

Updates on Common Rheumatological Disorders Hom Neupane, MD

MAY 2, 2026

Learning objectives

Review basic clinical and therapeutic aspects of rheumatologic conditions

- ▶ Improve interpretation skills for rheumatology laboratory testing
- ▶ Identify patients that can be managed in primary care practices, and patients that need to be referred to rheumatology
- ▶ Review up-to-date information about etiology, pathogenesis, and treatment of rheumatologic disorders

Partnering with the patient

- ▶ Rheumatological conditions are often difficult to understand for the medical professionals, more so for patients.
- ▶ With aggressive treatment, destructive consequences can be prevented.

Living comfortably with uncertainty

- ▶ Many criteria and classification schemes were developed for clinical trials, not making a specific diagnosis eg:
- ▶ A young woman with malar rash, GN and + ANA has lupus, may not have 4th criterion
- ▶ Another example of an elderly woman with myalgia, fever and visual deficit of new vision loss is c/w GCA, Rx should not be delayed for +biopsy.
- ▶ Pt has interstitial pneumonitis, malignancy and infection have been ruled out by extensive workup

Addressing the patient, not study results

- ▶ Inappropriate testing can increase diagnostic confusion and patient anxiety
- ▶ ANA is very sensitive but, non-specific
- ▶ AntiDS-DNA is highly specific but only mod. sensitivity
- ▶ ESR and CRP are helpful but should not be used as a sole criteria for disease flare-up such as in PMR.

Framing the clinical investigation

- ▶ Accurate medical history
- ▶ Thorough physical exam
- ▶ Review of system eg: 1.elderly man on diuretics for hypertension presents with recurrent acute inflammation of 1st MTP (ask for renal calculi or tophi, not photosensitivity)
- ▶ A young woman with multiple osteoporotic stress fractures should be asked about symptoms suggestive of malabsorptive states.

Thinking Like a Rheumatologist

- ▶ The diagnosis of many rheumatologic disorders is made clinically.
- ▶ Always treat the patient, not the laboratory results.
- ▶ Uncertainty is rife in rheumatology and must be accepted.
- ▶ Rheumatologic disorders are often variable in course and severity.
- ▶ Better education of the patient, especially with nature of the illness.

Chronic Inflammatory Arthritis

The Big One:

Rheumatoid

The Others:

Reactive

Psoriatic

Enteropathic

Infectious

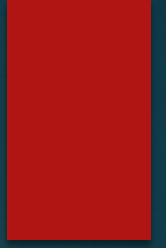


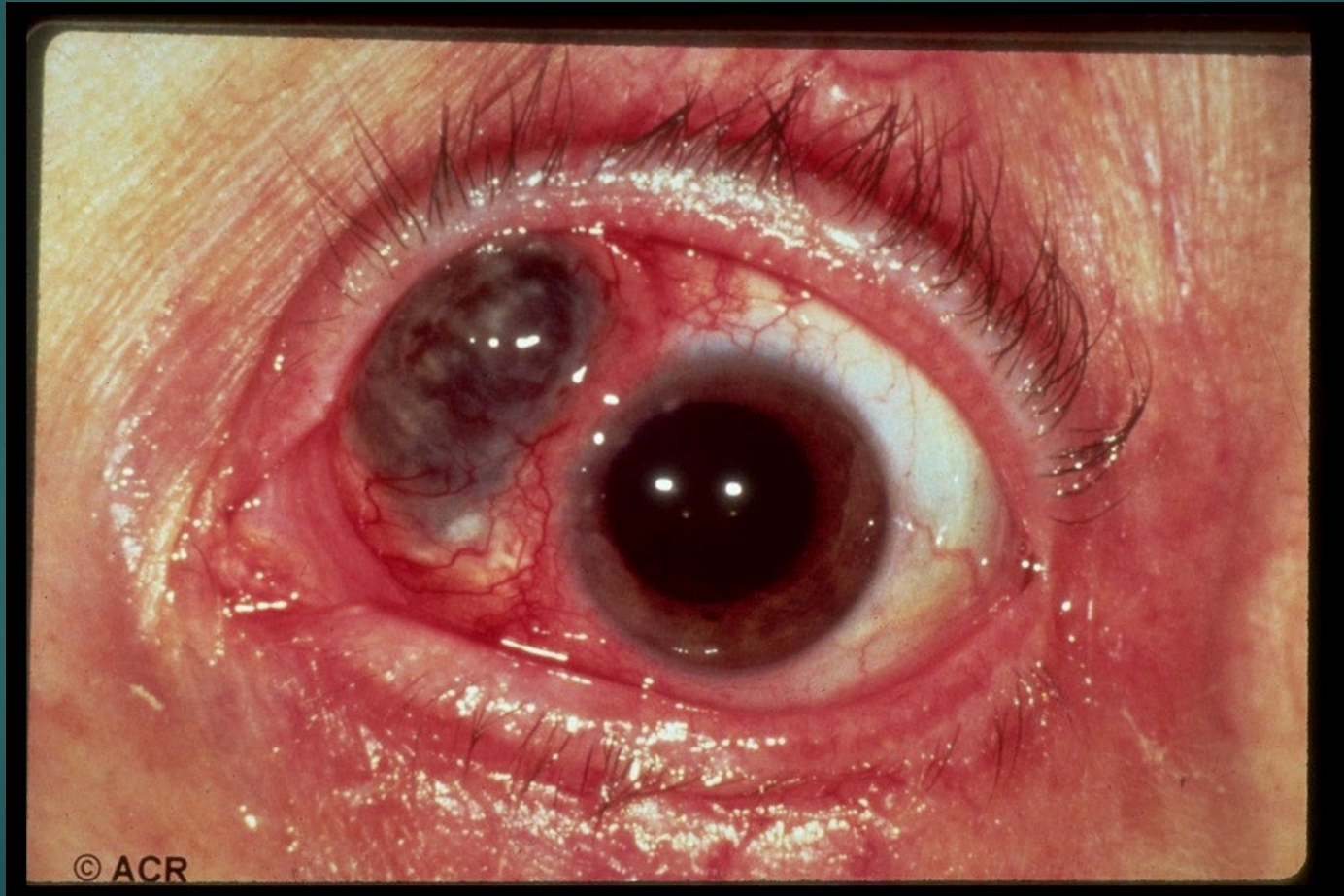


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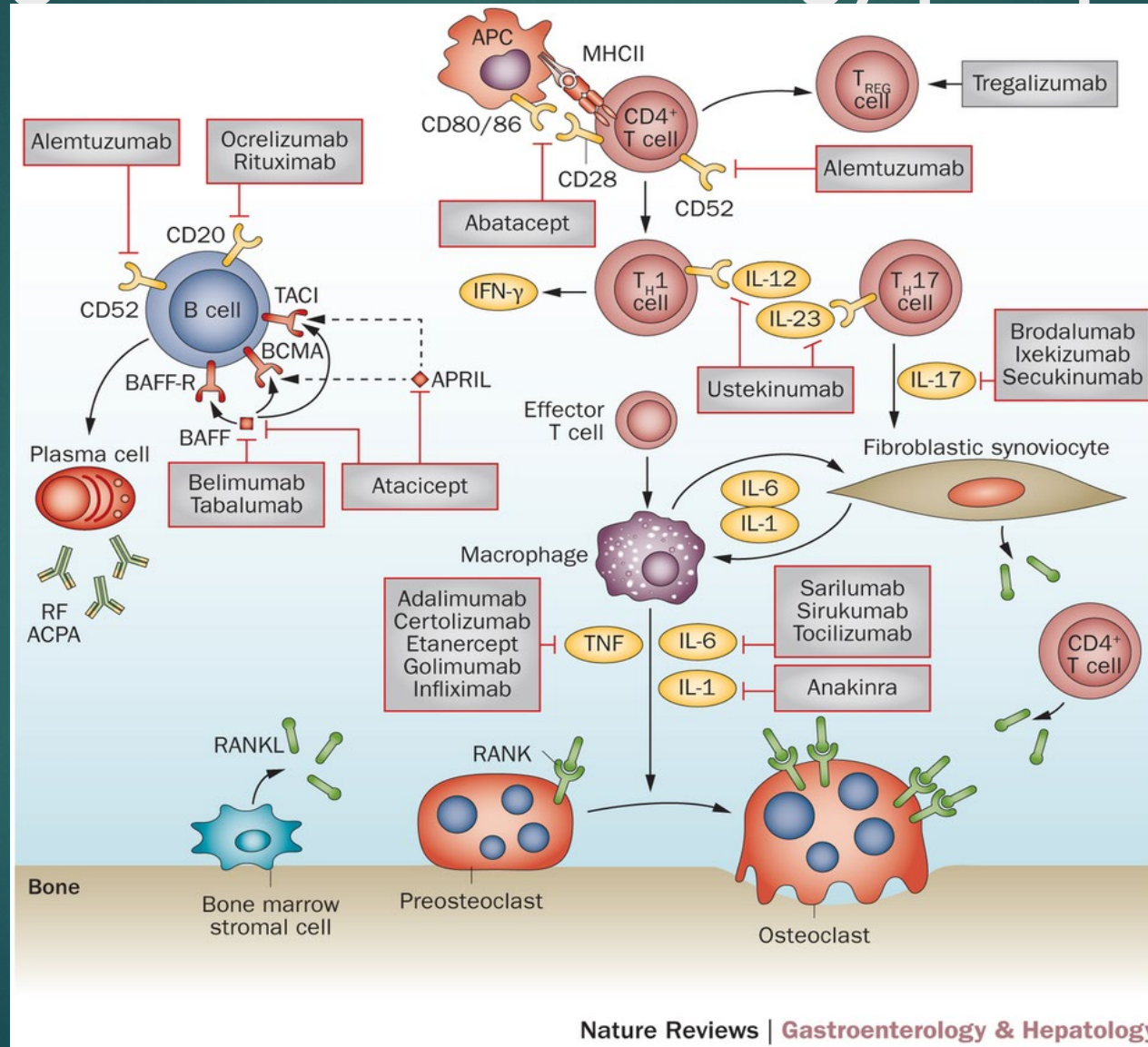


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Advances in use of immunomodulatory agents—a rheumatology perspective

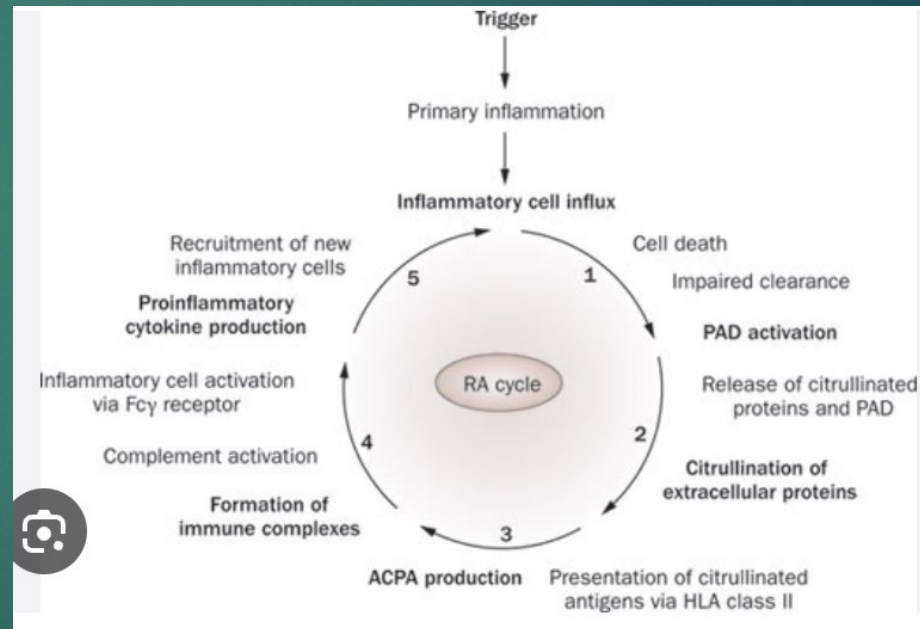


Management of RA

- ▶ Diagnose rheumatoid arthritis (RA) early and initiate disease-modifying antirheumatic drug (DMARD) therapy at the time of diagnosis.
- ▶ Treat all patients to a disease activity target—remission or low disease activity.
- ▶ It is not important what therapy patients receive as long as they are treated until they reach the target.
- ▶ For most patients, methotrexate will be the cornerstone of DMARD therapy.
- ▶ Many patients will require combinations of DMARDs with or without biologics to achieve the target.
- ▶ Many effective biologic DMARDs are available—all are more effective with methotrexate.
- ▶ NSAIDs may provide useful symptom control but are rarely indicated without DMARDs.
- ▶ Glucocorticoids are rapidly effective for most but have side effects. Therefore, use only with other DMARDs and ideally only as a bridge to effective DMARD therapy.
- ▶ Aggressively address the ubiquitous comorbidities of RA, especially cardiovascular disease.

Smoking increases risk of RA in genetically predisposed.

- ← Anti-CCP antibodies are directed against citrulline residues on various proteins formed by posttranslational deimination of arginine residues by the enzyme peptidylarginine deiminase (PAD).
- ← Both RF and anti-CCP can occur years before the onset of symptomatic disease.
- ← Environmental factors such as smoking may trigger an autoimmune reaction that involve the shared epitope (in HLA-DR4) and citrulline-modified peptides.



Smoking can lead to lung inflammation, activates PAD, which deaminates arginine to form citrullinated peptides.

| Clinical domains and criteria | Weight | Immunology domains and criteria | Weight |
|--|--------|------------------------------------|--------|
| Constitutional | | Antiphospholipid antibodies | |
| Fever | 2 | Anti-cardiolipin antibodies OR | |
| Hematologic | | Anti-β2GP1 antibodies OR | |
| Leukopenia | 3 | Lupus anticoagulant | 2 |
| Thrombocytopenia | 4 | Complement proteins | |
| Autoimmune hemolysis | 4 | Low C3 OR low C4 | 3 |
| Neuropsychiatric | | Low C3 AND low C4 | 4 |
| Delirium | 2 | SLE-specific antibodies | |
| Psychosis | 3 | Anti-dsDNA antibody* OR | |
| Seizure | 5 | Anti-Smith antibody | 6 |
| Mucocutaneous | | | |
| Non-scarring alopecia | 2 | | |
| Oral ulcers | 2 | | |
| Subacute cutaneous OR discoid lupus | 4 | | |
| Acute cutaneous lupus | 6 | | |
| Serosal | | | |
| Pleural or pericardial effusion | 5 | | |
| Acute pericarditis | 6 | | |
| Musculoskeletal | | | |
| Joint involvement | 6 | | |
| Renal | | | |
| Proteinuria >0.5g/24h | 4 | | |
| Renal biopsy Class II or V lupus nephritis | 8 | | |
| Renal biopsy Class III or IV lupus nephritis | 10 | | |

Total score:



Classify as Systemic Lupus Erythematosus with a score of 10 or more if entry criterion fulfilled.

SLE Classification criteria

Entry criterion

Antinuclear antibodies (ANA) at a titer of $\geq 1:80$ on HEp-2 cells or an equivalent positive test (ever)



If absent, do not classify as SLE
If present, apply additive criteria



Additive criteria

Do not count a criterion if there is a more likely explanation than SLE.

Occurrence of a criterion on at least one occasion is sufficient.

SLE classification requires at least one clinical criterion and ≥ 10 points.

Criteria need not occur simultaneously.

Within each domain, only the highest weighted criterion is counted toward the total score§.



Five clinical subtypes of psoriatic arthritis:

Table 37-1. Classification of Joint Involvement in Psoriatic Arthritis

| SUBTYPE | PERCENTAGE | TYPICAL JOINTS |
|--------------------------------------|------------|--|
| 1. Asymmetric oligoarticular disease | 15 to 20 | DIP joints and PIP joints of hands and feet. MCP joints, MTP joints, knees, hips, and ankles |



What clinical features suggest psoriatic arthritis rather than other polyarticular arthritic diseases such as rheumatoid arthritis?

- ← *Asymmetric joint involvement.*
- ← *Absence of rheumatoid factor.*
- ← *Significant **nail pits** (>60 total pits is pathognomonic) or nail dystrophy.*
- ← *Involvement of DIP joints in the absence of osteoarthritis.*
- ← ***“Sausage digits” (dactylitis):** seen in 30% to 50%. Due to synovitis and flexor tenosynovitis.*
- ← ***Enthesitis:** seen in 35% to 40%. Most common Achilles and plantar fascia insertion.*
- ← *Family history of psoriasis or psoriatic arthritis.*
- ← *Axial radiographic evidence of sacroiliitis, paravertebral ossification, and syndesmophytes.*
- ← *Peripheral radiographic evidence of erosive arthritis with relative lack of periarticular osteopenia.*
- ← *•Synovial biopsies show increased vascularity and the presence of macrophages (CD163+), lymphocytes, and neutrophils.*



Reiter's Syndrome

- ▶ The tetrad:
 - ▶ Arthritis
 - ▶ Urethritis
 - ▶ Conjunctivitis
 - ▶ Mucocutaneous





Periungueal erythema



The Shawl Sign

B



Gottron papules knees

Source: IMAG



Gottron papules



V-sign

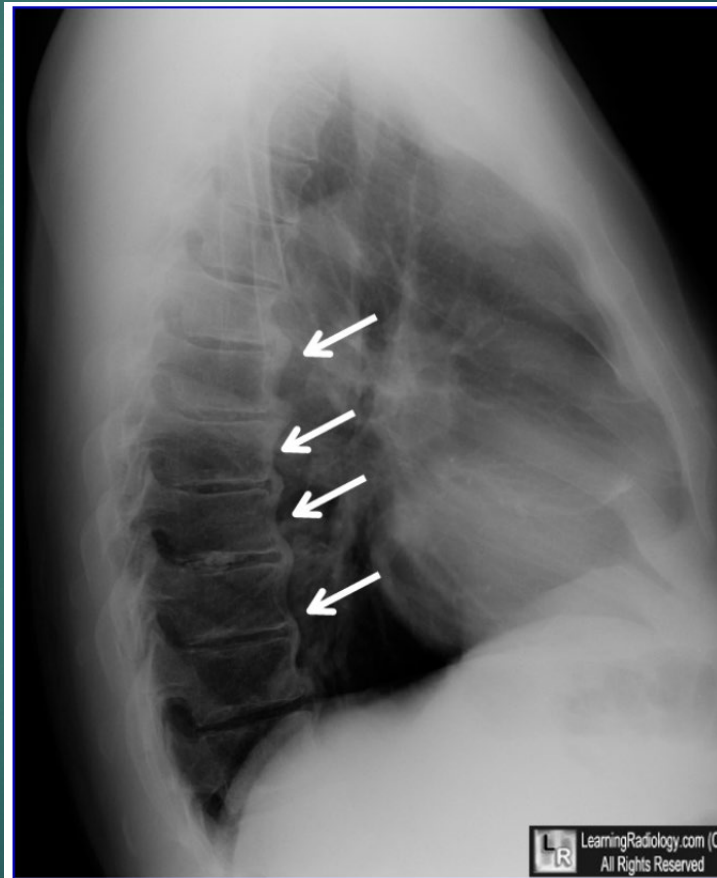


Heliotrope rash

A

Diffuse idiopathic skeletal hyperostosis

- Noninflammatory condition that causes back pain and stiffness without sacroiliac pain, typically in men > 45 yo.
- Associated with a distinctive radiographic finding consisting of flowing linear calcification and ossification along the anterolateral aspects of the vertebral bodies.
- Should involve four contiguous vertebral bodies while disc height maintained.



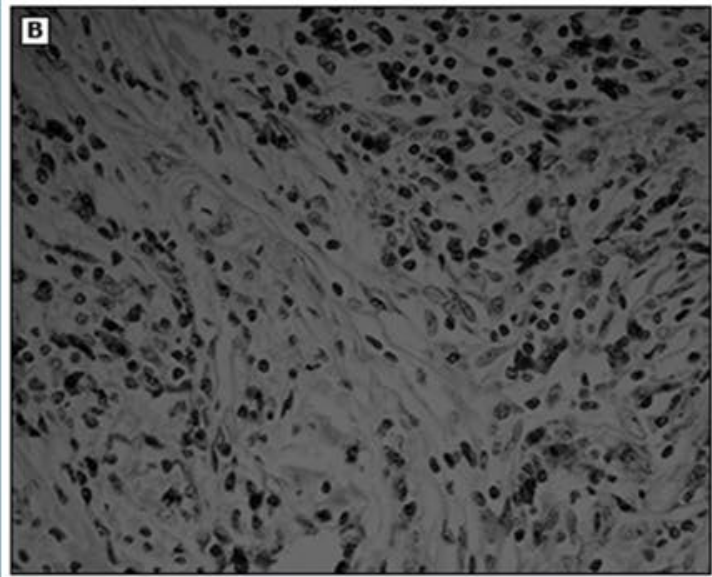
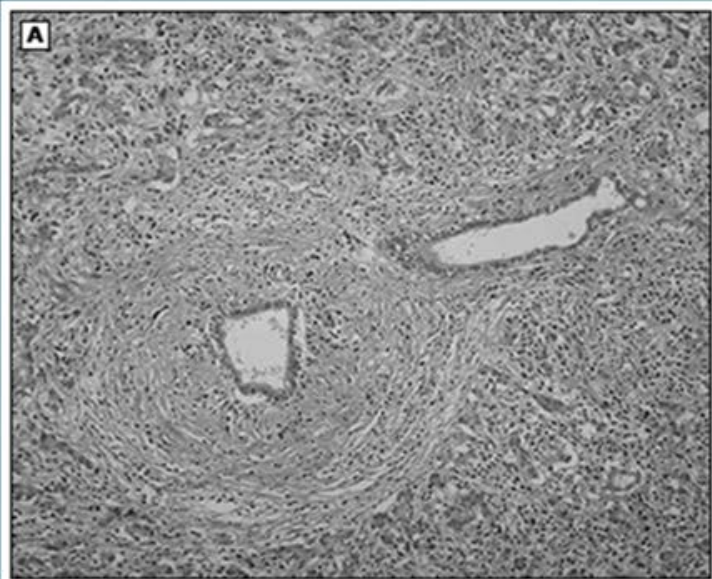
Osteonecrosis (ON)

- ← Death of cellular components of bone and bone marrow resulting from ischemia.
- ← Bones with limited vascular supply are most vulnerable. Most affected is femoral head.
- ← **At risk areas:** femoral head, carpal bones (lunate and scaphoid), humeral head, talus..etc.
- ← 10% to 30% of patients on GC develop ON. Especially those on prednisone 20mg or greater for over a month or receive >2g total over 2 to 3 months.
- ← Prednisone increases osteoblast apoptosis directly and indirectly increases hypercoagulability and decreased angiogenesis.
- ← Other causes: ETOH, genetic, proteinase inhibitors, hypercoagulable states

Hallmarks of IgG4-RD

- ▶ Dense lymphoplasmacytic infiltrations with a predominance of IgG4-positive plasma cells in the affected tissue,
- ▶ fibrosis
- ▶ most of the time by obliterative phlebitis and
- ▶ increased number of eosinophils
- ▶ Serum IgG4 levels are elevated (>135 mg/dL) in about two-thirds of the patients

“storiform” pattern



Autoimmune Pancreatitis
(A) Dense lymphoplasmacytic infiltration and storiform fibrosis (HE staining),
(B) abundant infiltration of IgG4-positive plasma cells (IgG4 immunostaining).

Classification of rheumatologic emergencies

- **Catastrophic antiphospholipid syndrome (cAPS)**

- **Kidney-lung syndrome**

- **Central nervous system (CNS) vasculitis**

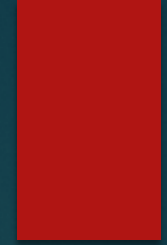
- **Anti-Ro syndrome (neonatal lupus)**

- **Macrophage activation syndrome (MAS)**

- **Scleroderma renal crisis**

- **Septic arthritis and**

Organ system involvement in cAPS



| | |
|-------------------------|-------------|
| Renal | 78 % |
| Pulmonary | 66 % |
| CNS | 56 % |
| Cutaneous | 50 % |
| Gastrointestinal | 38 % |
| Hepatic | 34 % |
| Adrenal | 13 % |
| Urogenital | 6 % |

Criteria for catastrophic APS

▶ Definite cAPS

- ▶ • Evidence of vessel occlusion or occlusive impact on >3 organs, systems, and/or tissues^a
- ▶ • Simultaneous or <1 week event occurrence
- ▶ • Anatomopathological confirmation of small-diameter vessel occlusion, at least in one organ or tissue^b
- ▶ • Persistent presence of antiphospholipid antibodies (APA/lupus anticoagulant) ≠ 6 weeks^c

▶ Probable cAPS

- ▶ • Two or more organs or systems affected
- ▶ • Occurrence of two events in less than 1 week and the third prior to week 4
- ▶ • The four criteria, except for absence of separate lab confirmation of at least 6 weeks due to early patient death.

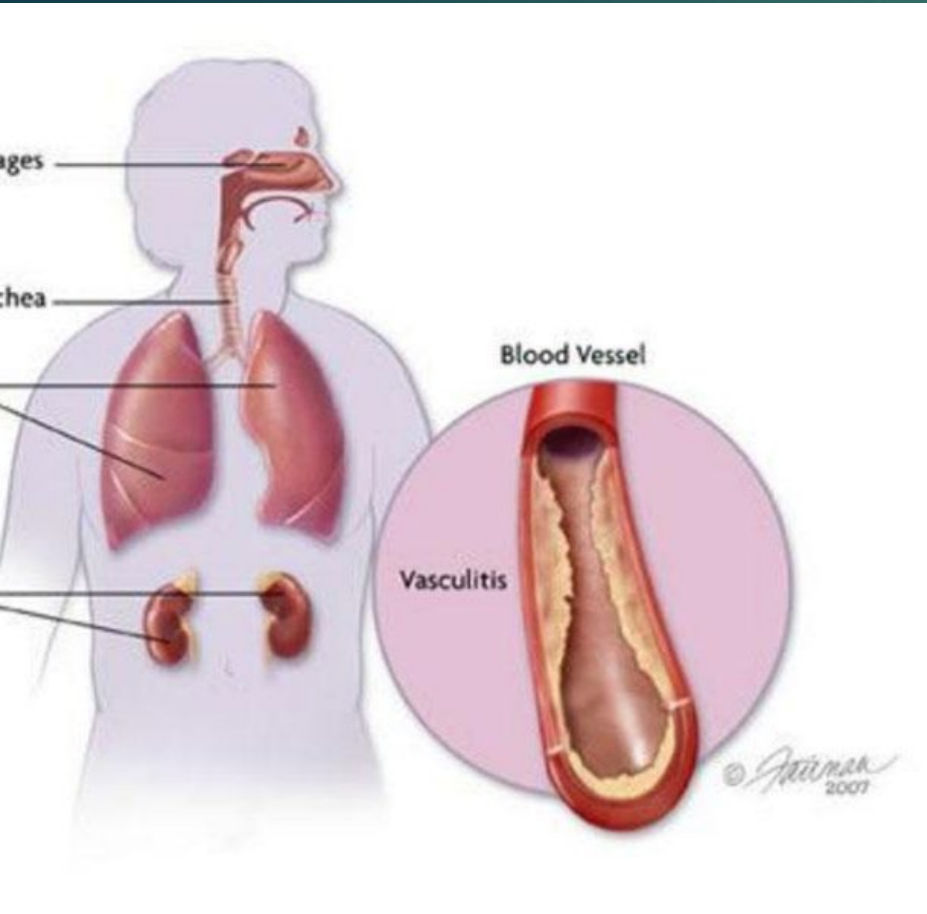
cAPS treatment

- ▶ ICU supportive care.
- ▶ Anticoagulant therapy ,a 5000 U bolus of nonfractionated heparin, followed by a continuous infusion of 1500 U/h , as enoxaparin is quite effective as well, at a dose of 1 mg/kg/day, coumadin as outpatient.
- ▶ Concomitant glucocorticoid (GC) therapy shall be started with anticoagulation
- ▶ If the patient fails to respond, gamma globulin 400 mg/kg/day for 5 days (average dose 25–30 g/day) .The use of cyclophosphamide (CYC)-type cytostatic agents is recommended, at a dose of 0.5–1 g/m² SC, always combined with gamma globulinfor patients failing to respond to GC therapy .
- ▶ For severely ill patients failing to respond to gamma globulin and CYC, the recommendation is to proceed to plasmapheresis for three to five continuous days, 100–150 ml/min

ANCA-associated vasculitides

- ← **Granulomatosis with polyangiitis (GPA)**- directed against **proteinase 3 (PR3)**
- ← **Microscopic polyangiitis (MPA)**- directed against **myeloperoxidase (MPO)**
- ← **Eosinophilic granulomatosis with polyangiitis (EGPA)**
- ← **Renal-limited vasculitis with pauci-immune necrotizing/crescentic glomerulonephritis (RLV)**

Granulomatosis with Polyangiitis (GPA)



Characterized by:

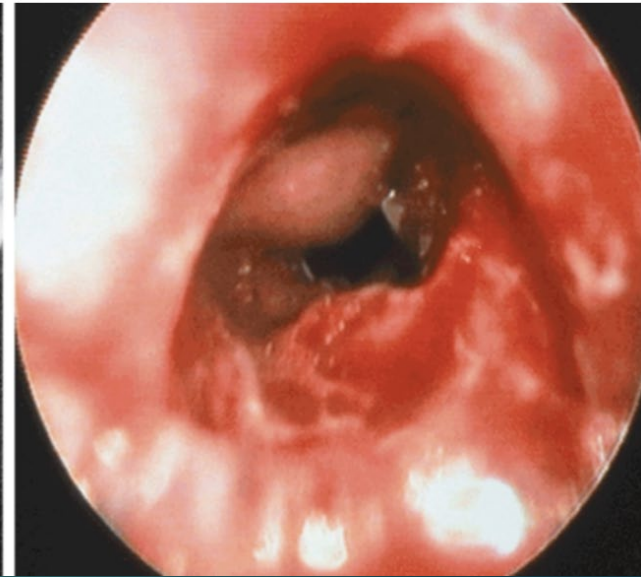
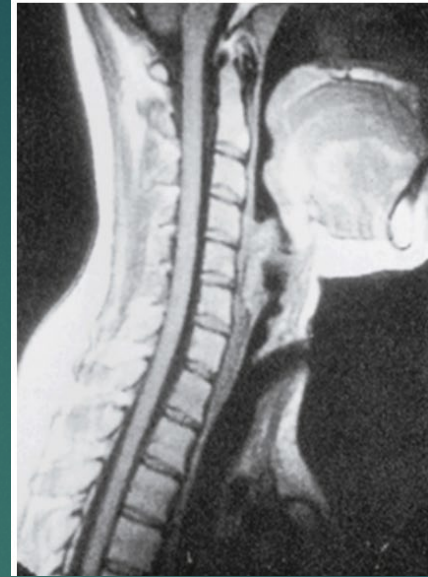
- **Upper and lower respiratory tract** involvement with granulomatous vasculitis.
- **Glomerulonephritis (GN)**- pauci-immune, focal, segmental, necrotizing and often crescentic
- Can also affect eyes, skin, MSK system, cardiac
- ↳ C-ANCA+ by IFA, anti-proteinase 3 (PR3) antibodies+ ELISA assay
- ↳ Generalized GPA: all 3 anatomic sites
- ↳ Limited: absence of renal involvement
- ↳ Renal bx is gold standard. Skin biopsy: non-specific vasculitis findings, thoracoscopic lung biopsy high risk procedure, transbronchial biopsy low yield



Saddle nose deformity



Pulmonary nodule



MRI of subglottic stenosis and endoscopic view



CT scan of the orbits, showing a retro-orbital mass (orbital pseudotumor)

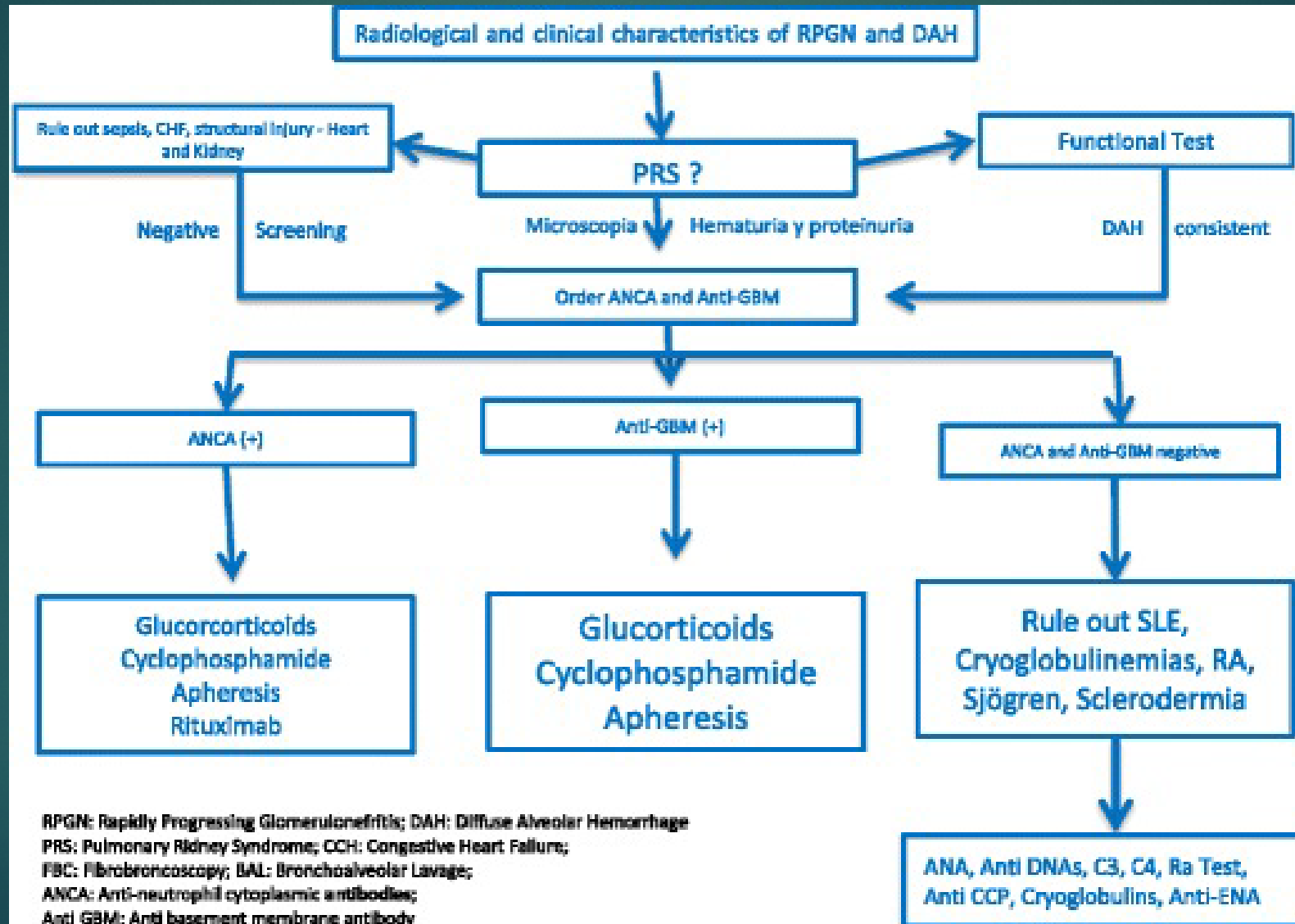
Pulmonary-renal syndrome

- ▶ vasculitis associated with neutrophil cytoplasmic antibodies (ANCA) in 56–77.5 % of the cases,
- ▶ Antiglomerular basement membrane antibody (anti-GBM Ab), representing 12.5–17.5 % of the patients. Some of the less frequent causes (<10 %) are double positive disease,
- ▶ APS-associated vasculitis, SLE-associated vasculitis, and IgA vasculitis (Purpura Henoch-Schönlein)

Double positive disease in PRS

- ▶ There is a subgroup among the PRS patients with both groups of antibodies present: ANCA and anti-GBM . The medical literature describes 5–14 % with ANCA (+) and detectable anti-GBM levels; another subgroup has 30–43 % anti-GBM with ANCA (+). The prevailing antigen in ANCA-associated PRS is myeloperoxidase (MPO) with positive ANCA in 82 %.

Double positive disease in PRS



PRS treatment

- ▶ There is no doubt that glucocorticoid therapy continues to be the battle horse for the treatment of vasculitis and in particular PRS vasculitis. Pulse dosing continues to give the best results, and the drug of choice is methylprednisolone 15–20 mg/day for three to five continuous days, followed by the maintenance dose of 1–2 mg/kg/dose (divided into three doses), with concomitant use of CYC-type cytostatic agents at a dose of 0.5–1 g/m² SC.
- ▶ Recent studies have shown that in anti-GBM-associated PRS, apheresis for 14 continuous days 100–150 ml/min or until the anti-GBM antibodies are removed reduces the mortality and the rate of relapses (as shown in the PEXIVAS trial). In contrast, in ANCA (+)-associated PRS, using biological therapies such as anti-CD20 (rituximab) at a dose of 350 mg m² SC × four doses per week has resulted in positive outcomes
- ▶ It is important to emphasize that the relapse rate in this patients ranges from 27 to 35 %, and hence, immunosuppressive therapy shall be maintained. The most commonly used agents are metotrexate, azathioprine, and mycophenolate mofetil

CNS vasculitis

- ▶ **Connective tissue diseases:** systemic lupus erythematosus, scleroderma, rheumatoid arthritis, Sjögren syndrome, mixed diseases of the connective tissue, and Behçet's disease.
- ▶ **Systemic necrotizing vasculitis:** polyarteritis nodosa, Churg-Strauss syndrome, microscopic polyangiitis, Kawasaki disease.
- ▶ **Systemic granulomatous vasculitis:** Wegener's granulomatosis, lymphomatoid granulomatosis, and lethal midline granuloma.

Diagnostic approach to CNS vasculitis

| | Acute phase reactants VSG/PCR | Pulses | Recurrent ulcerations | Antibodies |
|-----------------|----------------------------------|--------|-----------------------|-------------------|
| Wegener | ↑↑↑↑ | Normal | (-) | ANCA _c |
| Behçet | ↑↑↑↑ | Normal | (-) | (-) ^a |
| LES | ↑↑ | Normal | (+/-) | ANA, anti-dsDNA |
| Sjögren | ↑ | Normal | (-) | Anti-Ro/anti-LA |
| Takayasu | ↑↑↑ | ≠ | (+) | (-) |

. *Scleroderma renal crisis*

- ▶ The acute onset of renal failure.
- ▶ The abrupt onset of moderate to marked hypertension (although some patients remain normotensive).
- ▶ A urine sediment that is usually normal or reveals only mild proteinuria with few cells or casts

New onset **hypertension**.
Anemia,
thrombocytopenia, and
proteinuria are common
laboratory features.

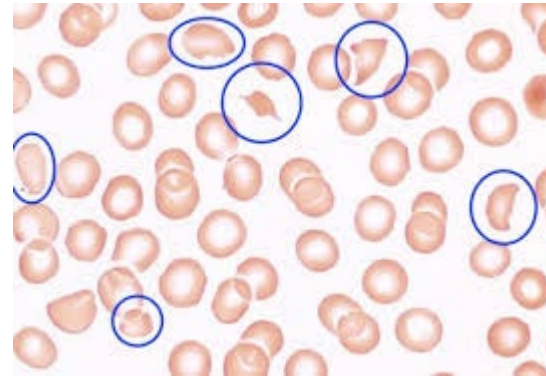
Evidence of
microangiopathic
hemolytic anemia with
schistocytes on the
peripheral blood smear is
a clue to the diagnosis

Patients with diffuse SSc
at risk

Higher risk with +anti-RNA
polymerase III

Angiotensin-converting
enzyme (ACE) inhibitors
work better than
angiotensin receptor
blockers (ARBs)

Avoid steroids- can
precipitate renal crisis,
prednisone >20mg.



Scleroderma renal crisis treatment

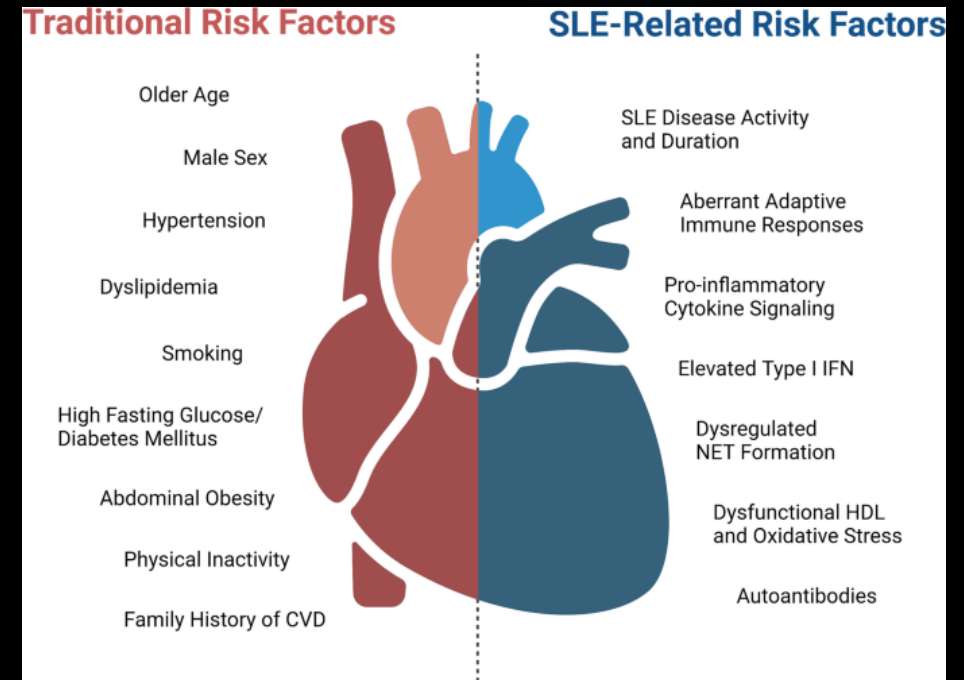
- ▶ Blood pressure control with angiotensin-converting enzyme (ACE) inhibitors with gradual reduction of malignant hypertension is the cornerstone of treatment.
- ▶ Other agents such as calcium channel-blocking agents may be added. Renal dialysis may even be required. It is important that the blood pressure be lowered gradually (i.e., avoid use of intravenous nitroprusside or labetalol) and do not let the patient develop hypovolemia

Increased risk Cardiovascular Disease in Systemic Lupus Erythematosus

Chronic inflammatory state—> acceleration of atherosclerotic process—> increased CVD

SLE, RA, APS increase risk of CVD

▶ Premature coronary heart disease is a major cause of morbidity and mortality in SLE compared to general population.



Take home message

- ▶ **Unusual (difficult) cases—targeted questioning: the personal and/or family history of autoimmunity is extremely relevant, as well as the use of oral contraceptives, past history of arterial or venous thrombosis, purpura, rheumatoid arthritis, lupus, abortions, and gangrenous ulcers.**
- ▶ **Always check the skin for lesions like livedo reticularis, Raynaud, nail pitting, Grotton papules, alopecia, splinter hemorrhage, malar rash, and photosensitivity.**
- ▶ **Use of paraclinical tests (Fast Lab): PCR, fibrinogen, procalcitonine, VDRL, C3, C4, Ra Test, COOMBS.**
- ▶ **Do not postpone glucocorticoids and immunosuppressors because of concomitant infections (keep in mind that the patient is hospitalized, monitored and severely ill).**



Thank You