Brigham and Women's Hospital
Founding Member, Mass General Brigham

Rheumatology Board Review

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- Clinical and research focus:
  spondyloarthritis (animal models and translational research)

Disclosures

- Consulting/Scientific Advisory Boards:
  Augurex, Eli Lilly, J&J
- Research Grants:
  Novartis

Question 1

A 52-year-old female presents with joint pain, swelling and morning stiffness lasting about 2 hours for the past 6 weeks. On examination, there are multiple tender and swollen joints with symmetric involvement of the wrists, MCP and PIP joints. → What is the most likely diagnosis?

A. Rheumatoid arthritis
B. Osteoarthritis
C. Psoriatic arthritis
D. Systemic lupus erythematosus
E. Gout

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Question 2

A 60-year-old male presents with sudden-onset of severe pain, erythema, and swelling in his left big toe. He denies any trauma. Symptoms began the night after a barbecue with friends. He is unable to wear a shoe or bear weight on the left foot. → What is the most likely diagnosis?

A. Rheumatoid arthritis
B. Psoriatic arthritis
C. Reactive arthritis
D. Gout
E. Calcium pyrophosphate deposition disease (CPPD)

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→ What is the most likely diagnosis?

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C. Reactive arthritis

D. Gout

E. Calcium pyrophosphate deposition disease (CPPD)

Question 3

A 38-year-old male presents with chronic right knee pain that worsens with activity and improves with rest. He has no other active musculoskeletal problems.
On examination, there is crepitus and bony enlargement of the right knee joint.
→ What is the most likely diagnosis?

A. Rheumatoid arthritis
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D. Systemic lupus erythematosus
E. Ankylosing spondylitis

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C. Psoriatic arthritis

D. Systemic lupus erythematosus

E. Ankylosing spondylitis

There are many types of “arthritis”

- Primary Inflammatory Arthritis
  - RA
  - Spondyloarthritis
    - Ankylosing Spondylitis
    - Psoriatic Arthritis
    - Arthritis associated with Inflammatory Bowel Disease
  - SLE
  - Crystal-induced arthritis
    - Gout (uric acid)
    - CPPD (calcium pyrophosphate)
- Infectious Arthritis
  - Septic arthritis
  - Parvovirus, Chikungunya
- Degenerative Arthritis (OA)

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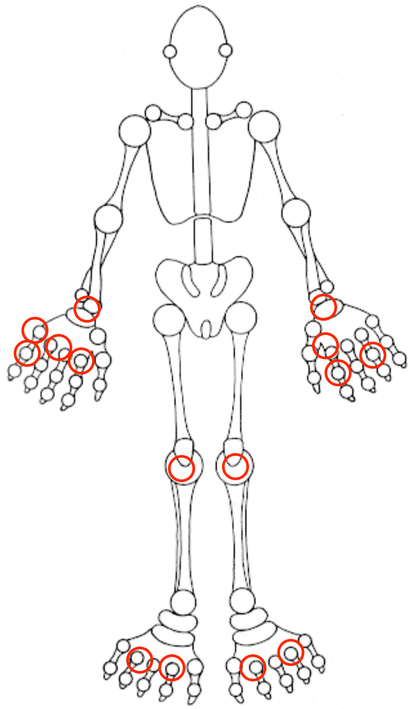
Apply pattern recognition:

- Symptom duration
- Demographics (sex, age)
- Joint involvement pattern
- Extra-articular manifestations

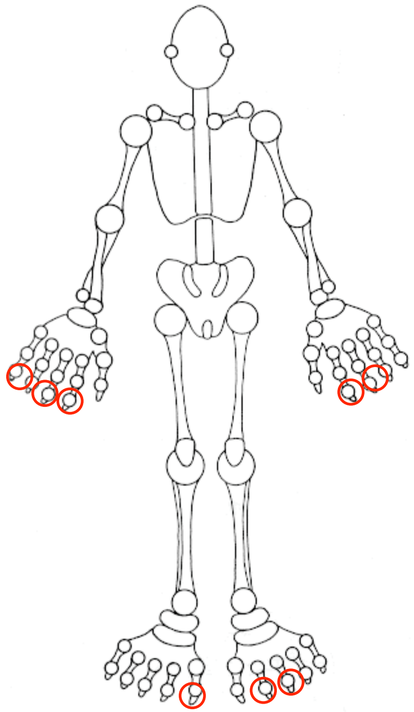
Joint involvement patterns

RA



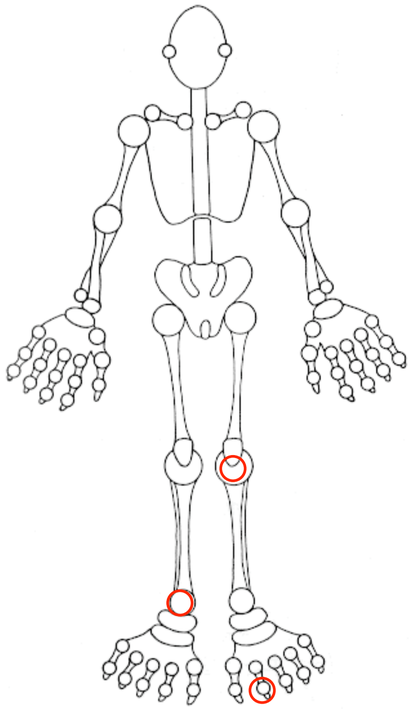
symmetric
polyarthritis

PsA



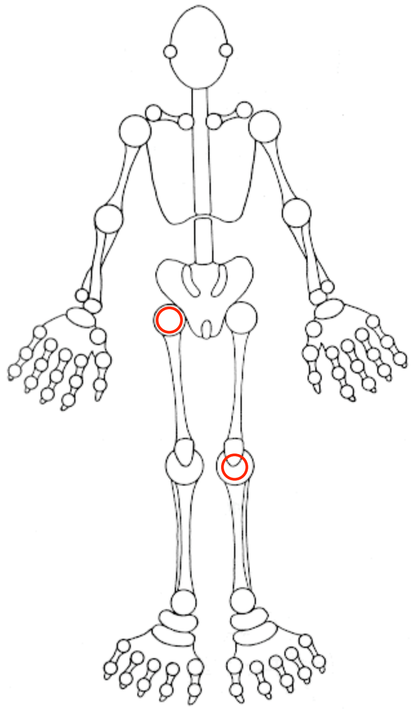
DIP arthritis

PsA



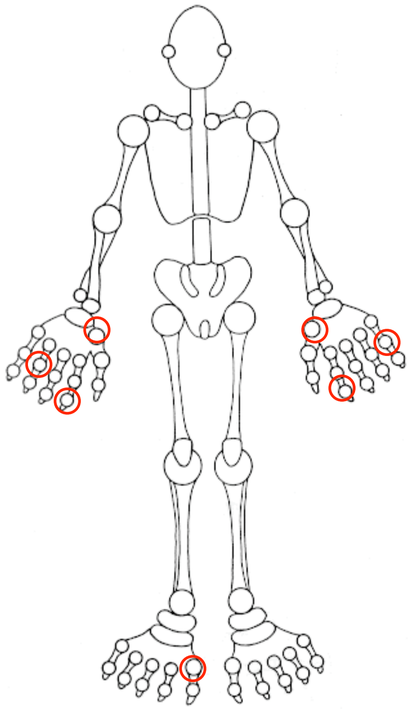
asymmetric
oligoarthritis

OA



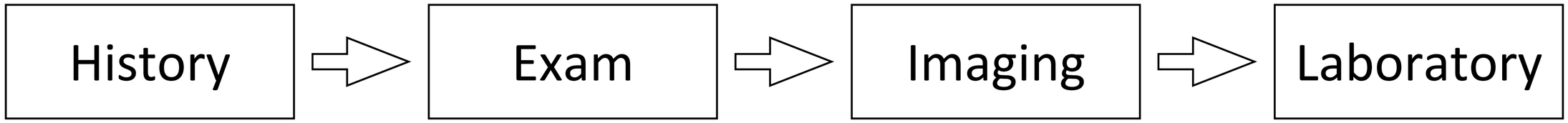
individual large
joints (hip, knee)

OA



DIPs, PIPs
CMC1, MTP1

Diagnostic approach



- patient age and sex
- symptom duration
- joint swelling
- morning stiffness
- h/o psoriasis
- pattern of involved joints
- family history

- synovitis
- pattern of involved joints
- dactylitis
- enthesitis
- skin/nail changes

- radiographs
  cheap, readily available, characteristic patterns, results of inflammation
- U/S
  cheap, user dependent, current inflammation
- MRI
  expensive, access issues, current inflammation

- CRP, ESR
- cave “rheum panel”
- RF, ACPA (anti-CCP)
  suspicion for RA
- ANA
  suspicion of SLE, CTD
- HLA-B27
  suspicion for axial SpA
- synovial fluid analysis in acute monoarthritis

Question 4

A 52 yo woman was recently diagnosed with seropositive rheumatoid arthritis. She has been treated with oral Methotrexate 10 mg weekly for 2 months. She continues to have significant joint pain and morning stiffness lasting one hour. She has 7 tender and 5 swollen joints on exam.

Labs:
RF and anti-CCP positive
ESR 50 mm/h, CRP 14.1 mg/l

What is the most appropriate next step?

A. add a TNF inhibitor
B. begin Rituximab infusions
C. switch MTX to Tofacitinib
D. increase MTX to 25 mg weekly
E. add prednisone 20 mg daily

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American College of Rheumatology
Empowering Rheumatology Professionals

2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis

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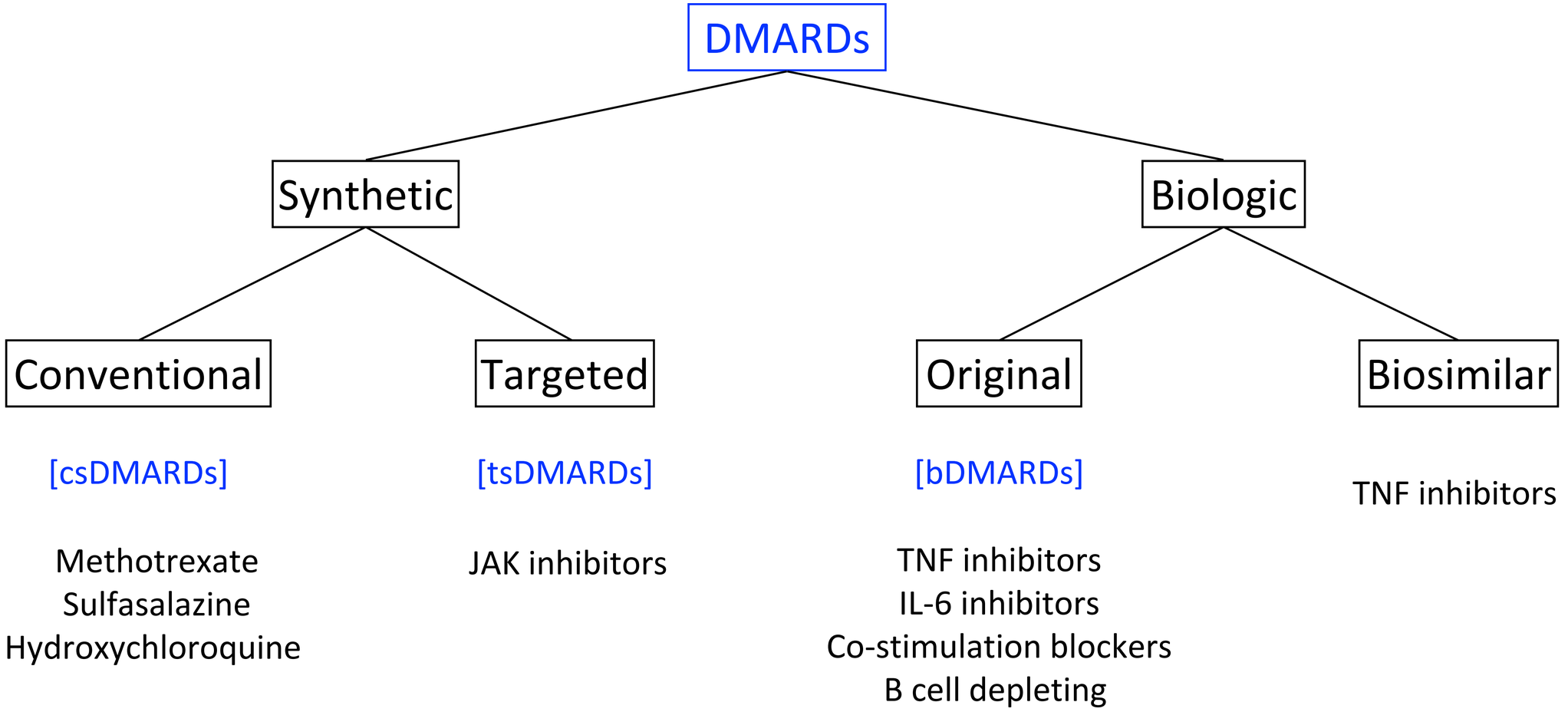
Treatment of rheumatoid arthritis

- Methotrexate
  - 1st line DMARD for most patients (“anchor drug”)
  - weekly dosing 15-25 mg, typically PO
  - folic acid 1 mg daily reduces side effects
  - CBC, LFT, Crea monitoring
- optimize treatment regimen before changing drugs
  - maximize dose to 25 mg weekly
  - split dosing
  - switch PO → SQ
- T2T = “treat to target” improves longterm outcomes
  strongly recommended

Fraenkel Arthritis Rheumatol 2021;73:1108-1123

Treatment of rheumatoid arthritis



Fraenkel Arthritis Rheumatol 2021;73:1108-1123

Question 5

Since the introduction of monoclonal antibodies into clinical practice ~20 years ago, biologics have revolutionized the care of patients with rheumatic diseases, cancer and other illnesses.

The patents for several of the early biologics have expired opening the market to biosimilars produced by competing manufacturers.

Which of the following statements regarding biosimilars is correct?

Compared with the reference product, biosimilars…

A. are structurally 100% identical
B. have similar efficacy
C. are less immunogenic
D. are cheaper but may be not as effective
E. can be given orally

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Biosimilars

- identical amino acid sequence as originator (reference) drug but structure may differ slightly due to post-translational modifications
- biosimilars ≠ generic drugs
- must be highly similar to an approved biological product (originator) in terms of structure, function, quality, clinical efficacy and safety
- at least 1 clinical trial in 1 indication → extrapolation to other indications

Lyman NEJM 2018; 378:2036-44

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Key messages for patients:

- biosimilars are as effective as the original drug
  company producing biosimilars are often the same as those producing original drugs (biosimilars are not cheap low quality copies)
- benefits and potential side effects are expected to be the same
  (cave: nocebo effect)

Lyman NEJM 2018; 378:2036-44

Question 6
How do JAK inhibitors work?

A. Block activation of the NLRP3 inflammasome
B. Inhibit the binding of IL-1α and IL-1β to the IL-1 receptors
C. Reduced adenosine deaminase activity→ increased extracellular adenosine
D. Prevent the phosphorylation of Stat proteins
E. Interfere with binding of JAK transcription factors to cytokine promoter regions

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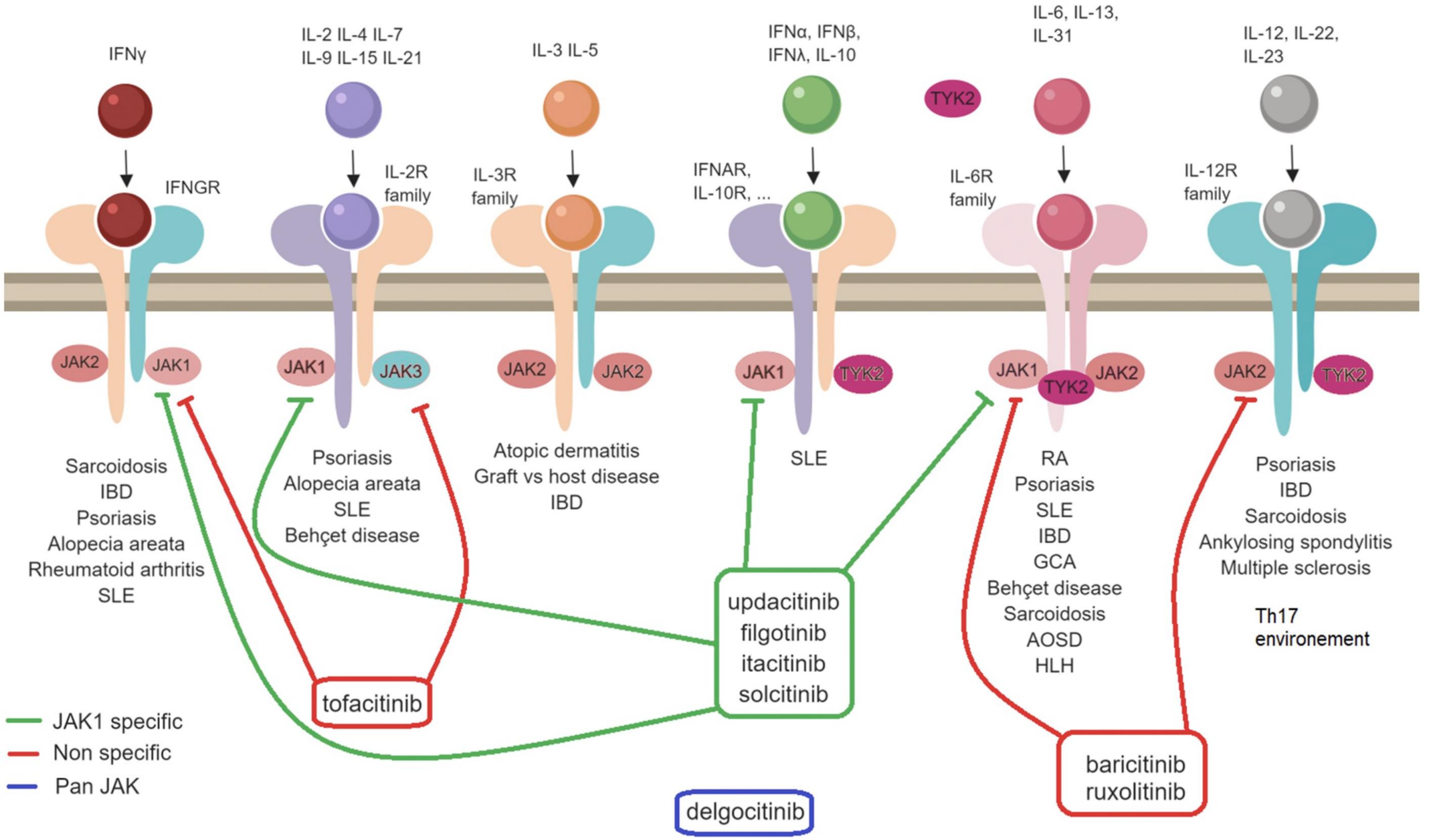

Jamilloux Autoimmun Rev 2019; 18: 102390

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B. Inhibit the binding of IL-1α and IL-1β to the IL-1 receptors Anakinra

C. Reduced adenosine deaminase activity→ increased extracellular adenosine Mtx

D. Prevent the phosphorylation of Stat proteins

E. Interfere with binding of JAK transcription factors to cytokine promoter regions

Question 7

The 52 yo female with seropositive rheumatoid arthritis was eventually started on a TNF inhibitor in addition to weekly Methotrexate 25 mg PO. Her arthritis is now well controlled.

She comes in for her annual physical. She plans to travel to South America later in the year. You review her vaccination records.

Which of the following vaccines should be avoided in this RA patient on a biologic?

A. Hepatitis A
B. Hepatitis B
C. Td booster
D. Yellow fever
E. Shingles

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Vaccination of patients on immunosuppressive drugs

- live-attenuated vaccines are generally not recommended
  - MMR
  - live-attenuated influenza
  - yellow fever
  (consider holding immunosuppressive drugs for an adequate time period)
- all adult patients on immunosuppressive drugs should receive
  - annual recombinant influenza
  - pneumococcal vaccine
  - recombinant zoster vaccine
  - other vaccines as indicated by age or other circumstances (SARS-CoV2)
- vaccinate ideally prior to initiation of therapy,
  continue immunosuppressive drug for non-live attenuated vaccinations,
  exception: hold Methotrexate for 2 weeks after flu shot

Furer Ann Rheum Dis 2020;79:39-52, Bass Arthritis Rheumatol 2023;75:333-348

Question 8

A 28 yo kindergarten teacher presents with 1 week of pain, swelling and morning stiffness in her hands and knees.

3 weeks ago, she had a cold with nasal discharge, fever, malaise, and muscle aches. Several children in her class had similar symptoms accompanied by an erythematous rash on the cheeks.

Exam:
Mild soft tissue swelling of several PIPs and MCPs. Minimally swollen + tender wrists and knees bilaterally.

Labs:
CBC unremarkable, ESR 40 mm/h
RF 24 IU

What is the most appropriate treatment at this time?

A. Naproxen 500 mg BID
B. Hydroxychloroquine 300 mg daily
C. Methotrexate 15 mg weekly + folic acid 1 mg daily
D. Prednisone 15 mg daily
E. Doxycycline 100 mg BID for 10 days

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Most likely diagnosis - acute viral arthritis

- presentation highly suggestive of Parvovirus B-19 infection
  - acute mild symmetric synovitis (RA-like)
  - exposure to sick children with facial rash (Fifth disease)
- generally a self limited disease, improvement over several weeks, minimal intervention required
- RF may be mildly elevated,
  better test: Parvo B19 IgM

Marks Clin Med (London) 2016; 16:129-34

What is the most appropriate treatment at this time?

A. Naproxen 500 mg BID viral arthritis, axSpA
B. Hydroxychloroquine 300 mg daily RA, SLE (≦ 5 mg/kg)
C. Methotrexate 15 mg weekly + folic acid 1 mg daily RA
D. Prednisone 15 mg daily PMR
E. Doxycycline 100 mg BID for 10 days Erythema migrans

Question 9

A 25 yo female medical student presents to the ED with fever, chills and a diffuse rash. This started the day after she returned from Haiti where she had spent one month as a volunteer in a health clinic. Within hours, she also developed severe widespread joint pain (affecting her PIPs, MCPs, wrists, ankles, knees, hips).

<u>Exam:</u>
T 103°F, HR 130/min, BP 130/71, O_2 98% on room air
diffuse, blanchable erythematous rash on trunk and limbs
swollen MCPs and wrists, multiple tender joints

<u>Laboratory:</u>
CRP 20 mg/l

Which of these viruses is the most likely cause for the patient's symptoms?

A. Borrelia
B. Chikungunya
C. Mayaro
D. O'nyong'nyong
E. Ross River

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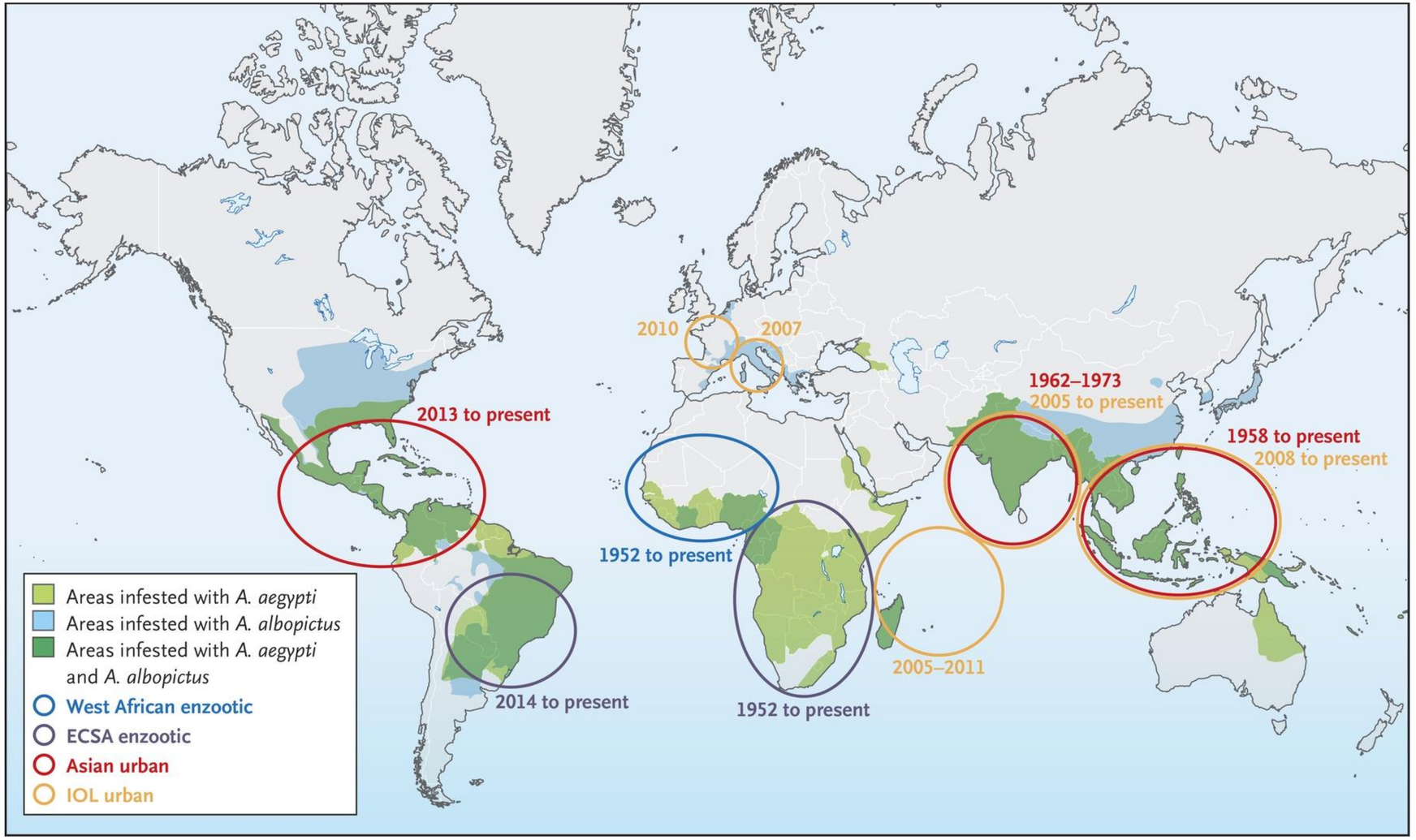
Chikungunya and other alpha viruses may induce arthritis

- consider viral arthritis in context of travel history
  Chikungunya - Caribbean, Central Africa, SE Asia
  Mayaro - South America
  O'nyong'nyong - East Africa
  Ross River - Australia
- arbovirus (arthrophod-born) transmitted by mosquitoes
  → acute disease with fever, rash, arthritis, myalgias,
  typically self-limited
- confirmation by antibody testing (IgM, IgG)
- treatment - NSAIDs

Waymouth Semin Arthritis Rheum 2013; 42:273-8, Weaver NEJM 2015; 372:1231-9, Sutaria Curr Opin Rheumatol 2018; 30:256-63

Origin, spread and distribution of Chikungunya virus and its vectors



Weaver NEJM 2015; 372:1231-9

Chikungunya vaccination (NEW)

- Two vaccines are available in the US, both single dose
  virus-like particle vaccine
  live-attenuated vaccine
- Recommended for
  - adults traveling to an area with a chikungunya outbreak
  - adults traveling or moving to an area with elevated risk if planning to stay for an extended period of time (≧ 6 months)
- virus-like particle vaccine - 12 years or older
  live-attenuated vaccine - 18 years or older, caution in older adults

https://www.cdc.gov/vaccines/

Question 10

A 72 yo female presents with 6 weeks of stiffness in the neck and both shoulder. She has shoulder pain when dressing herself in the morning. She also reports pain at night and sleeps poorly. Symptoms improve as the day progresses but then return in the early evening. No significant PMH except for HTN.

Exam:
Mildly decreased passive ROM in the shoulders. Mild OA changes in the hands. No synovitis. No muscle weakness.

Labs:
CBC unremarkable, ESR 40 mm/h

What is the most likely diagnosis?

A. polymyositis
B. early rheumatoid arthritis (RA)
C. fibromyalgia
D. polymyalgia rheumatica (PMR)
E. metabolic myopathy

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Polymyalgia rheumatica (PMR)

- clinical diagnosis
- pain and morning stiffness in neck, shoulders, hips
  age >50, +/- constitutional symptoms
- shoulder girdle (60%)
  hip girdle (5%)
  both (35%)
- Labs: ESR and/or CRP elevated in 80%
  anemia 15%
- associated with GCA (headache, visual loss, jaw claudication)

Kermani Lancet 2013; 381:63-72, Helfgott Arthritis Rheum 1996; 39:304-7

Question 11

An 80 yo woman was hospitalized two days ago for upper GI bleeding. She was found to have a peptic ulcer and was placed on omeprazole plus IV normal saline for hydration.
Today, she presents with acute painful swelling of the right knee. PMH is significant for OA of the hands and knees, for which she has been taking Ibuprofen.

<u>Exam:</u>
T 100.0 F
Heberden + Bouchard nodes in both hands
warmth and a large effusion in the right knee
knee aspiration → 60 ml of yellow cloudy fluid
(+ intracellular rhomboid positively birefringent crystals)

What is the likely cell count in the synovial fluid of this patient?

A. 500 cells/µl
B. 500 cells/ml
C. 15,000 cells/µl
D. 15,000 cells/dl
E. 15,000 cells/ml

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B. 500 cells/ml

C. 15,000 cells/µl

D. 15,000 cells/dl

E. 15,000 cells/ml

Synovial fluid analysis

- informative tests:
  - cell count + differential
  - Gram stain + culture
  - crystal analysis
- not informative: albumin, protein, glucose
- “inflammatory” >2,000 cells/µl
- septic arthritis more likely with
  - high cell count (>50,000 cells/µl)
  - high neutrophil fraction (>95%)

Courtney Best Pract Res Clin Rheumatol 2009; 23:161-92

Question 12: What is the serum uric acid target for most patients on uric acid lowering drugs?

A. less than 4 mg/dl
B. less than 5 mg/dl
C. less than 6 mg/dl
D. less than 7 mg/dl
E. less than 8 mg/dl

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Allopurinol dosing

- treat to target: serum uric acid <6 mg/dl in all patients
- alternative target:
  <5 mg/dl in severe gout for faster dissolution of crystals
- Flare prophylaxis during initiation!
  (e.g. low dose Colchicine)
- patients may require >300 mg daily to achieve target
- repeat uric acid test 1 month after dose adjustments

Khanna Arthritis Care Res 2012; 64:1431-46, Richette Ann Rheum Dis 2017; 76:29-42, FitzGerald Arthritis Rheum 2020; 72:879-895

Allopurinol toxicity

- clinical features:
  - rashes (mild → Stevens-Johnson syndrome)
  - LFT abnormalities
  - Allopurinol hypersensitivity syndrome
- low starting dose (100 mg daily) reduces risk for toxicity
- consider screening for HLA-B*58:01 in patients of Southeast Asian descent and African Americans
- alternatives
  - desensitization
  - Febuxostat
  - uricosuric drugs

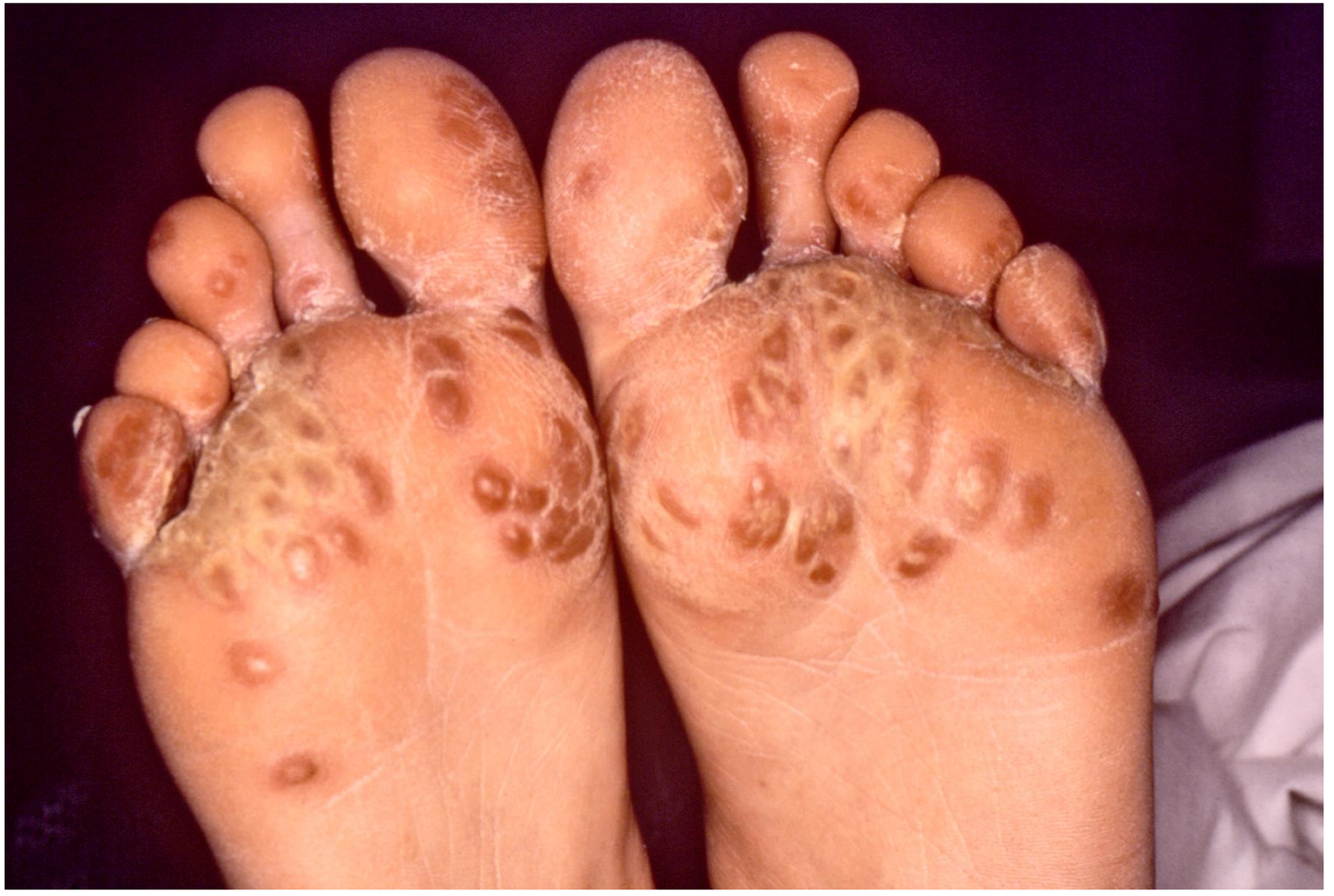
Khanna Arthritis Care Res 2012; 64:1431-46, Richette Ann Rheum Dis 2017; 76:29-42, FitzGerald Arthritis Rheum 2020; 72:879-895

Question 13

A 45 yo male presents with painful swelling of the 3rd and 4th toe of the right foot and a rash under the soles of his feet for 4 weeks. He denies fever, recent dysuria, diarrhea, eye problems, or a h/o psoriasis or back pain. He is sexually active. He takes no medications.

<u>Exam:</u>
dactylitis of the right 3rd and 4th toes
yellow-brown nodular/hyperkeratotic crusty plantar rash

<u>Laboratory + Imaging:</u>
CRP 8 mg/l
CBC unremarkable
X-ray foot - soft tissue swelling



Which of the following is the most appropriate test in this patient with reactive arthritis?

A. anti-CCP
B. ANA
C. urine PCR test for Chlamydia trachomatis
D. HLA-B27
E. X-ray of the pelvis

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Reactive arthritis

- within 4 weeks after UTI or infectious diarrhea
  Chlamydia, Yersinia, Salmonella, Shigella, Campylobacter
- synovial fluid: Gram-stain and culture negative
  other microbial analysis also often negative
- self-limited (50%) or chronic (50%)
  - asymmetric oligoarthritis, enthesitis, dactylitis
  - sacroiliitis
  - keratoderma blennorrhagica, circinate balanitis
- treatment with NSAIDs (+ DMARDs if chronic)
  no role for antibiotics

Carter Best Pract Res Clin Rheumatol 2011; 25:359-74

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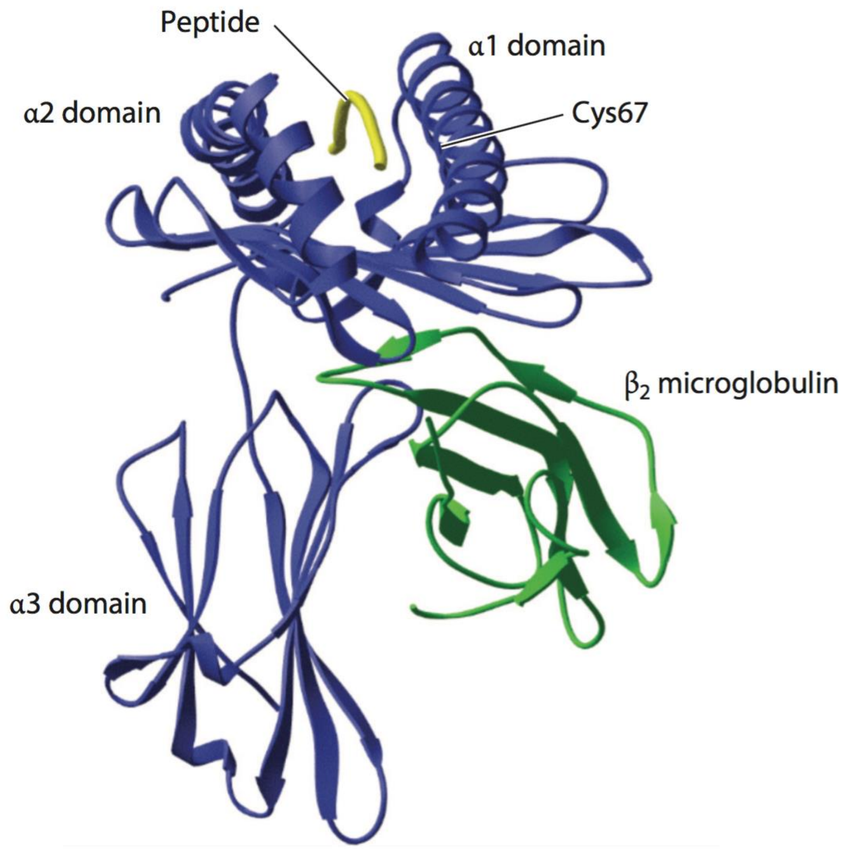
HLA-B27

- strongly associated with SpA
  - ankylosing spondylitis ~90%
  - reactive arthritis 30-70%
  - psoriatic arthritis 40-50%
- prevalence of HLA-B27+ in US
  - 6.1% overall
  - 7.5% non-Hispanic White
  - 4.6% Mexican American
  - 1.1% non-Hispanic Black
- HLA-B27 never makes a diagnosis of SpA



Khan Curr Rheumatol Rev 2010; 12:337-41, Reveille Arthritis Rheum 2011, 64:5, 1407-11

Question 14

A 29 yo male with axial spondyloarthritis diagnosed 2 years ago presents with worsening low back and buttock pain over the last 6 months. Morning stiffness lasts 3 hours. ROS is negative except for fatigue.

Symptoms had previously been well-controlled with physical therapy and Naproxen. A switch to Diclofenac 75 mg BID one month ago was without benefit.

<u>Exam:</u>
Tenderness to palpation over the SI joints.
Otherwise unremarkable.

<u>Labs:</u>
CRP 10 mg/l

What is the most appropriate addition to this patient's medical therapy?

A. Methocarbamol (muscle relaxant)
B. Methotrexate
C. Sulfasalazine
D. Adalimumab (TNF inhibitor)
E. Prednisone

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Management of axial spondyloarthritis/ankylosing spondylitis

- first line: NSAIDs and physical therapy
- inadequate NSAID response:
  - no response/intolerance to ≧2 NSAIDs over 1 month
  - incomplete response to ≧2 NSAIDs over 2 months
- second line: TNF inhibitors, IL-17A antagonists, JAK inhibitors
- no role for systemic corticosteroids or conventional DMARDs (e.g. Methotrexate)

Ward Arthritis Rheumatol 2016; 68:282-98, van der Heijde Ann Rheum Dis 2017; 76:978-991, Ward Arthritis Rheum 2019; 71:1599-1613

Question 15

A 35 yo high school teacher is evaluated for low back pain that started 2 weeks ago. The pain is constant, worse with movements and does not respond to OTC ibuprofen.

He has previously been fit and healthy. He denies a history of trauma, malignancy, fever, weight loss, numbness, tingling or weakness in the legs, bladder or bowel symptoms. He does not use IV drugs.

<u>Exam:</u>
uncomfortable, reduced ROM in L spine
sensation, strength, DTR in legs are symmetric and WNL
straight-leg-raise test → lumbar pain

What is the most appropriate next step?

A. X-ray lumbar spine
B. MRI of SI joints
C. corticosteroid taper
D. bedrest for 3 days, then graded exercise program
E. change NSAID

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Nonspecific low back pain

- pain without evidence for a serious underlying condition (e.g. cancer, infection, cauda equina syndrome), spinal stenosis, radiculopathy, or other specific spinal cause (e.g. compression fracture, AS)
- imaging not recommended
- management
  - education + reassurance
  - superficial heat, other non-pharmacological interventions
  - NSAIDs or muscle relaxants

Chou Ann Int Med 2007; 147:478-91, Qaseem Ann Int Med 2017; 166:514-530

Question 16

- A 40 yo colleague sees you for left shoulder pain. She is an avid tennis player and has had pain in the left deltoid area for the past 3 weeks. The pain is worse with movements and has prevented her from playing tennis.
- Exam:
  Subacromial tenderness. The AC joint is nontender.
  Full passive ROM in the glenohumeral joint.
  Resisted shoulder abduction causes pain, there is no weakness.
  Resisted forearm flexion is unremarkable.
- X-ray: normal

What is the the most likely diagnosis?

A. supraspinatus tendonitis
B. rotator cuff tear
C. bicipital tendonitis
D. calcific tendonitis
E. AC joint osteoarthritis

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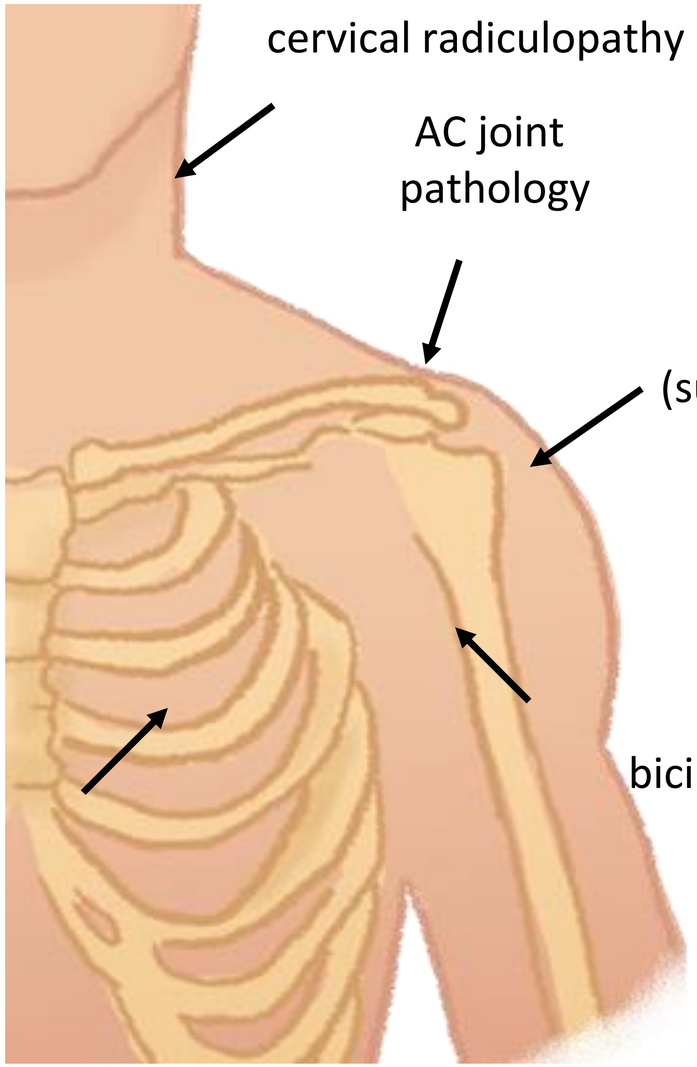
DD of shoulder pain



cervical radiculopathy

AC joint pathology

calcific tendonitis
frozen shoulder

rotator cuff impingement syndrome
(supraspinatus tendonitis, subacromial bursitis)

supraspinatus tear

OA of the glenohumeral joint
crystal-induced arthritis

bicipital tendonitis

referred pain
(heart,
gall bladder)

Beach NEJM 2016; 375:e24

Question 17

A 44 yo male computer programer presents with 3 months of lateral elbow pain. He is otherwise healthy and denies overt trauma to the elbow. He goes to the gym 3x per week.

The pain is noted when carrying stuff. No problems with typing. No problems in other joints.

No swelling on exam, active and passive ROM are full.
Tenderness over the lateral elbow and pain with resisted extension of the wrist.

What is the the most likely diagnosis?

A. Lateral epicondylitis (tennis elbow)
B. Medial epicondylitis (golfer’s elbow)
C. Bicipital tendinitis
D. Olecranon bursitis (student’s elbow)
E. Osteoarthritis of proximal radioulnar joint

What is the the most likely diagnosis?

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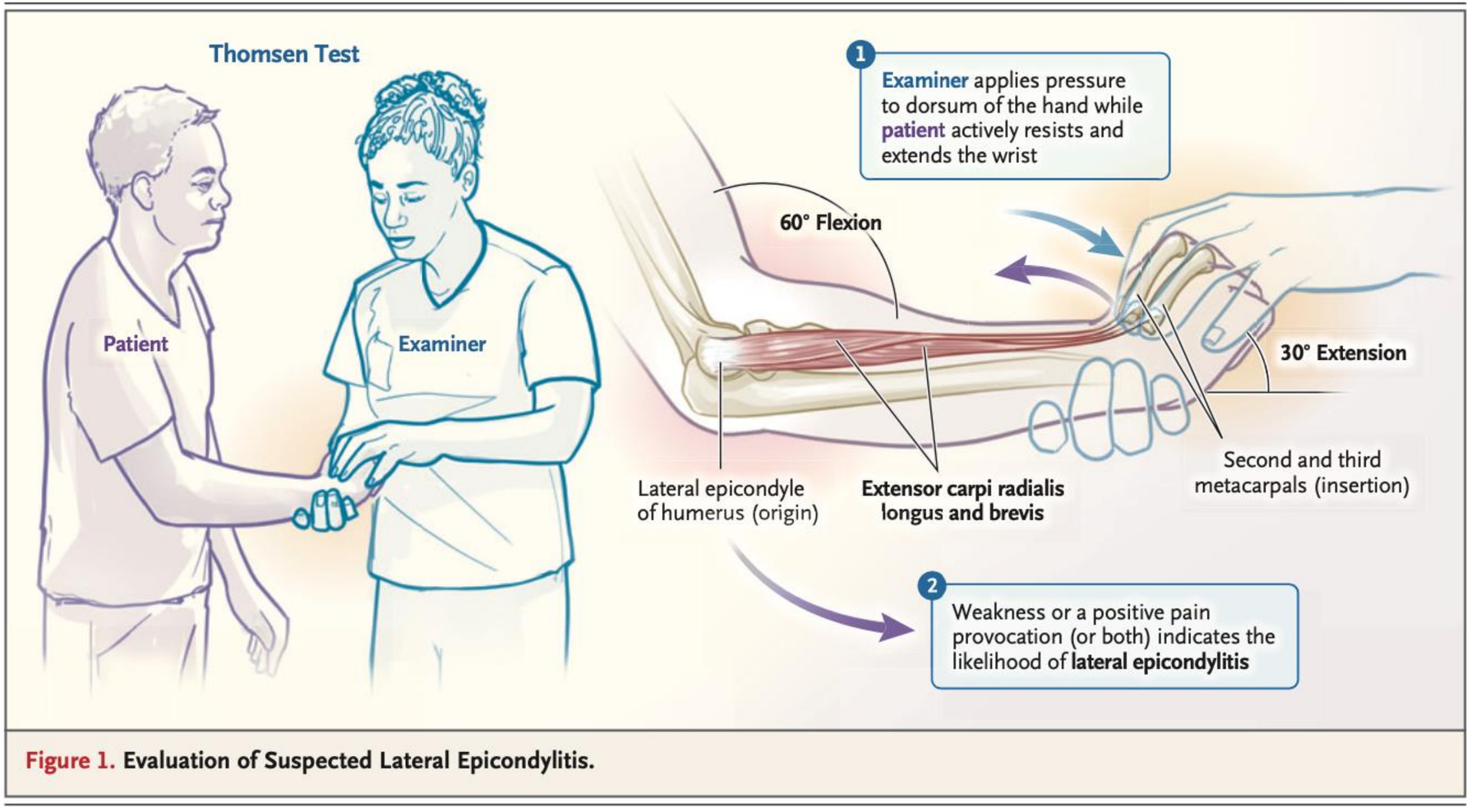

Figure 1. Evaluation of Suspected Lateral Epicondylitis.

Wolf NEJM 2023;388:2371-77

KEY CLINICAL POINTS

LATERAL EPICONDYLITIS

- Lateral epicondylitis (commonly known as tennis elbow) generally resolves without treatment in 6 to 12 months.
- There is no strong evidence to support substantive benefit from any intervention.
- There is no evidence that using the elbow, despite pain, causes harm.
- Some evidence, although inconsistent and of variable quality, supports the use of physiotherapy for lateral epicondylitis.
- Glucocorticoid injections can relieve pain in the short term but should be used with caution owing to potential adverse effects with regard to pain and function in the long term; additional adverse effects include skin atrophy and discoloration.
- Surgery may be considered after 1 year or more of persistent pain but is rarely indicated.

Wolf NEJM 2023;388:2371-77

Question 18

A 69 yo woman is admitted to the hospital with increasing shortness of breath on exertion.

The patient has a long history of Raynaud's and was told to have scleroderma several years ago. She has lost 30 lb over the last year in the setting of dysphagia. Facial telangiectasias and sclerodactyly are clearly present.

While obtaining the history you consider the differences between diffuse and limited cutaneous systemic sclerosis.

Which of the following is a characteristic feature of limited cutaneous systemic sclerosis?

A. skin involvement of proximal limbs and trunk
B. interstitial lung disease
C. pulmonary hypertension
D. increased risk for scleroderma renal crisis
E. anti-Scl 70 (topoisomerase 1) antibodies

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D. increased risk for scleroderma renal crisis

E. anti-Scl 70 (topoisomerase 1) antibodies

Denton Lancet 2017; 390:1685-99

Question 19

A 25 yo female presents with episodic painful color changes in her hands. This started after she moved to Boston three years ago to attend graduate school. Episodes are triggered by cold exposure. Typically, her fingers turn white and later blue.

She has no relevant past medical history and takes no medications except for birth control.

She feels chronically fatigued. ROS is otherwise unremarkable (no joint pain or swelling, rashes, photosensitivity, dry eyes or mouth, mucosal lesions, SOB, weakness).

Physical examination is unremarkable.

What is the most appropriate next step in evaluating this patient?

A. nailfold capillary microscopy + check ANA
B. check antiphospholipid antibodies
C. check scleroderma antibodies (Scl-70, anti-centromer)
D. check cryoglobulins
E. no additional tests needed

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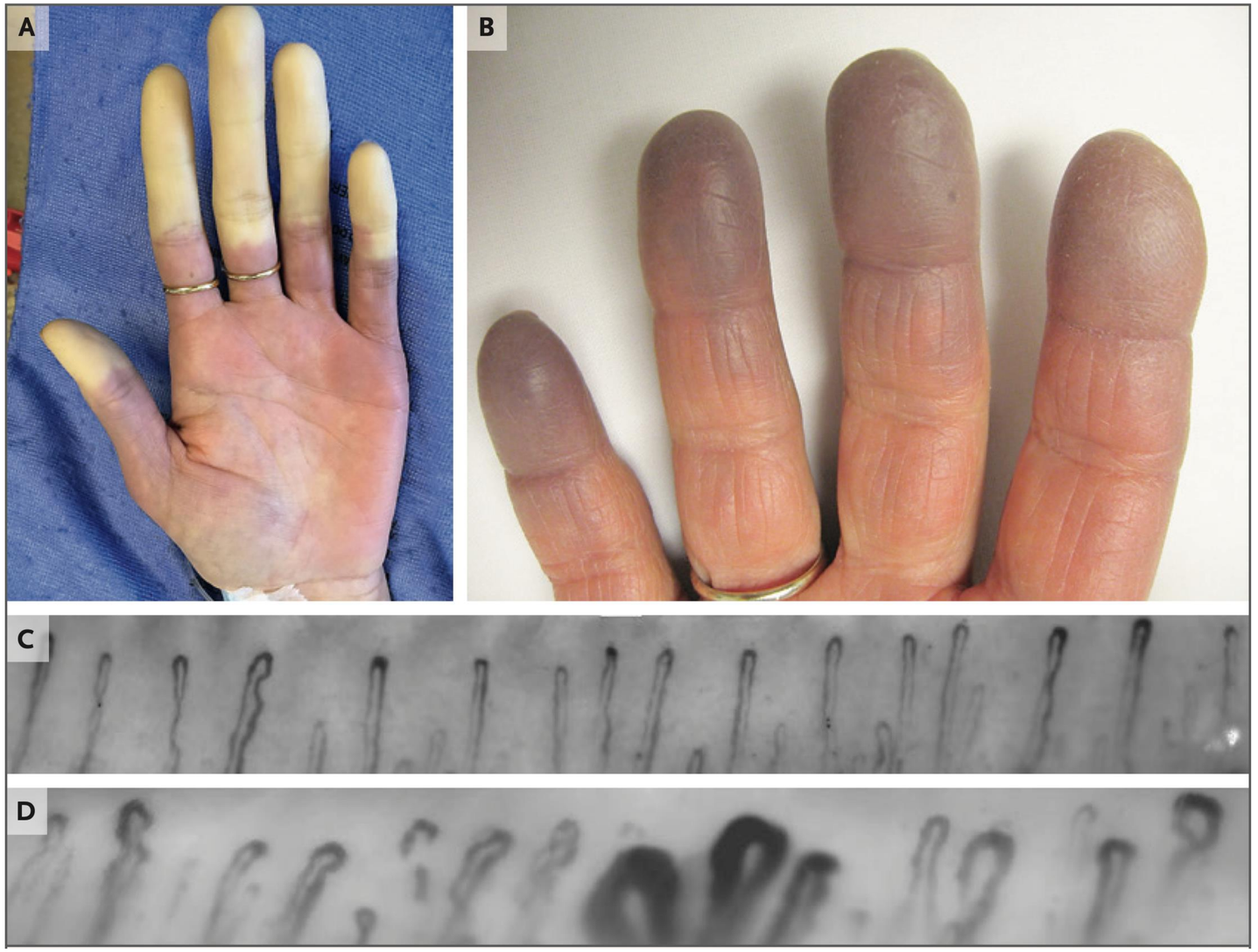

normal

pathological

Wigley NEJM 2016; 375:556-65

Question 20:

A 35-year-old woman has had three first-trimester miscarriages. Which test is essential to evaluate for antiphospholipid syndrome?

A. ANA
B. anti-dsDNA antibody
C. Lupus anticoagulant
D. complement levels (C3, C4)
E. anti-RO antibody

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Classification criteria for anti-phospholipid syndrome

The revised classification criteria for antiphospholipid syndrome (APS) are referred to as the Miyakis criteria[2]. A patient has to fulfil at least one clinical criteria and at least one laboratory criteria.

Clinical criteria

Vascular thrombosis

≥1 clinical episode of arterial, venous or small-vessel thrombosis. Thrombosis must be objectively confirmed. If histopathological confirmation is used, thrombosis must be present without inflammation of the vessel wall.

Pregnancy morbidity

- ≥1 unexplained death of a morphologically normal fetus ≥10 weeks of gestation
- ≥1 premature delivery of a morphologically normal fetus <34 weeks gestation because of severe pre-eclampsia or eclampsia (defined according to standard definitions) or recognized features of placental insufficiency
- ≥3 unexplained consecutive miscarriages at <10 weeks of gestation, with maternal and paternal factors (such as anatomical, hormonal or chromosomal abnormalities) excluded

Laboratory criteria

The presence of antiphospholipid antibodies on ≥2 occasions at least 12 weeks apart and <5 years before clinical manifestations, as demonstrated by ≥1 of the following:

- Presence of lupus anticoagulant in plasma
- Medium titre to high titre of anticardiolipin antibodies (>40 GPL* or MPL*, or >99th percentile‡) of immunoglobulin G (IgG) or IgM isotypes
- Anti-β2-glycoprotein 1 antibodies of IgG or IgM isotypes present in plasma

Miyakis J Thromb Haemost 2006; 4:295-306, Schreiber Nat Rev Dis Primers 2018; 4:17103

Question 21

A 52 yo man presents with new hemoptysis. He was previously in good health. Three weeks ago, he began experiencing muscle aches, joint pain, nose bleeds, and diminished hearing. One week ago, he developed a rash on both legs and weakness in his right hand.

Exam:
T 100.4, BP 152/100, HR 72, RR 24
bilateral conjunctival injection, tender maxillary sinuses, decreased hearing
diffuse rhonchi
reduced grip strength right hand
palpable purpura over the lower extremities

Labs:
Wbc 12,300, ESR 84
Crea 2.1
UA: 3+ protein, 50 Rbc, 20 Wbc, mixed cellular casts

Which of the following tests is most likely to establish the diagnosis?

A. anti-dsDNA
B. cryoglobulins
C. complement levels (C3, C4)
D. ANCA
E. urine electrophoresis

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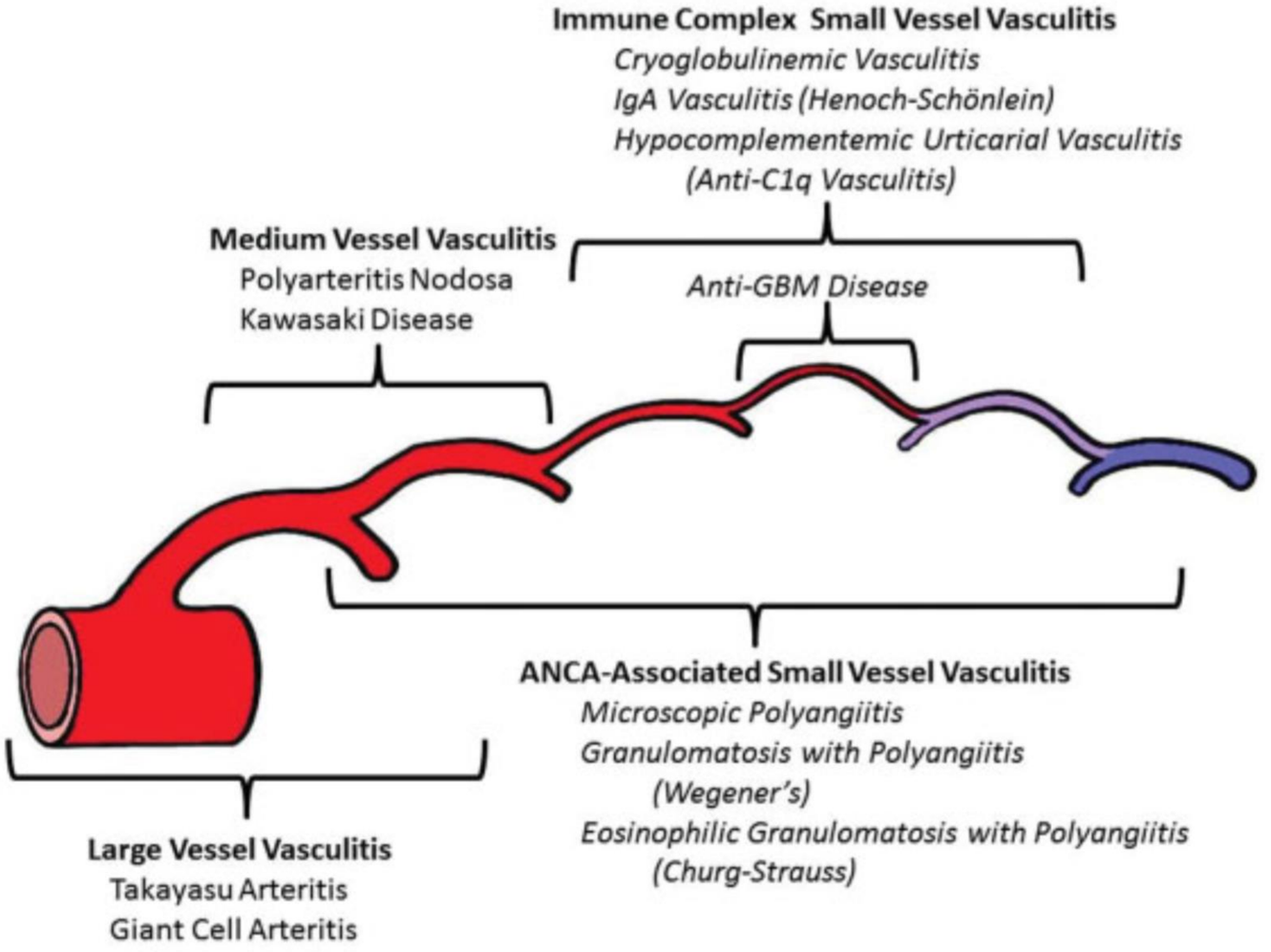
ANCA testing in the diagnosis of vasculitis

- useful test, especially when strongly positive,
  c-ANCA is more specific than p-ANCA
- indirect immunofluorescence: p-ANCA c-ANCA
  ELISA: anti-MPO anti-PR3
- ANCA-associated vasculitides:
  - GPA (Wegener's): c-ANCA, rarely p-ANCA
  - MPA (Microscopic polyangiitis): p-ANCA
  - EGPA (Churg-Strauss): c-ANCA or p-ANCA



Jennette Arthritis Rheum 2013; 65:1-11

Question 22: The Anti-Ro antibody is associated with all of the following EXCEPT:

A. Sjogren’s syndrome
B. neonatal lupus
C. subacute cutaneous lupus
D. diffuse proliferative glomerulonephritis
E. congenital heart block

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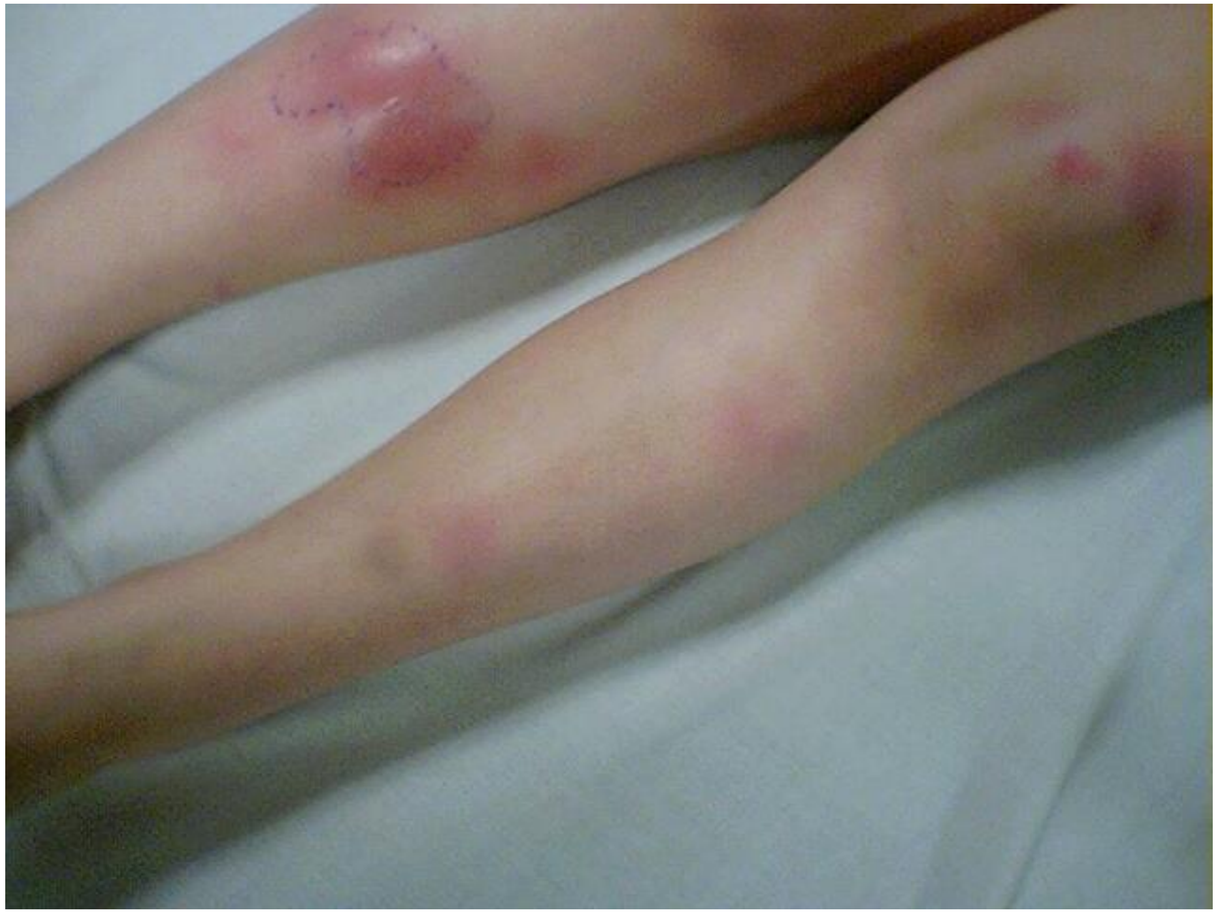
A. Sjogren's syndrome
B. neonatal lupus
C. subacute cutaneous lupus
D. diffuse proliferative glomerulonephritis
E. congenital heart block

Question 23

A 23 year old female college student is seen in the ER for acute bilateral ankle swelling and pain over both shins for 5 days. Symptoms have been getting worse and she has now difficulties walking. She denies any trauma or recent travel. No significant PMH.

Exam:
T 100.1, BP 110/65, P 85 reg, RR 18
bilateral swelling + tenderness of ankles
nodular lesions both lower legs, painful to palpation

Labs:
Hct 35%, ESR 35 mm/h



What is the most appropriate test to make a diagnosis ?

A. chest X-ray
B. skin biopsy
C. ACE level
D. Rheumatoid factor
E. urinalysis and ANCA

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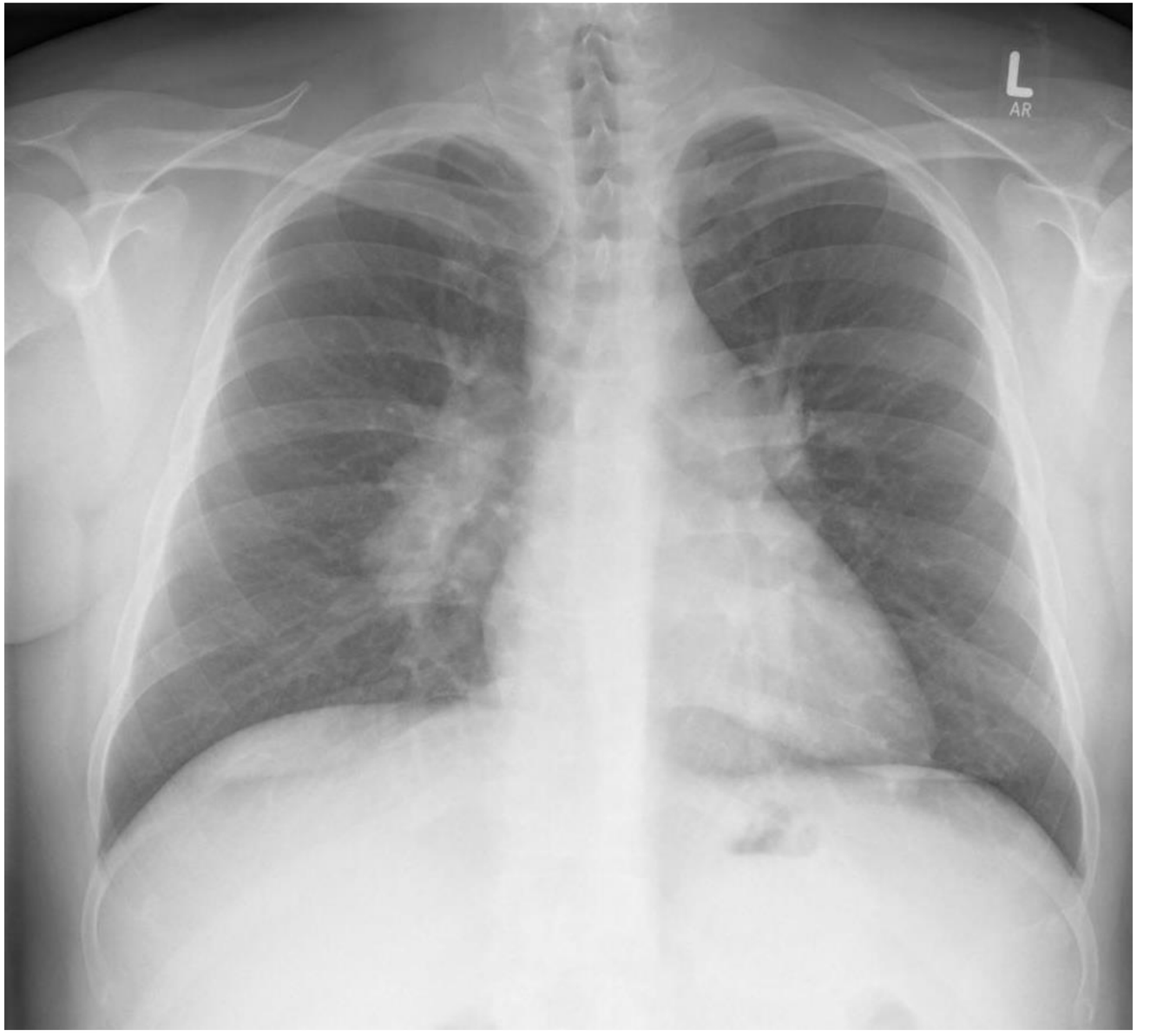
Lofgren syndrome

- acute presentation of sarcoidosis
  - erythema nodosum
  - ankle arthritis
  - bilateral hilar lymphadenopathy
- complete triade - 95% specific for sarcoidosis
  (DD coccidioidomycosis in endemic areas)
- 1st line treatment - NSAIDs

O'Regan Ann Intern Med 2012; 156



Courtesy of Dr Christoph Berliner, Radiopaedia.org, rID: 22067

Question 24

A 28-year-old female presents with chronic fatigue and generalized joint pain. She reports intermittent headaches and brain fog. She denies a history of rashes and photosensitivity. Her physical examination is unremarkable.

Her primary care physician orders an antinuclear antibody (ANA) test, which returns positive at a titer of 1:40. Her CBC, CRP and ESR are normal.

What is the most appropriate interpretation of the ANA titer (1:40)?

A. confirms a diagnosis of systemic lupus erythematosus (SLE)
B. indicates the presence of rheumatoid arthritis (RA)
C. specific for Sjögren's syndrome
D. not uncommon in the general population and typically not clinically relevant
E. suggests the need for immediate referral to a rheumatologist

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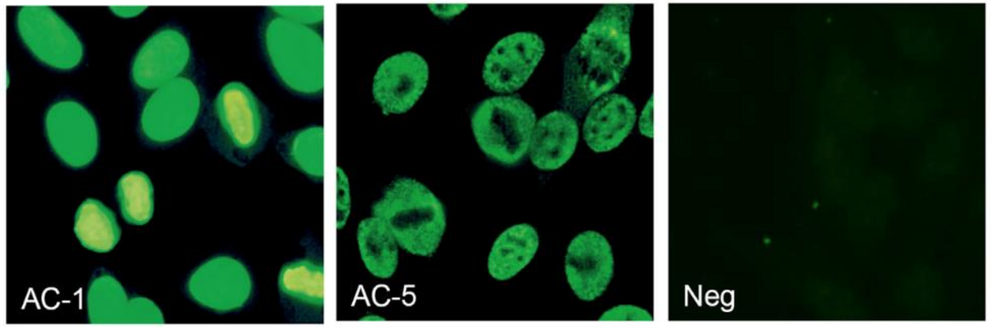
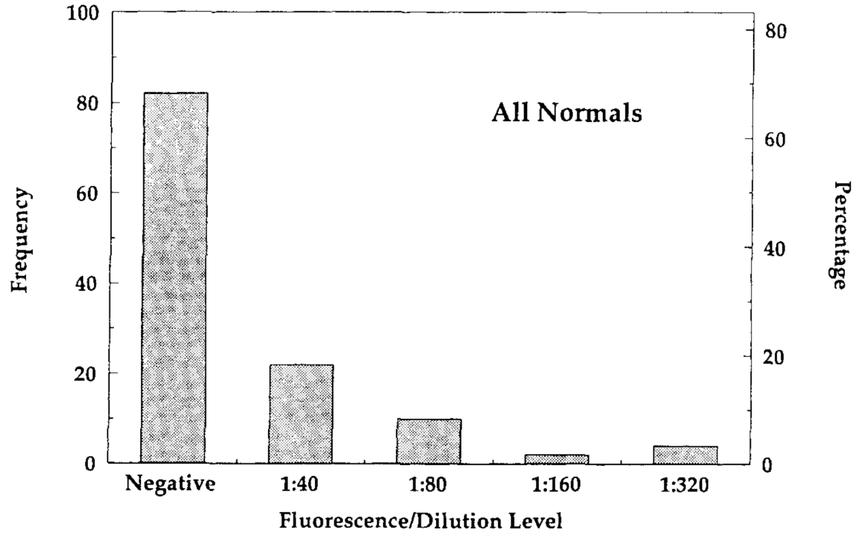
ANA testing





- traditionally done by indirect immunofluorescence (HEp-2 cells)
- two-fold serum dilutions are tested starting 1:40, higher titers indicate more autoantibody
- novel methods include
  - ELISA
  - multiplexed bead assays
- low titer ANA are common in the normal population
  Do not order as a screening test without specific symptoms or signs of SLE or other CTD!

Tan Arthritis Rheum 1997; 9:1601-11, Ricciuti Front Immunol 2018;9:927, Chow J Rheumatol 2015;42:682-9

Question 25: What do RA, PsA, AS and SLE have in common?

A. largely overlapping genetic risk factors
B. similar prevalence (~1%)
C. more common in women than in men
D. TNF inhibitors are first-line therapy
E. increased risk for cardiovascular disease

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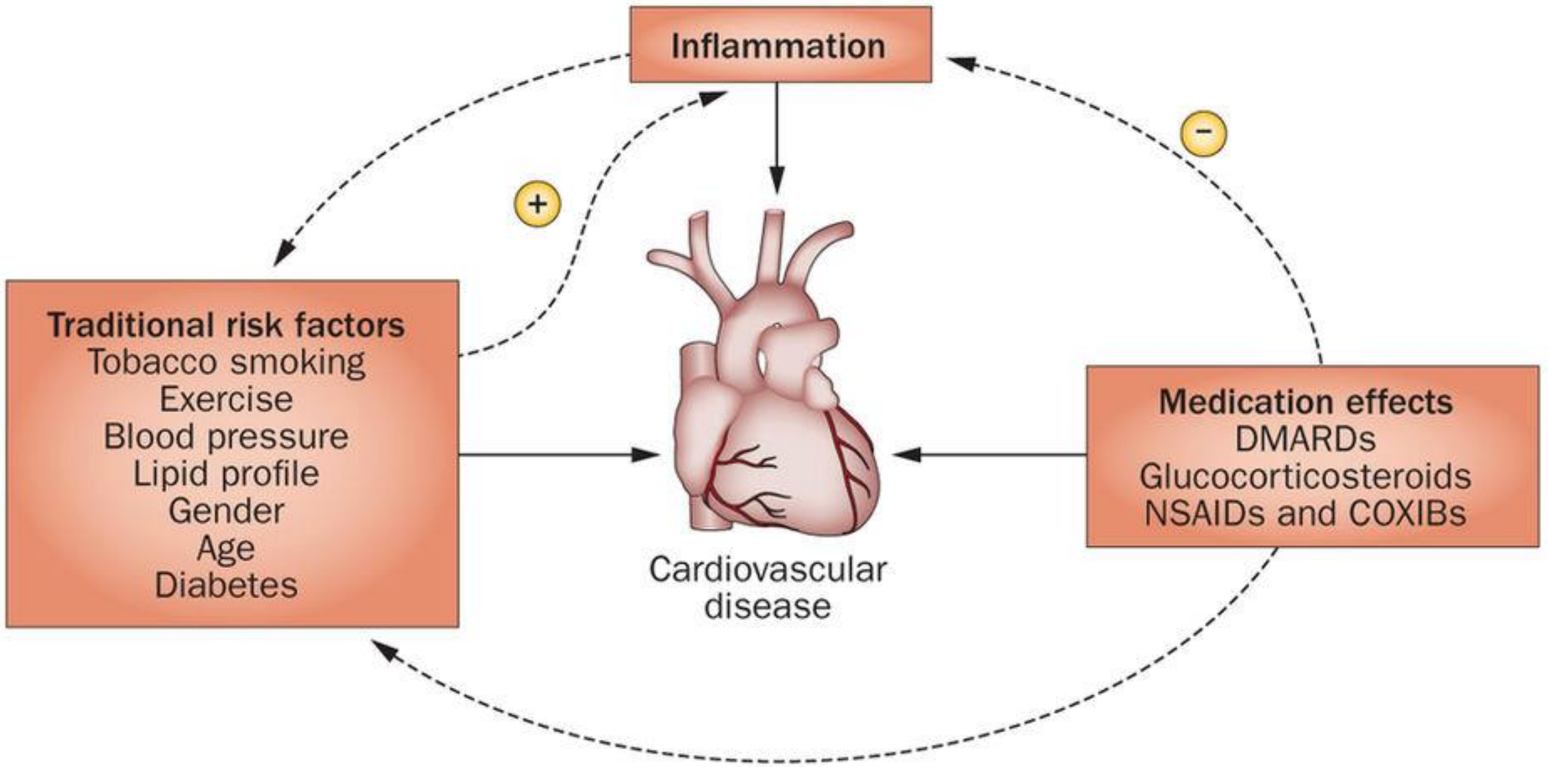
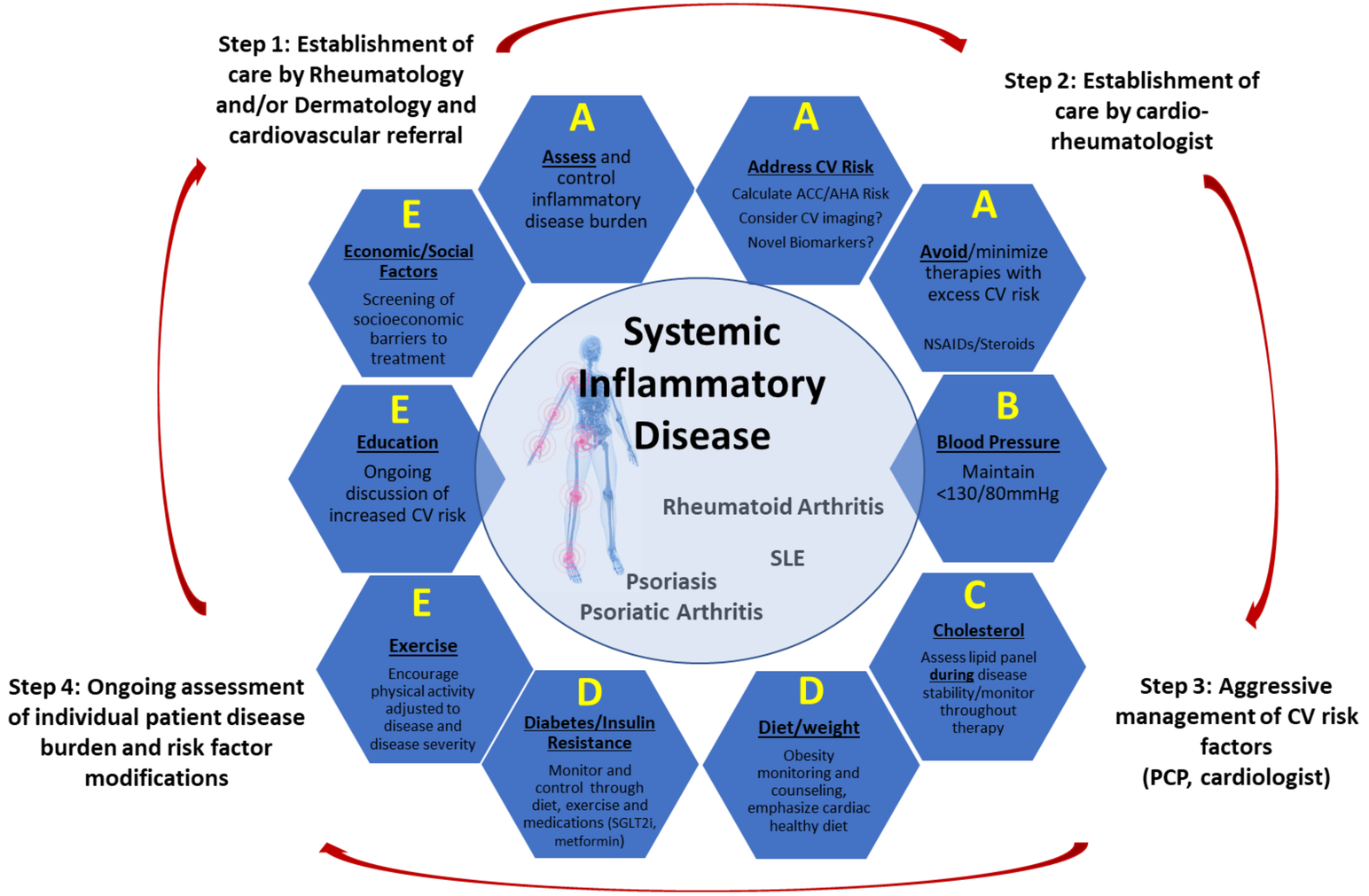
Patients with inflammatory rheumatic diseases have an increased risk for cardiovascular disease



Nurmohamed Nat Rev Rheumatol 2015; 11:693-704

ABCD for CVD prevention in systemic inflammatory diseases



- Early recognition of cardiovascular risk
- Risk Stratification
- Weight loss
- Lipid management
- Blood pressure management
- Lifestyle

→ need for collaborative care

Weber Curr Opin Cardiol 2021; 36:549-555

References

- Fraenkel Arthritis Rheumatol 2021;73:1108-1123
- Lyman NEJM 2018; 378:2036-44
- Ward Arthritis Rheum 2019; 71:1599-1613
- FitzGerald Arthritis Rheum 2020; 72:879-895