Rheumatology Test Review

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May, 2019

Question #1

- Answer: E (topical diclofenac)

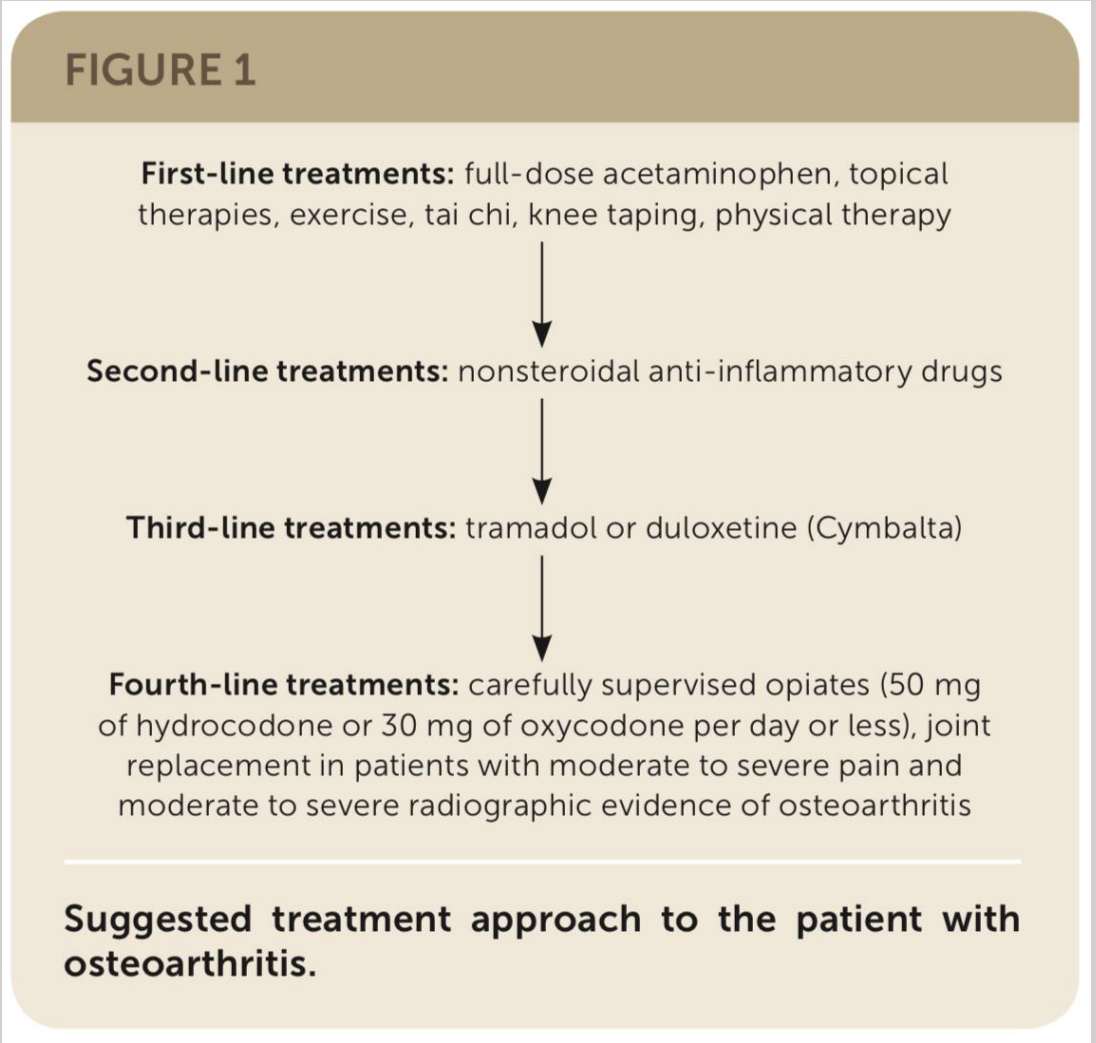
- 85 y/o F with knee pain, worse with activity and at night
- Stage 3 CKD
- Crepitus, decreased ROM, small effusion (WBC 1100)

- Management of osteoarthritis in an elderly patient

- *2012 ACR Recommendations for Management of Hand, Hip, and Knee OA*
  - We conditionally recommend that patients with knee OA should use one of the following:
    - Acetaminophen
      Oral NSAIDs
      Topical NSAIDs
      Tramadol
      Intraarticular corticosteroid injections

Question #1, continued

- “We conditionally recommend that persons age ≥75 years should use topical rather than oral NSAIDs. In persons age ≤75 years, the TEP expressed no preference for using topical rather than oral NSAIDs.”
- However,
  - Topical NSAIDs are associated with more skin reactions and are significantly more expensive than oral NSAIDs



Question #2

- Answer: D (order HLA-B*5801 allele testing)

- 53 y/o M with recurrent gout attacks
- Thai descent, stage 3 CKD
- No active inflammation
- Serum urate level 9.2 mg/dL

- Identify a patient at high risk for allopurinol hypersensitivity

- Risk factors:
  - Patients of Thai, Han Chinese, and Korean descent
  - CKD; esp when the initial dose of allopurinol exceeds 1.5 mg per mL/minute of creatinine clearance
  - Concomitant diuretic use

Question #2, continued

- Allopurinol Hypersensitivity Syndrome (AHS)
  - Erythematous rash
  - Fever
  - Hepatitis
  - Eosinophilia
  - Acute renal failure
- Occurs in 0.1% of treated patients
- Potentially life-threatening reaction, with a mortality rate approaching 25%
- Most cases occur within 8–9 weeks of commencing allopurinol
- Pretreatment testing for HLA-B*5801 and avoidance of allopurinol when positive reduces the risk of AHS in some ethnic groups
- A low starting allopurinol dose may reduce AHS risk, but the relationship between maintenance dose and AHS is more controversial
- Chronic kidney disease increases AHS risk, but slowly increasing the allopurinol dose in chronic kidney disease has not been associated with AHS

Question #3

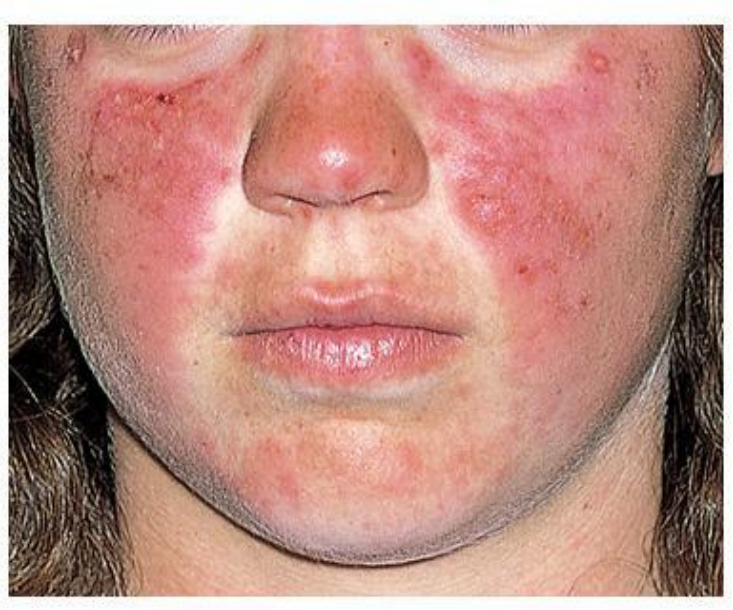
- Answer: A (acute cutaneous lupus erythematosus)

- 21 y/o F with 8 weeks of fatigue and low-grade fever
- Characteristic malar rash - bright erythematous patches over both cheeks and the nasal bridge, almost always sparing the nasolabial fold

- Diagnose acute cutaneous lupus erythematosus

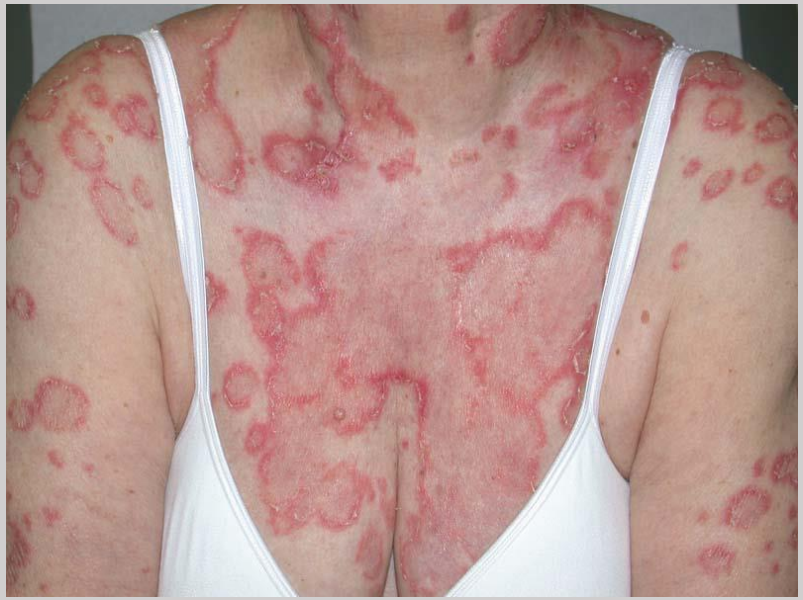
- Essentially all pts with ACLE will develop SLE

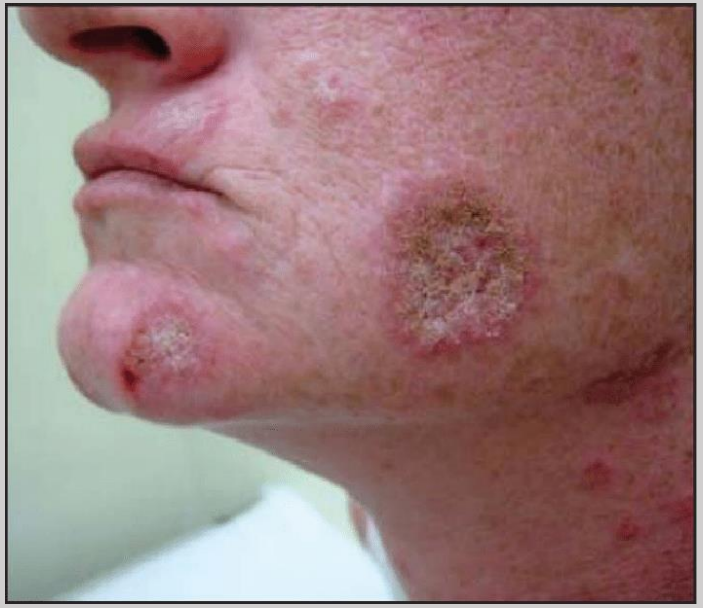
- Other answers:
  - Erysipelas - superficial cellulitis involving the lymphatics that presents as a violaceous-red, edematous, well-demarcated plaque on the face or lower extremities secondary to group A strep; **almost always unilateral**
  - Rosacea - inflammatory papules, small pustules, and telangiectasias, and **tends to involve the nasolabial folds**
  - Seborrheic dermatitis - characterized by a greasy scale and **tends to involve the nasolabial folds, eyebrows, and scalp**
  - Subacute cutaneous lupus erythematosus



Malar rash of **acute lupus erythematosus**

Subacute cutaneous lupus rash: erythematous, macular, or patchy skin lesions that are scaly and can evolve as annular/polycyclic lesions or papulosquamous plaques





Discoid lupus erythematosus is the most common **chronic** skin manifestation of SLE

Question #4

- Answer: A (antisynthetase syndrome)

- 47 y/o F with 2 weeks of low-grade fever
- Fingertip blanching with cold exposure
- Cracking/peeling of skin on hands and pain/swelling of PIP joints
- Erythema of the malar area, forehead, and chin
- Crackles at the lung bases
- Anti-Jo-1 antibody positive

- Diagnose antisynthetase syndrome

- Six predominant clinical manifestations:
  - Fever
  - Myositis
  - Interstitial lung disease
  - Mechanic's hands
  - Raynaud phenomenon
  - Inflammatory polyarthritis

Question #4, continued

- An important cause of autoimmune inflammatory myopathy in a subset of patients with polymyositis and dermatomyositis
- Should be included in the differential diagnosis in patients presenting with unexplained interstitial lung disease

- Key points:
  - Antisynthetase syndrome can present with a wide variety of clinical manifestations
  - The type and severity of interstitial lung disease usually determine the long-term outcome
  - The diagnosis is usually confirmed by the detection of antibodies to various aminoacyl-transfer RNA synthetases, anti-Jo-1 antibody being the most common
  - Glucocorticoids are considered the mainstay of treatment, steroid sparing drugs often added later
  - Cyclophosphamide is recommended if severe pulmonary involvement

Question #5

- Answer: B (inclusion body myositis)
- 67 y/o M with weakness, tripping, difficulty writing
- Exam with symmetric weakness of the forearm and thigh muscles; reduced grip strength, hands, wrists
- CK 1150 U/L; anti-Jo-1 negative
- Recognize inclusion body myositis

- Inclusion body myositis (IBM)
  - Inflammatory myopathy involving proximal and distal muscles, usually symmetric
  - Sporadic IBM is the most common muscle disease in elderly, M>F, usually >50 y/o
  - CK typically less than 10-12 x's ULN
  - Diagnosis of IBM is confirmed by muscle biopsy showing muscle fibers containing multiple rimmed vacuoles
  - IBM needs to be distinguished from polymyositis, as it is usually not treated with immunosuppressive therapy and has an overall poor response to treatment

Table 1. Criteria Supporting the Diagnosis of Inflammatory Myopathies.

Criterion	Dermatomyositis	Polymyositis	Necrotizing Autoimmune Myositis	Inclusion-Body Myositis
Pattern of muscle weakness	Subacute onset of proximal symmetric weakness with characteristic skin rash in patients of any age	Subacute onset of proximal symmetric weakness in adults (diagnosis is made when other causes have been ruled out)*	Acute or subacute onset of proximal, often severe weakness in adults	Slow onset of proximal and distal weakness; atrophy of quadriceps and forearms; frequent falls; mild facial muscle weakness in people older than 50 years of age
Creatine kinase level	High, up to 50 times the upper limit of normal; can at times be normal	High, up to 50 times the upper limit of normal in early active disease; may linger at up to 10 times the upper limit of normal	Very high; more than 50 times the upper limit of normal in early active disease	Up to 10 times the upper limit of normal; can be normal or slightly elevated
Electromyography	Myopathic units (active and chronic)	Myopathic units (active and chronic)	Active myopathic units	Myopathic units (active and chronic) with some mixed large-size potentials
Muscle biopsy	Perivascular, perimysial, and perifascicular inflammation; necrotic fibers in "wedge-like" infarcts; perifascicular atrophy; reduced capillaries†	CD8+ cells invading healthy fibers; widespread expression of MHC class I antigen; no vacuoles; ruling out of inflammatory dystrophies	Scattered necrotic fibers with macrophages; no CD8+ cells or vacuoles; deposits of complement on capillaries‡	CD8+ cells invading healthy fibers; widespread expression of MHC class I antigen; autophagic vacuoles,§ ragged-red or ragged-blue fibers; congophilic amyloid deposits¶
Autoantibodies	Anti-MDA-5, anti-Mi-2; anti-TIF-1 and anti-NXP-2 (implicated in cancer-associated dermatomyositis)	Antisynthetase antibodies (often seen in overlap myositis) associated with interstitial lung disease, arthritis, fever, and "mechanic's hands"	Anti-SRP and anti-HMGCR, specific for necrotizing autoimmune myositis	Anti-cN1A (of uncertain pathologic significance)
Magnetic resonance imaging	May show active inflammation	May show active inflammation; could guide biopsy site	May show active inflammation; could guide biopsy site	Shows selective muscle involvement, but might be difficult to distinguish atrophy from chronic inflammation

Drug-induced Myopathies		
Drug	**Time Course**	**Clinical Presentation**
Alcohol	Increased with long-term use	Asymptomatic elevations of serum creatine kinase; chronic muscle atrophy; acute, severe rhabdomyolysis with kidney failure
Antimalarials	Can occur after prolonged use	Infrequent elevation of serum creatine kinase (30%); muscle weakness (50%); myopathic electromyogram findings (100%); cardiomyopathy can occur
Cocaine	Can occur after single use	Asymptomatic elevations of serum creatine kinase; acute, severe rhabdomyolysis with kidney failure
Colchicine	Usually months to years; increased risk with coadministration of cytochrome P450 inhibitors	Proximal muscle weakness with elevations of serum creatine kinase; mild sensory symptoms; reduced reflexes
Glucocorticoids	Increased with long-term use	Proximal muscle weakness in the absence of elevations of serum creatine kinase
Statins	Usually weeks to months but can occur at any time; increased risk with preexisting neuromuscular disease, hypothyroidism, kidney failure, and/or coadministration of cytochrome P450 inhibitors; may also trigger immune-mediated necrotizing myopathy	Elevations of serum creatine kinase with myalgia and weakness
Zidovudine	Variable; may be more common after long-term use	Elevations of serum creatine kinase with myalgia and weakness

Question #6

- Answer: A (captopril)

- 32 y/o F with Raynaud's and GERD
- Presenting with headache and vomiting
- T 38, BP 240/140 mm Hg
- Fingers with digital pitting, thickening of the skin over the fingers and dorsum of the hands
- Hct 32%, platelets 75K, Cr 1.5 and u/a 2+ protein, no blood
- Peripheral smear: + schistocytes, decreased platelet count

- Recognize scleroderma renal crisis

- Scleroderma renal crisis
  - Hypertensive emergency
  - Headache, encephalopathy, seizures, hypertensive retinopathy
  - Microangiopathic hemolytic anemia
  - Acute Cr elevation
  - Proteinuria

- Risk factors:
  - DcSSc
  - Use of moderate to high dose steroids
  - Presence of anti-RNA polymerase III abs

- Management:
  - ACE inhibitor – even with rising Cr and need for HD
  - Some data for prophylaxis with CCB in those at high risk

A. Hypertensive scleroderma renal crisis (fulfills both A1 and A2)

1. New onset hypertension; defined as any of the following:
   a) Systolic blood pressure ≥ 140 mg Hg
   b) Diastolic blood pressure ≥ 90 mg Hg
   c) Rise in systolic blood pressure ≥ 30 mm Hg
   d) Rise in diastolic blood pressure ≥ 20 mm Hg

AND

2. One (1) of the following five (5) features:
   a) Increase in serum creatinine by 50+% over baseline
   OR serum creatinine ≥ 120% of upper limit of normal for local laboratory
   b) Proteinuria ≥ 2+ by dipstick
   c) Hematuria ≥ 2+ by dipstick or ≥ 10 RBCs/HPF
   d) Thrombocytopenia: < 100,000 plts/mm^3
   e) Hemolysis defined as anemia not due to other causes and either of the following:
      (1) Schistocytes or other RBC fragments seen on blood smear
      (2) increased reticulocyte count

B. Normotensive scleroderma renal crisis (fulfills both B1 and B2)

1. Increase in serum creatinine >50% over baseline
   OR serum creatinine ≥ 120% of upper limit of normal for local laboratory

AND

2. One (1) of the following five (5) features:
   a) Proteinuria ≥ 2+ by dipstick
   b) Hematuria ≥ 2+ by dipstick or ≥ 10 RBCs/hpf
   c) Thrombocytopenia: < 100,000 /mm^3
   d) Hemolysis defined as anemia not due to other causes and either of the following:
      (1) Schistocytes or other rbc fragments seen on blood smear
      (2) Increased reticulocyte count
   e) Renal biopsy findings consistent with scleroderma renal crisis (microangiopathy)

Question #7

- Answer: A (anakinra)

- 76 y/o M treated for heart failure now with painful, swollen left knee
- Microscopy of synovial fluid with needle-shaped intracellular crystals; negative gram stain and cultures
- Treated with intra-articular glucocorticoid as well as IV x 3 days; though still with warm, swollen knee

- Treat refractory acute gout

- Anakinra or canakinumab: IL-1 inhibitor

Management of treatment resistant inflammation of acute on chronic tophaceous gout with anakinra

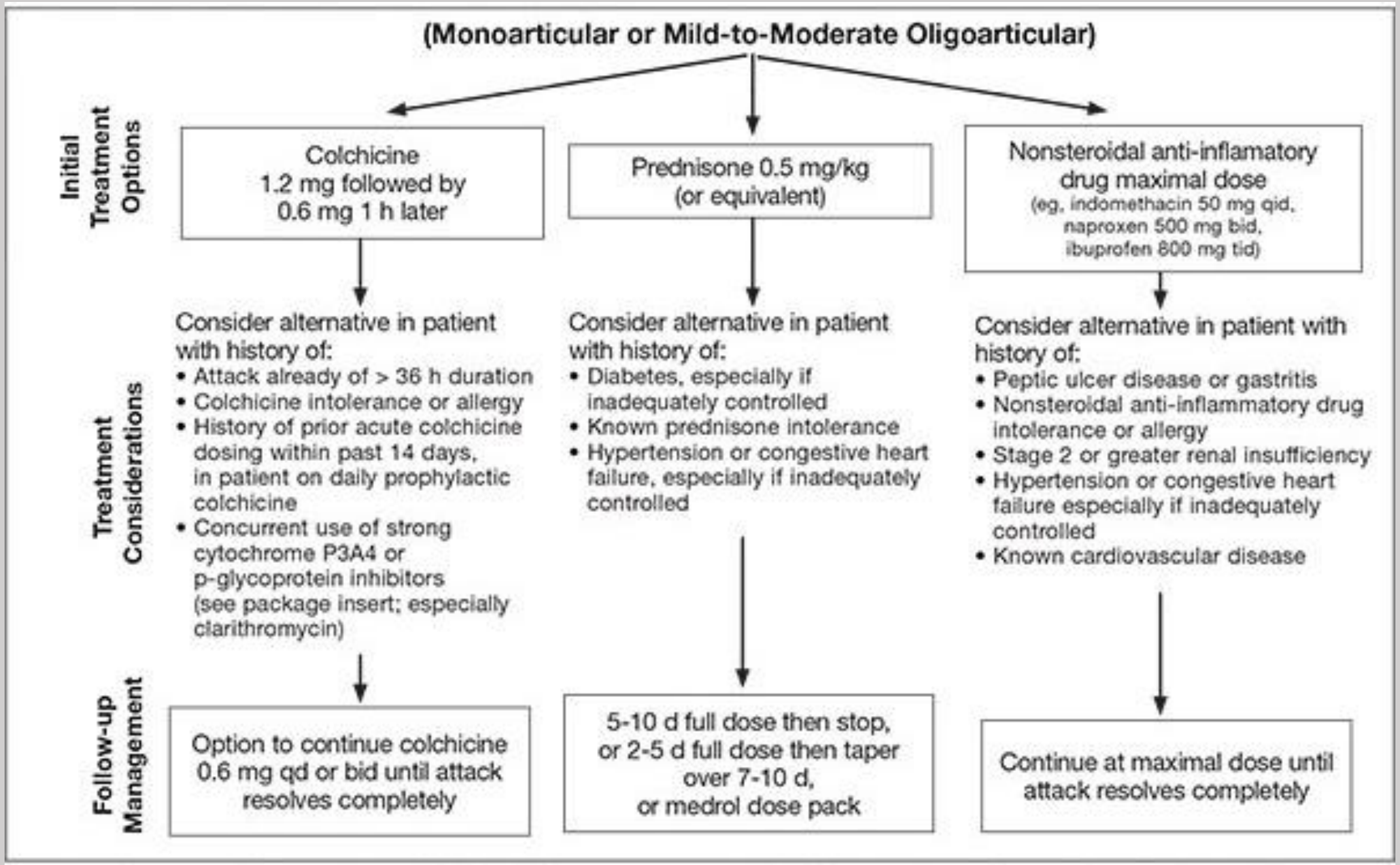
D McGonagle, A L Tan, S Shankaranarayana, J Madden, P Emery, M F McDermott

Anakinra for the treatment of acute gout flares: a randomized, double-blind, placebo-controlled, active-comparator, non-inferiority trial

Carly A Janssen Martijn A H Oude Voshaar Harald E Vonkeman Tim L Th A JansenMatthijs Janssen Marc R Kok Bea Radovits Caroline van Durme Hetty BaanMart A F J van de Laar

Efficacy of anakinra in gouty arthritis: a retrospective study of 40 cases

Sébastien Ottaviani,[1] Anna Moltó,[2] Hang-Korng Ea,[2] Séverine Neveu,[3] Ghislaine Gill,[1] Lauren Brunier,[1] Elisabeth Palazzo,[1] Olivier Meyer,[1] Pascal Richette,[2] Thomas Bardin,[2] Yannick Allanore,[4] Frédéric Lioté,[2] Maxime Dougados,[3] and Philippe Dieudé [1]


(Monoarticular or Mild-to-Moderate Oligoarticular)
Initial Treatment Options
Colchicine 1.2 mg followed by 0.6 mg 1 h later
Prednisone 0.5 mg/kg (or equivalent)
Nonsteroidal anti-inflamatory drug maximal dose (eg, indomethacin 50 mg qid, naproxen 500 mg bid, ibuprofen 800 mg tid)
Treatment Considerations
Consider alternative in patient with history of:
• Attack already of > 36 h duration
• Colchicine intolerance or allergy
• History of prior acute colchicine dosing within past 14 days, in patient on daily prophylactic colchicine
• Concurrent use of strong cytochrome P3A4 or p-glycoprotein inhibitors (see package insert; especially clarithromycin)
Consider alternative in patient with history of:
• Diabetes, especially if inadequately controlled
• Known prednisone intolerance
• Hypertension or congestive heart failure, especially if inadequately controlled
Consider alternative in patient with history of:
• Peptic ulcer disease or gastritis
• Nonsteroidal anti-inflammatory drug intolerance or allergy
• Stage 2 or greater renal insufficiency
• Hypertension or congestive heart failure especially if inadequately controlled
• Known cardiovascular disease
Follow-up Management
Option to continue colchicine 0.6 mg qd or bid until attack resolves completely
5-10 d full dose then stop, or 2-5 d full dose then taper over 7-10 d, or medrol dose pack
Continue at maximal dose until attack resolves completely

Question #8

- Answer: B (stop febuxostat; begin pegloticase infusions)

- 78 y/o F with more frequent and severe gout attacks
- HTN, CKD, nephrolithiasis, type 2 DM
- On max dose febuxostat, allergic to allopurinol
- ESR 76 mm/h, Cr 1.5 mg/dL, serum urate level 6.3 mg/dL

- Treat severe tophaceous gout

- Pegloticase:
  - IV-administered porcine-derived uricase (infused every 2 weeks)
  - Reduces serum urate level to zero within hours of administration
  - 30% to 50% of patients develop antibodies to the drug within a month
  - Indicated for severe recurrent and/or tophaceous gout that is intolerant or resistant to standard therapies

Gout Guidelines

Treat to symptom resolution (ACP)

ACP's new guideline does not recommend against a "treat-to-target approach" but advised that there is insufficient evidence to determine whether the benefits of escalating ULT to reach a target uric acid level outweigh the harms associated with repeated monitoring and increased medication.

Treat to target uric acid level (ACR and EULAR)

In its 2012 guideline, ACR recommends a target serum urate level below 6 mg/dL at a minimum, with some patients faring better when the serum urate level is below 5 mg/dL. A new guideline from EULAR released in 2016 includes the same recommendation.

Question #9

- Answer: C (increase allopurinol)

- 87 y/o F with gout x 15 years
- Recurrent attacks q3 months
- Hx of nephrolithiasis, CKD, HTN
- Tophi present on a few distal and proximal interphalangeal joints of both hands
- Current meds: allopurinol, 400 mg/d; colchicine, 0.6 mg/d; and lisinopril
- Cr level 1.0 mg/dL, serum urate level 5.8 mg/dL

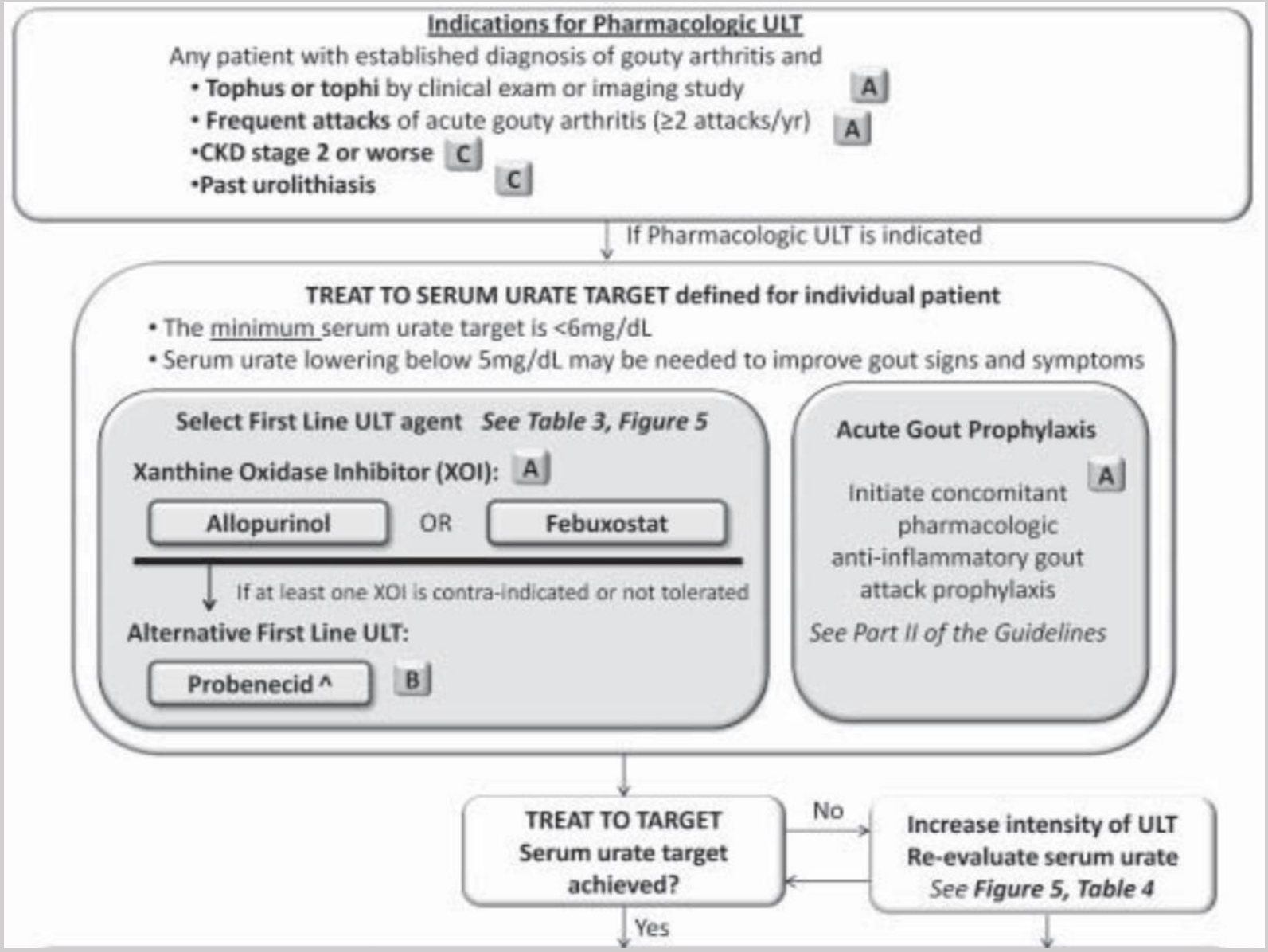
- Treat tophaceous gout with appropriate urate-lowering therapy.

- Allopurinol
  - Can be titrated to a maximum of 800 mg/d in 100-mg increments to alleviate symptoms
  - Dose-reduce if ≥ stage 3 CKD
  - Remember, watch and screen for hypersensitivity syndrome in certain populations

Question #9, continued

- Who should be on urate-lowering therapy:
  - Patients with gout plus any of the following:
    - (1) ≥ stage 2 CKD
    - (2) ≥ 2 acute attacks per year
    - (3) one or more tophi
    - (4) uric acid nephrolithiasis
- Contrary to prior practice, urate-lowering therapy can be initiated during an acute attack if adequate anti-inflammatory therapy is concurrently started

- Options for urate-lowering therapy:
  - Xanthine oxidase inhibitors (reduce urate production)
    - Allopurinol
    - Febuxostat (more expensive, concerns about cardiovascular safety)
  - Uricosuric agents (decrease renal urate resorption) - probenecid
    - Less effective; avoid with CKD, nephrolithiasis
  - Pegloticase, rasburicase (a uricase)


Indications for Pharmacologic ULT
Any patient with established diagnosis of gouty arthritis and
• Tophus or tophi by clinical exam or imaging study A
• Frequent attacks of acute gouty arthritis (≥2 attacks/yr) A
•CKD stage 2 or worse C
•Past urolithiasis C
If Pharmacologic ULT is indicated
TREAT TO SERUM URATE TARGET defined for individual patient
• The minimum serum urate target is <6mg/dL
• Serum urate lowering below 5mg/dL may be needed to improve gout signs and symptoms
Select First Line ULT agent See Table 3, Figure 5
Xanthine Oxidase Inhibitor (XOI): A
Allopurinol
OR
Febuxostat
If at least one XOI is contra-indicated or not tolerated
Alternative First Line ULT:
Probenecid ^ B
Acute Gout Prophylaxis
A
Initiate concomitant pharmacologic anti-inflammatory gout attack prophylaxis
See Part II of the Guidelines
TREAT TO TARGET
Serum urate target achieved?
No
Increase intensity of ULT
Re-evaluate serum urate
See Figure 5, Table 4
Yes

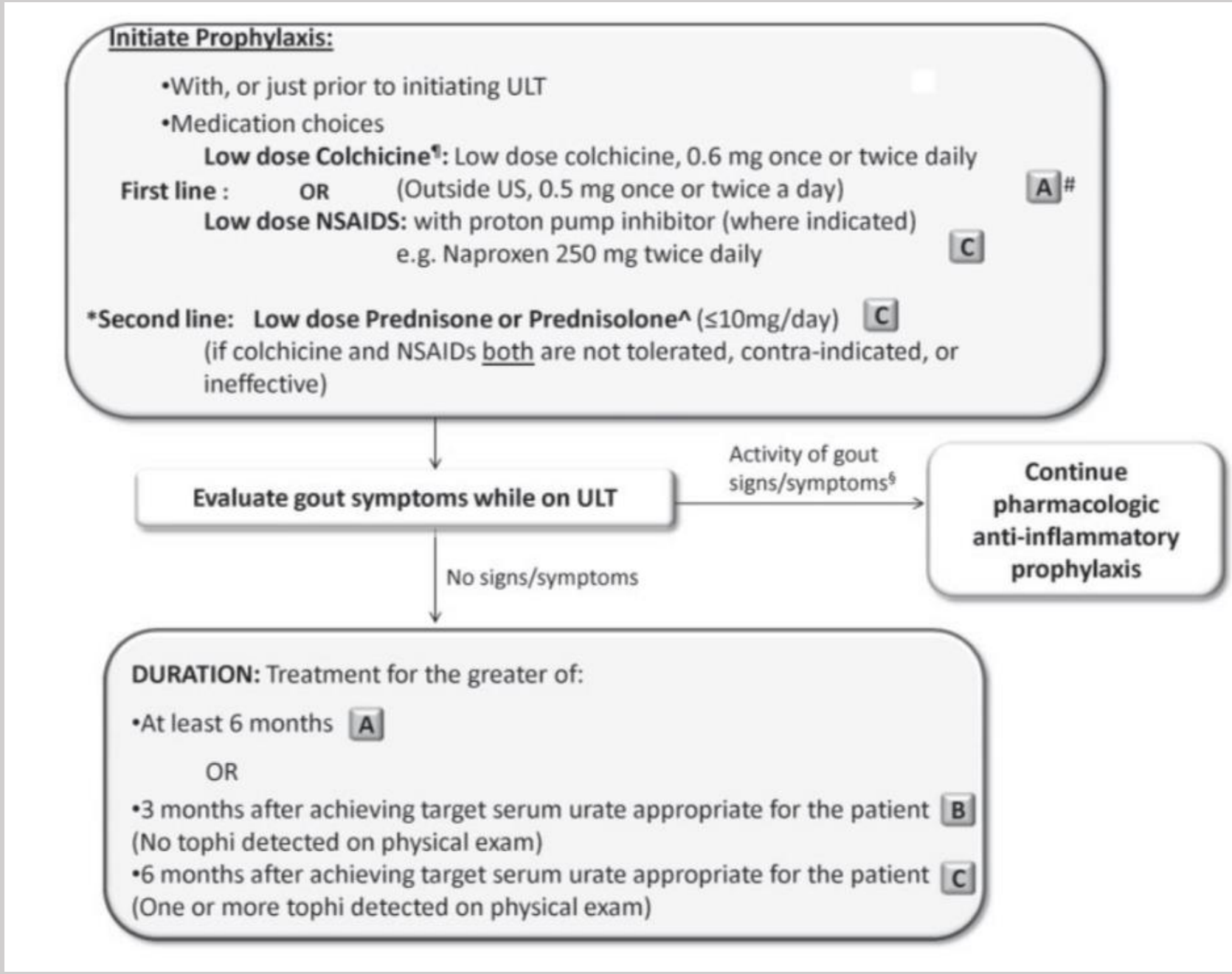
Question #10

- Answer: C (discontinue colchicine, begin meloxicam)

- 48 y/o M with gout, started on colchicine and allopurinol 2 months ago
- 3 acute gout attacks since initiation of therapy
- 2-3 daily episodes of diarrhea past 6 weeks
- Type 2 DM, on insulin
- Cr 0.8 mg/dL and serum urate level 5.5 mg/dL

- Prevent gout attacks during initiation of urate-lowering therapy

- Prophylaxis in the setting of initiation of urate-lowering therapy
  - Prevention/minimization of “mobilization attacks” at the initiation of urate-lowering therapy
  - Choice of therapy should be tailored to the individual's comorbid conditions
    - Consider SEs of diarrhea with colchicine, risk of hyperglycemia in pts with DM and CKD/PUD with NSAIDs


Initiate Prophylaxis:
•With, or just prior to initiating ULT
•Medication choices
Low dose Colchicine¶: Low dose colchicine, 0.6 mg once or twice daily
First line : OR (Outside US, 0.5 mg once or twice a day) A#
Low dose NSAIDS: with proton pump inhibitor (where indicated)
e.g. Naproxen 250 mg twice daily C
*Second line: Low dose Prednisone or Prednisolone^ (≤10mg/day) C
(if colchicine and NSAIDs both are not tolerated, contra-indicated, or ineffective)
Evaluate gout symptoms while on ULT
Activity of gout signs/symptoms§
Continue pharmacologic anti-inflammatory prophylaxis
No signs/symptoms
DURATION: Treatment for the greater of:
•At least 6 months A
OR
•3 months after achieving target serum urate appropriate for the patient B
(No tophi detected on physical exam)
•6 months after achieving target serum urate appropriate for the patient C
(One or more tophi detected on physical exam)

Question #11

- Answer: E (takayasu arteritis)

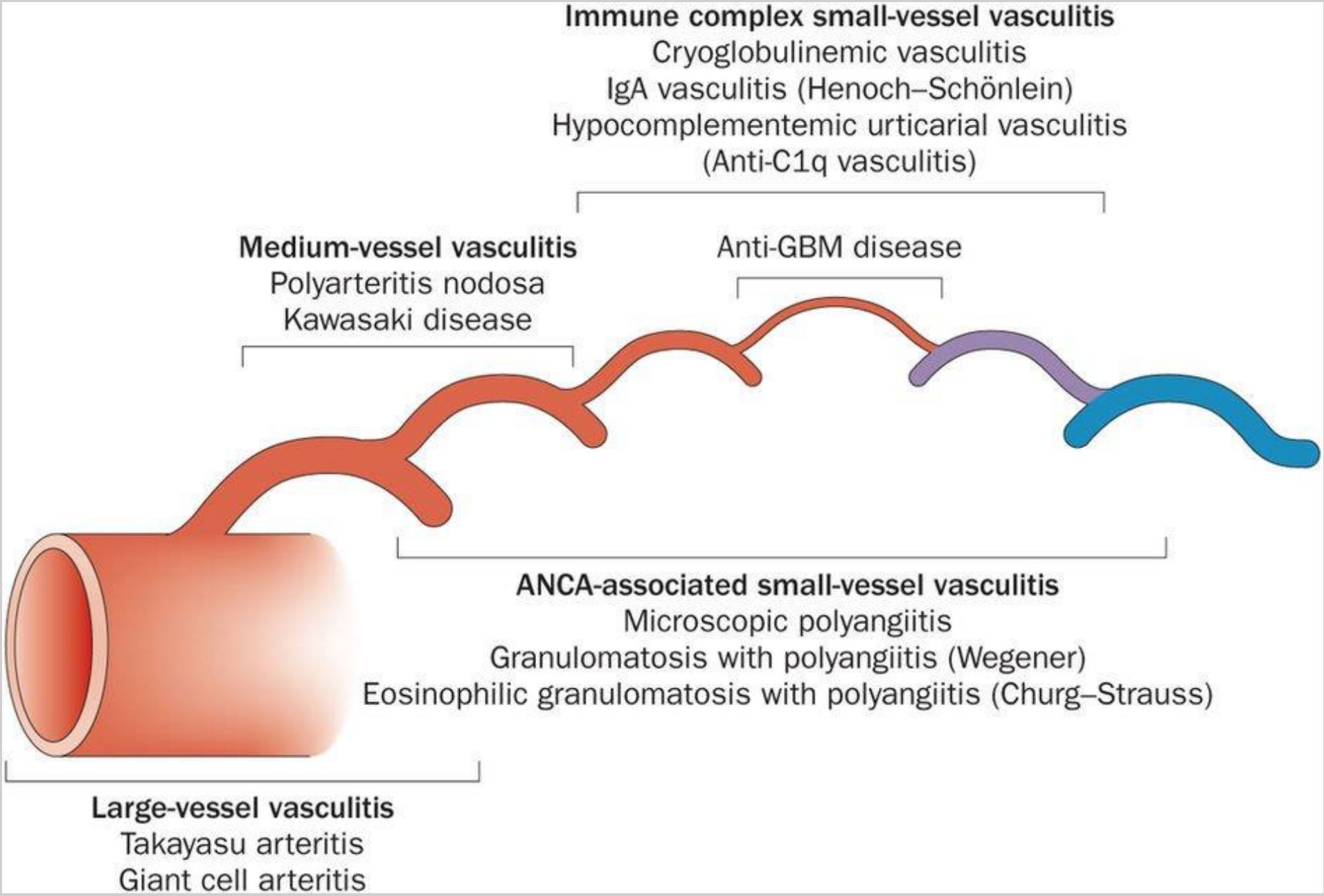
- 26 y/o F with 4 weeks of dyspnea on exertion
- 6 months of malaise and myalgia; arms ache with physical activity
- BP is 120/60 mm Hg in the right arm and 95/50 in the left arm
- Grade 2/6 decrescendo diastolic murmur at the left sternal border
- TTE: mild to moderate aortic valve regurgitation, dilated aortic root

- Recognize Takayasu arteritis

- Takayasu arteritis
  - Generally affects females ≤ 30 years and of Asian ancestry
  - Can lead to aortic insufficiency and heart failure
  - Aneurysms and stenoses of large arteries cause symptoms of claudication in the extremities, discrepancies in blood pressure between the arms, and reduced pulses
  - Involvement of the aorta

Question #11, continued

- Other answers:
  - GCA vasculitis: also large vessel and can affect the great vessels of the chest, but affects individuals > 50 y/o
  - IgA vasculitis: small-vessel vasculitis and almost always causes a rash
  - Kawasaki disease: medium-vessel vasculitis that begins in childhood, manifesting with a rash and other mucocutaneous findings; it can affect coronary vessels, leading to cardiac complications such as heart failure
  - Polyarteritis nodosa (PAN) is a medium-vessel vasculitis that can affect multiple organ systems


Immune complex small-vessel vasculitis
Cryoglobulinemic vasculitis
IgA vasculitis (Henoch–Schönlein)
Hypocomplementemic urticarial vasculitis
(Anti-C1q vasculitis)
Medium-vessel vasculitis
Polyarteritis nodosa
Kawasaki disease
Anti-GBM disease
ANCA-associated small-vessel vasculitis
Microscopic polyangiitis
Granulomatosis with polyangiitis (Wegener)
Eosinophilic granulomatosis with polyangiitis (Churg–Strauss)
Large-vessel vasculitis
Takayasu arteritis
Giant cell arteritis

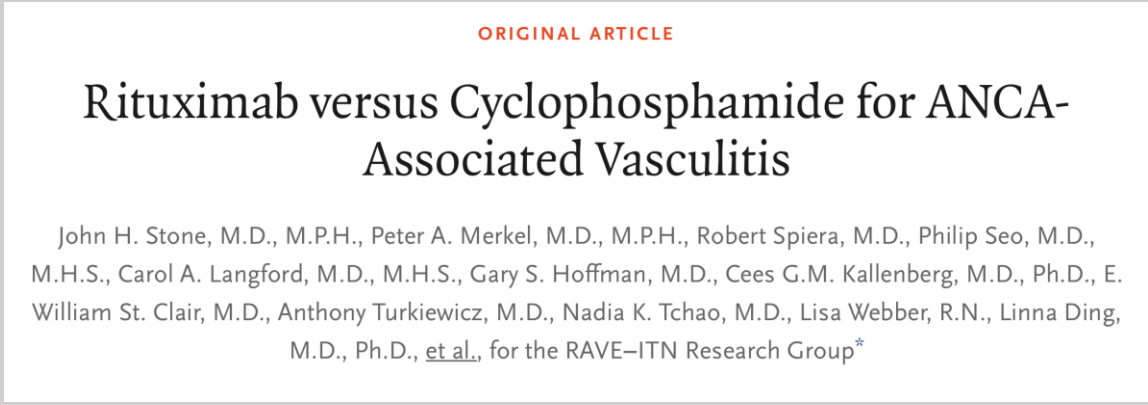
Question #12

- Answer: D (rituximab)

- 66 y/o M with hx of GPA previously treated with cyclophosphamide and on maintenance dose azathioprine
- Admitted with progressive dyspnea, started on IV solumedrol
- RR 25/min and O2 sat is 90% on 2 L
- ESR 90 mm/h and ANCA positive with a cytoplasmic pattern and a titer of 1:160; + proteinase 3 abs

- Treat relapsed granulomatosis with polyangiitis

- Relapse of GPA:
  - Occurs in more than 50% of patients within 5 years, and may occur in different organs from the initial presentation
  - Both rituximab and cyclophosphamide are efficacious for initial induction therapy in patients with severe GPA
  - Rituximab > cyclophosphamide in relapse


ORIGINAL ARTICLE

Rituximab versus Cyclophosphamide for ANCA-Associated Vasculitis

John H. Stone, M.D., M.P.H., Peter A. Merkel, M.D., M.P.H., Robert Spiera, M.D., Philip Seo, M.D., M.H.S., Carol A. Langford, M.D., M.H.S., Gary S. Hoffman, M.D., Cees G.M. Kallenberg, M.D., Ph.D., E. William St. Clair, M.D., Anthony Turkiewicz, M.D., Nadia K. Tchao, M.D., Lisa Webber, R.N., Linna Ding, M.D., Ph.D., et al., for the RAVE–ITN Research Group*

- 67% remission with rituximab > 42%

Question #12, continued

- Treatment of GPA:
  - Severe organ-threatening or life-threatening disease:
    - High-dose glucocorticoids plus cyclophosphamide or rituximab
    - Followed by maintenance therapy with azathioprine, mycophenolate mofetil, or rituximab for at least 12 to 24 months after stable remission has been achieved
  - Non-severe forms of disease:
    - Glucocorticoids plus either methotrexate or mycophenolate mofetil
  - Relapses are common (>50% 5 years after initial remission) and may respond better to rituximab than to cyclophosphamide
- Kidney failure and infection are the main causes of mortality

Question #13

- Answer: C (pulmonary arterial hypertension)

- 48 y/o F with 3 months of worsening exertional dyspnea
- Hx of limited cutaneous systemic sclerosis, Raynaud phenomenon and GERD
- Scattered telangiectasias, sclerodactyly at the fingers and tightness of the skin at the neck; increased intensity of the pulmonic sound and a widened split S_2

- Diagnose pulmonary arterial hypertension in a patient with limited cutaneous systemic sclerosis

- Vascular disease leading to pulmonary arterial hypertension may occur:
  - Secondary to interstitial lung disease (typically in patients with diffuse cutaneous systemic sclerosis) or
  - As an isolated process (typically in limited cutaneous systemic sclerosis)

Distinguishing Clinical Features of Limited Cutaneous and Diffuse Cutaneous Systemic Sclerosis

FEATURE	*LIMITED CUTANEOUS*	*DIFFUSE CUTANEOUS*
Skin fibrosis	Areas distal to the elbows and knees; may affect the face	Areas proximal or distal to the elbows and knees; may affect the face
Typical form of lung involvement	Pulmonary arterial hypertension	Interstitial lung disease
Characteristic visceral organ Involvement	Severe gastroesophageal reflux disease and Raynaud phenomenon	Scleroderma renal crisis
Physical examination Findings	Telangiectasia, calcinosis cutis, sclerodactyly, digital ischemic complications	Tendon friction rubs, pigment changes

Question #14

- Answer: D (no change in therapy)

- 28 y/o F with RA, + pregnancy test
- 2 year history of RA
- On hydroxychloroquine, stopped methotrexate 4 months prior in anticipation of conception

- Treatment of RA during pregnancy

- RA in pregnancy
  - 2/3 will go into remission/low disease activity
  - 1/3 will not improve or get worse
  - Disease activity typically returns, often with a flare, after delivery

Question #14, continued

- Contraindicated in pregnancy:
  - Leflunomide
    - Extremely teratogenic
    - Pregnancy must be avoided until the drug is no longer detectable in the serum
      - Cholestyramine may be used to hasten the elimination of leflunomide
  - Methotrexate
    - Highly teratogenic and abortifacient
    - Must be discontinued at least 3 months before pregnancy
- Safe in pregnancy:
  - Hydroxychloroquine crosses the placenta; however, there does not appear to be fetal toxicity with doses used for the treatment of RA
  - Sulfasalazine
  - TNF-α inhibitors: more data pointing to safety, risk/benefit assessment

Question #15

- Answer: C (rheumatoid pleuritis)

- 48 y/o M with 3 weeks of DOE, fever and L-sided chest pain
- Hx of anti-CCP + RA
- TB skin test non-reactive prior to starting TNF-α inhibitor
- Meds are MTX, folic acid and etanercept
- Moderate R-sided pleural effusion:
  - Leukocyte count of 3500/µL with 4% neutrophils, 87% lymphs, and 9% monos
  - Pleural fluid glucose of 6.0 mg/dL; a pH of 7.2; LDH 900 U/L; ADA is low, at 30 U/L

- Diagnose rheumatoid arthritis–related pleural effusion

- Pleuritis is the most common RA pulmonary manifestation
- Rheumatoid effusions
  - Pleural leukocyte count is typically less than 5000/µL, pleural fluid glucose is less than 60 mg/dL, and pH is less than 7.3

- Extremely low pleural fluid glucose levels found in rheumatoid effusions and empyema

Respiratory disease in rheumatoid arthritis

Interstitial
Interstitial pneumonitis/fibrosis (RA-ILD)
Usual interstitial pneumonitis (UIP)
Organizing pneumonia (OP)
Nonspecific interstitial pneumonitis (NSIP)
Lymphoid interstitial pneumonitis (LIP)
Desquamative interstitial pneumonitis (DIP)
Mixed morphology
Rheumatoid nodules
Rheumatoid pneumoconiosis (Caplan's syndrome)
Apical fibrobullous disease
Airway
Cricoarytenoid arthritis/central airway obstruction
Obliterative bronchiolitis
Bronchiectasis
Chronic small airway obstruction
Pleural
Pleuritis
Pleural effusion
Pleural thickening
Cholesterol (chyliform) effusions
Lung entrapment and trapped lung
Chest wall
Thoracic cage immobility
Pulmonary vascular
Pulmonary hypertension
Vasculitis
Other
Infection
Drug-related
? Lung cancer

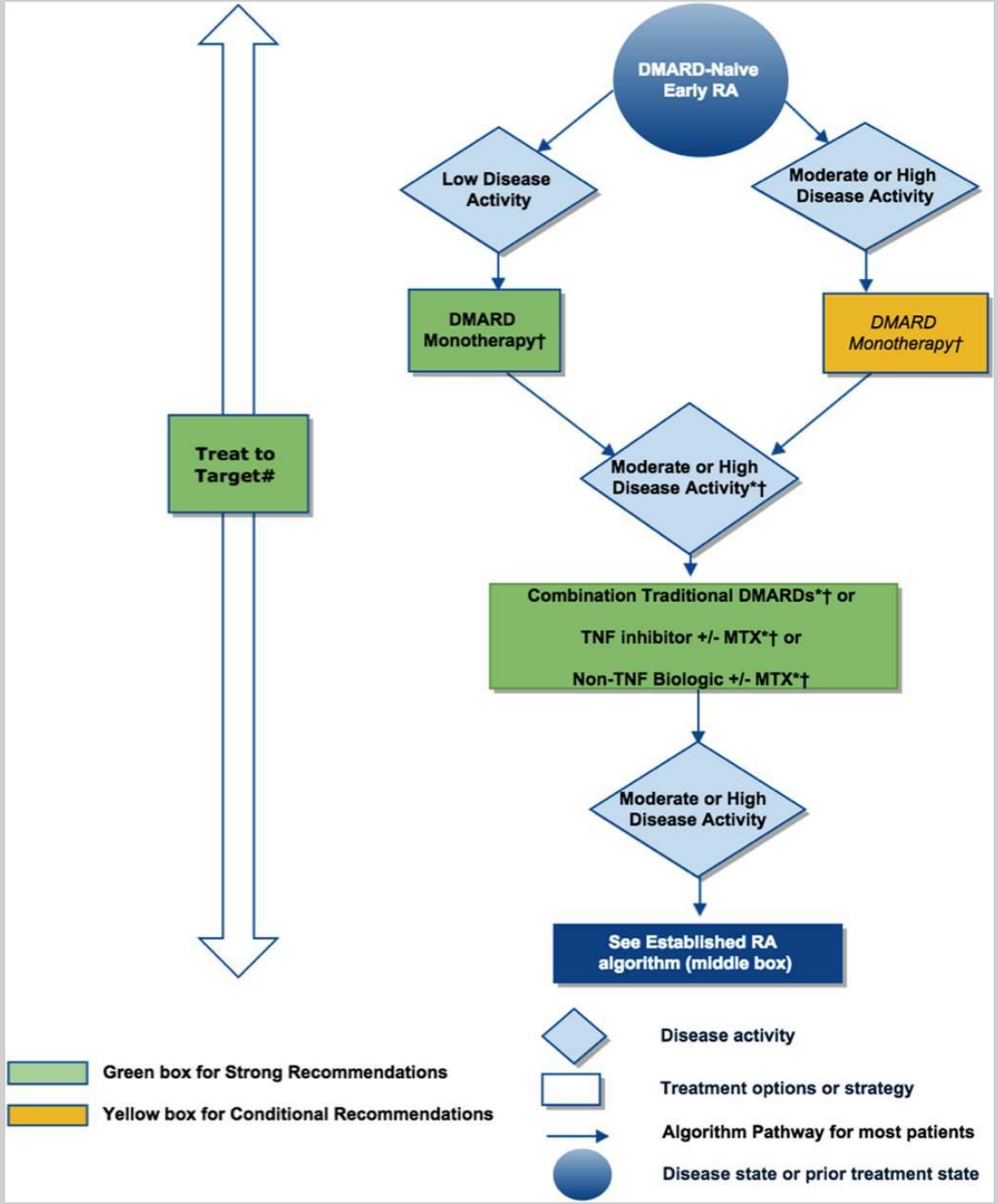
Question #16

- Answer: C (initiate methotrexate)

- 32 y/o F with 3 months of arthralgias, 9 tender and 6 swollen joints
- Started on prednisone 3 weeks ago which has helped with morning stiffness and pain
- ESR 38 mm/h and high levels of rheumatoid factor and anti–cyclic citrullinated peptide antibodies
- Clinical disease activity index score is 12, indicating moderate disease activity

- Treat early rheumatoid arthritis with methotrexate

- Methotrexate is the preferred initial monotherapy, as it both controls symptoms and prevents joint damage
- Clinical trials have demonstrated that 30% to 50% of patients treated with methotrexate monotherapy will show no disease progression as measured by hand and foot radiographs
- Close dose titration (up to as high as 25 mg per week) based on her CDAI score is necessary
- If methotrexate alone does not lead to remission, a second disease-modifying treatment should be added



BEST PRACTICES IN RHEUMATOLOGY

Recommendations from the Choosing Wisely Campaign

Recommendation	Sponsoring organization
Do not prescribe biologics for rheumatoid arthritis before a trial of methotrexate (or other conventional nonbiologic disease-modifying antirheumatic drugs).	American College of Rheumatology

Source: For more information on the Choosing Wisely Campaign, see http://www.choosingwisely.org. For supporting citations and to search Choosing Wisely recommendations relevant to primary care, see http://www.aafp.org/afp/recommendations/search.htm.

Question #16, continued

- Methotrexate side effects:
  - Stomatitis
  - Hepatic inflammation and fibrosis
  - Myelofibrosis, including megaloblastic anemia and pancytopenia

- Dosing:
  - Up to 25 mg per week
  - Daily folic acid supplementation

  - Guidelines from the ACR recommend monitoring of the CBC, CMP in pts on methotrexate
    - Every 2- 4 weeks for the first 3 months
    - Every 8-12 weeks thereafter

Question #17

- Answer: B (add pregabalin)

- 47 y/o F with 2 years of fibromyalgia symptoms, diagnosed 4 months ago
- Ongoing diffuse pain, fatigue, and difficulty concentrating
- Prescribed exercise and duloxetine 3 months ago with modest benefit
- On a 9-point pain scale, her pain was formerly an 8; after initiation of duloxetine, it decreased to a 5
- + tenderness between the shoulder blades and at the occiput, trapezius, elbows, and hips bilaterally

- Treat fibromyalgia

- 3 FDA-approved medications for fibromyalgia
  - Pregabalin, duloxetine, and milnacipran
  - ~ 30% reduction in pain symptoms

- Consider addition of a new treatment, acting through a complementary mechanism, to achieve better pain control
  - Pregabalin, gabapentin

- NSAIDs have not shown reliable benefit for fibromyalgia pain

- SNRIs are beneficial in fibromyalgia, but SSRIs as single agents have not been shown to be efficacious

Question #17, continued

Combination of pregabalin with duloxetine for fibromyalgia

a randomized controlled trial

Gilron, Ian[a,b,i,*]; Chaparro, Luis E.[c]; Tu, Dongsheng[d,e]; Holden, Ronald R.[f]; Milev, Roumen[g]; Towheed, Tanveer[h]; DuMerton Shore, Deborah[i]; Walker, Sarah[i]

- RCT compared a pregabalin–duloxetine combination to each monotherapy
- Participants (%) reporting ≥moderate global pain relief were 68% in the combination therapy group vs 39% in pregabalin alone and 42% in duloxetine alone
- Combining pregabalin and duloxetine for fibromyalgia improves multiple clinical outcomes vs monotherapy

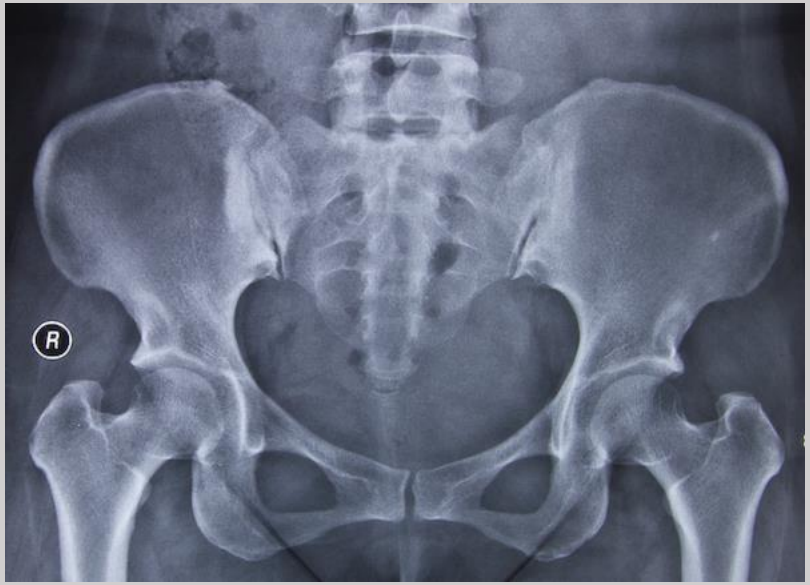
Question #18

- Answer: D (radiography of the sacroiliac joints)

- 49 y/o M with 10 years of intermittent low back pain with 30 to 60 minutes of morning stiffness, both of which improve with exercise
- Hx of anterior uveitis controlled with topical glucocorticoids
- Current medications are prn NSAIDs and ophthalmic glucocorticoid drops
- Lumbar spine range of motion is restricted on forward flexion

- Diagnose ankylosing spondylitis

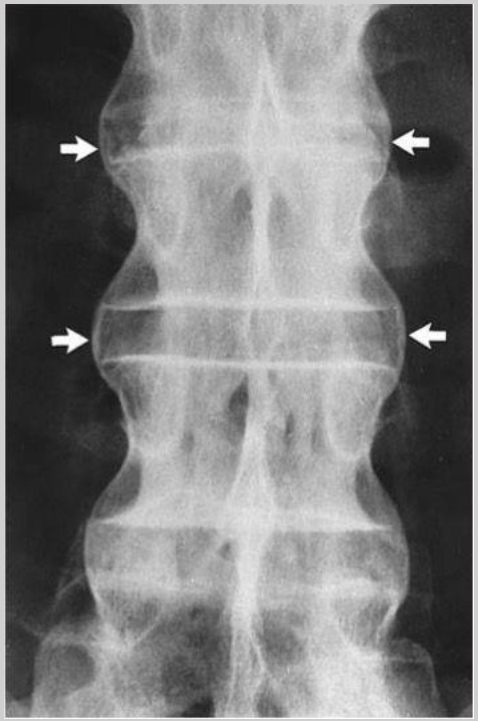
- American College of Radiology recommends radiography of the sacroiliac joints and spine as the initial evaluation of patients with inflammatory sacroiliac pain or back symptoms for evidence of sacroiliitis



Question #18, continued

- MRI is unnecessary in most cases of suspected ankylosing spondylitis, as the diagnosis can often be confirmed on radiography
- MRI is more sensitive than radiography or CT in detecting sacroiliitis
- MRI may be useful to detect inflammation in patients with high clinical suspicion but normal or equivocal radiographs

- Radiographic evidence of sacroiliitis includes pseudo-widening of the joints, erosions, sclerosis, and ankylosis
- In the spine, bony proliferation between vertebral bodies can result in formation of syndesmophytes (bony bridges) that can lead to a “bamboo spine” appearance in 10% to 15% of affected patients with ankylosing spondylitis



Question #19

- Answer: A (anti-double-stranded DNA antibodies)

- 20 y/o F with 2 weeks of worsening rash, arthritis and intermittent low-grade fever
- Hx of SLE x 5 years, on hydroxychloroquine
- Temp 37.8 °C (100.0 °F), malar rash is present as well as diffuse tenderness and swelling of multiple small joints of the hands
- Low C3 and C4 complement levels, a serum creatinine level of 1.8 mg/dL, a urine protein-creatinine ratio of 3200 mg/g

- Diagnose a flare of SLE

- Elevation of the ESR, rising anti–double-stranded DNA antibody titer, and low complement levels reliably diagnose an SLE flare
  - C3, C4 decrease due to excessive consumption
  - Increase in anti-double-stranded-DNA is most associated with a flare of lupus nephritis
- Interestingly, CRP levels do not rise during SLE flare-up

Question #19, continued

- Other answers:
  - Antinuclear antibody (ANA) testing is a useful screening tool for SLE but does not correlate with disease activity
  - Anti-Ro/SSA and anti-La/SSB antibodies correlate with SLE rashes and photosensitivity but do not correlate with disease activity
  - Anti-Smith antibodies are highly specific for the diagnosis of SLE but also do not correlate with disease activity
  - Anti-U1-ribonucleoprotein antibodies are found in patients with SLE and mixed connective tissue disease but do not correlate with disease activity

Question #20

- Answer: A (artificial tears and sugar-free candies)

- 66 y/o F with scratchy, itchy eyes, intermittent joint pain and dental carries
- No salivary pooling below the tongue, b/l parotid and lacrimal enlargement; mild tenderness without swelling of the 2nd-4th MCP joints b/l
- + RF, high-titer ANA and and anti-Ro/SSA antibodies
- A Schirmer test for ocular wetting is diminished at 3 mm

- Treat sicca symptoms associated with Sjögren syndrome

- Schirmer test:
  - Assessment of dry eyes
  - Strip of filter paper is placed under the lower eyelid and wetting is measured; less than 5 mm in 5 minutes indicates dryness

- Treatment of ocular symptoms:
  - Artificial tears and/or topical cyclosporine
  - Use of glasses with side panels to prevent surface drying
  - Plugging of the lacrimal ducts to promote tear retention

- Treatment of oral symptoms:
  - Meticulous dental care
  - Sugar-free candies can stimulate saliva flow
  - Artificial saliva may be used, but its effects are transient

Question #20, continued

ACR/EULAR classification criteria for primary Sjögren's syndrome

Item	Weight/score
Labial salivary gland with focal lymphocytic sialadenitis and focus score of ≥1 foci/4 mm^2*	3
Anti-Ro/SSA positive	3
Ocular staining score ≥5 (or van Bijsterveld score ≥4) in at least one eye¶Δ	1
Schirmer test ≤5 mm/5 minutes in at least one eye¶	1
Unstimulated whole saliva flow rate ≤0.1 mL/minute¶◇	1

- Sjögren syndrome:
  - Autoimmune exocrinopathy affecting salivary and lacrimal glands
  - Most common presentation being sicca (dryness of the eyes and/or mouth)
- Increased risk for non-Hodgkin lymphoma
- Diagnosis is typically triggered by a complaint of sicca and requires objective confirmation of exocrinopathy along with demonstration of autoimmunity
- Management of sicca is centered on preservation of moisture and relief of symptoms
- Extraglandular involvement is treated with immunosuppression