

Approach to a patient with polyarthrititis

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Estimated prevalence of musculoskeletal disorders in the population

	prevalence	Number of patients
All MSK disorders	15-20%	525000 - 700000
OA	12%	420000
RA	1-2%	35000 - 70000
Crystal arthropathies	1%	35000
spondyloarthropathies	0.25%	8750
SLE	< 0.1	< 3500
Scleroderma	< 0.01	< 350
Back/neck pain	15%	525000
Soft tissue rheumatism/FM	3-5%	105000 - 175000

What is the DDx
for polyarticular
pain?

A blue ribbon graphic with a 3D effect, featuring a darker blue shadow on the left side and a pointed bottom edge. The text is centered within the ribbon.

Polyarthrititis
Vs
Polyarthralgia

Joint count

- Poly: >4
- Oligo: ≤ 4
- Mon0: $=1$

- Arthralgia: joint pain

- Arthritis: joint inflammation

Symptoms and signs of arthritis:

- Pain/Tenderness
- Early morning stiffness/ inactivity stiffness.
- Swelling
- **↑ Temperature of the joint**
- **↓ Range of movement**
- Loss of function

DDx of polyarthralgia

- Osteoarthritis
- Soft tissue rheumatism or fibromyalgia
- Hypothyroidism
- Viral infection
- Depression
- Joints overuse

A blue speech bubble graphic with a white border and a dark blue shadow, pointing downwards. The text "DDx of polyarthrititis" is centered inside the bubble in white font.

DDx of polyarthrititis

DDx of polyarthrititis

- Infectious
- Post infectious
- Spondyloarthropathies (SpA)
- Rheumatoid arthritis
- Inflammatory osteoarthritis
- Crystal-induced arthritis
- Connective tissue diseases
- Vasculitis
- Systemic rheumatic illness
- Systemic illness

Polyarthrititis

Infectious	Connective tissue diseases
Bacterial	SLE
Viral	Scroderma
Other	Sjogren's
Post infectious	dermatomyositis
Infective endocarditis	Mixed connective tissue disease
Reactive arthritis	Vasculitis
Enteric arthritis	Large, medium, small vessel
Sero negative spondyloarthritides	Behcet's
Ankylosing spondylitis	Systemic rheumatic illnesses
Psoriatic arthritis	Adult Still's disease
Enteropatic arthropathy	Relapsing polychondritis
Rheumatoid arhritis	Autoinflammatory disordres
Crystal induced	Systemic illnesses
Gout	Sarcoid
CPPD	Malignancy

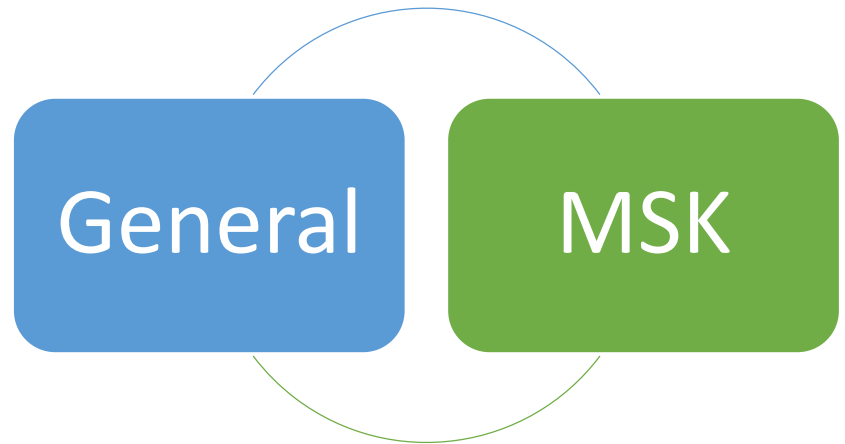
HPO

- Age and sex
- Onset
- Duration
- Distribution (axial, peripheral)
- Symmetrical vs asymmetrical
- Inflammatory vs non-inflammatory
- Extra-articular manifestation
- Function

Review of systems

- Constitutional
- Eyes
- Skin
- Cardiac / Vascular
- Respiratory
- GI
- GU / Obs & gyne
- Neuro

Physical
examination



Investigations

Hematology

Biochemistry

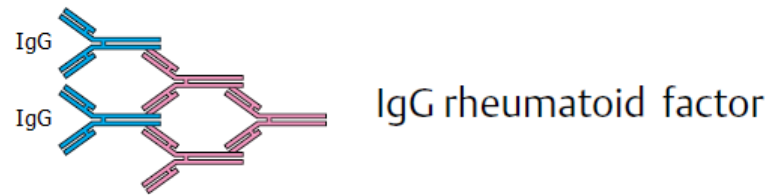
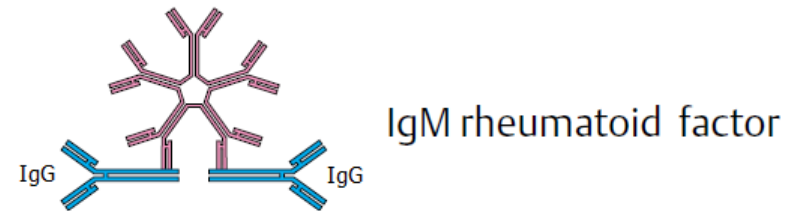
Virology

Immunology

Imaging

Rheumatoid Factor

- RF is an antibody against the Fc portion of IgG.
- RF can be of any immunoglobulin subclass (IgA, IgG, and IgM) but is **most commonly IgM**.
- RF is detectable during the disease in ~ 75% to 85% of patient with RA.
- ~ 50% are positive in the first 6 months of the illness and 85% become positive over the first 2 year.



The sensitivity of RF is 66%
the specificity of RF is 82%

Rheumatoid factor

CONDITION	FREQUENCY OF RF, PERCENT
Rheumatoid arthritis	80
Sjogren's syndrome	90
MCTD	50
Cryoglobulinemia	>95
SLE	25
Polymyositis/Dermatomyositis	<10

Non-rheumatic diseases associated with RF-positivity

Condition	Frequency of RF, %
Aging (>60years)	5 to 25
Infection	
Bacterial endocarditis	25 to 50
HBV or HCV	20 to 75
Tuberculosis	8
Syphilis	Up to 13
Parasitic	20 to 90
Leprosy	5 to 58
Viral infection	15 to 65

Condition	Frequency of RF, %
Pulmonary disease	
Sarcoidosis	3 to 33
Interstitial pulmonary fibrosis	10 to 50
Silicosis	30 to 50
Asbestosis	30
Miscellaneous diseases	
Primary biliary cirrhosis	45 to 70
Malignancy	5 to 25
After multiple immunizations	10 to 25

Frequency of positive RF in normal individuals of different ages

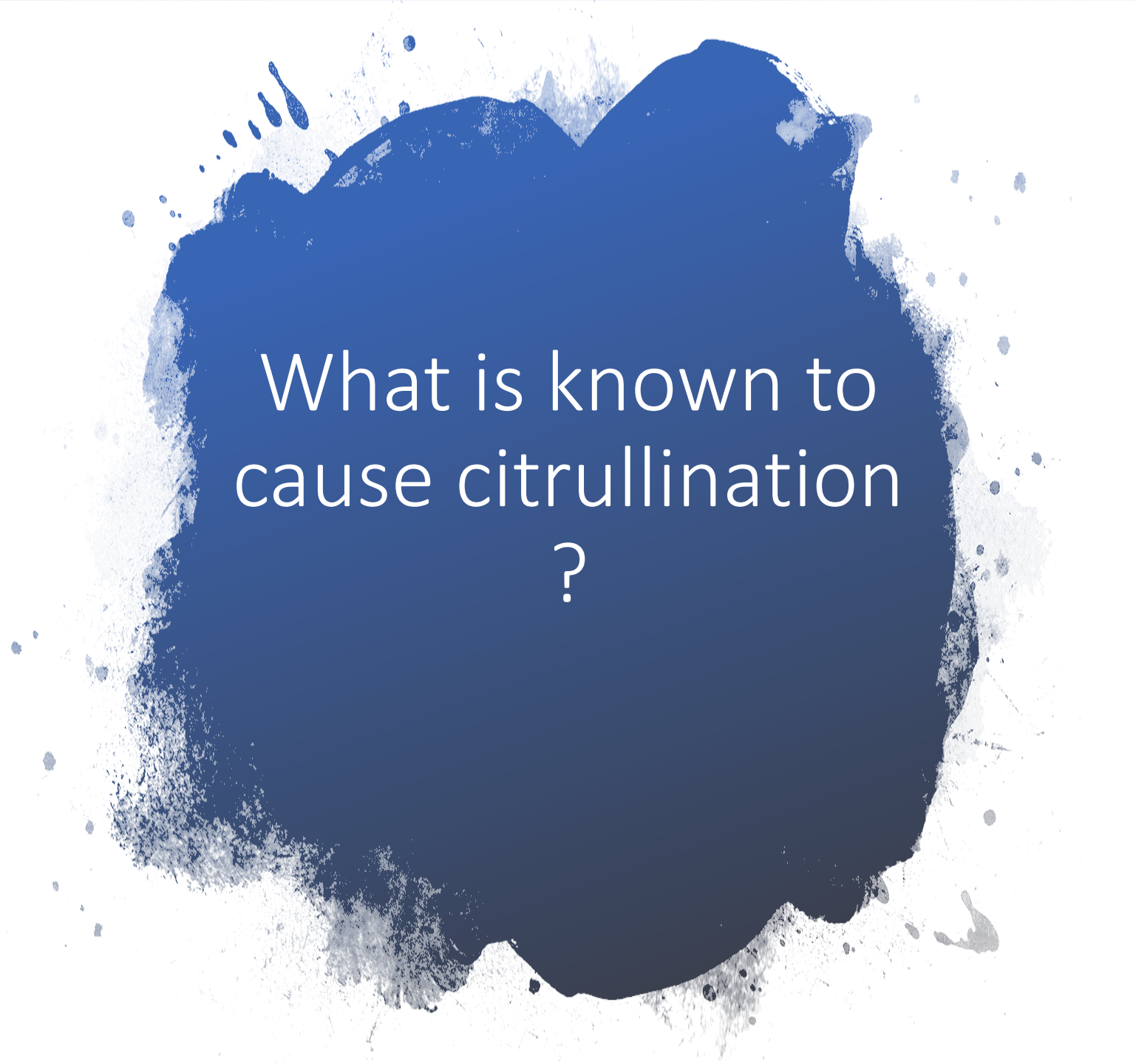
Age	Frequency of RF
20-60	2-4%
60-70	5%
> 70	10-25%

Anti-cyclic citrullinated antibodies (**anti-CCP**)

- Anti-CCP Abs are directed against citrullinated residues of proteins
- Citrulline is a non-naturally occurring amino acid generated by deimination of Arginine residues on proteins by enzyme called peptidylarginine deiminase (PAD)

The sensitivity of anti-CCP is 70%

The specificity of anti-CCP is 95%



What is known to
cause citrullination
?



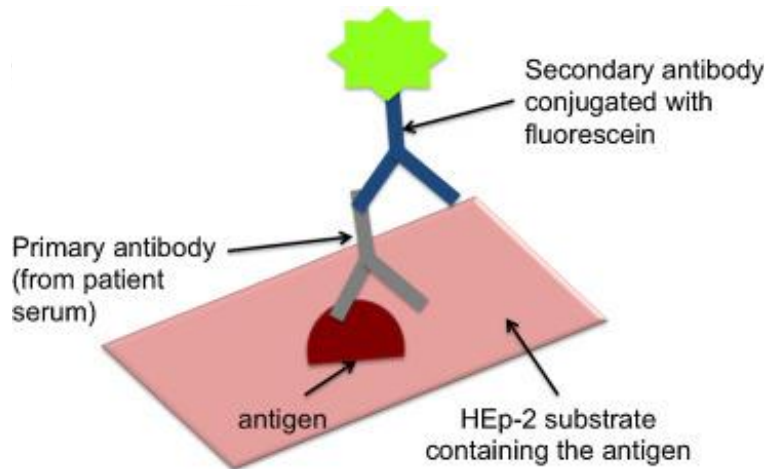


Anti-nuclear antibody (ANA)

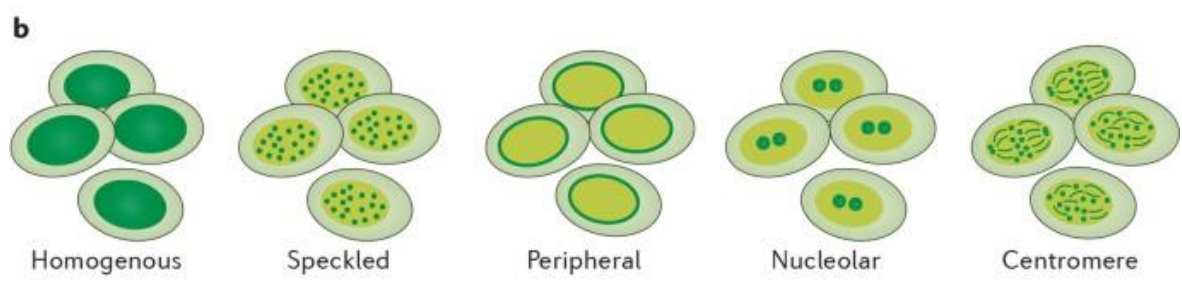
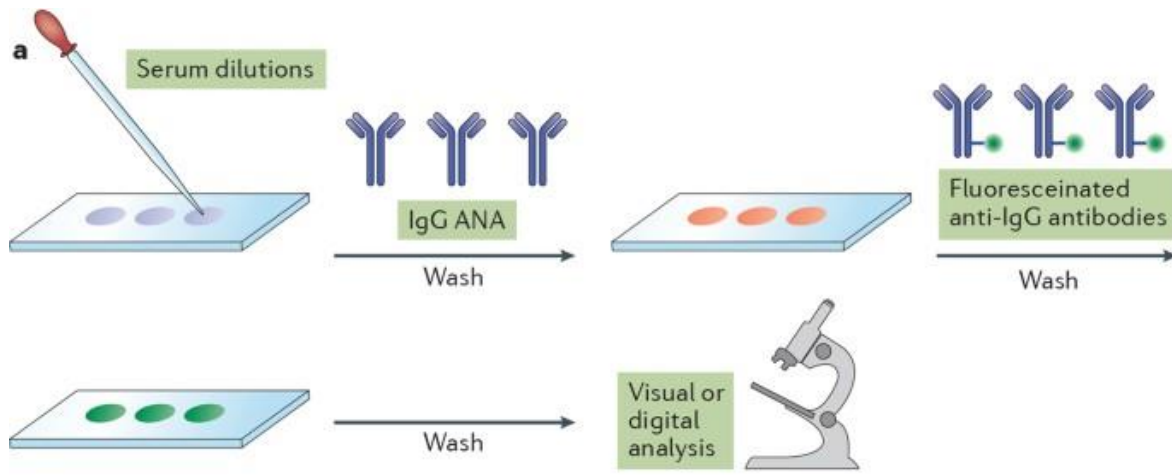
- **ANA** are autoantibodies that bind to contents of the cell nucleus.
- In normal individuals, the immune system produces antibodies to foreign proteins (antigens) but not to human proteins (autoantigens).
- In some individuals, antibodies to human antigens are produced.

- There are many subtypes of ANAs such as:
 - anti-Ro
 - anti-La
 - anti-Sm
 - anti-nRNP
 - anti-Scl-70
 - anti-dsDNA
 - anti-histone
 - anti-centromere
- Each of these antibody subtypes binds to different proteins or protein complexes within the nucleus.

The indirect immunofluorescence test

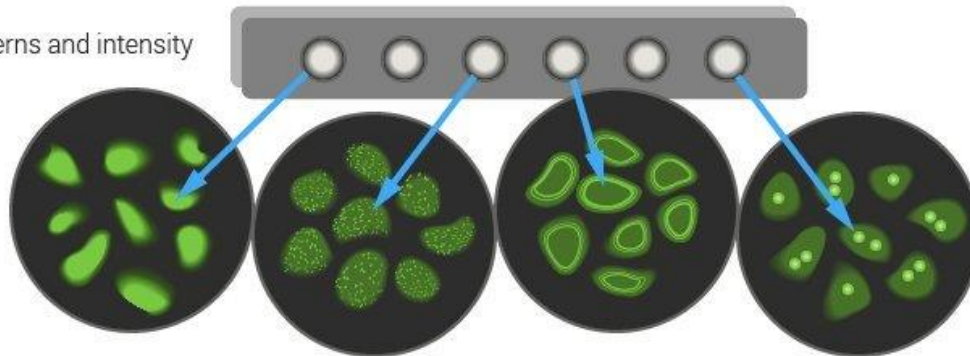
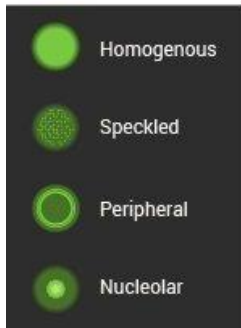


- The test takes advantage of a HEp-2 cell line, which has cells with large nuclei (making staining patterns easier to see).
- In addition, HEp-2 cells contain nearly all of the clinically important autoantigens, making these cells ideal for the detection of the corresponding autoantibodies.
- The cells are grown on and subsequently fixed to glass slides, permeabilized with a solvent, and then overlaid with diluted patient serum.
- After an initial incubation, the slides are washed to remove nonadherent immunoglobulins and other serum proteins, and the cells are then incubated with a fluorescein-conjugated antibody directed against human immunoglobulin.
- The fluorescein-conjugated secondary antibodies bind to human antibodies, which have reacted with antigens present in the HEp-2 cell substrate.



Common Procedure | Antinuclear Antibody Test

Flourescence patterns and intensity



Diagrammatic representation of common nuclear patterns observed under fluorescence microscopy.

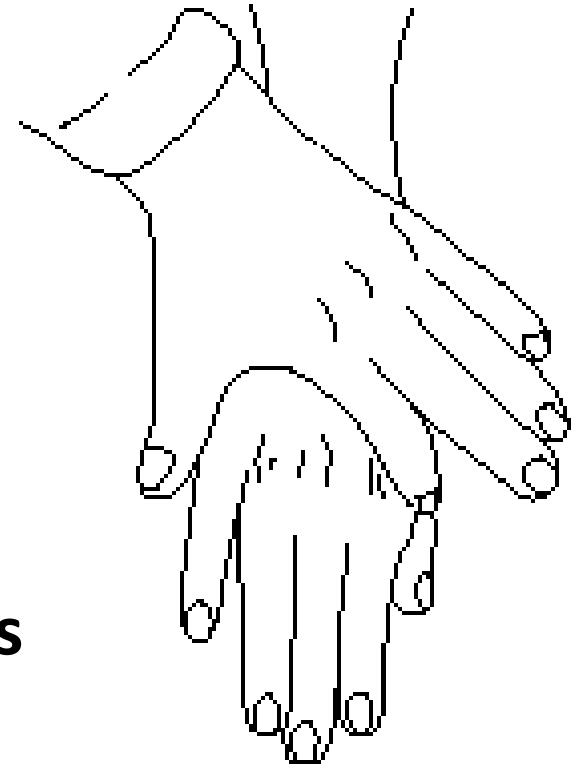
Medical conditions associated with +ve ANA

Condition	% ANA-positive
SLE	99
Drug-induced lupus	95-100
Mixed connective tissue disease	95-100
Autoimmune liver disease	60-100
Systemic sclerosis	> 90
Sjögren's syndrome	75-90
Polymyositis	30-80
Rheumatoid arthritis	30-50
Multiple sclerosis	25
Patients with silicone breast implants	15-25
Healthy relatives of SLE patients	15-25
neoplasia	15-25
Normal elderly (>70 years)	20

Early Referral Recommendations for *Potential RA*

Alarm signals

- ≥ 3 swollen joints
- MTP/MCP involvement
(Squeeze Test positive)
- Morning stiffness ≥ 30 minutes



Emery P, Breedveld FC, Dougados M, Kalden JR, Schiff MH, Smolen JS.
Ann Rheum Dis 2002; 61(4): 290-297.

Question #1

- A 42-year-old lady is evaluated for recurring pain and swelling of the left knee and right ankle that began 5 months ago. At that time she also had an episode of conjunctivitis as well as dysuria both of which resolved spontaneously. The joint pain and swelling persisted and aspiration of the left knee was performed which revealed leukocytosis without evidence of crystals or bacteria. She was started on naproxen which provides some relief.
- One month later she was switched to indomethacin but there was no improvement she then received corticosteroid joint infection which initially provided relief but now the pain and swelling and have recurred. Six months ago she also had an episode of non bloody diarrhea of 5 days duration that resolved spontaneously.
- On physical examination her vital signs are normal, cutaneous examination is normal, there is no evidence of conjunctivitis or iritis, musculoskeletal examination reveals swelling, tenderness and warmth of the left knee and right ankle.
- Rheumatoid factor, antinuclear antibody and anti-cyclic citrullinated peptide antibody testing is negative. Chlamydia trachomatis and neisseria gonorrhoeae test results are negative. Radiographs of the left knee and right ankle are normal
- Which of the following is the most appropriate treatment for this patient?
 - A) colchicine
 - B) Plaquenil
 - C) nitrofurantoin
 - D) sulfasalazine

Question #2

- **A 45-year-old man is evaluated for a 2-year history of recurrent pain and swelling of the wrists and knees which limits his ability to walk. He also has a 3-year history of psoriasis affecting the scalp scaling recurs periodically which was initially responsive to topical medication is but now is more resistant to treatment. He has no other pertinent personal or family medical history. His only medication is topical clobetasol propionate.**
- **On physical examination vital signs are normal cutaneous examination reveals erythematous plaques in the scalp with thick silver scaling, nail pitting in present. On musculoskeletal examination the wrists and knees are swollen and tender and there is pain on active and passive range of motion.**
- **Rheumatoid factor and anti-cyclic citrullinated peptide antibody test results are negative. Synovial fluid analysis is compatible with an inflammatory arthritis and there are no crystals. Gram stain and culture results are negative**
- **Which of the following is the most appropriate treatment for this patient?**
 - A) Sulfasalazine
 - B) methotrexate
 - C) prednisone
 - D) rituximab

Question #3

- **A 52-year-old male presents with increasing pain in the distal joints of the hands and feet for the last two months. The pain is worse in the morning associated with stiffness for more than an hour.**
- **His hands are so painful that he is having trouble writing. He denies fevers, weight loss, fatigue, cough, shortness of breath, or changes in bowel or bladder habits. He has no back pain, eye pain or skin rash. There is no history of arthritis in the family. His mother has psoriasis.**
- **On examination, there was tenderness over right 2nd MCP, PIP and DIP, and tenderness and swelling of the left 1st MCP joint. There was tenderness over most of his MTPs bilaterally. There was no other abnormality in his physical examination.**
- **His initial blood test showed normo-cytic anemia, ESR 36 and negative rheumatoid factor.**
- **Which of the following is the most likely diagnosis?**
 - a) Arthritis associated with inflammatory bowel disease
 - b) Gout
 - c) Osteoarthritis
 - d) Psoriatic arthritis
 - e) seronegative rheumatoid arthritis

Question #4

- A 46-year-old woman presents to your clinic with multiple complaints. She describes fatigue and general malaise over 2–3 months. Her appetite has decreased. She thinks she has unintentionally lost approximately 5.5 kg. Lately, she notes pain and stiffness in her fingers on both hands that is worse in the morning and with repetitive movement. She has a grandmother and a sister who have rheumatoid arthritis, and she is very concerned that she now has it as well.
- Which of her complaints represents the most common manifestation of established rheumatoid arthritis?
 - a) Fatigue and anorexia for more than 2 months with concomitant joint pain
 - b) Morning joint stiffness lasting for more than 1 hour
 - c) Pain in symmetric joints that is worsened with movement
 - d) Positive family history with two relatives with RA
 - e) Weight loss of more than 4.5 kg during period of active disease

Take
home
messages

Polyarthralgia is much more common than polyarthritis.

History and physical examination will help to reach a clinical diagnosis and guide management.

Do not order RF for patients with back pain.

Weakly positive RF or ANA are not always significant.



Questions
?



Thank you