Question 1

A 59-year-old man is evaluated for a 6-month history of gout. He was doing well on colchicine and allopurinol but developed hypersensitivity to allopurinol, which resolved with cessation of the agent. He then began to have more frequent gout flares; two flares occurred in the past month and were treated with prednisone. History is also significant for hypertension, chronic kidney disease, and dyslipidemia. Current medications are colchicine, lisinopril, metoprolol, and simvastatin.

On physical examination, temperature is 37.2 °C (98.9 °F), blood pressure is 142/86 mm Hg, pulse rate is 64/min, and respiration rate is 12/min. BMI is 30. The remainder of the examination is normal.

Laboratory studies reveal a serum creatinine level of 2.3 mg/dL (203.3 μmol/L), a serum urate level of 9.2 mg/dL (0.54 mmol/L), and normal liver chemistry studies; estimated glomerular filtration rate is 48 mL/min/1.73 m^2.

Which of the following is the most appropriate next step in management?

A
Discontinue colchicine

B
Start febuxostat

C
Start pegloticase

D
Start probenecid

Answer & Critique

Correct Answer: B

Educational Objective: Treat hyperuricemia with febuxostat in a patient with an adverse reaction to allopurinol.

Key Point

In patients with gout who require urate-lowering therapy, febuxostat is a viable alternative for those who have an adverse reaction to allopurinol.

Febuxostat is indicated for this patient with frequent gout attacks. He had been taking allopurinol, a first-line agent for serum urate reduction in patients with gout. Urate-lowering therapy is indicated for patients with gout who experience repeated attacks (?2 per year), have one attack in the setting of chronic kidney disease (CKD) of stage 2 or worse, have tophaceous deposits found on examination or imaging, or have a history of urolithiasis. This patient developed an adverse reaction to allopurinol but still needs urate-lowing therapy. Febuxostat is a newer non-purine, non-competitive xanthine oxidase inhibitor, which is a viable alternative to allopurinol. It can be used in patients with mild to moderate CKD and is safe to try after an adverse reaction or failure of allopurinol.

Anti-inflammatory prophylaxis to prevent gout attacks is recommended when urate-lowering therapy is initiated because of the paradoxical increased risk of acute gout attacks when serum urate levels are rapidly decreased by medication. Prophylaxis should be continued in the presence of any active disease (tophi or flares). Colchicine is a first-line option for gout prophylaxis and should not be discontinued in this patient who requires flare prophylaxis during urate-lowering therapy.

Pegloticase is an intravenous synthetic uricase replacement approved for treatment-failure gout. Pegloticase is immunogenic, and the development of antibodies eventually occurs in most patients taking the drug, which leads to reduced effectiveness and increases the risk of hypersensitivity reactions.

The uricosuric drugs probenecid and sulfinpyrazone promote kidney clearance of uric acid by inhibiting urate-anion exchangers in the proximal tubule responsible for urate reabsorption. These agents are relatively contraindicated in patients with impaired kidney function or those at risk for kidney stones.

Question 2

A 32-year-old woman undergoes a new patient evaluation. She was diagnosed with systemic lupus erythematosus 10 years ago; manifestations have included arthritis, pericarditis, leukopenia, and rash. She reports increasing difficulty using her hands due to joint deformities. Medications are hydroxychloroquine and prednisone.

On physical examination, temperature is 36.8 °C (98.2 °F), blood pressure is 130/85 mm Hg, pulse rate is 80/min, and respiration rate is 16/min. BMI is 24. Examination of the hands reveals subluxation and ulnar deviation of the metacarpophalangeal joints on both hands, swan neck deformity of fingers on both hands, flexion and subluxation of the metacarpophalangeal joint of both thumbs, and hallux valgus of the first metatarsophalangeal joints bilaterally.

Hand radiographs demonstrate no deformities or evidence of erosions.

Which of the following is the most likely diagnosis?

A
Hypermobility syndrome

B
Jaccoud arthropathy

C
Mixed connective tissue disease

D
Rheumatoid arthritis

Correct Answer: B

Educational Objective: Diagnose Jaccoud arthropathy in a patient with systemic lupus erythematosus.

Key Point

Jaccoud arthropathy is a nonerosive arthritis most commonly caused by systemic lupus erythematosus and is characterized by reducible subluxation of the digits, swan neck deformities, and ulnar deviation of the fingers due to attenuation of the joint-supporting structures.

The most likely diagnosis is Jaccoud arthropathy, which is most commonly caused by systemic lupus erythematosus (SLE). SLE arthritis is nonerosive, but persistent periarticular inflammation that affects the structural integrity of the joint capsule/supporting joint ligaments can result in Jaccoud arthropathy, or reversible hand deformities, which is characterized by reducible subluxation of the digits, swan neck deformities, and ulnar deviation of the fingers due to attenuation of the joint-supporting structures. It is reported to occur in 5% of patients with SLE and can be confused with rheumatoid arthritis. Jaccoud arthropathy can be seen in other inflammatory illnesses, including scleroderma, mixed connective tissue disease, and Sjögren syndrome, and was first described in patients with recurrent episodes of rheumatic fever. This patient with SLE demonstrates the classic features of Jaccoud arthropathy, including subluxation, ulnar deviation, and swan neck deformities, with radiographs that do not show evidence of erosions.

Joint hypermobility refers to the ability to painlessly move a joint beyond normal range of movement. Hypermobility syndrome describes a disorder characterized by musculoskeletal pain and generalized joint hypermobility occurring in otherwise healthy individuals. Patients with joint hypermobility can rarely have swan neck deformities but do not generally have deformities of the severity seen in this patient. In addition, the presence of another disease that can cause joint hypermobility (SLE in this patient) excludes hypermobility syndrome.

Mixed connective tissue disease (MCTD) is characterized by features of systemic sclerosis, polymyositis, and SLE and is by definition associated with high titers of anti-U1-ribonucleoprotein antibodies. This patient does not have any of the characteristic symptoms of MCTD, including Raynaud phenomenon, hand edema, puffy fingers, and/or prominent synovitis.

Rheumatoid arthritis generally causes nonreducible hand deformities; furthermore, severe hand changes associated with rheumatoid arthritis typically show erosions on radiograph and periarticular osteopenia, which are not present in this patient.

Question 3

A 30-year-old woman is evaluated for a 4-month history of increasing foot pain. She also has a 2-month history of increasing pain and swelling in her fingers and right wrist as well as morning stiffness for more than 1 hour. She has no other pertinent medical history and does not take any medications.

On physical examination, vital signs are normal. There are tenderness and swelling of the second and fifth proximal interphalangeal joints and the second and third metacarpophalangeal joints of the feet bilaterally, and tenderness with movement and swelling of the right wrist.

Radiographs of the hands and wrists are normal.

Which of the following combinatio n of tests is most helpful in confirming the diagnosis?

A
Anti–cyclic citrullinated peptide antibodies and antinuclear antibodies

B
Anti–cyclic citrullinated peptide antibodies and C-reactive protein

C
Anti–cyclic citrullinated peptide antibodies and rheumatoid factor

D
Antinuclear antibodies and rheumatoid factor

Answer & Critique

Correct Answer: C

Educational Objective: Diagnose rheumatoid arthritis with appropriate laboratory testing.

Key Point

The combination of anti–cyclic citrullinated peptide antibodies and rheumatoid factor has the greatest specificity for the diagnosis of rheumatoid arthritis.

This patient most likely has rheumatoid arthritis (RA), and testing for both anti–cyclic citrullinated peptide (CCP) antibodies and rheumatoid factor will be most helpful in confirming the diagnosis. RA is an autoimmune disorder that typically presents as a symmetric inflammatory polyarthritis affecting the proximal interphalangeal and metacarpophalangeal joints of the fingers, the wrists, and the analogous joints of the feet. Prolonged morning stiffness is common. Anti-CCP antibody testing has the greatest specificity (95%) for the diagnosis of RA. Although no single laboratory test will diagnose RA, the combination of a compatible clinical presentation and a positive rheumatoid factor and positive anti-CCP antibodies is more specific for the diagnosis than any other combination of tests. Approximately 75% of patients with RA are rheumatoid factor positive, but specificity is only around 80%. Rheumatoid factor positivity frequently occurs in other autoimmune disorders and chronic infections, most notably chronic active hepatitis C virus infection.

Testing for antinuclear antibodies (ANA) is usually performed in patients with suspected systemic lupus erythematosus (SLE). A new onset of polyarticular inflammatory arthritis as seen in this patient can be indicative of SLE; however, she has no other signs or symptoms suggestive of SLE such as alopecia, aphthous ulcers, malar rash, pericardial and pleural serositis, or cytopenias. Furthermore, an ANA test may be positive in 40% of patients with RA and would not distinguish between RA and SLE with as much specificity as the combination of anti-CCP antibodies and rheumatoid factor.

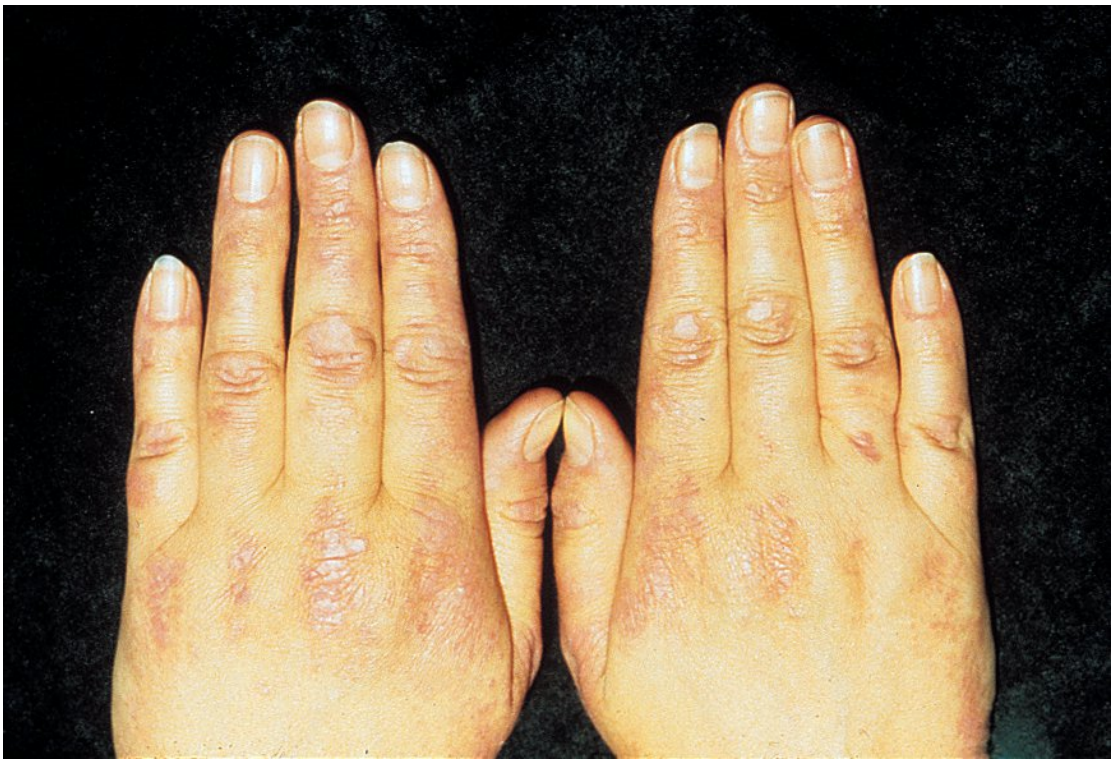
Although an elevated C-reactive protein may provide laboratory evidence of inflammation that can complement the physical examination findings of inflammatory synovitis, this inflammatory marker lacks diagnostic specificity and does not distinguish RA from other forms of inflammatory arthritis.

Question 4

A 46-year-old woman is evaluated for a 3-month history of a rash during the summertime. She is otherwise well and takes no medications.

On physical examination, vital signs are normal. BMI is 23. Examination of the skin reveals eyelid swelling and a periorbital violaceous rash, erythema and poikiloderma of the anterior chest and upper back, and an erythematous papular rash on the hands; there is no malar eruption, skin thickening, or digital ulcers. Muscle strength and reflexes are normal.

The appearance of the hands is shown.



Laboratory studies:

Complete blood count	Normal
Chemistry panel	Normal
Aldolase	5.1 U/L (normal range, 1.0-8.0 U/L)
Creatine kinase	100 U/L
Antinuclear antibodies	Titer of 1:640
Anti–Jo-1 antibodies	Negative
Urinalysis	Normal

Electromyogram and chest radiograph are normal.

Which of the following is the most likely diagnosis?

Top of Form

A

Amyopathic dermatomyositis

B

Polymorphous light eruption

C

Rosacea

D

Systemic lupus erythematosus

Answer & Critique

Correct Answer: A

Educational Objective: Diagnose amyopathic dermatomyositis.

Key Point

Amyopathic dermatomyositis refers to dermatomyositis with cutaneous involvement in the absence of clinical, laboratory, electromyogram, or biopsy evidence of myositis.

The most likely diagnosis is amyopathic dermatomyositis. This patient has a clinical presentation of heliotrope eruption in the form of a violaceous periorbital rash, Gottron papules over the extensor surface of small joints of the hands, and photodistributed violaceous poikiloderma (V sign and Shawl sign) without muscle weakness. These are findings of skin involvement seen in dermatomyositis without any clinical, serum, or electromyogram (EMG) findings of muscle involvement or myositis, suggesting the diagnosis of amyopathic dermatomyositis. Amyopathic dermatomyositis is seen in about 20% to 25% of patients with dermatomyositis, but some of these patients have evidence of myositis on one of the evaluation studies (muscle enzymes, EMG, or muscle biopsy) in the absence of muscle weakness. To qualify for the diagnosis of amyopathic dermatomyositis, the patient should have the characteristic rash but no clinical, laboratory, or muscle evaluation findings of myositis. Amyopathic dermatomyositis may be triggered by sunlight exposure and also is associated with an underlying malignancy. Treatment is usually with glucocorticoids and immunosuppressive agents.

Polymorphous light eruption (PMLE) is another dermatologic condition in which patients develop skin lesions after exposure to sunlight; these lesions last several days and resolve spontaneously in the absence of reexposure. A variety of skin lesions may be seen in PMLE, including urticarial wheals, papules, plaques, and vesicles. PMLE usually develops early in the spring, with the first few exposures to sunlight, and can be triggered by intense exposures. These lesions occur in photodistributed areas but lack characteristic heliotrope or Gottron eruptions. A diagnosis of PMLE is unlikely in this patient.

Rosacea is a chronic, inflammatory condition that causes an acneiform eruption and flushing on the mid-face. There are two types, vascular and papular pustular (inflammatory) rosacea. Vascular rosacea presents as persistent flushing, especially of the central face, with prominent telangiectasias. Pustules and papules are seen in the inflammatory variant, but in contrast to acne, rosacea pustules are not follicular based. The patient's findings are not consistent with rosacea.

Although this patient has positive antinuclear antibodies, she lacks the associated findings of systemic lupus erythematosus (SLE), including malar/discoid rash, arthritis, organ involvement, and kidney disease. SLE can cause a rash on the hands similar to Gottron papules, but it more typically involves skin located between the joints.

Question 5

A 62-year-old woman is evaluated for a 2-year history of progressively frequent and severe pain in the right knee. She has osteoarthritis with good control of her other joint symptoms with her current therapy that includes medication and a daily exercise regimen. She notes about 20 minutes of morning stiffness in the right knee with significant pain with use after rest; her activities are increasingly limited due to these symptoms. History is otherwise unremarkable. Medications are acetaminophen and celecoxib.

On physical examination, blood pressure is 135/82 mm Hg. BMI is 32. There are Heberden nodes of the second and fifth distal interphalangeal joints bilaterally and Bouchard nodes of the second and third proximal interphalangeal joints bilaterally. Bony hypertrophy of the knees is present. There is a positive bulge sign for effusion of the right knee with slight warmth but no erythema.

Standing radiographs of the knees show right (greater than left) medial joint-space narrowing, bilateral osteophytes, and bilateral peaking of the tibial spines.

Aspiration of the right knee is performed; synovial fluid analysis shows a leukocyte count of 250/μL (0.25×10^9/L) and no evidence of crystals.

Which of the following is the most appropriate next step in management?

A
Administer intra-articular glucocorticoids

B
Administer intra-articular hyaluronic acid

C
Refer for arthroscopic lavage

D
Substitute indomethacin for celecoxib

Answer & Critique

Correct Answer: A

Educational Objective: Treat inadequately controlled osteoarthritis with intra-articular glucocorticoids.

Key Point

Targeted therapy with an intra-articular glucocorticoid injection is appropriate in patients with osteoarthritis who have one symptomatic joint.

Intra-articular glucocorticoids are appropriate for this patient. She has osteoarthritis in multiple joints based on her history, physical examination, and plain radiographs. Although her overall osteoarthritis symptoms appear to be well controlled, the right knee is clearly more affected than any other joint. Therefore, therapy targeted toward this joint is indicated, and intra-articular glucocorticoids are the most appropriate choice for this patient to address her localized symptoms. Meta-analyses of clinical trials evaluating the use of glucocorticoid injection in osteoarthritis suggest that the technique may be particularly helpful. Individual studies have shown that the presence of an effusion, withdrawal of fluid from the knee, severity of disease, absence of synovitis, injection delivery under ultrasound guidance, and greater symptoms at baseline may all improve the likelihood of response.

Hyaluronic acid injections have shown only a minimal degree of benefit in the treatment of knee osteoarthritis. They generally require a series of three weekly injections and are more invasive, considerably more expensive, and less predictably efficacious than glucocorticoid injections.

Arthroscopic lavage for knee osteoarthritis is a technique in which fluid is instilled and aspirated from the joint through an arthroscope with the intention of removing the debris often present in these joints. Although observational studies originally suggested that the technique might be of benefit, more recent studies and meta-analyses have suggested otherwise. No differences in pain measured by visual analogue scale or function measured by the Western Ontario McMaster University Index have been identified in controlled trials using sham procedures.

The patient's symptoms are reasonably well controlled on her current NSAID. Therefore, there is no clear benefit to switching to another medication within this class.

Question 6

A 72-year-old man is evaluated in the emergency department for acute onset of pain and swelling of the left knee. He was diagnosed with community-acquired pneumonia 4 days ago, and a 7-day course of clarithromycin was started at that time. He reports marked improvement of his respiratory symptoms. History is also significant for gout, with attacks occurring approximately once a year; hypertension; diet-controlled diabetes mellitus; and chronic kidney disease. Other medications are nifedipine and hydrochlorothiazide.

On physical examination, temperature is 37.1 °C (98.8 °F), blood pressure is 117/86 mm Hg, pulse rate is 76/min, and respiration rate is 14/min. BMI is 32. Mildly decreased breath sounds in the right lung midfield are noted. The left knee is swollen, red, warm, tender, and fluctuant with limited range of motion.

Laboratory studies are significant for a leukocyte count of 7200/µL (7.2×10^9/L) and a serum creatinine level of 1.7 mg/dL (150.3 µmol/L).

A radiograph of the left knee is normal.

Aspiration of the left knee is performed; synovial fluid analysis reveals a leukocyte count of 20,000/µL (20×10^9/L), extracellular and intracellular urate crystals, and a negative Gram stain.

Which of the following is the most appropriate treatment?

A
Acetaminophen

B
Colchicine

C
Indomethacin

D
Intra-articular glucocorticoids

Answer & Critique

Correct Answer: D

Educational Objective: Treat an acute monoarticular gouty attack with intra-articular glucocorticoids.

Key Point

Intra-articular glucocorticoid injections are a good treatment strategy when only one or two joints are affected, the presence of joint infection has been ruled out, and oral therapies have potential adverse events.

Intra-articular glucocorticoid therapy is appropriate for this patient. Intra-articular glucocorticoid injections are a good treatment strategy when only one or two joints are affected, the presence of joint infection has been ruled out, and oral therapies have potential adverse events. This patient has a history of gout and currently presents with evidence of an acute gouty attack in the knee. Given the synovial fluid leukocyte count (<50,000/µL [50 × 10^9/L]), the documented presence of intracellular crystals, and the negative synovial fluid Gram stain, the probability of a joint infection is very low. The onset of gout in this patient was preceded by community-acquired pneumonia, which may have promoted the gout attack by causing fever and dehydration. Treatment for acute gout should focus on anti-inflammatory therapy, typically using colchicine, an NSAID, or a glucocorticoid. Although all three would effectively treat this patient's gout, the best choice would be an intra-articular glucocorticoid because of potential adverse effects of the other anti-inflammatories. Although both systemic and local glucocorticoid therapy are effective in treating acute gout, intra-articular glucocorticoids are preferred in this patient to avoid systemic immunosuppressive effects in the setting of resolving pneumonia and the possible adverse impact of systemic glucocorticoids in a patient with diabetes mellitus.

Acetaminophen is analgesic but not anti-inflammatory and does not promote the resolution of a gouty attack.

Colchicine effectively treats acute gout, especially in the early phases of an attack. However, colchicine is metabolized by the hepatic CYP3A4 enzyme, which clarithromycin strongly inhibits; coadministration raises the risk of colchicine toxicity and even death, and colchicine should be avoided while this patient is taking clarithromycin.

The presence of significant kidney disease makes the use of an NSAID such as indomethacin undesirable because cyclooxygenase inhibition adversely affects the kidneys.

Question 7

A 65-year-old man is evaluated for severe abdominal pain, joint pain, and a rash. He states that he had an upper respiratory infection about 10 days ago. Three days ago he noted a rash on his lower extremities. One day later, he experienced pain in his knees and ankles, along with abdominal pain that worsened over the past two days. He reports no visual symptoms, numbness, weakness, or other symptoms.

On physical examination, the patient appears uncomfortable. The chest and cardiac examinations are unremarkable. Decreased bowel sounds and diffuse abdominal tenderness without rebound are noted. The knees and ankles are tender and mildly swollen. Palpable purpuric lesions are present on the lower extremities, including the soles of the feet. The remainder of the physical examination reveals no abnormalities.

Laboratory studies show a normal complete blood count, an erythrocyte sedimentation rate of 88 mm/h, a serum creatinine level of 1.7 mg/dL (150.3 µmol/L), and a urinalysis showing 3+ protein, 20-30 erythrocytes/hpf, 20-30 leukocytes/hpf, and mixed granular and cellular casts. A stool test is positive for occult blood.

An abdominal ultrasound reveals thickening and edema of the ileum. A biopsy of an affected skin lesion demonstrates the presence of small-vessel, leukocytoclastic vasculitis accompanied by deposition of IgA.

Which of the foll owing is the most appropriate therapy at this time?

A
Cyclophosphamide

B
Dapsone

C
Ibuprofen

DPrednisone

Answer & Critique

Correct Answer: D

Educational Objective: Treat an adult with severe Henoch-Schönlein purpura using prednisone.

Key Point

Treatment with prednisone should be considered for patients who have severe Henoch-Schönlein purpura with involvement of multiple organ systems.

Prednisone is appropriate for this patient. His findings demonstrate the presence of a small-vessel vasculitis affecting the skin, joints, kidneys, and gastrointestinal tract. Deposition of IgA in the skin confirms the diagnosis of adult-onset Henoch-Schönlein purpura (HSP). In children, HSP is generally a benign, self-limited condition, and treatment is most commonly supportive pending spontaneous remission. HSP in adults is less common and typically is more severe. Although adult HSP also tends to run a self-limited course, adults with HSP are more likely to experience severe disease and to accumulate irreversible organ damage before the acute disease resolves. In this case, the involvement of multiple organ systems, including the gastrointestinal tract, probably warrants prednisone treatment based upon expert consensus recommendation.

Cyclophosphamide is an alkylating agent and potent immunosuppressant. It is commonly used for treatment of severe autoimmune disease such as systemic lupus erythematosus and ANCA-associated vasculitis. Its use in adult-onset HSP is less well established; although it is sometimes used in conjunction with prednisone for severe HSP nephritis, it would not be a first-choice therapy in the absence of prednisone use.

Dapsone is an antibiotic that has antileukocyte activity and is occasionally used to treat the leukocytoclastic vasculitides, including HSP. However, given the severity of this patient's condition, dapsone is less likely to be effective, and prednisone use is warranted.

Like all NSAIDs, ibuprofen may help alleviate joint pain and swelling and may have some modest effect on reducing the inflammation of small-vessel vasculitis. However, ibuprofen is unlikely to be adequately effective in a serious case such as this. Moreover, the nephrotoxic and antiplatelet effects of an NSAID would be undesirable in this patient who already has acute kidney injury and intestinal bleeding.

Question 8

A 28-year-old woman is evaluated for a 6-month history of joint pain and swelling. She was diagnosed with rheumatoid arthritis 5 years ago; current medications are etanercept, sulfasalazine, and etodolac. She was initially treated with methotrexate, which was stopped due to gastrointestinal intolerance, and she refuses to retry it.

On physical examination, temperature is 36.7 °C (98.0 °F), blood pressure is 126/74 mm Hg, pulse rate is 68/min, and respiration rate is 14/min. BMI is 24. Two proximal interphalangeal (PIP) joints of the left hand and one metacarpophalangeal (MCP) joint bilaterally are swollen and tender. Examination of the elbows, wrists, knees, and feet is normal. The remainder of the examination, including cardiopulmonary examination, is normal.

Laboratory studies, including complete blood count, chemistry panel, and liver chemistries, are normal; erythrocyte sedimentation rate is 35 mm/h, and C-reactive protein level is 1.1 mg/dL (11 mg/L).

Which of the following is the most appropriate next step in the management of this patient's disease activity?

A
Add abatacept

B
Add anakinra

C
Add leflunomide

D
Add rituximab

Answer & Critique

Correct Answer: C

Educational Objective: Avoid combining biologic agents when treating rheumatologic disease.

Key Point

Concurrent use of two or more biologic agents is not recommended because infection rates are significantly increased with minimal, if any, added efficacy.

Addition of the nonbiologic disease-modifying antirheumatic drug (DMARD) leflunomide is indicated for this patient. She has chronic moderate to severe rheumatoid arthritis with one or more poor prognostic markers, which may include young age, involvement of more than three joints, seropositivity, elevated inflammatory markers, and radiographic changes. She has continued to have active disease despite treatment with sulfasalazine and the biologic agent etanercept as suggested by continued synovitis of four joints and elevated inflammatory markers. A “treat to target” approach has been found to improve the outcomes in patients such as in this case, and additional therapy is needed to achieve a low disease activity or remission. A combination of a biologic agent (preferably a tumor factor necrosis ? inhibitor) and a nonbiologic DMARD is thought to be the best option to achieve this goal. Because of her side-effect history with methotrexate, the addition of the alternative nonbiologic DMARD leflunomide at this point would be the next best strategy.

Biologic agents are frequently used in combination with a nonbiologic DMARD. However, concurrent use of two or more biologic agents is not recommended because infection rates are significantly increased with minimal, if any, added efficacy. Therefore, the addition of abatacept, anakinra, or rituximab is inappropriate.

Question 9

A 42-year-old woman is evaluated for a 4-year history of diffuse muscle and joint pain, most notably of her shoulders, low back, hips, and knees. The pain is present in the morning and throughout the day. She wakes unrefreshed and reports problems with her memory. She also describes diarrhea alternating with constipation with no blood or mucus in the stool. She reports no weight loss. She quit working 2 years ago due to her symptoms, which were made worse by her work as a baker. She has been to multiple medical providers who have not established a diagnosis despite numerous tests.

On physical examination, temperature is 37.2 °C (99.0 °F), blood pressure is 134/88 mm Hg, pulse rate is 92/min, and respiration rate is 16/min. BMI is 36. Muscles are generally tender to light palpation but without weakness on muscle strength testing. The remainder of the examination is normal.

Laboratory studies, including complete blood count, chemistry panel, erythrocyte sedimentation rate, serum creatine kinase, and thyroid-stimulating hormone, are normal.

Which of the following is the most likely diagnosis?

A
Adrenal insufficiency

B
Fibromyalgia

C
Hypothyroidism

D
Polymyositis

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose fibromyalgia.

Key Point

Current criteria for the diagnosis of fibromyalgia include chronic widespread pain, fatigue, waking unrefreshed, and cognitive symptoms, with symptoms present for more than 3 months.

The most likely diagnosis is fibromyalgia, which is characterized by chronic widespread pain, tenderness of skin and muscles to pressure (allodynia), fatigue, sleep disturbance, and exercise intolerance. Previous lack of response to multiple medications, including NSAIDs, also provides a diagnostic clue. Examination is generally unremarkable except for allodynia. An association with other pain syndromes, including irritable bowel syndrome, irritable bladder, pelvic pain, vulvodynia, headache, and temporomandibular jaw pain, is not uncommon. This patient fulfills the 2010 American College of Rheumatology diagnostic criteria for fibromyalgia (widespread pain, wakes unrefreshed, significant fatigue, and cognitive difficulties), with symptoms present for more than 3 months.

The clinical manifestations of adrenal insufficiency are often insidious, with fatigue and malaise being the dominant symptoms; a high degree of clinical suspicion may be needed to pursue the diagnosis in the presence of subtle systemic symptoms. The patient's 4-year history of symptoms and a normal chemistry panel makes adrenal insufficiency unlikely.

The numerous and largely nonspecific clinical manifestations of hypothyroidism include fatigue, reduced endurance, weight gain, cold intolerance, constipation, impaired concentration and short-term memory, dry skin, edema, mood changes, depression, psychomotor retardation, muscle cramps, myalgia, menorrhagia, and reduced fertility. Some patients with mild hypothyroidism will exhibit few or none of these symptoms. A normal thyroid-stimulating hormone level makes hypothyroidism very unlikely.

The classic findings of polymyositis are symmetric proximal muscle weakness with little or no pain and elevation in muscle-associated enzymes. This patient has pain, a normal serum creatine kinase level, and no true weakness on examination, making polymyositis an unlikely diagnosis.

Question 10

A 28-year-old woman seeks preconception counseling. She has a 4-year history of systemic lupus erythematosus (SLE) with manifestations of photosensitive rash, arthritis, and pericarditis; she has been treated with hydroxychloroquine and low-dose prednisone with good control of her symptoms for 18 months. She has never been pregnant. She also takes vitamin D and calcium.

The physical examination and vital signs are normal.

Laboratory studies indicate that the patient's SLE is quiescent. A recent urinalysis is normal, and a previously checked antiphospholipid panel and lupus anticoagulant were negative.

SLE antinuclear antibody profile:

Antinuclear antibodies	Positive (titer: 1:320), speckled pattern
Anti-Ro/SSA antibodies	Positive
Anti–double-stranded DNA antibodies	Negative
Anti-U1-ribonucleoprotein antibodies	Negative
Anti-Smith antibodies	Negative

The increased risk of preeclampsia and preterm delivery in SLE as well as avoidance of NSAIDs prior to conception and in the later stages of pregnancy is discussed.

Which of the following also needs to be discussed with this patient based on her antibo dy profile?

A
Need to discontinue hydroxychloroquine

B
Risk of congenital heart block in her child

C
Risk of developing lupus nephritis

D
Risk of developing subacute cutaneous lupus

Answer & Critique

Correct Answer: B

Educational Objective: Provide preconception counseling to a patient with systemic lupus erythematosus who has positive anti-Ro/SSA antibodies.

Key Point

Neonatal congenital heart block affects approximately 2% of pregnancies in which the mother is positive for anti-Ro/SSA or anti-La/SSB antibodies.

Preconception counseling regarding congenital heart block in her child is appropriate for this patient with systemic lupus erythematosus (SLE) who is positive for anti-Ro/SSA antibodies. Patients with SLE experience miscarriage, stillbirth, preeclampsia and premature delivery two to five times more often than patients without the disease. This patient has mild SLE, and her disease has been quiescent for 18 months; therefore, this is an appropriate time to attempt pregnancy. Expert opinion recommends conception when SLE has been quiescent for at least 6 months. A major risk to her child would be congenital heart block, which affects approximately 2% of pregnancies in which the mother is positive for anti-Ro/SSA or anti-La/SSB antibodies. Some of these newborns require pacing from birth if there is complete heart block at delivery. Pregnancies in mothers who are positive for anti-Ro/SSA or anti-La/SSB antibodies should be monitored closely and should include input from high-risk obstetrics and neonatology because these antibodies can pass the placenta and affect the developing cardiac conduction system. If the mother has had a previously affected child, subsequent pregnancies carry a 12% risk of congenital heart block. Positivity for anti-Ro/SSA or anti-La/SSB antibodies also confers a risk for neonatal lupus erythematosus, which is characterized by rash as well as hematologic and hepatic abnormalities that generally resolve when the antibody dissipates. The use of phototherapy for neonatal hyperbilirubinemia may cause the rash to develop because the antibody is associated with photosensitivity.

Hydroxychloroquine is thought to be safe in pregnancy and has been shown to reduce the risk of congenital heart block in newborns whose mothers are positive for anti-Ro/SSA or anti-La/SSB antibodies. It should therefore not be discontinued in this patient.

This patient is not at an increased risk of lupus nephritis because it has not been a feature of her disease to date, and she is negative for anti–double-stranded DNA antibodies.

Although anti-Ro/SSA antibodies increase the risk of developing subacute cutaneous lupus, pregnancy does not increase this risk further and does not need to be part of preconception counseling. Because a photosensitive rash has been one of the features of this patient's illness, she is aware of the hazard of sun exposure.

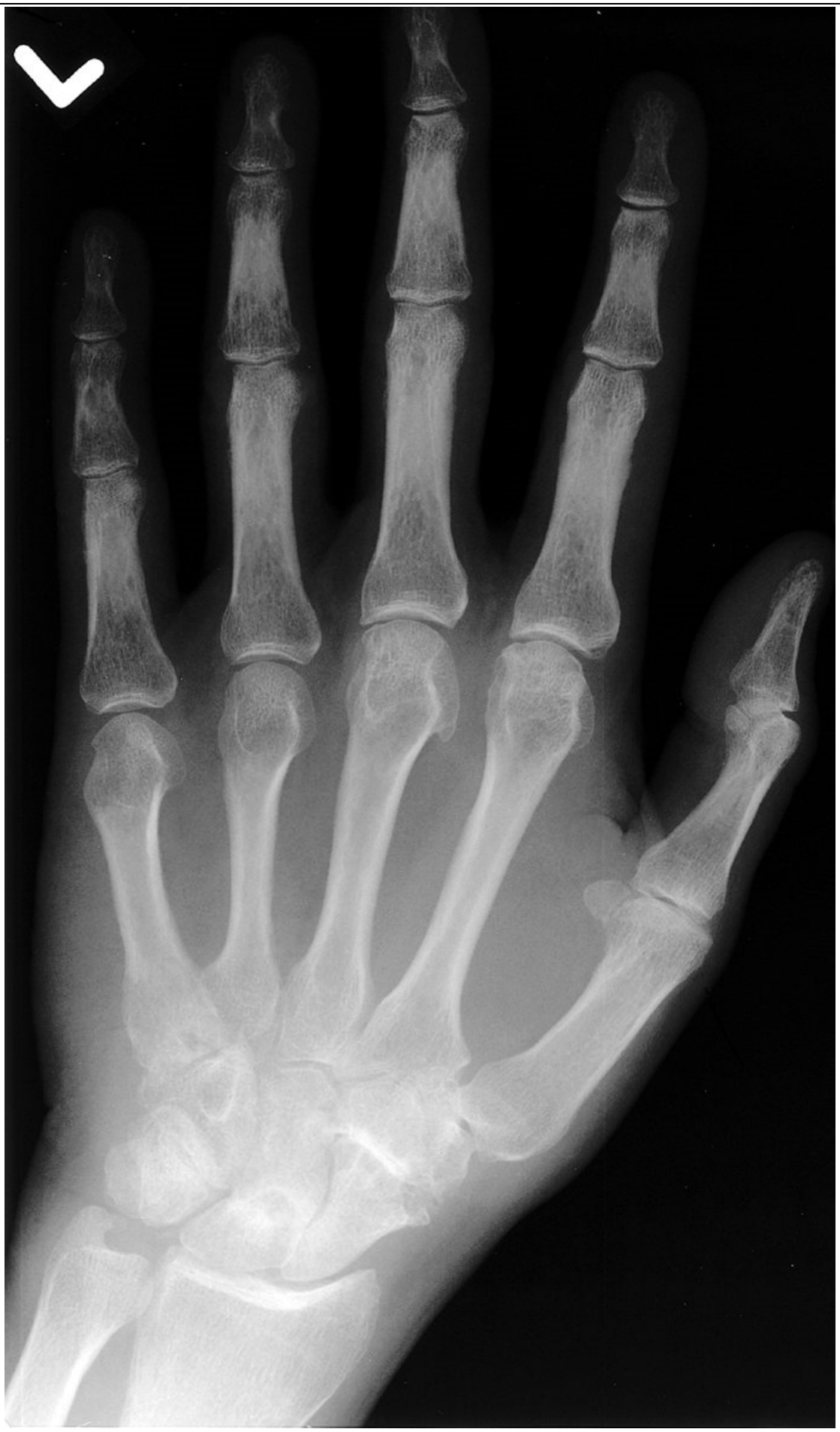
Question 11

A 50-year-old man is evaluated for an 8-year history of joint pain, particularly in the hands, and progressively worsening fatigue. Medical history is otherwise unremarkable. He takes ibuprofen as needed.

On physical examination, vital signs are normal. BMI is 32. There are swelling and tenderness of the second and third metacarpophalangeal (MCP) joints bilaterally, and tenderness but no swelling of the fourth and fifth MCP joints bilaterally. There is bony hypertrophy of the first MCP joints and knees bilaterally. The proximal interphalangeal joints and wrists are normal.

Laboratory studies are notable for an alanine aminotransferase level of 53 U/L and an aspartate aminotransferase level of 55 U/L; rheumatoid factor is negative.

A radiograph of the hand is shown.



Which of the following is the most appropriate diagnostic test to perform next?

A

Anti–cyclic citrullinated peptide antibody assay

B

Hepatitis C antibody assay

C

Serum ?-fetoprotein measurement

D

Transferrin saturation measurement

Answer & Critique

Correct Answer: D

Educational Objective: Diagnose hemochromatosis as a cause of secondary osteoarthritis.

Key Point

Secondary osteoarthritis may occur in the setting of hemochromatosis, which is associated with an arthropathy that is osteoarthritis-like, but characteristically involves the metacarpophalangeal and wrist joints.

Measurement of transferrin saturation is the most appropriate diagnostic test to perform next in this patient. He has signs and symptoms suggestive of hemochromatosis, an autosomal recessive disorder characterized by increased absorption of iron from the gut. Approximately 40% to 60% of patients with hemochromatosis develop arthropathy that is osteoarthritis-like, but characteristically involves the second and third metacarpophalangeal (MCP) or wrist joints. Transferrin saturation and serum ferritin levels are usually elevated in patients with arthropathy due to hemochromatosis. Although a variety of more specific diagnostic maneuvers may be undertaken, including liver biopsy and genetic testing for homozygosity for the C282Y mutation of the *HFE* gene, the most appropriate and cost-effective next step is measurement of transferrin saturation. A consensus does not exist for transferrin saturation cut-off levels for diagnosis of hemochromatosis, with some guidelines recommending a value of greater than 60% in men or greater than 50% in women, and others suggesting a level of greater than 55% for all patients. Measurement of ferritin levels is indicated in patients with an elevated transferrin saturation; a markedly elevated level further supports the diagnosis and predicts the development of symptoms. The presence of clinical MCP involvement with radiographic evidence of hook-shaped osteophytes is most characteristic of hemochromatosis.

Anti–cyclic citrullinated peptide antibodies are never associated with hemochromatosis, and rheumatoid factor is generally negative in patients with hemochromatosis as seen in this patient. These autoantibodies have specificity for rheumatoid arthritis.

Arthritis may occur in up to 20% of patients with hepatitis C virus infection and may mimic rheumatoid arthritis clinically and radiographically. However, the characteristic findings of hemochromatosis on this patient's radiographs and the lack of more typical findings of erosions or

bony decalcification adjacent to the involved joints make a diagnosis of hepatitis C–associated arthritis less likely.

Serum ?-fetoprotein is elevated in liver disease such as acute or chronic viral hepatitis infection as well as in hepatocellular and numerous other cancers. It would have little diagnostic specificity in this clinical setting.

Question 12

A 25-year-old man is evaluated for a 3-year history of low back and bilateral buttock pain that has gradually increased over the past year. The pain is worse in the morning and after inactivity; he feels better after stretching his back. He has 90 minutes of morning stiffness in his back. Ibuprofen provides moderate relief of symptoms. He reports no other arthritic symptoms, rash, or gastrointestinal symptoms. Family history is notable for his paternal uncle with long-standing back problems.

On physical examination, vital signs are normal. There is painful and diminished forward flexion and extension of the lumbar spine. Tenderness to palpation over both buttocks is noted.

Laboratory studies reveal an erythrocyte sedimentation rate of 35 mm/h; HLA-B27 testing is negative.

Plain radiographs of the lumbar spine and sacroiliac joints are normal.

Which of the following is the most appropriate diagnostic test to perform next?

A
CT of the sacroiliac joints

B
MRI of the sacroiliac joints

C
Technetium bone scan

D
Ultrasonography of the sacroiliac joints

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose spondyloarthritis using MRI.

Key Point

MRI is the most sensitive imaging technique for detecting early inflammation in the spine and sacroiliac joints in patients with suspected spondyloarthritis.

MRI of the sacroiliac joints and/or spine is the most appropriate diagnostic test to perform next in this patient with suspected spondyloarthritis, considered in patients with chronic inflammatory back pain beginning before the age of 45 years. It is important to establish the diagnosis of spondyloarthritis even if it will not change immediate management because it requires life-long monitoring for the development of cardiovascular and other major organ damage. A positive HLA-B27 can be supportive of this diagnosis, but a negative result does not rule it out. Conventional radiographs can demonstrate sacroiliitis (erosive changes and sclerosis) but may be normal in early disease. If there is high suspicion for axial inflammation and conventional radiographs are normal, MRI of the sacroiliac joints and/or spine should be considered to further evaluate for inflammation. MRI is the most sensitive imaging technique for detecting early inflammation in the spine and sacroiliac joints. Although his radiographs and HLA-B27 testing were negative, this 25-year-old patient has probable inflammatory back (morning stiffness lasting 90 minutes) and sacroiliac pain, making spondyloarthritis, specifically ankylosing spondylitis, a likely diagnosis. Advanced imaging is often needed to show sacroiliac joint abnormalities.

CT of the sacroiliac joints can provide evidence of erosive changes in the bone but has limited ability to detect soft-tissue inflammation of the spine and may be normal until bony changes are present.

When injected intravenously, technetium-99m binds to hydroxyapatite crystals. Increased uptake reflects increased bone turnover related to infection, cancer, trauma, and arthritis. Because of these characteristics, a positive scan is a sensitive but nonspecific indicator of bone, joint, and periarticular disorders and may be most useful when other first-line imaging modalities are negative but the suspicion of disease remains high.

Ultrasonography is relatively inexpensive, poses no radiation hazard, can scan across three-dimensional structures, and may be used concurrently with physical examination to evaluate

moving structures (for example, tendon evaluation). Musculoskeletal ultrasonography can be helpful in detecting evidence of peripheral enthesitis and arthritis but has not demonstrated usefulness in detecting axial involvement such as sacroiliitis.

Question 13

A 52-year-old woman is evaluated for an 8-week history of fatigue and shortness of breath. She has gastroesophageal reflux disease, hypertension, and a 3-year history of limited cutaneous systemic sclerosis. Medications are omeprazole, nifedipine, lisinopril, and aspirin.

On physical examination, temperature is 36.4 °C (97.6 °F), blood pressure is 126/72 mm Hg, pulse rate is 114/min, and respiration rate is 20/min. BMI is 24. Oxygen saturation is 88% on ambient air. A prominent single S_2 is heard. The chest is clear on auscultation. Sclerodactyly and multiple healed digital pits are noted. There is no rash.

Chest radiograph is normal.

Which of the following is the most appropriate diagnostic test to perform next?

A
Bronchoscopy with bronchoalveolar lavage

B
Doppler echocardiography

C
N-terminal proBNP (B-type natriuretic peptide) measurement

D
Right heart catheterization

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose pulmonary arterial hypertension in a patient with limited cutaneous systemic sclerosis.

Key Point

Echocardiography can rapidly and noninvasively estimate elevated pulmonary pressure as well as rule out some etiologies in the differential diagnosis of pulmonary arterial hypertension.

Doppler echocardiography is the most appropriate test to perform next in this patient with a 3-year history of limited cutaneous systemic sclerosis (LcSSc) who now presents with shortness of breath and fatigue, a prominent single S_2, and a normal pulmonary examination and chest radiograph. LcSSc is characterized by isolated distal skin thickening (face, neck, and hands distal to wrists), is typically not accompanied by internal organ fibrosis, and is more likely to be associated with pulmonary arterial hypertension (PAH). The initial screening test for those with systemic sclerosis who have suspected PAH is echocardiography, which can rapidly and noninvasively estimate elevated pulmonary pressure as well as rule out some etiologies in the differential diagnosis such as intracardiac shunts, valvular heart disease, or heart failure. A moderate to high tricuspid gradient correlates well with PAH confirmed with gold standard right heart catheterization, which is 97% specific but may not be sensitive.

Bronchoscopy with lavage is often used in immunocompromised patients with rapidly deteriorating lung function to assess for infection and/or pulmonary hemorrhage. This test is not indicated in a patient with findings suggestive of PAH.

B-type natriuretic peptide (BNP) or N-terminal proBNP levels should be assessed in patients suspected of having heart failure. Preliminary data suggest that N-terminal proBNP may be helpful in the assessment of PAH and may provide prognostic information. BNP and N-terminal proBNP measurement cannot be recommended at this time until further studies validate their usefulness in patients with PAH.

In patients with echocardiographic findings suggesting PAH, an array of studies (such as imaging of the chest to assess parenchymal lung disease; V/Q scanning to assess potential chronic thromboembolic disease; pulmonary function testing with D_{LCO}; serologic studies for connective tissue disease, liver disease, and HIV; and sleep studies) are helpful in selected patients. All

patients suspected of having PAH should be considered for right heart/pulmonary artery catheterization to confirm the diagnosis suggested by clinical presentation, echocardiography, and pulmonary function tests and to accurately measure the arterial pressure. It is also very useful in evaluating responsiveness to therapeutic medications and helps guide therapy. However, right heart catheterization follows these preliminary diagnostic tests and would not be done next.

Question 14

A 34-year-old woman is evaluated during a follow-up visit for polymyositis. She was diagnosed 1 year ago and has responded well to therapy. She reports no weakness, chest pain, or shortness of breath on exertion. Current medications are prednisone and azathioprine.

On physical examination, temperature is normal, blood pressure is 106/72 mm Hg, pulse rate is 84/min, and respiration rate is 26/min. BMI is 23. Oxygen saturation is 98% on ambient air. Cardiac and pulmonary examinations are normal. Strength is normal in proximal and distal muscles. Slight hyperkeratosis and cracking of the palmar surface of the hands are present. There are no other rashes, skin thickening, or digital ulcers.

Laboratory studies are notable for a serum creatine kinase level of 100 U/L, an antinuclear antibody titer of 1:1280, and anti–Jo-1 antibody positivity.

Electrocardiogram is normal.

Which of the following is the most appropriate diagnostic test to perform n ext?

A
6-Minute walk test

B
Cardiac MRI

C
Chest radiography

D Exercise stress testing

E No additional testing

Answer & Critique

Correct Answer: C

Educational Objective: Recognize the risk of interstitial lung disease in patients with polymyositis.

Key Point

Interstitial lung disease is strongly associated with polymyositis and the presence of positive autoantibodies to transfer RNA synthetases, including anti–Jo-1 antibodies.

Chest radiography is the most appropriate diagnostic test to perform next in this patient with polymyositis who has positive anti–Jo-1 antibodies and features of the antisynthetase syndrome. Pulmonary manifestations of dermatomyositis and polymyositis are common and may result from interstitial lung disease (ILD), hypoventilation (weakness of respiratory muscles), aspiration pneumonia, and, rarely, pulmonary arterial hypertension (PAH). Clinical manifestations of ILD range from being asymptomatic to severe progressive cough and dyspnea. ILD is strongly associated with the presence of positive autoantibodies to transfer RNA synthetases, including anti–Jo-1 antibodies. In clinical practice, chest radiography, high-resolution chest CT, and pulmonary function testing are used to evaluate for the presence of this manifestation, and periodic follow-up in an asymptomatic patient is appropriate. Various patterns of ILD occur, ranging from nonspecific interstitial pneumonitis (most common) to usual interstitial pneumonia or bronchiolitis obliterans organizing pneumonia. The pattern of involvement determines glucocorticoid responsiveness and, ultimately, prognosis.

6-Minute walk testing is an important test used in the evaluation and follow-up of patients with an established diagnosis of PAH, but there is no evidence that this patient has PAH.

Myocarditis has a highly variable presentation, including fatigue, chest pain, heart failure, cardiogenic shock, arrhythmias, and sudden death. This patient has no cardiovascular symptoms suggesting myocarditis, and a cardiac MRI is not necessary in a patient with a low suspicion for this condition.

Coronary artery disease most classically presents with exertional substernal chest pain relieved with rest or nitroglycerin. Variant presentation may include dyspnea on exertion and exertional fatigue. Exercise stress testing would be indicated if there was a high level of suspicion for coronary artery disease, which is not the case here.

No additional testing is incorrect because ILD may be asymptomatic in some patients and can be missed without additional testing.

Question 15

A 52-year-old woman is evaluated during a follow-up visit for a 6-year history of rheumatoid arthritis. She has not responded to combination therapy with methotrexate and etanercept, abatacept, or rituximab. Current medications are methotrexate and tofacitinib, which was initiated 1 month ago.

On physical examination, vital signs are normal. Examination of the joints shows mild swelling and tenderness of the proximal interphalangeal and metacarpophalangeal joints and wrists bilaterally.

Which of the following laboratory studies should be monitored in this patient?

A
Alkaline phosphatase

B
Bilirubin

C
Glucose

D
Lipid profile

Answer & Critique

Correct Answer: D

Educational Objective: Identify the association of tofacitinib with a risk of causing an abnormal lipid profile.

Key Point

The biologic agent tofacitinib is associated with a risk of causing an abnormal lipid profile.

The lipid profile should be monitored in this patient with rheumatoid arthritis who began taking tofacitinib 1 month ago. Elevation of all components of the lipid panel, including cholesterol, triglycerides, HDL cholesterol, and LDL cholesterol, has been found to occur as rapidly as 1 month after initiation of therapy with the biologic agent tofacitinib. Generally, these elevations remain stable over time. In the first 3 months of clinical trials evaluating the efficacy of tofacitinib, mean LDL cholesterol increased by 15%, and mean HDL cholesterol increased by 10%. In a subsequent clinical trial, statin therapy resulted in a return to pretreatment levels of LDL cholesterol. It is unknown to what extent these lipid abnormalities may impact the long-term risk of cardiovascular disease in patients treated with tofacitinib. Tofacitinib may initially raise then lower leukocyte counts. Furthermore, lymphopenia, neutropenia, and anemia may be seen with long-term use.

Elevated aminotransaminase levels may be seen with exposure to tofacitinib. However, abnormalities of bilirubin, glucose, and alkaline phosphatase would not be expected to result from exposure to 1 month of therapy with tofacitinib.

Question 16

A 56-year-old man is evaluated during a follow-up visit. He was diagnosed with gout 4 months ago based on recurrent episodes of podagra and a serum urate level of 7.2 mg/dL (0.42 mmol/L). Colchicine and allopurinol were initiated at that time and have been maintained at their initial doses. History is also significant for chronic kidney disease and hypertension, for which he takes losartan.

On physical examination, temperature is 37.1 °C (98.8 °F), blood pressure is 130/85 mm Hg, pulse rate is 75/min, and respiration rate is 15/min. BMI is 27. There is no swelling of the joints. The remainder of the examination is unremarkable.

Current laboratory studies reveal a serum urate level of 6.4 mg/dL (0.38 mmol/L) and a serum creatinine level of 2.1 mg/dL (185.6 μmol/L).

Which of the following is the most appropriate management?

A
Discontinue colchicine

B
Discontinue losartan

C
Increase allopurinol

D
No change in therapy

Answer & Critique

Correct Answer: C

Educational Objective: Prevent gout by titrating allopurinol to achieve a target serum urate level.

Key Point

Gradual dose escalation of allopurinol, with monitoring for side effects, is a safe approach for patients (even those with chronic kidney disease) with gout who have not reached a target serum urate level of less than 6.0 mg/dL (0.35 mmol/L).

The allopurinol dose should be increased for this patient with gout who has not yet reached the serum urate target goal of less than 6.0 mg/dL (0.35 mmol/L). Allopurinol is considered a first-line agent for serum urate reduction in patients with gout. Historically, concern has been expressed regarding allopurinol dosing and the risk of hypersensitivity reaction; however, it appears that gradual dose escalation with monitoring for side effects is a safe approach, even in patients with chronic kidney disease. Recent American College of Rheumatology recommendations advocate for a starting dose of 100 mg/d (or 50 mg/d in those with stage 4 or 5 chronic kidney disease) with titration upward every 2 to 5 weeks, aiming for a target serum urate level of less than 6.0 mg/dL (0.35 mmol/L). Despite the patient's kidney dysfunction, it is safe to up titrate the allopurinol gradually over several months to reach the target goal. If intolerance to allopurinol emerges, alternative urate-lowering therapy (such as the xanthine oxidase inhibitor febuxostat) should be pursued.

Gout flare prophylaxis such as colchicine should be maintained during urate-lowering therapy because patients are paradoxically at increased risk of gout flares during this time.

This patient is taking losartan to treat hypertension. This agent should not be discontinued because it has uricosuric effects and thus may be helping with efforts to lower his serum urate level.

This patient is not yet at the target serum urate goal; therefore, continuation of the same therapy is not appropriate.

Question 17

An 82-year-old woman is evaluated for a 2-week history of left-sided headaches with pain on chewing, accompanied by achiness in the shoulders and hips. She has no other pertinent personal or family history. She takes no medications.

On physical examination, temperature is 38.1 °C (100.6 °F), blood pressure is 132/86 mm Hg, pulse rate is 88/min, and respiration rate is 18/min. BMI is 25. Eye examination is normal. There are tenderness and swelling over the left temporal area. Moderate to severe pain on range of motion of the shoulders and hips is noted. There is no pain over the temporomandibular joints on palpation.

Laboratory studies, including basic metabolic panel, complete blood count, and liver chemistries, are normal; erythrocyte sedimentation rate is 85 mm/h.

Which of the following is the most approp riate immediate next step in management?

A
Initiate prednisone, 15 mg/d

B
Initiate prednisone, 60 mg/d

C
Obtain MRI of the head

D
Obtain temporal artery biopsy

Answer & Critique

Correct Answer: B

Educational Objective: Treat giant cell arteritis with high-dose prednisone.

Key Point

Immediate treatment with prednisone, 60 mg/d (or 1 mg/kg/d), is indicated for patients with suspected giant cell arteritis to prevent visual complications.

Treatment with prednisone, 60 mg/d (or 1 mg/kg/d), is indicated immediately for this patient. She has temporal artery pain and tenderness, along with jaw claudication in the setting of low-grade fever and a very high erythrocyte sedimentation rate. Given her age, these findings are most consistent with giant cell arteritis (GCA). The presence of shoulder and hip symptoms is consistent with polymyalgia rheumatica (PMR), which commonly co-occurs in patients with GCA (approximately 50% of cases). Despite a lack of visual symptoms to date, the patient is at risk of acute and potentially catastrophic visual loss. Immediate treatment is therefore warranted, the standard regimen being prednisone at a dose of 60 mg/d. (In the setting of severe visual loss, high-dose pulse glucocorticoids might be considered.) The addition of low-dose aspirin has been shown in limited studies to further reduce the risk of visual loss in patients with GCA already receiving prednisone and is favored by some experts.

Low-dose prednisone in the range of 10 to 20 mg/d is generally adequate treatment for isolated PMR but has not been shown to adequately treat GCA or to prevent visual complications.

MRI of the head permits the visualization of structures that could potentially be associated with headache and/or visual symptoms, including tumors, hydrocephalus, and/or large aneurysms. However, the presence of jaw claudication, as well as the presence of PMR symptoms, is not consistent with an intracranial lesion.

A temporal artery biopsy should be obtained as rapidly as possible to confirm the GCA diagnosis and to help direct long-term management; however, the histopathology of the disease will still be readable up to 1 to 2 weeks after initiation of treatment, and treatment should not be deferred pending biopsy.

Question 18

A 25-year-old woman is evaluated for a 2-month history of increasing joint pain and swelling. She was diagnosed with rheumatoid arthritis 1 year ago and initially treated with methotrexate with good response but recently has had more pain and swelling. With an increase of the methotrexate dosage and the addition of sulfasalazine and hydroxychloroquine, there was improvement but incomplete control of the disease. She also takes naproxen daily.

On physical examination, vital signs are normal. BMI is 23. Two metacarpophalangeal joints of both hands are tender and swollen. There is palpable warmth and tenderness of both wrists. The remainder of the examination is normal.

Laboratory studies, including complete blood count, chemistry panel, and liver chemistries, are normal; erythrocyte sedimentation rate is 45 mm/h, C-reactive protein level is 1.8 mg/dL (18 mg/L), and rheumatoid factor is 112 U/mL (112 kU/L). Hepatitis B and C serologies are negative.

The decision is made to start treatment with adalimumab.

Which of the following is the most appropriate screening test to perform before initiating adalimumab?

A
Chest radiography

B
Immunoglobulin level measurement

C
Interferon-γ release assay

D
Radiography of hands and feet

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Answer & Critique

Correct Answer: C

Educational Objective: Screen for tuberculosis prior to starting biologic therapy.

Key Point

Screening for tuberculosis is indicated before initiation of any biologic agent.

Screening for tuberculosis using an interferon-? assay is indicated for this patient before initiation of a tumor necrosis factor (TNF)-? inhibitor. This patient with rheumatoid arthritis has active disease despite treatment with triple therapy using nonbiologic disease-modifying antirheumatic drugs. In addition, she has poor prognostic markers, including positive rheumatoid serology and high inflammatory markers. Appropriate therapy with a biologic agent is being planned. TNF-? inhibitors are the mainstay of initial biologic therapy for rheumatoid arthritis. Reactivation of tuberculosis is a significant risk for most biologic agents, and particularly with TNF-? inhibitors because they inhibit formation of granuloma. Prior to starting any biologic agent, appropriate testing for latent tuberculosis is needed by obtaining either a tuberculosis skin test or an interferon-? release assay (IGRA). Either of these two tests can be used to screen for latent tuberculosis. IGRA is more costly but may be more sensitive in patients on immunosuppressive therapy.

Chest radiography will be needed if the patient is symptomatic with pulmonary symptoms or has positive testing for latent tuberculosis infection but is currently not necessary.

Common variable immunodeficiency (CVID) occurs in both adults and children. Serum IgG levels are markedly reduced, and serum IgA and/or IgM levels are frequently low. Patients with CVID frequently develop chronic lung diseases, autoimmune disorders such as rheumatoid arthritis, malabsorption, recurrent infections, and lymphoma. Recurrent sinopulmonary infections, ear infections, and conjunctivitis are common. Measuring immunoglobulin levels in this patient without evidence of recurrent infection is not indicated.

Radiographs of the hands and feet can confirm the presence of erosions in active rheumatoid disease but are not needed in this patient prior to starting a biologic because disease activity has already been established by physical examination and laboratory testing.

Question 19

A 30-year-old man is evaluated for a 1-year history of low back pain. The pain frequently spreads to the buttocks but does not radiate to the legs. The pain is worse in the morning and is associated with stiffness but improves 2 hours later after he starts working. Symptoms are worse at the end of the day and during the night. He takes ibuprofen with good relief of the pain. He is otherwise healthy and reports no other joint pain, rash, diarrhea, or dysuria.

On physical examination, vital signs are normal. Eye examination is normal. There is mild pain with normal range of motion in all directions of the lumbar spine. Tenderness over the buttocks is noted. There is no joint swelling or tenderness in the upper or lower extremities. There is no rash or nail pitting.

Laboratory studies are significant for an erythrocyte sedimentation rate of 40 mm/h, and HLA-B27 testing is positive.

Plain radiographs of the lumbar spine and sacroiliac joints are normal.

Which of the following is the most likely diagnos is?

A
Ankylosing spondylitis

B
Lumbar degenerative disk disease

C
Psoriatic arthritis

D
Reactive arthritis

Answer & Critique

Correct Answer: A

Educational Objective: Diagnose ankylosing spondylitis.

Key Point

Ankylosing spondylitis is characterized by inflammatory back pain that manifests as pain and stiffness in the spine that is worse after immobility and better with use.

The most likely diagnosis is ankylosing spondylitis, which is characterized by inflammatory back pain that manifests as pain and stiffness in the spine that is worse after immobility and better with use. Symptoms are prominent in the morning (>1 hour), and patients can be symptomatic during the night. Buttock pain is common and correlates with sacroiliitis, which is typically bilateral. This patient has symptoms/signs consistent with ankylosing spondylitis, including more than 3 months of inflammatory back pain of primarily axial involvement, age of onset younger than 45 years, a positive HLA-B27, and a good response to an NSAID. The lack of sacroiliitis or other inflammatory changes on his radiographs does not rule out this diagnosis; these changes may not be evident early in the disease course and may not be seen on plain radiographs if there are no bone erosions. He fulfills the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axial spondyloarthritis because he has a positive HLA-B27 plus at least two other features of spondyloarthritis, including inflammatory back pain and a good response to NSAIDs. The ASAS classification criteria use a nomenclature that defines spondyloarthritis as axial or peripheral, and ankylosing spondylitis would be the prototype disease in the spectrum of axial spondyloarthritis. These criteria allow patients who have not yet developed radiographic sacroiliitis to be classified as having “non-radiographic” axial spondyloarthritis.

Distinguishing between inflammatory and noninflammatory joint pain is critical in evaluating patients with musculoskeletal conditions. Inflammation may be the only symptom that distinguishes ankylosing spondylitis from lumbar degenerative disk disease. Subjective manifestations of joint inflammation include morning stiffness for more than 1 hour. Lumbar degenerative disk disease is not likely in this patient because his radiographs are normal and he has inflammatory back pain.

Characteristic features of psoriatic arthritis include enthesitis, dactylitis, tenosynovitis, arthritis of the distal interphalangeal joints, asymmetric oligoarthritis, and spondylitis. The HLA-B27 antigen

may be positive in patients with axial involvement. Psoriatic arthritis involving only the axial skeleton is possible in this patient but less likely because he has no evidence of psoriasis.

Reactive arthritis (formerly known as Reiter syndrome) is a postinfectious arthritis that occurs in both men and women. Infections may include urethritis or diarrhea, although patients may be asymptomatic. Arthritis, usually oligoarticular, develops several days to weeks after the infection. The HLA-B27 antigen may be positive in these patients. Reactive arthritis is also less likely as this patient has no history of a gastrointestinal or genitourinary infection preceding the onset of arthritis.

Question 20

A 52-year-old woman is evaluated for a 6-year history of Sjögren syndrome. During the past 3 months, she has had low-grade fevers up to 37.5 °C (99.5 °F), weight loss of 6.8 kg (15 lb), and increased fatigue and sicca symptoms. She recently noted a rash on her legs. She reports no current joint pain. Medications are hydroxychloroquine and acetaminophen as needed.

On physical examination, temperature is 37.2 °C (99.0 °F), blood pressure is 135/85 mm Hg, and pulse rate is 82/min. BMI is 28. The oral mucosa is dry. Bilateral parotid fullness is present. There is bilateral cervical adenopathy. The tip of the spleen is palpable. There are a few scattered palpable purpura on the lower legs. The remainder of the physical examination is unremarkable.

Laboratory studies show a normal complete blood count except for a hemoglobin level of 11 g/dL (110 g/L); serum C3 and C4 levels are low, and serum and urine protein electrophoresis reveals M-component.

Chest radiograph and echocardiogram are normal. CT scan of the abdomen shows numerous enlarged retroperitoneal lymph nodes and splenomegaly.

Which of the following is the most appropriate next step in the management of this patient?

A
Obtain a lymph node biopsy

B
Obtain a skin biopsy

C
Order heterophile antibody testing

D
Start prednisone

E
Start prednisone and cyclophosphamide

Answer & Critique

Correct Answer: A

Educational Objective: Recognize lymphoma in a patient with Sjögren syndrome.

Key Point

Patients with Sjögren syndrome have up to a 44-fold higher risk of developing lymphoma, the most common being diffuse B-cell and mucosa-associated lymphoid tissue (MALT) lymphomas.

The most appropriate next step in the management of this patient is to obtain a lymph node biopsy. This patient has Sjögren syndrome, an immune-mediated disease manifesting primarily as inflammation of exocrine glands, including the major and minor salivary glands, lacrimal glands, and, less commonly, other exocrine glands such as the pancreas. Patients with Sjögren syndrome are at significant risk of developing lymphoma, the most common being diffuse B-cell and mucosa-associated lymphoid tissue (MALT) lymphomas; this risk is up to 44-fold higher than in the general population. It is thought that chronic B-cell activation may lead to the development of a clone of malignant B cells. Hypocomplementemia, splenomegaly, lymphadenopathy, gammopathy, skin vasculitis, and cryoglobulinemia predict the development of, and accompany, lymphoma. With this patient's clinical history and findings, lymphoma must be in the differential and should be evaluated with a lymph node biopsy.

Biopsy of the rash will demonstrate leukocytoclastic vasculitis, which frequently accompanies lymphoma, but will not be able to diagnose the underlying lymphoma.

Heterophile antibody testing is not indicated because the complete blood count results do not demonstrate lymphocytosis, and the patient's symptoms and findings are much more concerning for lymphoma.

Prednisone and cyclophosphamide therapy may be helpful for some of this patient's symptoms, including vasculitis, but are premature at this time until lymphoma has been either identified or excluded. If there is no lymphoma and Sjögren syndrome is believed to be active and causing

vasculitis, then these therapies could be considered.

Question 21

A 30-year-old man is evaluated for a 6-month history of pain behind his right heel. The pain is worse after immobility, and he has morning stiffness in the foot lasting 1 hour. He has tried acetaminophen without much relief. History is also significant for a 3-year history of intermittent left eye uveitis treated with a prednisolone ophthalmic solution. He has no other symptoms.

On physical examination, vital signs are normal. There is no tenderness of the lumbar spine or sacroiliac joints; full range of motion of the lumbar spine is noted. Mild swelling and tenderness at the insertion of the Achilles tendon are noted. The remainder of the examination is normal.

Radiographs of the sacroiliac joints are normal. Radiographs of the right heel show soft-tissue swelling and an erosion at the insertion of the Achilles tendon.

Which of the following is the most appropriate diagnostic test to perform next?

A
Anti–cyclic citrullinated peptide antibody assay

B
Antineutrophil cytoplasmic antibody assay

C
Antinuclear antibody assay

D
HLA-B27 testing

Answer & Critique

Correct Answer: D

Educational Objective: Utilize HLA-B27 testing to aid in the diagnosis of spondyloarthritis.

Key Point

HLA-B27 testing can be helpful in supporting the diagnosis of spondyloarthritis in the absence of other sufficient manifestations.

The most appropriate diagnostic test to perform next is HLA-B27 testing. The patient has uveitis and enthesitis at the Achilles tendon, which are suggestive of peripheral spondyloarthritis. The Assessment of SpondyloArthritis international Society classification criteria for peripheral and axial spondyloarthritis are primarily used for research purposes, although they include many of the common symptoms, signs, and tests that are useful in diagnosing these disorders. Classification criteria include several other manifestations, including psoriasis, inflammatory bowel disease, preceding infection, and sacroiliitis, which are absent in this patient. HLA-B27 is included in the criteria and, in the absence of other sufficient manifestations, can be helpful in supporting the diagnosis of peripheral or axial spondyloarthritis. HLA-B27 testing has limitations because of its approximately 5% prevalence in the general population, which can lead to false positives in diagnosis. Therefore, HLA-B27 is not a useful test in a patient in whom clinical suspicion for spondyloarthritis is low (for example, a 65-year-old patient with noninflammatory or mechanical back pain). Furthermore, it does not add anything in the setting of a high suspicion for spondyloarthritis when there are sufficient other findings to establish a diagnosis (for example, a 35-year-old man with a 12-month history of anterior uveitis, chronic inflammatory back pain, and radiographic evidence of sacroiliitis).

Testing for anti–cyclic citrullinated peptide antibodies can be useful in patients with suspected rheumatoid arthritis, which is characterized by an inflammatory polyarthritis of small joints. Rheumatoid arthritis is unlikely in this patient because he only has enthesitis, an uncommon presentation of rheumatoid arthritis.

The ANCA-associated vasculitides include granulomatosis with polyangiitis (formerly known as Wegener granulomatosis), microscopic polyangiitis, and eosinophilic granulomatosis with polyangiitis (formerly known as Churg-Strauss syndrome). Granulomatosis with polyangiitis is a systemic necrotizing vasculitis that predominantly affects the upper and lower respiratory tract and

kidneys. More than 70% of patients have upper airway manifestations such as sinusitis or nasal, inner ear, or laryngotracheal inflammation. Microscopic polyangiitis is a necrotizing vasculitis that predominantly affects the lungs and kidneys. Eosinophilic granulomatosis with polyangiitis is an eosinophil-rich necrotizing vasculitis predominantly affecting the respiratory tract and other major organs. This patient does not have clinical evidence of ANCA-associated vasculitis; therefore, testing for ANCA is not indicated.

Antinuclear antibody testing is useful for patients with suspected systemic lupus erythematosus (SLE); however, SLE does not usually cause enthesitis or uveitis as seen in this patient.

Question 22

A 22-year-old woman is evaluated for a 2-year history of recurrent abdominal pain often accompanied by fever; episodes occur every 3 to 4 months and last 1 to 3 days and resolve completely. She went to the emergency department during an episode 6 weeks ago. She was noted to be mildly febrile, and laboratory studies showed an erythrocyte sedimentation rate of 84 mm/h and a leukocyte count of 16,000/μL (16×10^9/L) with neutrophilia. She was diagnosed with viral gastroenteritis and recovered completely with supportive treatment. She has been treated on several occasions for cellulitis that occurs on her foot or lower extremity, but the reason for repeated infection or a responsible organism has not been identified. On two occasions, she had pain and swelling in the knee that lasted several weeks and was not associated with the abdominal pain. She has tried naproxen without relief. She currently feels well and has no complaints.

On physical examination today, temperature is 36.6 °C (97.9 °F), blood pressure is 120/74 mm Hg, pulse rate is 74/min, and respiration rate is 14/min. BMI is 23. The cardiopulmonary and abdominal examinations are normal. There is no joint swelling.

Current laboratory studies, including complete blood count, chemistry panel, and erythrocyte sedimentation rate, are normal.

Which of the following is the most appropriate treatment?

A
Anakinra

B
Colchicine

C
Indomethacin

D
Prednisone

Answer & Critique

Correct Answer: B

Educational Objective: Treat a patient who has familial Mediterranean fever with colchicine.

Key Point

Familial Mediterranean fever is characterized by episodes of fever, polyserositis, arthritis, erysipeloid rash around the ankles, and elevated acute phase reactants; a response to colchicine is useful in the clinical diagnosis.

Colchicine is appropriate for this patient who has familial Mediterranean fever (FMF), an autosomal recessive disease characterized by episodes of fever, polyserositis, arthritis, erysipeloid rash around the ankles, and elevated acute phase reactants. Attacks last 1 to 3 days and are self-limited but can be dramatic. FMF is associated with mutation of the *MEFV*$_1$ gene; testing for *MEFV*mutations is available and should be considered as an aid to diagnosis, although not all mutations have been identified. AA amyloidosis is a potential long-term consequence of FMF due to the production and accumulation of serum amyloid A. Colchicine affects the function of various inflammatory cells that are thought to play a role in the cytokine overproduction seen in FMF. A response to colchicine is useful in the clinical diagnosis of FMF because it can prevent attacks as well as AA amyloidosis. Treatment with colchicine is therefore indicated for this patient who most likely has FMF, as manifested by her history of febrile attacks of abdominal serositis, erysipelas-like skin lesions that mimic cellulitis, and inflammatory arthritis occurring independently of the febrile episodes.

FMF genetic mutations affect the function of pyrin that results in overactivation of the inflammasome. The inflammasome is an important constituent of the innate immune system that is responsible for production of interleukin (IL)-1; dysregulation of the inflammasome, as in FMF, results in overproduction of IL-1. The IL-1 inhibitor anakinra can be used in patients with FMF who are unresponsive to colchicine; however, this agent is not first-line therapy.

NSAIDs and prednisone have not been shown to have a significant impact on the disease progression or symptoms associated with FMF.

Question 23

A 75-year-old woman is evaluated for progressive left knee pain. She has a 20-year history of bilateral knee osteoarthritis. There is no recent history of injury. She was recently discharged from the hospital for gastrointestinal bleeding related to her use of ibuprofen. She experienced only transient relief from previous glucocorticoid and hyaluronic acid injections. She is enrolled in physical therapy and exercises to increase her quadriceps strength. History is also significant for hypertension, coronary artery disease, hypercholesterolemia, and osteoporosis. Other medications are omeprazole, aspirin, lisinopril, propranolol, rosuvastatin, and alendronate.

On physical examination, vital signs are normal. BMI is 24. Mild weakness on muscle group testing and atrophy are noted in the quadriceps. There is marked bony hypertrophy of the left knee (greater than the right) without warmth, erythema, or effusion.

Which of the following is the most appropriate management for this patient?

A
Celecoxib

B
Duloxetine

C
Fentanyl

D
Prednisone

Answer & Critique

Correct Answer: B

Educational Objective: Treat osteoarthritis with duloxetine.

Key Point

Compared with placebo, duloxetine significantly reduces pain and improves physical functioning in patients with knee osteoarthritis.

The serotonin-norepinephrine reuptake inhibitor duloxetine is appropriate for this patient with osteoarthritis. The pharmacologic management of osteoarthritis pain can be difficult because therapy for symptom relief does not halt or reverse the disease process. Furthermore, all potential agents have side effects, some severe, and elderly patients can be at particularly high risk for developing them. The optimal choice of therapy relies on the risks and benefits of each agent in the context of the patient's comorbidities. This patient has already tried an NSAID (ibuprofen) as well as glucocorticoid and hyaluronic injections without symptomatic relief and has recently experienced an episode of gastrointestinal bleeding. Duloxetine is a reasonable choice given the patient's comorbidities and recent history of gastrointestinal bleeding. Compared with placebo, duloxetine significantly reduces pain and improves physical functioning in patients with knee osteoarthritis. In short-term studies, duloxetine was not associated with an increase in the adverse event rate compared with placebo. Unlike NSAIDs, duloxetine does not increase the risk for a recurrence of peptic ulcer disease. There are no medication interactions that contraindicate its use in this patient.

In an elderly patient who has had a recent bleeding peptic ulcer, the use of any NSAID, including the cyclooxygenase-2 inhibitor celecoxib, is inadvisable because the risk of recurrence with repeated exposure is high.

Narcotic use in the elderly, although not associated with ulcer risk or gastrointestinal bleeding, should also be approached cautiously. Short-acting narcotics should be tried first, and long-acting agents such as fentanyl may be used when other agents have failed. However, in this elderly patient at risk for falling due to her recent hospitalization, debilitation, quadriceps weakness, and a history of osteoporosis, fentanyl is not the optimal choice.

Although intra-articular glucocorticoids can be of benefit in the management of individual joints in osteoarthritis, there is no evidence that oral glucocorticoids would be of benefit. Furthermore, the likelihood of adverse effects with extended use is high in this patient.

Question 24

A 45-year-old woman is evaluated in the emergency department for progressive shortness of breath and fatigue for the past 6 weeks. She also has a 5-year history of diffuse cutaneous systemic sclerosis. Medications are nifedipine, lisinopril, omeprazole, and aspirin.

On physical examination, the patient is alert but short of breath. Temperature is 37.2 °C (99.0 °F), blood pressure is 126/92 mm Hg, pulse rate is 124/min, and respiration rate is 26/min. BMI is 25. Oxygen saturation is 98% on 2 L of oxygen. Cardiac examination is normal. Velcro-like crackles are heard throughout the chest. Diffuse skin thickening of the face, anterior chest, arms stopping at the elbows, and legs is present; sclerodactyly of the fingers is also noted. There is no rash. Pedal edema is present.

Chest radiograph shows bilateral reticulonodular infiltrates and ground glass opacities with normal cardiac silhouette. High-resolution CT scan is consistent with active nonspecific interstitial pneumonitis. An open lung biopsy confirms the diagnosis of nonspecific interstitial pneumonitis.

Which of the following is the most appropriate treatment?

A
Cyclophosphamide

B
D-penicillamine

C
Infliximab

D
Methotrexate

Answer & Critique

Correct Answer: A

Educational Objective: Treat a patient who has interstitial lung disease associated with diffuse cutaneous systemic sclerosis.

Key Point

Cyclophosphamide has been shown to have some benefit in patients who have interstitial lung disease associated with diffuse cutaneous systemic sclerosis.

Cyclophosphamide is appropriate for this patient who has interstitial lung disease (ILD) associated with diffuse cutaneous systemic sclerosis (DcSSc). This patient with DcSSc presents with dyspnea, decreased exercise tolerance, and characteristic Velcro-like crackles. These clinical findings are strongly suggestive of ILD and are supported by the imaging studies and confirmed by open lung biopsy. Patients with systemic sclerosis who have active inflammatory lung disease may be treated with immunosuppressive agents. Cyclophosphamide is the only treatment shown to have some benefit in patients with ILD associated with DcSSc. Cyclophosphamide given orally or intravenously for 1 year provides modest benefit. Although it has shown limited clinical improvement, it is the only evidence-based therapy and is therefore appropriate. High-dose glucocorticoids are frequently used in these patients but are of unclear benefit and may precipitate scleroderma renal crisis; therefore, if used, low doses are typically recommended by experts. Azathioprine may have a role as maintenance therapy.

Agents such as D-penicillamine or methotrexate have not been shown to be beneficial in these patients and should not be used to treat ILD.

Biologic agents, including tumor necrosis factor ? inhibitors such as infliximab, have not been shown to have therapeutic benefit in ILD or systemic sclerosis and should not be used in this patient.

Question 25

A 72-year-old man is evaluated in the emergency department for acute swelling, severe pain, and warmth of the right knee that woke him from sleep. He does not recall any inciting injury to the knee. Three months ago, he had an acutely swollen great toe that improved within 3 days, for which he did not seek treatment. History is also significant for hypertension and diabetes mellitus. Medications are hydrochlorothiazide and metformin.

On physical examination, temperature is 37.8 °C (100.1 °F), blood pressure is 130/75 mm Hg, pulse rate is 90/min, and respiration rate is 12/min. BMI is 33. The right knee is warm and swollen without overlying erythema; tenderness to palpation and decreased range of motion due to pain are noted. There is no skin breakdown or abrasions over the right knee. Examination of the other joints is unremarkable.

Which of the following is the most appropriate next step in management?

A
Obtain a knee MRI

B
Obtain a serum urate level

C
Perform joint aspiration

D
Start empiric colchicine

Answer & Critique

Correct Answer: C

Educational Objective: Perform joint aspiration to diagnose acute monoarticular arthritis.

Key Point

Analysis of synovial fluid from joint aspiration is the gold standard to diagnose gout and exclude infection.

Aspiration of the right knee is the most appropriate next step in management. This patient is likely to have gout based on his risk factors (older man, hypertension, diabetes mellitus, obesity), the description of the symptoms (sudden onset at night with severe pain), and the recent episode of great toe swelling consistent with podagra. The gold standard for diagnosing gout is identification of monosodium needle-shaped urate crystals within leukocytes via synovial fluid analysis. Furthermore, infectious arthritis must be excluded in a patient with monoarticular arthritis. This patient is at increased risk for joint infection given his age and presence of diabetes. Thus, joint aspiration should be performed and synovial fluid sent for Gram stain, cultures, leukocyte count, and crystal analysis. Although uncommon, it is important to note that gout and an infected joint can coexist.

MRI may be useful for a patient with a history of trauma or other reason to suspect a mechanical cause for knee pain. Although MRI may demonstrate inflammation, it does not typically distinguish between infectious and noninfectious causes. Therefore, MRI is not currently indicated in this patient with warmth over the joint as well as fever, which suggests an inflammatory process.

Obtaining a serum urate level may assist in the diagnosis of this patient because an elevated level (>6.8 mg/dL [0.40 mmol/L]) would help support a diagnosis of gout. However, this test is not definitive for the diagnosis. An elevated level does not prove that the patient has gout because asymptomatic hyperuricemia is common in the general population. A relatively low serum urate level also does not exclude gout because serum urate levels can be paradoxically low during acute gout attacks.

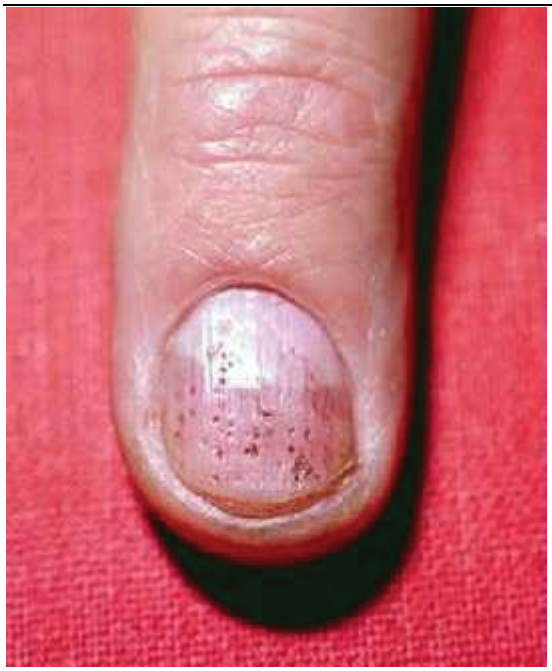
Starting colchicine would be an option for the treatment of acute gout in this patient, and resolution of inflammation with colchicine may in fact support a diagnosis of crystal-induced arthritis. However, the diagnosis must first be established and infectious arthritis excluded.

Question 26

A 40-year-old woman is evaluated for a 6-month history of pain and swelling in her left thumb, left fifth finger, and left foot. She also has morning stiffness lasting 2 to 3 hours. She has a 4-year history of lumbar and thoracic back pain that is worse with bending and lifting and is better with rest. Naproxen is only mildly helpful for the pain.

On physical examination, vital signs are normal. Patches of erythema and scaling behind the right ear and on the scalp at the occiput are noted. Fusiform swelling of the left thumb and left fifth finger is present. Tenderness and swelling at the left third metatarsophalangeal joint are noted. There is mild lumbar tenderness, and full range of motion of the lumbar spine and cervical spine is noted. No other joint swelling or tenderness is present.

Nail findings are shown.



Laboratory studies, including complete blood count with differential, comprehensive metabolic panel, rheumatoid factor, and urinalysis, are normal; HLA-B27 testing is positive.

Which of the following is the most likely diagn osis?

A
Ankylosing spondylitis

B
Inflammatory bowel disease–associated arthritis

C
Psoriatic arthritis

DReactive arthritis

Answer & Critique

Correct Answer: C

Educational Objective: Diagnose psoriatic arthritis.

Key Point

Psoriatic arthritis is associated with psoriasis, enthesitis, dactylitis, tenosynovitis, arthritis of the distal interphalangeal joints, asymmetric oligoarthritis, and spondylitis.

The most likely diagnosis is psoriatic arthritis. Although estimates of the prevalence of psoriatic arthritis in patients with psoriasis vary, more recent studies using standardized diagnostic criteria indicate that psoriatic arthritis is present in approximately 15% to 20% of those with psoriasis. Patients who have features consistent with psoriatic arthritis should be examined closely for psoriasiform skin lesions on the umbilicus, gluteal cleft, extensor surfaces, posterior auricular region, and scalp. Nails should be examined for pitting or onycholysis. Characteristic features of psoriatic arthriti s include enthesitis, dactylitis, tenosynovitis, arthritis of the distal interphalangeal joints, asymmetric oligoarthritis, and spondylitis. The recently developed Classification Criteria for Psoriatic Arthritis (CASPAR) have a sensitivity and specificity of more than 90%, especially for the diagnosis of early psoriatic arthritis. This patient fulfills the CASPAR criteria because she has inflammatory articular disease with psoriasis, psoriatic nail dystrophy, dactylitis, and a negative rheumatoid factor.

This patient does not have symptoms or findings of inflammatory back pain associated with ankylosing spondylitis; her back pain is related to use and improves with rest, which is noninflammatory. HLA-B27 positivity alone is insufficient to diagnose this dise ase, and peripheral articular disease is not typical for ankylosing spondylitis.

Nearly 50% of patients with inflammatory bowel disease (IBD) develop musculoskeletal symptoms. Peripheral arthritis may be acute and remitting with a pauciarticular distributi on commonly involving the knee. Peripheral arthritis can also be chronic or relapsing, with prominent involvement of the metacarpophalangeal joints and less correlation with intestinal inflammation. IBD-associated arthritis is also unlikely because this pa tient has no symptoms of bowel disease.

Reactive arthritis (formerly known as Reiter syndrome) is a postinfectious arthritis triggered by infections causing urethritis or diarrhea, although patients may be asymptomatic. Arthritis, usually oligoarticular, d evelops several days to weeks after the infection. Reactive arthritis can cause dactylitis; however, this patient has no history of a preceding infection, making this an unlikely diagnosis.

Question 27

A 42-year-old man is evaluated in the hospital for a 2-week history of progressive shortness of breath, with hemoptysis developing in the past 48 hours. During the past week he has also noted weakness of the left foot, numbness in the right hand, and the onset of a rash. He has a 7-year history of asthma. His only medication is an as-needed albuterol metered-dose inhaler.

On physical examination, temperature is 38.0 °C (100.4 °F), blood pressure is 142/87 mm Hg, pulse rate is 72/min, and respiration rate is 26/min. Diffuse crackles are heard in the lung fields. Diminished sensation in the right hand and weakness on dorsiflexion in the left foot are noted. There is palpable purpura on the arms and legs. The remainder of the physical examination is normal.

Laboratory studies:

Erythrocyte sedimentation rate	98 mm/h
Leukocyte count	16,000/µL (16 × 10^9/L), 22% eosinophils
Creatinine	0.8 mg/dL (70.7 µmol/L)
IgE	Elevated
ANCA	Negative
Antimyeloperoxidase antibodies	Negative
Antiproteinase 3 antibodies	Negative
Urinalysis	Normal

Chest radiograph shows diffuse pulmonary infiltrates.

Which of the following is the most likely diagnosis?

A Cryoglobulinemia
B Eosinophilic granulomatosis with polyangiitis
C Granulomatosis with polyangiitis
D Microscopic polyangiitis

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose eosinophilic granulomatosis with polyangiitis.

Key Point

Eosinophilic granulomatosis with polyangiitis is characterized by eosinophilia, migratory pulmonary infiltrates, purpuric skin rash, and mononeuritis multiplex in the setting of antecedent atopy.

This patient most likely has eosinophilic granulomatosis with polyangiitis (EGPA; formerly known as Churg-Strauss syndrome). EGPA is characterized by eosinophilia, migratory pulmonary infiltrates, purpuric skin rash, and mononeuritis multiplex in the setting of antecedent atopy. Although EGPA is considered an ANCA-associated vasculitis (specifically, antimyeloperoxidase/p-ANCA), 40% of patients with EGPA are negative for ANCA. This patient has involvement of the lungs (likely capillaritis with hemoptysis), nerves (mononeuritis multiplex), and skin. In the presence of systemic eosinophilia, elevated serum IgE levels, and a history of asthma, this patient's most likely diagnosis is EGPA. Other systemic multiorgan system diseases are less likely. For example, granulomatosis with polyangiitis (GPA; formerly known as Wegener granulomatosis) and microscopic polyangiitis would be unusual in the absence of ANCA and the presence of eosinophilia (and, in the case of GPA, lack of sinus involvement). Diagnosis of EGPA can be made most definitively by tissue biopsy. Sural nerve biopsy is most likely to yield pathology specific for EGPA, specifically, the presence of necrotizing vasculitis with eosinophilic granulomas. In addition, confirmation that the patient's neurologic findings are due to EGPA is important for characterizing the extent of disease and the level of immunosuppression needed. Such a biopsy would also allow the exclusion of other eosinophilic diseases, such as hypereosinophilic syndrome.

Although cryoglobulinemia commonly affects the nerves and skin (along with the kidneys, which are not involved in this patient), it uncommonly affects the lungs. Furthermore, the high level of eosinophilia is inconsistent with cryoglobulinemia.

Question 28

A 42-year-old woman is evaluated for a 3-month history of symmetric proximal muscle weakness. She takes no medications.

On physical examination, vital signs are normal. Symmetric weakness of the arm and thigh muscles is noted. There are no skin findings.

Laboratory studies are significant for a serum creatine kinase level of 2000 U/L and a normal thyroid-stimulating hormone level.

Electromyogram shows increased insertional activity, spontaneous fibrillations, and polyphasic motor unit potentials in the proximal muscles. MRI of the thighs shows inflammatory changes in the quadriceps.

A muscle biopsy is recommended, but the patient refuses.

Which of the following is the most appropriate treatment at this time?

A
Adalimumab

B
Cyclosporine

C
Leflunomide

D
Prednisone

Answer & Critique

Correct Answer: D

Educational Objective: Treat polymyositis using prednisone.

Key Point

The initial treatment of polymyositis or dermatomyositis with muscle involvement is glucocorticoids, most commonly prednisone.

Treatment with prednisone is indicated. This patient's findings of weakness, elevated muscle enzymes, electromyogram and MRI abnormalities, and no skin involvement suggest polymyositis. A definitive diagnosis can only be made by muscle biopsy, and every effort should be done to obtain it quickly. Nonetheless, treatment should be started as soon as possible to prevent complications of active disease, improve symptoms, and have a better long-term prognosis. Treatment should not be withheld if the biopsy is delayed or cannot be obtained. The initial treatment of polymyositis or dermatomyositis with muscle involvement is systemic glucocorticoids, most commonly prednisone given at 1 mg/kg/d. Some patients with severe disease require treatment with intravenous methylprednisolone, and many physicians use methotrexate or azathioprine at onset for their glucocorticoid-sparing benefits. If refractory or recurrent disease is noted, additional agents such as mycophenolate mofetil, intravenous immune globulin, rituximab, cyclophosphamide, or tumor necrosis factor (TNF)-? inhibitors can also be considered.

The TNF-? inhibitor adalimumab is not recommended as initial therapy prior to a trial of prednisone with or without a glucocorticoid-sparing agent in patients with polymyositis or dermatomyositis. TNF-? inhibitors have been reported to be effective in some patients with refractory disease.

Cyclosporine is an immunosuppressant agent that preferentially targets T cells and demonstrates efficacy in several rheumatologic and autoimmune diseases, including rheumatoid arthritis, systemic lupus erythematosus, inflammatory myositis, psoriasis, pyoderma gangrenosum, and inflammatory bowel disease. Toxicity is relatively common (hypertension, nephrotoxicity, tremor, hirsutism); therefore, cyclosporine is mainly used as a third-line agent in rheumatologic diseases.

Leflunomide is approximately as effective as methotrexate for rheumatoid arthritis; its use in other diseases is less explored. Toxicities include liver and hematopoietic abnormalities, infection, and

interstitial lung disease. This agent has an extremely long half-life (months) and undergoes enterohepatic circulation.

Question 29

A 71-year-old man is evaluated for long-standing stiffness, decreased range of motion, and pain of the neck, mid back, and low back. He has no history of falls or injuries. The stiffness and pain do not improve with activity and are not noticeably worse in bed or with inactivity. Acetaminophen provides minimal relief. He has no other medical problems.

On physical examination, vital signs and BMI are normal. Skin examination is normal. Bony hypertrophy of the second through fifth distal interphalangeal joints and the second and fifth proximal interphalangeal joints is present. Marked reduction in thoracic lateral bending and reduction of spinal flexion and extension are noted.

Plain radiographs of the thoracic spine show flowing osteophytes involving the anterolateral aspect of the thoracic spine at five contiguous vertebrae; there is normal disk height, the apophyseal joints are without osteophytes or bony sclerosis, and the sacroiliac joints are without erosions.

Which of the following is the most likely diagnosis?

A
Ankylosing spondylitis

B
Degenerative disk disease

C
Diffuse idiopathic skeletal hyperostosis

D
Psoriatic arthritis

Answer & Critique

Correct Answer: C

Educational Objective: Diagnose diffuse idiopathic skeletal hyperostosis.

Key Point

Diffuse idiopathic skeletal hyperostosis is a noninflammatory condition defined by the presence of flowing osteophytes involving the anterolateral aspect of the thoracic spine at four or more contiguous vertebrae with preservation of the intervertebral disk space and the absence of apophyseal joint or sacroiliac inflammatory changes such as erosions.

The most likely diagnosis is diffuse idiopathic skeletal hyperostosis (DISH), which is defined by the presence of flowing osteophytes involving the anterolateral aspect of the thoracic spine at four or more contiguous vertebrae with preservation of the intervertebral disk space and the absence of apophyseal joint or sacroiliac inflammatory changes such as erosions. DISH may occur with or without osteoarthritis or inflammatory arthritis and represents a separate finding of calcification and ossification of spinal ligaments and the regions where tendons and ligaments attach to bone (entheses). DISH is a noninflammatory condition of unknown cause that is common in the elderly population. Patients may be asymptomatic or may describe stiffness and reduced range of motion, particularly at the thoracic spine.

Ankylosing spondylitis is an inflammatory disorder that usually becomes symptomatic in adolescence and early adulthood. It is characterized by progressive morning stiffness and low back pain and typically becomes symptomatic in the lumbar spine rather than the thoracic spine early in the course. Radiographs of DISH and ankylosing spondylitis have similarities; however, ankylosing spondylitis demonstrates vertical bridging syndesmophytes rather than the flowing osteophytes that occur in DISH. Plain radiographs of ankylosing spondylitis also characteristically show changes of the sacroiliac joints that can include erosions, evidence of sclerosis, and widening, narrowing, or partial ankylosis.

Degenerative disk disease is thought to arise from age-related changes in proteoglycan content in the nucleus pulposus of the disk. Disks shrink as they become desiccated and more friable. Age-related changes also occur in the annulus fibrosus, which becomes more fibrotic, less elastic, and can shift its position. Vertebral body endplates adjacent to the disk develop sclerosis, and osteophyte formation occurs at the vertebral margins.

Psoriatic arthritis is an inflammatory disorder that can affect the spine as well as peripheral joints. When axial involvement is prominent, sacroiliitis and spondylitis can both be present; however, axial disease rarely presents in the absence of frank inflammatory arthritis of peripheral joints.

Question 30

A 46-year-old woman is evaluated for a 1-week history of symmetric polyarthritis of the hands, wrists, and knees, accompanied by a rash. She is a home health aide. She has no other pertinent history and takes no medications.

On physical examination, temperature is 37.7 °C (99.8 °F), blood pressure is 118/72 mm Hg, pulse rate is 78/min, and respiration rate is 13/min. BMI is 22. There are symmetric tenderness, warmth, erythema, and swelling of the wrists, proximal interphalangeal and metacarpophalangeal joints, and knees bilaterally. Bilateral knee effusions are noted. There is mild right upper quadrant pain. A maculopapular rash over the trunk and legs is present.

Laboratory studies:

Erythrocyte sedimentation rate	63 mm/h
Alanine aminotransferase	1050 U/L
Aspartate aminotransferase	800 U/L
Creatinine	Normal

Which of the following is the most likely diagnosis?

A
Autoimmune hepatitis

B
Hemochromatosis

C
Hepatitis B virus–associated arthritis

D
Primary biliary cirrhosis

Answer & Critique

Correct Answer: C

Educational Objective: Diagnose the acute prodromal arthritis of hepatitis B virus infection.

Key Point

The prodromal stage of hepatitis B virus infection is characterized by rapid-onset symmetric polyarthritis, which is often present before frank jaundice.

The most likely diagnosis is hepatitis B virus (HBV)–associated arthritis. The patient has rapid-onset symmetric polyarthritis, rash, and elevated aminotransferase levels, which are consistent with the prodromal phase of HBV infection. The differential diagnosis of this symmetric pattern encompasses numerous arthritides; however, the presence of elevated aminotransferase levels, a history of possible exposure risk (works as a home health aide), and the presence of a rash point toward the acute prodromal arthritis of HBV infection, which often presents before frank jaundice. Testing to document acute HBV infection, specifically assessment of hepatitis B core IgM and hepatitis B surface antigen, is indicated in this patient.

Hemochromatosis is characterized by excessive body stores of iron and can cause joint symptoms and liver dysfunction; unlike HBV-associated arthritis, it tends to occur gradually rather than abruptly, and the arthritis tends to resemble osteoarthritis without frank synovitis. Hemochromatosis is also uncommon in women, who are protected from iron accumulation due to menstruation.

Primary biliary cirrhosis and autoimmune hepatitis can cause acute liver enzyme elevation but do not cause acute arthritis or rash.

Question 31

A 65-year-old woman is seen at the request of her ophthalmologist. Two days ago, she was diagnosed with scleritis and began using an ophthalmic prednisolone solution. She notes progressive fatigue and intermittent episodes of sinus congestion during the past 5 weeks. She has a 10-year history of joint pain in her hands and low back pain that has not recently changed. History is also significant for hypertension diagnosed 3 months ago, for which she takes hydrochlorothiazide. She reports no dyspnea, cough, rash, diarrhea, or abdominal pain.

On physical examination, vital signs are normal. The ears are normal. Right eye scleral injection is present. There is mild redness and crusting of the nasal mucosa. There are no oral ulcerations. There is bony enlargement with tenderness over the distal interphalangeal joints bilaterally and squaring with tenderness over the first carpometacarpal joints bilaterally. Mild lumbar and paraspinal muscle tenderness is present; full range of motion of the lumbar spine is noted. There is no sacroiliac joint tenderness. The remainder of the physical examination is normal.

Laboratory studies:

Comprehensive metabolic panel	Normal
Erythrocyte sedimentation rate	55 mm/h
Hemoglobin	11 g/dL (110 g/L)
Leukocyte count	5000/µL (5.0×10^9/L)
Platelet count	550,000/µL (550×10^9/L)
Urinalysis	2+ protein; trace blood; no leukocytes; 1 erythrocyte cast

Chest radiograph is normal.

Which of the following is the most l ikely diagnosis?

A Ankylosing spondylitis
B Behçet syndrome
C Granulomatosis with polyangiitis
D Sarcoidosis

Answer & Critique

Correct Answer: C

Educational Objective: Diagnose vasculitis as a cause of scleritis.

Key Point

Scleritis can be caused by autoimmune diseases such as rheumatoid arthritis, relapsing polychondritis, inflammatory bowel disease, or vasculitis.

The most likely diagnosis associated with this patient's scleritis is granulomatosis with polyangiitis (formerly known as Wegener granulomatosis). Scleritis is inflammation of the fibrous layer of the eye underlying the conjunctiva and episclera. Scleritis can be caused by autoimmune diseases such as rheumatoid arthritis, relapsing polychondritis, inflammatory bowel disease, or vasculitis. This patient has evidence of systemic inflammation on laboratory testing, hypertension, and an abnormal urinalysis that could represent glomerulonephritis but no clinical evidence of rheumatoid arthritis, chondritis, or inflammatory bowel disease. Vasculitis, especially ANCA-associated vasculitis, should always be considered in the differential diagnosis of scleritis because delay in diagnosis can result in permanent loss of vision. In this case, the sinus symptoms, abnormal urinalysis suggestive of glomerulonephritis, and scleritis are suggestive of granulomatosis with polyangiitis.

Ankylosing spondylitis is characterized by inflammatory back pain that usually presents during the second to third decade of life. The type of ocular inflammation most commonly associated with this entity is anterior uveitis, not scleritis. Uveitis (inflammation of the uvea) commonly presents as a red eye with pain, photophobia, and blurred vision. Anterior uveitis is characterized by circumferential redness (ciliary flush) at the corneal limbus (junction of the cornea and sclera). Furthermore, the duration of this patient's back pain (which began after age 45 years) and evidence of osteoarthritis in her fingers suggest degenerative, rather than inflammatory, disease of the spine.

Behçet syndrome is characterized by recurrent oral and/or genital ulcers, eye and skin involvement, and pathergy. This patient has no clinical symptoms to suggest this diagnosis, and it is more commonly associated with uveitis rather than scleritis.

Sarcoidosis is a multisystem disease characterized by granulomas that form in tissues and most commonly affects the lungs. Sarcoidosis is more likely to cause uveitis than scleritis, and this

patient has no other clinical symptoms such as respiratory complaints or an abnormal chest radiograph to suggest this diagnosis.

Question 32

An 80-year-old man is evaluated for severe right knee pain that began yesterday. He has a 10-year history of gout that has affected his great toes and knees; his last attack was 2 years ago in the right great toe. Medications are allopurinol and ibuprofen as needed.

On physical examination, temperature is 37.8 °C (100.0 °F), blood pressure is 150/85 mm Hg, pulse rate is 80/min, and respiration rate is 16/min. BMI is 31. The right knee is warm, swollen, slightly erythematous, and tender; range of motion is limited to 90 degrees of flexion and associated with pain. There is no inflammation in the remainder of the joints.

Aspiration of the right knee yields 30 mL of cloudy yellow fluid. Synovial fluid leukocyte count is 55,000/μL (55×10^9/L), with 95% polymorphonuclear cells. Extracellular negatively birefringent needle-shaped crystals are seen under polarized light. Synovial fluid Gram stain is negative. Synovial fluid cultures are pending.

Which of the following is the most appropriate treatment?

A
Add probenecid

B
Increase allopurinol

C
Perform an intra-articular glucocorticoid injection

D
Start antibiotics

E
Start prednisone

Answer & Critique

Correct Answer: D

Educational Objective: Treat a suspected infected joint in the setting of gout.

Key Point

Empiric therapy with antibiotics should be started immediately in the setting of an acute inflammatory monoarthritis if infection is suspected, even if not yet confirmed on cultures.

Antibiotics are appropriate for this patient who has an acute inflammatory monoarthritis, possibly infectious arthritis. Acute crystalline attack can also cause fever and an inflammatory monoarthritis, but a negative Gram stain and/or the presence of crystals do not rule out infection. If infection is suspected, even if not yet confirmed on cultures, empiric therapy with antibiotics should be started without delay. The crystals seen in this patient's synovial fluid are extracellular, which is consistent with a diagnosis or history of gout but not diagnostic of an acute gouty attack; only intracellular crystals are diagnostic of an acute crystalline attack. In the absence of positive findings on Gram stain, initial empiric therapy usually includes coverage for gram-positive organisms (including methicillin-resistant *Staphylococcus aureus* [MRSA], which is increasing in prevalence in many communities) as well as coverage for gram-negative organisms if immunocompromised, at risk for gonococcal infection, or with trauma to the joint. Therapy can be adjusted once results from stains and cultures are available.

Probenecid is sometimes added to allopurinol to control gout when allopurinol alone is insufficient. If the patient were to experience persistent gout, increasing allopurinol to lower the serum urate below 6.0 mg/dL (0.35 mmol/L) would be more appropriate than combination therapy with two agents.

Allopurinol is considered a first-line agent for serum urate reduction in patients with gout. Increasing this patient's allopurinol will not be helpful in treating an acute gouty attack, and it will not treat an infected joint. It may be indicated long term if the patient has persistently elevated serum urate with recurrent attacks of gout.

An intra-articular glucocorticoid injection can be used to treat an acute crystalline attack; however, if an infected joint were suspected, it would not be appropriate because it may worsen infection. It

is therefore inappropriate at this time because the cause of this patient's acute inflammatory monoarthritis has not been determined.

Similarly, prednisone should not be started because it may cause worsening of infection. Prednisone is sometimes used short term to treat acute attacks of gout, but if a single large joint is involved, a local injection would avoid the systemic side effects of prednisone therapy.

Question 33

A 25-year-old woman is evaluated during a follow-up visit for an 18-month history of ankylosing spondylitis. She has minimal lower back pain with morning stiffness lasting 20 minutes. She is able to pursue her activities of daily living without any restrictions. She has been taking etanercept for 1 year with good results.

On physical examination, vital signs are normal. Full range of motion of the thoracic and cervical spine without tenderness is noted. There is no lumbar or sacroiliac tenderness. The Schober test increases by 5 cm (same as at the time of diagnosis).

Laboratory studies are notable for a normal erythrocyte sedimentation rate and a normal C-reactive protein level.

At the time of diagnosis, radiographs showed normal thoracic and lumbar spine and sacroiliac joints, and an MRI showed edema of the sacroiliac joints and in the lumbar and thoracic spine.

Which of the following should be performed next?

A Bone scan
B CT of the sacroiliac joints
C MRI of the sacroiliac joints
D Plain radiography of the sacroiliac joints
E No new imaging

Answer & Critique

Correct Answer: E

Educational Objective: Monitor ankylosing spondylitis disease activity with physical examination.

Key Point

Patients with ankylosing spondylitis who are responding well to treatment should be monitored clinically and do not require periodic imaging studies less than every 2 years unless absolutely necessary.

No new imaging is required for this patient with ankylosing spondylitis. She is currently feeling well, continues to respond well to treatment, and has normal inflammatory markers, making new imaging unnecessary. As with any test, imaging to follow disease activity should be performed only if clearly indicated by the clinical situation (for example, if the result is likely to change management). According to the 2010 Assessment of SpondyloArthritis international Society/European League Against Rheumatism (ASAS/EULAR) guidelines, serial imaging of patients with ankylosing spondylitis can be part of a comprehensive monitoring plan that also includes patient history (such as questionnaires like the Bath Ankylosing Spondylitis Functional Index [BASFI] or Bath Ankylosing Spondylitis Disease Activity Index [BASDAI]), clinical parameters (such as physical examination findings like the Schober test), and laboratory tests (such as erythrocyte sedimentation rate and C-reactive protein). The ASAS/EULAR recommendations state that spinal radiography should not be repeated more frequently than every 2 years unless absolutely necessary in specific cases. The Schober test measures range of motion of the lumbar spine and is an inexpensive and noninvasive physical examination tool for assessing spine involvement and progression; greater than 4 cm is normal.

Bone scan, CT, MRI, and plain radiography may demonstrate evidence of inflammation and/or progression of disease, but without a clear indication may unnecessarily expose the patient to radiation and to expense. This patient is feeling well, has intact activities of daily living, and had radiographs less than 2 years ago; therefore, no additional imaging is necessary at this time.

Question 34

A 35-year-old man is evaluated for a 2-month history of abrupt left knee swelling. He notes prominent stiffness of both joints but no significant pain. He previously felt well. He lives in Vermont and goes hiking during the summer. He has not had any episodes of diarrhea or abdominal pain and reports no trauma to the knee, fever, rash, or known insect bites. He does not have a history of sexually transmitted infections. He has no history of injection drug use and does not take any medications.

On physical examination, temperature is 37.1 °C (98.8 °F), blood pressure is 115/70 mm Hg, pulse rate is 82/min, and respiration rate is 12/min. BMI is 20. There is a large effusion over the left knee with warmth and mild tenderness but no overlying erythema; range of motion is limited by swelling, but stability is intact. There is no heart murmur. Lung and abdominal examinations are normal. There are no skin lesions.

Laboratory studies reveal an erythrocyte sedimentation rate of 12 mm/h and a leukocyte count of 6000/μL (6.0×10^9/L).

Radiograph of the left knee shows a large effusion but is otherwise unremarkable.

Which of the following is most likely to provide the diagnosis?

A
Blood cultures

B
Lyme serologic testing

C
MRI of the knee

D
Synovial fluid cultures

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose Lyme arthritis.

Key Point

In patients with risk factors for Lyme arthritis (even without a history of a tick bite), serologic tests showing an immunologic response to*Borrelia burgdorferi* are indicated to establish the diagnosis.

Serologic testing for Lyme disease is appropriate for this patient with arthritis characterized by prominent swelling with stiffness without significant joint pain. He has a risk factor for Lyme arthritis, given his frequent hiking in an endemic area. Patients may not recall a tick bite; therefore, Lyme disease should be suspected even without this history. The knee is most commonly affected, although other large joints can also be involved, usually in a monoarticular or oligoarticular pattern. Serologic testing for *Borrelia burgdorferi* is the diagnostic test of choice for this disease and is typically done with an enzyme-linked immunosorbent assay (ELISA) screening test, followed by confirmation by Western blot.

Blood cultures should always be obtained when there is a suspicion for bacterial infectious arthritis. This patient does not have risk factors for infectious arthritis, with Lyme being the most compelling diagnosis. Arthrocentesis is recommended for routine synovial fluid analysis and symptomatic relief, but blood cultures will not provide the correct diagnosis.

An MRI of the knee is unlikely to have diagnostic benefit in new-onset Lyme arthritis (and even in recurrent cases, it tends to be a nonerosive arthritis). MRI can be helpful in cases in which mechanical damage needs to be excluded or if there is concern for osteomyelitis or other bone pathology.

Synovial fluid cultures tend to be negative in Lyme arthritis. Synovial fluid will show inflammatory fluid with a neutrophil predominance. *B. burgdorferi* can be detected by polymerase chain reaction in synovial fluid.

Question 35

A 21-year-old woman is evaluated for a 3-week history of painful nodules and a rash in the lower extremities, along with pain and swelling of the wrists, knees, and ankles. She reports a low-grade fever and a 2.7-kg (6.0-lb) weight loss since the onset of symptoms. She has taken naproxen with some relief. History is significant for gastroesophageal reflux disease and acne. Medications are over-the-counter famotidine as needed and minocycline.

On physical examination, temperature is 38.2 °C (100.8 °F), blood pressure is 110/60 mm Hg, pulse rate is 92/min, and respiration rate is 16/min. BMI is 24. Mild swelling of the wrists, knees, and ankles is noted. There are scattered 1- to 2-cm painful erythematous nodules as well as livedo reticularis in the lower extremities beginning at the thighs. The remainder of the examination is normal.

Laboratory studies:

Antinuclear antibodies	Positive (titer: 1:320)
Anti–double-stranded DNA antibodies	Negative
Anti-Smith antibodies	Negative
Anti-U1-ribonucleoprotein antibodies	Negative
Anti-Ro/SSA antibodies	Negative
Anti-La/SSB antibodies	Negative
Antihistone antibodies	Negative
ANCA	Positive (titer: 1:320) in a perinuclear pattern; negative for myeloperoxidase
Urinalysis	Normal

Chest radiograph is normal.

Which of the following is the most appropriate next step in management?

A
Start azathioprine

B
Start high-dose prednisone

C
Discontinue famotidine

D
Discontinue minocycline

Answer & Critique

Correct Answer: D

Educational Objective: Treat a patient with drug-induced lupus erythematosus caused by minocycline.

Key Point

The diagnosis of drug-induced lupus erythematosus is typically confirmed when symptoms resolve several weeks to months after discontinuation of the offending agent.

Discontinuation of minocycline is indicated for this patient. Minocycline is one of the known causes of drug-induced lupus erythematosus (DILE). Criteria for DILE include a positive antinuclear antibody (ANA) test, exposure to a drug associated with DILE, and at least one clinical feature of lupus in a patient without a known history of lupus. Common symptoms include malaise, fever, arthritis, and rash. Diagnosis is typically confirmed when symptoms resolve several weeks to months after discontinuation of the offending agent. The agents classically associated with DILE, such as procainamide and methyldopa, are not commonly used at present. However, the spectrum of DILE includes other medications that are more commonly used, including hydralazine, diltiazem, isoniazid, minocycline, and certain tumor necrosis factor ? inhibitors (such as infliximab and etanercept). Other agents that possibly cause DILE include specific anticonvulsants, antithyroid agents, and certain antibiotics.

The diagnostic laboratory evaluation for DILE is similar to that for patients with suspected idiopathic systemic lupus erythematosus. Antinuclear antibodies are typically positive, whereas anti–double-stranded DNA antibodies are usually negative in DILE, as are most other lupus-associated extractable nuclear autoantibodies. Antihistone antibodies have traditionally been associated with DILE caused by older medications, but their presence may be more variable with DILE induced by newer agents. In addition to causing DILE, certain medications, such as minocycline and hydralazine, may be associated with a p-ANCA syndrome that may also cause a small- to medium-vessel vasculitis with organ involvement. Treatment of DILE, regardless of offending agent, requires discontinuation of the drug. The patient can also be treated symptomatically until manifestations resolve. An NSAID such as naproxen may be helpful, as can low-dose prednisone. Rarely, more substantial therapy may be needed if there is internal organ involvement.

Neither azathioprine nor high-dose prednisone is indicated in this patient because she does not have evidence of internal organ involvement.

Famotidine has not been associated with DILE.

Question 36

A 61-year-old man is evaluated for a 10-month history of generalized weakness. He reports no pain or myalgia. History is significant for hypercholesterolemia treated with a stable dose of simvastatin for the past 3 years.

On physical examination, temperature is normal, blood pressure is 138/74 mm Hg, pulse rate is 70/min, and respiration rate is 16/min. BMI is 27. There is symmetric weakness of the arm and thigh muscles with slightly reduced grip and power of the finger flexors. No muscle tenderness is noted. There is no rash, skin thickening, or digital ulcers. Reflexes and the remainder of the physical examination are normal.

Laboratory studies are notable for a normal complete blood count, an erythrocyte sedimentation rate of 23 mm/h, and a serum creatine kinase level of 365 U/L.

Chest radiograph is normal. Electromyogram and nerve conduction studies show myopathic changes in the proximal and distal muscles of the extremities as well as some neurogenic changes.

Which of the following is the most likely diagnosis?

A
Amyotrophic lateral sclerosis

B
Inclusion body myositis

C
Myasthenia gravis

D
Statin-induced myopathy

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose inclusion body myositis.

Key Point

Inclusion body myositis has an insidious onset, with muscle weakness that may be diffuse and involve both the distal and proximal muscles.

The most likely diagnosis is inclusion body myositis (IBM), an insidious and slowly progressive inflammatory myopathy that occurs more commonly in men and in those over the age of 50 years. Muscle weakness may be diffuse and involve both the distal and proximal muscles. Although typically symmetric, IBM muscle involvement may be asymmetric in up to 15% of patients. Skin is generally spared. IBM is rarely associated with extramuscular manifestations such as rash, fever, or pulmonary involvement. Patients with IBM typically have only mildly elevated (typically <1000 U/L), or even normal, levels of muscle enzymes. The characteristic triad of electromyographic findings for myopathy includes short-duration, small, low-amplitude polyphasic potentials; fibrillation potentials at rest; and bizarre, high-frequency, repetitive discharges. This older male patient has developed slowly progressive weakness affecting both the proximal and distal muscles without any significant pain or stiffness. This presentation suggests a myopathy with weakness based on his history and physical examination, mild elevation of muscle enzymes, and abnormal electromyogram (EMG) results, all of which are most consistent with IBM.

Amyotrophic lateral sclerosis is characterized by progressive dysfunction of both upper motoneuron and lower motoneuron pathways in one or more areas of the body. Common upper motoneuron features are spasticity, hyperreflexia, and pathologic reflexes, including extensor plantar responses. Typical lower motoneuron features are muscle weakness, atrophy, fasciculations, and cramps. These findings are not present in the patient.

Myasthenia gravis is characterized by fluctuating, fatigable muscle weakness that worsens with activity and improves with rest. Neurologic examination may reveal bilateral asymmetric ptosis worsened by prolonged upward gaze, an expressionless or sagging appearance of facial muscles, a “snarling” smile, nasal speech worsened by prolonged speaking, and limb weakness that increases with exercise. None of these findings are present in this patient.

Statin-induced myopathy most commonly presents with muscle pain, tenderness, and cramping typically within the first 6 months of therapy, and EMG results are normal. This patient has no muscle pain, has an abnormal EMG, and has been taking a stable dose of a stain for years, making statin-induced myopathy unlikely.

Question 37

A 72-year-old man is evaluated for a 1-year history of progressive worsening of bilateral knee pain and stiffness. He has had no locking, popping, or giving way in either knee. He has pain in both knees at rest and at night, which awakens him from sleep. He has no history of injury. Acetaminophen and over-the-counter ibuprofen improve his pain temporarily.

On physical examination, vital signs are normal. BMI is 35. Bilateral bony hypertrophy and valgus deformity of the knees are noted. There is no warmth, erythema, swelling, or effusion. Anterior drawer sign is negative, and there is no compromise in stability.

Which of the following studies of the knees is the most appropriate diagnostic test to perform next?

A
Bone scintigraphy

B
MRI

C
Standing plain radiography

D
Ultrasonography

Answer & Critique

Correct Answer: C

Educational Objective: Diagnose knee osteoarthritis with standing plain radiography.

Key Point

In patients with suspected osteoarthritis, confirmatory plain radiographs with standing views are appropriate to solidify the diagnosis and rule out less common findings such as avascular necrosis, fractures, and malignancies.

Standing plain radiography is appropriate for this patient who most likely has osteoarthritis. Osteoarthritis is often clinically identifiable by the presence of bony hypertrophy in a characteristic pattern of joint involvement and the absence of overt inflammatory synovitis. The history generally consists of long-standing and gradually worsening symptoms in middle-aged or older patients. Confirmatory plain radiographs are appropriate to solidify the diagnosis and rule out less common findings such as osteonecrosis, fractures, or malignancies. They are also noninvasive, widely available, and the least expensive radiographic modality. Standing views of the knees can demonstrate a more accurate picture of the joint-space narrowing that is present during functioning, including standing and walking, than radiographs that are obtained supine.

Bone scintigraphy can visualize areas of bone turnover change due to osteophyte formation, subchondral sclerosis, subchondral cyst formation, and bone marrow lesions. However, its limited anatomic resolution and the use of ionizing radiation make it less useful for the diagnosis of osteoarthritis.

MRI is capable of demonstrating numerous findings in soft tissue and cartilage that provide information about the joint as a whole organ. As such, MRI is a critical tool in osteoarthritis research, but its high cost argues against its routine use, particularly because there are no end points apart from joint-space narrowing (easily assessed on plain radiographs as well) visualized on MRI that confer prognostic information.

Although ultrasonography is noninvasive and is appealing because it provides real-time information, its primary use in the management of osteoarthritis is for needle placement in difficult arthrocenteses. Limitations of ultrasonography include that it is an operator-dependent technique

and that the physical properties of sound limit its ability to assess deep articular structures and the subchondral bone.

Question 38

A 60-year-old woman is evaluated during a follow-up visit for Sjögren syndrome. She reports persistent eye discomfort described as a sandy or gritty sensation. She has had recurrent corneal abrasions and erosions. She has been using artificial tears with minimal improvement. She saw her ophthalmologist who inserted punctal plugs, but they caused excessive tearing and were removed. She otherwise feels well and reports no fever, chills, weight loss, rash, joint pain, chest pain, or dyspnea.

On physical examination, temperature is 36.7 °C (98.0 °F), blood pressure is 135/80 mm Hg, pulse rate is 75/min, and respiration rate is 18/min. The oral mucosa is dry. Moderately injected sclerae are noted. There is no cervical or supraclavicular adenopathy and no parotid gland swelling. Lung, heart, musculoskeletal, and skin examinations are normal.

Which of the following is the most appropriate treatment?

A
Certolizumab pegol

B
Cyclosporine drops

C
Hydroxychloroquine

D
Olopatadine drops

E
Prednisone

Answer & Critique

Correct Answer: B

Educational Objective: Treat dry eyes in a patient with Sjögren syndrome.

Key Point

Topical cyclosporine improves the symptoms of dry eyes in patients with primary Sjögren syndrome.

Cyclosporine drops are appropriate for this patient. She has primary Sjögren syndrome with dry eyes (keratoconjunctivitis sicca), which has not responded to topical lubrication or punctal plugs. Sjögren syndrome is an immune-mediated disease of unknown cause manifesting primarily as inflammation of exocrine glands, including the major and minor salivary glands, lacrimal glands, and, less commonly, other exocrine glands such as the pancreas. The most prominent clinical feature is dryness (sicca), particularly of the eyes and mouth. Dry eyes can lead to corneal damage and visual impairment. Sicca symptoms are primarily treated with hydration and lubrication, although other local measures and medications may be helpful. Topical cyclosporine has been demonstrated in trials to improve the symptoms of dry eyes in patients with primary Sjögren syndrome. An alternative therapy is punctal occlusion (placement of plugs in the tear drainage duct openings of the lower eyelids to increase eye moisture). There is controversy as to the timing and type of plug to use when performing this procedure.

Certolizumab pegol is a tumor necrosis factor (TNF)-? inhibitor used to treat diseases such as rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. This agent is not appropriate for this patient because trials of other TNF-? inhibitors (etanercept and infliximab) did not demonstrate benefit for sicca symptoms.

Hydroxychloroquine is used to treat diseases such as systemic lupus erythematosus and rheumatoid arthritis. This agent has not been demonstrated to improve sicca symptoms, although it could be useful for treating arthritic and other systemic symptoms associated with Sjögren syndrome.

Olopatadine drops reduce histamine release from mast cells and are used to treat allergic conjunctivitis; they would therefore not be helpful for Sjögren-related sicca symptoms.

Prednisone is a potent anti-inflammatory agent that is very effective in many rheumatologic diseases. It has not been demonstrated to improve sicca symptoms, although it could be useful for treating systemic manifestations of Sjögren syndrome.

Question 39

A 25-year-old man undergoes a new patient evaluation. He has Marfan syndrome. His clinical course has been unremarkable. History is significant for inguinal hernia repair; family history is notable for his father who has Marfan syndrome. The patient takes no medications.

On physical examination, temperature is 37.4 °C (99.3 °F), blood pressure is 134/89 mm Hg, pulse rate is 80/min, and respiration rate is 14/min. BMI is 22. Tall stature and pectus excavatum are noted. Oral examination demonstrates a high arched palate. Arachnodactyly is noted. Scoliosis is present on forward bending. Examination of the feet reveals bilateral pes planus without obvious osteoarthritic mid-foot changes.

Which of the following is the most appropriate periodic imaging tes t for this patient?

A
Abdominal ultrasonography

B
Chest radiography

C
Echocardiography

D
Spine radiography

Answer & Critique

Correct Answer: C

Educational Objective: Monitor a patient with Marfan syndrome using echocardiography.

Key Point

In patients with Marfan syndrome, echocardiography should be performed at the time of diagnosis to determine aortic root and ascending aortic diameters and 6 months later to determine their rate of enlargement.

Echocardiography to evaluate for aortic root dilatation is the most appropriate routine monitoring test for this patient with Marfan syndrome. This autosomal dominant condition is characterized by a mutation in the gene *FBN1*responsible for producing fibrillin 1, a structural protein in tissues that contain elastic fibers, such as the arterial wall. Clinical features include tall stature, arachnodactyly, anterior thoracic deformity, spinal curvature, and skin hyperextensibility. The most common cause of morbidity and mortality is aortic root dilatation with possible dissection, rupture, or aortic valve insufficiency. Current guidelines recommend that echocardiography should be performed at the time of diagnosis to determine aortic root and ascending aortic diameters and 6 months later to determine their rate of enlargement. Annual imaging is recommended if stability of the aortic diameter is documented. If the maximal aortic diameter is 4.5 cm or greater, more frequent imaging should be considered.

Patients with Marfan syndrome may develop abdominal aortic aneurysm, but thoracic involvement or thoracic and abdominal aneurysms are much more common. There currently are no recommendations from any organization to routinely screen these patients with abdominal ultrasonography.

Apical lung bullae can form and lead to pneumothorax in patients with Marfan syndrome; however, there are no data to suggest that monitoring with annual chest radiography has any impact on morbidity or mortality.

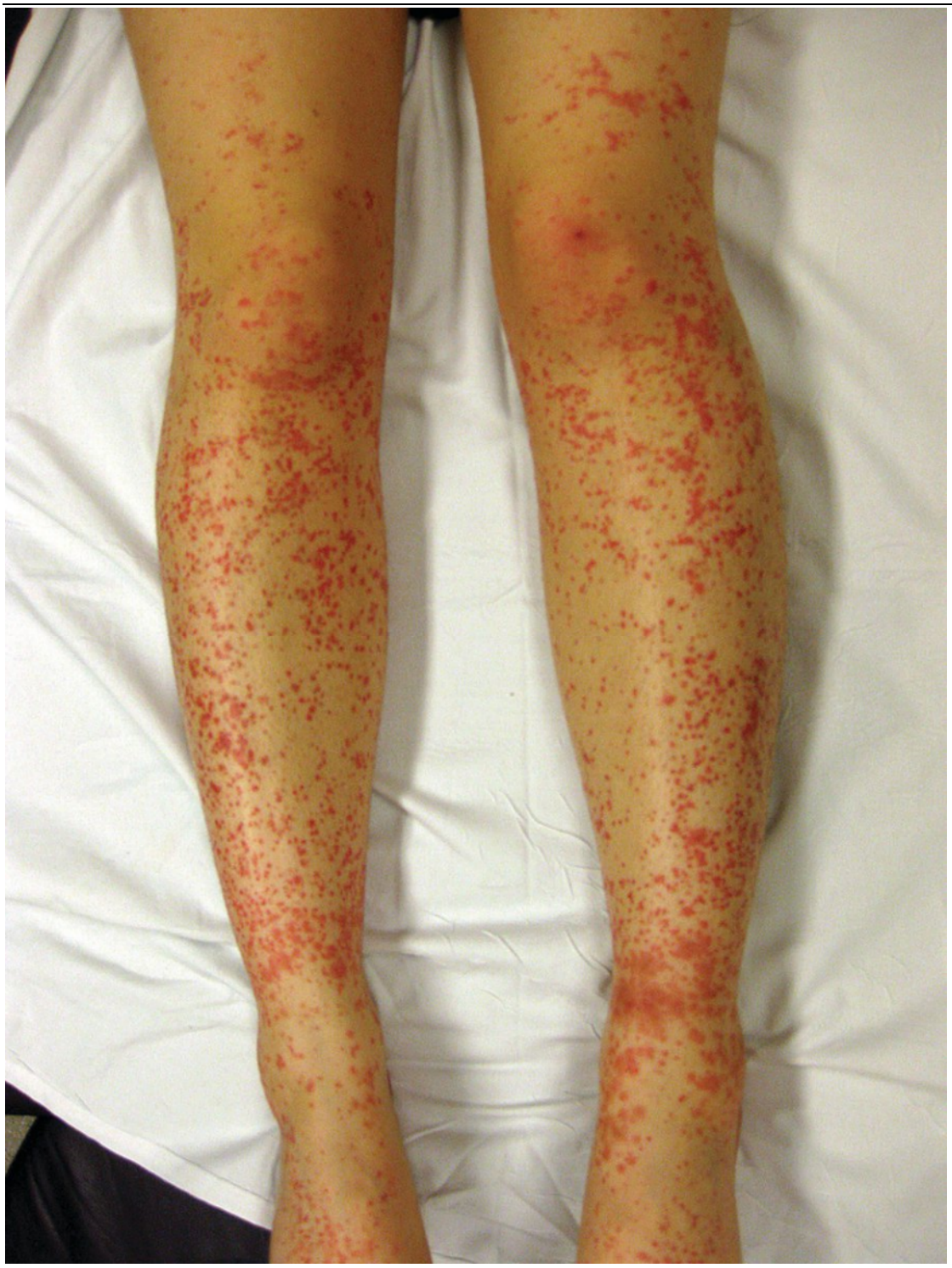
Likewise, routine monitoring for progressive skeletal abnormalities, including annual spine radiography to monitor this patient's scoliosis, is not indicated because it has no impact on outcome and should be evaluated only when symptomatic. However, counseling regarding joint protection to prevent osteoarthritis is useful.

Question 40

A 32-year-old woman is evaluated for a new rash on her legs. She was diagnosed with pyelonephritis 4 days ago and was started on a 7-day regimen of trimethoprim-sulfamethoxazole based on urine culture and sensitivity data; her urinary symptoms have improved. Medical history includes Hashimoto thyroiditis treated with levothyroxine; her dose was increased 4 weeks ago based on thyroid function studies. Medical history is otherwise unremarkable.

On physical examination, temperature is normal, blood pressure is 124/82 mm Hg, pulse rate is 66/min, and respiration rate is 13/min. BMI is 21. Cardiopulmonary examination is unremarkable. The abdomen is soft and nontender. Musculoskeletal examination shows no evidence of joint swelling, warmth, or tenderness. The remainder of the examination is normal.

The appearance of the legs is shown.



Which of the following is the most appropriate next step in management?

A

Discontinue trimethoprim-sulfamethoxazole

B

Initiate prednisone

C Measure antihistone antibodies

D Obtain skin biopsy

Answer & Critique

Correct Answer: A

Educational Objective: Treat a patient who has hypersensitivity vasculitis.

Key Point

Hypersensitivity vasculitis is caused by a hypersensitivity reaction to antigens s uch as medication or infection and typically resolves when the offending agent is removed.

Discontinuation of trimethoprim-sulfamethoxazole is indicated for this patient who developed palpable purpura within days of starting trimethoprim -sulfamethoxazole for a urinary tract infection. The most likely diagnosis is hypersensitivity vasculitis, which is caused by a hypersensitivity reaction to antigens such as medication or infection. Hypersensitivity vasculitis typically resolves when the offending agent is r emoved. Similar to other forms of small-vessel vasculitis, hypersensitivity vasculitis results from antibodies directed toward the antigens that result in immune complex formation. Complement is activated, and neutrophils are attracted to accumulate in cap illaries, arterioles, and post-capillary venules. Although a similar reaction associated with the infection itself may occur, this is less likely given the time course of onset and the high degree of association of trimethoprim-sulfamethoxazole with this r eaction. Because her reaction is mild and limited to the skin, the most important aspect of treatment is to remove the likely offending agent, after which the condition will resolve.

Prednisone has shown efficacy in hypersensitivity vasculitis and can be u sed if the vasculitis is severe, is causing discomfort of the skin or other organ damage, or if it is imperative that the agent be continued despite the reactions. Because this is not the case, discontinuing the offending agent remains the highest priority .

Antihistone antibodies occur frequently in patients with either systemic or drug -induced lupus erythematosus. This patient's disease is more consistent with hypersensitivity vasculitis without specific features of drug -induced lupus (for example, malar r ash); however, even if drug-induced lupus were the likely diagnosis, discontinuing the offending agent would still be the highest priority.

Palpable purpura is a clinical diagnosis for which a skin biopsy is not generally needed. A skin biopsy could be useful in cases where the mechanism of the rash needs to be understood to facilitate diagnosis or treatment, or when the rash fails to resolve despite management. In this case, the cause of the rash is known, and management should consist of removal of the offending agent before any further work -up is considered.

Question 41

A 30-year-old woman is evaluated during a follow-up visit for systemic lupus erythematosus. She was diagnosed 3 months ago after presenting with pericarditis and arthritis. She was initially treated with prednisone, 40 mg/d, with improvement of her presenting symptoms. The prednisone has been tapered over 3 months to her current dose of 10 mg/d with no recurrence. She also takes vitamin D and a calcium supplement.

On physical examination, vital signs are normal. BMI is 25. Cardiac examination is normal. There is no evidence of arthritis. The remainder of the examination is normal.

Which of the following is the most appropriate next step in treating this patient?

A
Add azathioprine

B
Add hydroxychloroquine

C
Add mycophenolate mofetil

D
Add a scheduled NSAID

Answer & Critique

Correct Answer: B

Educational Objective: Treat mild systemic lupus erythematosus.

Key Point

Antimalarial therapy such as hydroxychloroquine in systemic lupus erythematosus (SLE) has documented benefit for reducing disease activity, improving survival, and reducing the risk of SLE-related thrombosis and myocardial infarction.

Hydroxychloroquine is an appropriate agent to address milder systemic manifestations of systemic lupus erythematosus (SLE) such as arthritis and pericarditis, and it can act as a glucocorticoid-sparing agent. All patients with SLE who can tolerate it should be taking hydroxychloroquine. Antimalarial therapy such as hydroxychloroquine in SLE has documented benefit for reducing disease activity, improving survival, and reducing the risk of SLE-related thrombosis and myocardial infarction.

Azathioprine is generally reserved for more severe manifestations of SLE not responsive to low-dose prednisone and hydroxychloroquine but can be associated with serious toxicity. Azathioprine has generally been supplanted by the use of mycophenolate mofetil in SLE.

Mycophenolate mofetil may be appropriate for this patient if she had more serious disease activity such as nephritis or if her arthritis or pericarditis recurred while taking hydroxychloroquine.

NSAIDs, often with colchicine, are first-line therapy for most patients with pericarditis, although glucocorticoids may be indicated in patients with pericarditis associated with a systemic inflammatory disease such as in this patient. However, there is no indication to start an NSAID now given resolution of her symptoms, and doing so would increase her risk of gastrointestinal complications if used along with her daily glucocorticoid.

Question 42

A 65-year-old man is evaluated during a follow-up visit for gout. He initially presented 6 months ago with acute pain and swelling of the right great toe and a serum urate level of 7.2 mg/dL (0.42 mmol/L); symptoms resolved with naproxen. He then presented last week with recurrent symptoms of great toe pain, redness, and swelling that began during sleep. Colchicine was initiated, and symptoms resolved. History is also significant for hypertension, coronary artery disease, hyperlipidemia, and urolithiasis. Current medications are colchicine, metoprolol, simvastatin, and low-dose aspirin.

On physical examination, temperature is 37.1 °C (98.8 °F), blood pressure is 138/80 mm Hg, pulse rate is 60/min, and respiration rate is 15/min. BMI is 30. Examination of the joints reveals no swelling.

Laboratory studies reveal a serum urate level of 7.6 mg/dL (0.45 mmol/L) and normal kidney and liver chemistries.

Which of the following is the most appropriate treatment for this patient?

A
Discontinue aspirin

B
Discontinue colchicine

C
Start allopurinol

D
Start probenecid

Answer & Critique

Correct Answer: C

Educational Objective: Treat gout with urate-lowering therapy.

Key Point

Urate-lowering therapy should be initiated in patients with gout who have had two or more attacks within a 1-year period, one attack in the setting of chronic kidney disease of stage 2 or worse, one attack with the presence of tophi visible on examination or imaging, or one attack with a history of urolithiasis.

Initiation of allopurinol is appropriate for this patient with gout who has had two attacks of podagra within the past year. The American College of Rheumatology (ACR) guidelines currently recommend that urate-lowering therapy should be initiated in patients with gout who have had two or more attacks within a 1-year period, one attack in the setting of chronic kidney disease of stage 2 or worse, one attack with the presence of tophi visible on examination or imaging, or one attack with a history of urolithiasis. Allopurinol, a xanthine oxidase inhibitor, is an appropriate first-line agent for urate reduction. Flare prophylaxis should be maintained when urate-lowering therapy is undertaken.

Low-dose aspirin can increase serum urate due to effects on renal uric acid transport; however, the ACR does not currently recommend aspirin discontinuation in patients for whom it is indicated, such as this patient with coronary artery disease.

This patient needs to begin urate-lowering therapy, and his flare prophylaxis (colchicine) should be maintained during this period given the paradoxical increased risk of flare during acute serum urate reduction. In the absence of active disease, the ACR currently recommends that prophylaxis should be continued for the greater of the following: 6 months; 3 months after achieving the target serum urate level for a patient without tophi; or 6 months after achieving the target serum urate level where there has been resolution of tophi.

Probenecid is a uricosuric agent (promotes kidney uric acid excretion) and is a viable alternative first-line urate-lowering agent in patients who cannot tolerate or have a contraindication to xanthine oxidase inhibitor therapy. However, allopurinol is generally more appropriate in patients such as in this case who have no contraindication to urate-lowering therapy. Moreover, the

patient's history of urolithiasis makes probenecid relatively contraindicated because this medication increases the risk of kidney stones.

Question 43

A 50-year-old woman is evaluated for slowly worsening joint pain in her fingers for the past 5 years. She notes swelling, morning stiffness lasting 10 minutes, and pain that is worse after housework or typing. She has no other joint pain and otherwise feels well. She reports no fevers, weight loss, rashes, alopecia, oral ulcers, dyspnea, chest pain, or abdominal pain. The patient takes no medications.

On physical examination, vital signs are normal. There is squaring, crepitus, and tenderness of the first carpometacarpal joints. Bony enlargement and tenderness over all distal interphalangeal (DIP) joints are present. Limited range of motion of the thumbs and DIP joints is noted. There is no joint warmth, redness, or effusions. The remainder of the joint examination is normal.

Which of the following is the most appropriate next step in management?

A
Anti–double-stranded DNA antibody testing

B
Antinuclear antibody testing

C
Radiography of the hands

D
Rheumatoid factor testing

E
No further testing

Answer & Critique

Correct Answer: E

Educational Objective: Clinically diagnose osteoarthritis of the hands.

Key Point

Additional testing such as autoantibody measurements or radiography is unnecessary in patients with clinically diagnosed hand osteoarthritis.

No further testing is necessary for this patient who clinically appears to have hand osteoarthritis. Osteoarthritis is a clinical diagnosis, and the cardinal symptom is pain with activity that is relieved with rest. Affected patients also typically experience morning stiffness that lasts for less than 30 minutes daily. Bony hypertrophy is commonly detected in the fingers, and Heberden and Bouchard nodes may be easily palpated. Osteoarthritis also may cause squaring or boxing of the carpometacarpal joint at the base of the thumb.

This patient has no clinical signs or symptoms suggestive of a systemic inflammatory disease and therefore does not require diagnostic testing with antinuclear antibodies (ANA) or anti–double-stranded DNA antibodies. A positive ANA test result has low predictive value when the pretest probability of systemic lupus erythematosus or a related disease is low. Therefore, this test should not be used to screen indiscriminately for the presence of rheumatologic disease. The American College of Rheumatology recommends not testing ANA subserologies such as anti–double-stranded DNA without the combination of a positive ANA and elevated clinical suspicion of autoimmune disease, which is not present in this patient.

Radiography is not needed to confirm the diagnosis of osteoarthritis in patients with a history and physical examination compatible with this condition. Clinical examination is more sensitive and specific for the diagnosis of hand osteoarthritis compared with radiography.

The key features of rheumatoid arthritis (RA) are swelling and tenderness in and around the joints. Prominent morning stiffness that usually lasts more than 1 hour characterizes early RA. Rheumatoid factor positivity is characteristic of RA, although rheumatoid factor has a low specificity for diagnosis of RA. Rheumatoid factor may be present in healthy persons, especially at older ages. Because this patient has no clinical evidence of RA, testing for rheumatoid factor is unnecessary.

Question 44

A 74-year-old man is evaluated for a 2-month history of progressively worsening bilateral shoulder and hip pain. He currently has difficulty rising from a chair and reaching overhead because of the pain. He also reports fatigue, malaise, and 4.5-kg (10-lb) weight loss during this period. He reports no other symptoms. He takes acetaminophen as needed for pain with little or no relief.

On physical examination, the patient appears depressed. Temperature is 37.9 °C (100.2 °F), blood pressure is 126/66 mm Hg, pulse rate is 72/min, and respiration rate is 18/min. BMI is 26. There is markedly limited range of motion of the shoulders and hips due to pain; strength cannot be adequately assessed. The remainder of the physical examination is normal.

Laboratory studies, including basic metabolic panel, complete blood count, liver chemistries, and thyroid-stimulating hormone level, are normal. Erythrocyte sedimentation rate is 68 mm/h.

Which of the following is the most appropriate treatment?

A
Aspirin, 81 mg/d

B
Aspirin, 650 mg three times daily

C
Duloxetine, 60 mg/d

D
Prednisone, 15 mg/d

E
Prednisone, 60 mg/d

Answer & Critique

Correct Answer: D

Educational Objective: Treat polymyalgia rheumatica with low-dose prednisone.

Key Point

Treatment of polymyalgia rheumatica typically consists of low-dose prednisone, initially at 10 to 20 mg/d, which should result in rapid resolution of symptoms.

Treatment with prednisone, 15 mg/d, is appropriate. This 74-year-old man presents with shoulder and hip girdle pain and limitation accompanied by signs of systemic inflammation, including low-grade fever, weight loss, malaise, and a markedly elevated erythrocyte sedimentation rate (ESR). This constellation of findings is classic for polymyalgia rheumatica (PMR), especially in this age group. Treatment of PMR, typically prednisone initiated at a dose of 10 to 20 mg/d, is warranted and should result in rapid resolution of symptoms. Prednisone can be tapered over a 6-month period in some patients, but others experience flares with tapering and require more prolonged therapy, for as long as 1 to 3 years. Methotrexate can be tried as a glucocorticoid-sparing agent, but studies suggest limited efficacy.

Low-dose aspirin (81 mg/d) may be useful to reduce ocular complications in patients with giant cell arteritis (GCA), which can co-occur with PMR; however, this patient has no signs or symptoms consistent with GCA such as jaw claudication, temporal headache, or visual loss.

Aspirin, 650 mg three times daily, functions in a manner similar to other traditional NSAIDs, with analgesic, anti-inflammatory, and antipyretic effects. However, like other NSAIDs, it is not a treatment for PMR and is not effective for this condition.

Duloxetine is a dual serotonin-norepinephrine reuptake inhibitor that is used as an antidepressant, to modulate pain due to fibromyalgia and other chronic central pain syndromes, and for chronic musculoskeletal pain. Although the patient has pain and a depressed affect—a common constellation in fibromyalgia—his pain is in a classic distribution for PMR and his depressed affect is common in patients with PMR pain. Since low-dose prednisone will likely be curative, duloxetine therapy should not be needed.

High-dose prednisone is indicated for GCA and severe or life-threatening forms of autoimmunity but carries a high rate of toxicity. This patient has no signs or symptoms of GCA or any other disease except PMR; therefore, high-dose prednisone is not warranted.

Question 45

A 45-year-old man is evaluated for a 2-week history of progressive pain and swelling of the third and fourth toes of the right foot. He has a rash on the soles of his feet that appeared 4 weeks ago. He reports no fever, back pain, chest pain, dyspnea, dysuria, diarrhea, ocular problems, oral ulcers, Raynaud phenomenon, psoriasis, or photosensitivity. He is sexually active. He takes no medications.

On physical examination, vital signs are normal. There is no nail pitting. Dactylitis and diffuse swelling of the right third and fourth toes are noted. The soles of the feet have yellow-brown vesicles and hyperkeratotic nodules with overlying keratotic crust. The remainder of the examination is normal.

Laboratory studies reveal an erythrocyte sedimentation rate of 35 mm/h; complete blood count with differential and urinalysis are normal.

Radiographs of the toes reveal diffuse soft-tissue swelling of the right third and fourth toes but are otherwise normal.

Which of the following is the most appropriate diagnostic test to perform next?

A
Anti–cyclic citrullinated peptide antibody assay

B
Antinuclear antibody assay

C
DNA amplification urine test for *Chlamydia trachomatis*

D
HLA-B27 testing

Answer & Critique

Correct Answer: C

Educational Objective: Diagnose chlamydia infection associated with reactive arthritis.

Key Point

Patients with reactive arthritis, even if asymptomatic, should be tested for chlamydia infection using a DNA amplification urine test.

The most appropriate diagnostic test to perform next is a DNA amplification urine test for *Chlamydia trachomatis*. This patient has a presentation consistent with reactive arthritis (oligoarticular lower extremity dactylitis, keratoderma blennorrhagicum). Up to 30% of patients with reactive arthritis develop keratoderma blenorrhagicum, a hyperkeratotic rash found on the soles and palms that may be indistinguishable from pustular psoriasis. Chlamydia infection is a common cause of reactive arthritis and is often asymptomatic. Patients with reactive arthritis, even if asymptomatic, should be tested for chlamydia because they may have persistent infection or carriage of this organism. If chlamydia is identified, these patients, as well as their partners, should receive treatment to prevent recurrence or transmission of infection. More studies are needed to determine whether antibiotics are helpful in treating arthritic symptoms. Antibiotics are not indicated for non–chlamydia-related reactive arthritis unless there is documentation of persistent infection because they have not been shown to alter the course of arthritis.

Anti–cyclic citrullinated peptide antibodies are associated with rheumatoid arthritis, which is characterized by a symmetric small joint polyarthritis typically without dactylitis. This patient does not have this typical presentation; therefore, testing for these antibodies is not indicated.

Antinuclear antibodies are associated with systemic lupus erythematosus (SLE); with the exception of arthritis, this patient has no clinical evidence of SLE, including alopecia, aphthous ulcers, pericardial and pleural serositis, kidney disease, rash, and cytopenias, and does not need to be tested for these antibodies.

Although many patients with reactive arthritis are positive for HLA-B27, it will not add any further value to the diagnosis or management. This patient has several typical features to establish a diagnosis of reactive arthritis, and management with anti-inflammatory medication for arthritis will be effective in the presence or absence of HLA-B27.

Question 46

A 52-year-old man is evaluated during a follow-up visit for a 2-year history of progressively symptomatic rheumatoid arthritis. He reports increased difficulty with his job due to persistent pain and swelling in the first proximal interphalangeal joints, second and third metacarpophalangeal joints, and bilateral wrists. He also has increased difficulty climbing stairs due to persistent pain and swelling in the right knee. Medications are methotrexate, 25 mg weekly; prednisone, 10 mg/d; naproxen; and folic acid.

On physical examination, vital signs are normal. There is 1+ tenderness to palpation and 1+ swelling of the affected joints.

Plain radiographs of the hands and wrists show periarticular osteopenia, multiple erosions, and carpal joint-space narrowing. Plain radiographs of the knees show medial and lateral joint-space narrowing.

Which of the following is the most appropriate next step in management?

A
Add etanercept

B
Add rituximab

C
Increase methotrexate

D

Increase prednisone

Answer & Critique

Correct Answer: A

Educational Objective: Treat inadequately controlled rheumatoid arthritis.

Key Point

In patients with inadequately controlled rheumatoid arthritis who are taking methotrexate, the addition of a tumor necrosis factor ? inhibitor is appropriate to improve signs and symptoms of disease.

Addition of a tumor necrosis factor (TNF)-? inhibitor such as etanercept is indicated for this patient with inadequately controlled rheumatoid arthritis (RA). He has been appropriately started on the recommended initial agent, methotrexate, with the dose appropriately titrated up because of continued disease activity. Symptomatic relief has been sought with the use of prednisone and naproxen, but he continues to have active synovitis. Because he has been given an appropriate dose of methotrexate for an adequate period of time, the most appropriate next step is to add a TNF-? inhibitor such as etanercept. TNF-? inhibitors remain the most widely used biologics for RA and are highly effective in the treatment of RA, leading to a 20% improvement in signs and symptoms of disease within weeks for over half of patients.

Rituximab is indicated for use in patients with moderate to severe RA who are also taking methotrexate but have not responded to TNF-? inhibitors. Having never been treated with a TNF-? inhibitor, it is most appropriate to add a TNF-? inhibitor to this patient's regimen rather than rituximab. Other biologics are available, and a number have different mechanisms of action and can be used in combination with methotrexate.

The patient has been on methotrexate since diagnosis and is taking a dose that would be expected to improve his symptoms; however, he continues to have significant disease activity. It is unlikely that continuing to increase the dose will adequately control his disease; this will also increase the risk of toxicity.

Increasing prednisone may offer short-term relief of flares in patients with RA. However, this patient has been on chronic glucocorticoids and high-dose methotrexate, yet continues to have a considerable amount of synovitis. Given the chronic nature of RA and need for long-term treatment, exposing patients to the numerous side effects associated with higher doses of glucocorticoids is not optimal. Furthermore, in this patient with known seropositive erosive

disease, therapy with disease-modifying agents is required, and prednisone does not halt bony destruction.

4Question 47

A 39-year-old man is evaluated for a lower extremity rash of 3 weeks' duration. He has no recent history of a cold, flu, or other infection. He takes no medications.

On physical examination, temperature is 37.3 °C (99.2 °F), blood pressure is 136/86 mm Hg, pulse rate is 66/min, and respiration rate is 12/min. BMI is 24. Small vascular infarctions are observed on the ears and fingertips. There are scattered palpable purpuric lesions on the bilateral lower extremities, which are less prominent on the soles. Strength is reduced in the right wrist.

Laboratory studies:

Erythrocyte sedimentation rate	66 mm/h
C3	Normal
C4	Decreased
Creatinine	2.1 mg/dL (185.6 µmol/L)
Rheumatoid factor	Positive
Hepatitis C antibodies	Positive, genotype 2
Serum protein electrophoresis	Monoclonal spike in IgG band
Urinalysis	Positive for erythrocytes, leukocytes, erythrocyte casts

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

A Anti–cyclic citrullinated peptide antibody levels
B Anti–glomerular basement membrane antibody levels
C Antinuclear antibody levels
D p-ANCA levels
E Serum cryoglobulin levels

Answer & Critique

Correct Answer: E

Educational Objective: Diagnose cryoglobulinemic vasculitis.

Key Point

Patients presenting with a multisystem vasculitic disease should be considered for cryoglobulinemia, particularly if the C4 is low, the C3 is relatively preserved, and rheumatoid factor is present.

Measurement of serum cryoglobulin levels is most likely to establish the diagnosis of cryoglobulinemic vasculitis. This patient presents with palpable purpura, glomerulonephritis (elevated serum creatinine, active urine sediment with cellular casts), mononeuritis, and skin infarctions of the fingers and ears. Although several vasculitic diseases may present with this picture, the presence of ear infarctions is most consistent with a diagnosis of cryoglobulinemia. Moreover, low C4 with a normal (or relatively unaffected) C3, in the presence of rheumatoid factor and a monoclonal paraprotein (the rheumatoid factor itself), is the classic pattern for cryoglobulinemic vasculitis. Thus, the test most likely to establish the diagnosis is a serum cryoglobulin level. Because more than 90% of patients with essential mixed cryoglobulinemia are infected with hepatitis C virus, this patient should be screened and treated for this infection.

Anti–cyclic citrullinated peptide antibodies are found in patients with rheumatoid arthritis (RA). Because this patient lacks arthritis, this diagnosis can be excluded, with the rheumatoid factor (also associated with RA) explained by the patient's cryoglobulinemia.

Anti–glomerular basement membrane antibodies can produce glomerulonephritis but would be less likely to cause the skin findings that are seen in this patient and would be inconsistent with the other serologies presented.

Antinuclear antibodies are present in nearly all patients with systemic lupus erythematosus, a disease of protean manifestations that could indeed present in this manner. However, the presence of a normal C3 with a low C4 is atypical in lupus.

p-ANCA is found in several forms of vasculitis, all of which may involve the kidneys and the skin. However, external auricular involvement is not classic, and the C4 is not reduced.

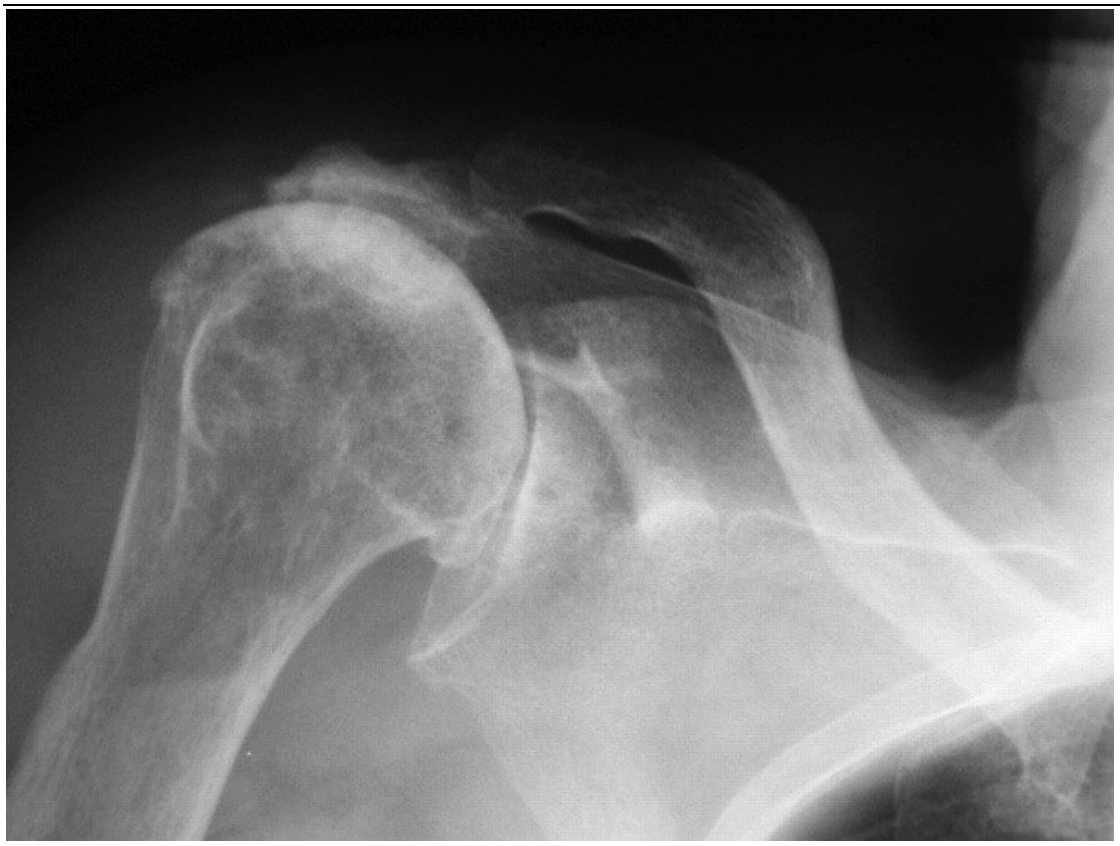
Question 48

A 71-year-old woman is evaluated during an office visit. Four months ago, she fell on an outstretched hand. During the next several weeks, she noted gradual pain, stiffness, and swelling of her right shoulder; the pain occurs with movement and at night. History is significant for knee osteoarthritis, gout, and hypertension. Medications are acetaminophen, colchicine, allopurinol, and lisinopril.

On physical examination, vital signs are normal. BMI is 25. The right shoulder has a large effusion without warmth or overlying erythema; range of motion is limited by pain and swelling, and prominent crepitus is palpable with motion.

Erythrocyte sedimentation rate, leukocyte count, C-reactive protein level, and serum urate level are within normal limits.

A radiograph of the shoulder is shown.



Aspiration of the right shoulder shows blood-tinged synovial fluid with a leukocyte count of 8300/µL (8.3×10^9/L); Gram stain is negative, and there are no crystals.

Which of the following is t he most likely diagnosis?

A
Acute calcium pyrophosphate crystal arthritis

B
Acute gouty arthritis

C
Basic calcium phosphate deposition

D
Infectious arthritis

Answer & Critique

Correct Answer: C

Educational Objective: Diagnose basic calcium phosphate deposition.

Key Point

Milwaukee shoulder syndrome, caused by basic calcium phosphate deposition, is characterized by pain, stiffness, and swelling that tend to occur gradually over time, often with a preceding trauma or history of overuse on the affected side, with a predilection for women older than the age of 70 years.

This patient has Milwaukee shoulder syndrome, caused by basic calcium phosphate deposition. Milwaukee shoulder syndrome is characterized by symptoms of pain, stiffness, and swelling that tend to occur gradually over time, often with a preceding trauma or history of overuse on the affected side; this entity is classically described in women over the age of 70 years. This patient has typical features of the syndrome, including a large effusion on examination and synovial fluid that is blood tinged with a low leukocyte count. The crystals are often not visible by routine light microscopy due to their small size, and they are not birefringent (hence, not appreciated with a polarizing microscope); however, they may be revealed with alizarin red staining (with crystals visualized as red, globular clumps). This patient's shoulder radiograph reveals narrowing of the glenohumeral joint, calcification of the periarticular cartilage, and erosive changes of the humeral head, all typical findings in this syndrome. Upward subluxation of the humeral head due to rotator cuff destruction and bony cysts are also common.

Acute calcium pyrophosphate crystal arthritis (also known as pseudogout) can lead to significant joint swelling; however, the absence of inflammatory synovial fluid makes this diagnosis unlikely.

This patient has a history of gout; however, her current symptoms are atypical for a gout attack, particularly the gradual onset of these symptoms. The synovial fluid is also very uncharacteristic for gout, which typically causes an inflammatory effusion. The absence of crystals in the synovial fluid further speaks against gout, although monosodium urate crystals are sometimes missed on synovial fluid analysis.

Monoarticular joint swelling must always raise suspicion for an infected joint; however, in this case, the slow onset of symptoms, lack of fever, and normal serum leukocyte count go against this

diagnosis. Synovial fluid with low leukocyte count and negative Gram stain also point away from a diagnosis of an infected joint.

Question 49

A 23-year-old woman is evaluated for a 1-week history of fevers, malaise, aches of her elbows and left knee, and pain of her wrists, hands, and ankles that is worse with movement. She has noticed transient skin lesions resembling pustules. She reports no urinary symptoms or vaginal discharge. She has no history of illicit drug use; she drinks alcohol socially and is sexually active. She has not traveled recently. Her only medication is an oral contraceptive.

On physical examination, the patient appears uncomfortable. Temperature is 38.3 °C (100.9 °F), blood pressure is 115/75 mm Hg, pulse rate is 95/min, and respiration rate is 12/min. BMI is 23. Ulnar deviation of the wrists while holding the thumbs down elicits pain over the radial side of the wrists (positive Finkelstein test). There is generalized swelling of several fingers with tenderness to palpation diffusely. The left knee is warm, with a small effusion and pain with range of motion. The ankles have tenderness to palpation over the posterior aspects, with erythema along the Achilles tendons and pain with range of motion bilaterally. There are a few scattered vesiculopustular lesions over the palmar aspect of the hands and upper extremities.

Laboratory studies reveal a leukocyte count of 13,500/μL (13.5×10^9/L) and normal kidney and liver chemistries.

Which of the following is most likely to provide the diagnosis?

A
Cervical culture

B
Hepatitis B serologies

C
Rapid streptococcal antigen testing

D
Synovial fluid analysis

Answer & Critique

Correct Answer: A

Educational Objective: Diagnose disseminated gonococcal infection.

Key Point

Blood cultures or cultures of the genitourinary tract or pharynx are useful diagnostic tests in the setting of bacteremia from disseminated gonococcal infection.

Cervical culture is the most appropriate diagnostic test to perform in this patient who most likely has disseminated gonococcal infection (DGI). DGI occurs in up to 3% of patients with *Neisseria gonorrhoeae*and can cause two distinct clinical presentations. In the setting of bacteremia from DGI, patients present with vesiculopustular or hemorrhagic macular skin lesions, fever, polyarthralgia, and tenosynovitis. Arthritis typically is nonpurulent, and synovial fluid cultures tend to be negative. Blood cultures or cultures of the genitourinary tract or pharynx are often positive. Therefore, a cervical culture is appropriate for this patient; cultures of the throat, skin, and rectum should also be ordered to maximize the chance of organism identification.

The second presentation of DGI is purulent arthritis without the rash or other features of gonococcal bacteremia. Synovial fluid cultures are often positive for *N. gonorrhoeae* in these patients. This patient does not exhibit these symptoms; therefore, synovial fluid analysis is unnecessary.

Hepatitis B virus infection can also present with arthralgia, fever, and rash; however, this patient's rash is not typical for hepatitis B, and her liver chemistry studies are normal. Hepatitis B serologies therefore will not be diagnostic.

A positive rapid streptococcal antigen test is helpful to diagnose acute rheumatic fever; however, this patient lacks the sore throat, characteristic rash, and other findings such as cardiac or neurologic involvement that are associated with acute rheumatic fever.

Question 50

A 26-year-old woman seeks preconception counseling. She has a 3-year history of rheumatoid arthritis. Medications are methotrexate, hydroxychloroquine, low-dose prednisone, and folic acid. Currently her disease is under excellent control.

On physical examination, vital signs are normal. There is no warmth, erythema, swelling, or tenderness of the joints.

Which of the following is the most appropriate next step in management?

A
Discontinue hydroxychloroquine

B
Discontinue methotrexate

C
Discontinue prednisone

D
Discontinue prednisone, methotrexate, and hydroxychloroquine

Answer & Critique

Correct Answer: B

Educational Objective: Manage rheumatoid arthritis medications in a patient of childbearing age.

Key Point

Women taking methotrexate must discontinue this medication 3 months prior to attempting to conceive.

Discontinuation of methotrexate is indicated for this patient with rheumatoid arthritis (RA) who is interested in becoming pregnant. This nonbiologic disease-modifying antirheumatic drug is both highly teratogenic and abortifacient and must be discontinued 3 months prior to attempting to conceive. Although this patient is taking folic acid to help reduce her incidence of methotrexate side effects, taking folic acid supplements during pregnancy can reduce the risk of certain neural tube birth defects. Therefore, she should not discontinue folic acid even if she discontinues methotrexate.

Considerable epidemiologic evidence in patients with systemic lupus erythematosus as well as RA supports the use of hydroxychloroquine during pregnancy. The risks to mothers and their fetuses appear low, particularly when balanced against the consequences of discontinuing treatment in anticipation of pregnancy. Greater disease activity during pregnancy is associated with small gestational age and preterm delivery. In addition, patients in whom all medications are stopped, including hydroxychloroquine, run the risk of flare, which can impair their physical functioning and make coping with pregnancy more difficult. No increases in adverse maternal or fetal outcomes have been observed in a number of studies in which hydroxychloroquine has been continued throughout pregnancy.

Low-dose glucocorticoids are frequently used but should be avoided if possible before 14 weeks of gestation because of the risk of cleft palate. Glucocorticoid use can contribute to gestational diabetes and hypertension. However, they can be useful in the management of RA in pregnancy if the benefit of treatment is thought to exceed risk.

Question 51

A 52-year-old man is evaluated for a 4-month history of slowly progressive unilateral proptosis. He reports enlargement of the glands under his jaw on both sides. He generally feels well and has no other medical problems. He takes no medications.

On physical examination, vital signs are normal. Marked proptosis of the left eye is noted; there is no inflammation of the sclerae or conjunctivae. There is bilateral enlargement of the lacrimal, parotid, and submandibular glands. There is an enlarged lymph node at the angle of the jaw on the right. The remainder of the examination is normal.

Laboratory studies include a normal complete blood count with differential, chemistry panel, liver chemistries, antinuclear antibody panel, and urinalysis.

MRI of the head and orbits demonstrates a homogeneous enhancing mass behind the left eye and enlargement of the parotid and submandibular glands. Biopsy of the ocular mass demonstrates a lymphoplasmacytic infiltrate with storiform fibrosis and obliterative phlebitis, rare neutrophils, and no granulomas; a monoclonal population of cells is not identified.

Which of the following is the most likely diagnosis?

9%

A

Hodgkin lymphoma

44%

B

IgG4-related disease

12%

C

Sarcoidosis

36%

D

Sjögren syndrome

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose IgG4-related disease.

Key Point

IgG4-related disease is characterized by the lymphoplasmacytic infiltration and enlargement of various structures, including the pancreas, lymph nodes, salivary glands, periaortic region leading to retroperitoneal fibrosis, kidneys, and skin.

The most likely diagnosis is IgG4-related disease, a recently described condition characterized by lymphoplasmacytic infiltration and enlargement of various structures, including the pancreas, lymph nodes, salivary glands, periaortic region leading to retroperitoneal fibrosis, kidneys, and skin. Most patients are men (60%-80%) over the age of 50 years. Typical presentation is the subacute development of a mass in the affected organ (for example, an orbital pseudotumor) or diffuse organ enlargement. Up to 90% of patients have multiple organ involvement. Lymphadenopathy is common, as is lacrimal and salivary gland involvement. Most patients lack constitutional symptoms at the time of diagnosis and generally feel well. Staining for IgG4-producing plasma cells reveals large numbers in the tissue.

Hodgkin lymphoma usually presents with palpable lymphadenopathy or a mediastinal mass that requires tissue biopsy for diagnosis. Biopsy is likely to show mainly clonal malignant Hodgkin/Reed-Sternberg cells in a background of granulocytes, plasma cells, and lymphocytes. Reed-Sternberg cells appear as large cells with large, pale nuclei containing large purple nucleoli, and their appearance is indicative of Hodgkin disease. The patient's biopsy findings are not consistent with Hodgkin lymphoma.

Sarcoidosis is a multisystem disease characterized by noncaseating granulomas that form in tissues and most commonly affects the lungs. The absence of granulomas on biopsy is helpful to distinguish IgG4-related disease from sarcoidosis.

Sjögren syndrome can present with enlargement of the salivary glands. However, it is associated with focal, centrilobular collections of lymphocytes on biopsy without the histology characteristic for IgG4-related disease present in this patient. Patients with Sjögren syndrome also usually have positive anti-Ro/SSA and anti-La/SSB antibodies, which are not present in this patient.

Question 52

A 58-year-old woman is evaluated for a 2-year history of hand pain and increasing difficulty using her hands. She reports worsening grip strength as well as increasing pain in the distal interphalangeal (DIP) and proximal interphalangeal (PIP) joints. She has intermittent erythema and swelling in some of these joints (such as the fifth DIP joint and the right second PIP and left third PIP joints) sometimes lasting for weeks at a time. She takes naproxen twice daily.

On physical examination, vital signs are normal. BMI is 29. Bony hypertrophy and malalignment of the DIP joints are noted; there is mild erythema over the right fifth DIP joint. There are bony hypertrophy of the PIP joints and swelling and tenderness of the right second PIP joint and the left third PIP joint. There is bony hypertrophy of the first carpometacarpal (CMC) joint bilaterally.

Laboratory studies, including a complete blood count, erythrocyte sedimentation rate, C-reactive protein, serum creatinine, rheumatoid factor, anti–cyclic citrullinated antibodies, and urinalysis, are normal.

Plain hand radiographs show central erosions and collapse of the subchondral bone in the right second PIP joint and the left third PIP joint; osteophytes at the second, third, and fifth DIP joints bilaterally; and joint-space narrowing at the first CMC joint bilaterally. There is no periarticular osteopenia or marginal erosions.

Which of the following is the most likely diagnosis?

A
Erosive osteoarthritis

B
Reactive arthritis

C
Rheumatoid arthritis

D
Tophaceous gout

Answer & Critique

Correct Answer: A

Educational Objective: Diagnose erosive osteoarthritis.

Key Point

In contrast to rheumatoid arthritis, erosive osteoarthritis is common in the distal interphalangeal and carpometacarpal joints, is associated with erosions that are centrally located in the joint and accompanied by proliferative changes, does not typically affect the wrists or elbows, and is not associated with inflammatory markers.

The most likely diagnosis is erosive osteoarthritis (OA). Distinguishing erosive OA from rheumatoid arthritis (RA) can be difficult because both diseases disproportionately affect women, are polyarticular, and preferentially affect the hand joints. Signs of inflammation (warmth, erythema, swelling, tenderness, reduced function) are present in both entities, although generally involving more joints for longer periods of time in RA. In contrast to RA, erosive OA is common in the distal interphalangeal and carpometacarpal joints, does not typically affect the wrists or elbows, and is not associated with rheumatoid factor, anti–cyclic citrullinated peptide antibodies, or an elevated erythrocyte sedimentation rate or C-reactive protein level. Both types of arthritis can lead to erosions seen on plain radiographs. In erosive OA, these erosions are centrally located in the joint and are accompanied by proliferative changes. In RA, erosions are located at the joint margins, and periarticular osteopenia is likely to be present.

Reactive arthritis is a noninfectious inflammatory arthritis that can occur after a gastrointestinal or genitourinary infection. It is not commonly associated with erosive changes on radiographs.

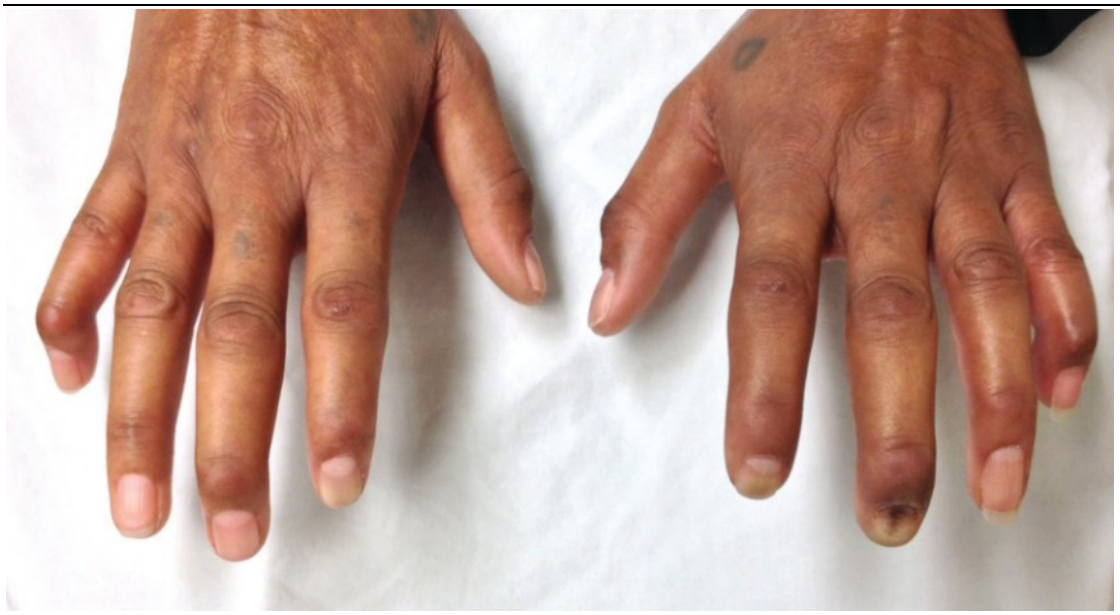
Tophaceous gout can occur in either gender and is more frequent in women after menopause. It can occasionally have a polyarticular presentation in the hands, but extensive disease is typically accompanied by the obvious presence of multiple tophi in the skin. When inflammation is evident, an acute gout flare is occurring in the presence of tophaceous gout. Tophi can occur in many locations and can create the appearance of erosions with overhanging edges in affected bones, which are sometimes found adjacent to joints. Highly destructive changes can occur that can lead to loss of joint space with long-standing tophaceous gout.

Question 53

A 44-year-old man is evaluated for a 2-month history of color change in the hands when exposed to the cold, finger skin tightness with palpable nodules, fatigue, and pruritus. He has no other medical problems and takes no medications or nutritional supplements.

On physical examination, vital signs are normal. BMI is 23. Skin thickening of the face and fingers is noted. There are a few firm, gritty nodules on the palmar aspect of the digits. There is no rash or digital pits.

The appearance of the hands is shown.



Which of the following is the most likely diagnosis?

A

Eosinophilia myalgia syndrome

B

Limited cutaneous systemic sclerosis

C

Morphea

D

Primary biliary cirrhosis

Correct Answer: B

Educational Objective: Diagnose limited cutaneous systemic sclerosis.

Key Point

Limited cutaneous systemic sclerosis is characterized by distal skin thickening (face, neck, and hands) and is typically not accompanied by internal organ fibrosis; patients may display features of the CREST (calcinosis cutis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia) syndrome.

The most likely diagnosis is limited cutaneous systemic sclerosis (LcSSc), a form of systemic sclerosis that is characterized by distal (face, neck, and hands) but not proximal skin thickening and is typically not accompanied by internal organ fibrosis. Patients with LcSSc may display features of the CREST (calcinosis cutis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia) syndrome and are more likely to develop Raynaud phenomenon early in the disease course. Pulmonary arterial hypertension is more common in patients with LcSSc compared with diffuse cutaneous systemic sclerosis. This patient presents with skin thickening involving the distal extremities and face as well as Raynaud phenomenon; he also has nodules on the extremities, which are suggestive of calcinosis cutis. A number of patients may present with only one or two clinical features, and negative serologies (including antinuclear antibodies) are seen in up to 10% to 25% of patients with LcSSc. He does not have CREST syndrome, which is a variant of LcSSc characterized by the presence of telangiectasias and esophageal dysmotility as well as positive antinuclear and anticentromere antibodies.

Eosinophilia myalgia syndrome is characterized by fasciitis and dermal induration linked to consuming contaminated L-tryptophan, a nutritional supplement. Patients also develop neuropathy and myopathy but not Raynaud phenomenon or scleroderma-specific autoantibodies. New cases are rare since the identification of the toxin several years ago. This patient consumes no nutritional supplements and has Raynaud phenomenon, making eosinophilia myalgia syndrome unlikely.

Morphea is characterized by a localized area of skin thickening, usually on the torso; systemic manifestations or Raynaud phenomenon is extremely rare in patients with this condition.

Primary biliary cirrhosis (PBC) is a chronic cholestatic liver disease of unknown cause affecting middle-aged women. Fatigue, dry eyes, dry mouth, and pruritus are the most common symptoms. Jaundice, cutaneous hyperpigmentation, hepatosplenomegaly, and xanthelasmas are rarely observed at diagnosis. Raynaud phenomenon and skin thickening are not consistent with PBC.

Question 54

A 42-year-old woman is evaluated for a 6-month history of pain and swelling of several small hand joints, an elbow, and an ankle. She gets modest relief with naproxen. She has no other medical problems and takes no additional medications.

On physical examination, vital signs are normal. There are tenderness to palpation and swelling of the second and third proximal interphalangeal joints bilaterally, second and fifth metacarpophalangeal joints bilaterally, left wrist, right elbow, and right ankle. The remainder of the physical examination is normal.

Laboratory studies are significant for a rheumatoid factor of 85 U/mL (85 kU/L) and positive anti–cyclic citrullinated peptide antibodies.

Radiographs of the hands and wrists show periarticular osteopenia at the metacarpophalangeal joints and a marginal erosion at the right second metacarpal head.

Which of the following is the most appropriate initial treatment?

A
Hydroxychloroquine

B
Methotrexate

C
Rituximab

D
Tofacitinib

Answer & Critique

Correct Answer: B

Educational Objective: Treat rheumatoid arthritis with methotrexate.

Key Point

Methotrexate is the initial treatment of choice for patients with new-onset, rapidly progressive, or erosive rheumatoid arthritis.

Treatment with methotrexate is indicated for this patient with rheumatoid arthritis (RA). She has a polyarticular inflammatory arthritis involving the small joints of the hands as well as a wrist and an ankle, with radiographically demonstrated marginal erosions and periarticular osteopenia and positive anti–cyclic citrullinated peptide antibodies and rheumatoid factor, all of which support a diagnosis of RA. Methotrexate with or without the addition of another disease-modifying antirheumatic drug (DMARD) should be instituted immediately in patients with erosive disease documented at disease onset. Methotrexate is the gold standard therapy because it is usually better tolerated than other DMARDs and has good efficacy, long-term compliance rates, and relatively low cost.

Hydroxychloroquine is indicated to treat early, mild, and nonerosive disease. Hydroxychloroquine therapy alone has not been shown to retard radiographic progression of RA and therefore should be used only in patients whose disease has remained nonerosive for several years. This patient has erosive disease, and hydroxychloroquine as a single agent is not appropriate.

Rituximab, the anti-CD20 B-cell depleting monoclonal antibody, is FDA approved for the treatment of moderately to severely active RA in combination with methotrexate in patients who have had an inadequate response to tumor necrosis factor ? inhibitor therapy. Rituximab may also be considered for patients with high disease activity and poor prognostic features despite sequential nonbiologic DMARDs or methotrexate in combination with other DMARDs. It is not appropriate initial treatment for RA in a patient who has not been given a trial of methotrexate.

Tofacitinib is also indicated for use in the management of RA but only in patients who have already not responded to methotrexate alone. This relatively recent addition to the treatment armamentarium for RA is the first oral agent to be introduced in decades but is indicated for use in patients who are intolerant to or have had an inadequate response to methotrexate.

Question 55

A 40-year-old woman is evaluated for a 7-year history of color changes associated with pain that occurs in her fingers. Her second and third fingertips turn white in the cold, then become blue, and eventually become dark red and painful. These symptoms last approximately 15 minutes before resolving. She also reports a 3-month history of pain and swelling in the second and third metacarpophalangeal joints. History is also significant for dry eyes and dry mouth of 5 years' duration as well as recent onset of diffusely puffy hands and increasing fatigue. She reports no gastrointestinal symptoms, including gastroesophageal reflux disease. She takes no medications.

On physical examination, vital signs are normal. No rash or oral ulcers are noted. Slightly cool, diffusely edematous fingers are noted. Scattered palmar telangiectasias are present. There is swelling and tenderness of the second and fourth metacarpophalangeal joints.

Laboratory studies:

C3	Normal
C4	Normal
Creatine kinase	596 U/L
Creatinine	Normal
Antinuclear antibodies	Positive (titer: 1:320)
Anti–double-stranded DNA antibodies	Negative
Anti-Ro/SSA antibodies	Negative
Anti-La/SSB antibodies	Negative
Anti-Scl-70 antibodies	Negative
Anti-Smith antibodies	Negative
Anti-U1-ribonucleoprotein antibodies	Positive
Urinalysis	Negative

Which of the following is the most likely diagnosis?

A
Mixed connective tissue disease

B
Polymyositis

C
Systemic lupus erythematosus

D
Systemic sclerosis

E
Undifferentiated connective tissue disease

Answer & Critique

Correct Answer: A

Educational Objective: Diagnose mixed connective tissue disease.

Key Point

Mixed connective tissue disease is an overlap syndrome that includes features of systemic lupus erythematosus, systemic sclerosis, and/or polymyositis in the setting of positive anti-U1-ribonucleoprotein antibodies.

The most likely diagnosis is mixed connective tissue disease (MCTD), an overlap syndrome that includes features of systemic lupus erythematosus (SLE), systemic sclerosis, and/or polymyositis in the setting of positive anti-U1-ribonucleoprotein (RNP) antibodies. Patients with MCTD must have positive anti-U1-RNP antibodies and at least three of the following five features: Raynaud phenomenon, edema of the hands, sclerodactyly, synovitis, and myositis. Patients with MCTD usually have positive antinuclear antibodies (ANA), negative anti–double-stranded DNA antibodies, normal complement levels, and a low incidence of kidney disease. These criteria have a sensitivity of 63% and specificity of 86% in the diagnosis of MCTD. These patients are more likely to have myositis and pulmonary hypertension, an important cause of mortality, than patients with SLE.

Polymyositis is a form of inflammatory myopathy characterized by symmetric proximal muscle weakness with little or no pain, and muscle enzymes such as creatine kinase are usually elevated 10- to 50-fold the upper limit of normal. However, polymyositis is not associated with anti-U1-RNP antibodies and does not result in puffy hands or sicca symptoms.

Although the patient has a positive ANA, the diagnosis of SLE is less likely in the context of the negative anti-Smith and anti–double-stranded DNA antibodies as well as the normal complement levels, serum creatinine, and urinalysis.

The absence of sclerodactyly, sclerodermatous skin changes, and esophageal involvement makes systemic sclerosis an unlikely diagnosis.

Undifferentiated connective tissue disease (UCTD) is not an overlap syndrome but instead refers to nonspecific clinical features (such as Raynaud phenomenon and arthralgia), no disease-specific findings, and nonspecific positive autoantibodies (such as ANA). UCTD may exist for some time

prior to a clear emergence of symptoms characteristic enough to define a single rheumatologic disease.

Question 56

A 28-year-old woman is evaluated in the emergency department for a 1-day history of progressive shortness of breath, cough, and hemoptysis. She reports a fever but no chills. She has a 2-year history of systemic lupus erythematosus. Medications are mycophenolate mofetil, hydroxychloroquine, prednisone, naproxen as needed, vitamin D, and calcium.

On physical examination, temperature is 38.9 °C (102.0 °F), blood pressure is 100/60 mm Hg, pulse rate is 110/min, and respiration rate is 24/min. Oxygen saturation is 88% on ambient air. BMI is 29. Diffuse hair thinning is noted. A malar rash is present. There is symmetric swelling of metacarpophalangeal and proximal interphalangeal joints as well as both wrists and knees. There are no cardiac rubs or murmurs. Diffuse crackles are heard on lung auscultation.

Laboratory studies:

Hematocrit	22% (30% in office 1 week ago)
Leukocyte count	3200/µL (3.2×10^9/L)
Platelet count	90,000/µL (90×10^9/L)
Creatinine	1.3 mg/dL (115 µmol/L)
Urinalysis	3+ blood; 2+ protein; erythrocyte casts

Chest radiograph reveals diffuse bilateral pulmonary infiltrates with sparing of the apices.

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

A
Bronchoalveolar lavage and biopsy

B
Chest CT

C
MRI of the chest

D
Pulmonary angiography

Answer & Critique

Correct Answer: A

Educational Objective: Diagnose diffuse alveolar hemorrhage in a patient with systemic lupus erythematosus.

Key Point

The triad of hypoxemia, new pulmonary infiltrates on chest radiograph, and decreasing hematocrit is highly predictive of underlying diffuse alveolar hemorrhage associated with systemic lupus erythematosus.

Bronchoscopy with bronchoalveolar lavage (BAL) and biopsy is the most appropriate diagnostic test to perform next in this patient with suspected diffuse alveolar hemorrhage (DAH), a rare but severe manifestation of systemic lupus erythematosus (SLE). The triad of hypoxemia, new infiltrates found on chest radiograph, and decreasing hematocrit is highly predictive of underlying DAH; only about 50% of patients have hemoptysis. DAH occurs in the setting of active SLE, and up to 90% of patients have evidence of nephritis. Chest radiograph demonstrates bilateral infiltrates often sparing the lung apices. Diagnosis is by BAL during bronchoscopy to demonstrate bleeding and rule out infection. Lung biopsy is the definitive diagnostic test, which typically shows a capillaritis with immune complex deposition. Mechanical ventilation and aggressive immunosuppression are generally required, but mortality rates still are as high as 70%.

Although DAH can be suggested by the presence of ground-glass opacities on chest CT, the diagnosis is established only with bronchoalveolar lavage and biopsy.

MRI of the chest can be used to determine if the infiltrates are blood and could be used in rare cases in which bronchoalveolar lavage and biopsy are unable to be done.

Because DAH is typically a pulmonary capillaritis, angiography will not image vessels of this size and will not be useful in establishing the diagnosis.

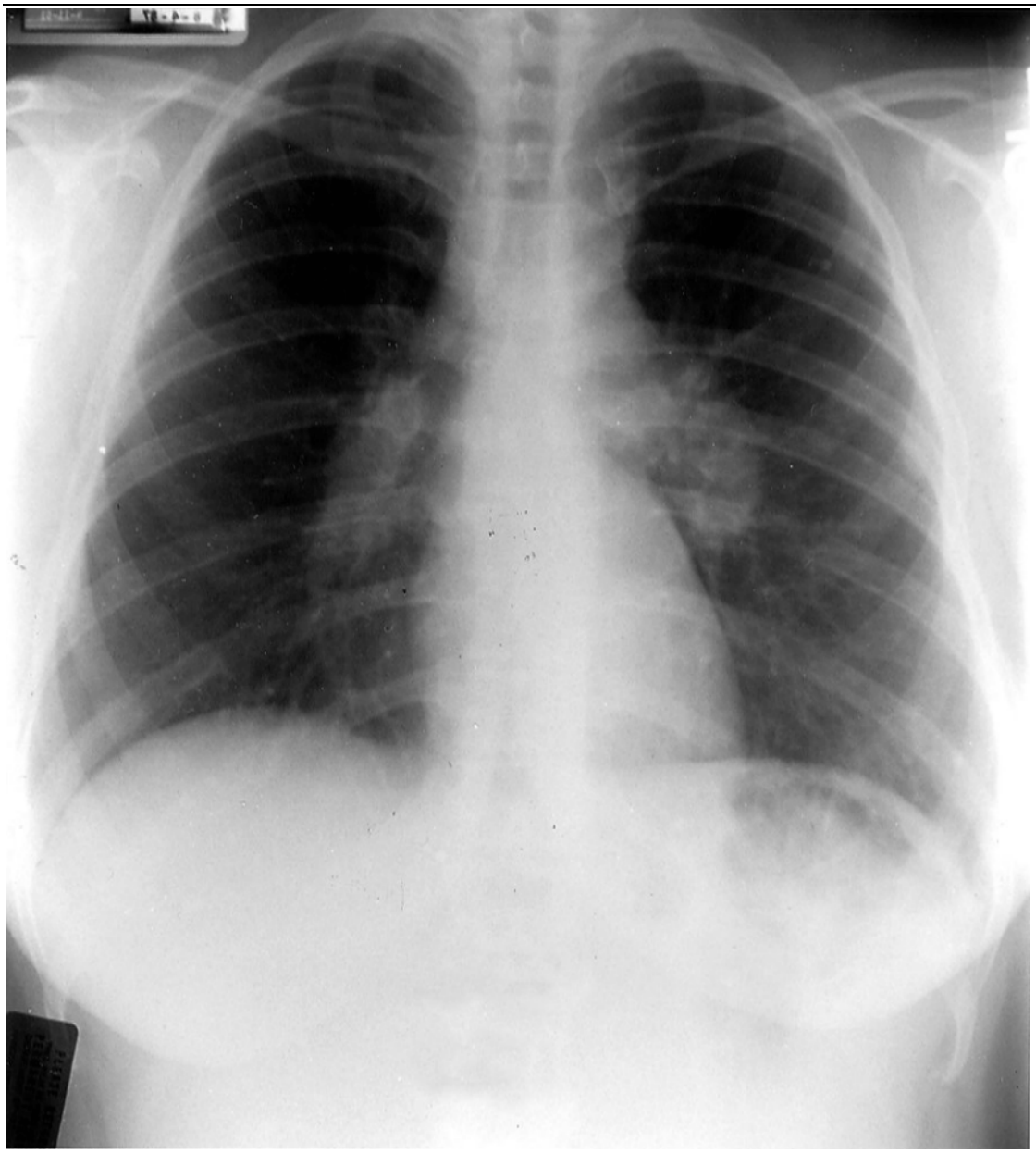
Question 57

A 24-year-old woman is evaluated for a 1-week history of tender nodules over the legs about 2 to 3 cm in size along with pain and stiffness in the ankles. She also notes a nonproductive cough of 3 days' duration. Her only medication is an oral contraceptive.

On physical examination, temperature is 38.4 °C (101.1 °F), blood pressure is 110/65 mm Hg, pulse rate is 85/min, and respiration rate is 18/min. BMI is 24. There are four 3-cm erythematous tender nodules on the left anterior lower leg and three on the right. Swelling of both ankles with tenderness at the right Achilles tendon insertion into the calcaneus is noted; no other joints are swollen. Cardiopulmonary examination is normal.

Laboratory studies reveal an erythrocyte sedimentation rate of 38 mm/h and a hematocrit of 35%; leukocyte and platelet counts are normal.

A chest radiograph is shown.



Which of the following is the most appropriate treatment?

A

Adalimumab

B

High-dose prednisone

C

Methotrexate

D

Naproxen

Answer & Critique

Correct Answer: D

Educational Objective: Treat a patient who has Löfgren syndrome.

Key Point

Löfgren syndrome is a self-limiting form of sarcoidosis characterized by acute arthritis, bilateral hilar lymphadenopathy, and erythema nodosum.

An NSAID such as naproxen is appropriate for this patient who has Löfgren syndrome, a self-limiting form of sarcoidosis characterized by a triad of acute arthritis in combination with bilateral hilar lymphadenopathy and erythema nodosum. The “arthritis” associated with Löfgren syndrome is actually a nondestructive periarthritis of the soft tissue, entheses, and tenosynovium around the joints. Symmetric involvement of the ankles is classic, but knees, wrists, and elbows can also be involved. Ninety percent of patients remit within 12 months. When the triad of features occurs, it has a 95% specificity for diagnosis, and further diagnostic tests (such as radiography or serologic testing) are unnecessary. This patient presents with the classic triad of hilar lymphadenopathy, erythema nodosum, and acute arthritis involving the ankles and therefore has Löfgren syndrome. Erythema nodosum may occur in association with a wide array of causes, including infections, medications, and systemic disease, or it may be idiopathic. Sarcoidosis and inflammatory bowel disease are the most frequently associated systemic diseases. The lesions of erythema nodosum are tender, subcutaneous nodules presenting as barely appreciable convexities on the skin surface, with a reddish hue in the acute phase. As the lesions resolve, a dull brown circular patch is often left behind. Erythema nodosum is frequently bilateral and symmetric, and it usually occurs on the distal lower extremities. Löfgren is more common among Europeans. Initial treatment is generally with NSAIDs (such as naproxen), colchicine, or low-dose prednisone.

Methotrexate, high-dose prednisone, or a tumor necrosis factor ? inhibitor such as adalimumab are reserved for patients with chronic, organ-damaging forms of sarcoidosis.

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Question 58

A 35-year-old man is evaluated for a 4-week history of persistent pain and swelling in the left knee and right ankle. Symptoms are worse in the morning and associated with stiffness lasting 1 hour. Ibuprofen is beneficial. Seven weeks ago he had diarrhea that lasted one week and resolved without treatment. One week ago he was diagnosed with anterior uveitis, which is resolving with a prednisolone ophthalmic solution. He reports no current gastrointestinal or genitourinary symptoms, rash, or cardiorespiratory symptoms.

On physical examination, vital signs are normal. Slightly injected sclera of the right eye is noted. There are swelling, warmth, and tenderness of the right knee joint. Tenderness and swelling at the right Achilles tendon insertion to the calcaneus are noted. There is no rash or nail pitting. The remainder of the physical examination is normal.

Laboratory studies done at the time of the visit:

Complete blood count with differential	Normal
Erythrocyte sedimentation rate	30 mm/h
Stool cultures	Negative
Urinalysis	Normal
DNA amplification urine test for *Chlamydia trachomatis*	Negative

Aspiration of the left knee is performed; synovial fluid analysis reveals a leukocyte count of 15,000/µL (15 × 10^9/L) with 70% monocytes and no crystals. Gram stain is negative, and cultures are pending.

Radiographs of the knee and ankle are normal.

Which of the following is the most likely diagnosis?

A
Infectious arthritis

B
Psoriatic arthritis

C
Reactive arthritis

D
Rheumatoid arthritis

Answer & Critique

Correct Answer: C

Educational Objective: Diagnose reactive arthritis.

Key Point

Reactive arthritis can occur after a gastrointestinal or genitourinary infection and is characterized by an asymmetric monoarthritis or oligoarthritis in the lower extremities as well as enthesopathy, dactylitis, and sacroiliitis.

The most likely diagnosis is reactive arthritis (formerly known as Reiter syndrome), a noninfectious inflammatory arthritis that can occur approximately 3 to 6 weeks after a gastrointestinal or genitourinary infection. It is common for infection to have resolved and stool culture to become negative by the time arthritis begins. Asymmetric monoarthritis or oligoarthritis in the lower extremities is the most common presentation, but up to 20% of patients have polyarthritis. Enthesopathy (inflammation at the site where ligaments, tendons, joint capsule or fascia attaches to bone), dactylitis, and sacroiliitis may occur. Erosive disease is uncommon. Ophthalmologic inflammation is a feature of this disease in up to 30% of patients and can manifest as uveitis or conjunctivitis. This patient's manifestations, including a diarrheal illness that preceded the onset of arthritis by 2 to 3 weeks, inflammatory oligoarticular involvement of lower extremities, inflammation of the insertion of the Achilles tendon, and anterior uveitis, are typical of reactive arthritis.

In bacterial infections, synovial fluid analysis typically reveals a neutrophilic leukocytosis (typically >50,000/µL [50 × 10^9/L]), but synovial fluid leukocyte counts ?50,000/µL (50 × 10^9/L) do not definitively rule out infection. In this patient, infectious arthritis is less likely because this patient has no fever or leukocytosis on complete blood count.

Although psoriatic arthritis can present as an oligoarthritis, it is also less likely because the patient has no evidence of psoriasis on physical examination.

Rheumatoid arthritis is unlikely because it usually is a symmetric small joint polyarthritis rather than large joint oligoarthritis, and enthesopathy is not common.

Question 59

A 68-year-old man is evaluated during a follow-up visit for long-standing tophaceous gout that caused almost monthly gout flares. Five months ago, colchicine and allopurinol were initiated. He reached his serum urate goal (<6.0 mg/dL [0.35 mmol/L]) within 3 months of starting therapy, and he has not had a gout flare since reaching this target. He has not developed any new tophi; his original tophi on his hands and elbows have begun to shrink in size. History is also significant for hypertension, for which he takes losartan.

On physical examination, temperature is 37.2 °C (98.9 °F), blood pressure is 133/79 mm Hg, pulse rate is 79/min, and respiration rate is 12/min. BMI is 28. A moderate-sized tophus is visible on the right elbow as well as two small tophi on different distal interphalangeal joints. There is no swelling or tenderness to palpation of any joints.

Current laboratory studies reveal a serum urate level of 5.4 mg/dL (0.32 mmol/L) and normal kidney and liver chemistries.

Which of the following is the most appropriate next step in management?

A
Add probenecid

B
Change allopurinol to febuxostat

C
Continue colchicine and allopurinol

D
Discontinue colchicine

Answer & Critique

Correct Answer: C

Educational Objective: Treat tophaceous gout.

Key Point

In patients with gout, continuation of flare prophylaxis and urate-lowering therapy is currently indicated if there is any evidence of active disease, including flares or tophi.

Continuation of colchicine for flare prophylaxis and allopurinol for urate lowering is indicated for this patient with tophaceous gout. He is having a good response to colchicine and allopurinol, with a serum urate level currently at the target goal of less than 6.0 mg/dL (0.35 mmol/L), resolution of flares, and reduction in size of tophi (reservoirs of monosodium urate). The American College of Rheumatology currently recommends continuation of flare prophylaxis if there is any evidence of active disease, including flares or tophi as seen in this patient. Hence, both agents should be continued at this time. The guidelines further suggest that in the absence of active disease and once target serum urate is reached, colchicine should be continued for the longer of the following: 6 months; 3 months after reaching target serum urate in a patient without baseline tophi; or 6 months after reaching target serum urate in a patient with baseline tophi that have resolved.

Changing this patient's urate-lowering regimen by adding probenecid or changing allopurinol to febuxostat is unnecessary in this patient who has reached the target serum urate level by taking allopurinol. His gout symptoms have improved, and the tophi have begun to shrink in size. If he was not at goal or was having ongoing flares or resistance of tophi to dissolve on his current regimen, options would be to further increase allopurinol, switch to febuxostat (a newer, more expensive xanthine oxidase inhibitor), or add probenecid.

Colchicine should be maintained at daily dosing because the patient still needs ongoing protection against flares, given the presence of tophi.

Question 60

A 27-year-old man is evaluated for a 2-year history of ankylosing spondylitis. Symptoms were initially responsive to physical therapy and naproxen; however, for the past 6 months he has experienced increasing back and buttock pain and stiffness, with difficulty bending downward. One month ago naproxen was discontinued, and indomethacin was initiated but with no improvement.

On physical examination, vital signs are normal. BMI is 25. Tenderness to palpation over the sacroiliac joints and lower lumbar spine is noted. There is limited range of motion of the lumbar spine manifested by an increase of 1 cm of change on forward flexion.

Laboratory studies reveal an erythrocyte sedimentation rate of 40 mm/h.

In addition to continuing physical therapy, which of the following is the most appropriate treatment?

A
Adalimumab

B
Methotrexate

C
Rituximab

D
Sulfasalazine

Answer & Critique

Correct Answer: A

Educational Objective: Treat ankylosing spondylitis with a tumor necrosis factor ? inhibitor.

Key Point

In patients with ankylosing spondylitis, treatment with a tumor necrosis factor ? inhibitor is currently recommended if first-line therapy with NSAIDs is inadequate.

Treatment with adalimumab is appropriate for this patient with ankylosing spondylitis, a form of spondyloarthritis that predominantly affects the axial skeleton. Inflammatory back pain is a hallmark feature, manifesting as pain and stiffness in the spine that is worse after immobility and better with use. Symptoms are prominent in the morning and can be symptomatic during the night. Buttock pain is common and correlates with sacroiliitis. Fusion of the spine may occur over time, leading to rigidity and kyphosis. Exercise to preserve range of motion and strengthen the spine extensor muscles to prevent kyphosis is essential. Physical therapy may be indicated to assist patients in developing a home exercise routine. NSAIDs are considered first-line therapy for symptomatic patients. If the patient does not adequately respond to a minimum of two different trials of NSAIDs used at least 4 weeks total, the Assessment of SpondyloArthritis international Society/European League Against Rheumatism (ASAS/EULAR) guidelines recommend treatment with a tumor necrosis factor (TNF)-? inhibitor. This patient has not adequately responded to either naproxen or indomethacin; therefore, a TNF-? inhibitor such as adalimumab is appropriate. The currently available TNF-? inhibitors appear to be equally effective when compared with placebo. Response is rapid, often within the first 6 weeks of therapy. Patients who do not respond to one agent may respond to an alternative. Because long-term safety is unknown, TNF-? inhibitors remain second-line therapy to NSAIDs.

Nonbiologic disease-modifying antirheumatic drugs (DMARDs) such as methotrexate and sulfasalazine have not been demonstrated to be efficacious for axial disease but may be considered for peripheral arthritis.

Rituximab is a biologic DMARD used to treat moderate to severe rheumatoid arthritis in combination with methotrexate in patients who have had an inadequate response to TNF-? inhibitor therapy and is also used in ANCA-associated vasculitis. There is no evidence showing benefit of this agent in ankylosing spondylitis.

Question 61

A 28-year-old woman is evaluated for a 2-week history of left hip pain that occurs at night and with walking. She has a 1-year history of systemic lupus erythematosus with class IV nephritis. Treatment has included prednisone as high as 60 mg/d and cyclophosphamide. Current medications are mycophenolate mofetil, hydroxychloroquine, prednisone, furosemide, lisinopril, calcium, and vitamin D.

On physical examination, vital signs are normal. BMI is 26. She has a cushingoid appearance. There is pain on internal rotation of the left hip. There is no pain on hip adduction or with pressure over the lateral hip. The remainder of the examination is normal.

Laboratory studies reveal an erythrocyte sedimentation rate of 18 mm/h, normal complement (C3 and C4) levels, and stable anti–double-stranded DNA antibodies.

Anterior-posterior pelvis and lateral left hip radiographs are normal.

Which of the following is the most appropriate diagnostic test to perform next?

A

CT of the left hip

B

MRI of the left hip

C

Repeat plain radiography in 1 month

D

Ultrasonography of the left hip

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose acute osteonecrosis in a patient with systemic lupus erythematosus.

Key Point

Patients with systemic lupus erythematosus who have pain or limitation of motion of the large joints, especially the hips, should be evaluated for osteonecrosis using MRI when plain radiographs are normal.

MRI of the left hip is the most appropriate diagnostic test to perform next in this patient with systemic lupus erythematosus (SLE) who has symptoms associated with osteonecrosis. Patients with SLE who have pain or limitation of motion of the large joints, especially the hips, should be evaluated for osteonecrosis. MRI is the best method for detecting early bone edema caused by osteonecrosis when plain radiographs are normal. MRI can also be prognostic: If more than 20% of the femoral volume demonstrates necrosis and edema on MRI, progressive disease (subchondral fracture and femoral head collapse) is the rule, whereas smaller infarcts rarely progress. Up to 37% of patients with SLE may have osteonecrosis by serial MRI monitoring, although less than 10% become symptomatic. Cushingoid features indicate a risk for osteonecrosis because enlargement of fat cells in the face is a marker for enlargement of fat cells in the ends of long bones. Increased adipose volume causes compression of small sinusoidal vessels that leads to interosseous hypertension and impairment of arterial inflow. Use of daily oral prednisone more than 20 mg/d for 4 to 6 weeks is also a risk factor, whereas use of intravenous glucocorticoids may not have the same risk. This patient has hip pain, cushingoid features, and recent use of high-dose prednisone, all indicators that she should be evaluated for osteonecrosis despite the normal hip radiograph.

MRI remains the gold standard to diagnose osteonecrosis. CT is less sensitive than MRI and exposes the patient to unnecessary radiation.

Plain radiography may not detect changes of osteonecrosis for several months following the onset of symptoms. Early radiographic findings include bone density changes, sclerosis, and, eventually, cyst formation. Subchondral radiolucency producing the “crescent sign” indicates subchondral collapse. End-stage disease is characterized by collapse of the femoral head, joint-space narrowing, and degenerative changes.

Ultrasonography can be used to evaluate for trochanteric bursitis as the cause of lateral hip pain but would not be useful to check for osteonecrosis. Trochanteric bursitis can be confirmed in patients in whom hip adduction intensifies the pain or in those in whom the examination reveals pain and tenderness over the bursa. Pain at night is present when the patient sleeps on the

affected side.

Question 62

A 58-year-old woman is evaluated in the hospital for a 3-month history of fatigue and a 4.5-kg (10-lb) weight loss. She also has dermatomyositis that was diagnosed 1 year ago, at which time she underwent detailed evaluation for myopathy and age-appropriate malignancy screening. She has also noticed worsening muscle weakness and rash in the past 2 weeks.

On physical examination, temperature is normal, blood pressure is 148/94 mm Hg, pulse rate is 90/min, and respiration rate is 16/min. BMI is 27. Cardiac and pulmonary examinations are normal. Abdominal examination reveals ascites without organomegaly. There is symmetric weakness of the arm and thigh muscles. A violaceous rash is present on the extensor surface of the metacarpophalangeal joints. A few areas of palpable purpura on the lower extremities are noted.

Laboratory studies:

Complete blood count	Normal
Chemistry panel	Normal
Aldolase	31 U/L (normal range, 1.0-8.0 U/L)
Aspartate aminotransferase	98 U/L
Creatine kinase	1400 U/L
Antinuclear antibodies	Titer of 1:640
Urinalysis	Normal

Which of the following is the most appropriate diagnostic test to perform next?

A

Chest CT with contrast

B Liver biopsy

C PET scan

D Thigh muscle MRI

E Transvaginal pelvic ultrasonography

Answer & Critique

Correct Answer: E

Educational Objective: Diagnose ovarian cancer in a patient with dermatomyositis.

Key Point

The risk of ovarian cancer may be especially increased in women with dermatomyositis.

Transvaginal pelvic ultrasonography is indicated for this patient with dermatomyositis, which may be associated with an underlying malignancy, especially in the first 2 years after diagnosis. Malignancy risk may also be higher in the presence of vasculitis (as seen in this patient) or cutaneous necrosis as well as in patients who are of older age at onset. Patients with dermatomyositis have an increased standardized incidence ratio of solid malignancies such as adenocarcinomas of the lung, cervix, ovaries, pancreas, colorectal, stomach, and bladder as well as non-Hodgkin lymphoma. Risk of ovarian cancer may be especially increased. In a population-based study, the standardized incidence ratio was 10.5 for ovarian cancer, highest among all cancers diagnosed. Therefore, obtaining a transvaginal pelvic ultrasonography to look for ovarian pathology, especially ovarian cancer, is recommended for this patient who has worsening dermatomyositis and new-onset ascites on examination.

Chest CT is helpful in diagnosing interstitial lung disease in patients with myositis and in evaluating malignancy; however, this patient has no evidence of respiratory symptoms but does have new-onset ascites, making ovarian cancer a more likely diagnosis.

Although this patient has elevated aspartate aminotransferase, it is likely of muscle origin and abnormal due to active myositis. Liver biopsy is not needed prior to obtaining other noninvasive studies for her abnormal liver chemistry tests and evaluation for ovarian cancer.

The diagnosis of advanced ovarian cancer is usually made by CT- or ultrasound-guided biopsy of a suspicious mass or cytologic examination of ascitic fluid. PET scan is likely to show abnormalities in her abdomen but will not lead to the correct diagnosis and is not cost-effective.

Thigh muscle MRI with specialized (STIR protocol) images may show evidence of actively involved muscle with myositis and support the diagnosis of dermatomyositis. However, this study

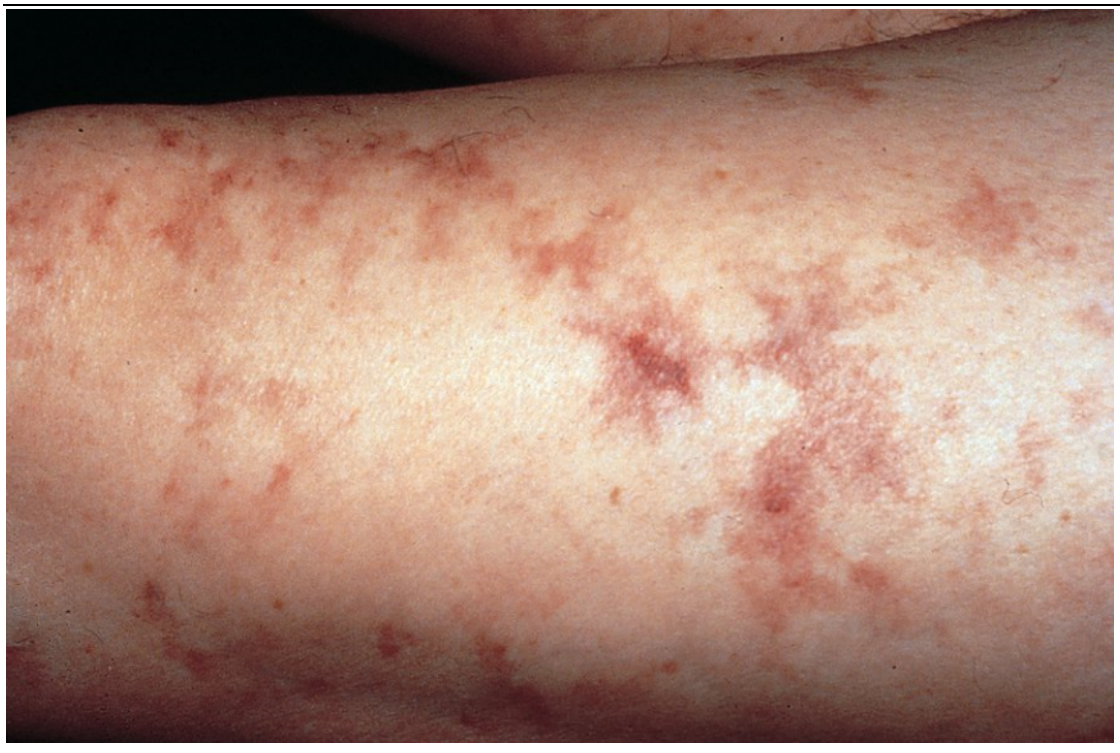
is not needed in this patient who already has been diagnosed with dermatomyositis and has evidence of the classic rash, weakness, and elevated muscle enzymes.

Question 63

A 52-year-old man is evaluated in the hospital for fever, malaise, arthralgia, left foot drop, abdominal pain that is worse after eating, and a 4.5-kg (10-lb) weight loss, all of which gradually developed over the past 2 months.

On physical examination, temperature is 38.4 °C (101.1 °F), blood pressure is 154/92 mm Hg, pulse rate is 76/min, and respiration rate is 18/min. BMI is 29. There is no temporal or sinus tenderness. The nasal passages and oropharynx are normal. The chest is clear. An abdominal bruit is heard on the right, inferior to the costal margin. The abdomen is otherwise normal. The testicles are tender to palpation. The joints are tender to palpation without synovitis. Weakness of the left foot to dorsiflexion is noted.

The appearance of the trunk and thighs is shown.



Laboratory studies:

Erythrocyte sedimentation rate	72 mm/h
Complements (C3 and C4)	Normal

Creatinine	2.2 mg/dL (194.5 µmol/L)
IgA	Normal
Hepatitis B surface antigen	Positive
Hepatitis B surface antibodies	Negative
Hepatitis C antibodies	Negative
ANCA	Negative
Urinalysis	Negative

Chest radiograph is unremarkable. Abdominal angiogram shows aneurysms and stenoses of the mesenteric and renal arteries.

Which of the following is the most likely diagnosis?

A
Goodpasture syndrome

B
Granulomatosis with polyangiitis

C
Henoch-Schönlein purpura

D
Polyarteritis nodosa

Answer & Critique

Correct Answer: D

Educational Objective: Diagnose polyarteritis nodosa.

Key Point

Patients with polyarteritis nodosa typically present with fever, arthralgia, myalgia, skin findings, abdominal pain, weight loss, and peripheral nerve manifestations, most commonly mononeuropathy or mononeuritis multiplex.

The most likely diagnosis is polyarteritis nodosa (PAN), the most common medium-sized vasculitis that affects the mesenteric and renal arteries. Patients usually present with nonspecific inflammatory symptoms as well as abdominal symptoms (chronic or intermittent ischemic pain), neurologic involvement (mononeuritis multiplex), and skin findings (livedo reticularis, purpura, and painful subcutaneous nodules). Kidney disease is based on decreased renal artery blood flow rather than glomerulonephritis. The presence of hepatitis B virus (HBV) infection is a strong risk factor for the development of PAN, although in areas where HBV vaccination is common, the incidence of HBV-associated PAN has diminished greatly. This patient with HBV infection (positive hepatitis B surface antigen) presents with involvement of the abdomen, kidneys, nerves, joints, and skin, accompanied by hypertension but sparing the upper and lower respiratory tracts. He also has mononeuropathy, arthralgia, fever, and livedo reticularis (shown in the figure) but lacks the active urine sediment characteristic of glomerulonephritis. Together these findings suggest a systemic vasculitis of which PAN is the most likely. Testicular involvement is also common, as in this case. Diagnosis of PAN is best established by demonstrating necrotizing arteritis in biopsy specimens, or characteristic medium-sized artery aneurysms and stenoses on imaging studies of the mesenteric or renal arteries using either angiography or CT angiography.

Goodpasture syndrome affects the kidneys and often the lungs. The lack of active urine sediment and the presence of medium arterial involvement are inconsistent with Goodpasture syndrome, as are the abdominal symptoms.

Granulomatosis with polyangiitis (GPA; formerly known as Wegener granulomatosis) can involve the kidneys, and neuropathy and purpura can occur; however, this disease is associated with glomerulonephritis, which is absent in this patient. Furthermore, medium-sized artery involvement does not occur in GPA, and the absence of ANCA makes GPA much less likely.

Henoch-Schönlein purpura (HSP) can affect the kidneys, nerves, and skin as well as cause abdominal pain. However, HSP is an immune complex disease affecting small vessels; active urine sediment is common, complements (particularly C4) are typically low, and IgA levels may be elevated, none of which is the case in this patient.

Question 64

A 34-year-old man is evaluated for progressive left knee pain. The pain causes difficulty with his work as a mail carrier, particularly when walking. His occupation does not require repetitive bending. He played football in college and experienced left knee trauma during sports participation; he underwent left meniscectomy and stopped playing sports. His mother has osteoarthritis of the hands that developed at age 65 years.

On physical examination, vital signs are normal. BMI is 27. Bone hypertrophy of the left knee is noted. There is crepitus but no warmth, erythema, swelling, or effusion of the knees.

Plain radiographs (anteroposterior views) show medial joint-space narrowing of both knees but greater on the left as well as osteophytes and bony sclerosis of the tibial plateau of the left knee; there is no periarticular osteopenia or erosive or destructive changes.

Which of the following is the most likely cause of this patient's left knee osteoarthritis?

A

BMI

B

Family history

C

Meniscectomy

D

Occupation

Answer & Critique

Correct Answer: C

Educational Objective: Recognize the risk of early-onset knee osteoarthritis following meniscectomy.

Key Point

There is an increased risk of early-onset knee osteoarthritis in patients with a history of prior injury followed by meniscectomy.

The most likely cause of this patient's left knee osteoarthritis is meniscectomy. The history of prior injury followed by meniscectomy puts this patient at substantial risk for the development of osteoarthritis at an earlier age than would otherwise be predicted. A recent prospective study with a 40-year follow-up concluded that meniscectomy leads to osteoarthritis of the knee with a resultant 132-fold increase in the rate of total knee replacement in comparison to their matched controls. The risk of osteoarthritis of the knee following meniscus injury and removal is also well documented for adolescent athletes and, as recognition of this link has become more widespread, the incidence of meniscus repair rather than meniscectomy has risen.

Other factors for osteoarthritis are advancing age, obesity, female gender, and genetic factors. For example, obesity is the most important modifiable risk factor for osteoarthritis of the knee, but this patient is not obese. The incidence of knee osteoarthritis is also increased by occupations with repetitive bending, which this patient does not experience. The prevalence of osteoarthritis of the hip and knee is nearly two times higher in women than in men. Osteoarthritis of the hand has strong female and genetic predilections; it is also associated with obesity. His mother's hand osteoarthritis is probably not relevant for this patient who developed knee osteoarthritis at an early age following meniscectomy.

Bibliography

Question 65

A 62-year-old woman is evaluated in the emergency department for right knee pain. Three days ago she developed increasing pain, swelling, warmth, and erythema of the right knee as well as fevers and chills. She underwent total knee replacement of her right knee 2 months ago.

On physical examination, temperature is 38.4 °C (101.2 °F), blood pressure is 110/75 mm Hg, pulse rate is 98/min, and respiration rate is 12/min. BMI is 23. The right knee has a well-healed surgical scar, but there are significant knee joint swelling, warmth, tenderness to palpation, mild overlying erythema, and decreased range of motion. The remainder of the examination is normal.

Laboratory studies reveal a leukocyte count of 15,500/µL (15.5×10^9/L) with 89% neutrophils, a C-reactive protein level of 6.8 mg/dL (68 mg/L), and an erythrocyte sedimentation rate of 45 mm/h.

Radiograph of the right knee shows only an effusion.

Which of the following is the most appropriate next step in management?

A

Begin vancomycin and cefepime

B

Obtain blood and synovial fluid cultures

C

Obtain a bone scan

D

Obtain a CT of the knee

Answer & Critique

Correct Answer: B

Educational Objective: Manage a prosthetic joint infection.

Key Point

In patients with suspected prosthetic joint infection, blood and synovial fluid cultures should be obtained before initiation of antibiotics to allow for more accurate culture data.

Obtaining blood and synovial fluid cultures is the most appropriate next step in management for this patient with suspected prosthetic joint infection. Infections may occur early (within 3 months of surgery), have delayed onset (3-12 months), or have late onset (>12 months after surgery). Early-onset infections typically present with joint swelling, erythema, wound drainage, and/or fever. Delayed-onset infections present more insidiously with prolonged joint pain, often without fever. Late-onset infections present as acute pain and swelling, often in the setting of a nidus for hematogenous seeding such as a vascular catheter or other site of infection remote from the affected joint. This patient has acute onset of pain and swelling of the right knee, along with fevers, an elevated leukocyte count with a left shift, and elevated inflammatory markers, occurring 2 months after knee replacement. Urgent surgical consultation is warranted, and blood and synovial fluid cultures should be obtained before administration of antibiotics, whenever possible, to allow for more accurate culture data. Blood cultures are essential (even when fever is absent); although the infection likely arose locally at the surgical site in this patient, most cases of infectious arthritis arise from hematogenous spread. Blood cultures are also important because, even in cases in which the infection arises directly at the joint, the organism may occasionally be identified in the blood cultures. Before initiating antibiotics, synovial fluid cultures should be obtained via arthrocentesis or in the operating room if surgical intervention is imminent and the patient is stable enough to withhold antibiotics until surgery.

This patient will need antibiotics shortly, but she is stable enough to await surgical evaluation and collection of blood and synovial fluid cultures.

More advanced imaging such as a CT, bone scan, or MRI is generally not indicated in the preliminary evaluation and treatment of a suspected prosthetic joint infection because these studies delay the more urgent management of the patient and do not change the initial management.

Question 66

A 76-year-old man seeks advice regarding dietary modifications to help prevent gout flares. He recently experienced his first episode of podagra. At his initial visit, serum urate level was 7.2 mg/dL (0.42 mmol/L). History is also significant for hypertension, for which he takes losartan.

On physical examination, temperature is 37.1 °C (98.8 °F), blood pressure is 135/80 mm Hg, pulse rate is 80/min, and respiration rate is 15/min. BMI is 27. The remainder of the examination is unremarkable.

In addition to meat restriction, increased intake of which of the following may help to decrease this patient's risk of gout flares?

A

Leafy green vegetables

B

Low-fat dairy products

C

Red wine

D

Shellfish

Answer & Critique

Correct Answer: B

Educational Objective: Manage gout with dietary modifications.

Key Point

In patients with gout, lifestyle and dietary modifications, including weight loss if appropriate, reduction of high-fructose and high-purine foods, alcohol restriction, and increased low-fat dairy intake, may help decrease the risk of gout flares.

The addition of low-fat dairy products is appropriate for this patient with gout. Low-fat dairy products have been shown to decrease the risk of gout flares both through uricosuric and anti-inflammatory properties. He should also be advised to reduce intake of high-fructose beverages such as soft drinks because they are associated with gout flares due to metabolic pathways utilized in the metabolism of fructose, which lead to increased uric acid generation. Obesity is also a risk factor for gout and should be addressed as needed.

Some leafy green vegetables are high in purines, the nucleic acid component that is metabolized to uric acid. Thus, a recommendation to increase leafy greens as a dietary approach to gout treatment would be incorrect. However, intake of leafy green vegetables has not been shown to increase the risk of flares in population-based studies.

Alcohol is a well-established trigger for gout, probably due to several mechanisms, including uric acid production and kidney urate handling. Although wine has been found less likely to trigger gout flares than beer, alcohol consumption of any sort will increase the risk of flares overall.

Shellfish have long been established as a food that is likely to trigger a gout flare due to the high purine load and should therefore be restricted in this patient's diet.

Question 67

A 29-year-old woman is evaluated for increasing fatigue and diffuse pain of 6 months' duration. The pain becomes more severe for several days if she “overdoes it.” She reports chronically poor sleep and has difficulty concentrating at work. History is also significant for hypothyroidism, for which she takes levothyroxine. She takes ibuprofen as needed for the pain, which provides minimal benefit.

On physical examination, vital signs are normal. BMI is 25. Tenderness to palpation of multiple muscle groups is noted. Muscle strength is normal. There is no joint swelling or rash. The remainder of the examination is normal.

Laboratory studies, including complete blood count, chemistry panel, erythrocyte sedimentation rate, and thyroid-stimulating hormone, are normal.

Which of the following is the most appropriate next step in management?

A

Begin scheduled ibuprofen

B

Increase levothyroxine

C

Obtain an antinuclear antibody panel

D

Start an aerobic exercise program

Answer & Critique

Correct Answer: D

Educational Objective: Treat a patient who has fibromyalgia.

Key Point

Nonpharmacologic therapy, including regular aerobic exercise, is the cornerstone of fibromyalgia treatment and should be initiated in all affected patients.

An aerobic exercise program is appropriate for this patient with fibromyalgia, which is characterized by chronic widespread pain, tenderness of skin and muscles to pressure, fatigue, sleep disturbance, and exercise intolerance. Nonpharmacologic therapy is the cornerstone of treatment and should be initiated in all affected patients. Regular aerobic exercise has been shown to be effective in this setting. Exercise regimens should be individualized and titrated up to 30 minutes most days of the week. Physical therapy may also be helpful initially to develop a stretching and progressive aerobic program. Cognitive behavioral therapy has been shown to be beneficial but is not always covered by insurance plans.

NSAIDs such as ibuprofen have not been shown to be particularly useful in fibromyalgia, and most patients have tried them before seeking medical care for their symptoms. Although possibly helpful when taken on an as-needed basis for other musculoskeletal pain, NSAIDs as a primary therapy for fibromyalgia would not be appropriate.

This patient also has hypothyroidism but has a normal thyroid-stimulating hormone level, indicating that she is being treated properly and does not need an increase of her levothyroxine dose.

Fibromyalgia may co-occur in patients with inflammatory diseases such as rheumatoid arthritis, systemic lupus erythematosus, and Sjögren syndrome, but this patient does not have any clinical signs or laboratory features that would suggest an inflammatory disease. Thus, an antinuclear antibody (ANA) panel would not be helpful, and a clinically insignificant low-level positive ANA may actually lead to further unnecessary testing and specialist referral.

Question 68

A 75-year-old man is evaluated for gradual progression of right knee pain. He has a 10-year history of right knee osteoarthritis, which was previously controlled with acetaminophen. He recently discontinued the acetaminophen because of continued pain and began over-the-counter oral naproxen, with good results. He can walk again without pain or difficulty. He has no other medical problems and takes no other medications.

On physical examination, blood pressure is 124/82 mm Hg. The right knee demonstrates evidence of bony enlargement and crepitus on flexion and extension; no warmth, tenderness, or effusion is noted.

Which of the following is the most appropriate next step in management?

A

Continue oral naproxen

B

Discontinue oral naproxen; begin celecoxib

C

Discontinue oral naproxen; begin a topical NSAID

D

Refer for knee joint replacement

Answer & Critique

Correct Answer: C

Educational Objective: Manage NSAID gastrointestinal risk in an older patient by using topical NSAID therapy.

Key Point

Older patients with osteoarthritis who require NSAID therapy to control pain should be considered for topical NSAID therapy to manage gastrointestinal toxicity.

Discontinuation of oral naproxen and initiation of a topical NSAID is the most appropriate therapy for this 75-year-old patient with knee osteoarthritis. The major risks of NSAIDs include gastrointestinal toxicity, cardiovascular disease, hypertension, and kidney disease. Among these, NSAID gastrointestinal risk is higher among older patients and needs to be managed. The American College of Rheumatology currently recommends topical NSAIDs rather than oral NSAIDs for patients aged 75 years or older. A 2012 Cochrane review of topical NSAIDs for chronic musculoskeletal pain included 34 studies with 7688 participants. Topical NSAIDs were superior to placebo for pain relief, with the most data available for topical diclofenac. Topical and oral NSAIDs did not differ with regard to pain relief. Topical NSAIDs led to more skin reactions than placebo or oral NSAIDs and fewer gastrointestinal events than oral NSAIDs.

Discontinuing naproxen and adding celecoxib would reduce the risk of gastrointestinal toxicity to an extent similar to that of adding a proton pump inhibitor (PPI) to naproxen but would be unwarranted in the setting of a good response to topical naproxen. In patients with particularly high risk who require therapy with oral NSAIDs, simultaneously switching to celecoxib and adding a PPI could be considered.

Joint replacement should be considered in patients who have knee osteoarthritis with function and/or pain that cannot be managed using nonsurgical interventions. Because this patient has neither pain nor limitation on his current therapy, consideration of joint replacement would be premature.

Question 69

A 52-year-old man is evaluated for a 6-month history of increasingly swollen and painful joints of the fingers of both hands, both wrists, and the left ankle associated with 90 minutes of morning stiffness. He has tried over-the-counter ibuprofen and naproxen without sustained benefit. He has no other symptoms.

On physical examination, vital signs are normal. There are swelling and tenderness of the second, third, and fifth proximal interphalangeal joints; first, second, and third metacarpophalangeal joints; both wrists; and left ankle. Decreased range of motion of the right wrist is noted. The remainder of the physical examination is normal.

Laboratory studies reveal an erythrocyte sedimentation rate of 45 mm/h and a C-reactive protein level of 5.2 mg/dL (52 mg/L); rheumatoid factor and anti–cyclic citrullinated peptide antibody tests are negative.

Hand radiographs show an erosion of the second right metacarpal head with mild symmetric joint-space narrowing and mild periarticular osteopenia of the metacarpophalangeal joints; there is no bony sclerosis or osteophytes.

Which of the following is the most likely diagnosis?

A

Osteoarthritis

B

Rheumatoid arthritis

C

Sarcoidosis

D

Systemic lupus erythematosus

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose seronegative rheumatoid arthritis.

Key Point

Seronegative rheumatoid arthritis has an identical clinical appearance as seropositive rheumatoid arthritis but is more likely to occur in men.

The most likely diagnosis is rheumatoid arthritis (RA), which is characterized by a symmetric inflammatory polyarthritis of the small joints. Autoantibodies such as rheumatoid factor or anti–cyclic citrullinated peptide (CCP) antibodies may be present, although autoantibodies are neither necessary nor sufficient for diagnosis. Anti-CCP antibodies occur less frequently than rheumatoid factor, but their presence has more diagnostic specificity for RA. Some patients with RA also lack rheumatoid factor. Seronegative RA has an identical clinical appearance as seropositive RA but is more likely to occur in men. Despite a negative rheumatoid factor and anti-CCP antibodies, this patient's clinical presentation of polyarticular inflammatory arthritis involving multiple and bilateral interphalangeal joints of the fingers, metacarpophalangeal joints, a wrist, and an ankle as well as prolonged morning stiffness and radiographic findings of marginal erosion and periarticular osteopenia, is characteristic of RA. Over time, some patients who are initially seronegative develop a positive rheumatoid factor.

This patient does not have monoarticular or oligoarticular disease or radiographs showing bony sclerosis or osteophyte formation, all of which are typical of osteoarthritis. This patient's symmetric polyarticular inflammatory arthritis associated with prolonged morning stiffness is not consistent with osteoarthritis, in which joint swelling is not found and morning stiffness lasts less than 30 minutes.

Although sarcoidosis can occasionally cause joint involvement, it is unlikely to present with joint symptoms alone. Chronic sarcoid arthropathy most commonly involves the ankles, knees, hands, wrists, and metacarpophalangeal and proximal interphalangeal joints and is usually accompanied by parenchymal pulmonary disease. It is unlikely to be the cause of inflammatory polyarthritis in a previously healthy middle-aged man.

Although systemic lupus erythematosus (SLE) can cause seronegative polyarticular inflammatory arthritis, the initial presentation in a middle-aged man as an explanation for polyarticular

inflammatory arthritis would be exceedingly unlikely, and erosions are not seen as a result of arthritis in SLE. The patient has no signs or symptoms otherwise suggestive of SLE such as brain, kidney, lung, heart, or skin manifestations.

Question 70

A 41-year-old man is evaluated for a 1-month history of daily fever as high as 39.0 °C (102.2 °F), a 4.5-kg (10.0-lb) weight loss, myalgia, and swollen lymph nodes. He reports joint pain and stiffness in the shoulders, hands, wrists, and knees. He has also noted a pink rash over the trunk and extremities associated with the fever.

On physical examination, temperature is 38.4 °C (101.1 °F), blood pressure is 128/78 mm Hg, pulse rate is 100/min, and respiration rate is 18/min. BMI is 28. Multiple enlarged lymph nodes in the anterior cervical chain are present. Splenomegaly is noted. There is an erythematous maculopapular rash on the trunk and extremities. Swelling of the wrists and knees is present. The remainder of the examination is normal.

Laboratory studies:

Erythrocyte sedimentation rate	100 mm/h
Hematocrit	31%
Leukocyte count	30,000/µL (30 × 109/L), with 80% neutrophils; no blasts
Platelet count	350,000/µL (350 × 109/L)
Alanine aminotransferase	68 U/L
Aspartate aminotransferase	75 U/L
C-reactive protein	30 mg/dL (300 mg/L)
Creatinine	0.9 mg/dL (79.6 µmol/L)
Ferritin	20,000 ng/mL (20,000 µg/L)
Urinalysis	Normal

Chest radiograph is normal.

Which of the following is the most likely diagnosis?

A Acute myeloid leukemia

B

Adult-onset Still disease

C

Granulomatosis with polyangiitis

D Systemic lupus erythematosus

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose adult-onset Still disease.

Key Point

Adult-onset Still disease is characterized by high spiking fevers, arthritis, rash, high neutrophil counts, and markedly elevated serum ferritin.

The most likely diagnosis is adult-onset Still disease (AOSD), a multisystem inflammatory disease characterized by high spiking fevers, arthritis, rash, high neutrophil counts, and markedly elevated serum ferritin. The rash is a nonpruritic salmon-colored macular/maculopapular rash on the trunk or extremities. Serum ferritin is elevated in many patients, often to extremely high levels, and is a marker of macrophage activation. Erythrocyte sedimentation rate and C-reactive protein can also be impressively elevated. Diagnosis is clinical, based on exclusion of infection, malignancy, or other rheumatologic diseases. Clinical criteria have been developed to assist in the diagnosis of AOSD. The most sensitive of these are the Yamaguchi classification criteria. Diagnosis requires fulfilling at least five criteria, two of which must be major. This patient fulfills three major criteria (fever, rash, joint involvement) and three minor criteria (splenomegaly, lymphadenopathy, elevated liver chemistries). Very few other diseases elevate ferritin to this level, although this is not currently one of the criteria.

Acute myeloid leukemia (AML) is a malignancy of myeloid progenitor cells. Clinical manifestations of bone marrow failure develop over days to months and include fatigue, dyspnea, and easy bleeding. Fever is commonly caused by infection. The leukocyte count can be low, normal, or high, but circulating myeloblasts are present in most cases. This patient has a significant leukocytosis but no circulating blasts, thus excluding the diagnosis of AML.

Granulomatosis with polyangiitis (formerly known as Wegener granulomatosis) is also a multisystem disorder characterized by upper respiratory, lower respiratory, and kidney involvement. More than 70% of patients have upper airway manifestations such as sinusitis or nasal, inner ear, or laryngotracheal inflammation. This patient has none of these manifestations.

Systemic lupus erythematosus (SLE) is also a multisystem disease with early nonspecific constitutional symptoms, including fever, fatigue, and weight loss. Common presentations include

a photosensitive rash and symmetric polyarthritis. Cytopenia is common, whereas leukocytosis and extremely elevated serum ferritin levels are not characteristic of SLE.

Bibliography

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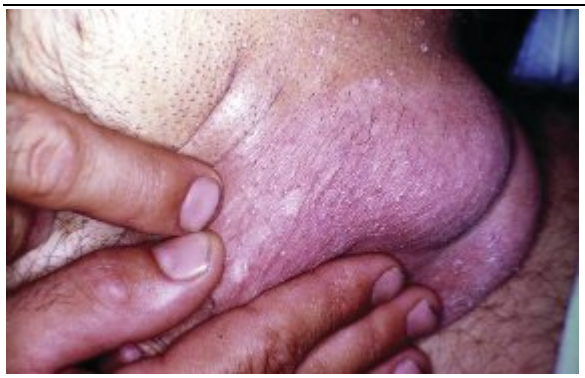
Question 71

A 29-year-old man is evaluated for pain and photophobia in the left eye that began 3 days ago. He reports a 6-month history of recurrent painful oral and genital ulcers that last 1 to 2 weeks and then resolve, as well as waxing and waning knee, ankle, and wrist pain during this time. Medical history had been unremarkable until the onset of these symptoms, and he takes no medications.

On physical examination, temperature is 38.2 °C (100.7 °F), blood pressure is 134/82 mm Hg, pulse rate is 90/min, and respiration rate is 14/min. BMI is 22. The left eye is diffusely erythematous, and a small amount of white fluid on the bottom of the anterior chamber is noted. There is an ulcer on the right side of the tongue.

The genital ulcers are shown.



Laboratory studies show an erythrocyte sedimentation rate of 76 mm/h as well as a normal complete blood count and metabolic profile. The patient is urgently referred to an ophthalmologist.

Which of the following is the most likely diagnosis?

89%

A

Behçet syndrome

B

Cytomegalovirus infection

C

Herpes simplex virus type 1 infection

D

Reactive arthritis

Answer & Critique

Correct Answer: A

Educational Objective: Diagnose Behçet syndrome.

Key Point

Behçet syndrome is characterized by recurrent painful oral ulcers plus at least two of the following: recurrent painful genital ulcers, eye involvement, skin involvement, and pathergy.

The most likely diagnosis is Behçet syndrome, a form of vasculitis that can affect small to large arterial vessels and is one of the few forms of vasculitis that also can affect veins. Behçet syndrome has an increased prevalence in a belt from East Asia to Turkey and therefore conveys an ethnic/genetic risk in those with a Mediterranean/Asian background. Behçet syndrome is characterized by recurrent painful oral ulcers plus at least two of the following: recurrent painful genital ulcers, eye involvement, skin involvement (typically acneiform lesions), and pathergy (development of a pustule following a needle stick). Oral ulcers typically resolve spontaneously after 1 to 3 weeks. Eye involvement can be severe, especially when there is a posterior uveitis/retinal vasculitis, and can lead to blindness. Hypopyon (suppurative fluid seen in the anterior chamber) is also a distinctive feature. The combination of recurrent painful oral ulcerations, genital ulcerations, and uveitis make Behçet syndrome the most likely diagnosis in this patient. Other clinical findings include gastrointestinal ulceration that may make it challenging to differentiate Behçet syndrome from Crohn disease with extraintestinal manifestations. Arthritis affecting medium and large joints is common, and the vasculitic process may cause neurologic, cardiopulmonary, kidney, and vascular complications.

Clinical manifestations of cytomegalovirus infection (CMV) include a mononucleosis-like illness with findings ranging from fever and lymphadenopathy to colitis, hepatitis, and even retinitis. Oral ulcers, genital ulcers, and hypopyon are not features of acute CMV infection.

Herpes simplex virus type 1 (HSV-1) infection has been classically associated with causing recurrent painful oral ulcerations. Although HSV-1 is being increasingly recognized as a cause of genital ulceration, it is much less common than with HSV type 2 infection. Systemic symptoms, such as fever, may be associated with primary herpes virus infection but are less common with recurrent episodes of viral activation. Additionally, HSV-1 may also be associated with ocular disease, although keratitis is the most common manifestation seen with HSV-1 infection and not hypopyon, as seen in this patient.

Reactive arthritis (formerly known as Reiter syndrome) is a postinfectious, noninfectious arthritis that occurs in both men and women. Arthritis, usually oligoarticular, develops several days to weeks after a genitourinary or gastrointestinal infection and can be associated with oral and genital lesions as well as uveitis. Unlike Behçet, the oral ulcers are painless, the genital lesions are hyperkeratotic rather than ulcerative, and hypopyon is not typical.

Question 72

A 66-year-old man is evaluated for a 2-month history of right knee pain. The pain is worse with walking and is accompanied by approximately 5 minutes of morning stiffness. Medical history is significant for chronic kidney disease, hypertension, and mild gastroesophageal reflux disease. Medications are lisinopril, hydrochlorothiazide, and ranitidine as needed for heartburn.

On physical examination, vital signs are normal. BMI is 29. Medial joint line tenderness and mild crepitus are noted in the right knee. There is no redness, warmth, or instability of the affected joint; minimal swelling is noted.

Laboratory studies reveal a serum creatinine level of 1.6 mg/dL (141.4 μmol/L).

Radiographs of the right knee show mild medial joint-space narrowing, subchondral sclerosis of the same region, and small osteophytes at the medial femoral and tibial joint margins.

In addition to an exercise program, which of the following is the most appropriate initial treatment?

A

Acetaminophen

B

Celecoxib

C

Colchicine

D

Ibuprofen

Answer & Critique

Correct Answer: A

Educational Objective: Select acetaminophen as a first-line pharmacologic agent in the treatment of knee osteoarthritis.

Key Point

In patients with osteoarthritis, initial treatment with acetaminophen for pain control is generally recommended.

Treatment with acetaminophen is appropriate for this patient with knee osteoarthritis (OA). The presence of progressive knee pain in this older individual that is worse with walking and is accompanied by unicompartmental joint-space narrowing and osteophytosis in the absence of extensive inflammation is pathognomonic for OA. Although OA includes a component of low-level inflammation, the goal of treatment is relief of pain and restoration of function. Most treatment guidelines suggest the initial use of acetaminophen for pain control in patients with knee OA. Acetaminophen is usually at least moderately effective in OA management; at doses of up to 3 to 4 g/d, it is considered safe and well tolerated. Additionally, it causes little or no gastrointestinal intolerance in most patients, does not affect blood pressure, and has significantly less nephrotoxicity than NSAIDs.

Both selective cyclooxygenase (COX)-2 inhibitors and traditional nonselective NSAIDs (such as ibuprofen) are of proven benefit in patients with OA and may be incrementally more effective than acetaminophen; selective COX-2 inhibitors have improved gastrointestinal tolerance and might be a better choice than a traditional NSAID in this patient given his gastric symptoms. However, both selective COX-2 inhibitors and traditional NSAIDs promote hypertension and can cause or exacerbate kidney disease; this patient's chronic kidney disease therefore makes them even less desirable as first-line therapy compared with acetaminophen. Other options for pharmacotherapy include local and topical therapy, intra-articular management, tramadol, and, if absolutely necessary, opiates.

Colchicine is an anti-inflammatory agent commonly used in gout and is not recommended for OA therapy.

Question 73

A 24-year-old woman is evaluated for a 6-month history of color change in her hands and feet, which is worse during stress. She is a nonsmoker. Family history is negative.

On physical examination, temperature is normal, blood pressure is 116/72 mm Hg, pulse rate is 64/min, and respiration rate is 12/min. BMI is 22. There is mild reversible discoloration of the fingertips upon exposure to cold. Cool tips of the fingers without digital pits are noted. Cardiopulmonary examination is normal. Muscle strength and reflexes are normal. There is no rash. The remainder of the examination is normal.

Laboratory studies, including complete blood count and chemistry panel, are normal. Nailfold capillary examination is normal.

Which of the following is the most appropriate next step in management?

A

Measure antinuclear and anti-U1-ribonucleoprotein antibodies

B

Measure antiphospholipid antibody panel and cryoglobulins

C

Obtain digital arteriography

D

Clinical observation

Answer & Critique

Correct Answer: D

Educational Objective: Evaluate a patient with primary Raynaud phenomenon.

Key Point

Raynaud phenomenon may be the initial symptom of an underlying connective tissue disease; the predictors/features include severe and prolonged vasospastic episodes, asymmetric involvement of the digits, and abnormal nailfold capillary examination and/or digital pitting.

Clinical observation is the most appropriate next step in management. This patient's presentation is suggestive of primary Raynaud phenomenon, a common occurrence in young women that may be seen in up to 30% of women who are white. Raynaud phenomenon may also be the initial symptom of an underlying fibrosing connective tissue disease (CTD) such as mixed connective tissue disease or systemic sclerosis; the predictors/features include severe and prolonged episodes of vasospasm, asymmetric involvement of the digits, and abnormal nailfold capillary examination and/or digital pitting. This patient has none of these features, has a negative family history for CTD, and has undergone nailfold capillary examination, which is normal. She is at a low risk for progressing to a CTD, should be reassured, and can be followed periodically. In these patients, most episodes of Raynaud phenomenon are self-limiting and do not require treatment. Persistently symptomatic patients can be treated with a peripherally acting calcium channel blocker such as nifedipine or amlodipine. Sildenafil and endothelin-1 blockers can be used in refractory cases.

This patient's likelihood of developing a CTD is low, and measuring antinuclear and anti-U1-ribonucleoprotein antibodies would be of extremely low yield and would not be cost-effective.

Similarly, obtaining an antiphospholipid antibody panel and cryoglobulins in a patient who has no history or evidence of thrombosis, pregnancy loss, or vasculitis is unnecessary and not cost-effective.

Digital arteriography is an invasive test and is usually normal in patients with Raynaud phenomenon. Obtaining this study would be appropriate if thromboangiitis obliterans (“Buerger disease”) were suspected, which is a nonatherosclerotic vascular inflammatory disease affecting

the medium and small vessels of the extremities and digits that has a strong association with smoking and male gender

Question 74

A 64-year-old man is evaluated in the emergency department for progressively deteriorating mental status. His wife states that he has been experiencing episodic headaches during the past several months, and his mental status has changed progressively over the past several days. History is significant for atherosclerosis, hypertension, and coronary artery disease. He has a 40-pack-year history of smoking. Medications are atorvastatin, lisinopril, and low-dose aspirin.

On physical examination, the patient is alert and oriented to self but not to place or year. Vital signs are normal. BMI is 26. On the Mini–Mental State Examination, he is unable to do serial sevens, is able to recall only one object out of three, and cannot draw a geometric figure that is shown to him. The remainder of the examination, including the neurologic assessment, is within normal limits.

Laboratory studies, including complete blood count, basic metabolic panel, liver chemistries, and urinalysis, are normal; erythrocyte sedimentation rate is 22 mm/h.

Lumbar puncture is performed; cerebrospinal fluid analysis reveals a leukocyte count of 15/μL (15×10^6/L), 90% lymphocytes, and a protein level of 45 mg/dL (450 mg/L).

Chest radiograph is unremarkable. A brain MRI shows scattered lesions, mainly in the white matter, and an MR angiogram shows possible narrowing of the intracerebral arteries.

Which of the following is the most appropriate next step in management?

A

Initiate azathioprine

B

Initiate cyclophosphamide and glucocorticoids

C

Obtain functional MRI

D

Obtain intracerebral angiography and brain biopsy

Answer & Critique

Correct Answer: D

Educational Objective: Evaluate a patient for primary angiitis of the central nervous system.

Key Point

Intracerebral angiography with brain biopsy can provide a definitive diagnosis in patients with suspected primary angiitis of the central nervous system.

The most appropriate next step in management is to obtain an intracerebral angiography and brain biopsy. This patient, presenting with recurrent headaches and rapidly progressive encephalopathy but no clear evidence of stroke or infection, requires consideration for primary angiitis of the central nervous system (PACNS). PACNS is a rare and challenging, but treatable, diagnosis because it is isolated to the CNS with no evidence of systemic involvement. His change in mental status could alternatively represent Alzheimer disease, or dementia on a vascular basis given his history of hypertension and smoking; however, the time course would be unusual, headaches are somewhat atypical for dementia, and the presence of an abnormal cerebrospinal fluid suggests an inflammatory process. Other diagnoses to consider include reversible vasoconstriction syndrome, infection, and intravascular malignancy. MR angiography (MRA) is insufficiently sensitive for a negative result, as in this patient's case, to suggest an absence of vasculitis, and insufficiently specific for a positive finding to abrogate further work-up. Because treatment of PACNS is aggressive and not without hazard, it is important to definitively establish a diagnosis whenever possible. Angiography is generally used to define the extent of vasculitic disease. Although it is more sensitive than MRA, it is still insufficiently sensitive and specific to establish a PACNS diagnosis alone. Brain biopsy is the gold standard, although it also has sensitivity limitations. The combination of intracerebral angiography and brain biopsy is therefore the preferred approach.

If PACNS were confirmed, treatment would generally require initiation of cyclophosphamide and high-dose glucocorticoids; however, such treatment should only be initiated after the brain biopsy or empirically if a brain biopsy cannot be carried out.

Azathioprine is a somewhat safer immunosuppressant than cyclophosphamide but has not been shown to be a treatment of first choice in PACNS; however, azathioprine may be utilized to reduce relapse rates among patients already treated and in remission.

Functional MRI (fMRI) could provide information about this patient's overall brain functioning; however, to date there are no specific signatures on fMRI that would permit specific diagnosis of

PACNS.

Question 75

A 45-year-old woman is evaluated for a 2-week history of nausea, right upper quadrant abdominal pain and fullness, and malaise. She has rheumatoid arthritis that was diagnosed 2 years ago. Initial treatment with methotrexate lost its efficacy after 6 months, and she was switched to leflunomide. She had partial response to leflunomide and was started on etanercept in combination. Other medications are sulfasalazine and naproxen. In the past 6 months, she has had no active swollen or tender joints.

On physical examination, vital signs are normal. BMI is 28. Icterus is noted. The liver is palpable with slight tenderness. Murphy sign is negative. The remainder of the examination is normal.

Laboratory studies:

Hemoglobin	11.1 g/dL (111 g/L)
Leukocyte count	12,500/μL (12.5×10^9/L)
Alkaline phosphatase	162 U/L
Alanine aminotransferase	73 U/L
Aspartate aminotransferase	81 U/L
Total bilirubin	2.6 mg/dL (44.5 μmol/L)
Hepatitis B serologies	Negative
Hepatitis C serologies	Negative

Abdominal ultrasound shows multiple gallstones, no thickening of the gallbladder, and normal extrahepatic bile ducts.

Which of the following is the most appropriate next step in management?

A

Discontinue etanercept

B

Discontinue leflunomide

C

Schedule a cholecystectomy

D

Schedule a liver biopsy

Answer & Critique

Correct Answer: B

Educational Objective: Manage liver toxicity in a patient taking leflunomide.

Key Point

Leflunomide can induce elevation of liver chemistries, which is usually reversible with dose reduction or drug discontinuation.

Discontinuation of the nonbiologic disease-modifying antirheumatic drug leflunomide is appropriate for this patient with rheumatoid arthritis who has developed abdominal pain and tenderness with acute hepatitis. The most likely diagnosis is leflunomide-induced hepatitis. Leflunomide-induced elevation of liver chemistries can occur in up to 20% of patients taking the medication, and a threefold elevation of serum aminotransferase levels has been noted in up to 13% of patients treated with leflunomide. She is at a slight increased risk for it due to concomitant NSAID use. Mild elevations less than three times the upper limit of normal are usually reversible with dose reduction or drug discontinuation. Hence, temporary or permanent discontinuation of leflunomide is indicated in this patient. In patients with more severe elevations (> three times), additional therapy with cholestyramine to quickly decrease the drug levels would also be indicated because leflunomide undergoes significant enterohepatic circulation. The current American College of Rheumatology treatment guidelines recommend periodic monitoring of liver chemistry tests (every 8-12 weeks) in patients being treated with leflunomide.

Etanercept is a receptor fusion protein, which blocks tumor factor necrosis ?. Etanercept-induced liver disease is extremely rare and should not be considered the likely diagnosis.

The usual presentation of biliary colic is episodic, with severe abdominal pain typically in the epigastrium and/or right upper quadrant. The pain rapidly intensifies over a 15-minute interval to a steady plateau that lasts as long as 3 hours and resolves slowly. The pain is often associated with nausea or vomiting, and there is no jaundice. This patient's symptoms are not suggestive of biliary colic; therefore, cholecystectomy is not indicated.

Liver biopsy may be needed to evaluate the cause of liver disease, but it is an invasive process and is only recommended if repeat testing and discontinuation of a known offending agent do not

lead to resolution, if the cause of liver disease is uncertain, or if there is evidence of chronic liver disease.

Bibliography

Question 76

A 55-year-old man is evaluated during a follow-up visit for gout. Two years ago, he had been treated with allopurinol and developed a hypersensitivity reaction. Over the past several months, he has had recurrent attacks of acute, episodic swelling of the first metatarsophalangeal joints with increasing involvement of other joints, including the ankles and knees. Laboratory studies showed significant hyperuricemia. History is also significant for Crohn disease, hypertension, chronic kidney disease (estimated glomerular filtration rate of 55 mL/min/1.73 m^2), and nonalcoholic fatty liver disease. Current medications are diltiazem and azathioprine, which he has been taking for the past 9 months.

On physical examination, temperature is 37.1 °C (98.8 °F), blood pressure is 125/70 mm Hg, pulse rate is 80/min, and respiration rate is 12/min. BMI is 28. The examination is unremarkable, including no joint abnormalities.

Which of the following is a contraindication to the use of febuxostat in this patient?

A

Azathioprine

B

Diltiazem

C

Mild to moderate chronic kidney disease

D

Nonalcoholic fatty liver disease

Answer & Critique

Correct Answer: A

Educational Objective: Identify azathioprine as a contraindication to the use of febuxostat.

Key Point

The xanthine oxidase inhibitor febuxostat is contraindicated in patients taking azathioprine, which undergoes metabolism via xanthine oxidase; concomitant use of these agents can lead to dangerously high levels of azathioprine.

Azathioprine is a contraindication to the use of febuxostat in this patient with gout. Febuxostat is a purine analogue that blocks urate synthesis by inhibiting xanthine oxidase, the final enzyme in the pathway of urate synthesis from purine precursors. It can be utilized when a patient has intolerance to or failure of allopurinol. Azathioprine, a purine analogue used in the treatment of inflammatory bowel disease, undergoes metabolism via xanthine oxidase. Thus, concomitant use of febuxostat (a xanthine oxidase inhibitor) can lead to dangerously high levels of azathioprine. Of note, use of allopurinol (also a xanthine oxidase inhibitor) concomitantly with azathioprine also poses a risk and is relatively contraindicated; however, some practitioners have used allopurinol in this setting with dose reduction and careful monitoring.

Use of diltiazem is a relative contraindication to colchicine, not febuxostat. Diltiazem is a moderate CYP34A inhibitor, and coadministration of this agent with colchicine can cause elevated colchicine levels.

Moderate chronic kidney disease (estimated glomerular filtration rate, 30-59 mL/min/1.73 m^2) is not a contraindication to the use of febuxostat; no dose adjustment to this medication is needed in the setting of mild to moderate kidney impairment.

Nonalcoholic fatty liver disease is not a contraindication to febuxostat use, although monitoring of hepatic function with administration of the drug is indicated.

Question 77

A 28-year-old woman is evaluated in the emergency department for a 3-week history of progressively worsening pain in the left arm. The pain worsens with use of the arm. She also notes fatigue, malaise, and the inability to walk long distances due to discomfort in her legs. She reports no cough, nausea, vomiting, or burning on urination. She takes no medications.

On physical examination, temperature is 38.1 °C (100.5 °F), blood pressure is 166/95 mm Hg in the right arm and 115/56 mm Hg in the left arm, pulse rate is 72/min, and respiration rate is 14/min. BMI is 27. Pallor of the fingertips and delayed capillary refill of the nail beds are noted in the left hand. A diminished radial pulse of the left arm and decreased dorsalis pedis pulses bilaterally are noted. A bruit is heard over the mid abdomen. There is no rash.

Laboratory studies:

Erythrocyte sedimentation rate	115 mm/h
Creatinine	1.3 mg/dL (115 µmol/L)
Partial thromboplastin time	Normal
Prothrombin time	Normal
D-dimer	Negative
Urinalysis	Normal

Which of the following is the most appropriate diagnostic test to perform next?

A

Antimyeloperoxidase antibody assay

B

Antiphospholipid antibody assay

CAortic arteriography

D\Temporal artery biopsy

Answer & Critique

Correct Answer: C

Educational Objective: Diagnose Takayasu arteritis.

Key Point

Arteriography of the aorta and its branches can be used to confirm the diagnosis of Takayasu arteritis.

The most appropriate diagnostic test to perform next is aortic arteriography in this patient who most likely has Takayasu arteritis. She presents with arterial compromise in the setting of a systemic febrile illness. Asymmetric blood pressure in the arms suggests arm involvement, and a midabdominal bruit, leg symptoms, and hypertension suggest aortic and renal artery obstruction. The differential diagnosis includes other forms of vasculitis and/or thrombosis. Given her age, sex, and high erythrocyte sedimentation rate, a diagnosis of Takayasu arteritis is likely. Because there are no specific laboratory tests used to diagnose or define Takayasu arteritis, arteriography of the aorta and its branches is used to confirm the diagnosis and define the extent of the problem. Alternative imaging modalities such as CT angiography or MR angiography might also be used for the same purpose.

An antimyeloperoxidase antibody assay would be useful if microscopic polyangiitis (MPA) were a diagnostic consideration; however, the kidney disease seen in this patient is due to renal artery obstruction and occurs in the absence of active urine sediment such as would be expected in MPA glomerulonephritis. Moreover, peripheral artery involvement would not be expected in MPA, a small-vessel disease.

The presence of antiphospholipid antibodies would be consistent with the antiphospholipid antibody syndrome and with the presence of thrombotic disease potentially occluding the arm, aorta, and renal arteries. However, her normal prothrombin and partial thromboplastin times indicate the absence of a lupus anticoagulant (one criterion for antiphospholipid antibody syndrome), and the lack of elevation in fibrin degradation products (D-dimer) argues against a thrombotic disease.

Although Takayasu arteritis and giant cell arteritis (GCA) share remarkably similar pathology, GCA occurs in older patients and is characterized by temporal arteritis, whereas Takayasu arteritis is a

disease of the young that rarely, if ever, involves temporal arteries. Thus, a temporal artery biopsy is not indicated.

Question 78

A 28-year-old woman seeks preconception counseling. She has a 5-year history of systemic lupus erythematosus, which initially presented with nephritis, rash, and arthritis. Her disease has been well controlled for 1 year with hydroxychloroquine, mycophenolate mofetil, and prednisone, 5 mg/d.

On physical examination, vital signs are normal. BMI is 28. There is a discoid rash on the ear pinna, unchanged since the last examination. No other rashes or ulcers are noted. The remainder of the examination, including cardiopulmonary examination, is normal.

Laboratory studies, including complete blood count, chemistry panel, liver chemistries, complement levels, and urinalysis, are normal.

Which of the following is the most appropriat e next step in management?

A

Discontinue hydroxychloroquine

B

Discontinue mycophenolate mofetil

C

Discontinue prednisone

D

Continue current regimen

E

Stop all medications

Answer & Critique

Correct Answer: B

Educational Objective: Manage pregnancy planning in a patient with systemic lupus erythematosus who is taking mycophenolate mofetil.

Key Point

Mycophenolate mofetil is teratogenic and must be stopped for 3 months prior to becoming pregnant.

Discontinuation of mycophenolate mofetil is indicated for this patient with systemic lupus erythematosus (SLE) who plans to become pregnant. Pregnancy outcomes in patients with SLE are better if their disease has been well controlled for 6 months prior to becoming pregnant. SLE can worsen during pregnancy in up to one third of patients, and hydroxychloroquine can reduce this risk. In addition, most rheumatologists continue stable low-dose prednisone during the pregnancy. Many medications used in SLE are contraindicated in pregnancy; permitted medications include prednisone, hydroxychloroquine, and azathioprine. Mycophenolate mofetil was developed to prevent transplant rejection but in recent years has been used as a treatment for SLE. Mycophenolate works by inhibiting the purine pathway in nucleotide synthesis and may be at least as effective as cyclophosphamide for SLE (including lupus nephritis) but with fewer and milder side effects. This agent is teratogenic and must be stopped for 3 months prior to becoming pregnant. Mycophenolate mofetil use may also be associated with difficulty in conception in some cases. This patient with SLE plans to become pregnant and has stable disease, and her laboratory parameters show no significant activity. Stopping mycophenolate is the only necessary intervention, and both hydroxychloroquine and prednisone should be continued unchanged.

Stopping all three medications would put this patient at unnecessary increased risk of a flare-up during pregnancy.

Question 79

A 42-year-old woman is evaluated for a 4-month history of progressive right hip pain. Plain radiographs obtained 2 months ago showed early osteoarthritis. Her symptoms have steadily worsened and are now limiting mobility. She reports no recent trauma or injuries, fevers, or pain of other joints. She is originally from India. She has lived in the United States for 15 years but visits her family abroad occasionally. She reports no injection drug use and is not sexually active. She was found to be positive for latent tuberculosis infection several years ago and underwent standard treatment at that time. History is significant for rheumatoid arthritis, for which she takes methotrexate and folic acid; she also started etanercept 3 months ago.

On physical examination, temperature is 37.1 °C (98.8 °F), blood pressure is 135/80 mm Hg, pulse rate is 75/min, and respiration rate is 12/min. BMI is 23. Range of motion of the right hip is limited by pain without overlying erythema or warmth. There are no visible joint or skin abnormalities. There are no heart murmurs, and the lungs are clear.

Laboratory studies reveal an erythrocyte sedimentation rate of 40 mm/h; complete blood count and kidney and liver chemistries are normal.

Radiograph of the right hip reveals an effusion and new erosive changes.

Arthrocentesis of the right hip is performed.

Which of the following is the most likely cause of this patient's hip pain?

A

Gout

B

Mycobacterium tuberculosis infection

C

Neisseria gonorrhea infection

D

Rheumatoid arthritis

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose *Mycobacterium tuberculosis* infection.

Key Point

Patients should be screened for latent tuberculosis prior to start of tumor necrosis factor ? inhibitor therapy and monitored for signs of infection during therapy.

The most likely diagnosis is *Mycobacterium tuberculosis* infection of the hip. Joint infections with*M. tuberculosis* present as an indolent process, often in the hip, knee, or spine (Pott disease). Constitutional symptoms are frequently absent, and imaging may reveal nonspecific erosions that may be interpreted as osteoarthritis. Moderate elevation of the erythrocyte sedimentation rate is common. The diagnosis is made by joint aspiration with fluid sent for mycobacterial cultures. This patient is at increased risk due to origination from and travel to an endemic area (India) and the recent initiation of the tumor necrosis factor (TNF)-? inhibitor etanercept for treatment of rheumatoid arthritis. TNF-? inhibitors increase the risk of tuberculosis reactivation. Patients should be screened for latent infection prior to start of therapy and monitored for signs of infection during therapy. In this case, the patient had appropriate treatment for latent tuberculosis infection in the past but may have had an incomplete response or contracted another latent infection.

Gout rarely occurs in premenopausal women and typically presents in peripheral joints, with the great toe (podagra) the classic site of the first attack.

This patient is not sexually active and thus is not at risk for *Neisseria gonorrhoeae* infection. Furthermore, gonococcal arthritis typically spares the axial skeleton.

Rheumatoid arthritis (RA) is always a consideration in a patient with RA and joint pain. However, it is unusual for a single joint to be involved in an RA flare, and her arthritis appears well controlled overall. Isolated inflammation of a single joint out of proportion to other joints is a clue to infection.

Question 80

A 35-year-old woman is evaluated for weakness in the right foot and left wrist with paresthesia in the right leg, right foot, left forearm, and left hand. She also reports facial erythema and joint stiffness. She has a 6-year history of systemic lupus erythematosus (SLE). Medications are hydroxychloroquine, prednisone, vitamin D, and calcium.

On physical examination, vital signs are normal. There is a new malar rash. Swelling of the second through fourth metacarpophalangeal joints of the hands is present. There is dorsiflexion weakness of the right ankle and a left wrist drop. Reflexes are normal. The remainder of the examination is normal.

Laboratory studies indicate that her SLE appears to be active with an elevation of erythrocyte sedimentation rate compared with baseline, leukopenia, and anemia typical of her previous SLE flares.

Which of the following is the most appropriate next step in management?

A

Discontinue hydroxychloroquine

B

Obtain electromyography/nerve conduction studies

C

Obtain MRI of the cervical spine

D

Obtain skin biopsy for small-fiber neuropathy

Answer & Critique

Correct Answer: B

Educational Objective: Evaluate a patient with systemic lupus erythematosus who has developed mononeuritis multiplex.

Key Point

Mononeuritis multiplex is characterized by abnormal findings in the territory of two or more nerves in separate parts of the body and is highly specific for vasculitis but can occur in systemic inflammatory disorders such as systemic lupus erythematosus.

Electromyography (EMG) and nerve conduction studies (NCS) are appropriate for this patient with systemic lupus erythematosus (SLE) who most likely has mononeuritis multiplex. Mononeuritis multiplex is characterized by abnormal findings in the territory of two or more nerves in separate parts of the body. She has a foot drop with normal reflexes that suggests an injury to the peroneal nerve and wrist drop that suggests injury to the radial nerve. EMG/NCS would most likely document a peripheral neuropathy. Mononeuritis multiplex is highly specific for vasculitic disorders that affect the vasa vasorum or nerve vascular supply but can also occur in systemic inflammatory disorders such as SLE. The peroneal nerve is the most commonly affected nerve. Approximately 14% of patients with SLE have a peripheral neuropathy with the majority (60%) due to SLE. Risk factors for the development of SLE-associated peripheral neuropathy include moderate to severe disease and the presence of other neuropsychiatric SLE manifestations. Approximately two thirds of patients improve with more aggressive immunosuppression. EMG/NCS can identify a nerve (usually the sural nerve) that might be amenable to biopsy to document the vasculitis prior to aggressive immunosuppression.

Hydroxychloroquine can cause a neuromyopathy manifested by proximal muscle weakness and areflexia. Biopsy demonstrates vacuoles in the muscle cells. However, hydroxychloroquine has not been associated with mononeuritis multiplex.

SLE may rarely cause transverse myelitis, which is characterized by a rapidly progressing paraparesis associated with a sensory level. Autonomic symptoms, including increased urinary urgency, bladder and bowel incontinence, and sexual dysfunction, may be present. The patient has no symptoms suggesting transverse myelitis, and a spine MRI is not indicated.

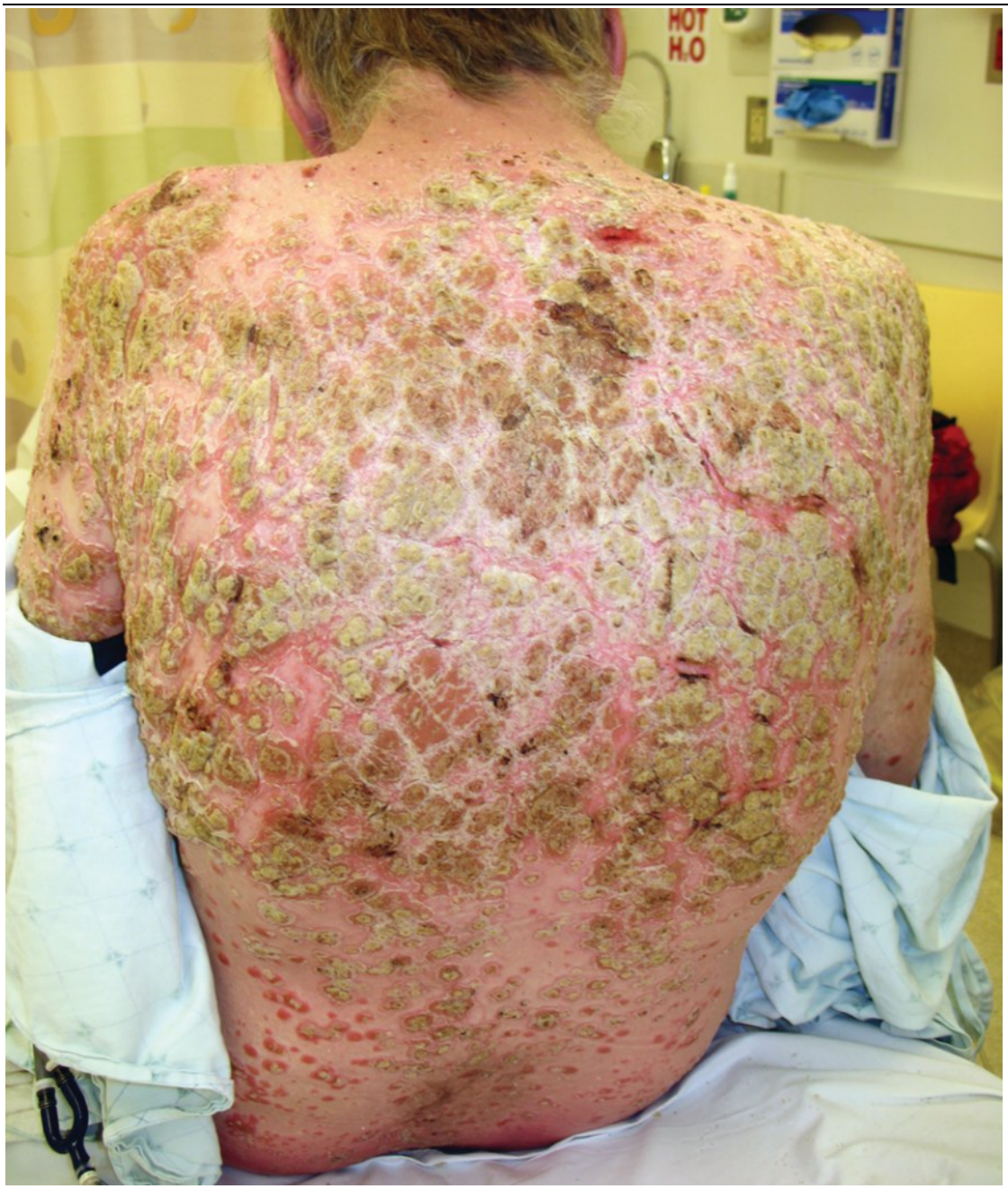
A small-fiber neuropathy causes a burning pain in the extremities and has been associated with autoimmune diseases such as SLE but does not cause motor symptoms. Diagnosis is made by skin biopsy, which demonstrates a reduced density of small sensory nerve fibers in the skin.

Question 81

A 40-year-old man has a 15-year history of well-controlled chronic plaque psoriasis and psoriatic arthritis and is now evaluated for a severe flare of both the skin and joint disease. One month ago, he developed severe pain and swelling of the hands, elbows, knees, ankles, and toes; symptoms have been unresponsive to ibuprofen. He also developed sudden worsening of psoriasis over the trunk and extremities. He notes increased fatigue and intermittent lymphadenopathy in the neck for the past 3 months. He has no other symptoms. His only medication is sulfasalazine.

On physical examination, temperature is 37.8 °C (100.0 °F), blood pressure is 130/85 mm Hg, and pulse rate is 80/min. Swelling and tenderness of the bilateral elbows, wrists, proximal interphalangeal joints, knees, ankles, and metatarsophalangeal joints are noted. Oropharyngeal candidiasis is present. Cervical lymphadenopathy is noted bilaterally. Except for the skin, the remainder of the physical examination is normal.

The appearance of the skin is shown.



Which of the following is the most appropr iate diagnostic test to perform next?

A

Heterophile antibody testing

B

HIV antibody testing

C

HLA-B27 testing

D

Lyme antibody testing

ERapid streptococcal testing

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose HIV infection as the cause of a severe flare of psoriatic arthritis.

Key Point

The development of explosive onset or severe flare of psoriatic arthritis should raise suspicion for concomitant HIV infection.

HIV antibody testing is indicated for this patient with a severe flare of psoriatic arthritis. HIV infection can trigger the onset of or exacerbate preexisting psoriatic arthritis and psoriasis. Skin and joint symptoms tend to be severe. Explosive onset or severe flare-up of psoriatic arthritis should therefore raise suspicion for concomitant HIV infection. This patient had previously well-controlled psoriatic arthritis until a recent severe flare, as manifested by severe pain and swelling of multiple joints and psoriasis, and should therefore be tested for HIV infection.

Although viral infections other than HIV can trigger flares of psoriasis, infectious mononucleosis is characterized by sore throat, lymphadenopathy, and splenomegaly, none of which (except adenopathy) is seen in this patient. Therefore, heterophile antibody testing is not indicated.

HLA-B27 is associated with psoriatic arthritis but not with psoriasis; furthermore, it neither confirms the diagnosis nor explains the flare-up of psoriasis.

The initial clinical manifestation of early localized Lyme disease is erythema migrans, an erythematous skin lesion that is noted in 70% to 80% of patients with confirmed infection. Early disseminated Lyme disease develops several weeks after the initial infection. Patients frequently present with a febrile illness associated with myalgia, headache, fatigue, and lymphadenopathy. Although Lyme disease may trigger a flare of psoriasis, as most acute infections can, it cannot account for the patient's thrush.

Streptococcal pharyngitis is a common trigger of guttate psoriasis, especially in children. Guttate psoriasis can also be the first sign of a flare in previously stable chronic plaque psoriasis. Guttate psoriasis consists of many small raindrop-like papules and plaques on the trunk. This patient's psoriatic pattern does not suggest guttate psoriasis, and testing for streptococcal infection is not indicated.

Question 82

A 28-year-old woman is evaluated for a 1-week history of pain and morning stiffness in her hands. Three weeks ago, she had muscle aches, malaise, fevers, and coryza, all of which have resolved. She is an elementary school teacher; prior to her initial illness, several children in her class had similar symptoms accompanied by an erythematous rash on the cheeks. She does not have other pertinent personal or family history, and she takes no medications.

On physical examination, temperature is 37.3 °C (99.2 °F), blood pressure is 120/78 mm Hg, pulse rate is 66/min, and respiration rate is 13/min. BMI is 22. Symmetric wrist, metacarpophalangeal, and proximal interphalangeal joint tenderness and pain with motion are noted without significant joint swelling. The remainder of the examination is normal.

Laboratory studies are significant for an erythrocyte sedimentation rate of 38 mm/h.

Which of the fo llowing is the most appropriate initial treatment?

A

Azithromycin

B

Ibuprofen

C

Interferon alfa

D

Prednisone

Answer & Critique

Correct Answer: B

Educational Objective: Treat a patient who has parvovirus B19 infection.

Key Point

Parvovirus B19 infection and its associated arthritis are generally self-limited; therefore, management is symptomatic, and an NSAID such as ibuprofen should alleviate symptoms until the episode resolves.

This patient has parvovirus B19 infection, and an NSAID such as ibuprofen is the appropriate initial treatment. This infection most commonly occurs in children and is characterized by acute polyarthritis with symmetric swelling and stiffness, the classic “slapped cheek” rash, and flu-like symptoms. Adults tend to contract the virus from children, but the rash may be absent or atypical in adults. Therefore, diagnosis should be suspected in adults with other characteristic findings as well as exposure to sick children. This patient shows evidence of a symmetric, small joint arthritis of the hands, a pattern consistent with rheumatoid arthritis as well as several forms of viral arthritis, most characteristically the arthritis that accompanies parvovirus B19 infection. This patient is at risk for parvovirus B19 infection given her occupation as an elementary school teacher, and the presence of IgM antibodies for parvovirus is definitive and establishes the diagnosis. Parvovirus B19 infection and its associated arthritis are generally self-limited; therefore, management is symptomatic, and an NSAID such as ibuprofen should alleviate symptoms until the episode resolves.

Azithromycin therapy may be appropriate for treatment of *Chlamydia* infection associated with reactive arthritis, a form of spondyloarthritis associated with a specific group of urogenital and gastrointestinal pathogens. However, antibiotic therapy is not indicated for parvovirus B19 infection.

Interferon alfa is of value for treating some viruses, particularly hepatitis. However, this agent is not needed to treat parvovirus B19 infection, which is self-limited.

Glucocorticoid therapy is not indicated in uncomplicated parvovirus B19 infection due to the self-limited nature of the infection and associated arthritis.

Question 83

A 52-year-old man is evaluated in the hospital for several episodes of hemoptysis that developed over the past day. He reports feeling well until about 3 weeks ago when he developed myalgia, arthralgia, occasional epistaxis, and diminished hearing. One week ago he developed a rash and weakness in his right hand. History is otherwise unremarkable, and he takes no medications.

On physical examination, temperature is 38.0 °C (100.4 °F), blood pressure is 152/100 mm Hg, pulse rate is 72/min, and respiration rate is 24/min. Conjunctivitis is present in both eyes. Decreased hearing in both ears is noted. Bilateral maxillary sinus tenderness is present. Chest examination reveals diffuse rhonchi. The right hand has decreased grip strength. Palpable purpura of the bilateral lower extremities is present.

Laboratory studies:

Erythrocyte sedimentation rate	84 mm/h
Leukocyte count	12,300/µL (12.3 × 10^9/L), eosinophils <2%
Complements (C3, C4)	Normal
Creatinine	2.1 mg/dL (185.6 µmol/L)
Urinalysis	3+ protein; 50 erythrocytes/hpf; 20 leukocytes/hpf; several mixed cellular casts

Sinus radiograph shows bony erosion of the septum and turbinates. Chest radiograph shows diffuse infiltrates.

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

A

Anti–double-stranded DNA antibody levels

B Antimyeloperoxidase antibody levels

C Antiproteinase 3 antibody levels

D Serum cryoglobulin levels

Answer & Critique

Correct Answer: C

Educational Objective: Diagnose granulomatosis with polyangiitis.

Key Point

The presence of antiproteinase 3 antibodies is sufficient to establish a diagnosis of granulomatosis with polyangiitis in patients with classic upper airway manifestations, pulmonary infiltrates/nodules, and urinary abnormalities consistent with glomerulonephritis.

The presence of antiproteinase 3 (PR3) antibodies will be diagnostic in this patient who most likely has granulomatosis with polyangiitis (formerly known as Wegener granulomatosis), a systemic necrotizing vasculitis that predominantly affects the upper and lower respiratory tract and kidneys. More than 70% of patients have upper airway manifestations such as sinusitis or nasal, inner ear, or laryngotracheal inflammation. Purpura and ulcers are common skin manifestations. Mononeuritis multiplex may also occur. Pulmonary manifestations can present as cough, hemoptysis, and pleurisy. Characteristic radiographic findings include multifocal infiltrates or nodules, some of which may cavitate; diffuse opacities are seen in patients with pulmonary hemorrhage. Pauci-immune glomerulonephritis occurs in up to 80% of patients. Diagnosis is best established by lung or kidney biopsy. However, the presence of anti-PR3 antibodies is sufficient to establish a diagnosis in patients with classic upper airway manifestations, pulmonary infiltrates/nodules, and urinary abnormalities consistent with glomerulonephritis.

Anti–double-stranded DNA antibodies are specific but relatively insensitive for systemic lupus erythematosus (SLE). SLE is an unlikely diagnosis in this patient because the involvement of the upper airways, particularly with erosion of the sinuses, is uncommon in SLE, the disease is much less common in men than women, and complement levels are typically reduced during active disease.

Antimyeloperoxidase antibodies reflect the presence of ANCA in a perinuclear rather than cytosolic pattern and are associated with microscopic polyangiitis, eosinophilic granulomatosis with polyangiitis (formerly known as Churg-Strauss syndrome), and rapidly progressive glomerulonephritis. However, the presence of upper airway disease essentially rules out these conditions in this patient.

Serum cryoglobulins can be elevated in cryoglobulinemia, which can characteristically affect the kidneys, skin, and nerves and can less commonly affect the lungs. However, upper airway involvement is uncommon, and the normal complement levels, especially a normal C4, also argue against cryoglobulinemia as a diagnosis.

Question 84

A 31-year-old woman is evaluated during a follow-up visit for systemic lupus erythematosus. She was diagnosed 6 months ago after presenting with a malar rash, pericarditis, and arthritis. She was initially treated with prednisone, 40 mg/d, and hydroxychloroquine with good control of symptoms. The prednisone was subsequently tapered to the current dose of 5 mg/d.

On physical examination, temperature is normal, blood pressure is 130/92 mm Hg, pulse rate is 90/min, and respiration rate is 16/min. BMI is 27. There is edema of the lower extremities to just above the ankles. There are no cardiac or pleural rubs. No rash is present.

Laboratory studies:

	One month ago	Today
C3	Normal	Decreased
C4	Normal	Decreased
Creatinine	0.7 mg/dL (61.9 µmol/L)	1.3 mg/dL (115 µmol/L)
Anti–double-stranded DNA antibodies	225 U/mL	721 U/mL
Urinalysis	Trace erythrocytes; trace protein	1+ erythrocytes; 2+ protein; 1 erythrocyte cast; no bacteria
Spot urine protein-creatinine ratio	300 mg/g	1200 mg/g

In addition to an increase in prednisone, which of the following is the most appropriate next step in management?

Top of Form

A

Add methotrexate

B

Repeat laboratory testing in 1 month

C

Schedule kidney biopsy

D

Schedule renal artery Doppler examination

Answer & Critique

Correct Answer: C

Educational Objective: Evaluate a patient with suspected lupus nephritis using a kidney biopsy.

Key Point

The diagnosis of lupus nephritis, suggested by proteinuria (>500 mg/24 h) or cellular casts (erythrocytes or leukocytes) in the urine sediment, must be confirmed and classified with a kidney biopsy.

A kidney biopsy is appropriate for this patient with systemic lupus erythematosus (SLE). Kidney disease occurs in some form in up to 70% of patients with SLE, especially in those who express anti–double-stranded DNA antibodies, which typically rise and fall with disease activity. Diagnosis of lupus nephritis is suggested by proteinuria (>500 mg/24 h) or cellular casts (erythrocytes or leukocytes) in the urine sediment of patients fulfilling the formal criteria for the diagnosis of SLE. Most patients with active lupus nephritis have low serum complement levels. According to the 2012 American College of Rheumatology guidelines for evaluating and treating lupus nephritis, this patient meets the criteria for kidney biopsy. Unless contraindicated, biopsy should be done before initiating therapy. This patient will most likely have a proliferative form of lupus nephritis (class III/IV) and will require aggressive immunosuppressive therapy.

The usual therapeutic agents for proliferative forms of lupus nephritis are either cyclophosphamide or mycophenolate mofetil. There are no data to suggest that methotrexate is useful in this setting. Methotrexate is renally excreted, and toxicity increases in the setting of kidney disease.

Without adequate management, class III, class IV, or class V combined with class III or class IV generally are progressive, with a probability of end-stage kidney disease as high as 50% to 70% after 5 to 10 years of diagnosis. Therefore, there is no reason to wait another month to repeat laboratory testing in this patient given the present abnormalities.

Because the vascular lesion in lupus nephritis is at the level of the arteriole, a renal artery Doppler examination will not be useful for treatment decisions.

Question 85

A 55-year-old man is diagnosed with hypertension. Other than a single episode of podagra 6 months ago, his medical history is unremarkable. He takes no medications. Family history is notable for his father and brother who have gout and hypertension.

On physical examination, temperature is 36.6 °C (97.9 °F), blood pressure is 152/100 mm Hg, pulse rate is 82/min, and respiration rate is 14/min. BMI is 24. The remainder of the physical examination is unremarkable.

Laboratory studies are significant for normal blood urea nitrogen, serum creatinine, and electrolyte levels; the serum urate level is 7.9 mg/dL (0.47 mmol/L).

Which of the following antihypertensive drugs is the most appropriate for this patient?

A

Hydrochlorothiazide

B

Lisinopril

C

Losartan

D

Metoprolol

Answer & Critique

Correct Answer: C

Educational Objective: Treat hypertension in a patient with hyperuricemia who is at increased risk for acute gout.

Key Point

The angiotensin receptor blocker losartan and calcium channel blockers lower serum urate and may be useful to treat patients in whom hypertension and gout are both clinical concerns.

The angiotensin receptor blocker (ARB) losartan is the most appropriate antihypertensive drug for this patient with hyperuricemia who is at increased risk for acute gout. Hypertension is a common comorbidity of gout and is found in approximately 74% of patients with gout. Antihypertensive drugs have variable effects on serum urate levels and risk of acute gout. A population-based, nested-case control study compared nearly 25,000 patients with a new diagnosis of gout with 50,000 control patients. The risk of gout was assessed according to antihypertensive drug class. Losartan, but not other ARBs, and calcium channel blockers were associated with a reduced risk of gout (relative risk for losartan: 0.81 [95% CI, 0.7-0.84]; relative risk for calcium channel blockers: 0.87 [95% CI, 0.82-0.93]). Both losartan and calcium channel blockers lower serum urate. Losartan, like probenecid, interferes with the urate-reabsorbing transporter, thereby promoting kidney urate excretion. The mechanism by which calcium channel blockers lower urate levels is unclear but may be mediated through increased glomerular filtration rate and increased urate clearance. Based upon these data, losartan and calcium channel blockers are the preferred antihypertensive agents if reducing the risk of gout is clinically relevant.

In this same study, ACE inhibitors, non-losartan ARBs, ?-blockers, and diuretics were all associated with an increased risk of gout. The absolute risk of gout was greatest with diuretics, with an estimated risk of six events per 1000 person-years.

Bibliography

Question 86

A 71-year-old man is evaluated for severe tophaceous gout. Colchicine has been effective in reducing flares to approximately two in the past year. On initial evaluation 1 year ago, serum urate level was 10.2 mg/dL (0.60 mmol/L). Allopurinol was initiated but subsequently discontinued because of gastrointestinal intolerance. He was switched to febuxostat, which was increased to maximum dose without success in reaching the serum urate goal of less than 6.0 mg/dL (0.35 mmol/L). He recently had a gout flare of his right great toe, which has nearly resolved.

On physical examination, temperature is 36.6 °C (97.9 °F), blood pressure is 140/80 mm Hg, pulse rate is 89/min, and respiration rate is 15/min. BMI is 32. Bulky tophi are present over bilateral elbows, hands, and feet with drainage of pasty material from a large tophus over the second metacarpophalangeal joint of the left hand. There are mild swelling and tenderness to palpation over the right first metatarsophalangeal joint.

Laboratory studies reveal a serum urate level of 10.9 mg/dL (0.64 mmol/L), an estimated glomerular filtration rate of 42 mL/min/1.73 m^2, and a normal glucose-6-phosphate dehydrogenase level.

Which of the following is the most appropriate next step in management?

A

Add pegloticase

B

Start prednisone

C

Switch colchicine to anakinra

D

Switch febuxostat to pegloticase

Answer & Critique

Correct Answer: D

Educational Objective: Treat tophaceous gout with pegloticase in a patient who has not responded to oral urate-lowering therapy.

Key Point

Pegloticase may be considered for patients with resistant gout who have not responded to oral urate-lowering therapy.

Switching febuxostat to pegloticase is appropriate for this patient. He has severe tophaceous gout and persistent hyperuricemia and has not responded to oral urate-lowering therapy, including the xanthine oxidase inhibitors allopurinol and febuxostat. He therefore warrants a trial of the synthetic uricase replacement pegloticase, an intravenous medication FDA approved for treatment-failure gout. Patients with bothersome persistent tophi or recurrent gout flares despite oral urate-lowering therapy (or with contraindications to available oral therapy) should be considered for pegloticase treatment, in consultation with a rheumatologist.

Xanthine oxidase inhibitors such as febuxostat should be discontinued when initiating pegloticase. Immunogenicity to pegloticase can result in infusion reactions; loss of response to the drug suggests the presence of neutralizing antibodies to the drug and indicates increased risk of infusion reactions. Therefore, drugs that might otherwise lower the serum urate level should be discontinued because they may mask a rising serum urate level that would signal the presence of pegloticase antibodies and its attendant loss of effectiveness and increased risk of a serious infusion reaction. Pegloticase is contraindicated in patients with glucose-6-phosphate dehydrogenase deficiency.

This patient's current gout flare is nearly resolved and therefore does not require prednisone. Moreover, prednisone is not effective in reducing serum urate levels, and it is not an appropriate drug to prevent recurrent attacks of acute gout due to its many long-term side effects.

Colchicine is generally working well in reducing gout flares in this patient. If this were ineffective or not tolerated, another agent would need to be considered for prophylaxis (or treatment of acute flares). Anakinra is an interleukin-1? inhibitor that may be considered for off-label use for gout prophylaxis and flare treatment in patients in whom other more conventional agents are ineffective or contraindicated, which is not the case for this patient.

Question 87

A 25-year-old woman is evaluated during a follow-up visit for systemic lupus erythematosus. She was feeling well until 2 weeks ago when she developed increased fatigue and diffuse arthralgia. Medications are hydroxychloroquine and ibuprofen as needed.

On physical examination, temperature is 37.2 °C (99.0 °F), blood pressure is 140/80 mm Hg, pulse rate is 80/min, and respiration rate is 16/min. There is diffuse alopecia of the scalp. Malar erythema is noted. Heart sounds are normal, and the chest is clear. Examination of the abdomen is normal. Tenderness with minimal swelling of the proximal interphalangeal joints is present bilaterally. Small effusions on both knees with pain on range of motion are noted.

Laboratory studies:

Leukocyte count	3000/µL (3.0 × 10^9/L), with 900 lymphocytes
Creatinine	Normal
Electrolytes	Normal
Urinalysis	2+ protein; trace blood

Which of the following tests should be obtained next?

A

Anti–double-stranded DNA antibodies

B

Antinuclear antibodies

C

Anti-Ro/SSA and anti-La/SSB antibodies

D

Anti-Smith antibodies

E

Anti-U1-ribonucleoprotein antibodies

Answer & Critique

Correct Answer: A

Educational Objective: Confirm a flare of systemic lupus erythematosus with an anti–double-stranded DNA antibody measurement.

Key Point

Anti–double-stranded DNA antibodies correlate with systemic lupus erythematosus disease activity, particularly active kidney disease or glomerulonephritis.

Measurement of anti–double-stranded DNA antibodies is appropriate for this patient who is having a flare of systemic lupus erythematosus (SLE). She has symptoms of fatigue, joint pain, rash, leukopenia, and lymphopenia. Urinalysis shows proteinuria and hematuria, indicating that she may have glomerulonephritis as well. Levels of anti–double-stranded DNA antibodies correlate with SLE disease activity; in particular, they correlate with active kidney disease or glomerulonephritis and might prompt further evaluation such as kidney biopsy. Thus, measuring anti–double-stranded DNA antibody titers may be useful in assessing this patient's recent symptoms. Following anti–double-stranded DNA antibody titers over time can be useful because it is a marker for risk of developing lupus nephritis.

Antinuclear antibody (ANA) testing is a useful screening tool for SLE because more than 95% of patients with SLE are positive for ANA; however, ANA does not correlate with disease activity.

Anti-Ro/SSA and anti-La/SSB antibodies can be present in patients with Sjögren syndrome as well as SLE. These antibodies correlate with SLE rashes and photosensitivity and are a risk factor for the development of neonatal lupus erythematosus; however, they do not correlate with disease activity.

Anti-Smith antibodies are highly specific for the diagnosis of SLE; however, these antibodies also do not correlate with disease activity.

Anti-U1-ribonucleoprotein antibodies are found in patients with SLE and with mixed connective tissue disease but do not correlate with disease activity.

Question 88

A 31-year-old woman is evaluated in the hospital for headache, blurred vision, and nausea occurring for the past 12 hours. She has a 2-year history of diffuse cutaneous systemic sclerosis with recent worsening of Raynaud phenomenon that is treated with nifedipine.

On physical examination, the patient is alert but is somnolent and has altered sensorium. Temperature is normal, blood pressure is 150/92 mm Hg, pulse rate is 104/min, and respiration rate is 16/min. BMI is 22. Oxygen saturation is 95% on ambient air. Cardiopulmonary examination is normal. Examination of the skin reveals diffuse skin thickening of the face, anterior chest, and distal extremities; sclerodactyly; and multiple healed digital pits. Neurologic examination is nonfocal.

Laboratory studies:

Complete blood count	Normal
Albumin	3.0 g/dL (30 g/L)
Bicarbonate	32 mEq/L (32 mmol/L)
Creatinine	4.2 mg/dL (371.3 µmol/L); baseline, 0.8 mg/dL (70.7 µmol/L)
Urinalysis	2+ protein; 3 erythrocytes/hpf; 5 leukocytes/hpf; few granular casts
Urine protein-creatinine ratio	1200 mg/g

Chest radiograph is normal. Noncontrast CT of the head is normal. MRI of the brain shows bilateral parietal lobe white matter prominence.

Which of the following is the most appropriate treatment?

A

Captopril

B

Cyclophosphamide

C

Methylprednisolone

D Sildenafil

Answer & Critique

Correct Answer: A

Educational Objective: Treat a patient who has scleroderma renal crisis.

Key Point

In patients with scleroderma renal crisis, treatment with an ACE inhibitor is essential to restore kidney function and manage hypertension.

The ACE inhibitor captopril is the most appropriate treatment for this patient who most likely has scleroderma renal crisis (SRC) in the setting of diffuse cutaneous systemic sclerosis (DcSSc). SRC occurs in 10% to 15% of patients with systemic sclerosis and is more frequent in DcSSc compared with limited cutaneous systemic sclerosis. Vascular involvement of afferent arterioles leads to glomerular ischemia and hyperreninemia. The typical presentation is acute onset of oliguric kidney disease and severe hypertension, mild proteinuria, urinalysis with few cells or casts, microangiopathic hemolytic anemia, and thrombocytopenia. Some patients develop pulmonary edema and hypertensive encephalopathy. Normal blood pressure may be present in up to 10%. This patient presents acutely with a rapid rise in serum creatinine consistent with acute kidney injury, with a bland urinalysis and non–nephrotic-range proteinuria as well as neurologic symptoms suggestive of encephalopathy. Although her blood pressure is almost normal, these findings are highly suggestive of SRC. Treatment with an ACE inhibitor is essential to restore kidney function and manage hypertension associated with SRC. Captopril is the preferred ACE inhibitor because it has been the most extensively studied agent in this clinical setting, and its short half-life allows rapid titration.

Cyclophosphamide is a potent immunosuppressant used to treat severe or life-threatening manifestations of certain diseases such as systemic lupus erythematosus or systemic vasculitis. It is ineffective in treating SRC, which is vascular and noninflammatory.

This patient does not have inflammatory end-organ involvement; therefore, methylprednisolone is not needed. Glucocorticoids are not useful in SRC, and intravenous glucocorticoids may cause worsening symptoms.

Sildenafil can be used to treat pulmonary hypertension or finger ulcerations but is not appropriate for SRC, which is primarily mediated through the renin-angiotensin axis.

Question 89

A 55-year-old woman is evaluated for a 3-year history of gradual left knee pain. She reports increased difficulty with stair climbing and an increase in pain over the past 6 months. She has no history of injury. She was prescribed acetaminophen, 1000 mg three times daily, and an exercise program 3 months ago but continues to have activity-limiting symptoms. Family history is notable for her mother who had a total knee replacement at the age of 65 years.

On physical examination, vital signs are normal. BMI is 31. There is bony hypertrophy of the left knee and the first metacarpophalangeal joints without warmth, erythema, swelling, or effusion.

Laboratory studies, including an erythrocyte sedimentation rate and serum creatinine, are normal.

Knee radiographs (including standing views) show medial joint-space narrowing and small osteophytes of the left knee; there is no periarticular osteopenia or marginal erosions.

Which of the following is the most appropriate next treatment?

A

Capsaicin

B

Diclofenac

C

Duloxetine

D

Hyaluronic acid

E

Hydrocodone

Answer & Critique

Correct Answer: B

Educational Objective: Treat a patient who has inadequately controlled knee osteoarthritis.

Key Point

An NSAID should be initiated in patients with osteoarthritis if first-line therapy with acetaminophen does not provide adequate relief.

An NSAID such as diclofenac is indicated for this patient with knee osteoarthritis. In addition to the implementation of nonpharmacologic measures such as an exercise regimen and/or assistive devices, the initial pharmacologic management of osteoarthritis recommended in guidelines issued by various societies is acetaminophen in doses ?3 g/d. If this offers inadequate relief, NSAIDs can be used. NSAIDs are more efficacious than acetaminophen in the relief of osteoarthritis pain. Treatment guidelines suggest using the lowest possible effective dose for the shortest time period because side effects are common and occasionally severe. However, many patients require years of NSAID use given the prolonged timeframe over which the disease is symptomatic and the small number of alternative pharmacologic treatments. NSAIDs are associated with important toxicities, particularly with prolonged exposure. The risk of peptic ulcer disease and gastrointestinal bleeding can be reduced with concomitant use of proton pump inhibitors. Cardiovascular risks can be mitigated by appropriate patient selection for chronic NSAID use.

Topical capsaicin can be used at any time to treat osteoarthritis as well; however, in the absence of an effect from acetaminophen, an NSAID is likely to give this patient more substantial relief of symptoms.

Duloxetine is a serotonin-norepinephrine reuptake inhibitor approved to treat osteoarthritis pain but is slower acting than NSAIDs and requires ongoing, rather than intermittent and as-needed, administration.

Hyaluronic acid injections have shown only a minimal degree of benefit in the treatment of knee osteoarthritis; they also require an invasive procedure for administration and are expensive. Therefore, they would not be preferred to treatment with an NSAID.

Narcotics such as hydrocodone should be reserved for patients who have not responded to nonpharmacologic measures in addition to NSAIDs. An alternative to hydrocodone is tramadol, a centrally acting synthetic opioid analgesic that binds to ?-opioid receptors and inhibits reuptake of norepinephrine and serotonin. It can be used for analgesia when NSAIDs are not tolerated or are contraindicated. Side effects include headaches and dizziness. Tolerance can occur with long-term use; withdrawal symptoms can occur with discontinuation.

Question 90

.A 56-year-old man is evaluated for painless intermittent bloody urine of 6 weeks' duration. History is significant for granulomatosis with polyangiitis (formerly known as Wegener granulomatosis) diagnosed 10 years ago, which is now in remission; he was treated with prednisone for 3 years and oral cyclophosphamide for 1 year. He also has hypertension and hyperlipidemia. Current medications are metoprolol and atorvastatin.

On physical examination, temperature is 36.7 °C (98.0 °F), blood pressure is 146/94 mm Hg, pulse rate is 68/min, and respiration rate is 14/min. BMI is 28. There are no rashes or ulcers. Genitalia are normal. The remainder of the examination, including cardiopulmonary examination, is normal.

Laboratory studies:

Chemistry panel and kidney function tests	Normal
Hemoglobin	12.1 g/dL (121 g/L)
Erythrocyte sedimentation rate	35 mm/h
p-ANCA	Negative
Antimyeloperoxidase antibodies	Negative
Antiproteinase 3 antibodies	Negative
Urinalysis	Trace protein; 10-20 erythrocytes/hpf; 0-2 leukocytes/hpf; no casts
Urine cultures	Negative

A chest radiograph is normal.

Which of the following is the most appropriate diagnostic test to perform next?

A

CT of the abdomen and pelvis with contrast

B Cystoscopy

C

Kidney and bladder ultrasonography

D

Urine eosinophil measurement

E

Urine protein-creatinine ratio

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose bladder cancer in a patient who has received cyclophosphamide.

Key Point

The use of cyclophosphamide is associated with increased risk of malignancy, especially bladder cancer, and patients should be evaluated accordingly.

Cystoscopy is the most appropriate diagnostic test to perform next in this patient. He has painless hematuria with a history of granulomatosis with polyangiitis (formerly known as Wegener granulomatosis), which was treated with the nonbiologic disease-modifying antirheumatic alkylating agent cyclophosphamide. Both the underlying rheumatologic condition and the medication used for its treatment are associated with increased risk of malignancy, especially bladder cancer. Bladder cancer usually presents with painless frank (usually not microscopic) hematuria, and cystoscopy with biopsy is most likely to lead to the correct diagnosis. In contrast, kidney involvement due to the disease is associated with glomerulonephritis, and urinalysis shows erythrocyte casts or dysmorphic erythrocytes, which is not the case here. The risk of bladder cancer is higher if the patient has received oral cyclophosphamide because there is prolonged daily exposure to the metabolites associated with causing mucosal irritation and metaplasia. The incidence of cystitis and bladder cancer is lower with intermittent intravenous cyclophosphamide, especially when given with mesna, an adjuvant therapy given with cyclophosphamide to detoxify urotoxic metabolites. Importantly, bladder cancers associated with cyclophosphamide exposure may be more aggressive and should be urgently evaluated even when suspicion is low.

CT and ultrasonography may show large lesions affecting the kidneys and gastrointestinal tract but do not detect small and superficial lesions, which can only be detected on cystoscopy.

The patient had no new drug exposure, and urinalysis does not show significant findings of nephritis; therefore, there is no reason to suspect a drug reaction or interstitial nephritis and obtain urine eosinophils.

Urine protein-creatinine ratio to look for glomerular disease is not helpful in evaluating a patient with hematuria when suspicion for the underlying vasculitis is low, as seen in this patient with a negative p-ANCA.

Question 91

A 35-year-old woman is evaluated in the hospital for a 6-month history of worsening fatigue and a 3-week history of progressive shortness of breath. Over the past 2 weeks she has developed orthopnea and leg edema. Medical history is significant for diffuse cutaneous systemic sclerosis and gastroesophageal reflux disease. Her only medication is omeprazole.

On physical examination, the patient is alert but in respiratory distress. Temperature is 37.2 °C (99.0 °F), blood pressure is 106/74 mm Hg, pulse rate is 108/min, and respiration rate is 24/min. BMI is 31. Oxygen saturation is 92% on ambient air. An S_3 and elevated jugular venous pressure are noted. Crackles are noted at the lung bases. Diffuse skin thickening of the face, anterior chest, arms stopping at the elbows, and legs is noted; there is sclerodactyly of the hands. There is lower extremity edema to the knees.

Laboratory studies are normal except for a serum creatinine level of 2.2 mg/dL (194.5 µmol/L).

Chest radiograph shows bilateral pleural effusions and diffuse alveolar infiltrates. Echocardiogram shows generalized myocardial hypokinesis and a left ventricular ejection fraction of 20%. Electrocardiogram shows nonspecific T-wave changes.

Which of the following is the most likely cause of this patient's clinical presentation?

A

Cardiomyopathy

B

Constrictive pericarditis

C

Pulmonary arterial hypertension

D

Scleroderma renal crisis

Answer & Critique

Correct Answer: A

Educational Objective: Diagnose cardiomyopathy in a patient with systemic sclerosis.

Key Point

Microvascular cardiomyopathy is the most common symptomatic manifestation of heart involvement in systemic sclerosis and presents with heart failure.

The most likely diagnosis is cardiomyopathy in this patient with systemic sclerosis. Cardiomyopathy due to systemic sclerosis–induced coronary vasospasm and microvascular disease leading to patchy myocardial fibrosis is the most common symptomatic manifestation of heart involvement in systemic sclerosis. Although accelerated macroscopic coronary atherosclerosis has been associated with other autoimmune inflammatory diseases, coronary vascular involvement in systemic sclerosis is most often microvascular, with ischemia due to structural changes and recurrent spasm of small vessels. This results in contraction band necrosis, a pathologic finding due to episodes of myocardial ischemia followed by reperfusion. This process may ultimately lead to patchy fibrosis resulting in cardiomyopathy and heart failure. Patients who have systemic sclerosis with symptomatic cardiac involvement have a poor prognosis and mortality rate of 75% at 5 years. This patient presents with evidence of fluid overload due to heart failure as seen on her physical examination and confirmed by an abnormal chest radiograph and an echocardiogram suggesting diffuse myocardial dysfunction, consistent with this cause. Infiltrative myocardial fibrosis and conduction abnormalities may also contribute to the cardiac dysfunction but are less common causes of systemic sclerosis heart disease.

Constrictive pericarditis is a chronic disorder resulting from inflammation and fibrosis of the pericardium with loss of elasticity and resulting noncompliance of the pericardium. Although it may be associated with connective tissue disease, this patient does not have specific clinical findings typically associated with constrictive pericarditis such as a pericardial knock or pulsus paradoxus; furthermore, her echocardiogram shows evidence of diffuse myocardial dysfunction and no evidence of impaired cardiac filling with normal ventricular function as would be expected with constrictive pericarditis.

Pulmonary arterial hypertension is a common complication of systemic sclerosis and may lead to cor pulmonale and primarily right-sided heart failure. This patient's clinical presentation is more consistent with generalized myocardial dysfunction due to cardiomyopathy.

The kidneys are frequently involved in systemic sclerosis, with scleroderma renal crisis (SRC) occurring in 10% to 15% of patients. SRC causes acute-onset oliguric kidney disease, severe hypertension, and often microangiopathic hemolysis and thrombocytopenia. Except for evidence of impaired kidney function likely due to heart failure, this patient's clinical presentation is not consistent with SRC.

Bibliography

Question 92

A 32-year-old woman is evaluated for a 2-month history of weight loss, abdominal cramping, and loose stools. Her stools are malodorous, but she has not noted any blood associated with her bowel movements. Although her appetite is good, she has lost 3.2 kg (7.0 lb). She has an 8-year history of diffuse cutaneous systemic sclerosis.

On physical examination, temperature is normal, blood pressure is 146/92 mm Hg, pulse rate is 94/min, and respiration rate is 16/min. BMI is 19. Cardiopulmonary examination is normal. The abdomen is soft and nontender with normal bowel sounds. Diffuse skin thickening of the face, anterior chest, and distal extremities is noted as well as sclerodactyly and multiple healed digital pits. There is no rash. Muscle strength and reflexes are normal.

Laboratory studies:

Hematocrit	30%
Albumin	2.6 g/dL (26 g/L)
Alanine aminotransferase	Normal
Aspartate aminotransferase	Normal
Total bilirubin	Normal
Lipase	Normal
Urinalysis	Normal

Which of the following is the most appropriate diagnostic test to perform next?

Top of Form

A

Colonoscopy

B

CT of the abdomen and pelvis with contrast

C

Endoscopic retrograde cholangiopancreatography

D

Glucose hydrogen breath test

Answer & Critique

Correct Answer: D

Educational Objective: Diagnose bacterial overgrowth syndrome due to systemic sclerosis–associated intestinal disease.

Key Point

In patients with systemic sclerosis, malabsorption due to bacterial overgrowth is evaluated by obtaining a glucose hydrogen breath test.

A glucose hydrogen breath test is indicated. This patient has an 8-year history of diffuse cutaneous systemic sclerosis (DcSSc) and now presents with weight loss, abdominal cramping, and loose stools. She is at high risk for developing malabsorption from bacterial overgrowth (also known as blind loop syndrome) due to altered peristalsis caused by fibrosis associated with her underlying disease. She has unexplained weight loss as well as loose stools without any increase in symptoms of dysphagia, nausea, or vomiting. The most appropriate study for her evaluation at this time is the glucose hydrogen breath test. The gold standard for the detection of bacterial overgrowth is small bowel aspiration, but this study is not frequently performed because it is invasive. By comparison, the glucose hydrogen breath test is noninvasive and has a high sensitivity and specificity. Barium study may also be done to confirm these findings, but obtaining a CT scan at this point is unnecessary and costly. MRI may also be useful in the future for assessment of disease and exclusion of other pathologies.

She does not have bloody bowel movements or colitis, and performing a colonoscopy is unlikely to lead to the correct diagnosis because the primary pathology is in the small bowel and not the colon.

Endoscopic retrograde cholangiopancreatography is the diagnostic test of choice for suspected pancreatic or extrahepatic biliary tract pathology. She has no evidence of biliary tract blockage or pancreatic disease.

Question 93

A 65-year-old woman is evaluated for bilateral hand and wrist pain that worsens with activity. She reports no swelling or redness but has morning stiffness lasting less than 30 minutes. History is also significant for hypertension and diabetes mellitus. There is no personal or family history of psoriasis. Medications are hydrochlorothiazide and metformin.

On physical examination, vital signs are normal. BMI is 29. The right wrist has a mild effusion and slightly reduced range of motion. There is mild pain with range of motion of both wrists. The hands have bony hypertrophy of the proximal and distal interphalangeal joints, with mild tenderness to palpation but no swelling. Bilateral crepitus of the knees is noted. There are no rashes or nail changes.

Laboratory studies reveal a negative rheumatoid factor, and erythrocyte sedimentation rate, C-reactive protein, and serum urate levels are within normal limits.

A radiograph of the wrist is shown.

Aspiration of the wrist is performed, and results are pending.

Which of the following is the most likely diagnosis?

A
Chronic gouty arthropathy

B
Osteoarthritis with calcium pyrophosphate deposition

C
Psoriatic arthritis

D
Rheumatoid arthritis

Answer & Critique

Correct Answer: B

Educational Objective: Diagnose osteoarthritis with calcium pyrophosphate deposition.

Key Point

Osteoarthritis with calcium pyrophosphate deposition is a form of pyrophosphate arthropathy in which patients often have osteoarthritis in joints not typically involved with traditional osteoarthritis, including non–weight-bearing joints such as the shoulders and wrists.

This patient most likely has pyrophosphate arthropathy, specifically osteoarthritis with calcium pyrophosphate deposition (CPPD). She has symptoms consistent with degenerative arthritis (pain worse with activity, brief morning stiffness) and signs of osteoarthritis of her hands. Her radiograph shows calcification (also known as chondrocalcinosis) of the triangular fibrocartilage, seen as calcific densities in the region of the distal ulna and ulnar styloid, consistent with CPPD; there is also some narrowing of the carpal metacarpal joints consistent with osteoarthritis. In osteoarthritis with CPPD, patients often have osteoarthritis in joints not typically involved with traditional osteoarthritis, including non–weight-bearing joints such as the shoulders and wrists.

This patient has risk factors for gout (postmenopausal woman, hypertension and taking a diuretic, diabetes mellitus, overweight). However, she lacks a history of episodic joint inflammation that typically precedes chronic gouty arthropathy.

The distribution of involved joints, including the distal interphalangeal (DIP) joints, is consistent with psoriatic arthritis; however, there is no evidence or symptoms of inflammatory arthritis. This patient also has no skin or nail findings to support the diagnosis of psoriasis. Although some patients develop skin involvement after the onset of arthritis, psoriatic arthritis cannot account for the finding of chondrocalcinosis seen in this patient.

The absence of synovial thickening and limited morning stiffness are not consistent with inflammatory arthritis such as rheumatoid arthritis. Rheumatoid factor is also negative, and inflammatory markers are within normal limits. Finally, examination and radiographic findings indicate involvement of the DIP joints, which tend to be spared in rheumatoid arthritis.

Question 94

A 74-year-old woman is evaluated during a follow-up visit for polymyalgia rheumatica diagnosed 8 weeks ago after developing shoulder and hip girdle pain and morning stiffness. Symptoms resolved on prednisone, 15 mg/d. She feels well and reports no headache, jaw claudication, visual changes, or recurrence of myalgia or stiffness. History is significant for type 2 diabetes mellitus and hypertension. Medications are metformin, lisinopril, and prednisone, which has been tapered to 10 mg/d.

On physical examination, temperature is normal, blood pressure is 140/80 mm Hg, pulse rate is 70/min, and respiration rate is 14/min. BMI is 31. There is no temporal tenderness or induration. No carotid or subclavian bruits are present. Good range of motion without pain in the shoulders and hips is noted. Proximal strength is normal.

Laboratory studies:

	Initial	Current
Erythrocyte sedimentation rate	90 mm/h	42 mm/h
Hemoglobin	11.5 g/dL (115 g/L)	12 g/dL (120 g/L)

Which of the following is the most appropriate management at this time?

A

Increase prednisone

B

Increase prednisone and add methotrexate

C

Schedule temporal artery biopsy

D

Continue current treatment

Answer & Critique

Correct Answer: D

Educational Objective: Identify the cause of an elevated erythrocyte sedimentation rate.

Key Point

Noninflammatory conditions (kidney disease, diabetes mellitus, pregnancy, obesity) as well as normal aging can cause an elevated erythrocyte sedimentation rate.

Continuing this patient's current treatment is appropriate at this time. This patient has polymyalgia rheumatica (PMR); she feels well, and her laboratory studies have improved over time. Although her erythrocyte sedimentation rate (ESR) remains elevated, it likely does not represent ongoing disease activity. The most likely cause of this patient's persistently elevated ESR is her age; it may also be elevated because of uncontrolled diabetes mellitus (possibly exacerbated by prednisone). The degree of elevation is related to the serum globulin concentration, the albumin-globulin ratio, the serum fibrinogen concentration, and the percent of hemoglobin A_{1c} but not the fasting serum glucose concentrations. ESR is dictated by characteristics of the erythrocytes themselves and by the presence of specific plasma proteins that alter the normal repulsive forces between erythrocytes and influence their ability to aggregate, form rouleaux, and sediment more quickly. These plasma proteins include acute phase reactants (such as fibrinogen) produced by the liver in response to proinflammatory cytokines occurring in rheumatologic disease, infection, and malignancy that neutralize these negative surface charges and increase ESR. Noninflammatory conditions causing elevated fibrinogen, including kidney disease, diabetes, pregnancy, and obesity, can also result in an elevated ESR. Normal aging can also cause an elevated ESR; for this female patient, an equation to find the estimate of the maximal expected ESR is (age in years + 10)/2, resulting in 42 mm/h.

It is important to recognize underlying factors that influence laboratory studies such as ESR; misinterpreting an elevated ESR as indicative of persistent inflammation or other disease can lead to inappropriate treatment such as prolongation or increase of glucocorticoid therapy. Thus, increasing prednisone or adding methotrexate is not indicated at this time.

This patient reports no headache, jaw claudication, or visual changes, all of which are clinical signs of giant cell arteritis; therefore, temporal artery biopsy is not indicated.

Question 95

A 47-year-old woman is evaluated in the emergency department for sharp mid-chest pain that developed abruptly. The pain is exacerbated by lying down, deep inspiration, or coughing but improves when she sits up.

On physical examination, temperature is 37.8 °C (100.0 °F), blood pressure is 140/88 mm Hg, pulse rate is 100/min, and respiration rate is 22/min. A friction rub at the left sternal border is heard. The lungs are clear. There are swelling and tenderness of the second and third proximal interphalangeal and metacarpophalangeal joints.

Electrocardiogram shows diffuse ST-segment elevations in all leads except aVR and V_1 and PR-segment depression in leads V_2 to V_6.

Which of the fol lowing is the most likely cause of this patient's pericarditis?

A

Ankylosing spondylitis

B

Polymyalgia rheumatica

C

Psoriatic arthritis

D

Rheumatoid arthritis

Answer & Critique

Correct Answer: D

Educational Objective: Identify rheumatoid arthritis as the cause of pericarditis.

Key Point

Pericarditis is the most common cardiac manifestation of rheumatoid arthritis and is often asymptomatic.

Rheumatoid arthritis (RA) is the most likely cause of this patient's pericarditis. RA is an independent risk factor for both coronary artery disease and heart failure; patients with severe extra-articular disease are at particularly increased risk of cardiovascular death. Pericarditis is the most common cardiac manifestation of RA and is often asymptomatic. Approximately one third of patients with RA can be found to have an asymptomatic pericardial effusion, and 10% of patients with RA will have symptomatic pericarditis at some point during the course of their disease. Most of those with symptomatic disease have a positive rheumatoid factor and active synovitis; however, when symptomatic, the manifestations are likely to be similar to those of any other cause of pericarditis. Diagnosis is most often made by confirming two of three classic findings: chest pain, often with a pleuritic component; friction rub; and diffuse ST-segment elevation on electrocardiogram.

Ankylosing spondylitis is a form of spondyloarthritis that manifests primarily by axial inflammation and bony ankylosis (fusion across joints). Inflammatory arthritis involvement of the hands tends to present as “sausage digits” rather than the symmetric polyarthritis seen in RA. Although conduction defects and aortitis with dilatation of the aortic valve ring and aortic regurgitation occur, pericarditis is not seen in patients with ankylosing spondylitis.

Polymyalgia rheumatica occurs in patients over the age of 50 years and causes diffuse achiness at the neck, shoulder girdle, and pelvic girdle. It is rarely associated with synovitis and is not associated with pericarditis.

Psoriatic arthritis is associated with an increased risk of coronary artery disease, as is RA. It can also cause a symmetric polyarticular inflammatory arthritis involving the small joints of the hands. However, psoriatic arthritis is not a common cause of pericarditis.

Question 96

An 80-year-old woman was hospitalized 2 days ago for upper gastrointestinal bleeding due to peptic ulcer disease. She was placed on omeprazole and given intravenous normal saline for hydration. Today she has developed right knee pain and swelling. History is also significant for osteoarthritis of the hands and knees. Her only medication prior to admission was ibuprofen as needed.

On physical examination, temperature is 37.8 °C (100.0 °F); the remainder of the vital signs is normal. Hand findings are consistent with osteoarthritis. The right knee is warm with a large effusion, is tender to palpation, and has limited flexion to 90 degrees.

Aspiration of the right knee is performed; the synovial fluid is yellow and cloudy, and the leukocyte count is 15,000/μL (15×10^9/L).

Which of the following synovial fluid tests will be most helpful in establishing a diagnosis?

A

Antinuclear antibody measurement

B

Glucose measurement

C

Gram stain, culture, and crystal analysis

D

Protein measurement

Answer & Critique

Correct Answer: C

Educational Objective: Evaluate synovial fluid for infection and crystal-related disease.

Key Point

The most useful tests to obtain from synovial fluid are leukocyte count, Gram stains, cultures, and crystal analysis to evaluate for infection and crystal-related disease and to distinguish between inflammatory and noninflammatory disease.

Gram stain, culture, and crystal analysis are the most helpful and appropriate diagnostic tests to perform next on this patient's synovial fluid. Synovial fluid aspiration is essential when evaluating for infection and crystal-related disease and is useful in distinguishing between inflammatory and noninflammatory disease. On physical examination, this febrile patient has evidence of a monoarthritis with inflammation in her knee, which is confirmed by the cloudy appearance of the synovial fluid at the bedside and her elevated synovial fluid leukocyte count (15,000/µL [15 × 10^9/L]). Synovial fluid leukocyte counts greater than 2000/µL (2.0 × 10^9/L) are consistent with inflammatory fluid; the higher the count is, the more inflammatory the fluid and the greater the suspicion for crystal-related or infectious disease. An acute hospitalization or illness can precipitate an attack of crystal-related arthritis (either gout or pseudogout) and/or infection, and these entities can be evaluated for by synovial fluid analysis. It is important to note that the presence of crystals does not rule out concomitant infection. The most useful tests to obtain when analyzing synovial fluid are leukocyte count, stains, cultures, and crystal analysis. Sometimes the amount of synovial fluid available for analysis may be small; therefore, it is important to order only the most useful tests.

Antinuclear antibodies, glucose levels, and protein levels do not add any useful information and do not distinguish between infectious and noninfectious synovial fluid.
