Short notes

in

Rheumatology

Collagen Diseases

Def. : C.T. diseases characterized by fibrinoid degeneration, vasculitis and immune disturbance.

They include : (R +3S + 3P +G)

1- Rheumatoid Arthritis.
2- S.L.E. (Systemic Lupus Erythematosus).
3- Scleroderma.
4- Serum Sickness.
5- Polymyositis & Dermatomyositis.
6- Polymyalgia rheumatica.
7- P.A.N. (Poly-Arthritis Nodusa)
8- Giant Cell Arthritis.

Rheumatoid Arthritis, (Rheumatoid Disease)

Def. : Collagen disease specially characterized by : **(1) Arthritis** with Articular & periarticular damage, **(2) Systemic** manifestations, **(3)** painful course with **remissions** and **exacerbations**.

It was previously called "Rheumatoid Arthritis" but now it is called "Rheumatoid Disease" due to the presence of systemic manifestations.

Incidence : (1-3 % of population)

- Age : 30 – 40 years.
- Sex : ♀ : ♂ = 3 : 1

Etiology :

1- Genetic Factor : evidenced by :
   a. +ve family history.
   b. ↑ incidence in identical twins.
   c. ↑ incidence in HLADR3 & DR4.
2- Environmental Infection : [may act by autoimmune mechanism] as
   a. Mycoplasma. B. Viral infection. c. Diphtheroids.
3- Immune disturbance :
   Infection → body forms IgG (ẅ is abnormal Ab acting as Ag) → Antibody formation (IgM) → Ag/Ab complex (+ complement) → engulfed by neutrophils as :
   a. Rheumatoid factor (IgM)
   b. L.E. cells (in 150/0) [neutrophils]

C / P :

A- Extra-articular (= Systemic) :

1) S.C. nodules : in 20-30% (only in sero +ve).
   - sites : pressure areas & extensor surface.
   - Shape : rounded or oval, firm, not tender, not attached to the overlying skin.

2) Vasculitis :
   - small vessels → palmar erythema & ulceration of nail folds.
   - Large vessels → A.R. (rare)
3) Neuropathy :
   - usually sensory → parasthesia than anaesthesia.
   - Carpal-tunnel or Tarsal-tunnel syndrome.
4) Myopathy : proximal than distal.
5) Pallor (due to anemia)
6) Proeinuria & HSM .
7) Eye : scleritis, uveitis, Sjogren's syndrome [↓ lacrimation → keratoconjuctivitis sicca]
8) Chest :
   - pleurisy & pleural effusion.
   - Fibrosing alveolitis → interstitial fibrosis.
   - Caplan's syndrome [rhd. nodules on a background of pneumoconiosis]
9) Heart :
   - pericarditis & pericardial effusion.
   - Rare → cardiomyopathy , A.R.
10) Constitutional manifestations : low-grade fever, anorexia, malaise, easy fatigability and weight loss.

B- Arthritis :

1) Prodroma :
   i. general : fever, malaise, anorexia and fatigue.
   ii. Local :
      1. parasthesia in hands and feet.
      2. painful sensation when hands are put in cold water.
      3. Palmar erythema.
      4. Pain in the proximal joint on vigorous hand shaking.
2) Distribution :
   i. centripetal affecting small joints at 1st then large joints.
   ii. The distal interphalangeal joints are usually spared.
3) Features :
   i. Morning stiffness > 1 hour. [characteristic]
   ii. Criteria of inflammation : swelling, tenderness and thick synovial membrane.
4) Deformities.

Investigations :

1- Blood picture :
   - RBCs → anemia.
   - ↑ ESR > 100
   - WBCs → normal or leucopenia (hypersplenism in Felty's)
2- Urine analysis : Albuminuria.

3- Biochemical :
- **CRP** → +ve
- **L.E.** cells is +ve in 15% of patients.
- Rheumatoid factor (**RF**), detected by :
  * **Rose Waaler test**, (most specific test) :
    - pt. serum + suspension of sheep RBCs coated with IgG → agglutination.
    - Diagnostic titre is 1/32 .
  * **Bentonite test** , (using a neutral clay) :
    - Diagnostic titre is 1/32 .
  * **Latex agglutination test** :
    - Diagnostic titre is 1/160 .
- These tests are +ve only in 85% of cases (seropositive).
- False +ve result: - old patient, relatives of a patient.
  - infective endocarditis.
  - T.B., $, Leprosy.
  - SLE, PAN, Scleroderma.

4- X-ray on joint :
- Early → soft tissue shadow, osteoporosis.
- Late → Narrowing of joint space & bony cysts.
- Very late → joint deformity & ankylosis.

5- Aspiration of synovial fluid :
- turbid.
- ↑ " cells, enzymes & protein ".
- ↓ " complement, glucose & mucin (pathognomonic)".

6- Biopsy :
1. from synovial membrane :
- proliferation of cells (villous formation).
- infiltration of plasma cells & lymphoceyts.

2. S.C. nodules : central fibrinoid degeneration surrounded by radially arranged C.T. cells + fibrous capsule.

Variants of rheumatoid arthritis :

1- Sjogren Syndrome :
a. *Type I* (1ry or glandular) :
   i. Sicca Syndrome [exocrine gland destruction].
   ii. Xerophthalma, Xerostomia & Bronchitis sicca.
b. *Type II* (2ry or extraglandular) :
- Same as *type I* plus :
  - Collagen diseases : Rhd arthritis (30%), SLE (10%).
  - Lymphadenopathy.
  - Hashimoto's thyroiditis, in upto 50% of cases.
  - Renal involvement.

2- **Felty's Syndrome** :
- occurs in 5% of adults.
- *C/P* : [of Felty's synd.]
  - skin pigmentation & generalized lymphadenopathy.
  - HSM, Liver cirrhosis, Hypersplenism may occur.
  - Highly erosive & deforming arthritis.
  - Sero +ve cases.. L.E. cells are +ve.

3- **Chronic juvenile arthritis (CJA)** :
- Age : children < 16 years.
- Classification :
  - Monoarticular.
  - Pauciarticular (2-3 joints) :
    - Male → sacroiliitis.
    - Female → uveitis.
  - Polyarticular :
    - Sero +ve → severe arthritis, of poor prognosis.
    - Sero –ve → (1) systemic manifestations (Still's dse). [e.g.: fever, skin rash, HSM, lymphadenopathy & iritis] → (2) Dwarfism + affection of DIP joints & Cervical spines.

Treatment :

1- **Rest** : during the acute stage, for 2 weeks & rest of the joints by splint.
2- **Physiotherapy** (after acute stage) :
   a. Hydrotherapy : by paraffin wax bath.
   b. Faradic stimulation of the muscles.
   c. Massage to blood flow.
   d. Passive exercise to minimize the fibrosis.
   e. Active exercise to strengthen the muscles.

3- **Medical treatment** (drugs) :

I) First line, NSAIDs :
- aim : relief of pain & inflammation.
- Acts by : ↓ PGs.
  - **Aspirin** :
    - *Dose* : 4-6 gm/day.
    - *S/E* : Allergy, Salicylism, Peptic ulcer, bleeding, resp. Alkalosis, metabolic acidosis, GIT irritation, nephropathy.
  - **Phenylbutazone** :
    - *Dose* : 100 m.g. t.d.s.
    - *S/E* : B.M. depression, nephrotoxicity, hepatotoxicity, GIT irritation, Optic neuritis, Hypersensitivity.

- **Paracetamol** :
  - *Dose* : 500 m.g. t.d.s.
  - *S/E* : Hepatotoxicity (large dose).
- **Indomethacin** (Indocid) :
  - *Dose* : 25 m.g. t.d.s.
  - *S/E* : GIT irritation, neurotoxicity (headache, vertigo...)

II) Second line, DMARDs [Disease Modifying Anti-Rheumatic Drugs] :

- Indications : Progressive damage of the joints.

1. Gold (Na thiomalate) :

- *Action* : ↓ lysosomal enzymes & phagocytosis.
- *Dose* : 10 mg IM (test dose) → if no hypersensitivity;
  - 50 mg/ week, when a therapeutic response occurs;
  - 50 mg/ 2weeks, then every 3 weeks, then 4 weeks
  - total dose : 1-1.5 gm
- *S/E* : neuropathy, renal toxicity, skin rash, B.M. depression, Hepatotoxicity.

2. D-penicillamine :

- *Dose* : 125 mg t.d.s., gradual ↑ up to 250 mg t.d.s.
- *S/E* : As Gold + Myasthenia.

3. Chloroquine : [used for malaria]

- *Dose* : 250 mg t.d.s.
- *S/E* : corneal opacities, retinopathy, GIT irritation.

III) Third line, Corticosteroids :

1. Prednisone : 10 mg/day orally.

- *S/E* :
  - Hyperglycemia & Hypertension.
  - Moon face & buffalo hump.
  - Osteoprosis & ms. Weakness.
  - Trunkal obesity & peptic ulcer.
  - Hemorrhage & purpura.
  - Activation of healed T.B. lesion.
  - Androgenic stimulation of the female.

2. Intra-articular injection of Hydrocortisone acetate :

- shouldn't exceed 3 times/ year.
- *Dose* :
  - Small joint : 2-5 mg.
  - Large joint : 20-50 mg.

IV) Fourth line, Immunosuppressive drugs :

1. **Azathioprine** : 1.5 – 2 mg/kg/day Orally.
2. **Cyclophosphamide** : 1.5 – 2 mg/kg/day Orally.
3. **Methotrexate** : 1 mg/kg/day Orally.

- *Precautions* : regular liver function tests, CBC, Folic acid supplementation.
- *S/E* :
  - B.M. depression.
  - Gonadal destruction.
  - Hepato- & nephro- toxicity.
  - Teratogenicity.

- recent regimen for treatment of rheumatoid disease :
  - corticosteroids → 4th line.
  - Methotrexate → 2nd line.
  - Immunosuppressive drugs → 3rd line.

4- Surgery :

a. Synovectomy → early (before deformity).
b. Arthrodesis, Arthroplasty → late.

Spondylyloarthropathy
Sero –ve arthropathy

(1) Reiter's syndrome, **(2)** Ankylosing spondylitis, **(3)** Colitic arthropathy, **(4)** Psoriatic arthropathy, **(5)** Still's disease, **(6)** whipple's disease, **(7)** Behcet's disease.

1- Reiter's syndrome :

- AE : 1- post-dysentery : G. –ve bacilli (schigella, salmonella)
  2- post-venereal : Non gonococcal urethritis.
- C/P : * Articular : oligo-articular; mainly in L.L. and asymmetrical.
  * Extra-articular : - urogenital manifestations.
  - Dysentery.
  - conjunctivitis.
- Investigations : * R.F. : -ve . * HLAB27 +ve .
- Treatment : - NSAIDs for arthritis.
  - Corticosteroids for conjunctivitis.

2- Ankylosing spondylitis :

- C/P : - old male patient
  * Articular : sacroiliitis, kyphosis.
  * Extra-articular : Prostatitis, iritis & A.R.
- Investigations : - same as Reiter's.
  + X-ray → Bamboo spine.
- Treatment : - NSAIDs.
  - Physiotherapy.
  - Surgical correction of spine deformities.

3- Colitic arthropathy :

In chronic Inflammatory Bowel Disease : there are 2 types of arthropathy :

1- Arthropathy identical to ankylosing spondylitis :
   - It appears 1st then after months or years, it is followed colitic arthropathy.
   - It's not related to the severity of the bowel disease.

2- Reactive Arthropathy :
   - It appears after colitic disease.
   - It's proportionally related to the severity of the bowel dse.
   - No deformities.

4- Psoriatic Arthropathy :

- C/P : * Evidence of Psoriasis; nail pitting & Auspitz sign.
  * Arthropathy : affects DIP joints.
  - Sacroiliitis ē spondylitis in 20% of cases.
- Treatment : as rheumatoid disease; but chloroquine is contraindicated.

5- Still's disease :

- C/P : * Fever, skin rash, HSM, lymphadenopathy & iritis.
  * Dwarfism, affection of DIP joints & cervical spinces.

6- Whipple's disease :

- C/P : * Malabsorption (due to deposition of macrophages in the wall of the small intestine.
  * Arthritis & serositis.

7- Behcet's disease :

- C/P :
  - Mucous memb. → orogenital ulcers.
  - Articular → Arthropathy.
  - Cutaneous → Erythema nodosum.
  - Cardiac → Cardiomyopathy.
  - Ocular → Iridocyclitis, uveitis.
  - Cerebral → Encephalopathy, myelopathy & neuropathy.

Osteoarthritis

Def. : Degeneration of the articular cartilage with osteophytic formation.

AE :

1- Primary (commonest) :
   - Hereditary (from mother to her daughters).
   - Any joint can be affected; except wrist.
   - The **DIP** joints are affected → **Heberden** nodules; which are cystic at the first then become hard (bony).

2- Secondary (commonly affects the knee; but other joints may be involved) :
   1. Rheumatoid arthritis.
   2. Obesity (most common cause in Egypt).
   3. Joint trauma.
   4. Infections.
   5. Endocrinal (hyperparathyroidism, D.M. & acromegally)

C / P :

1- Pain & stiffness (may be present but not as Rhd. Arthritis)
2- Crepitus on movement.
3- Wasting of the muscles around the joint.
4- Heberrden's nodules; early they are painful, then painless.
5- Minimal deformities.
6- No systemic manifestations.

Investigations :

All investigations are normal (unless other disease is present), but **X-ray** shows:
- sclerosis of the edge of the joint (subchondrial sclerosis).
- osteophytes (new bone formation).
- Bone cysts may be present.

Treatment :

1- Causal : ↓ weight (in obese patients).
2- Analgesics : to ↓ pain (NSAIDs).
3- Physiotherapy. [especially if muscle wasting occurs].
4- Surgical : Osteotomy, Arthrodesis & Arthroplasty.

	Rheumatoid disease	1ry Osteoarthritis
Age :	30 – 40 years	30 years
Morning stiffness :	characteristic	absent
DIP joints :	spared	involved
Arthropathy :	synovitis, effusion and ↓ movements	crepitus on movement
Deformities :	severe	minimal
Nodules :	**S.C. nodules**	**Heberden's nodules**
Syst. Manifestations :	+ve	-ve
Lab. Findings :	abnormal	normal

GOUT

Def. : Clinical syndrome due to hyperuricemia.
- normal serum uric acid : 2-7 mg/dL.

AE. : maybe due to :

1- ↑ **production** of uric acid :
   a. Hereditary; ↓ **HGPRT** enzyme (Hypoxanthine Guanine Phospho-Ribosyl Transferase).
   b. Acquired :
      i. Leukemia, polycythemia.
      ii. Sarcoidosis.
      iii. Psoriasis.

2- ↓ **excretion** of uric acid :
   a. Hereditary tubular defect.
   b. Acquired :
      i. C.R.F.
      ii. Drugs (Thiazide, loop-diuretics & Aspirin).

Pathology :

- Acute gout : rapid ↑↑ in serum uric acid which are phagocytosed by leucocytes → release of lysosomal enzymes & Uric acid → acute gouty arthritis.
- Chronic gout : deposition of uric acid in :
  - Skin → gouty tophi.
  - Joint → osteoarthritis.
  - Kidney → stones & C.R.F.

C/P :

- **Acute gout** :
  - Acute monoarticular arthritis is the initial presentation of gout in 90% of patients.
  - It involves the metatarsophalangeal joint of big toe in 50% of cases, however; any distal joint may be affected.

- The attacks begin abruptly and reach maximum intensity in 8-12 hours. The joints are red, hot, swollen and extremely tender.
- Untreated, the first attacks resolve spontaneously in less than 2 weeks. Intermittent inflammatory arthritis, in which the joints return to normal between attacks.

- **Chronic gout** :
  - **Skin** : Tophi; (Tophi are collections of uric acid crystals in the soft tissues. They occur in more than half of untreated patients. While the classic location is along the helix of the ear, they can be found in multiple locations, including the fingers, toes, in the olecranon bursae, and along the olecranon, where they can resemble rheumatoid nodules. They appear as yellow white nodules, may ulcerate and discharge chalky paste material).
  - **Joints** :
    - The attacks become more polyarticular.
    - More proximal and upper-extremity joints become involved
    - Eventually, patients may develop a chronic polyarticular arthritis, sometimes nearly symmetrical (that may resemple rheumatoid arthritis)
  - **Kidney** :
    - Patients with gout have a 1000-fold increased incidence of renal stones and therefore may have a history of renal colic. Indeed, renal stones may precede the onset of gout in 40% of patients. [obstructive uropathy].
    - Patients with gout also may develop urate nephropathy (or hyper-uricaemic nephropathy), in which uric acid crystals are deposited in the medullary interstitium and pyramids.
    - Later on, C.R.F. may develop.

Investigations :

1- serum uric acid : > 7 mg/dL. (This is the most misused test in the diagnosis of gout).
2- Urine : urate crystals & hematuria (bcz of renal stones).
3- Biopsy from tophi : uric acid crystals.
4- Joint X-ray : punched-out lesion in bone ends.
5- Joint aspiration : urate crystals.
6- Kidney U/S : stones.

Differential Diagnosis :

1- Other causes of arthritis (e.g.: Rheumatoid arthritis, psoriatic arthritis, septic arthritis, gonococcal arthritis & Ca++ pyrophosphate deposition disease).
2- Other causes of nephropathy. [refer to nephrology].

Treatment :

1- **Acute gouty attacks :**

a. **Colchicine** : ↓ release of the lysosomal enzymes.
   - *Dose* : 1mg [2 tab.] at first, then 1 tab./3hours; till pain is relieved or *S/E* appear (GIT troubles; diarrhea and vomiting)

b. **Indomethacin** & **NSAIDs** (**1st** choice) : ↓ pain.
   - Aspirin should be avoided as it can alter the urate level in the blood, COX-2 inhibitors have been used with success.
   - NSAIDs should be avoided in patients with GIT bleeding, peptic ulcer or renal & hepatic insufficiency.

c. **Corticosteroids** (if the 1st choice drugs are contraindicated).
   - refer to " rheumatoid arthritis " for *S/E*.

d. **Rest** of the affected joint or even **Aspiration** of the effusion (if complicated) + steroid injection.

2- **Chronic gout :**

a. ↓ production of uric acid :
   i. **Allopurinol** :
      - acts by inhibition of Xanthine-Oxidase enzyme (which converts xanthine to uric a.).
      - *Dose* : 300 – 400 mg/day orally.
      - the dose should be reduced if renal sufficiency is present, monitor Liver function & CBC.
      - *S/E* : skin rash, headache & diarrhea.

b. ↑ excretion of uric acid (uricosuric drugs) :
   * **Probencid** * **Sulphinpyrazone**
   - *Contra-indications :*
      1- high uric a. excretion (>700 mg/day).
      2- renal insufficiency or stones. (GFR < 50ml/min).
      3- not used with Aspirin as Aspirin blocks its action.

c. Colchicine : used to control the serum uric a.

d. Excess fluid intake.

e. Alkalinization of urine (to prevent stone formation).

f. Others :
   i. Follow up for cardiac function and B.p.
   ii. Surgical removal of tophi.
   iii. Treatment of renal troubles; if present.

Systemic Lupus Erythematosus

Def. : SLE is an autoimmune disorder that involves multisystem microvascular inflammation with the generation of autoantibodies.

* Multiple factors are associated with the development of the disease. These include genetic, environmental & Immune factors.
* Antinuclear antibodies (ANAs) are present in the serum in virtually all patients with active SLE, and antibodies to native double-stranded DNA (dsDNA) are relatively specific for the diagnosis of SLE.

Incidence :

- Age : 15-30 years.
- Sex : ♀ : ♂ = 9 : 1 .

AE :

1- Genetic factor; evidenced by :
   a. +ve family history.
   b. High incidence in identical twins.
   c. High incidence in HLADR3, DR4.
2- Environmental :
   a. Infections. [viral].
   b. Sun exposure.
   c. Drugs
      i. SLE- like condition : hydralazine, INH, procainamide.
      ii. Ppt attack in SLE patient : sulpha, penicillamine.
3- Immune disturbance; evidenced by :
   a. +ve L.E. cells
   b. Autoantibodies.

C/P :

1- Systemic manifestations :
   - Low-grade fever, weakness.
   - Tachycardia, anorexia, malaise & weight loss.
2- Musculoskeletal :
   - Myalgia.
   - Arthropathy :
     i. Arthralgia > arthritis. (pain without significant clinical findings).
     ii. Small-joint arthritis of the hands and wrists is most frequent, followed by arthritis of the knees.
     iii. Jaccoud arthropathy is the term for the nonerosive hand deformities due to chronic arthritis and tendonitis that develop in 10% of patients with SLE.
     iv. Fibromyalgia may be concomitant with SLE, causing generalized widespread pain, arthralgia, and myalgia.
3- Skin changes :
   - **Malar rash** describes an erythematous rash over the cheeks and nasal bridge with classic nasolabial fold sparing.

- **Photosensitive rash** is often macular or diffusely erythematous in sun-exposed areas of the face, arms, or hands.
- **Discoid lesions** are plaquelike lesions with follicular plugging, which may create scarring. Discoid lesions may represent limited discoid lupus or systemic SLE.
- **Alopecia** commonly affects the temporal regions or creates a patchy pattern.
- **Raynaud's phenomenon** may be observed with blue, white, and red color change at the distal digital tips.

4- C.N.S. :
- Altered mental status may be secondary to aseptic meningitis, seizures, psychosis, or organic brain lesion (transverse myelitis, epilepsy or encephalitis)
- Focal neurological deficits may represent stroke, TIA, or mononeuritis.
- Mononeuritis is observed in some patients with SLE vasculitis.

5- Eyes :
- Conjunctivitis, scleritis & cytoid bodies.
- Sjogren syndrome. (10% of cases)
- Retinal infarction; due to vasculitis.

6- Chest :
- Shortness of breath or dyspnea may be due to many causes. Serositis due to pulmonary effusions, pulmonary embolism, lupus pneumonitis, chronic lupus interstitial lung disease.
- Pulmonary hypertension due to vasculitis.

7- C.V.S. :
- Pericarditis that manifests as chest pain is the most common cardiac manifestation of SLE and may occur with or without a detectable pericardial effusion.
- Libman-Sacks endocarditis is noninfectious but may manifest with symptoms similar to those of infective endocarditis.
- Myocarditis may occur in SLE with symptoms of heart failure.
- Ischemic heart diseases & thrombosis.

8- Renal :
- The kidney is the most commonly involved visceral organ in SLE. Although only approximately 50% of patients develop clinically evident renal disease, biopsy studies demonstrate some degree of renal involvement in almost all patients.
- Lupus nephritis; may be manifested by HTN or hematuria.
- Later on; renal failure may occur.

9- G.I.T. :
- Abdominal pain in SLE is significant because it may be directly related to active lupus, including peritonitis, pancreatitis, mesenteric vasculitis, and bowel infarction.

- Jaundice due to autoimmune hepatitis. (lupus hepatitis)
- Painless mouth ulcers & malabsorption.

10- R.E.S. :
- Generalized painless lymphadenopathy.
- Hepatosplenomegally.

11- Hematological :
- Multiple cytopenias such as leucopenia, lymphopenia, anemia, or thrombocytopenia may suggest SLE.
- Bleeding tendency. [due to thrombocytopenia & auto-Ab]

Investigations :

1- Blood picture :
a. cytopenia (pan-, bi- or monocytopenia)
b. ↑↑ ESR. c. B.T. & C.T. may be ↑ .

2- Biochemical :
* ↓ C3, C4 * RF +ve in 15% * L.E. cells in 85%

3- Immunological :
a. **ANA** - Screening test; sensitivity 95%; not diagnostic without clinical features.
b. **Anti-dsDNA** - High specificity.
c. **Anti-Sm** - Most specific antibody for SLE; only 30-40% sensitivity.
d. **Anticardiolipin** - IgG/IgM variants measured by ELISA.
e. Anti-cell antibody. (e.g.: anti-red-cell Ab.)
f. Anticoagulation factor Ab.

4- Other investigations may be important :
a. Urine analysis; to evaluate kidney function.
b. Echocardiography; to assess the cardiac function.
c. Chest radiography.
d. Joint radiography.

Treatment :

1- Prophylaxis :
- avoid drugs inducing SLE, infections or long sun-exposure.
- Avoid psoralin rich diet. (e.g.: figs)

2- NSAIDs :
- symptomatic relief for serositis, arthralgia & fever.

3- Corticosteroids :
- Topical : for skin lesions.
- Systemic : for major & multi-system manifestations.
- Pulse steroids (large IV doses); for severe lupus, renal, CNS, cardiopulmonary or blood abnormalities.

4- Anti-malarials (as Chloroquine) :
- The mechanism of action of anti-malarials in SLE is unknown, but they do not cause generalized immuno-suppression. They are useful

to prevent and treat lupus skin rashes, constitutional symptoms, arthralgias, and arthritis.

5- Cytotoxic drugs :
For severe cases; which are refractory to steroid therapy.
- Cyclophosphamide.
- Methotrexate.
- Azathioprine.

6- Treatment of complication :
e.g.: HTN, infections, cerebral lupus or other underlying conditions.

Causes of Mono-arthritis :
1- gouty arthritis.
2- Pseudo-gout.
3- Hypertrophic osteoarthropathy.
4- Acute pyogenic arthritis.
5- Monoarthritic form (CJA).
6- Hemoarthrosis.

Scleroderma
Progressive Skin Sclerosis

Def. : multi-system disease caused by over-production of collagen fibers.

Incidence :
- Age : 20-50 years.
- Sex : ♀ : ♂ = 3 : 1 .

Pathology :
1- collagen deposition all over the body.
2- Vasculitis.

Scleroderma is a systemic disease that affects many organ systems. It is most obvious in the skin; however, the gastrointestinal tract, the respiratory, renal, cardiovascular, and musculoskeletal systems, as well as numerous vascular structures, are frequently involved. The symptoms result from inflammation and progressive tissue fibrosis and occlusion of the microvasculature by excessive production and deposition of types I and III collagens.

C/P :
1- Skin :
- Raynaud's disease. [due to vasculitis]
- Diffuse cutaneous scleroderma is skin thickening; present on the trunk and proximal aspects of the extremities in addition to the face.
- Limited movements. [e.g.: inability to open the mouth completely, limited chest expansion & limited movement of the fingers].

- Acrosclerosis : sausage-shaped fingers + ulceration and calcification of the finger tips.

2- GIT :
- Reflux from decreased LES pressure, oesophagitis & dysphagia.
- Small intestine → malabsorption.
- Large intestine → wide-mouth diverticula.

3- Renal :
- Vasculitis of renal bl. Vessels → HTN & R.F.
- Glomerulonephritis.

4- Cardiac :
- Cardiomyopathy (+++)
- Pericarditis.
- C.H.D. [due to vasculitis]

5- Chest :
- Pulmonary hypertension.
- Interstitial pulmonary fibrosis.
- Recurrent aspiration pneumonia.

6- Musculoskeletal :
- Proximal myopathy.
- Rheumatoid-like arthritis.
- Arthralgia.

Investigations :

1- laboratory : many are +ve especially;
- (1) RF, (2) LE cells, (3) ↑ ESR, (4) anemia & (5) leukocytosis.
- (6) auto-antibodies. (anti-centromere Ab.)
- (7) ↑ urinary hydroxyproline. (index of collagen turn-over)

2- Skin biopsy.

3- Invest. For complications :
- Chest x-ray, ECG, Barium swallow..etc.

Treatment :

1- anti-platelets drugs; e.g.: Aspirin, dipyridamole.

2- Anti-collagen fibers :
   a. Colchicines : destruction of collagen fibers.
   b. D-penicillamine : ↓ synthesis of the collagen fibers.
   c. Cyclophosphamide.

3- Treatment of complications :
   - as reflux oesophagitis, glomerulonephritis, cardiomyopathy, pulmonary troubles..etc.