitely.

- Add additional antihypertensives as needed.

- **Avoid beta blockers**.

- **Disposition:**
  - Consult nephrology as > 50% of patients require renal replacement therapy.
  - Consider ICU admission.

Alveolar hemorrhage

1. Diffuse Alveolar Hemorrhage:
   Widespread extravasation of blood from the pulmonary capillaries into the alveolar space, resulting in destruction of the capillary-alveolar basement membrane this destruction is caused by injury or inflammation of the arterioles, venules, or alveolar wall or interstitial capillaries.

.

Etiology:

1. Autoimmune Disorders:
Granulomatosis Polyangiitis (GPA)
Goodpasture Syndrome

2. Severe lung infections:
such as certain types of pneumonia or tuberculosis

3. Toxic Inhalation:
Exposure to environmental toxins, chemicals, or irritants

4. Blood Disorders:
Antiphospholipid Syndrome and ANCA Vasculitis

Management of diffuse alveolar hemorrhage (DAH)

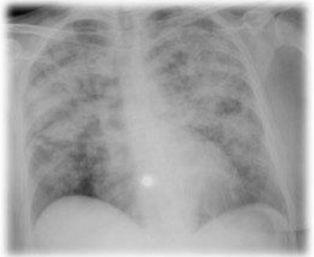
FVSG FRENCH VASCULITIS STUDY GROUP

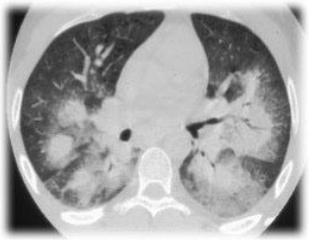
Blood escaping through the capillary wall into the alveoli, due to injury, inflammation or hypertension of arterioles, venules, or alveolar septal capillaries

1 Positive diagnosis of DAH

- **DAH triad:** lung opacities, hemoptysis, anemia
- **Chest CT scan:** diffuse ground-glass opacities, non localized alveolar infiltrates, no pleural effusion nor cardiomegaly
- **Bronchoscopy + BAL**

⚠ *Do not confuse with bronchial hemorrhage ± alveolar flooding (much more frequent +++)*





2 Etiological workup

Nonimmune

Alveolar injury

Barotrauma
Infection
Inhalation injury (toxic gases, …)

Venous hypertension

Left ventricular dysfunction
Renal failure
Hypervolemia
Mitral stenosis, veno-occlusive disease…

Immune

Vascular disease

Systemic vasculitides (AAV +++)
Goodpasture
Connective tissue diseases (LES, SAPL)
Vascular tumors
PAH

Blood clotting

Coagulation abnormality
Toxic, drugs, infection
Thromboembolic diseases
Endovascular metastasis

3 Assess severity

⚠ ***Never forget the heart***

Immune cause if score ≥4

Variables	Points
Time since the first respiratory symptoms ≥11 days	+ 2
Fatigue and/or weight loss	+ 2
Arthralgia/arthritis	+ 3
Proteinuria ≥1 g/L	+ 3

Poor prognostic factors in DAH

- Shock
- GFR <60 ml/min
- LDH > 2 x N

Similar outcome between immune and nonimmune DAH

Poor prognostic factors in immune DAH

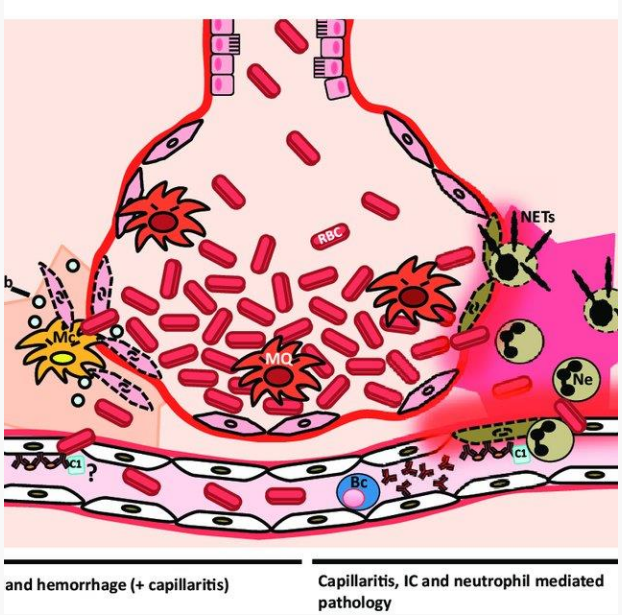
- Cardiac failure
- aPL antibodies
- Hypoxemia
- SAPS

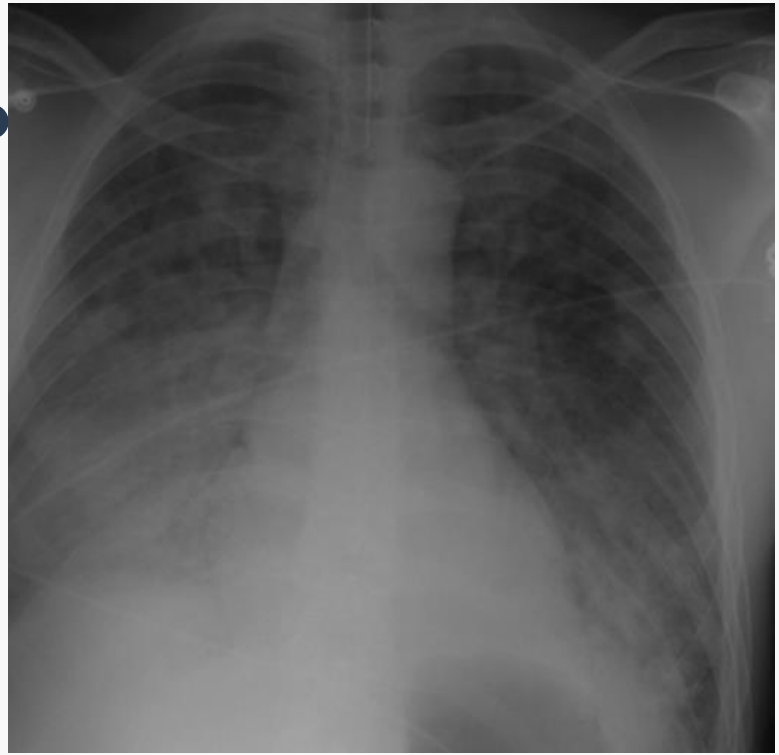
Corticoids +++

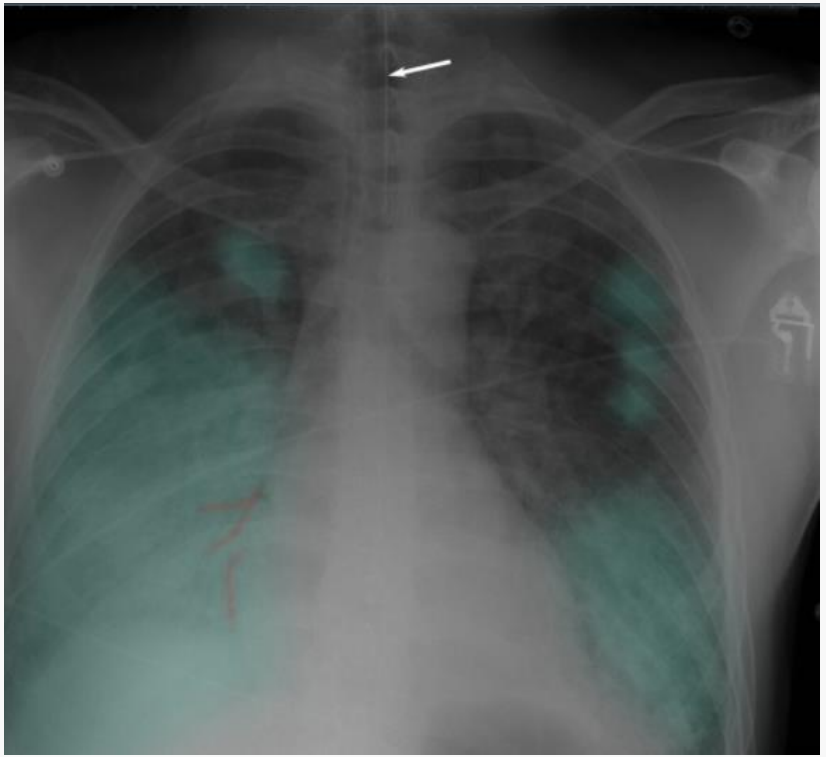
Diffuse alveolar hemorrhage Presents as:

Dyspnea and cough
Fall in blood hemoglobin level
Hemoptysis
Diffusion capacity of carbon monoxide typically increased

*** High mortality rate



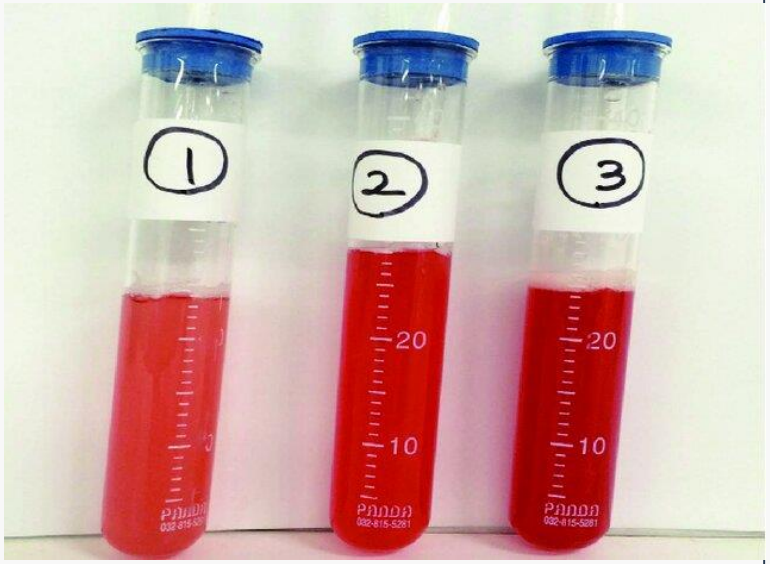




1) X-ray chest (AP view) of a patient with adult respiratory distress syndrome (ARDS)
*Confluent and multifocal airspace opacities (examples indicated by green overlay) predominate in the lower zones of the lungs. Air bronchograms (examples indicated by red lines) are visible in some locations. There are no Kerley lines or pleural effusions. The cardiac silhouette size is normal. An endotracheal tube (arrow) is present.

2) CT/MRI

3) Bronchoscopy with bronchoalveolar lavage (BAL) is important in ruling out infection and confirming the diagnosis. progressive hemorrhagic BAL in the serial samples (Number 1 is the first BAL, number 2 is the second, and number 3 is the third.). BAL fluid analysis shows an increase in red blood cells.



4) Biopsy is often indicated to determine underlying etiology.

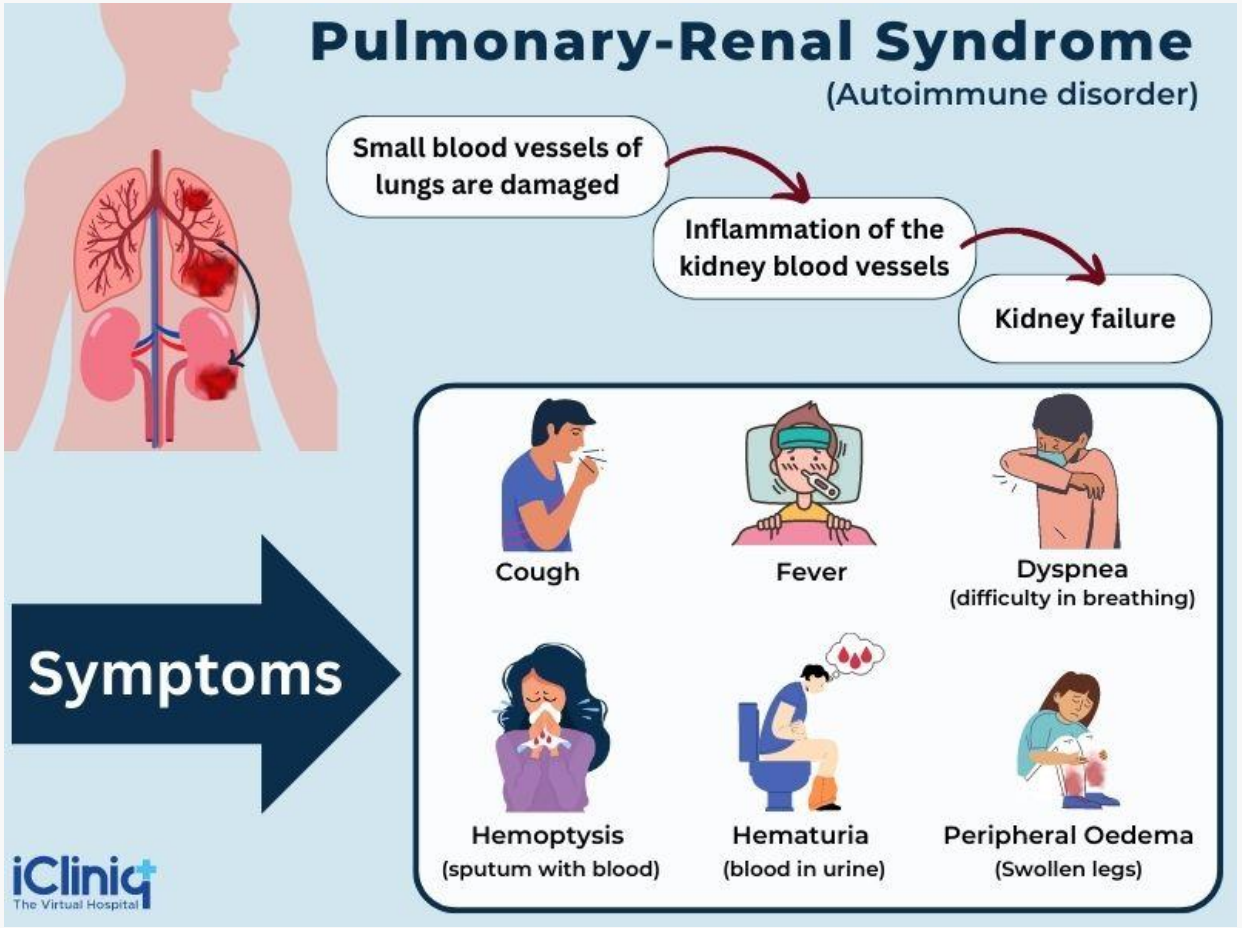
Treatment:

- Aggressive immunosuppression with steroids and cyclophosphamide
- Plasmapheresis (clinical benefit in Goodpasture syndrome)

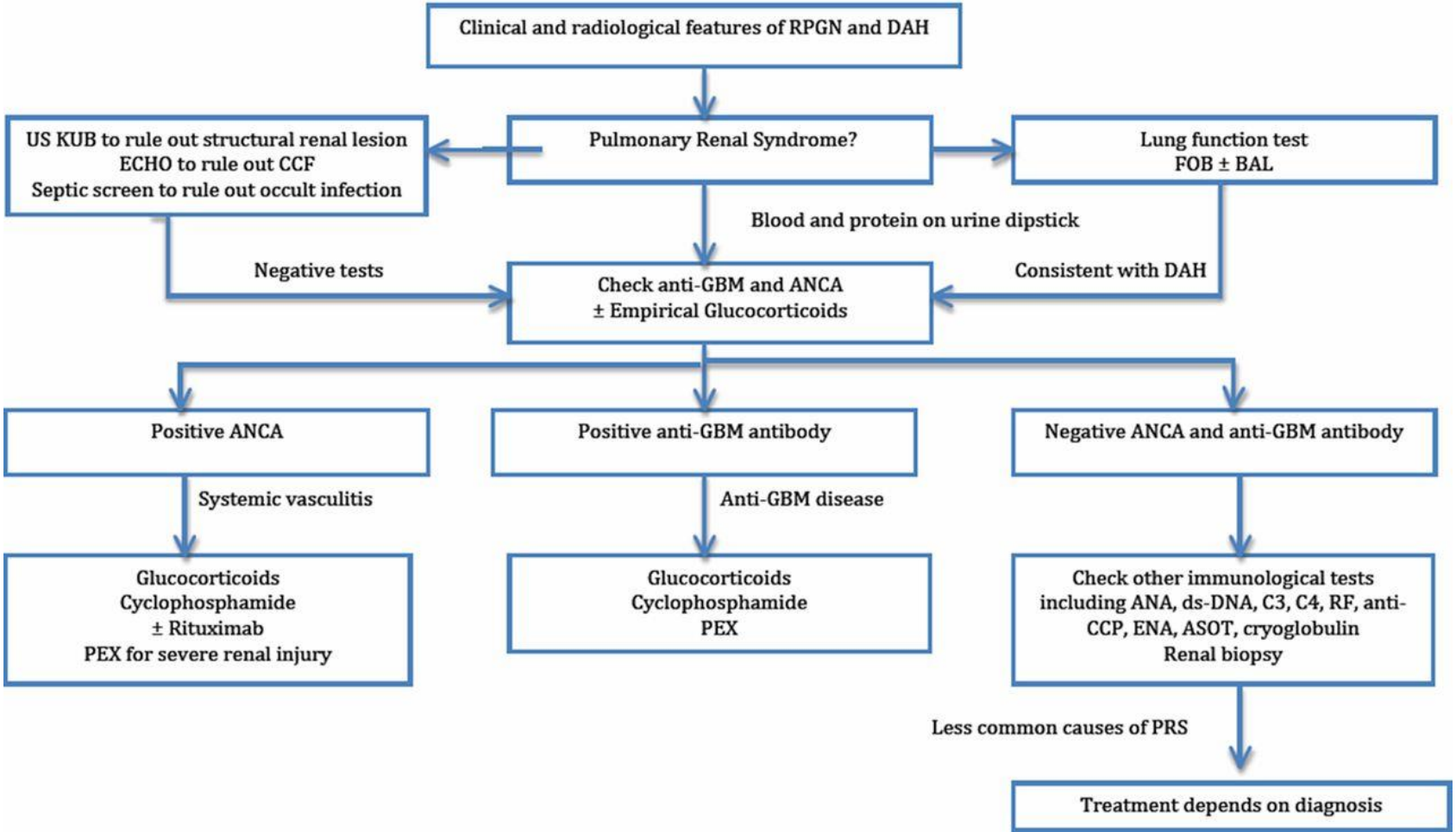
PULMONARY-RENAL SYNDROME

Pulmonary-renal syndrome is diffuse alveolar hemorrhage plus glomerulonephritis, often occurring simultaneously.

Occurs in patients with:
ANCA vasculitis (Wegener /microscopic polyangitis)
Good pasture syndrome(Anti-Glomerular Basement Membrane disease)


Pulmonary-Renal Syndrome
(Autoimmune disorder)
Small blood vessels of lungs are damaged
Inflammation of the kidney blood vessels
Kidney failure
Symptoms
Cough
Fever
Dyspnea
(difficulty in breathing)
Hemoptysis
(sputum with blood)
Hematuria
(blood in urine)
Peripheral Oedema
(Swollen legs)
iClinic
The Virtual Hospital

Diagnostic algorithm for Pulmonary Renal Syndrome



POLYARTERITIS NODOSA AND TAKAYASU'S ARETERITIS

Polyarteritis nodosa (PAN) is a systemic vasculitis of medium-sized vessels that most commonly affects the skin, peripheral nerves, muscles, joints, gastrointestinal tract, and kidneys, but usually spares the lungs. Most cases are idiopathic, but it is associated with certain viral infections, most commonly hepatitis B virus (HBV) infection.

Takayasu arteritis (TAK) is classified as a large-vessel vasculitis because it primarily affects the aorta and its primary branches.

Patients typically present with systemic symptoms. The kidneys, skin, joints, muscles, nerves, and gastrointestinal tract are commonly involved.

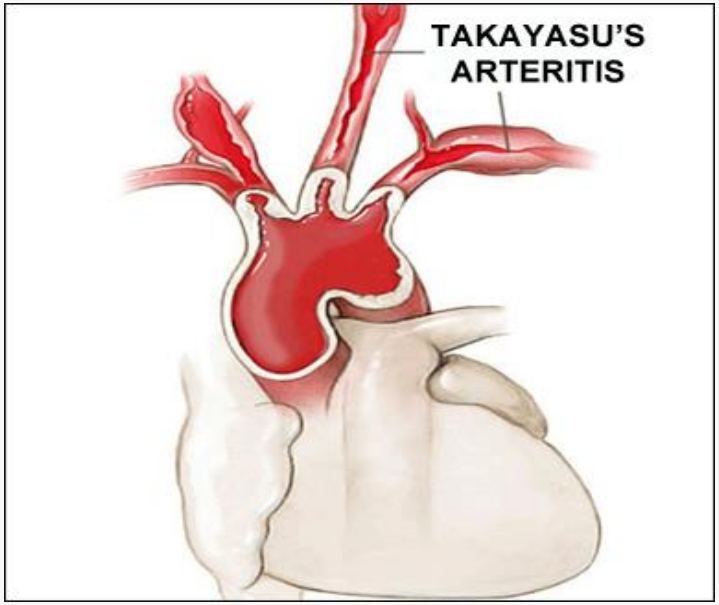
GI COMPLICATIONS IN POLYARTERITIS NODOSA AND TAKAYASU'S

In PAN : Abdominal pain is an early symptom in patients with mesenteric arteritis
Weight loss may ensue due to decreased food intake and/or malabsorption.
Progressive disease can result in bowel infarction with perforation .
Nausea, vomiting, melena, bloody or nonbloody diarrhea, and life-threatening gastrointestinal bleeding.
Ischemia due to vasculitis affects the small intestine more commonly than other areas of the gastrointestinal tract.

IN TAKAYASU'S: Abdominal pain, diarrhea, and gastrointestinal hemorrhage may result from mesenteric artery ischemia.

Diagnosed best with biobsy or conventional angiography which will show aneurysms in PAN and trans mural thickening in Takayasu's

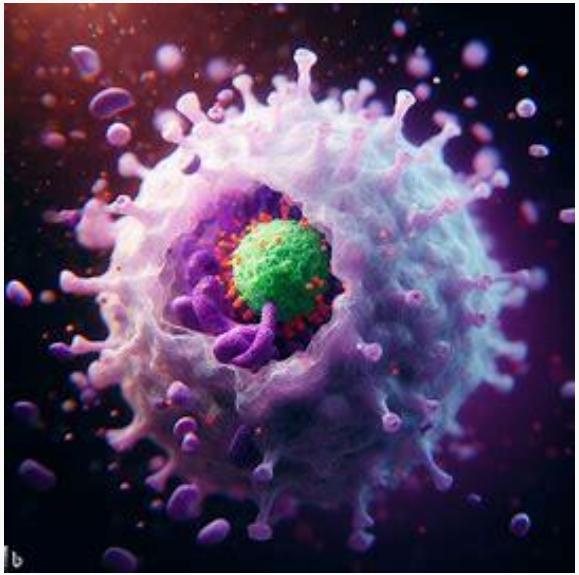
Treatment : Pulsed dose steroids
tocilizumab in Takayasu's
Cyclophosphamide in PAN
Surgery is indicated in cases of necrosis or bowel perforation



Macrophage activation syndrome

A form of secondary hemophagocytic Lymphohistiocytosis due to an underlying Rheumatological disease.

is an aggressive and life-threatening syndrome of excessive immune activation. It is most common in infants and young children but can affect patients of any age, with or without a predisposing familial condition.

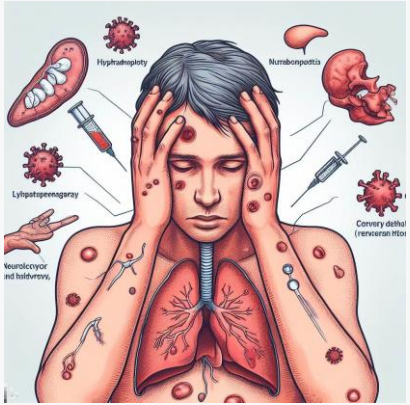


Severe inflammatory response caused by immune system over-activation leading to cytokine storm

Overactive macrophages start to engulf RBCs and other cells.

Signs and symptoms

*Most patients with HLH are acutely ill with multiorgan involvement. Common findings include:
fever,
hepatosplenomegaly,
rash,
lymphadenopathy,
neurologic symptoms,



Patients may have already experienced a prolonged hospitalization or clinical deterioration without a clear diagnosis before the possibility of HLH is raised.

If not treated, leads to death from multi organ failure

initial evaluation:

*complete blood count with differential(pancytopenia)
*coagulation studies,
*serum ferritin(high)
*liver function tests(high)
*triglycerides(high)
*blood cultures, and viral testing.

The bone marrow should be examined for the cause of cytopenias

The pathognomonic feature of the syndrome is bone marrow examination that reveals numerous well-differentiated macrophages actively phagocytosing hematopoietic cells

Treatment:

1. urgently refer to a haematology or oncology specialist.
2. Pretreatment testing of cardiac function and disease markers should be done in all patients.

3. HLA typing of all patients and appropriate family members, and genetic testing of potential sibling donors should be sent in anticipation of possible hematopoietic cell transplant (HCT).

4. Treat underlying Rheumatological condition (or infection) after the patient is clinically stable.

5. Among patients who are acutely ill or deteriorating, we suggest HLH-specific therapy based on the HLH-94 protocol

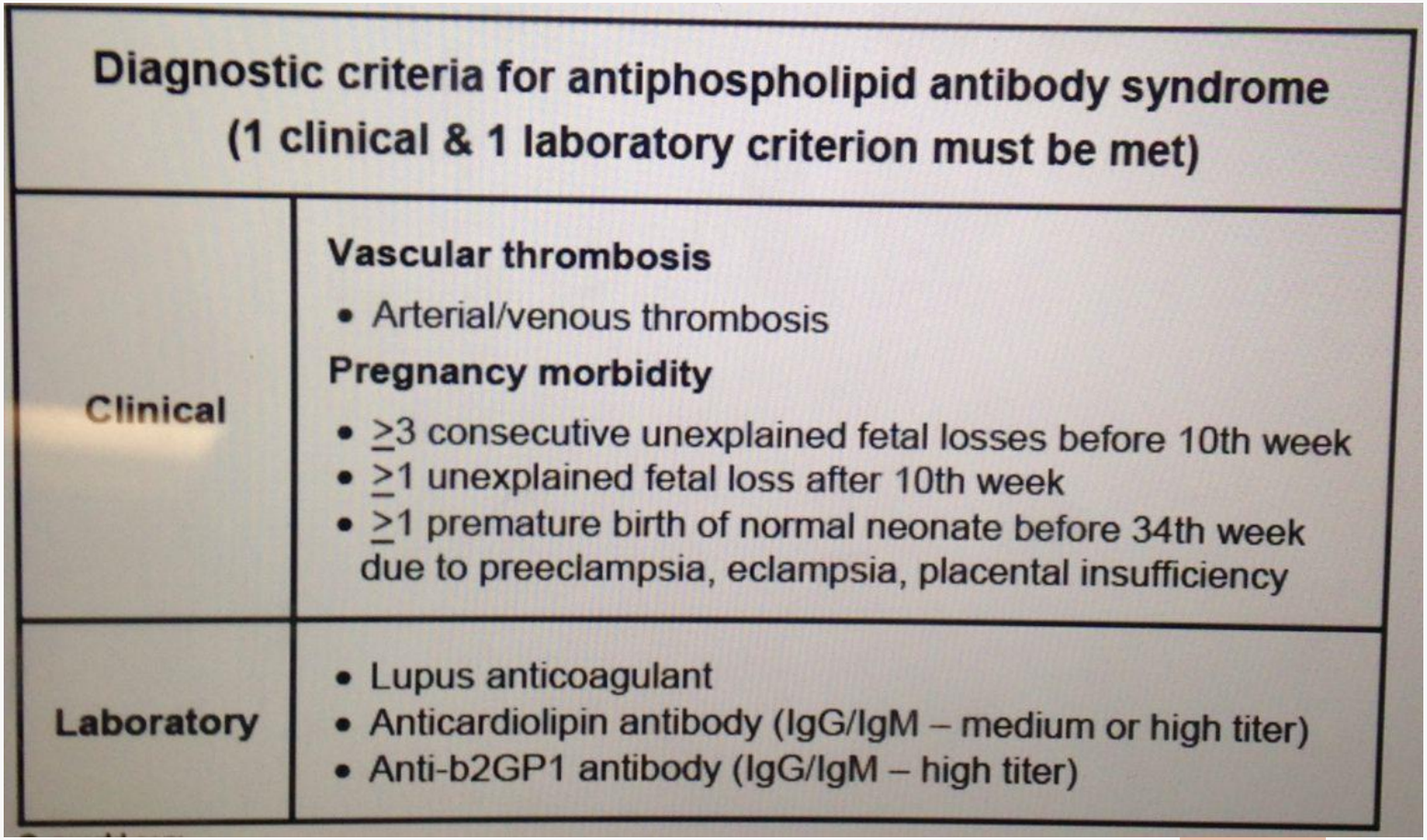
** therapy includes etoposide and dexamethasone given at tapering doses over eight weeks, with intrathecal methotrexate and hydrocortisone for those with central nervous system (CNS) involvement.

6. Patients should receive transfusions of red blood cells and platelets as needed (target platelet count >50,000/microL during induction); we give fresh frozen plasma, thawed plasma, or cryoprecipitate for bleeding if the fibrinogen is low.

Catastrophic antiphospholipid syndrome (CAPS)

Antiphospholipid syndrome (APS)

- Antiphospholipid syndrome (APS) is characterized by venous and/or arterial thrombosis and/or an adverse pregnancy outcome in the presence of persistent laboratory evidence of antiphospholipid antibodies (aPL).
- APS occurs either as a primary condition or in the setting of an underlying disease, usually systemic lupus erythematosus (SLE).
- Clinical manifestations range from asymptomatic aPL positivity (no history of vascular or pregnancy events) to catastrophic APS (multiple thromboses occurring over days).
- Diagnosis of the antiphospholipid syndrome (APS) requires that a patient have both a clinical event (thrombosis or pregnancy morbidity) and persistent antiphospholipid antibodies .



Diagnostic criteria for antiphospholipid antibody syndrome
(1 clinical & 1 laboratory criterion must be met)

Clinical	**Vascular thrombosis** • Arterial/venous thrombosis **Pregnancy morbidity** • ≥3 consecutive unexplained fetal losses before 10th week • ≥1 unexplained fetal loss after 10th week • ≥1 premature birth of normal neonate before 34th week due to preeclampsia, eclampsia, placental insufficiency
Laboratory	• Lupus anticoagulant • Anticardiolipin antibody (IgG/IgM – medium or high titer) • Anti-b2GP1 antibody (IgG/IgM – high titer)

- **Catastrophic antiphospholipid syndrome (CAPS)** is a rare, life-threatening form of APS characterized by severe thrombotic complications, usually microvascular as well as large-vessel thrombosis, affecting multiple organs, that develop simultaneously or over a short period of time.

- Approximately 1 percent of patients with APS develop the severe clinical picture of CAPS. Approximately one-half of all patients with APS present with CAPS as their initial manifestations of APS.

- The mechanism by which a "thrombotic storm" occurs , is not well understood. most individuals with CAPS have triple aPL positivity with high titer immunoglobulin G (IgG) anticardiolipin and anti-beta2GPI antibodies.

- Precipitating factors for CAPS may include infections, drugs, major/minor surgical procedures, and anti-coagulation withdrawal.

CLINICAL FEATURES

- **Pulmonary involvement** – Pulmonary involvement may progress to acute respiratory distress syndrome (ARDS) and may be complicated by PE or pulmonary hemorrhage. Pulmonary microvascular involvement is generally in the form of alveolar hemorrhage, which can be asymptomatic with ground glass opacities on chest computed tomography (CT) or may present with gross hemoptysis.

- **Cardiac involvement-**myocardial infarction

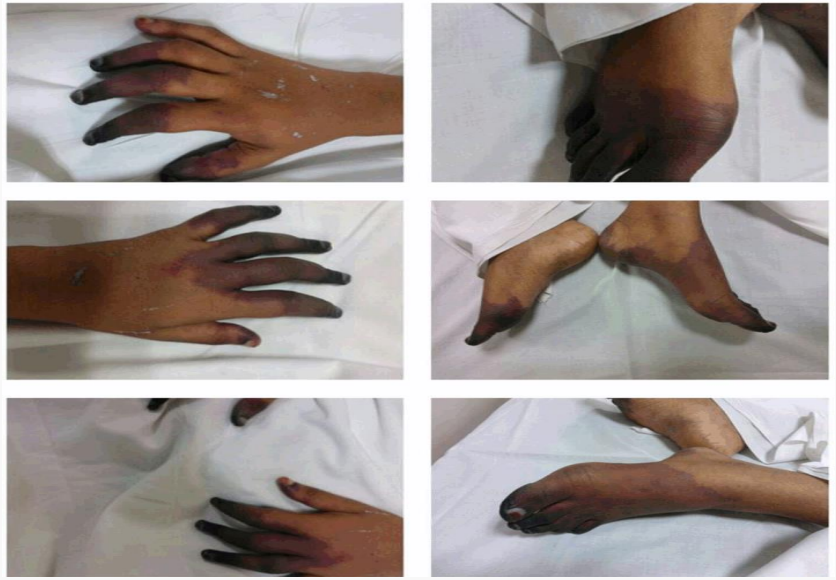
- **Skin involvement** – Cutaneous manifestations can include, purpura, subungual hemorrhage, and skin necrosis.

- **Visceral organ involvement** – Abdominal pain may reflect intra-abdominal thrombotic complications affecting the vasculature of the kidneys, liver, adrenal glands, spleen, intestines, mesentery, or pancreas.

- **Kidney involvement** – Individuals with kidney involvement often have fever, hypertension, proteinuria, and hematuria. A urinalysis may show proteinuria and hematuria.

- **Central nervous system (CNS)** – CNS changes include acute ischemic encephalopathy with confusion, seizures, and/or focal findings.

- Patients often have moderate thrombocytopenia and other features of thromobotic microangiopathies.



Diagnosis

When to suspect — A high level of suspicion for CAPS should be maintained in any patient with features of multiorgan involvement (often with evidence of ischemic changes on imaging), rapid clinical deterioration, and findings suggestive of microangiopathic hemolytic anemia (MAHA) such as thrombocytopenia and schistocytes on peripheral blood smear.

A prior diagnosis of APS or systemic lupus erythematosus (SLE) should further increase the clinical suspicion.

Classification criteria for CAPS.

1. Evidence of involvement of three or more organs, systems and/or tissues
2. Development of manifestations simultaneously or in less than a week
3. Confirmation by histopathology of small vessel occlusion in at least one organ or tissue
4. Laboratory confirmation of the presence of antiphospholipid antibodies (lupus anticoagulant and/or anticardiolipin antibodies)

Definite catastrophic APS

- All 4 criteria

Probable catastrophic APS

- All 4 criteria, except for only two organs, systems and/or tissues involvement
- All 4 criteria, except for the absence of laboratory confirmation at least 6 weeks apart due to the early death of a patient never previously tested for aPL prior to the catastrophic APS event
- Criteria 1, 2 and 4
- Criteria 1, 3 and 4 and the development of a third event in more than a week but less than a month, despite anticoagulation

Treatment

CAPS is typically treated with a combination of anticoagulation, glucocorticoids, and therapeutic plasma exchange (TPE) or intravenous immune globulin (IVIG), sometimes referred to as triple therapy.

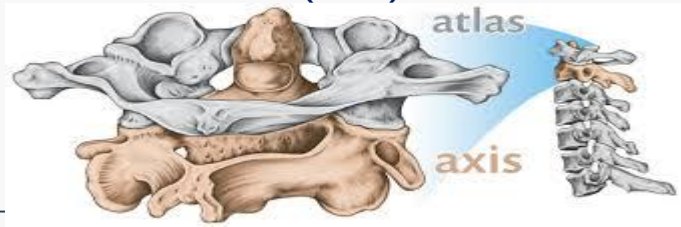
Parenteral anticoagulant – The choice of initial anticoagulant is intravenous unfractionated heparin. hemodynamically stable patients may be transitioned to warfarin.

Glucocorticoids-A typical dose is methylprednisolone, 0.5 to 1 g intravenously, once daily for three days. This is followed by oral or parenteral therapy with the equivalent of 1 mg/kg of prednisone per day with a taper started once the patient is clinically improving.

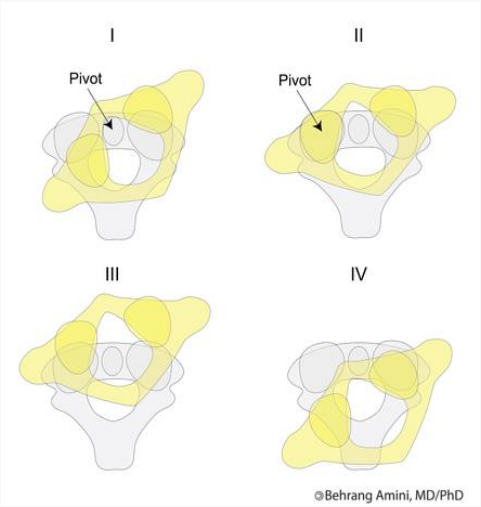
Refractory disease — CAPS that does not improve despite anticoagulation, glucocorticoids, and TPE or IVIG. In such cases, we typically add rituximab (a monoclonal antibody against the B cell antigen CD20) or eculizumab (a monoclonal antibody against the complement component C5).

atlantoaxial (C1-C2) subluxation

- Cervical spine involvement reported in as many as 80% of patients with RA.
- Of the cervical spine findings observed in RA, the most serious clinical presentations relate to atlantoaxial (C1-C2) subluxation.
- risk factors for cervical spine involvement in RA include erosive disease, glucocorticoid use, treatment failure, and early age at disease onset.
- increased mobility or laxity between the body of the first cervical vertebra (atlas) and the odontoid process of the second cervical vertebra (axis).

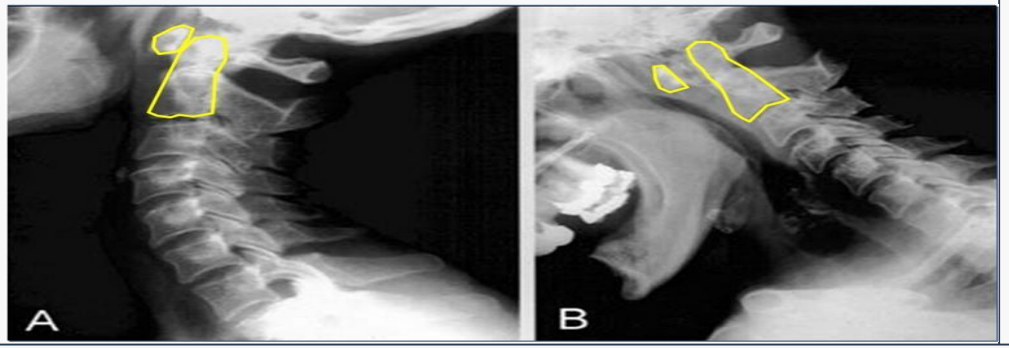


- The atlas (C1) can move anteriorly, posteriorly, vertically, laterally, or rotationally relative to the axis .
- the earliest and most common symptom of cervical subluxation is pain radiating superiorly towards the occiput.
- A sensation of the head falling forward.
- in patients with atlantoaxial subluxation, symptoms may include those of a myelopathy, sensory loss, paresthesias in the C2 area (greater occipital neuralgia), decreased sensation in the distribution of the fifth cranial nerve, and nystagmus.
- Vertical subluxation of the odontoid process of C2 may cause transient episodes of medullary dysfunction (such as respiratory irregularity) and the potential for vertebral artery compression and the development of Symptoms of vertebrobasilar insufficiency including dizziness ,syncopal episode; vertigo; bilateral leg weakness and hemiparesis; diplopia and visual loss; numbness and paresthesia.



diagnosis

- plain radiographs of the cervical spine
- appropriate images include upright (preferably standing) anteroposterior, open-mouth odontoid, and lateral radiographs of the cervical spine with additional lateral images taken in flexion and extension.
- In patients with deformity, instability, or narrowing (<14 mm) of the space available for the (spinal) cord (SAC), magnetic resonance imaging (MRI) of the cervical spine is indicated to assess the spinal cord and brainstem



Treatment

- Patients with minimal neurologic symptoms and minor degrees of radiographic subluxation can be followed periodically.

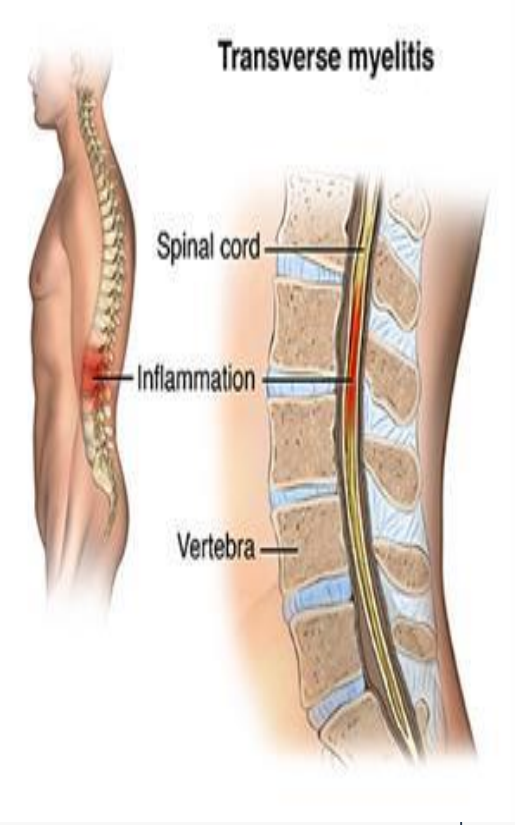
- The indications for surgery include:

Neurologic compromise (myelopathy and/or radiculopathy)
Vertebrobasilar insufficiency (VBI)
Radiographic spinal instability
Stenosis with spinal cord signal changes on MRI
Severe unremitting pain.

Transverse myelitis

- Acute transverse myelitis (TM) is a rare, acquired neuro-immune spinal cord disorder that can present with the rapid onset of weakness, sensory alterations, and bowel or bladder dysfunction.

- TM can occur as an independent entity, or as a postinfectious complication , or as a continuum of neuro-inflammatory disorders that includes acute disseminated encephalomyelitis, multiple sclerosis.



CLINICAL FEATURES

- The onset of TM is characterized by acute or subacute.

- **Motor symptoms** — Motor symptoms include a rapidly progressing paraparesis that can involve the upper extremities (depending on location of the lesion within the spinal cord), with initial flaccidity followed by spasticity if caused by white matter damage.

- **Sensory symptoms** — Typical sensory symptoms are pain, and paresthesia. Most patients have a sensory level.

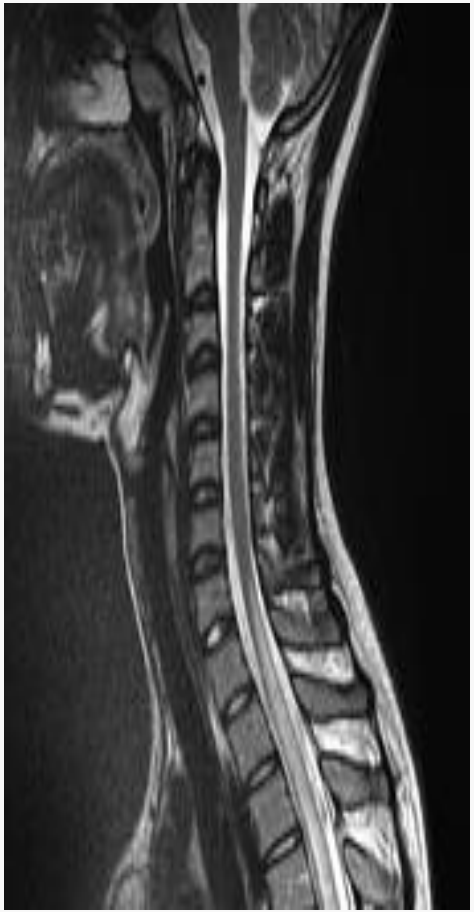
- **Autonomic symptoms** — Autonomic symptoms include increased urinary urgency, bladder and bowel incontinence.

Diagnosis

- MRI of the spine is the preferred diagnostic study for suspected TM(T2 hyperintense signal change , gadolinium enhancement on MRI).

- perform a lumbar puncture (with pleocytosis and/or an elevated IgG index).

- **Diagnostic criteria** — Although a set of diagnostic criteria for TM has been developed for research purposes, not all are necessarily required to make the diagnosis in clinical practice .



- Sensory, motor, or autonomic dysfunction attributable to the spinal cord
- T2 hyperintense signal change on spinal magnetic resonance imaging (MRI)
- No evidence of compressive cord lesion
- Bilateral signs and/or symptoms
- Clearly defined sensory level
- Inflammation defined by cerebrospinal fluid pleocytosis, elevated immunoglobulin G (IgG) index, or gadolinium enhancement on MRI
- Progression to nadir between 4 hours and 21 days

- **Treatment**

- high-dose intravenous glucocorticoid (methylprednisolone (30 mg/kg up to 1000 mg daily) or dexamethasone (120 to 200 mg daily for adults) for three to five days.)
- plasma exchange.
- intravenous cyclophosphamide for patients with aggressive TM has been associated with good outcomes.

Structural disorders of the Eye

Episcleritis

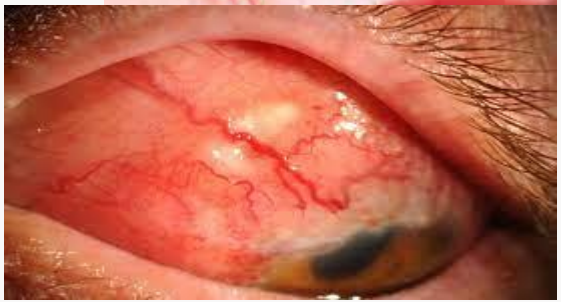
- is a common, benign, self-limiting and frequently recurrent disorder.
- It is seldom associated with a systemic disorder.
- Presentation is with unilateral mild discomfort, tenderness to touch and watering.
- **Two clinical types :**

Simple episcleritis is characterized by sectoral or, rarely, diffuse redness. it usually resolves spontaneously with 1-2 weeks.
Nodular episcleritis is localized to one area of the globe, forming a nodule with surrounding injection.

- if discomfort is annoying, topical steroids and/or topical non-steroidal antiinflammatory drugs (NSAIDs) may be helpful.

Scleritis

- Scleritis is a granulomatous inflammation of the scleral.
- The condition covers a spectrum of ocular disease which extends from trivial self-limiting episodes of inflammation to a necrotizing process.
- may cause sight-threatening complications such as uveitis, cataract. glaucoma, keratitis, retinal oedema and optic neuropathy.



- The classification is based on the primary anatomical site of the inflammation and the following associated changes in the scleral vasculature:

Anterior scleritis Non-necrotizing: diffuse or nodular.
Necrotizing: with or without inflammation.
Posterior scleritis

- in up to 50 percent of patients, scleritis is associated with an underlying systemic illness such as rheumatoid arthritis or granulomatosis with polyangiitis .

CLINICAL FEATURES

- Subacute onset of symptoms.
- Scleritis is usually characterized by severe, constant, boring pain that worsens at night or in the early morning hours and radiates to the face and periorbital region.
- The pain generally limits activity and often prevents sleep
- dark red eyes.
- Photophobia and/or loss of vision

Treatment

- NSAIDs: first-line therapy in mild to moderate cases
- Systemic glucocorticoids: in patients unresponsive to NSAIDs.
- . Systemic immunosuppressive therapy (e.g., azathioprine, methotrexate): in patients unresponsive to steroids.

uveitis

- uveitis is characterized by inflammation of the uvea, which is the middle portion of the eye; the anterior portion of the uvea includes the iris and ciliary body, and the posterior portion of the uvea is known as the choroid.

- There are four types of uveitis:

1. Anterior (Iris, ciliary body).
2. Posterior (vitreous body, choroid, retina).
3. Intermediate (vitreous body).
4. Complete, also called panuveitis

- its associated with systemic inflammatory conditions such as seronegative spondyloarthropathies, RA, SLE and Behçet disease. infectious causes are also possible

Clinical features:

1. Anterior uveitis (most common): pain, red eye, Photophobia, Decreased visual acuity (blurry vision), Increased lacrimation, Hypopyon.

2. Posterior uveitis: Painless, Floaters, Decreased visual acuity (blurry vision).

3. intermediate uveitis same as Posterior uveitis.

Treatment:

- Initial treatment:Glucocorticoids, Cycloplegics (e.g., atropine, scopolamine), Analgesics (e.g., NSAIDs).
- Severe cases or those resistant to initial treatment: Systemic glucocorticoids, Immunosuppressants (e.g., azathioprine, cyclosporin, infliximab).