Clinical features.

The peak age of onset is about 45 y.in men while in predisposed women it occurs some years after menopause.

Gout classically occurs in obese middle or young men who drinks more alcohol than average.

The patient wakes early hours in the morning with sever agonizing pain usually in the

metatarsophalangeal joint of the big toe (the joint is usually red, swollen, warm & tender).The overlying skin is shinny with periarticular edema, & there is often fever.

75% of the first attack is monoarticular, at half involve metatarsphalageal joint of big toe.

Attack lasts days or weeks befor subsiding spontaneously . Patient might have one attack or may have reccurences at monthly or yearly intervals.

Reccurent attacks may merge in to each other. No synovial joint is immune from gout . Boney erosion & joint destruction might occur & lead to disability.

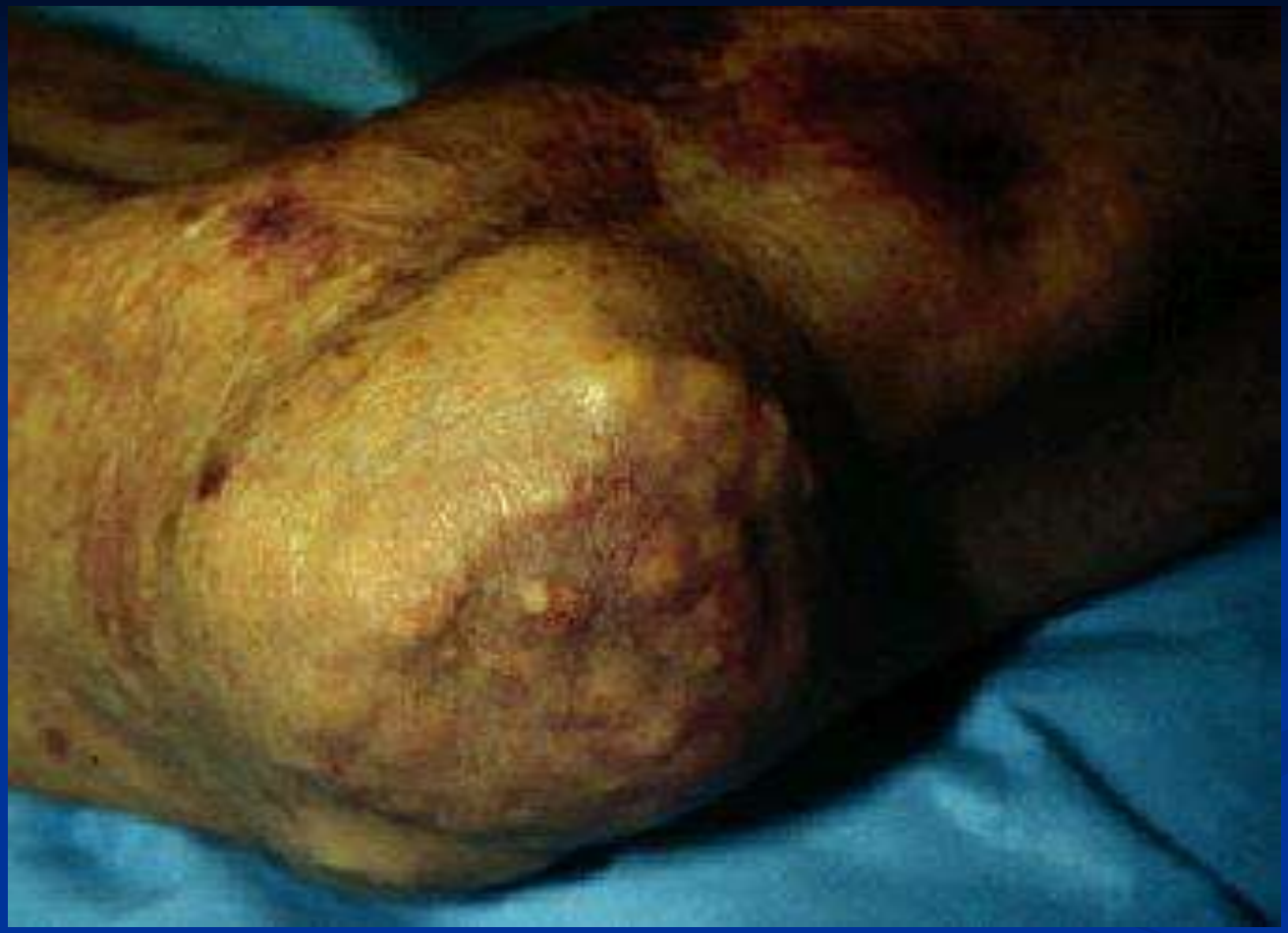
Acute gout could occur in nonarticular sites i.e olecranon bursa , achillis tendon & prepatellar bursa.

Tophi.

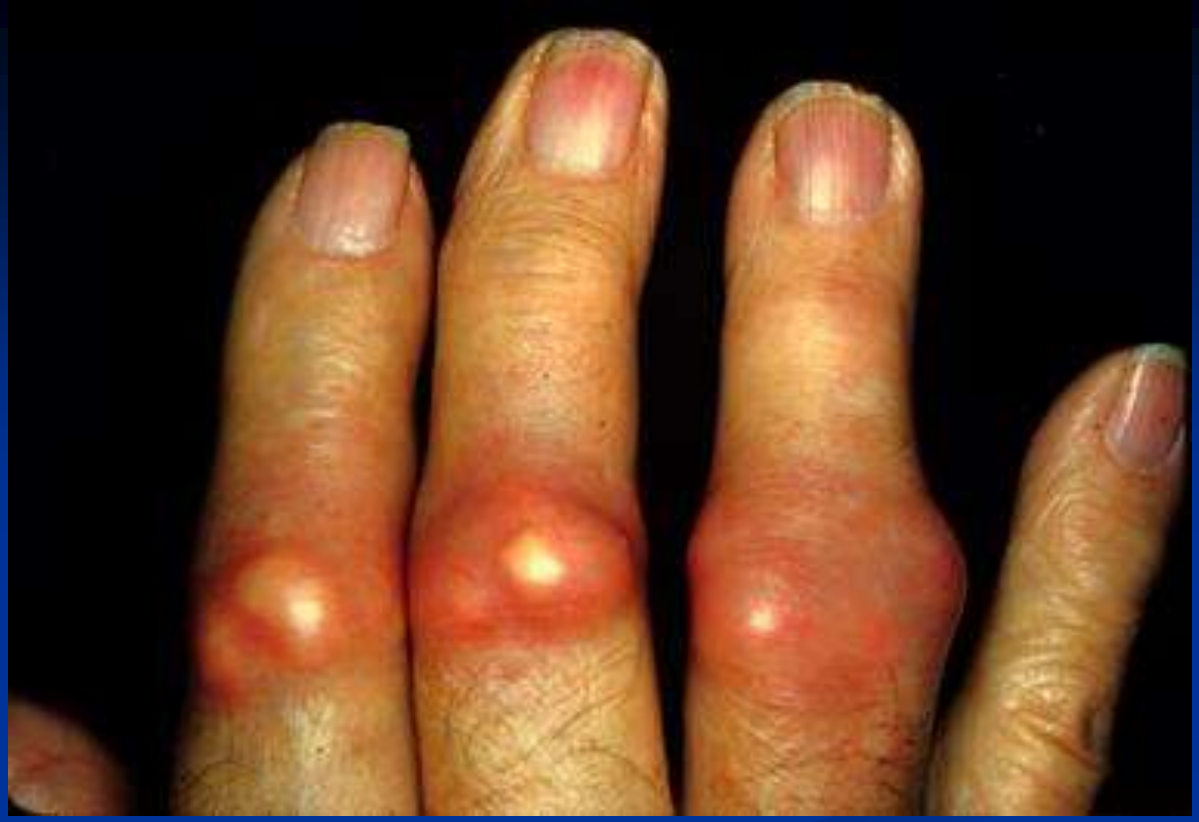
A tophus is a deposite of fine needle (msu) surrounded by grnuloma & giant cells. They are found in the articular cartilage,ear cartilage, synovium, tendon sheath, bursae & other periarticular structure..Patient possessing tophi is said having chronic tophaceous gout either or not experiencing episodes of acute gouty arthritis. Presence of tophi is an indication for long term treatment to lower the serum uric acid.

Renal calculi

is present in 10% of gout & renal nephropathy might be found on autopsy.



Large tophus of the knee in patient with chronic uncontrolled gout.



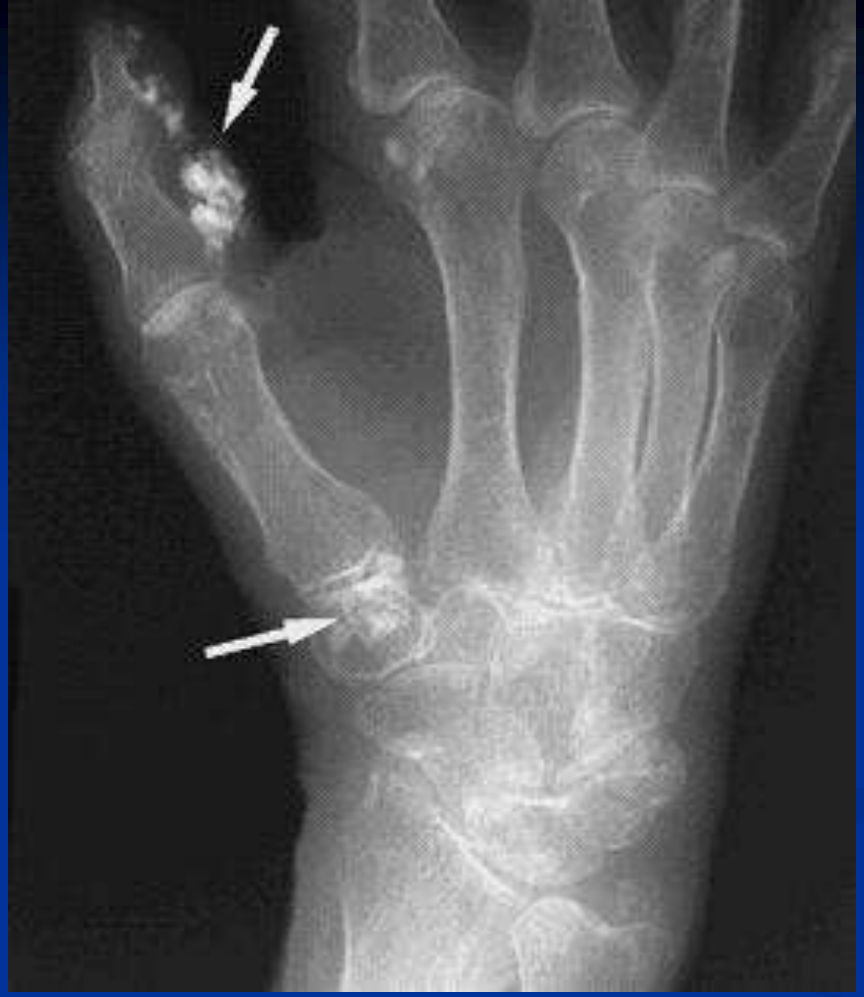
Three inflamed tophi over the proximal interphalangeal joints in a patient with chronic tophaceous gout. Several of the lesions ruptured spontaneously over the next three days, exuding a pasty material composed of urate crystals and inflammatory cells but no organisms.

Dfferential diagnosis.

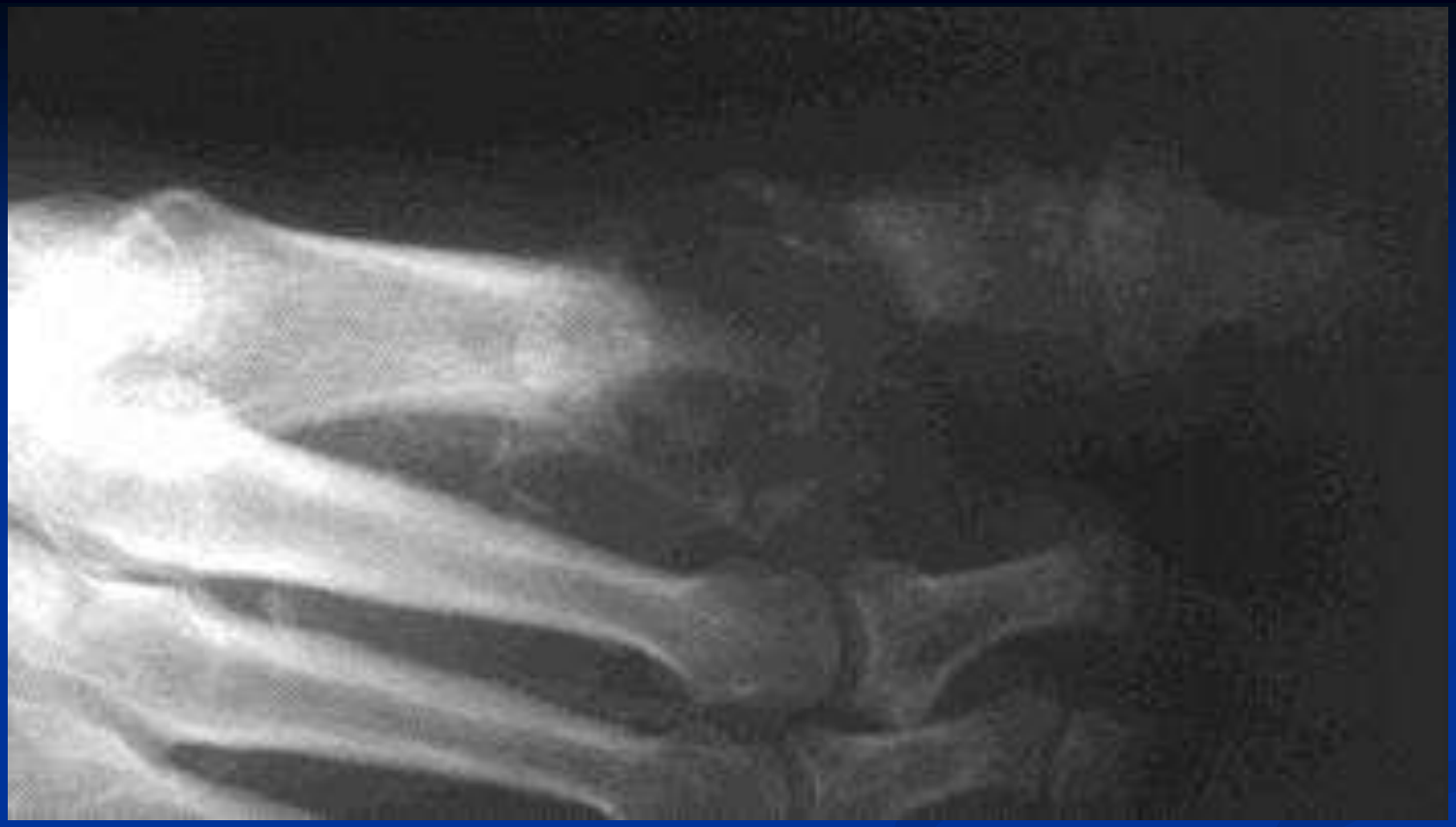
- Pseudogout
- Acute rheumatic fever
- RA
- Pyogenic arthritis
- Cellulites
- Bursitis,
- Tendonitis
- Thrombophelibitis.

Investigation .

- ESR is elevated in acuter attack .
- Serum uric acid could be high but it is not necessary to be so & high serum uric acid alone doesn't justify the diagnosis of gout.
- In acute gout the presence of long needle shaped negatively birefringent nmonosodium crystals in the synovial fluid is diagnostic.
- X- ray shows punched out area , joint destruction & might be ankylosis.]



Plain radiograph of the hand demonstrating soft tissue calcifications adjacent to interphalangeal joints and at the base of the thumb (arrows). These findings represent calcification within gouty tophi.



Plain radiograph of the foot demonstrating features consistent with gout. There is soft tissue swelling and extensive erosions involving the first metatarsophalangeal joint, as well as calcifications within a tophus.

Management.

The aims are to reduce acute synovitis , prevent further crystal formation & identify associated disease.

In acute attack :

1. NSAID (often indomethacine)
2. Oral colchicine.
3. I.V colchicine.
4. Itraarticular corticosteroids.
5. Oral corticosteroid.

Azapropazone (600 twice a day) is both antiinflamatory & uricosuric agent.

When long term treatment is necessary xanthine oxidase inhibitor (allopurinol) or uricosuric drugs are started after several weeks from controlling the acute attack.

Indications for long term therapy include :

1. Reccurent attacks
2. Tophaceous gout
3. Renal calculi.

Uricosuric drugs inhibit renal tubular reabsorption of uric acid, (Probenecid, Sulphinpyrazone & Salicylate in high doses). They are ineffective in renal failure.

Allopurnol :

Is the most popular hypourecemic agent , it is a xanthin oxidase inhibitor , reduces the oxidation of hypoxanthin to xanthin & xanthin to uric acid.

Indications are :

- Extensive topaceous gout ,
- Renal impairment & ston ,
- Hyperuricemia due to antimitotic drug therapy
- Intolerance or failure of uricosuric therapy.

Side effects include dyspepsia& skin rash.

Oxypurinol is also could be used (having longer half life 28 hours).

Connective Tissue Diseases

The term C.T diseases is used for three conditions:

1. Systemic lupus erythematosus
2. Systemic sclerosis
3. polymyositis & dermatomyositis.

They some sharing features:

Arthritis or arthralgia, multisystem involvement, vasculitis & immunological abnormalities such as ciculating autoantibodies & immune complex deposition.

Features of all three diseases appear in mixed connective tissue disease.

Systemic Lupus Erythematosus

I s a disease of unknown cause, characterized by the presence of , in serum, antibodies against nuclear components . It is a multisystem disease with :

Arthralgia & rash the commonest clinical features while renal & cerebral involvement are the most serious problems.

The clinical course of the disease is characterized by periods of remission & acute or chronic relaps, mltisystem pathologiese & presence of immune abnormalitiese especially antibodies to a number of nuclear & cellular antigens.

Epidemiology :

It s a world wide disesease , affects about 0.1% of the population, it is 20 times less common than RA, it is much more commoner in black womens in USA. Fmales/ males is about 9 / 1. The peak age of onset is between 15 & 40 years. In children female to male ratio is 5/1.

Pathogensis & aetiology.

The cells & tissue are damaged by pathogenic autantibodies & immune complexes , the classical example is that of diffuse prolefrative glomerulonephritis …. Immun complexes deposits in glomerular basement membrane. This will lead to attraction & infiltration of leucocyte which then phagocyte immune complexes & cause release of mediators (such as activators of clotting system) . With continuing immune complex deposition , chronic inflammation may ensuea(come) , ultimately leading to fibrinoid necrosis & scarring (crescent) & loss of renal function.

The cause of SLE is unknown but is probably multifactorial including a variable genetic predisposition & environmental factors that tigger the disease.

Predisposing factors include :

- **Heredity : The identical twine of SLE patient has a 30% chance to develop the disease, first degree relatives have 5% chance, while certain races are especially prone to the disease i.e black Americans & Africans.**
- **Sex hormone status : Females are much more affected than males.**
- **Complement deficiencies of all types.**
- **Environmental triggers.**
- **Drugs: such as hydralazine, & ultra violate light.**
- **Infection : a virus infection is a popular theory for the cause of lupus.**

Immnological mechanism of the disease.

1. Polyclonal B-cell activation ; increased number of B-cells lead to hyperglobulinaemia.
2. Antinuclear antibodies & other autoantibodies are produced.
3. Impaired T-cell regulation of the immune response.
4. Failure to remove immune complxes from the circulation, circulating immune complexes cause arthralgia, deposition of immune complexes in tissue cause vasculitis & other features of the disease including glomerulonephritis .

SLE may coexist with other autoimmune diseases such as haemlytic anemia , thyroiditis, & idiopathic thrombocytopenic purpura.

Pathology.

SLE is characterized by wide spread vasculitis affecting capillaries , arteriols ,& venules. Vascular changes include perivascular mononuclear cells , luman obliteration , enlarged endothelial cells & thrombi .

Pleura & pericardium are infiltrated by mononuclear cells . Coronary arteries often demonstrate premature onset athresclerosis.

Biopsy from malar erythema may reveal some minor basal layer abnormalities as well as immune complex deposits at the dermal – epidermal junction.

Fibrinoid (an eosinophilic amorphous material) is found along blood vessels & tissue fibers . The synovium of joint may be oedematous & may contain fibrinoid deposits.

Haemotoxyline bodies (which are rounded blue homogenous haemtoxyline stained deposits) are seen in inflammatory infiltrates & thought to result from the interaction of antinuclear antibodies and cell nuclei.

The onion skin lesions are found in the spleen & consist of concentric layers of fibrosis surrounding the vessels (arteries).

Necrotising vasculitis occurs in the small & medium sized arteries in the skin with inflammation & degeneration in the dermal—epidermal junction may also cause skin lesions.

Clinical Features.

Are variable. Most of the features are due to VASCULITIS.

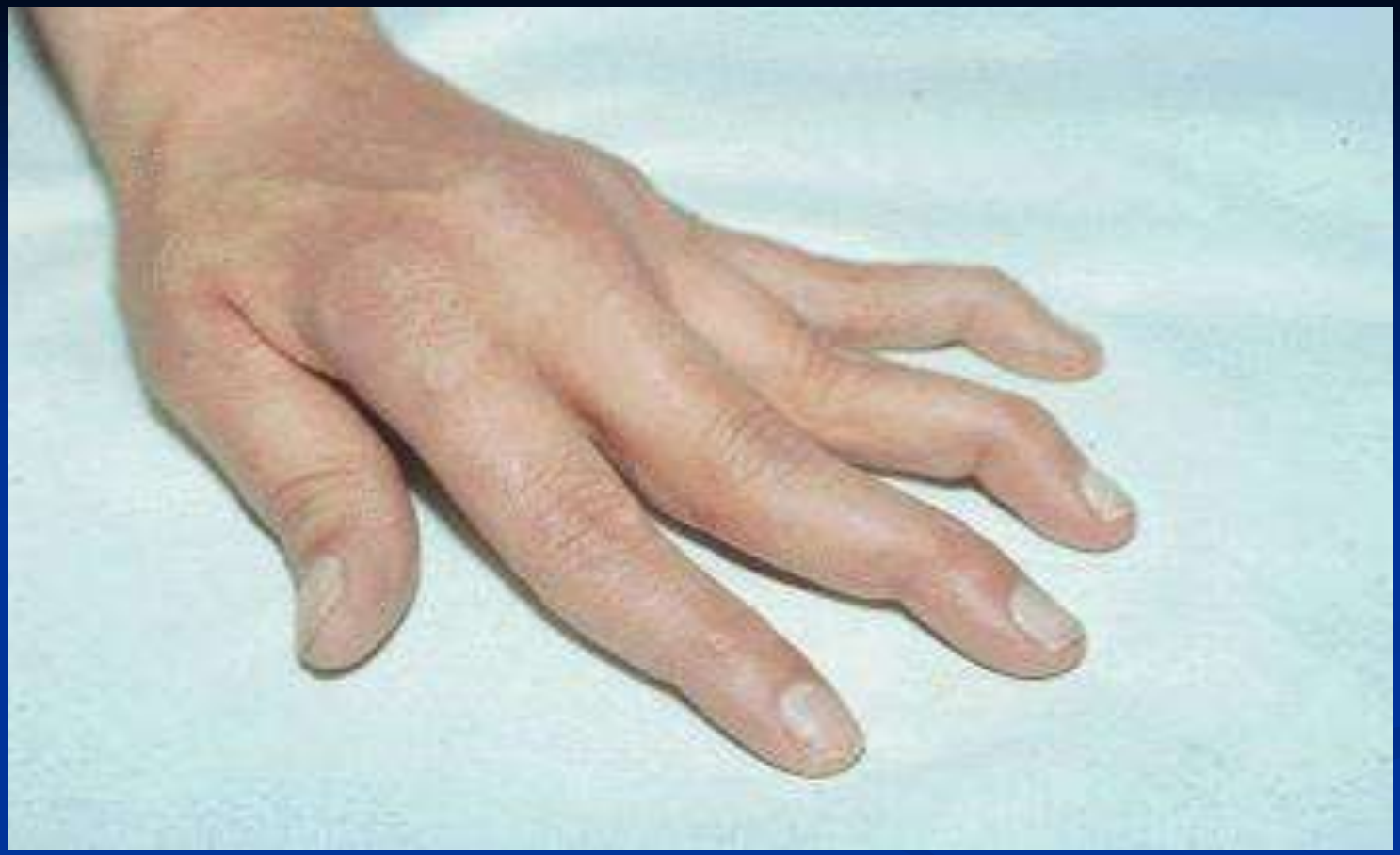
Mild cases may presents with only Artralgia whilst in sever cases there might be Multisystem involvement.

General features : fever is common in exacerbations (80%), malaise, tiredness& fatgue.

Joint involvement: is a commonest manifestation (90%) & is similar to that of RA in distribution but erosion & deformities are rare (could be arthralgia).

Tenosynovitis could be a feature.

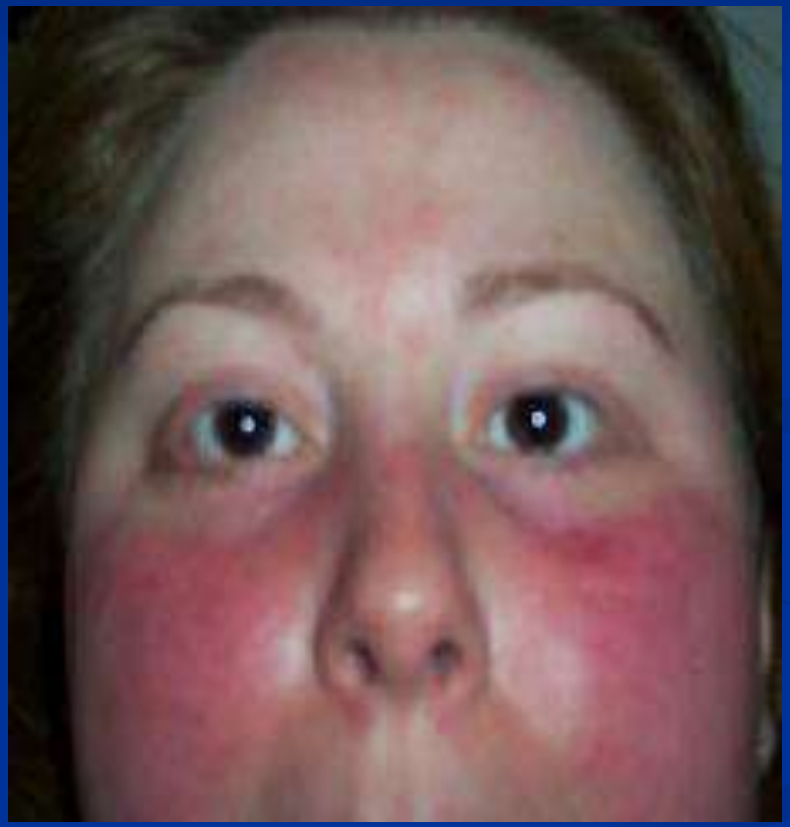
Subcutaneous nodules may occur.



Patient with long-standing lupus has developed subluxation at the MCP joints and swan neck deformities of her fingers. These deformities are reducible (probably being due to lax tendons) and x-rays reveal no erosions or cysts, both of which differentiate these findings from those in rheumatoid arthritis.

Skin features : (80%).

Malar (Butterfly) rash.

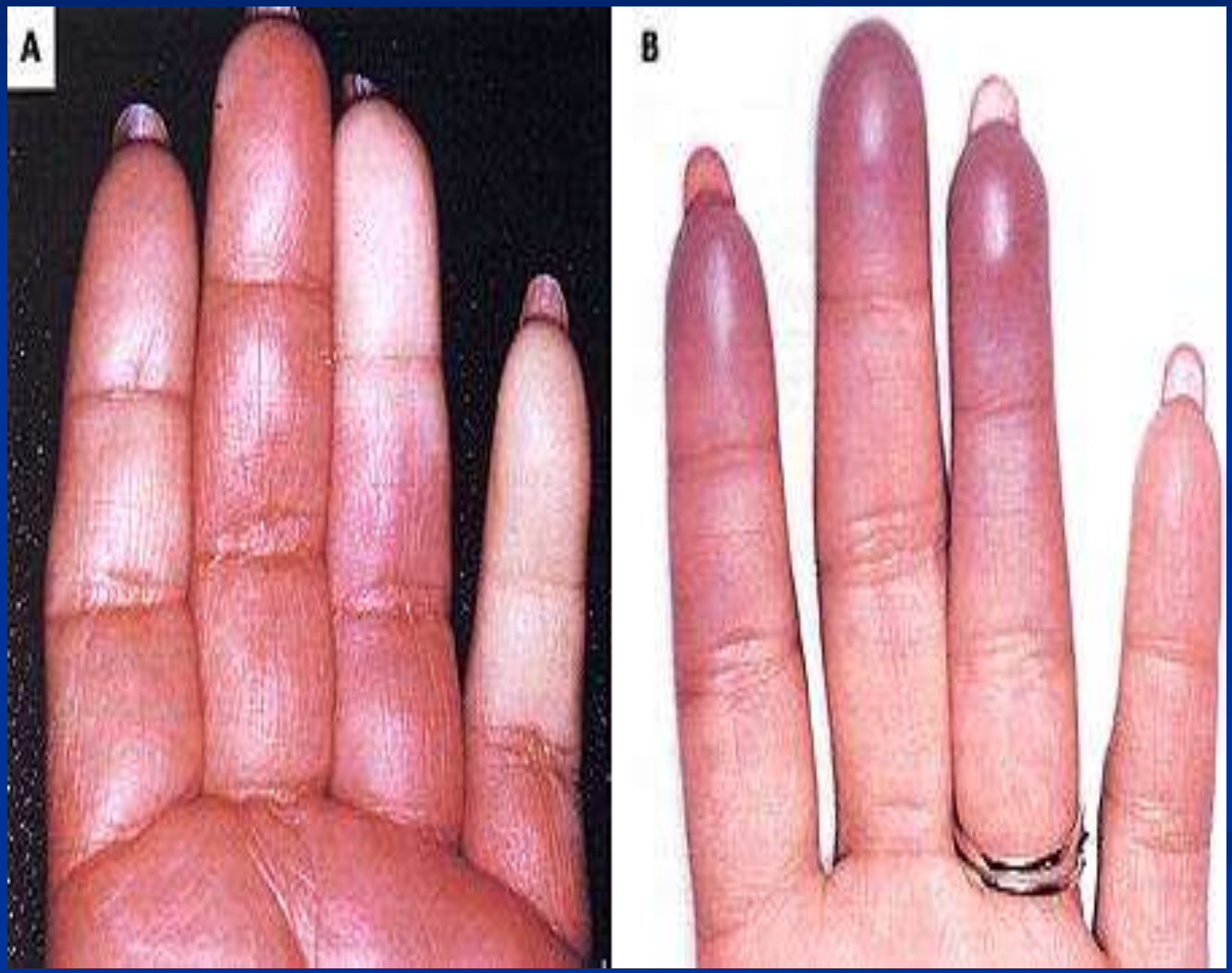


Butterfly Rash (Malar Rash) .

Discoid rash

Photosensivity.

Raynaudes phenomenon.



Vsculitic lesions on the finger tips & around nails folds , purpura & urtecaria occur.

Livedo reticularis, palmar & plantar erythema.

Pigementation & alopecia which may be diffuse or patchy.

Band test in the skin (seen by immunofluorescent, is deposition of immunoglobuline & complements in dermo—epidermal junction).

In mucosmembrane:(mouth ulcers, vaginal ulcers & nasal septal erosions.

Lungs ; PLeursy & exudates effusion.& pneumonitis.(70%).

The heart : (40%) Pericarditis , small effusion, mild myocarditis, aortic valve lersion & cardiomyopathy.

The kidneys : means bad prognosis (30—40 %) protienuria less than 1 gm / 24 hours is common, various types of glomerulonephritis could occur. Hypertension duo to renal involvement could occur.

The nervous system : (60%) depression, Epilepsy , cerebellar ataxia, CVA, or peripheral neuropathymay be seen . These lesions may be due to vasculitis or immune complex deposition , CNS involvement means bad prignosis.

Eyes ; could be involveddue to retinal vasculitis.

Investigations

Blood : Anemia usually normochromic normocytic., Neutropenia & thrombocytopenia. ESR is raised proportional to disease activity.

While CRP is usually normal.

Serum antinuclear antibodies (ANAs) are positive in almost all cases .

Antiduoble strand antibodies (anti DNA) were found to more specific but present in about 50—70% of cases particularly those with sever systemic involvement i.e. renal disease.

- Sreum rheumatoid factor is seen in half of cases.
- Serum complement levels are reduced during active phase. Immunoglobulins are usually raised (IgM & IgG)
- False positive tests for syphilis are found in 1/3 of SLE patients.

Management .

Aims :

1. Relieving symptoms.
2. Suppression of inflammation.
3. Preventing future pathology.

The risk to benefit ratio of potentially toxic drugs must be tailored to the patient

Should avoid sulfonamide , penicillin & high oestrogen pills which exacerbate the disease.

Treatment.

1. Avoid over exposure to sunlight & ultraviolate light & use sunblock .
2. Take low fat diet & add fish oil derivatives . Give Calcium & vit. D for healthy bones.

Drug therapy:

This depends on the organ involvement but steroid is the main stay in the mainstay of the treatment.

- In mild disease (artharlgia & fever) ----- NSAIDs.
- Artharlgia, myalgia& lethargy ---------- Antimalarials +-- NSAIDs.
- Skin without joint involvement ---------- Antimalarials + sunblock.
- Skin & joints---------- NSAIDs + Antimalarials.

- Serositis/ arthritis/ myositis--------Steroid (if mild serositis --- NSAIDs may be enough).
- Renal ---------- Steroid + azathioprine. (might need monthly i.v. steroid &Cyclophosphamide for six months then 2—3 monthly for 2 years.
- CNS ---------- Steroid (anticonvulsant).

Pregnancy in SLE.

1. No major contraindication for pregnancy.
2. Fertility is normal except when there is sever renal involvement.
3. There is an increased rate of a fetal loss, recurrent abortion can occur befor or during the clinical course of SLE.
4. Exacerbation may occur at any time during the course of pregnancy. (but 30% go to remission in psregnancy).
5. A postpartum deterioration is common .
6. Apatient with active renal disease have much worse prognosis.

Course & prognosis.

1. An episodic course is characteristic, with exacerbation & complete remission.
2. Chronic course is occasionally seen.
3. Unless there is sever renal or CNS involvement the outlook is now much improved. 5—10 y. survival is about 95%.
4. In most of the cases the pattern of the disease becomes established in the first few years , if serious problems haven't developed in this time they are unlikely to do so.
5. The arthritis is usually not erosive or destractive.

Revised criteria of the ARA for the classification of SLE.

1. Malar rash.
2. Discoid rash.
3. Photosensitivity.
4. Oral ulcers usually painless.
5. Arthritis nonerosive , not deforming.
6. Serositis. Pleuritis or pericarditis.

7. Renal disorder persistent proteinuria of more than 0.5 gm/24 h or cellular cast.

8. Neurological disorder seizure or psychosis.

9. Haematological disorders Haemolytic anemia, leucopenia, lymphopenia & thrombocytopenia.

10. Immunological disorders
Raised antinative DNA antibody binding.
Anti—Sm antibody.
Positive antiphispholipid antibodies.

11. Antinuclear antibody in raised titre.