# **RHEUMATOID ARTHRITIS**

Most Rheumatic diseases are : chronic , inflammatory , systemic , autoimmune , affect joint with variable extent .

Most joints affected here are **small joints** : pip , mcp , wrists , mtp , ankles , knees

## NOTES

- $\rightarrow$  DIP joints <u>not</u> affected , its go with OA + psoriasis
- → RA affect **both** small and large joints , **but if** small joints aren't affected then the diagnosis of RA should be questioned !!
- $\rightarrow$  Large joints are the least joints affected (central joints : Hip , shoulder)
- → They begin distal to proximal ( **progressive** )
- → Symmetrical , if Asymmetrical it go against RA
- Asymmetrical involve : the sero negative arthritis ( ankylosing spondylitis , Reactive arthritis , (IBD) Related arthritis , psoriasis which behave away from the group ) and they affect Large joints , except psoriasis : affect small joints .
- CHRONIC : long duration
- Pattern : additive ( today complain tow joints , next week 5 joints ... )
- Non-remitting : don't remit alone without treatment except in rare cases .

And so : The old criteria for diagnosis require <u>persistent symptom</u> for six weeks at least ; to exclude viral and reversible arthritis .

Rheumatic fever : <u>don't cause</u> chronic joint symptom (more than 1 month)
 , it cause short lived arthritis (less than 1 month)

**NOTE** : if you see that joint symptoms persist for more than month **most likely** you're not dealing with Rheumatic fever !

- Morning stiffness : since it's an inflammatory process
  - due to edema inside the joints and the intra articular

pressure is high.

- (duration more than 1 hour)

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Criterion	Definition
A patient is classified as RA if 4/7 criteria are satisfied. Criteria 1-4 must have been present for ≥6 weeks	
1. Morning stiffness	Morning stiffness in and around the joints, lasting at least an hour before maximal improvement
2. Arthritis of ≥3 joints areas	≥3 joints areas simultaneously have had synovitis observed ay a physician
3. Arthritis of hand joints	At least 1 area swollen in a wrist, MCP or PIP joint
4. Symmetric arthritis	Simultaneous involvement of the same joint areas on both sides of the body
5. Rheumatoid nodules	Subcutaneous nodules, over bony prominences, extensor surfaces or juxta-articular regions
6. Serum rheumatoid factor (RF)	Positive RF
7. Radiographic changes	Radiographic changes typical of RA in posteroanterior hand and wrist radiographs

New criteria

Target population:      Patients who (i) have at least one joint with clinical synovitis,      and (ii) the synovitis not better explained by another disease	core
Add score of categories A-D, score of ≥6/10 needed to classify patient as having definite RA	
A. Joint involvement (tender/swollen)	
1 large joint 2-10 large joints 1-3 small joints (with or without involvement of large joints) 4-10 small joints (with or without involvement of large joints) >10 joints (at least 1 small joint)	0 1 2 3 5
B. Serology	
Negative RF /ACPA Low-positive RF/low positive ACPA High positive RF/high-positive ACPA	0 2 3
C. Acute phase reactants	
Normal CRP&ESR Abnormal CRP/ESR	0 1
D. Duration of symptoms	
<6 weeks ≥6 weeks	0 1

2010 ACR/EULAR Classification criteria for RA[5]

1987 ACR Classification criteria for RA[3]

# In old criteria [7], 1987 :

- $\rightarrow$  Symptom must last for 6 weeks at least
- → Patient must exhibit **four** of them
- $\rightarrow$  you can diagnosed here by history only !
- → No anti CCP ?! ما كان وقتها مكتشف

**NOTE** : **subcutaneous nodules** present also in Rheumatic fever ! ( see the Jones criteria for rheumatic fever )

Rheumatic fever	Rheumatoid arthritis
Large / major joints	Small joints
Migratory	Additive
No morning stiffness	✓ morning stiffness
Short duration	Long / chronic

**[RA nodules]** : large , on **extensor aspect** of forearm , long duration ( months to years ) .

# # In new criteria [4] , 2010 :

ACPA : anti citrulinated peptide antibody , the same with other name : ( anti ccp )

**RF ( rheumatoid factor )** : antibody against FC portion of another antibody .

- Acute phase reactant : positive [ CRP , ESR (fibrinogen) , platelet , ferritin ] and negative (albumin ) .
- ✤ Advantages of new criteria :
- $\rightarrow$  The new criteria follow SCORING system
- → \* allow you to make an early diagnosis ( how ) as it **not** require the duration just to be more than 6 weeks.
- to be diagnosed with RA in new criteria you need score of more or equal to 6/10.
- THE Difference between old and new criteria : ( this points not found in new criteria ) :
  - 1- Morning stiffness
  - 2- The symmetry
  - 3- The Nodules
  - 4- X-ray findings
- Other manifestation of RA :
- pericarditis

### - neuropathy

scleritis

- felty's syndrome (RA, splenomegaly, neutropenia)
- **sjogren syndrome** ( xerostomia + xerophthalmia ) , they called Sicca symptoms
- pulmonary involvement ( interstitial fibrosis )

**NOTE** (now the explanation of pictures ) important findings in RA : ( see the findings on Google or doctor's slides ) :

- → nodules on **extensor** aspect and large >>> nodules of RA
- → scleromalacia : thinning in sclera ( dangerous sign ! it can cause rapture of globe and loss of vision )
- $\rightarrow$  digital infarction / vasculities
- → chest x- ray show interstitial lung disease ( bilateral reticular nodular shadow )
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- NOTES :
  - RA age (30-55) : as patient younger think of SLE , as older think in RA
    , so age is important in ddx here !
  - No morning stiffness in SLE .
  - x-ray of bone show joint erosion >> destruction >> deformity ( it occur in first 2 years of disease so early treatment and diagnosis very important )

- Most have fluctuation course (exacerbation + remission) Cont. of pictures :

- $\rightarrow$  PIP joint swelling & swan neck
  - >> swan neck deformity : extension of PIP , flexion of DIP
  - >> boutonniere deformity : extension of DIP , flexion of PIP
- $\rightarrow$  Wrist & PIP joint swelling
- → **Z-deformity** of thumb
- ightarrow Ulnar deviation
- → Volar subluxation of MCP joint ( step sign ) & clubbing !!! why ? lung fibrosis of RA.
- → Muscle wasting ( dorsal interossus muscle )
- $\rightarrow$  Pus from the joint coming out = septic arthritis
- $\rightarrow$  Turbid (CSF) in RA ! ( high inflammatory fluid )
- → Neck sub laxation in C1 & C2 ( patient come with electric like pain in back when he looking down )
- $\rightarrow$  BAKER cyst
  - NOTE :

>> when you see deformity <u>look for reversibility</u>, if reversible then the disease NOT in the joint, but could be periartcular (ligaments, capsules, muscles, nerves)

**So** : <u>Fixed deformity</u>  $\rightarrow$  disease in joint , as **RA** 

<u>Not Fixed / reversible</u>  $\rightarrow$  periartcular ( ex : **SLE** & rheumatic fever )

- → joint aspiration , usually we don't do it in RA ( not routinely ) , but we do it when I have MONO ARTHRITIS as ( gout , septic arthritis, haemarthrosis )
- In RA we do aspiration if one of joint painful more than other joints

#### ✤ GENETIC PREDESPOSITION :

- >> HLA-DR4 → most common
- >> HLA DRB1  $\rightarrow$  bad prognosis ( here the Anti CCP positive : worse disease )

### PATHOLOGY :

- Active T-cell activate macrophages :
- cytokine **TNF alpha** , **IL-6** , **IL1** ( high inflammatory cytokine ) that activate :
  - 1- Osteoclast
  - 2- Chondrocyte
  - 3- Synoviocyte hypertrophy & inflammatory cell → PANUS ( highly destructive pathology )
- B-cell → produce RF & Anti ccp

### NOTES

- >> RF & Anti ccp mean → worse prognosis
- >> anti ccp is specific factor for RA

The Importance of CCP :

- 1- Good for diagnosis
- 2- Prognosis
- 3- Help in prediction

REMEMPER  $\rightarrow$  damage of joint start early in course

Pregnancy :

>> **RA** : <u>improve</u> due to placental steroids , and the methotrexate is stopped before 3 month .

>> SLE : mostly worse more and more .

#### If you see X-ray of hand you can see :

- 1- Soft tissue swelling
- 2- Osteopenia
- 3- Joint space narrowing
- 4- Joint erosion (very important)

#### Poor prognosis RA in :

- 1- Poly articular joint disease
- 2- Persistent active disease
- 3- Extra articular manifestation
- 4- Positive (RF / Anti ccp )
- 5- Elderly
- 6- HLA DRB1

# **TREATMENT**

Only controlled NOT cured .

- ♦ NSAIDS → pain control ( selective COX2 : no GI symptom + don't affect platelet, they end by – COXIB)
- ◆ DMARDs → methotrexate ( best initial DMARD ) , hydroxychoroquine , cyclosporine
- >> Monitor of MTX by :
  - 1- liver function test (risk of hepatitis)
  - 2- bone marrow / CBC ( risk bone marrow suppression )

Corticosteroids in :

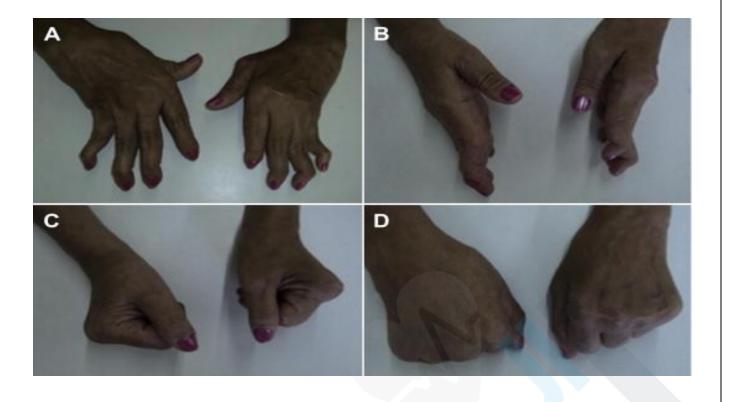
- 1- Acute disease
- 2- Interval ( 6 weeks ) until methotrexate act
- 3- If there is vasculities
- Gold injection : not used now ( nephrotoxicity )
- New Biological agent [anti TNF] : etanrcept (sc), infliximab (IV)
- Disadvantages of biological agents :
  - 1- Risk to recurrent infection esp. TB
  - 2- Very expensive
- Surgery >> Joint replacement

**Final NOTE :** methotrexate times of action is 6 weeks and we use corticosteroid in this interval to gain an action and it's not safe in pregnancy as it can end the pregnancy or cause birth defect .

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You can see here a **reversible** sawn neck deformities , which is not considered as RA , instead it's mostly SLE patient !!