- The disappearance of eosinophilia is considered a poor prognostic sign; it may represent the development of superimposed bacterial infections.

- Compared to other skeletal muscles, the diaphragm has a relatively high density of encysted larvae.

- There is no therapeutic role for intravenous immune globulin.

Educational objective: To identify the clinical features of trichinosis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Drug-induced myopathies
2. Clinical manifestations and diagnosis of inclusion body myositis
3. Trichinosis
4. Viral myositis

Answer to Question 18
Answer: D

This patient has multiple compression fractures suggestive of osteoporosis. Many of the causes of secondary osteoporosis have been ruled out by the normal laboratory results already obtained. Of the remaining choices, all would be useful except measurement of the urinary excretion of cross-linked N-telopeptides (NTX).

Hypogonadism secondary to testicular dysfunction may lead to low serum testosterone and premature osteoporosis with compression fractures. In addition, secondary osteoporosis may be a result of hyperthyroidism or hypovitaminosis D.

Bone densitometry would help to quantify the degree of bone loss and may provide a baseline value of bone density that can be used over time to measure response to therapy.

Biochemical markers of bone loss, such as the urinary excretion of cross-linked N-telopeptides (NTX) of type 1 collagen, are not useful in making the diagnosis of osteoporosis because the values in normal subjects and patients with osteoporosis overlap substantially. In addition, the diagnostic utility of a single measurement is limited.

Educational objective: To be familiar with the laboratory evaluation of osteoporosis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Epidemiology and causes of osteoporosis
2. Use of biochemical markers of bone turnover in osteoporosis
3. Bone disease with hyperthyroidism and thyroid hormone therapy

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Answer to Question 19
Answer: E

The vast majority of patients with late onset prosthetic joint infections will not be cured until the prosthesis is removed, particularly if the prosthesis is both infected and loosened. Surgical debridement with prolonged antibiotic therapy may be curative in 25 to 33 percent of patients with early prosthetic joint infections, but this approach is seldom successful in patients with late infections.

The procedure most likely to result in cure and successful replacement of a new prosthesis is the "two-stage" procedure outlined in answer E. The five-year success rate for this technique, when S. aureus is the causative microorganism, has been as high as 95 percent in one series.

In patients who are poor surgical candidates or refuse surgery, chronic suppressive antibiotic therapy may be successful for several months or years, however, the failure rate is high.

A "one-stage" replacement procedure and arthroscopic debridement have high failure rates and would not be recommended for this patient.

Educational objective: To understand the approach to the treatment of late prosthetic joint infections.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Treatment and prevention of prosthetic joint infections

Answer to Question 20
Answer: D

Calcitonin is considered by some investigators to be an effective first-line therapy in patients who have substantial pain from an acute osteoporotic fracture, because of its analgesic actions. However, most clinical trials to date have shown more improvement in bone mineral density and a greater reduction in fracture rates with bisphosphonate therapies such as alendronate or risedronate.

Nasal calcitonin has not been shown to be an effective therapy in premenopausal women. It can be used with estrogen replacement therapy, although this combination has never been formally investigated as a therapy for osteoporosis.

There is concern that tachyphylaxis to nasal calcitonin can occur. This is based on observations of its use in patients with Paget's disease where this phenomenon has occurred.

Treatment with oral bisphosphonates lowers serum calcium concentrations, although clinically important hypocalcemia has been reported only in patients with hypoparathyroidism, vitamin D, or calcium deficiency.

Educational objective: To understand the differences between the various antiresorptive therapies for osteoporosis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Overview of the management of osteoporosis in women
2. Calcitonin in the prevention and treatment of osteoporosis

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Answer to Question 21
Answer: B

The treatment of patients with Raynaud's phenomenon (RP) includes the use of conservative measures such as the avoidance of cold temperatures and careful transitions from warm to cold environments. It is essential that anyone with Raynaud's phenomenon stop smoking, as this habit clearly contributes to vasoconstriction and endothelial injury.

Sympathomimetic drugs (such as decongestants, amphetamines, diet pills, and herbs containing ephedra) should be avoided since they may exacerbate Raynaud's phenomenon.

Some studies have noted the benefit of behavioral training for some patients. The goal is to train the patient with Raynaud's phenomenon to voluntarily control their peripheral circulation.

Many published studies have used both short and long acting preparations of the calcium channel blockers in the treatment of Raynaud's phenomenon. In particular, nifedipine has been noted to be a useful therapeutic agent.

It was initially suggested that nonselective beta blockers could cause Raynaud's phenomenon. However, more recent studies have shown that beta blockers do not induce vasoconstriction in these patients.

Educational objective: To understand and treat Raynaud's phenomenon.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Treatment of Raynaud's phenomenon

2. Clinical manifestations and diagnosis of Raynaud's phenomenon

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Answer to Question 22
Answer: C

Aspirin-induced asthma is mediated by increased leukotriene production. When the cyclooxygenase pathway is blocked by NSAIDs or aspirin in these patients, there is an abnormal increase in leukotriene production. Any drug that significantly blocks the cyclooxygenase pathway could provoke a similar asthma exacerbation. Choline magnesium salicylate and salicylic acid, both non-acetylated salicylates, have weak to absent cyclooxygenase inhibitory properties and can be used with appropriate caution in these patients.

In contrast, all the other NSAIDs including non-selective inhibitors and cyclooxygenase-2 selective inhibitors of the cyclooxygenase pathway may induce an asthma exacerbation in a susceptible patient and thus these drugs should be avoided. If there is a question as to whether this patient's episode of angioedema was coincidental to her aspirin ingestion, she could be challenged in a supervised setting if the potential benefit warrants the risk.

Educational Objective: An increased understanding of aspirin-induced asthma and the implications for NSAID use in these patients.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Aspirin-induced asthma
2. NSAID: Overview of adverse effects
3. Aspirin: Efficacy and toxicity in rheumatic and other disorders

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Answer to Question 23
Answer: E

This patient presents with dry eyes and mouth, mild parotid swelling, fatigue, worsening myalgia, and peripheral neuropathy. The chest radiograph demonstrates interstitial lung abnormalities and laboratory data reveals a polyclonal gammopathy, a mildly elevated sedimentation rate, and negative serologic studies for autoantibodies. Although suggestive of Sjögren's syndrome, these features are not uniquely specific for the diagnosis. For example, alcoholism could explain the neuropathy and parotid swelling. Amitriptyline therapy may contribute to the sicca symptoms. Other systemic disorders such as sarcoidosis or amyloidosis may also fit the clinical picture.

Before recommending a therapeutic plan, a more definitive diagnostic test is required. Since the anti-Ro and La antibodies are negative, biopsy of a labial salivary gland would provide the best choice for establishing the diagnosis of Sjögren's syndrome. It is also a minimally invasive test. Thus, choice E is correct.

A sural nerve biopsy may be useful in establishing the diagnosis of vasculitis or amyloidosis, particularly if symptoms worsened or persisted, or if motor loss occurred. However, neither condition is the likely cause of this patient's illness, and a nerve biopsy is less desirable in this patient given its invasive nature.

The Schirmer test may confirm decreased tear production and the Rose Bengal stain may identify areas of corneal and conjunctival damage from decreased tear production. These tests would confirm xerophthalmia but could not establish the diagnosis of Sjögren's syndrome in this patient.

The use of bronchoscopy with BAL and TBBx is not warranted in this case. Although one could consider these studies at a later point, less invasive procedures such as the labial salivary gland biopsy should be performed first.

Educational objective: Consider the multiple disorders that mimic many of the manifestations of Sjögren's syndrome.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Classification and diagnosis of Sjögren's syndrome
2. Clinical manifestations of Sjögren's syndrome
3. Treatment of Sjögren's syndrome

Answer to Question 24
Answer: B

This patient has radiographic evidence of sarcoidosis. Features include the presence of multiple phalangeal cysts and cortical erosions. Bony lesions are cystic and rarely sclerotic. The involvement of the phalangeal shafts, lack of cartilage loss, and sparing of the wrist and metacarpophalangeal joints rule out the diagnosis of rheumatoid arthritis. In addition, the ocular involvement noted in the past is also consistent with sarcoidosis. Bone involvement in this condition occurs in about 5 percent of patients. Although bone involvement generally implies a more chronic and severe course, almost half of affected patients are asymptomatic. Thus, choice B is false.

The other statements are true, and therefore, incorrect answers:

- Bone involvement in patients with sarcoidosis is unusual in the absence of infiltrative skin lesions.
- Involvement of the skull may be associated with the development of painless nodules in the scalp.
- Sarcoidosis involvement of bone and Paget's disease may share similar radiographic and radionuclide imaging features. A distinction between the two can be made by measuring the serum alkaline phosphatase which is raised in active Paget's disease but not in sarcoidosis.
- As mentioned, bony lesions are rarely sclerotic.

Educational objective: To review the features of bony involvement in sarcoidosis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Overview of sarcoidosis
2. Rheumatic manifestations of sarcoidosis

Answer to Question 25
Answer: C

This patient's illness has features of three connective tissue diseases: systemic lupus erythematosus (SLE) (inflammatory arthritis resolving with hydroxychloroquine and a nonsteroidal anti-inflammatory drug); polymyositis (proximal weakness with an elevated CPK and abnormal nailfold microscopy); and scleroderma (sclerodactyly and abnormal nailfold microscopy). The disease overlap and the presence of antibodies to U1 ribonucleoprotein is diagnostic of mixed connective tissue disease (MCTD).

Choice C is correct since she has clinical features of trigeminal neuropathy, the most frequent CNS finding in both MCTD and scleroderma. By comparison, the more characteristic CNS findings in SLE, such as cerebritis, psychosis, and seizures, are not found in MCTD.

The absence of severe renal disease is a hallmark of MCTD. It is possible that high titers of anti-U1 RNP antibodies may protect against the development of diffuse proliferative glomerulonephritis, independent of whether these antibodies occur in MCTD or classic SLE.

Hydralazine is a known cause of drug-induced lupus; however, it has not been linked to MCTD.

An inflammatory myopathy, clinically and histologically identical to classic polymyositis, is a hallmark feature of MCTD.

Whereas malignancy should be suspected in patients with dermatomyositis over the age of 50, there is no known association with MCTD.

Educational objective: Diagnose mixed connective tissue disease and know its clinical presentation and natural history.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical manifestations of mixed connective tissue disease
2. Anti-U1 RNP antibodies in mixed connective tissue disease
3. Definition and diagnosis of mixed connective tissue disease

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Answer to Question 26
Answer: E

This patient has an abnormally low serum TSH suggesting over-replacement of thyroid hormone. This is a well-known cause of accelerated bone loss leading to osteoporosis. Thus, the appropriate therapeutic decision is to reduce the dose of levothyroxine.

The patient is already taking appropriate doses of calcium and vitamin D. Increasing the hydrochlorothiazide is not likely to add any therapeutic value to a plan that already includes appropriate calcium intake. Initiating alendronate therapy without correcting her thyroid dose first would also not be an effective treatment plan.

Educational objective: To be able to identify causes of bone loss.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Bone disease with hyperthyroidism and thyroid hormone therapy
2. Epidemiology and causes of osteoporosis
3. Overview of the management of osteoporosis in women
4. Clinical use of the bisphosphonates in osteoporosis

Answer to Question 27
Answer: B

Two alleles, DRB1*0401 (previously called Dw4) and DRB1*0404 (previously called Dw14), primarily account for the DR4 association with disease in Caucasians. All of the associated alleles share the presence of a region of highly similar sequence called the shared epitope, a short amino acid sequence in the beta chain of the DR4 molecule. It has been postulated that this portion of the DRB molecule (amino acids 67-74) controls susceptibility to disease. This hypothesis has been further bolstered by the remarkable finding that among ethnic populations in which DR4 is rare, the alleles associated with RA still contain the shared epitope. This "shared epitope" can also be found in certain other HLA class II molecules, including DR1 and DR6.

Not all populations fit the shared epitope hypothesis. For example, the majority of African-American patients with RA do not carry the shared epitope in their DR genes.

Most studies have found a correlation between DR4+ RA-associated alleles and more severe, erosive disease, as measured by the severity of radiographic changes. In addition, having two "doses" of shared epitope-positive genes increases the risk for and disease severity of RA.

Educational objective: To understand the role of histocompatibility genes in the genetics of rheumatoid arthritis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. HLA and other susceptibility genes in rheumatoid arthritis
2. Pathogenesis of rheumatoid arthritis
3. Risk factors for and possible causes of rheumatoid arthritis

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Answer to Question 28
Answer: B

The differential diagnosis of this patient's illness includes a connective tissue disease such as SLE or a systemic necrotizing vasculitis such as Wegener's granulomatosis or MPA. However, the presence of a C-ANCA by immunoflu-

orescence would essentially rule out the diagnosis of SLE. This was noted in a large study of patients with various connective tissue diseases; none had a positive C-ANCA. In contrast, P-ANCA was detected in 31 percent of patients with systemic lupus erythematosus and in 0 to 5 percent of patients with other types of connective tissue disease.

Almost all patients with active systemic Wegener's granulomatosis have a positive ANCA. This disorder is most clearly associated with the presence of ANCA directed against a specific target antigen, which is most commonly PR3. Eighty to 95 percent of all ANCA found in patients with Wegener's granulomatosis are C-ANCA by immunofluorescence and PR3 by ELISA. Although patients with Churg-Strauss syndrome may have similar clinical features, she lacks the characteristic history of asthma and there is no peripheral eosinophilia.

Neither Takayasu's arteritis or polyarteritis nodosa are associated with a positive ANCA.

Educational objective: To be able to identify the distinguishing characteristics of various connective tissue diseases.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical spectrum of antineutrophil cytoplasmic antibodies
2. Pulmonary manifestations of systemic lupus erythematosus
3. Pathogenetic role of ANCA in Wegener's granulomatosis and related vasculitides
4. Churg-Strauss syndrome (allergic granulomatosis and angiitis)

Answer to Question 29
Answer: B

This patient probably has GCA, based on her history of antecedent jaw claudication (a highly specific finding), abrupt visual loss, and the fundoscopic examination showing the characteristic changes of ischemic optic neuropathy. If untreated, the second eye is likely to become affected within one to two weeks. Thus, it is necessary to initiate therapy with corticosteroids immediately. Awaiting the results of a temporal artery biopsy before initiating prednisone would be inappropriate.

An initial dose of 40 to 60 mg of prednisone or its equivalent in single or divided daily doses is adequate in nearly all cases of GCA, while some patients have responded to doses as low as 20 mg/day. The role of methotrexate is unclear; it has not yet been proven to be an effective or steroid sparing therapy for GCA.

Educational objective: To review the issues related to visual loss in GCA.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical manifestations and diagnosis of giant cell (temporal) arteritis
2. Treatment of giant cell (temporal) arteritis

Answer to Question 30
Answer: B

This patient with RA and the new onset of fever and selected painful joints most likely has developed a septic arthritis. Although a flare of RA is a possibility, it would not typically be associated with a fever or chills.

The following results are typically obtained from synovial fluid analysis in patients with bacterial arthritis:

- Synovial fluid culture is positive in the majority of patients with nongonococcal bacterial arthritis. Negative cultures may occur in those who have received recent antimicrobial therapy or are infected with a fastidious organism such as some streptococci or mycoplasma. Blood cultures are positive in 50 percent of cases.

- Gram stain is positive in most but not all cases. However, false positive results can be obtained because precipitated crystal violet and mucin in the synovial fluid can mimic gram-positive cocci.

- The synovial fluid glucose is often depressed and lactic acid concentration is elevated; however, these tests are not sufficiently sensitive to be of widespread diagnostic utility.

• The infected fluid is usually purulent with an average leukocyte count ranging between 50,000 to 150,000 cells/mm3.

Educational objective: Recognition of the clinical presentation and important diagnostic tests in patients with rheumatoid arthritis and suspected superimposed septic arthritis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Bacterial (nongonococcal) arthritis
2. Synovial fluid analysis and the diagnosis of septic arthritis

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Answer to Question 31
Answer: B

The patient clearly has SLE, as manifested by a photosensitive rash, alopecia, arthritis, and a positive ANA and anti-dsDNA. The finding of an extremely low serum albumin with moderate proteinuria is a clinical clue suggesting the presence of a protein losing enteropathy, which may be asymptomatic. It is diagnosed via a tagged serum albumin study, which reveals a large loss of albumin in stool. It is a (rare) complication of SLE and responds well to moderate doses of corticosteroids.

Although she also has concurrent renal disease, the degree of proteinuria is not within the nephrotic range. In addition, she is unlikely to have significant liver dysfunction without liver function test abnormalities and physical signs of hepatic disease. She is not clinically malnourished.

Educational objective: To understand the clinical characteristics and evaluation of SLE with protein losing enteropathy.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Gastrointestinal manifestations of systemic lupus erythematosus
2. Protein-losing gastroenteropathy

Answer to Question 32
Answer: A

This patient has an acute episode of pseudogout due to calcium pyrophosphate dihydrate crystal deposition disease (CPPD). The diagnosis is based upon the finding of weakly positively birefringent crystals in synovial fluid by compensated polarized light microscopy along with radiographic documentation of chondrocalcinosis.

Aside from peripheral joint involvement, there may be axial involvement, especially in familial forms of the condition. These include bony ankylosis, deposition of crystals in the ligamentum flavum, the longitudinal ligaments, the intervertebral discs, and the sacroiliac joints. These patients may develop a more accelerated form of osteoarthritis of the lumbosacral spine. Thus, his back pain may be a manifestation of this condition.

CPPD crystal deposition disease can occur in association with a variety of metabolic and endocrine conditions including hemochromatosis, hyperparathyroidism, chronic hypomagnesemia, and hypophosphatasia. Thus, it would be appropriate to measure the serum iron, total iron binding capacity, calcium, and phosphorus.

In a subset of patients with CPPD crystal deposition, a familial basis has been established for the disease. Numerous affected kindreds have been described from a variety of geographic regions. An autosomal dominant inheritance of the disorder has been discovered in nearly all of these families.

CPPD can mimic gout, osteoarthritis, spondyloarthropathy, and in up to 5 percent of patients, rheumatoid arthritis.

Educational objective: To review salient clinical features of calcium pyrophosphate dihydrate crystal deposition disease.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical manifestations; diagnosis; and treatment of calcium pyrophosphate crystal deposition disease
2. Pathogenesis and etiology of calcium pyrophosphate crystal deposition disease
3. Clinical manifestations of hereditary hemochromatosis

Answer to Question 33
Answer: C

This patient presents with polyarthralgias, palpable purpura, hypocomplementemia, and a positive rheumatoid factor. The absence of joint swelling makes the diagnosis of RA unlikely. The biopsy reveals PAS-positive microthrombi, which is pathognomic for the presence of cryoprecipitates. Thus, this presentation is most consistent with cryoglobulinemia. The incidence of circulating cryoglobulins in chronic liver disease has been found to be highest in patients infected with hepatitis C virus. One study noted their presence in over 50 percent of patients compared to an incidence of 15 percent in patients with hepatitis B and 25 percent of patients with forms of autoimmune liver disease. The rheumatoid factor positivity is also consistent with hepatitis C infection; it has been observed that hepatitis C-infected lymphocytes may secrete molecules with rheumatoid factor activity.

Although SLE can be associated with polyarthralgias and palpable purpura, the ANA titer is too low to consider it to be a positive result. In addition, the diagnosis of SLE would not explain the elevated RF.

Educational objective: To recognize the presentation of hepatitis C in patients with joint complaints.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical manifestations and natural history of hepatitis B virus infection
2. Malignancy and rheumatic disorders
3. Extrahepatic manifestations of hepatitis C virus infection
4. Cutaneous manifestations of systemic lupus erythematosus

Answer to Question 34
Answer: B

The clinical manifestations of Henoch-Schönlein purpura (HSP) include the following classic tetrad that can occur in any order and at any time over a period of several days to several weeks: rash, arthralgias, abdominal pain, and renal disease. This patient's presentation is consistent with this disorder.

HSP is characterized by the tissue deposition of IgA-containing immune complexes. The pathogenesis of this disorder may be similar to that of IgA nephropathy, which is associated with identical histologic findings in the kidney. With HSP, renal disease is usually noted within a few days to four weeks after the onset of systemic symptoms. This patient's clinical presentation, particularly the presence of palpable purpura, is most consistent with HSP and not an isolated IgA nephropathy.

There is a general, but not absolute, correlation between the severity of the clinical manifestations and the findings on renal biopsy. Patients with only asymptomatic hematuria, for example, usually have only focal mesangial proliferation. By comparison, the appearance of significant proteinuria and renal insufficiency is associated with more marked cellular proliferation and frequent crescent formation. Thus, the biopsy finding of crescentic glomerulonephritis with IgA deposition (choice B) is most consistent with these clinical findings, rather than mesangial proliferation with IgA deposition on immunofluorescence

Crescentic glomerulonephritis with negative immunofluorescence and no deposits on electron microscopy would be characteristic of pauci-immune disorders, such as Wegener's granulomatosis or other systemic necrotizing vasculitides. However, this patient's presentation, particularly the presence of purpura, is atypical for these diseases.

In this clinical setting, a proliferative glomerulonephritis with subendothelial immune deposits would be most consistent with poststreptococcal glomerulonephritis. Although the presentation is consistent with this diagnosis, the presence of palpable purpura over the lower extremities is uncommon with this disorder.

Educational objective: To recognize the typical histological findings on renal biopsy in Henoch-Schönlein purpura (HSP).

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Henoch-Schönlein purpura
2. Course of poststreptococcal glomerulonephritis
3. Hematuria following upper respiratory infection

Answer to Question 35
Answer: C

This patient's presentation is characteristic of Sweet's syndrome. This disorder of unknown etiology with a striking predilection for women, presents with the abrupt onset of fever, rash, and a leukocytosis. The rash generally consists of erythematous plaques infiltrated by neutrophils.

Further follow-up is required since approximately 50 percent of affected patients have an associated disorder. These include malignancies (myelodysplastic disorders in 20 to 25 percent and solid tumors in 15 percent), bacterial and viral infections, inflammatory bowel disease, rheumatologic conditions such as rheumatoid arthritis and systemic lupus erythematosus, and ingestion of certain drugs. These drugs include oral contraceptives, minocycline, lithium, and furosemide. Thus choice C is correct.

Cytokine dysregulation is thought to play a key role in the pathogenesis of Sweet's syndrome. Granulocyte colony-stimulating factor (G-CSF) and interleukins 1, 3, 6 and 8 seem to play important roles. However, no clear role for TNF has been identified. Thus, the use of anti-TNF therapies is unwarranted.

The diagnostic histopathology consists of a nodular and dense perivascular neutrophilic infiltrate with neutrophil karyorrhexis without vasculitis.

Educational objective: To recognize the clinical features of Sweet's syndrome.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Neutrophilic dermatoses

Answer to Question 36
Answer: A

Takayasu's arteritis typically afflicts women between the ages of 10 and 40, with a predilection for the aorta and its primary branches. Vascular insufficiency ensues, usually starting with the left middle or proximal subclavian artery and later involving the left common carotid, vertebral, and brachiocephalic arteries. CT angiography may be more sensitive than conventional angiography in establishing the diagnosis and detecting mural vessel changes. In addition, it may be used to follow patients in response to treatment. Thus, choice A is correct.

The other choices are incorrect for the following reasons:

- Autoantibodies, such as ANCA or antiphospholipid antibodies, cannot be detected in the sera of patients with this disease.

- The following complications of Takayasu's disease: the development of aneurysms, aortic (not mitral) regurgitation, hypertension, and retinopathy, are all predictors of a poor outcome.

- Approximately one-half of all patients have chronic active disease that requires immunosuppressive therapies in addition to the use of systemic corticosteroids.

- The synovitis seen in patients with Takayasu's arteritis typically involves large joints such as the wrists or knees.

Educational objective: To understand the clinical presentation and therapy of Takayasu's arteritis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Takayasu's arteritis
2. Clinical manifestations and diagnosis of giant cell (temporal) arteritis

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Answer to Question 37
Answer: A

This patient with Sjögren's syndrome and xerophthalmia has developed worsening symptoms of eye irritation after using an artificial tear preparation. Although worsening of the Sjögren's syndrome sicca symptomatology could account for increased eye irritation, the temporal relation between the onset of irritation following treatment with artificial tears suggests that the artificial tears are the more likely culprit. Most of the standard preparations contain preservatives, stabilizers, and solubilizers which extend the lifetime of the product. However, in some patients they may cause itching and eye irritation. Appropriate management would be to discontinue the use of the product and recommend the use of preservative-free artificial tears. Thus, choice A is correct.

Although artificial tears can worsen blepharitis, the lack of lower conjunctival erythema makes this diagnosis unlikely. Similarly, the lack of conjunctival discharge does not support the diagnosis of a bacterial conjunctivitis.

Acetylcysteine is a mucolytic agent added to some artificial tear preparations. Its use would not be helpful in this case.

Episcleritis or scleritis can occur in patients with RA. However episcleritis usually presents unilaterally. Scleritis, a more serious manifestation, presents with pain, photophobia, and increased tear production.

Educational objective: To understand the purpose of the different components of artificial tears preparations used in the treatment of Sjögren's syndrome.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Treatment of Sjögren's syndrome
2. Episcleritis and scleritis

Answer to Question 38
Answer: C

This elderly patient presents with a common problem, namely the development of asymptomatic hyperuricemia in the setting of diuretic therapy. The proximal tubule is the major site of urate handling; both reabsorption and secretion occur in this segment, with the net effect being the reabsorption of most of the filtered urate. Diuretics decrease urate excretion by increasing net urate reabsorption; this can occur either by enhanced reabsorption or by reduced secretion. Volume depletion plays an important role in this response, since urate retention does not occur if the diuretic-induced fluid losses are replaced.

The degree of urate retention is dose-dependent. In patients with hypertension, for example, 12.5 mg of hydrochlorothiazide (or its equivalent) is often as effective as 50 mg in lowering the blood pressure; the lower dose, however, does not induce hyperuricemia.

Treatment of asymptomatic hyperuricemia is not necessary, even though the plasma urate concentration may exceed 15 mg/dL. These patients are not at risk for the development of uric acid nephropathy, since the elevation in the plasma urate level is due to an initial decrease in the rate of urate excretion. Gouty arthritis is also not common in this setting, occurring primarily in patients with a personal or family history of the disease. This patient did not have either of those risk factors. However, careful observation of this patient over time will determine whether this approach will need to be modified.

Educational objective: To understand the mechanisms of diuretic-induced hyperuricemia and its appropriate management.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Diuretic-induced hyperuricemia and gout
2. Etiology and management asymptomatic hyperuricemia

Answer to Question 39
Answer: B

This patient with RA has developed rheumatoid nodules. Palpable nodules are present in 20 to 35 percent of patients with RA, and almost all nodule formers have positive tests for rheumatoid factor. Methotrexate use has been associated with the development of nodules in some patients with RA. This may occur despite the concurrent effective suppression of synovial inflammation by methotrexate. Among susceptible individuals this complication may be due to the activation of adenosine A1 receptors by methotrexate, which leads to enhanced cellular fusion and the formation of multinucleated giant cells.

Palpable nodules are present in 20 to 35 percent of patients with RA. Almost all nodule formers have positive tests for rheumatoid factor.

Similar to rheumatoid nodules, gouty tophi can involve the olecranon surface.

Rheumatic fever nodules are typically firm, nontender, and are present for one or more weeks, rarely for more than a month. Thus, choice B is correct.

Educational objective: To review the manifestations of nodule formation associated with methotrexate use.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Ganglia and nodules
2. Major side effects of methotrexate

Answer to Question 40
Answer: B

This patient has developed a saddle nose deformity, which is caused by a chondritis with destruction of nasal cartilage. The differential diagnosis of this lesion includes: infectious granulomatous lesions such as tuberculosis, leprosy, and syphilis; idiopathic granulomatous inflammation due to Wegener's granulomatosis or relapsing polychondritis; or neoplasms including diffuse large B-cell lymphoma (lymphomatoid granulomatosis), extranodal natural killer/T cell nasal type lymphoma (lethal midline granuloma), other types of lymphoma and carcinoma.

The most likely cause in this patient's case is relapsing polychondritis since it is the only disorder that is associated with asthma, which this patient recently developed.

Educational objective: To be able to identify upper airway features of rheumatic diseases.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical manifestations and diagnosis of Wegener's granulomatosis and microscopic polyangiitis
2. Diagnostic evaluation of relapsing polychondritis
3. Clinical and pathologic features of mature peripheral T and NK cell lymphomas
4. Clinical and pathologic features of diffuse large B cell lymphoma

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Answer to Question 41
Answer: B

Parvovirus infection should be considered in all adults presenting with acute polyarthralgias or arthritis and skin rash. The onset of disease mimics acute rheumatoid arthritis; primary involvement of the small joints of the hands and knees is frequently followed by additive involvement of the wrists, feet, elbows, and shoulders. The rash may be

evanescent or overlooked by the patient.

The diagnosis of acute parvovirus infection would be confirmed by the detection of circulating IgM antibody to parvovirus. IgM antibody develops within 10 to 12 days after infection and is present in over 90 percent of patients with erythema infectiosum at the onset of rash. The presence of an IgG antibody is evidence of preexisting infection and may be found in a substantial portion of the normal population. Thus, its detection in this patient would not be helpful diagnostically.

Although tests such as the ANA and ESR might be helpful, they would unlikely be diagnostic in this situation. The ESR is nonspecific, and if elevated, would only confirm the presence of an inflammatory process. The patient lacked other features suggesting a connective tissue disease. The history and physical exam is not consistent with Lyme disease.

Educational objective: To recognize the typical presentation of acute arthritis associated with human parvovirus infection.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Specific viruses that cause arthritis
2. Epidemiology and laboratory diagnosis of parvovirus B19 infection
3. Clinical manifestations and pathogenesis human parvovirus B19 infection
4. General symptomatology and diagnosis of systemic lupus erythematosus

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Answer to Question 42
Answer: B

Inherited deficiencies of complement components can predispose to immune complex excess syndromes such as systemic lupus erythematosus or bacterial infections and tissue damage. These conditions are inherited as autosomal codominant or recessive traits, except for the deficiencies of C1 inhibitor (which is autosomal dominant) and properdin (which is X-linked).

Deficiencies are inherited in an autosomal codominant or recessive fashion and result from "null" (Q0) alleles in which no protein is produced. Heterozygotes inherit a single Q0 gene and a "normal" gene and usually have one-half of the plasma levels normally present. On the other hand, homozygotes inherit a Q0 gene from each parent and do not have detectable levels of the protein. Thus, choice B is correct.

A total deficiency of C4 (Q0 alleles at all four C4 loci) is exceedingly rare. When present, however, it is associated with an early onset, severe form of SLE. In contrast, partial deficiencies of C4 are very common and predispose to the development of SLE and related disorders. As an example, 10 to 15 percent of Caucasian patients with SLE are null for C4A.

A deficiency of either of the serine proteases C1r or C1s is associated with the development of SLE; these deficiencies generally have prominent renal and cutaneous manifestations.

Deficiency of components of the membrane attack complex (MAC, C5-C9) is primarily associated with infection by Neisseria species (meningococcal and gonococcal). The infections are often caused by unusual serotypes and are rarely fulminant. Individuals carrying these genotypes are otherwise surprisingly healthy.

Educational objective: To understand the mechanisms by which complement deficiency states predispose to rheumatic diseases.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. General symptomatology and diagnosis of systemic lupus erythematosus
2. Inherited and acquired disorders of the complement system

Answer to Question 43
Answer: E

Osteonecrosis is a pathological process that has been associated with numerous conditions and therapeutic interventions. Compromise of the bone vasculature leading to the death of bone and marrow cells and ultimate mechanical failure, appear to be common to most proposed etiologies. If left untreated, progressive joint destruction within three to five years is common. Depending upon the imaging technique used to establish the diagnosis, osteonecrosis is seen in 3 to 30 percent of patients with SLE. Risk factors for osteonecrosis have been identified in SLE and include the following:

- The use of regular doses of prednisone greater than 20 mg per day
- The presence of antiphospholipid antibodies
- Raynaud's phenomenon
- Hyperlipidemia

Male sex does not confer any added to risk for the development of osteonecrosis in patients with SLE.

Educational objective: To identify the risk factors for the development of osteonecrosis in patients with SLE.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Osteonecrosis

Answer to Question 44
Answer: A

This patient with scleroderma presents with dyspnea of recent onset. The physical examination reveals an increased P2 heart sound and normal lung auscultation. The chest x-ray shows an enlarged right pulmonary artery with attenuation of the smaller vessels. These features are most consistent with the diagnosis of pulmonary hypertension. Another helpful clue is an isolated reduction in the pulmonary diffusion capacity, DLCO, to less than 65 percent of predicted, in the absence of significant restrictive ventilatory abnormalities. Thus, choice A is correct.

The lack of interstitial changes on chest radiograph along with the absence of pulmonary rales make the diagnosis of interstitial lung disease less likely.

The patient has no systemic features such as fever or chills and does not have a cough. Along with the lack of a history of immunosuppressive drug therapy, there is little evidence to support a diagnosis of an opportunistic lung infection.

Although recurrent pulmonary emboli could conceivably present in this fashion, there is no history of any pain suggesting prior thromboembolic events.

The radiographic findings with pulmonary sarcoidosis include bilateral hilar adenopathy; prominent pulmonary arteries are not observed.

Educational objective: To review the pulmonary manifestations of systemic sclerosis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Rheumatic manifestations of sarcoidosis
2. Clinical manifestations and diagnosis of secondary pulmonary hypertension
3. Clinical manifestations and evaluation of scleroderma lung disease
4. Overview of sarcoidosis

Answer to Question 45
Answer: D

The insidious onset and progressive development of asymmetric weakness in this middle aged male patient is most consistent with the diagnosis of an inclusion body myositis. By comparison, the asymmetric and distal muscle involvement are not typical features for polymyositis. The mildly elevated CPK level is an additional feature com-

monly seen with inclusion body myositis. The muscle histopathology typically reveals endomysial inflammation in over 90 percent of cases and basophilic rimmed vacuoles are seen in the muscle fiber sarcolemma in virtually all cases. There is no effective treatment for this disorder; treatment with corticosteroids may provide only short-term relief.

The patient's symptoms are not consistent with a metabolic myopathy. Usually, these patients complain of exercise-induced weakness. Thus, a forearm ischemic muscle test would not be helpful.

Myasthenia gravis, an autoimmune disease of the neuromuscular junction, presents with a history of "fatigue" from continued muscle use. Ocular manifestations are usually present. The CPK is normal.

The periodic paralyses are related to disorders of either thyroid or potassium metabolism. Symptoms of profound weakness and even paralysis develop, but are episodic in nature. Between flare-ups, the patient may have normal muscle strength.

Educational objective: To recognize the distinct features of inclusion body myositis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Paraneoplastic syndromes of the nervous system
2. Clinical manifestations and diagnosis of inclusion body myositis
3. Approach to the metabolic myopathies
4. Musculoskeletal symptoms in thyroid disease

Answer to Question 46
Answer: D

This patient has some clinical features suggesting that plain radiographs of the lumbar spine should be obtained. These include the prior history of cancer, her age over 50, and pain lasting more than one month. Thus, in this situation, there is a role for obtaining plain radiographs prior to considering more costly alternatives such as a MRI.

Common radiographic findings may include fracture, vertebral end-plate destruction, disc degeneration and osteoarthritic changes, or structural anomalies such as spondylolysis or spondylolisthesis.

A normal plain radiograph does not entirely rule out malignancy. Further imaging studies may be required in a patient at risk for metastatic disease.

Oblique views are of little value and add to the radiation dose. On the other hand, flexion-extension views are helpful in the evaluation of spondylolisthesis. Spondylolisthesis is the forward slipping of one vertebra on another. Most often, the defect is thought to result from repeated and increased stress on the pars interarticularis.

Educational objective: To be familiar with the indications and limitations of plain radiographs in the evaluation of patients with low back pain.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Laboratory evaluation of low back pain

Answer to Question 47
Answer: A

This patient developed an illness consistent with sarcoidosis. His symptoms related to this disorder, such as fever, dyspnea, and ankle pain, resolved. The persistent fatigue that developed afterwards, along with the normal physical examination and laboratory studies, is consistent with a post-sarcoid chronic fatigue syndrome that occurs in some patients. Thus, choice A is correct.

Fifty percent of affected patients exhibit bilateral hilar adenopathy as the initial manifestation of sarcoidosis. Regression of hilar nodes within one to three years occurs in 75 percent of these patients, while 10 percent develop

chronic enlargement, which can persist for 10 years or more. However, persistence of the adenopathy is not associated with fatigue. Biopsy of a hilar node would not be indicated since the appearance of the adenopathy remains unchanged.

Since the chest radiograph revealed hilar adenopathy without parenchymal changes, a high-resolution computed tomography study of the lungs is unlikely to provide additional helpful information regarding the cause of this patient's fatigue.

The serum angiotensin converting enzyme (ACE) level is elevated in 75 percent of untreated patients with sarcoidosis. However, the value of monitoring the ACE level to assess the course of the disease remains unclear. Furthermore, this patient does not have any objective evidence for ongoing sarcoidosis, rendering the interpretation of an ACE level even more confusing.

Approximately 5 percent of patients with sarcoidosis have neurologic involvement. The protean central nervous system (CNS) manifestations usually occur in the early phase of the disease, while peripheral nerve and skeletal muscle involvement are characteristically seen in the more chronic stages. Because his neurologic examination is normal, the likelihood of active CNS disease is low in this patient. Thus, a head MRI is not indicated.

Educational objective: To understand the management issues of sarcoidosis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Overview of sarcoidosis
2. Rheumatic manifestations of sarcoidosis
3. Neurologic sarcoidosis

Answer to Question 48
Answer: D

Non-pharmacologic treatments for osteoarthritis include many modalities such as weight loss, exercise, and the use of assistive devices. The general goals are to control pain, reduce disability, improve function, improve quality of life, and prevent progression of disease.

Weight loss is inversely correlated with the development of osteoarthritis. In one study, a 10-pound weight loss over 10 years decreased the risk of developing osteoarthritis of the knee by 50 percent. Although the benefits of weight loss as an intervention in patients with established osteoarthritis are less clear, weight loss is generally recommended since it may have an impact in slowing progression of the disease and is beneficial for overall health.

Rest relieves pain in osteoarthritis, but prolonged rest may lead to muscle atrophy and decreased joint mobility. Rest is therefore recommended only for short periods of time (ie, 12 to 24 hours for acute pain and/or inflammatory signs). Rest is not known to slow progression of the disease.

The use of a cane may unload a lower extremity joint and thereby reduce stresses across the joint, which have the potential to accelerate the osteoarthritis. As an example, a cane can reduce force across the hip by as much as 50 percent. However, it is not clear that it reduces forces across the knee to the same extent.

Some patients have abnormal knee joint loading at heel strike, leading to a 30 percent increase in force. This abnormality may reflect the inability of musculoskeletal structures to absorb forces due to injury. Altering the distribution of walking forces by muscular structures in patients with knee osteoarthritis may be beneficial for some patients. Such techniques include the use of padded shoes and quadriceps training. Padded, protective shoes can decrease the joint load on impact by up to one-half. Viscoelastic or wedged inserts worn with ordinary shoes may also be beneficial.

An appropriate exercise program is an integral part of the treatment for osteoarthritis. Exercise such as walking can correct deficiencies in strength and gait and can improve pain and function in patients with osteoarthritis of the knees and hips.

Educational objective: To understand the theory behind non-pharmacologic therapies for osteoarthritis of the knee.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Nonpharmacologic therapy of osteoarthritis
2. Weight-resistance training in patients with osteoarthritis

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Answer to Question 49
Answer: D

This patient with Paget's disease has an elevated serum calcium and alkaline phosphatase and reduced serum phosphorus. Although an elevated alkaline phosphatase is consistent with Paget's disease, the other concentrations are normal in most patients with Paget's disease. More likely, this patient has developed primary hyperparathyroidism. It is not clear if there is a relationship between these two diseases, but primary hyperparathyroidism has been reported in as many as 15 to 20 percent of patients with Paget's disease. Increased osteoclast activity due to hyperparathyroidism will worsen Paget's bone disease; thus, removal of a parathyroid adenoma in a patient with Paget's disease often leads to improvement in bone symptoms.

The classic manifestations of hyperparathyroid bone disease are osteitis fibrosa cystica and brown tumors. Subperiosteal bone resorption on the radial aspect of the middle phalanges is the most sensitive radiologic sign of primary hyperparathyroidism. These findings are now very rare, being found only in patients with prolonged, severe disease, especially those with parathyroid carcinoma.

Paget's disease of the skull can cause 8th nerve compression, resulting in hearing loss. This is one of the more common complaints, being present in 37 percent of respondents in a recent survey of 2,000 patients with Paget's disease. Other causes of hearing loss include pagetic involvement of the middle ear ossicles, which dampens the motion of these ossicles.

Educational objective: To be familiar with the presentation of Paget's disease.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical manifestations and diagnosis of Paget's disease of bone
2. Diagnosis and differential diagnosis of primary hyperparathyroidism
3. Clinical manifestations of primary hyperparathyroidism

Answer to Question 50
Answer: A

For a variety of reasons, including the low incidence of the disease, and the lack of large, prospective, multicenter trials, the data pertaining to therapies for scleroderma are limited. In general, there are limited indications for the use of specific agents in the treatment of diffuse scleroderma. For example, long-term, high-dose corticosteroid therapy is potentially toxic and has been implicated in precipitating renal crisis. Thus, their use should be limited to patients with myositis, active fibrosing alveolitis, symptomatic serositis, refractory arthritis and tenosynovitis, and the early edematous phase of the skin disease.

The interferons are potent, in vitro inhibitors of collagen synthesis. A multicenter double-blind study noted that treatment with interferon-alfa was associated with worsening skin disease and a significantly greater deterioration in lung function, compared to the placebo-treated group.

In uncontrolled studies, interferon-gamma has been associated with considerable vascular side effects, including renal hypertensive crisis. Thus, there is currently no role for its use in the treatment of scleroderma.

Educational objective: To be familiar with the therapeutic options available for the treatment of scleroderma.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. General approach to the treatment of scleroderma

Answer to Question 51
Answer: D

This patient presents with features of an acute infectious disease. The diagnosis of Lyme disease may be considered, but the high fever, headache and hematologic findings are not typical features of this diagnosis. Other arthropod-borne illnesses, especially Rocky Mountain spotted fever, and the human ehrlichial diseases, including human monocytic and human granulocytic ehrlichiosis, should be considered in the differential diagnosis because they may also cause fever, rash, leukopenia, and thrombocytopenia. However, the petechial rash, elevated liver enzyme levels, and the finding on blood smear of ring-like parasites, in a patient who has not traveled to an area where malaria is endemic, is most consistent with the diagnosis of babesiosis.

Babesiosis is a tick-borne illness caused by a malaria-like protozoa that infects red blood cells and causes hemolysis. Clinical manifestations range from asymptomatic, or self-limited infection, to life-threatening disease characterized by severe hemolysis, jaundice, and renal failure. The treatment of choice for babesiosis consists of a combination of clindamycin and quinine given for 7 to 10 days.

The typical rash of Rocky Mountain spotted fever begins on the ankles and wrists and spreads both centrally and to the palms and soles. It often begins as a macular or maculopapular eruption and then usually becomes petechial. Only a minority of patients with ehrlichiosis have rash. In a patient with similar features, without a blood smear diagnostic for babesiosis, it would be prudent to institute anti-rickettsial therapy with doxycycline in addition to treating for babesiosis.

As noted above, a diagnosis of Lyme disease is unlikely. The positive Lyme antibody test is a manifestation of her previous bout with this disease five years earlier.

Educational objective: To distinguish joint complaints associated with early Lyme disease from those due to other infections.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Cases illustrating clinical dilemmas in Lyme disease
2. Diagnosis; treatment; and prevention of babesiosis
3. Clinical manifestations and diagnosis of Rocky Mountain spotted fever
4. Human ehrlichiosis

Answer to Question 52
Answer: B

This patient's history, physical examination, and imaging studies are most consistent with mild prostatitis and an undifferentiated spondyloarthropathy. The latter term is currently recommended to describe patients who lack the triad of features associated with classical Reiter's syndrome (arthritis, conjunctivitis, and urethritis) and whose disease has not resulted from a preceding infection (reactive arthritis). In the case presented, dysuria, pyuria, and positive test for Chlamydia trachomatis provide evidence of an ongoing infection that may have triggered the arthritis. One quarter of men with Chlamydia trachomatis infection may have no genitourinary symptoms. Some patients come to medical attention because they develop arthritis, or alternatively, because of symptomatic illness in their sexual partners.

The prognosis is worse for patients with post-venereal rather than with post-dysenteric disease. As an example, one study noted a 68 percent incidence of chronic arthritis developing post-chlamydia Reiter's syndrome compared with 2.4 percent following Yersinia infection. These general prognostic observations may be difficult to apply to an individual patient; more likely, the particular strain of the organism is an important determinant of prognosis.

A number of studies have found that the presence of HLA-B27 would increase the likelihood of chronicity of his condition.

Following the acute episode of arthritis associated with an undifferentiated spondyloarthropathy, approximately 75 percent of patients are in complete remission after two years. In about 25 percent of patients, the attack never com-

pletely subsides and a waxing and waning course continues.

An age of onset of less than 16 years has been associated with a poorer prognosis.

Educational objective: To be able to identify features in patients with reactive arthritis or undifferentiated spondyloarthropathy, which are associated with a worse prognosis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Course and treatment of Reiter's syndrome and reactive arthritis
2. Screening for Chlamydia trachomatis

Answer to Question 53
Answer: D

Rheumatic fever nodules have the following features:

- They are firm, painless, and subcutaneous.
- They usually occur only in patients with carditis.
- Their size varies from a few millimeters to one or two centimeters.
- There may be a single to dozens of nodules present.
- When numerous, the nodules are usually symmetric.

Compared to rheumatoid nodules, rheumatic fever nodules are smaller and short-lived. Although the elbows are the most frequently involved site in both conditions, rheumatic fever nodules are more common on the olecranon surface, whereas rheumatoid nodules are usually found 3 to 4 centimeters distally.

Rheumatic fever nodules are generally present for one to four weeks; it is rare for them to persist beyond this time. Therefore, choice D is the correct answer.

Educational objective: To recognize the features of rheumatic fever nodules.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Ganglia and nodules
2. Clinical manifestations and diagnosis of acute rheumatic fever

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Answer to Question 54
Answer: C

Calcium carbonate, citrate, lactate, and gluconate are all effective calcium supplements. Calcium carbonate is the least expensive supplement. Oyster shell calcium is not recommended due to unacceptably high levels of lead. Calcium absorption from vegetables such as spinach is less than that from dairy products. Calcium supplements should not be seen as an alternative to estrogens. The beneficial effect of calcium on bone is much less than that of estrogen alone or the combination of calcium plus estrogen. The recommended daily intake of calcium for postmenopausal woman should be 1500 mg. Amounts in excess of this can lead to the development of nephrolithiasis or hypercalcemia and should be discouraged.

Educational objective: To be familiar with the proper use of calcium supplementation in the management of osteoporosis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Calcium supplementation in osteoporosis

Answer to Question 55
Answer: E

Scleritis is an inflammatory process involving the sclera, which is due primarily to an immune-mediated vasculitis in which inflammatory cells are activated by deposited immune complexes or local antigens. It is a chronic, painful, destructive, and potentially blinding disorder commonly associated with systemic disease.

The reported incidence of scleritis in patients with RA has ranged from 0.7 to 6.3 percent, although as many as 33 percent of all patients presenting to an ophthalmologist with scleritis may have associated RA.

Other associated disorders include Wegener's granulomatosis, polyarteritis nodosa, granulomatous diseases such as sarcoidosis, infectious diseases including syphilis and tuberculosis, and inflammatory bowel disease.

Ocular manifestations of GCA are frequent and include blurred vision, diplopia, and blindness. Ischemic optic neuropathy is the most frequent pathologic consequence within the eye. Retinal involvement with giant cell arteritis is manifested as cotton wool spots, hemorrhages, or both. Other less common retinal findings include central and branch retinal artery occlusions, ocular ischemic syndrome, hypotony, choroidal ischemia, and cortical blindness. Although scleritis has been described in GCA, her age makes this diagnosis extremely unlikely.

Educational objective: Recognize the differential diagnosis of scleritis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. General symptomatology and diagnosis of systemic lupus erythematosus
2. Episcleritis and scleritis
3. Retinal vasculitis associated with systemic disorders and infections

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Answer to Question 56
Answer: C

Although uncommon, a spinal epidural abscess (SEA) is an important infection, which requires prompt recognition and proper management to avoid potentially disastrous complications. Many SEAs begin as a focal pyogenic infection, such as an infectious diskitis involving the vertebral disc or the junction between the disc and the vertebral body. The leading bacterial pathogen causing SEA is Staphylococcus aureus, which accounts for about two-thirds of all cases. Longitudinal extension of the infection is common, sometimes involving the whole length of the spinal column.

The initial manifestations of infection can be nonspecific, such as fever and malaise. The abscess itself causes symptoms, which progress in a typical sequence, beginning with back pain, which is often focal and severe. The pain is often described as "shooting" or "electric shocks" in the distribution of the affected nerve root. Subsequently, motor weakness, sensory changes, and bladder or bowel dysfunction may develop. Finally, in severe cases there may be paralysis. Painless loss of motor function is not observed with SEA.

Fever is a helpful diagnostic clue because it is not present in most cases of musculoskeletal back pain such as a herniated disc. Fever in a patient with severe, localized back pain, especially if the pain is worsened by percussion, should suggest the diagnosis of SEA.

Educational objective: Recognize the clinical features of rare but important causes of back pain.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Epidural abscess

Answer to Question 57
Answer: D

Renal transplant recipients are predisposed to hyperuricemia due to reduced uric acid secretion. In addition, the use of cyclosporine may reduce uric acid secretion further through reduction of the glomerular filtration rate and tubular damage. Patients on diuretic therapy are also prone to developing hyperuricemia.

This patient has developed chronic tophaceous gout, but he is not currently experiencing acute gouty arthritis. Antihyperuricemic therapy is indicated, with a goal of reducing serum urate to a range between 5 and 6 mg/dL. Allopurinol interferes with azathioprine metabolism through its inhibition of xanthine oxidase, thus enhancing the risk of azathioprine toxicity. One strategy would be to discontinue azathioprine and replace it with mycophenolate, which does not interact with allopurinol.

When allopurinol is initiated for the prophylaxis of acute gouty attacks, a low dose of colchicine is recommended as acute gouty episodes can be precipitated during the initiation of antihyperuricemic therapy.

Colchicine alone does not constitute adequate treatment for chronic tophaceous gout; it is not effective in lowering serum uric acid levels, which is the basic goal in treatment of this disorder. In addition, this patient is taking cyclosporine, which decreases the hepatic clearance of colchicine. Thus, his dose of colchicine should not exceed 0.6 mg per day.

The use of selective COX-2 inhibitors and NSAIDs in general should be avoided in patients with significant renal disease. In addition, the patient is currently not experiencing an acute gouty episode.

Educational objective: To understand strategies for the treatment of tophaceous gout in the renal transplant recipient.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical manifestations and diagnosis of gout
2. Treatment of gout
3. Hyperuricemia and gout in renal transplant recipients

Answer to Question 58
Answer: C

Osteomalacia is a disorder of newly formed bone matrix which may present with radiographic changes such as osteopenia. The radiographic appearance of the patient's hip and pelvis reveals the presence of Looser's pseudofractures, which are narrow radiolucent lines two to five millimeters in width with sclerotic borders. As in this patient, they are often found in the femoral neck. In addition to the pelvis, they may involve upper extremity bones including the ulna, radius, and clavicle.

Another distinguishing feature is the bilateral, symmetric nature of these pseudofractures, which would not be typical for "true" fractures.

It has been suggested that Looser's pseudofractures may represent stress fractures which have been repaired by the deposition of inadequately mineralized osteoid. A second theory suggests that since the fractures often lie in apposition to arteries, they may occur by erosion of the bone matrix by the pulsating blood vessels.

In patients with osteomalacia due to vitamin D deficiency, the serum calcium is in the low to low-normal range, the serum phosphate is low, and the alkaline phosphatase is elevated.

Educational objective: To recognize the clinical features of osteomalacia.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Diagnosis and treatment of osteomalacia
2. Clinical manifestations and etiology of osteomalacia

Answer to Question 59
Answer: E

This patient most likely has fibromyalgia. Other diagnostic considerations for this 61-year-old patient with fatigue and myalgia include polymyalgia rheumatica, thyroid disease, metabolic or inflammatory myopathies, and occult systemic diseases.

The CBC and chemistry panel are appropriate basic screening studies to look for hematologic, hepatic, renal, or calcium abnormalities.

The ESR screens for polymyalgia rheumatica and may provide a clue for the need of additional studies to rule out other systemic or hematologic disorders.

Since fatigue and myalgia may be manifestations of thyroid disease, measurement of the serum TSH is appropriate. Similarly, a CPK may be necessary to rule metabolic or inflammatory myopathies that can be present with these symptoms.

There is no clinical indication to support the measurement of the ANA in this patient. The review of systems is completely unremarkable for any features consistent with SLE or other ANA-associated disorders. Since there may be an increased prevalence of false positive (low titer) ANA tests, this result may be misleading and cause unnecessary testing and delay in initiation of appropriate therapies.

Educational objective: Understand the appropriate laboratory evaluation for a patient with fibromyalgia.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical manifestations and diagnosis of fibromyalgia
2. Differential diagnosis of fibromyalgia

Answer to Question 60
Answer: E

This patient with diffuse systemic sclerosis presents with complaints suggesting malabsorption including weight loss and steatorrhea. Bowel involvement is common in systemic sclerosis often leading to small intestine dysmotility. Intestinal stasis and bacterial overgrowth are the major treatable causes of malabsorption in these patients. Diagnosis can be established by small bowel aspiration or less invasively by a glucose hydrogen breath test. Treatment involves the use of broad-spectrum antibacterial therapy for varying periods of time depending on the severity of symptoms and response to therapy.

D-penicillamine in the treatment of scleroderma is controversial, but there is no data to support its use for the treatment of gastrointestinal disorders. Similarly, there is no known role for the use of cyclophosphamide in this patient.

H2-blockers such as ranitidine can be helpful in improving symptoms of gastroesophageal reflux in some patients with scleroderma, but his present symptoms are referable to small intestinal disease.

Diphenoxylate (Lomotil) is an antidiarrheal agent, which is unlikely to benefit this patient with a bacterial overgrowth syndrome.

Educational objective: Recognize bacterial overgrowth as an important cause of malabsorption in patients with systemic sclerosis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Treatment of gastrointestinal disease in scleroderma
2. Gastrointestinal manifestations of scleroderma
3. Organ-based therapy in scleroderma

Answer to Question 61
Answer: D

Pulmonary involvement is a major cause of morbidity and mortality in patients with systemic sclerosis, and occurs in as many as 70 percent of patients. The two main types of involvement are interstitial lung disease and pulmonary vascular disease leading to pulmonary vascular hypertension. In patients with limited scleroderma, pulmonary hypertension is the main clinical concern. The patient described has limited scleroderma and presents with exertion-

al dyspnea, which should raise concerns regarding pulmonary hypertension. The presence of an A-wave in the jugular venous pulse distention is also a helpful clue for the diagnosis of pulmonary hypertension. A recent preliminary study in patients with scleroderma suggested that echocardiography can accurately predict pulmonary hypertension, which was subsequently confirmed by right heart catheterization. Using right heart catheterization as the gold standard, echocardiography had a 90 percent sensitivity and 75 percent specificity for the detection of pulmonary hypertension.

Exertional dyspnea due to a cardiomyopathy would be an unusual finding in a patient with limited scleroderma. Thus, CPK determination is not likely to be helpful.

High-resolution chest CT is valuable in identifying interstitial lung disease in patients with scleroderma. In this patient, however, the more likely cause of her dyspnea is pulmonary vascular disease, which would be better assessed by echocardiography.

Pulmonary function studies can be useful in the diagnosis of pulmonary hypertension, usually reflected by an isolated impairment of the DLCO (less than 65 percent of predicted) in the absence of a significant restrictive ventilatory abnormality. Again, echocardiography is a more sensitive and specific test for this diagnosis.

A ventilation perfusion scan is unlikely to be helpful. Although thromboembolic disease can be a cause of dyspnea and also of secondary pulmonary hypertension, it would not seem likely as a cause of dyspnea in this patient.

Educational objective: Recognize pulmonary hypertension as an important cause of exertional dyspnea in the patient with limited scleroderma.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical manifestations and evaluation of scleroderma lung disease
2. Overview of the manifestations and diagnosis of scleroderma

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Answer to Question 62
Answer: A

Polyarthritis is a relatively common symptom complex, which often is not clearly diagnosed by history and physical examination alone. Laboratory and radiological studies can often be of value but also can be misleading. As an example, serum positivity for rheumatoid factor has been associated most commonly with rheumatoid arthritis, but up to 25 percent of RA patients remain seronegative throughout their course. Despite these observations, high titer rheumatoid factor titers have a much better predictive value for RA and probably predict poorer outcomes.

The ESR is a non-specific measure of systemic inflammation; however, it can help distinguish between inflammatory and non-inflammatory joint processes. Unfortunately, it is affected by many factors unrelated to inflammation and may be normal in a minority of patients with inflammatory polyarthritis.

Plain radiographs may aid in the diagnosis of chronic conditions (such as osteoarthritis or rheumatoid arthritis) and are occasionally helpful in the diagnosis of some acute arthritis syndromes (such as calcium pyrophosphate deposition disease). However, x-rays in early osteoarthritis occasionally do not reveal any significant findings.

MRI is particularly sensitive for the detection of soft tissue processes. However, this modality lacks specificity.

Synovial fluid cell count can frequently help evaluate synovitis. The likelihood of septic arthritis increases with cell count and percentage of polymorphonuclear leukocytes on the differential. However, a value lower than 50,000/mm3 does not exclude septic arthritis, particularly in the setting of immunosuppression or infections involving mycobacterial or Neisserial organisms.

Educational objective: To recognize the roles of various diagnostic studies in the evaluation of polyarthritis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Approach to the patient with polyarticular joint pain
2. Approach to the patient with knee pain
3. Approach to the patient with monoarticular joint pain

4. Synovial fluid analysis and the diagnosis of septic arthritis

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Answer to Question 63
Answer: B

The patient most likely has developed atlantoaxial subluxation secondary to rheumatoid arthritis. Symptoms of spinal cord compression that require immediate attention include a sensation of the head falling forward upon flexion of the cervical spine, changes in levels of consciousness, loss of sphincter control, vertigo, dysarthria, peripheral paresthesia without evidence of peripheral nerve disease. Neurologic findings include hemiplegia, nystagmus, ataxia, or positive Babinski responses without evidence of peripheral nerve disease.

Among the joints of the cervical spine, the atlantoaxial joint is prone to subluxation in multiple directions. Anterior movement on the axis is most common; it results from laxity of the ligaments induced by proliferative synovial tissue in an adjacent synovial pouch.

The earliest and most common symptom of cervical subluxation is pain radiating superiorly towards the occiput.

In the proper clinical context, the presence of brisk deep tendon reflexes in the upper extremities should suggest the diagnosis of a cervical myelopathy which, in patients with RA, may be due to cervical spine disease.

There are two possible mechanisms for involvement of the intervertebral joints in the cervical spine in rheumatoid arthritis. These include an extension of the inflammatory process from adjacent neurocentral joints into the discovertebral area or chronic cervical instability initiated by apophyseal joint destruction, subsequently leading to vertebral malalignment or subluxation. This may produce microfractures of the vertebral endplates, disc herniation, and degeneration.

Educational objective: To identify the clinical features of cervical spine involvement in rheumatoid arthritis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Cervical subluxation in rheumatoid arthritis

Answer to Question 64
Answer: E

The upper GI with small bowel follow through shows dilated loops of small bowel, some of which have a "wire spring" appearance due to closely packed valvulae in a dilated bowel. These are findings noted in patients with scleroderma involving the small bowel.

Abnormal small bowel function has been reported in 20 to 60 percent of patients with scleroderma. The pathophysiology is thought to be similar to the neuromuscular involvement observed in patients with esophageal disease. Light microscopy reveals few clues; the villous structure is normal, and there are few inflammatory cells present. Collagen deposition around Brunner's glands leading to periglandular sclerosis is thought to be pathognomonic of intestinal scleroderma. However, small intestine biopsies rarely include the submucosal layer.

Colonic disease occurs in 10 to 50 percent of patients with scleroderma, with the anorectum being the most frequently affected area. In some series of patients, the colon is almost as frequently involved as the esophagus. In addition, patients with abnormal esophageal manometry almost always have abnormal anorectal motility.

The major cause of malabsorption, which occurs in up to one third of patients with scleroderma, is intestinal stasis with bacterial overgrowth. These patients have persistent diarrhea and steatorrhea.

The glucose hydrogen breath test is a useful, noninvasive method to screen for the presence of bacterial overgrowth. Although false negative results may occur when the predominant organisms produce CO_2, false positives rarely occur in patients with scleroderma.

Educational objective: To recognize the clinical and therapeutic issues related to scleroderma involvement of the

small intestine.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Gastrointestinal manifestations of scleroderma
2. Treatment of gastrointestinal disease in scleroderma

Answer to Question 65
Answer: B

This patient has features that may suggest the development of a connective tissue disease, thus serologic evaluation is helpful. Antibodies to topoisomerase-1 (also known as anti-Scl-70) are highly specific for the diagnosis of scleroderma. However, they are not sensitive, being observed in only 15 to 20 percent of patients. They correlate with the development of interstitial pulmonary fibrosis and are associated with a reduced incidence of pulmonary hypertension.

Other autoantibodies observed with some forms of scleroderma include those targeting U1-RNP and the centromere. The latter are more common, seen in 25 to 30 percent of patients. Most commonly, these patients develop the limited CREST variant. They have a greater risk for the development of pulmonary hypertension; the risk for pulmonary fibrosis though, is reduced.

Antibodies to U1-RNP are seen in about 10 percent of patients and correlate with muscle involvement.

Antibodies to U3-RNP are seen in less than 5 percent of patients. They are associated with a poor prognosis in black males and are associated with the development of pulmonary hypertension and myositis.

Educational objective: The use of serologies in the diagnosis of scleroderma spectrum disorders.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Overview of the manifestations and diagnosis of scleroderma
2. Classification of scleroderma

Answer to Question 66
Answer: C

Corticosteroid-related toxicities and adverse effects are generally related to both the average dose and cumulative duration of use. The most common toxicities attributable to prednisone are skin thinning and purpura. One large study noted 32 cases of purpura for every 1000 patient-years of follow-up.

Cataracts commonly occur after prolonged use. Children are more susceptible than adults for this complication.

Patients with a family history of depression may be at increased risk for the development of an affective disorder when given corticosteroids. Lithium has been found to be an effective treatment for these conditions. In addition, corticosteroid therapy does not block the antibody response to influenza vaccine.

The development of osteoporosis is a serious concern in an elderly, postmenopausal female treated with corticosteroids. It does not appear that alternate day dosing protects against the development of osteoporosis. Thus, choice C is false.

Educational objective: To be familiar with corticosteroid related toxicities.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Major side effects of corticosteroids

Answer to Question 67
Answer: B

Polymyalgia rheumatica (PMR) is classically characterized by aching and morning stiffness in the shoulder, hip girdles, neck, and torso in patients over the age of 50. The symptoms are usually symmetric, but asymmetric pain can occur. Physical examination may reveal decreased active range of motion of the shoulders, neck, and hips due to pain. Although the shoulders may be tender to palpation, these findings are usually less prominent than expected given the severity of the symptoms. Muscle strength is usually normal. However, weakness may become a problem because of disuse atrophy or lack of effort on examination because of pain.

The characteristic laboratory finding of PMR and GCA is an elevation in the erythrocyte sedimentation rate which can exceed 100 mm/hr. However, values below 40 mm/hr are seen in as many as one-fifth of patients. This is most likely to occur in patients with limited disease and fewer systemic symptoms.

This patient fits this diagnostic category. Given his lack of response to nonsteroidal antiinflammatory drugs and his ongoing symptoms involving the proximal shoulder girdle, it would be appropriate to empirically treat the patient with a trial of corticosteroids and assess the clinical response. Because of the near universal response of PMR to corticosteroids, some rheumatologists consider a prompt response of symptoms to corticosteroids as an additional criterion for PMR.

Preliminary evidence suggests that elevated levels of C-reactive protein (C-RP) may be more sensitive than a high ESR for the diagnosis of PMR. However, this patient should first be treated with a trial of prednisone, since the serum C-RP value would not change the need for the trial. Similarly, repeating the ESR would not eliminate the need for a therapeutic trial of prednisone.

Although the statin drugs may cause myalgias and elevated serum CPK levels, the degree of morning stiffness and nocturnal pain would be unusual features of this disorder.

The symptoms and findings in the shoulders in PMR may be similar to subdeltoid bursitis or rotator cuff tendinitis. However, tenderness is minimal in most cases of polymyalgia rheumatica, while patients with bursitis or tendinitis lack constitutional symptoms. Thus, shoulder radiographs and corticosteroid injections are not appropriate options.

Educational objective: To understand the presentation of polymyalgia rheumatica with normal laboratory results.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Polymyalgia rheumatica

Answer to Question 68
Answer: D

Approximately 15 percent of patients with GCA have involvement of branches of the aortic arch, particularly the subclavian and axillary arteries. These patients often present with features of arm claudication. Compared to patients with cranial GCA, patients with large-vessel GCA have a younger mean age of onset. The majority of affected individuals are female.

In the largest series of patients observed to date, those with large-vessel vasculitis had a substantially lower frequency of headaches than patients with cranial GCA.

An ANCA test is of no benefit in the evaluation of patients with GCA, since it is negative in those with either large-vessel or cranial GCA.

Educational objective: To be able to distinguish the clinical features of large-vessel GCA.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical manifestations and diagnosis of giant cell (temporal) arteritis
2. Pathogenesis of giant cell (temporal) arteritis

Answer to Question 69
Answer: C

This patient has features consistent with osteomalacia and secondary hyperparathyroidism related to long term anticonvulsant use and hypovitaminosis D. The patient's severe mental incapacity may be associated with poor dietary intake and lack of sun exposure causing hypovitaminosis D. In addition, patients on long-term anticonvulsant treatment develop bone loss related to low calcium, hypovitaminosis D and secondary hyperparathyroidism due to increased catabolism of vitamin D and decreased intestinal calcium absorption. This results in the development of osteomalacia and an increased fracture risk. Looser pseudofractures, fissures, or narrow radiolucent lines, two to five mm in width with sclerotic borders, are the characteristic radiologic finding in osteomalacia.

Paget's disease, osteoporosis, and hypoparathyroidism do not cause the laboratory or radiographic findings in this case.

This patient's findings are consistent with a secondary not primary hyperparathyroidism, for the reasons stated earlier.

Educational objective: To identify the clinical features of metabolic bone disease.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical manifestations and etiology of osteomalacia
2. Diagnosis and treatment of osteomalacia
3. Causes of vitamin D deficiency and resistance

Answer to Question 70
Answer: A

This patient displays classic features of Reiter's syndrome. The pathogenesis of Reiter's syndrome remains to be fully elucidated, but several observations support molecular mimicry in eliciting the disease. The introduction of the human genes for HLA-B27 and beta-2 microglobulin into rats results in a syndrome with features of Reiter's syndrome, including peripheral joint arthritis, spondylitis, and cutaneous cardiac, gastrointestinal and genitourinary tract inflammation. Susceptibility to the disease in individual rat strains correlated with the level of B-27 gene expression in the particular rat strain. Thus, choice A is correct.

There are several factors, which indicate a poor prognosis and increase the likelihood of chronicity. These include HLA-B27 and, to a lesser degree, male gender and the presence of extraarticular lesions. Overall, individuals who are HLA-B27 positive have a 20-fold increased risk of developing a spondyloarthropathy. However, determining the HLA-B27 status of an individual is not helpful in predicting the likelihood of response to therapy.

As part of the class I major histocompatibility complex, HLA-B27, is expressed by nearly all nucleated cells of the body and not only on antigen presenting cells.

Educational objective: To understand the role of HLA-B27 in the pathogenesis of the spondyloarthropathies

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Course and treatment of Reiter's syndrome and reactive arthritis
2. Definition and diagnosis of Reiter's syndrome, reactive arthritis and undifferentiated spondyloarthropathy
3. HLA-B27 and the pathogenesis of Reiter's syndrome and ankylosing spondylitis

Answer to Question 71
Answer: A

This previously healthy 33-year-old woman presents with an acute stroke. An extensive work-up is notable for a

moderately elevated ESR and an abnormal angiogram suggestive of vasculitis. The absence of findings indicating a systemic disorder suggests the diagnosis of isolated central nervous system vasculitis (ICNSV), also known as primary angiitis of the central nervous system. The angiographic findings, although strongly suggestive of vasculitis, are relatively nonspecific. Such "vasculitic" angiographic changes may be observed in a number of disorders, including drug-induced vasospasm (such as phenylpropanolamine), and infections.

In this critically ill patient, corticosteroids were appropriately administered to provide an immediate immunosuppressive effect for presumed vasculitis. Subsequently, confirmation of the diagnosis by biopsy of involved tissue is indicated since additional therapies, principally cytotoxic agents, have potentially life-threatening side effects. Thus, choice A is correct.

Although intravenous cyclophosphamide may ultimately be necessary, this agent should not be started without confirming a tissue diagnosis because of the possible induction of adverse effects. In addition, a minimal delay in initiating therapy is acceptable since cyclophosphamide does not have an immediate immunosuppressive effect.

There is no known role for the use of intravenous heparin, aspirin, or a calcium channel blocker for the treatment of patients with a primary angiitis of the central nervous system.

Educational objective: Appreciate the difficulties involved in establishing the diagnosis of isolated central nervous system vasculitis (ICNSV).

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Isolated central nervous system vasculitis

Answer to Question 72
Answer: B

This patient has features compatible with hereditary hemochromatosis. These include: arthritis of the MCP joints, elevated transferrin saturation, fatigue, and diabetes mellitus. Elevation of the AST and ALT could reflect hepatic involvement as well.

Arthropathy associated with hereditary hemochromatosis runs the entire spectrum of calcium pyrophosphate crystal deposition disease, including chondrocalcinosis, pseudogout, and chronic arthropathy. Distinguishing features include a number of distinctive articular radiographic findings described specifically in hemochromatosis, such as hook-like osteophytes of the metacarpal heads, as well as a tendency for degenerative changes to favor the MCP joints over the scapholunate. Small, 1 to 3 mm cysts may develop relatively early in the course of the arthropathy. In comparison to primary CPPD crystal deposition disease, narrowing of the MCP joints, including the fourth and fifth, tends to be more pronounced, and scapholunate separation is less prevalent in the arthritis of hereditary hemochromatosis.

CPPD deposition is not related to age or to the amount of iron deposited. Radiologic progression of CPPD deposition (and arthritis) does not decrease or disappear with treatment.

Symptoms are more severe in those over 50 years of age. Ulnar deviation, a common finding in rheumatoid arthritis, has not been reported in hereditary hemochromatosis.

Phlebotomy is the mainstay of treatment for hereditary hemochromatosis and is indicated for extraarticular manifestations. It is utilized even in asymptomatic patients to forestall progressive organ involvement. However, it usually fails to improve arthritic symptoms of this disease. Therefore, the correct answer is B.

Educational objective: To review aspects of hereditary hemochromatosis and its associated arthropathy.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Rheumatic manifestations of hereditary hemochromatosis
2. Clinical manifestations of hereditary hemochromatosis
3. Genetics of hereditary hemochromatosis

Answer to Question 73
Answer: B

This patient presents with typical symptoms and findings of de Quervain's tenosynovitis, but osteoarthritis of the thumb CMC joint is also a common cause of pain in this area. The Finkelstein maneuver may be positive in both de Quervain's and CMC osteoarthritis. Other measures such a local injection of an anesthetic may be needed to differentiate these conditions.

Tendon calcification is rarely seen in this disorder. Ganglia may cause pain in this area, but should be apparent as a mass-like swelling.

Up to 90 percent of patients treated within six months of developing symptoms have relief of pain following corticosteroid injection; complications are rare, and most can resume normal activities within three weeks. Surgery is reserved for those few patients with severe, refractory pain and loss of function.

Educational objective: Recognize the typical presenting features and physical findings in de Quervain's tenosynovitis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. de Quervain's tenosynovitis
2. Evaluation of the patient with thumb pain

Answer to Question 74
Answer: A

This patient presents with features suggestive of a septic olecranon bursitis. The relatively short duration of symptoms and findings of surrounding cellulitis increase the likelihood of a septic, rather than a purely traumatic process. The lack of bursal fluid crystals makes gout less likely. Bursal fluid leukocyte counts in cases of proven septic bursitis are frequently much lower than those seen in septic joints. They may be normal and the Gram stain is frequently negative. Septic bursitis requires identification of the causative organism (usually Staphylococcus aureus) and selection of the appropriate antibiotic. Antibiotic therapy continued for five days after sterilization of the bursal fluid is usually sufficient. Since this patient is not systemically ill, he can be managed as an outpatient with oral antibiotics. He should be instructed to return within two days to reaspirate and reculture the bursal fluid. In addition, given his history of diabetes, it would be inappropriate to wait several weeks for follow-up.

Indications for hospitalization and/or intravenous antibiotic therapy for septic bursitis include the presence of fulminant local infection, evidence for systemic toxicity, or infection in an immunocompromised patient.

At the initial visit the possibility for a bursal infection is high. Therefore, the bursa should not be injected with corticosteroids until infection has been ruled out.

The use of naproxen alone would be insufficient therapy for this patient's bursitis.

Educational objective: To recognize and plan appropriate management of septic bursitis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical manifestations and treatment of bursitis

Answer to Question 75
Answer: E

Between 10 and 50 percent of patients with scleroderma have colonic involvement, with the anorectum being the most frequently involved segment. Patients with abnormal esophageal manometry almost always have abnormal anorectal motility. Disordered anorectal function is an early finding in systemic sclerosis and is a major factor in the development of fecal incontinence. Manometry is the best means of identifying disease involvement in this location.

Thus, choice E is correct.

Colonoscopy or an air contrast barium enema study might reveal wide-mouthed diverticuli but would be unlikely to document the cause of this patient's incontinence.

A glucose hydrogen breath test would be useful in the evaluation of bacterial overgrowth syndromes. However, bacterial overgrowth syndrome is not likely the cause of this patient's problem given the absence of a history of diarrhea.

In the absence of diarrhea, use of loperamide or antibiotics (for bacterial overgrowth) is unlikely to be of benefit. However, these interventions may help reduce fecal soiling for those with liquid stools.

Educational objective: To review the recognition and evaluation of anorectal complaints in scleroderma.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Treatment of gastrointestinal disease in scleroderma
2. Gastrointestinal manifestations of scleroderma
3. Fecal incontinence

Answer to Question 76
Answer: D

Although the presence of a particular autoantibody is rarely pathognomonic for a particular diagnosis, some are commonly associated with certain clinical settings. These include:

- Anti-dsDNA antibodies with the development of lupus nephritis
- Anti-Ro antibodies with C2 deficiency
- Anti-La antibodies with neonatal lupus and Sjögren's syndrome

By comparison, patients with U1-RNP antibodies seldom develop diffuse proliferative glomerulonephritis, psychosis, or seizures.

Educational objective: To be familiar with specific autoantibody-disease associations seen in rheumatologic practice.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. General symptomatology and diagnosis of systemic lupus erythematosus
2. Clinical significance of anti-Ro/SSA and anti-La/SSB antibodies

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Answer to Question 77
Answer: A

This patient has developed a multisystem disease, characterized by a pronounced eosinophilia. The presence of cardiopulmonary and neurologic features suggest a possible diagnosis of either a hypereosinophilic syndrome of unknown cause (HES) or Churg-Strauss syndrome (CSS). There are no specific tests diagnostic of HES; the diagnosis is considered when there is a blood eosinophilia exceeding 1500/uL for at least six months as well as signs and symptoms of end-organ dysfunction. Parasitic diseases and allergic disorders must be excluded.

CSS is characterized by multi-system involvement including the respiratory tract, nose and sinuses, skin, and heart, along with a prominent eosinophilia. Renal involvement appears to be more common than is generally reported. On renal biopsy, focal segmental glomerulonephritis is the predominant lesion and is often associated with necrotizing features and crescents. Extravascular granulomata and eosinophilic infiltrates were relatively rare. By comparison, renal disease in patients with HES is exceedingly rare. Thus, choice A is correct.

Neurologic disease is common to both HES and CSS. HES may be complicated by cerebral thromboemboli, encephalopathy, or peripheral neuropathy. In patients with CSS, a peripheral neuropathy may be seen. In addition, cerebral hemorrhage and infarction are important causes of death.

Cardiac disease is a major cause of morbidity and mortality among patients with either condition. In HES, the eosinophil-mediated heart damage evolves through three stages including an acute, necrotic stage, an intermediate phase characterized by thrombus formation, and a fibrotic stage. In CSS, there may be features of pericarditis, heart failure, and myocardial infarction. Cardiovascular disease accounts for one-half of all deaths attributable to CSS.

Skin lesions or subcutaneous nodules can be observed in patients with either condition.

Educational objective: To be able to distinguish systemic illnesses associated with eosinophilia.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Causes of eosinophilia
2. Idiopathic hypereosinophilic syndrome
3. Churg-Strauss syndrome (allergic granulomatosis and angiitis)

Answer to Question 78
Answer: C

After fresh and salt water exposure a wide array of microorganisms can cause soft tissue infections, particularly in sites of prior trauma or skin breakdown. Infection with Mycobacterium marinum (also known as "fish tank granuloma" or "waterman's disease") characteristically results in a slowly progressive, indolent oligoarthritis and tenosynovitis. Diagnosis is often delayed, sometimes for many months. However, this infection tends to remain localized peripherally, without systemic spread, possibly due to the tendency for this organism to grow better at lower temperatures. Diagnosis can often be confirmed by stains and cultures of synovial fluid, although tissue cultures may be required in some patients.

Most forms of bacterial arthritis and tenosynovitis would be more rapidly progressive and associated with systemic toxicity. For example, other organisms associated with water exposure, such as Vibrio vulnificas, usually present with a more fulminant infection. Erysipelothrix infection is usually associated with a chronically draining cutaneous lesion.

Most forms of fungal arthritis and tenosynovitis are associated with either obvious skin lesions or coexistent pulmonary infection. This patient had neither of these features.

Although gout is a possibility, it tends to be associated with more pain and discomfort than described in this case. Gouty tenosynovitis would be unusual in a patient without a prior, well-characterized history of gout.

Educational objective: To recognize the typical presentation of mycobacterium marinum musculoskeletal infection.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Soft tissue infections following water exposure
2. Diagnosis and treatment of disseminated histoplasmosis
3. Epidemiology of nontuberculous mycobacterial infections
4. Erysipelothrix infection

Answer to Question 79
Answer: B

This patient with primary Raynaud's phenomenon presents with an acutely ischemic digit and early gangrene. The key to reversing any or all of this ischemia is early, aggressive intervention. The drugs of choice should include vasodilators such as calcium channel blockers, which can be given intravenously if necessary, and an antiplatelet agent, such as aspirin. If calcium channel blockers are ineffective, other vasodilators such as nitroglycerin or prostaglandins should be considered. Aspirin should be used with caution because it could theoretically worsen vasospasm via the inhibition of vasodilating prostaglandins. Thus, choice B is correct.

Sympathectomy should be considered if vasodilator therapy fails. This may not be as effective in treating secondary RP.

Treating this patient as an outpatient with nitroglycerin and aspirin may be ineffective. The time lost with this intervention may enhance the risk of eventually requiring amputation of the digit. Thus, choice D is incorrect.

Heparin may be an appropriate therapy in a patient with antiphospholipid antibodies or a known thrombotic disorder. However, there is no information to suggest that the patient has either disorder.

Unless there is an underlying vasculitis, there is no evidence that the use of corticosteroids, such as intravenous solumedrol, plays a role in the treatment of this condition.

Educational objective: To understand the management of acute ischemia in the patient with a history of Raynaud's phenomenon.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Treatment of Raynaud's phenomenon

Answer to Question 80
Answer: D

It has been proposed that there is a bimodal pattern of mortality in patients with SLE; within the first two years following the diagnosis, infections, in part due to immunosuppression, are the most common cause, whereas coronary artery disease is predominant beyond the first few years. An additional risk factor may be the long-term use of corticosteroids. This patient has had longstanding SLE, requiring long term corticosteroid therapy. At the time of presentation, there was no clinical evidence to suggest the presence of an underlying vasculitis. The normal cardiopulmonary auscultation does not support the diagnosis of cardiac tamponade.

Extensive atherosclerosis involving the major coronary arteries, rather than the small myocardial vessels, appears to be a common finding among SLE patients.

Libman-Sacks or verrucous endocarditis is not uncommonly observed in patients with SLE. Generally this is an asymptomatic finding in SLE, although occasionally the verrucae can fragment and produce systemic emboli. However, the development of an arrhythmia and cardiac arrest would be a highly unlikely event.

Educational objective: To understand the cardiac complications of patients with SLE.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Cardiac manifestations of systemic lupus erythematosus
2. Clinical manifestations and diagnosis of the antiphospholipid antibody syndrome

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Answer to Question 81
Answer: D

This patient has the characteristic clinical features of chronic fatigue syndrome: progressive fatigue following a respiratory tract infection, arthralgias, myalgias, and headaches. The fatigue is so debilitating that it is affecting her occupational and social life.

A psychiatric history is common in many patients with chronic fatigue syndrome. Depression or other psychiatric disorders should be investigated as an underlying cause. Although patients often resist the notion that their symptoms may have a psychiatric basis, it is best to be frank about this possibility. Thus, the treating rheumatologist should consider obtaining a psychiatric consultation.

Since the cause of chronic fatigue syndrome is unclear, costly laboratory testing should be avoided. Recent hypotheses have included Epstein Barr virus infection, chronic Lyme disease, chronic candidiasis, "immune dysfunction syndrome," and endocrine-metabolic dysfunction; however, none of these etiologies have been scientifically linked to chronic fatigue syndrome.

Educational objective: To understand the clinical features of chronic fatigue syndrome and its relationship to psychiatric illness.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical features of chronic fatigue syndrome
2. Treatment of chronic fatigue syndrome

Answer to Question 82
Answer: A

This patient has linear scleroderma involving the left leg. There is resultant atrophy of the soft tissues and muscles. In younger patients, this may result in disfiguring growth defects in either all or part of a limb. Linear scleroderma is one form of localized scleroderma, the others being morphea and the "en coup de sabre" variant, involving the cranial structures. These conditions are distinguished from systemic scleroderma by the relative absence of vasospasm, structural vascular damage, internal organ involvement, and by the distribution of the skin lesions.

Localized scleroderma rarely transforms into a systemic illness. However, patients need to be monitored extremely carefully because linear lesions are quietly progressive for long periods of time and may be associated with considerable morbidity.

Cranial, perioral skin, and oral cavity involvement can occur. However, bilateral involvement of extremities in linear scleroderma is rarely seen.

The use of L-tryptophan has been associated with the development of the eosinophilia-myalgia syndrome. Some of these patients developed a "peau d'orange" appearance. However, there is no associated muscle and soft tissue atrophy as noted in this patient.

Educational objective: To be familiar with the features of localized scleroderma.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Scleroderma and fasciitis in childhood
2. Pathogenesis and clinical manifestations of eosinophilia-myalgia syndrome

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Answer to Question 83
Answer: E

The asymptomatic elevation of the ESR is a frequent problem confronting rheumatologists. In the absence of a defined rheumatic disease, infection and malignancy should be considered. Among the malignant disorders, multiple myeloma is the most common cause for an elevated ESR. A monoclonal spike noted on the serum protein electrophoresis and confirmed by an immunoglobulin electrophoresis may be due to myeloma or may be of undetermined significance. Some of these patients remain asymptomatic over time, whereas others develop multiple myeloma or another lymphoproliferative disorder, such as Waldenstrom's macroglobulinemia or amyloidosis. Factors that favor a more benign likely course include the presence of fewer than 10 percent plasma cells in the bone marrow, a monoclonal protein concentration of 3.0 g/dL or less, and the absence of light chains in the urine (Bence-Jones protein). A recent study has demonstrated that a normal MRI of the thoracolumbar spine confers a favorable prognosis and makes the diagnosis of myeloma unlikely.

On the other hand, an elevated serum creatinine would raise the possibility of renal involvement by amyloidosis, macroglobulinemia, or myeloma, rather than monoclonal gammopathy of undetermined significance. Thus, choice E is correct.

Educational objective: To be familiar with the evaluation of an elevated ESR in the absence of rheumatic disease.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Monoclonal gammopathy of undetermined significance
2. Recognition of monoclonal proteins

Answer to Question 84
Answer: C

The gradual development of hypertension, proteinuria, and edema in pregnancy is most often due to preeclampsia, particularly in a primigravida. Since these features may also be seen in patients with active SLE, it is important for the clinician to be able to distinguish these two entities. Preeclampsia is typically associated with a rise in the plasma urate level to above 5.5 mg/dL (327 mmol/L).

Urinary calcium excretion tends to be below 100 mg/day (2.5 mmol/day) in preeclampsia. However, it is typically above 200 mg/day (5 mmol/day) in normotensive pregnant women in the third trimester.

The urine sediment in preeclampsia typically is free of any cells or casts. Proteinuria of some degree is always present. The plasma creatinine concentration is generally normal or only slightly elevated (1.0 to 1.5 mg/dL [88 to 133 µmol/L]) in preeclampsia. However, renal failure is an unusual complication, which can occur only in patients who develop severe disease with disseminated intravascular coagulation. This patient did not demonstrate any features worrisome for this diagnostic possibility.

Thus, answer C is correct since this combination of a normal serum creatinine, elevated serum uric acid, low 24-hour calcium excretion, and an acellular urine sediment is the combination of results which is most supportive of preeclampsia.

Educational objective: To understand physiologic differences between lupus nephritis and preeclampsia.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Pathogenesis and clinical feature of preeclampsia
2. Pregnancy in women with underlying renal disease
3. Pregnancy in women with systemic lupus erythematosus

Answer to Question 85
Answer: D

This patient presents with an insidious onset of polyarthritis/polyarthralgia involving shoulders, elbows, wrists, fingers, lumbar spine, and knees. The hand radiographs show evidence of tufting of the terminal phalanges, widening of the MCP joint spaces, and degenerative changes at the thumb and first CMC joints. These findings are consistent with a diagnosis of acromegaly. Nonrheumatologic features of this condition include macroglossia, the presence of multiple skin tags, and hyperhidrosis.

Although amyloidosis or hypothyroidism may be associated with an insidious onset of polyarthritis and the development of macroglossia, other findings such as skin tags and hyperhidrosis are not observed. In addition, the radiographic features are not consistent with either of these conditions.

The arthropathy associated with hyperparathyroidism is characterized by subperiosteal bone resorption of the middle phalanges. This was not observed in this case. In addition, the clinical features would not be explained by this disorder.

Calcium pyrophosphate deposition disease (CPPD) can be associated with a wide range of metabolic disorders including acromegaly, thyroid, and parathyroid conditions. However, this patient's clinical scenario and radiographs are not consistent with this condition.

Educational objective: Recognize the musculoskeletal manifestations and presentation of acromegaly.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical manifestations of acromegaly
2. Rheumatic and bone disorders associated with acromegaly
3. Clinical manifestations; diagnosis; and treatment of calcium pyrophosphate crystal deposition disease

4. Diagnosis of primary (AL) and secondary (AA) amyloidosis

Answer to Question 86
Answer: B

The majority of patients with AS are able to maintain almost full functional and employment capacity. In some surveys, however, almost one-third of male patients develop a functional decline that affects their work capabilities. One study of over 300 patients with spondyloarthropathy noted seven variables at entry that correlated with increased disease severity. These include all five listed above along with the presence of an oligoarthritis and an age of onset less than 16 years of age. However, the greatest odds ratio for the development of severe disease is seen with hip arthritis, odds ratio (OR) of 23, compared with OR ranging from three to eight for all the others. Thus, choice B is correct.

Educational objective: To be familiar with the prognostic indicators for disease outcome in patients with AS.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Treatment and prognosis of ankylosing spondylitis

Answer to Question 87
Answer: C

The patient's presentation is strongly suggestive of a myopathy with proximal muscle weakness, elevated CK values, and a positive ANA. Myopathy has been observed with the use of penicillamine in patients with rheumatoid arthritis. The development of myositis appears to bear no relationship to either daily dose or the duration of penicillamine therapy. It has been reported in patients taking as little as 50 mg/day and in patients on the drug for as long as six years. Affected patients present with symmetric proximal muscle weakness. Muscle enzymes are elevated; EMG shows myopathic changes; and muscle biopsy reveals perifasicular cellular infiltrates and muscle fiber necrosis and regeneration. Muscle weakness resolves and muscle enzymes return to normal within a few weeks to months of stopping the drug plus treatment with high dose corticosteroids, 40 to 60 mg of prednisone per day. In some cases, clinical recovery has occurred just by stopping penicillamine without adding corticosteroids.

Many of the lipid-lowering agents can cause myalgia and elevation in CK values, which typically resolve with drug discontinuation; however, nicotinic acid has not been implicated.

Both hypo- and hyperthyroidism are associated with a myopathy. The slight elevation in the TSH would not be significant enough to explain the patient's presentation.

Methotrexate is not associated with the development of a myopathy. While severe nutritional deficits of folate or vitamin B12 can produce a myopathy, significant depletion is unlikely in a patient with no history of malabsorption, who ingests multivitamins and supplemental folate.

Corticosteroid use may be associated with a proximal myopathy. However, the CK is not elevated in this situation.

Educational objective: To be familiar with muscle disease associated with drugs, endocrine disorders and nutritional deficiencies.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Drug-induced myopathies
2. Subclinical hypothyroidism
3. Major side effects of methotrexate
4. Major side effects of corticosteroids

Answer to Question 88
Answer: D

Oral contraceptives and estrogens have been shown to increase the serum concentrations of glucocorticoids by decreasing their metabolism and clearance. Theoretically, this can result in a greater incidence of glucocorticoid-induced toxicities such as weight gain, although estrogens themselves may also be directly responsible.

Cyclosporine levels may be increased by the concomitant use of corticosteroids. However, the corticosteroid concentration is not affected by the cyclosporine. Similarly H2-blocking drugs such as ranitidine and cimetidine have no substantial interaction.

Assuming hepatic function is normal, methotrexate does not significantly alter prednisone concentrations. In addition, calcium supplements do not affect steroid levels, but large doses of aluminum or magnesium can decrease bioavailability by 30 to 40 percent.

Educational objective: To recognize which medications can alter serum concentrations of synthetic glucocorticoids.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Determinants of corticosteroid dosing

Answer to Question 89
Answer: D

The more selective COX-2 inhibitors that are currently available in the United States include celecoxib, rofecoxib, and meloxicam. In clinical trials, these agents have been shown to have similar analgesic and anti-inflammatory effects to traditional NSAIDs, but with fewer gastric and duodenal ulcers as detected by serial endoscopy.

COX-2 activation may promote colon tumor growth. Based on this finding, COX-2 inhibition using celecoxib has shown a reduction in rectal polyp formation in patients with familial adenomatous polyposis.

The molecular structure of celecoxib includes a sulfonamide moiety, whereas rofecoxib contains a sulfone. Thus, the use of celecoxib, but not rofecoxib, is contraindicated in patients with sulfonamide allergy.

The incidence of hypertension and peripheral edema increases with higher doses of rofecoxib. In one study, the incidence of peripheral edema was 6 percent, and hypertension was noted in 8 percent of patients treated with rofecoxib 50 mg daily. The use of 12.5 mg or 25 mg daily doses did not show this increase.

Some older NSAIDs are also relatively selective for the COX-2 receptor at low doses. For example, nabumetone and etodolac appear to be more effective inhibitors in some experimental systems of COX-2 than COX-1. Thus, D is correct.

Educational objective: To be familiar with the use of COX-2 NSAIDs.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Overview of selective COX-2 inhibitors

Answer to Question 90
Answer: D

This patient appears to have a spondyloarthropathy, possibly ankylosing spondylitis (AS). The first radiographic changes observed in these patients are usually in the sacroiliac joints (SI). However, the sacroiliac changes may be detectable only on CT scanning in the first few months of the disease. This is an important consideration since the presence of sacroiliitis is essential for the diagnosis.

Radiographs of the lumbar spine or oblique views of the SI joints may not show changes at this early stage. Radionuclide bone scans are nonspecific for this diagnosis and are not recommended.

Only 50 percent of African-American patients with AS carry the HLA-B27 antigen. The presence of this gene in this

patient would be supportive, but not diagnostic of the diagnosis.

Educational objective: To be familiar with the appropriate selection of radiographic imaging in patients with recent onset of a spondyloarthropathy.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical manifestations and diagnosis of ankylosing spondylitis

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Answer to Question 91
Answer: C

The diagnosis of vertebral osteomyelitis can present many clinical challenges. Features of infection such as fever or bacteremia may be absent in a majority of patients. There is no diagnostic characteristic to the pain caused by this infection. The most reliable clinical sign is the observation of local tenderness to gentle percussion of the spine. MRI is the most sensitive radiologic technique to detect vertebral osteomyelitis. The MRI abnormalities may predate the changes seen on plain radiographs by several weeks. However, this technique cannot be used because of the presence of a pacemaker.

If a MRI cannot be obtained, radionuclide imaging is the next best technique to detect vertebral osteomyelitis. Three-phase bone scintigraphy using labelled technetium, a relatively sensitive and specific test, is usually performed first to document the presence of a localized abnormality of bone. When positive, a gallium scan should be performed, which may reveal intense uptake in two adjacent vertebrae with loss of the intervening disk space. Thus, choice C is correct.

Labelled-leukocyte scans are rarely useful. Abnormalities detected with this technique are nonspecific photopenic defects.

Although CT scans may be diagnostic, they can reveal nonspecific findings, such as end plate irregularities (particularly in a patient with abnormalities observed with plain radiography) or fail to detect epidural abscesses. In the absence of neurologic deficits, contrast myelography should also not be performed in this patient.

Educational objective: To recognize the presentation of vertebral osteomyelitis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Vertebral osteomyelitis
2. Epidural abscess

Answer to Question 92
Answer: B

This young boy has features consistent with the diagnosis of Kawasaki disease (KD). KD is a form of a childhood vasculitis, characterized by fever, cervical lymphadenopathy, conjunctivitis, mucositis, and rash. Vasculitis of the coronary arteries appears in up to 25 percent of untreated patients. This may result in complications including aneurysms, thrombosis, myocardial infarction, arrhythmias, and sudden death. Thus, choice B is correct.

Approximately one-half of patients develop lymphadenopathy involving the anterior cervical lymph nodes. However, diffuse lymphadenopathy and/or splenomegaly are distinctly uncommon, and if present, suggest alternative diagnoses.

The use of corticosteroids for the treatment of KD is controversial. There is conflicting data whether corticosteroids promote or prevent the development of coronary aneurysms. By comparison, intravenous immune globulin and aspirin help prevent several complications of KD, including coronary artery aneurysms, and remain the therapeutic agents of choice for KD.

Lipid abnormalities may occur in KD. These typically consist of elevations of the serum triglycerides and low-density lipoproteins, with reduction in the serum levels of high density lipoproteins.

Anticoagulation is indicated only in patients who develop coronary artery abnormalities, vascular obstruction, or thrombosis. This group constitutes a minority of KD patients.

Educational objective: To understand the clinical presentation and management of Kawasaki disease.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Etiology and clinical manifestations of Kawasaki disease
2. Diagnosis and treatment of Kawasaki disease
3. Cardiovascular sequelae of Kawasaki disease

Answer to Question 93
Answer: C

This patient has features consistent with degenerative joint disease involving the lumbar spine. These patients may present with one of the following four subtypes: lumbago, which describes a low back ache which is usually self-limited in nature; osteoarthritis of the facet joints with severe central low back pain; lumbar spinal stenosis due to narrowing of the spinal canals with nerve root compression; and herniated disc syndrome, which occurs infrequently in this population and may present with sciatic pain. A positive Romberg sign, in which patients have difficulty maintaining balance with their eyes closed, and a wide-based gate are highly specific for spinal stenosis, but not very sensitive.

The cauda equina syndrome is an uncommon, neurologic emergency. These patients generally present with genitourinary symptoms including urinary retention or overflow incontinence. Physical examination may reveal loss of anal sphincter tone or saddle anesthesia. However, the vast majority of patients with spinal stenosis treated conservatively do not go on to develop this condition.

As noted above, a herniated disc would be an unlikely finding in this patient, given the lack of radicular pain and the low frequency of this finding in the elderly. Despite the prior history of breast cancer, metastatic disease does not present with the pain pattern described in this case. Pain is generally focal, unrelenting and not relieved by rest.

Educational objective: To recognize and appropriately evaluate lumbar spinal stenosis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Approach to diagnosis and evaluation of low back pain
2. Evaluation of low back pain in older subjects: Degenerative spinal disease and lumbar stenosis

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Answer to Question 94
Answer: D

This patient presents with features that are most consistent with a metabolic myopathy. These include muscle achiness, weakness associated with strenuous activity, and an episode suggestive of myoglobinuria. Most studies in these patients, including serum CK, electromyelography (EMG), and routine muscle biopsy are generally normal when the patient is examined during normal resting conditions. Since exercise is required to induce symptoms, a forearm ischemic exercise test is useful in this setting. Thus, choice D is correct.

Educational objective: To review features of metabolic myopathies.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Metabolic myopathies: Disorders of lipid metabolism
2. Approach to the metabolic myopathies

Answer to Question 95
Answer: D

The major goal for treatment of ITP is to provide a safe platelet count to prevent major bleeding rather than correcting the disease. Major bleeding is rare in patients with ITP, primarily occurring in those with platelet counts below 10,000/µL. Among patients with initial platelet counts above 30,000 to 50,000/µL, fewer than 10 percent develop more severe thrombocytopenia and require treatment at three to seven year follow-ups. These data suggest that such patients require careful follow-up but no specific initial therapy.

In adults, the standard practice is to initiate treatment with prednisone, 1 mg/kg given as a single daily oral dose. Most adults respond to prednisone treatment within the first few weeks.

Immune complex deposition may be enhanced in patients with cryoglobulinemia and high titers of rheumatoid factor. Thus, the use of IVIG in such patients may be relatively contraindicated.

Anti-D (WinRho) is effective only in Rh-positive patients in whom the immunoglobulin binds to the erythrocyte D antigen; immune-mediated clearance of the sensitized erythrocytes occupies the Fc receptors in the reticuloendothelial system, thereby minimizing removal of antibody-coated platelets. The response rate in one series was 70 percent with the increase in platelet count lasting more than 21 days in 50 percent of the responders.

Splenectomy is traditionally considered to be the second-line treatment in adults with ITP who fail to achieve a safe platelet count with initial prednisone therapy. Many case series have reported large numbers of patients undergoing splenectomy and all have comparable results: approximately two-thirds of patients recovered to a normal platelet count, which persisted for the duration of observation.

Educational objective: To be familiar with the therapeutic options for IVIG.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. General principles of the use of intravenous immune globulin
2. Treatment and prognosis of idiopathic thrombocytopenic purpura

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Answer to Question 96
Answer: A

The two main clinical manifestations of lung involvement in scleroderma are interstitial lung disease (ILD), also called fibrosing alveolitis or pulmonary fibrosis, and pulmonary vascular disease leading to pulmonary hypertension. ILD occurs in more than three-quarters of patients with scleroderma; and pulmonary vascular disease occurs in at least 10 percent and possibly many more. ILD is seen in both diffuse and limited cutaneous scleroderma, although it usually occurs at an earlier stage and may progress more rapidly in the diffuse form.

Thin section (3 mm or less) high-resolution computed tomography (HRCT) scanning of the lung has revolutionized the approach to interstitial lung disease (ILD) in scleroderma. It can demonstrate the character and distribution of fine structural abnormalities that may not be visible on chest radiographs. A ground-glass appearance of opacification on HRCT is associated with a biopsy showing predominantly cellular infiltration. It is likely to respond to therapy; in contrast, fibrotic disease on HRCT is irreversible and therapy is given in an attempt to prevent progression in less affected regions of the lung.

His HRCT findings of a ground glass appearance are not consistent with the diagnosis or subsequent development of pulmonary hypertension. In addition, his pulmonary function studies, demonstrating a reduction in the DLCO along with reduced lung volumes and FEV1, are consistent with interstitial lung disease.

In the absence of immunosuppressive therapy his lung findings do not place him at risk for the development of an opportunistic lung infection. However, his risk for this type of infection will increase if he is treated with cyclophosphamide and corticosteroids.

Without treatment, the likelihood for progression of his pulmonary disease is quite high. He has diffuse cutaneous disease of recent onset, and these patients are more likely to develop worsening lung disease over time.

Educational objective: Recognize the clinical presentation of ILD in scleroderma.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical manifestations and evaluation of scleroderma lung disease
2. Overview of the manifestations and diagnosis of scleroderma.

Answer to Question 97
Answer: D

This young male college student has features characteristic of infectious mononucleosis (IM), including a prodrome of fatigue, myalgias, lymphadenopathy, and tonsillitis. The skin rash following the administration of ampicillin is very commonly seen in patients with IM. The blood smear demonstrates the characteristic feature of IM, namely atypical lymphocytes with abundant cytoplasm. The abdominal pain is due to splenic rupture, a rare but potentially life-threatening complication of IM, estimated to occur in one to two cases per thousand. Almost all cases have been in males. Splenic rupture can be the first symptom of IM that brings the patient to medical attention; it is spontaneous in over one-half of reported cases, with no history of specific injury. Rupture has occurred between the fourth and twenty-first day of symptomatic illness, and has not correlated with the clinical severity of IM or with laboratory findings. Nonoperative treatment with intensive supportive care and splenic preservation has been successfully carried out in some cases, while others require splenectomy.

Although lymphadenopathy, skin rash, and fever may be seen in patients with Adult Still's disease (ASD), Kawasaki's disease, or SLE, they are less likely:

- The lack of a history suggesting a quotidian fever spike and a low rather than elevated platelet count go against the diagnosis of ASD.

- Kawasaki's disease is unlikely given the absence of conjunctivitis, mucositis, and a history of palmar erythema followed by desquamation of the affected skin.

- SLE is a diagnostic consideration, but at this point in time the lack of serologic findings (eg, autoantibodies) along with the presence of atypical lymphocytes on blood smear point to another diagnosis. Most importantly, the abdominal pain along with the atypical lymphocytes on blood smear should lead the clinician to suspect IM.

Educational objective: To recognize the presentation of viral syndromes that may mimic rheumatic diseases.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
Adult Still's disease
General symptomatology and diagnosis of systemic lupus erythematosus
Pathogenesis and diagnosis of viral arthritis
Infectious mononucleosis

Answer to Question 98
Answer: A

Marfan syndrome (MFS) is an autosomal dominant condition with a reported incidence of 1 in 10,000 to 20,000 individuals. It is among the most common inherited disorders of connective tissue. Patients may demonstrate a wide range of clinical severity depending upon the involved tissues. These include ocular, cardiovascular, and musculoskeletal abnormalities, as well as lung, skin, and central nervous system involvement. Many cases of the Marfan phenotype involve mutations of the fibrillin-1 (FBN1) gene.

Aortic root disease leading to the formation of aneurysmal dilatation, aortic regurgitation, and dissection is the main cause of morbidity and mortality in the MFS. Mitral valve prolapse may also occur; however, aortic stenosis is not a feature of MFS.

Kyphosis and scoliosis with greater than a 20 degree angulation of the spine is a common finding.

Displacement of the lens occurs often; secondary myopia (due to increased axial length of the globe), retinal detachment, glaucoma, and iritis with loss of vision are responsible for most of the ocular-related morbidity in MFS.

Retinal tears and detachment are commonly bilateral in MFS and may be associated with a proliferative retinopathy.

An enlargement of the spinal canal owing to progressive ectasia of the spinal dura and neural foramina along with erosion of vertebral bone occurs in more than 90 percent of patients with MFS. This abnormality usually involves the lower spine. The clinical significance of dural ectasia, which is best assessed by magnetic resonance imaging, remains to be established.

Educational objective: To recognize the presentation of Marfan syndrome.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. The Marfan syndrome

Answer to Question 99
Answer: E

The preference and experience of the surgeon is the primary determinant for the choice of carpal tunnel release surgery. Long-term success rates are equivalent with either an open incision or an endoscopic approach. Because of better visualization, open carpal tunnel release is generally cited as the safer option. It does, however, have a higher rate of post-operative incision pain and a larger scar. Endoscopic release is associated with a smaller scar, less incision pain, and an earlier return to work.

Educational objective: To understand the benefits of various surgical approaches for carpal tunnel release.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Surgery for carpal tunnel syndrome

Answer to Question 100
Answer: C

This patient has symptoms of estrogen deficiency and has osteoporosis. Treatment of both problems requires daily systemic estrogen. The best treatment option for this patient is daily continuous estrogen and progesterone that is more likely to result in an atrophic endometrium and amenorrhea than cyclic hormonal treatments. Thus, choice C is correct.

The other choices are incorrect:

- Daily oral estrogen therapy unopposed by progesterone in a woman with a uterus increases the risk of endometrial hyperplasia that can lead to endometrial cancer.

- Daily oral estrogen and cyclic progesterone treatment may lead to uterine bleeding and probable discontinuation of the therapy due to patient preference.

- Although the effects of raloxifene upon serum lipids suggest some usefulness for the prevention of cardiovascular disease, there are no direct data in these areas. In addition, raloxifene does not relieve menopausal symptoms.

- Alendronate is an effective anti-osteoporosis therapy but lacks any effect on relieving menopausal symptoms or reducing cardiac risk factors.

Educational objective: To be familiar with the merits and drawbacks of various therapies used for management of bone density and other perimenopausal issues.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Hormone preparations for estrogen replacement therapy
2. Use of selective estrogen receptor modulators in postmenopausal women
3. Estrogen replacement therapy: Benefits and risks
4. Clinical use of the bisphosphonates in osteoporosis

Answer to Question 101
Answer: D

Clinically, this patient has an illness characterized by arthritis, myalgias, painful loss of visual acuity, nasal ulcers, and a lung infiltrate. Her blood pressure is slightly elevated and there are some red blood cells in the urine. These features could be consistent with a systemic necrotizing vasculitis. Almost all patients with active systemic Wegener's granulomatosis have a positive ANCA, most commonly targeting the PR3 proteinase antigen. The diagnostic accuracy of ANCA becomes greater in patients with classic presentations of systemic vasculitis such as the case described above. If an underlying infectious cause of disease has been excluded, this patient's presentation is most consistent with a diagnosis of Wegener's granulomatosis. Thus, choice D is correct.

A renal arteriogram would not be recommended in this setting since it would most likely be associated with nonspecific findings and carries some risk. Although this test could be helpful in the evaluation of a patient suspected of having polyarteritis nodosa, the pulmonary infiltrate makes this diagnosis unlikely.

Alveolar infiltrates, usually associated with hemoptysis, may also be seen in Goodpasture's syndrome, which would be screened for by an anti-glomerular basement membrane antibody. However, this patient's other manifestations could not be explained by this condition.

Behcet's disease is a chronic, relapsing, inflammatory disease characterized by recurrent oral aphthae and any of several systemic manifestations including genital aphthae, ocular disease, skin lesions, neurologic disease, vascular disease, or arthritis. Ocular disease occurs in 25 to 75 percent of patients, depending upon the population studied. Many patients progress to blindness. There are no pathognomonic laboratory tests in Behcet's disease. However, a positive pathergy test, which is characterized by skin inflammation 24 to 48 hours after oblique insertion of a 20 to 25 gauge needle, can be a helpful clinical clue. However, pathergy is only noted in 10 to 20 percent of Northern European and North American patients, making it a test with high specificity but low sensitivity.

The patient's clinical presentation is atypical for SLE, particularly the ocular involvement. Thus, an anti-double stranded DNA antibody test would not be helpful.

Educational objective: To recognize the clinical manifestations of systemic necrotizing vasculitis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical manifestations and diagnosis of Wegener's granulomatosis and microscopic polyangiitis
2. Clinical manifestations and diagnosis of Behcet's disease
3. Clinical spectrum of antineutrophil cytoplasmic antibodies

Answer to Question 102
Answer: D

Celiac sprue is among the most frequent causes of chronic vitamin D deficiency that become clinically evident as osteomalacia. The patient's history does not suggest hepatic or renal disease as a cause of vitamin D deficiency. There is no history to suggest inflammatory bowel disease, cystic fibrosis nor any history of prior gastrointestinal surgery. However, bone loss due to osteomalacia can occur in patients with celiac disease in the absence of gastrointestinal symptoms. IgA endomysial antibody testing is moderately sensitive and highly specific for untreated celiac disease. The very high specificity of the IgA endomysial test has led to debate as to whether a positive result in the appropriate clinical setting can be considered diagnostic and eliminate the need for small bowel biopsy. However, it is recommended that both IgA endomysial and small bowel biopsy be performed prior to dietary treatment, since additional diseases that result in villous atrophy may mimic sprue on biopsy. This approach provides the best means of making a definitive diagnosis of celiac disease from the outset. By comparison, antigliadin antibody tests are not as helpful when there is a moderate or high probability of celiac disease, since it is associated with an unacceptably high rate of false positives. Thus, choice D is correct.

Although vitamin D supplements may be appropriate in the short-term, screening for celiac disease is of greater long-term importance, as nutritional deficiencies in this setting will correct after initiation of a gluten-free diet.

Educational objective: To be familiar with the differential diagnosis of osteoporosis in younger individuals.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Diagnosis and treatment of osteomalacia
2. Causes of vitamin D deficiency and resistance
3. Pathogenesis; epidemiology; and clinical manifestations of celiac disease
4. Use of serum antibodies to diagnose celiac disease

Answer to Question 103
Answer: C

Sulfasalazine can be safely continued throughout pregnancy and nursing. The incidence of decreased birth weight, prematurity, spontaneous abortion, stillbirths, or birth defects is similar in children born to mothers taking sulfasalazine and in the general population. In addition, the amount of sulfasalazine found in the breast milk and serum of nursing infants is minimal, therefore, this medication may be used in lactating women. The use of sulfasalazine in the pregnant woman or nursing mother with rheumatoid arthritis is the same as it is with nonpregnant patients.

Educational objective: To be familiar with the use of sulfasalazine during pregnancy.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Sulfasalazine in the treatment of rheumatoid arthritis
2. Use of immunosuppressive drugs in pregnancy

Answer to Question 104
Answer: C

Stiff-person syndrome is a rare autoimmune disorder characterized by progressive stiffness and episodic severe, painful spasms of axial muscles. Most patients have serum antibodies to glutamic acid decarboxylase, an enzyme with an important role in neuroinhibitory pathways. Patients usually present with low back pain; with time, they may gradually assume a lordotic posture. The EMG may demonstrate continuous motor unit activity without other findings of insertional irritability, fibrillations, or high frequency discharges typical of myositis or neuropathic myopathies.

The other choices are incorrect:

- Radiographs are completely normal, excluding ankylosing spondylitis and diffuse skeletal hyperostosis.

- The abnormal posture and EMG findings are not consistent with either fibromyalgia or myotonic dystrophy. In this latter disorder, weakness and muscle wasting are characteristic features.

Educational objective: To recognize the clinical presentation of the stiff-person syndrome.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical manifestations and diagnosis of ankylosing spondylitis
2. Inherited muscular dystrophies other than Duchenne and Becker dystrophies
3. Stiff-man syndrome
4. Diffuse idiopathic skeletal hyperostosis

Answer to Question 105
Answer: D

Following carpal tunnel surgery, improvement in numbness and weakness is generally slower than wound recovery. The paresthesias and pain typically improve within the first six weeks post-operatively. Improvement in muscle

weakness, as determined by grip and pinch strength, takes much longer. The weakness may actually worsen initially with a return to preoperative at three months and maximum recovery of strength by two years.

Educational objective: To become familiar with the expected time course of surgical response to carpal tunnel syndrome surgery.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Surgery for carpal tunnel syndrome

Answer to Question 106
Answer: C

This patient has most likely developed a reflex sympathetic dystrophy syndrome (RSDS, also known as complex regional pain syndrome-type I). The findings of pain, swelling, warmth, and hyperhidrosis of the lower extremity along with the described radiographic and scintigraphic features are characteristic of the disorder. Although the cause of RSDS is generally unknown, it has been observed in some transplant patients treated with cyclosporine. In one series of patients, symptoms improved with a reduction of the cyclosporine dose. Thus, choice C is correct.

Although higher doses of corticosteroids may be an effective therapy for some patients with RSDS who are not taking cyclosporine, a reduction in the cyclosporine dose would be the preferred course of action in this patient.

RSDS may mimic gouty arthritis. There is insufficient evidence to establish a diagnosis of gout in this patient; thus, neither colchicine therapy nor intraarticular corticosteroids are recommended.

Azathioprine has not been implicated as a precipitating cause for RSDS. Adjusting the dose would not affect this patient's condition.

Educational objective: Recognize cyclosporine as a potential precipitant of reflex sympathetic dystrophy.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Reflex sympathetic dystrophy (complex regional pain syndrome)
2. Hyperuricemia and gout in renal transplant recipients
3. Osteonecrosis

Answer to Question 107
Answer: B

This patient with a prior history of a positive PPD most likely has developed spinal TB or Pott's disease. The radiograph demonstrates destruction of the T7-8 disk space and adjacent vertebral bodies. A paraspinal mass is apparent. Pott's disease typically involves the lumbar and lower thoracic region of the spine. The most common symptom is local pain that tends to increase over weeks to months. There is often an intense degree of muscle spasm and surrounding soft tissue pain. Once the infection is established, it may spread down behind the anterior ligament to involve the adjacent vertebral body. Local destruction often produces collapse of bony structures and herniation of the disk material into the vertebral bodies.

The most important complication of spinal tuberculosis is cord compression resulting in paraplegia. In highly endemic areas, 40 to 70 percent of patients have symptoms and signs of cord compression at the time of diagnosis. Patients with upper thoracic or cervical spine involvement may face even greater risks for this complication. Thus, answer B is correct.

The other answers are incorrect.

- The absence of constitutional features is common, being noted in less than 40 percent of cases.

- Plain radiographs of the spine may show involvement of the anterior aspect of a vertebral body, with demineralization of the end plate and loss of definition of the bony margin early in the course of the disease. The opposing ver-

tebra soon becomes involved and a paravertebral abscess may become apparent. As disease progresses, the disc space becomes obliterated with anterior wedging and angulation.

- The presence of skeletal TB does not predict the HIV status of an individual.

- A chest radiograph is likely to be normal since more than 50 percent of patients with skeletal TB do not have evidence of active chest disease.

Educational objective: To be familiar with the presentation of tuberculous arthritis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Skeletal tuberculosis

Answer to Question 108
Answer: C

This patient has developed a cutaneous vasculitis in the setting of long-term use of PTU for the treatment of Graves' disease. PTU-induced vasculitis is characterized by the development of a positive ANCA with specificities to several different target antigens, including proteinase-3 (PR3), myeloperoxidase (MPO), and elastase. With PTU, highly reactive oxidative products are generated utilizing activated neutrophil myeloperoxidase/hydrogen peroxide/chloride; the products are all thought to be reactive and form macromolecules that bind covalently to the neutrophil membrane.

The leukocytoclastic vasculitides are not typically associated with the development of a positive ANCA, except for those cases due to ingestion of drugs known to cause an ANCA-positive vasculitis. These include hydralazine, minocycline, and PTU.

Although a leukocytoclastic vasculitis has been associated with SLE in some cases, there are no other clinical features to support this diagnosis in this patient. In addition, the ANA titer is generally higher in these patients.

Graves' disease is not associated with a leukocytoclastic vasculitis.

Educational objective: To be able to recognize the presentation of a drug-induced vasculitis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Hyperthyroidism in childhood and adolescence
2. Clinical spectrum of antineutrophil cytoplasmic antibodies

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Answer to Question 109
Answer: A

Metabolic done disease or hepatic osteodystrophy is commonly found in patients with primary biliary cirrhosis. The pathogenesis is not well understood. Plasma concentrations of vitamin D metabolites and calcium are normal in most patients. Biochemical and bone histomorphometric studies have suggested that these patients have a low-turnover osteoporosis. Bone formation is inhibited and bone resorption is low or normal. Thus, choice A is correct.

The other choices are incorrect:

- The axial skeleton is more commonly affected than the appendicular skeleton.

- Although it was initially suggested that malabsorption of vitamin D may be the underlying cause of this condition, this hypothesis has been proven to be incorrect for most patients. Plasma concentrations of vitamin D metabolites have been normal in these patients, and high dose vitamin D supplementation has little effect on this condition.

- The risk of spontaneous fracture actually increases in the first three to six months following liver transplant. This is due to an accelerated bone loss that occurs following the procedure. Corticosteroids used for immunosuppres-

sion along with immobility contribute to fracture development in one-third of patients in the first year post-transplant. In subsequent years, there is a progressive increase in bone mineral density.

Educational objective: To understand the pathophysiology of metabolic bone disease in primary biliary cirrhosis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical manifestations and etiology of osteomalacia
2. Metabolic bone disease in primary biliary cirrhosis

Answer to Question 110
Answer: B

Joint injections are commonly used to treat arthritis flares, tendonitis, and other causes of acute musculoskeletal pain. Many clinicians consider shoulder injections to be a useful therapeutic modality. A local post-injection flare may be easily confused with infection. Infection should be suspected if the flare lasts longer than or begins later than 48 hours after injection. Other findings suggestive of an iatrogenic septic joint include a crescendo pattern of pain, redness, drainage around the injection site, and fever or malaise.

The other choices are incorrect:

- The risk for infection following a joint injection has been estimated to be approximately 6 cases per 100,000 injections.

- Post-injection flares are most commonly associated with injections of corticosteroid preparations other than triamcinolone.

- The use of a local anesthetic such as lidocaine appears to reduce the risk of tendon rupture and soft tissue atrophy by diluting the concentration of corticosteroid to be injected. It also decreases the risk of post-injection flares caused by the crystalline nature of the corticosteroid preparation.

Educational objective: To understand the potential benefits and complications of joint injections.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Intraarticular and soft tissue steroid injections: What agent(s) to inject and how frequently?
2. Joint aspiration or injection: Complications

Answer to Question 111
Answer: E

The development of dialysis-related amyloidosis (DRA) can occur in patients treated with either hemodialysis or continuous ambulatory peritoneal dialysis. The diagnosis of DRA is dependent upon the typical clinical features, as shown in this patient, supported by documented tissue deposition of amyloid or the characteristic x-ray picture of multiple bone cysts that enlarge over time. Amyloid deposition can be shown via aspirate of joint effusions. By comparison, skin biopsy is generally negative. Thus, choice E is correct.

The plasma ß2-microglobulin concentration is increased in dialyzed patients. However, elevated ß2-microglobulin levels alone do not establish the diagnosis, since they may be seen in patients without (or prior to) DRA.

Educational objective: To review clinical features and diagnosis of dialysis-related amyloidosis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Dialysis-related amyloidosis

Answer to Question 112
Answer: D

Because of a potentiation of the immunosuppressive and cytolytic effects of 6-mercaptopurine and azathioprine, which are metabolized in part by xanthine oxidase, allopurinol should generally be avoided in patients treated with these drugs. If, however, the patient has severe gout and allopurinol must be used, the dose of azathioprine should be reduced by at least 50 percent and the white blood cell count carefully monitored. A possible alternative in some disorders is switching from azathioprine to mycophenolate, which does not interact with the allopurinol. Similarly, there is no apparent interaction between methotrexate and allopurinol. Thus, choice D is false.

The use of intravenous colchicine should be restricted to hospitalized patients who are supervised by physicians experienced in the use of colchicine by this route of administration. Leukopenia, hepatic disease, renal insufficiency, and recent use of oral colchicine should be considered contraindications to the use of intravenous colchicine.

The major side effects of uricosuric drugs include rash, precipitation of acute gouty arthritis, gastrointestinal intolerance, and uric acid stone formation. Probenecid also increases urinary calcium excretion in gouty patients, reinforcing the contraindication for its use in patients with a history of nephrolithiasis.

The allopurinol hypersensitivity syndrome, consisting of an erythematous skin rash, fever, hepatitis, eosinophilia, and renal failure, is an unusual but potentially life threatening reaction. It appears to be more likely to occur in patients with mild renal insufficiency who are treated with standard doses of allopurinol and a diuretic.

Educational objective: To determine the best treatment for tophaceous gout.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Treatment of gout

Answer to Question 113
Answer: E

This patient's radiographs demonstrate the characteristic appearance of diffuse idiopathic skeletal hyperostosis (DISH). The diagnosis is based upon radiographic criteria which include the following: the sacroiliac joints are usually spared; the apophyseal joints are not ankylosed; there is exuberant osteophyte formation and flowing calcification occurs; at least four contiguous vertebral bodies are ossified; and disc height is maintained. This is a common degenerative enthesopathy affecting both the spine and the peripheral joints, with an increased prevalence in obese and possibly diabetic individuals. Patients may therefore have extraspinal involvement with hyperostosis noted in the region of the entheses of the olecranon, patella, calcaneus, shoulder, or acetabulum. Thus, choice E is correct.

It is not associated with Stiff-man syndrome, an autoimmune disorder resulting in severe muscle stiffness and spasm, vertebral fractures or iritis. The clinical features of DISH are typically mild and often asymptomatic. Pain in the distribution of a lumbar radiculopathy would not typically be due to DISH.

The radiographic features are in contrast to spinal involvement due to a spondyloarthropathy. Vertebral fractures and iritis are not a feature of DISH.

Educational objective: To review the radiographic and clinical manifestations of diffuse idiopathic skeletal hyperostosis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Diffuse idiopathic skeletal hyperostosis
2. Clinical manifestations and diagnosis of ankylosing spondylitis

Answer to Question 114
Answer: E

This patient's skin lesions are consistent with the diagnosis of erythema nodosum. Lofgren's syndrome is defined as the triad of hilar adenopathy, acute polyarthritis, and erythema nodosum. Patients with erythema nodosum tend to be women, possess the HLA-DR3 allele, and have involvement of multiple joints, typically the ankles and knees. It is usually a self-limiting condition as the erythema nodosum typically disappears in a few months and the joint symptoms within two years. However, approximately one-third of patients have a more persistent arthritis. Nevertheless, the arthritic symptoms are rarely recurrent.

The presence of arthritis in a patient with erythema nodosum and hilar adenopathy does not assure the diagnosis of sarcoidosis. Histoplasmosis, coccidioidomycosis, Yersinia, and chlamydia pneumoniae can all produce this constellation of findings. However, the presence of bilateral ankle arthritis or uveitis strongly suggests the diagnosis of sarcoidosis in patients with erythema nodosum and hilar adenopathy. In these cases, the differential diagnosis must be narrowed largely on geographic and epidemiological grounds as well as laboratory testing.

Educational objective: To review features of Lofgren's syndrome.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Rheumatic manifestations of sarcoidosis
2. Erythema nodosum

Answer to Question 115
Answer: B

This patient's presentation of ascending weakness and paresthesia, absent reflexes, and an elevated protein level in the cerebrospinal fluid is consistent with a demyelinating polyneuropathy, Guillain-Barré syndrome. Symptoms usually develop two to four weeks following a diarrheal or respiratory tract illness. Thus, one would expect that his upper extremities will become involved as well. Choice B is correct.

Marked elevation of serum CK is not associated with Guillain-Barré syndrome. And the mild elevation of CK seen in this case does not suggest the presence of rhabdomyolysis that could lead to acute renal failure.

Inflammatory myositis, such as polymyositis or dermatomyositis, presents with proximal weakness, but without paresthesias. The deep tendon reflexes are usually preserved. The mildly elevated CK is nonspecific; it is not, by itself, diagnostic of an inflammatory myopathy. Other features of these disorders such as Raynaud's phenomenon, photosensitivity, and dysphagia are unlikely to be present in this patient.

A metabolic myopathy or muscular dystrophy disorder that has a genetic basis would normally not present in this abrupt fashion, and the sensory features are also inconsistent. Although mild to moderate elevation of serum CK may be observed, paresthesia and numbness develop insidiously in these diseases.

Educational objective: To be familiar with the presentation of muscle weakness.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1.Hereditary primary motor sensory neuropathies; including Charcot-Marie-Tooth disease
2. Skeletal tuberculosis
3. Guillain-Barré syndrome
4. Clinical features and diagnosis of epidural spinal cord compression

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Answer to Question 116
Answer: A

Celiac disease or gluten enteropathy is an inflammatory disorder of the proximal small intestine triggered by the ingestion of gluten, the alcohol-soluble fraction of wheat protein. The primary findings of mucosal inflammation, crypt hyperplasia, and villous atrophy can result in marked degrees of malabsorption. This can result in weight loss, growth retardation in children, anemia, and vitamin deficiencies particularly of the B and D groups. Thus, osteomalacia can develop. Affected patients may present with diffuse achiness and bone pain, which is most prominent in the

lower spine, pelvis, and legs.

Arthritis may be seen in patients with celiac disease. It may present as an axial or peripheral arthritis. Some patients have features of both. The arthritis may only partially respond to diet therapy.

An association between selective IgA deficiency and celiac disease has been well established. Approximately 10 percent of patients with IgA deficiency have been found to have celiac disease.

There is no known association between polymyalgia rheumatica and celiac disease. Thus, choice A is correct.

Educational objective: To be able to recognize the manifestations of celiac sprue.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Pathogenesis; epidemiology; and clinical manifestations of celiac disease
2. Clinical manifestations and etiology of osteomalacia

Answer to Question 117
Answer: B

This patient presents with features that are consistent with the diagnosis of the sternoclavicular hyperostosis or SAPHO syndrome (Synovitis, Acne, Pustulosis, Hyperostosis, and Osteomyelitis). This is a unique arthropathy, which frequently involves the anterior chest wall. Affected patients may present with pain, tenderness, and swelling of the sternum and its articulations. Radiographs may show enlargement and sclerosis of one or both medial clavicles. There may be osteolytic lesions noted within the sclerotic areas. Other bony involvement includes the ribs and sacroiliac joints. The histopathology of the bony lesions resembles a sterile osteomyelitis. It has been proposed that an occult disseminated infection by a low virulence organism such as Propionibacterium acnes may be the cause of this disorder. Thus, answer B is correct.

The other answers are incorrect.

- Treatment of the SAPHO syndrome is usually nonspecific and conservative. Among the therapies reported to be effective are the nonsteroidal antiinflammatory drugs, colchicine, corticosteroids, and intramuscular calcitonin. A response to antibiotics has not been reported.

- As noted, biopsy findings are characteristic of osteomyelitis, not synovitis.

- There is no association with any particular HLA haplotype.

- There are no known long-term sequelae to this condition.

Educational objective: To be familiar with the presentation and treatment of the SAPHO syndrome.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Neutrophilic dermatoses
2. Major causes of musculoskeletal chest pain

Answer to Question 118
Answer: D

The patient's recent travel to an area endemic for Lyme disease and the development of a bull's eye rash two weeks following a tick bite constitute strong evidence in support of the diagnosis of Lyme disease. The appropriate course of action would be to initiate therapy with oral amoxicillin 1.0 to 2.0 grams per day for three to four weeks' duration. There is no data to support the use of a more prolonged course of therapy. Since this patient's Lyme disease is considered to be in the early stages, intravenous antibiotics are not indicated. In addition, there is no data to support the use of intravenous antibiotics for the treatment of early Lyme disease in pregnancy.

The use of doxycycline would be indicated for the treatment of non-pregnant patients with early Lyme disease. However, it should not be used in pregnancy because of its deleterious effects on fetal dentition.

There is no data to suggest that Lyme disease predisposes to congenital anomalies.

Since this patient recalls being bitten by a tick two weeks earlier, it is possible that Lyme antibody testing may be falsely negative at this time. Even without the antibody results, there are sufficient findings as noted above, to suggest a diagnosis of Lyme disease. Thus, awaiting the results of Lyme antibody testing before recommending antibiotic therapy would not be indicated.

Educational objective: To be familiar with the appropriate therapeutic decisions for pregnant women with Lyme disease.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Pregnancy complicated by Lyme disease

Answer to Question 119
Answer: A

The muscle biopsy shows characteristic features of polymyositis; there is an intense interstitial mononuclear infiltrate with some myocyte degeneration. The majority of patients with polymyositis respond to high doses of corticosteroids. As steroids are tapered, it is not uncommon to observe a relapse of the disease. These patients will require the addition of an immunosuppressive agent either to improve disease control or to serve as a steroid-sparing agent. Along with azathioprine, methotrexate is the drug of choice in this situation.

Increasing the patient's dose of prednisone to 60 mg/day may provide some short term benefit, but given the history that two previous attempts to lower the prednisone dose were unsuccessful, it is unlikely that this strategy would be effective.

Intravenous immune globulin therapy is used in some patients with refractory polymyositis. Because of its high cost and development of tachyphylaxis after a few months of therapy, it should not be considered as a second-line therapy ahead of methotrexate or azathioprine.

Patients with thyroid-related muscle disease do not respond to corticosteroid therapy. In addition, the muscle biopsy is typically minimally noninflammatory in appearance.

Malignant disease may be present in some patients with dermatomyositis and polymyositis, although more frequently in the former. The clinical features of this patient, including the positive ANA, EMG findings, response to corticosteroids, and initially negative evaluation, did not suggest a paraneoplastic myositis. Thus, a more extensive workup for occult malignancy is not indicated at this time.

Educational objective: To understand the use of immunosuppressive therapy in polymyositis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Malignancy and rheumatic disorders
2. Clinical manifestations and diagnosis of adult dermatomyositis and polymyositis
3. Treatment of adult dermatomyositis and polymyositis
4. Malignancy in dermatomyositis and polymyositis

Answer to Question 120
Answer: D

This patient with a history of Wegener's granulomatosis successfully treated three years earlier with oral cyclophosphamide presents with microscopic hematuria. There is a mildly elevated ESR, anemia, and a low titer ANCA. These features may suggest active Wegener's granulomatosis; however, they are not sensitive or specific enough to establish this diagnosis. Nearly all patients with active systemic Wegener's granulomatosis have a positive ANCA (range of 65

to over 90 percent). However, ANCA alone, including C-ANCA, which is more specific for Wegener's granulomatosis, does not appear to be sufficiently accurate to make or exclude the diagnosis. The sensitivity of the C-ANCA may be as low as 65 to 70 percent in patients with limited Wegener's granulomatosis or inactive disease.

Furthermore, the patient's anemia and elevated ESR may be due to an underlying urologic problem causing the hematuria, such as a bladder cancer. In one study of patients treated with cyclophosphamide for at least 12 months for an ANCA-associated vasculitis, an 11-fold enhanced risk for bladder cancer was observed. Thus, in this context, the patient should first undergo urologic evaluation including cystoscopy prior to initiation of any immunosuppressive therapy.

Renal biopsy would not be appropriate in this setting. It should be considered only if the urologic work-up is unrevealing and the diagnosis remains uncertain.

Educational objective: Recognize the possibility of cyclophosphamide bladder toxicity occurring years after discontinuation of the therapy.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Treatment of Wegener's granulomatosis and microscopic polyangiitis
2. General principles of the use of cyclophosphamide in rheumatic and renal disease

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Answer to Question 121
Answer: B

This patient has developed an ischemic toe in the setting of atrial fibrillation with the recent initiation of warfarin therapy and a history of hyperlipidemia (given his use of a statin drug). The use of warfarin or thrombolytic agents may interfere with the healing of ulcerated atheromatous plaques and allow them to shear off and embolize.

The presence of livedo reticularis over the legs and intact pedal pulses may be consistent with either vasculitis or atheroembolic disease. Similarly, hypocomplementemia and an elevated serum creatinine may be seen in either condition.

The finding of eosinophiluria is consistent with renal atheroemboli. It can also be observed in patients with other conditions, such as acute interstitial nephritis, prostatitis, and rapidly progressive glomerulonephritis.

In patients with atheroemboli, a skin or renal biopsy may show a pathognomonic biconcave, needle-shaped cleft within the occluded vessel. In addition, the intraluminal lesions are often accompanied by a perivascular inflammatory reaction that may contain eosinophils.

In essential cryoglobulinemic vasculitis, aggregates consisting of immunoglobulins and complement components are deposited in the walls of capillaries, venules, or arterioles, resulting in small vessel inflammation. However, atheroembolic disease is not a feature of this condition.

Educational objective: To be able to recognize the clinical characteristics of systemic atheroemboli, which may often mimic systemic vasculitis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical characteristics of renal atheroemboli
2. The significance of urinary eosinophils
3. Classification of and approach to the vasculitides

Answer to Question 122
Answer: E

This patient presents with an isolated retinal vasculitis. There are no clinical findings that could help to narrow the differential diagnosis. Retinal vasculitis is associated with two broad groups of disorders: the systemic diseases and infectious illnesses. The former group includes the systemic necrotizing vasculitides such as polyarteritis nodosa and

Wegener's granulomatosis, Cogan's syndrome, Behcet's disease, and relapsing polychondritis. In addition, inflammatory bowel disease, SLE, and sarcoidosis may be associated with a retinal vasculitis.

The development of retinal vasculitis is a rare occurrence in patients with multiple sclerosis, and when present, is most often limited to perivascular sheathing and increased numbers of inflammatory cells in the vitreous. However, vascular occlusions, capillary closure, vitreous hemorrhage, and neovascularization may occur. When present, retinal vasculitis may serve as a strong predictor for the eventual development of multiple sclerosis in patients presenting with optic neuritis.

Although giant cell arteritis may involve the retina, this diagnosis is extremely unlikely given her relatively young age. Thus, choice E is correct.

Infectious diseases that may be associated with a retinal vasculitis include toxoplasmosis, tuberculosis, and syphilis.

Educational objective: Recognize the differential diagnosis of retinal vasculitis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical manifestations and diagnosis of Behcet's disease
2. Retinal vasculitis associated with systemic disorders and infections
3. Epidemiology, risk factors, and clinical features of multiple sclerosis
4. Clinical manifestations and diagnosis of giant cell (temporal) arteritis

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Answer to Question 123
Answer: E

This elderly male patient's Lyme serology suggests a previous exposure to Borrelia burgdorferi. The Western blot test would be considered positive by CDC (Centers for Disease Control) criteria, since 5 out of 10 bands are positive. However, he is asymptomatic. While one might wish that the serologic testing had not been performed, the results suggest he was infected at some time in the past with B burgdorferi. The optimal approach to a person with evidence of prior infection, which was never treated, is currently unknown.

In the absence of symptoms of active disease, some experienced physicians consider this situation similar to that of latent syphilis and recommend treating with either amoxicillin 500 mg PO TID or doxycycline 100 mg PO BID orally for 30 days. Other physicians consider positive serology in an asymptomatic person to be evidence of a prior infection, which has been successfully controlled by the host and therefore do not recommend antibiotic treatment. While the use of intravenous ceftriaxone would probably be as effective as either of the oral regimens suggested, it would be much more costly.

The Lyme vaccine would not be useful because he was already exposed to Lyme disease and has developed antibodies to the major Borrelia antigens, Osp A and B. A recommendation to use tick repellants, wear proper attire when walking through wooded areas, and to perform a check for ticks after outdoor activities is appropriate.

Discussing the conflicting recommendations from opinion leaders in the care of Lyme disease, the risks and potential benefits of antibiotic treatment, and involving the patient in the decision making is the most appropriate management approach when the optimal choice is not known. Thus, choice E is correct.

Educational objectives: To understand the management of asymptomatic seropositive Lyme disease.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Prevention of Lyme disease
2. Treatment of Lyme disease
3. Laboratory confirmation of the diagnosis of Lyme disease
4. Cases illustrating clinical dilemmas in Lyme disease

Answer to Question 124
Answer: C

The diagnosis of late-onset prosthetic joint infection is often difficult. Plain radiographs may show evidence of loosening, but similar findings can be seen in aseptic loosening. In late infections , such as in the case described above, synovial fluid is often difficult to obtain and may yield unreliable culture results. Thus, an open surgical biopsy is frequently required to obtain synovial tissue for proper culture. In addition, frozen section histopathology showing significant neutrophil or plasma cell infiltration is highly suggestive of infection, which should be confirmed by careful aerobic and anaerobic cultures.

Organisms involved in late-onset prosthetic joint infections usually reach the joint from distant sites by hematogenous spread, while infections occurring earlier are often the result of an infection at the operative site.

Antimicrobial prophylaxis of prosthetic joint infections is indicated at the time of surgery to prevent early infections, and any occult or minor infection present at the time of joint replacement should be treated prior to joint replacement. However, there is no evidence that antimicrobial prophylaxis is indicated in patients with prosthetic joints who undergo dental procedures. There have been fewer than 25 documented cases of late-onset prosthetic joint infection after dental procedures, and the association between dental treatment and prosthetic joint infection in these cases is at best extremely weak.

In late infections, the most common complaint is joint pain. Fever is present in less than half the cases, and chills are very uncommon.

Although the plain radiographs may demonstrate prosthetic loosening, this is a nonspecific finding which may also occur due to mechanical (aseptic) causes.

Educational objective: To understand pathogenic factors and diagnostic approach in patients with suspected late-onset prosthetic joint infection.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Treatment and prevention of prosthetic joint infections
2. Pathogenesis and clinical manifestations of prosthetic joint infections
3. Total joint replacement for severe rheumatoid arthritis

Answer to Question 125
Answer: E

The clinical challenge in making the diagnosis of HIV myopathy may involve distinguishing this disorder from zidovudine myopathy. Successful distinction often requires a trial of stopping AZT and monitoring the response. Muscle enzymes and strength generally return to normal one to two months after the drug is discontinued. If there is partial or no response, it is likely that HIV myopathy is present. Thus, E is the correct answer.

In contrast to patients with HIV myopathy, light microscopy of the affected muscle in patients with AZT myopathy generally shows no inflammatory infiltrate or a very mild endomysial collection of T lymphocytes, scattered muscle fiber necrosis, and variable muscle fiber atrophy. Most investigators have found evidence of a mitochondrial myopathy. However, discontinuation of AZT is preferable to muscle biopsy as the initial intervention in this patient.

The other choices are also incorrect:

- Muscle enzymes are typically increased up to ten-fold in patients with both disorders.
- EMG shows myopathic changes in both disorders.
- The development of HIV myopathy does not correlate with the circulating CD4+ T cell level.

Educational objective: To understand the manifestations of HIV muscle disease.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Muscle disease in HIV-infected patients

Answer to Question 126
Answer: B

Antiphospholipid antibodies, such as lupus anticoagulants (LA) and anticardiolipin antibodies (aCL), are recognized causes of thromboembolic phenomenon, thrombocytopenia, and several adverse obstetrical outcomes. The presence of these antibodies is confirmed when titers exceed 20 GPL units, measured on at least two occasions six weeks apart. Along with her prior history of a venous thrombosis, she fulfills the criteria for the diagnosis of the antiphospholipid antibody syndrome.

Most physicians recommend starting low dose aspirin (81 mg per day) as soon as conception is attempted. In addition, this patient should immediately begin anticoagulation with either unfractionated or low molecular weight heparin (LMWH). Unfractionated heparin should be continued until term and stopped once labor has begun. It is subsequently resumed postpartum (12-hours post-cesarean section and 6-hours post-vaginal birth) and either continued or switched to warfarin.

Heparin-induced osteoporosis with fracture has been reported as a complication in up to 2 percent of pregnant women on long-term heparin therapy. LMWH has the advantages of once a day dosing and lower risks of hemorrhage, thrombocytopenia, and osteoporosis, although it is generally more expensive than unfractionated heparin. There is a heightened risk for the development of epidural hematomas associated with LMWH therapy in patients receiving regional anesthesia for childbirth. Thus, therapy should be halted at 36 weeks gestation, or earlier if preterm delivery is anticipated, and unfractionated heparin should be substituted.

Educational objective: To understand the issues regarding pregnancy and anticoagulation therapy in women with the antiphospholipid syndrome.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Monitoring and treatment of pregnant women with the antiphospholipid antibody syndrome
2. Clinical manifestations and diagnosis of the antiphospholipid antibody syndrome
3. Prognosis and therapy of the antiphospholipid antibody syndrome

Answer to Question 127
Answer: C

The patient described has diffuse scleroderma and presents with hypertension, borderline elevated creatinine, and an abnormal urinalysis. The most critical issue to address is the possibility that he is developing renal disease due to his scleroderma. Angiotensin converting enzyme (ACE) inhibitors are the mainstay of treatment, both for achieving adequate blood pressure control and for preserving and improving renal function.

Prior to the introduction of ACE-inhibitor therapy, the control of blood pressure and survival was extremely poor. The use of these agents has increased antihypertensive efficacy, is associated with improved survival, and leads to better preservation of renal function. The addition of calcium channel blocking drugs such as nifedipine should be considered in patients who fail to respond to an ACE inhibitor.

Although low doses of corticosteroids can be helpful in treating arthralgias, arthritis, and friction rubs in some patients with scleroderma, they should be used cautiously. Use of moderate dose corticosteroids has been implicated as a risk factor for developing hypertensive scleroderma renal crisis.

The selective COX-2 inhibitors may prove useful for arthralgias, arthritis, and tendon friction rubs associated with scleroderma. However, they may adversely affect renal function, and should not be used in this patient.

It would be prudent to initiate therapy with an ACE inhibitor for the reasons listed above. Patients with scleroderma renal crisis must be closely followed, which should take place within a matter of days and not weeks.

Educational objective: To recognize the importance of early detection and treatment of hypertension and renal disease in scleroderma.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Scleroderma renal disease
2. Organ-based therapy in scleroderma
3. Overview of the manifestations and diagnosis of scleroderma
4. Overview of selective COX-2 inhibitors

Answer to Question 128
Answer: B

This patient's new ocular complaints may be related to either her Sjögren's syndrome or due to direct involvement of the eye by her RA. For example, scleritis and episcleritis are also extensions of synovial pathology in RA; they occur in less than 5 percent of patients.

Patients with episcleritis usually complain of the abrupt onset of redness, irritation, and watering. Pain is unusual and vision is not affected. One eye is usually affected, but both eyes may occasionally be involved.

Scleritis is a painful disorder; it is typically a constant, severe, boring pain that worsens at night or in the early morning hours and radiates to the face and periorbital region. The pain is severe enough to limit activity and often to prevent sleep. Additional symptoms include watering, redness, and photophobia. This patient's presentation is most compatible with scleritis.

Primary-open angle glaucoma affects both eyes and is associated with a slow, painless loss of vision.

A vitreous hemorrhage presents with a sudden, painless loss of vision without ocular erythema or redness.

The major long-term toxicity of hydroxychloroquine use is the development of macular changes and loss of color vision. This is gradual in onset and painless.

Educational objective: To be familiar with the potential emergency ocular complications that can be seen in patients with rheumatoid arthritis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Evaluation of the red eye
2. Ocular manifestations of rheumatoid arthritis
3. Episcleritis and scleritis

Answer to Question 129
Answer: C

Chronic GVHD is the single major factor determining long-term outcome and quality of life following bone marrow transplantation. Clinical aspects of chronic GVHD may mimic features observed with systemic lupus erythematosus, scleroderma, sicca syndrome, eosinophilic fasciitis, rheumatoid arthritis, and primary biliary cirrhosis. The skin, liver, gastrointestinal tract, and lungs are the principal target organs.

However, significant renal involvement is an extremely rare feature of chronic GVHD. His renal dysfunction is more likely due to cyclosporine nephrotoxicity.

Patients with GVHD may experience dysphagia due to esophageal narrowing or ulcerations. A high frequency of antimitochondrial antibodies is observed, suggesting a common pathogenesis between chronic GVHD and primary biliary cirrhosis.

Thrombocytopenia can be a manifestation of chronic GVHD and may have prognostic importance.

Bronchiolitis obliterans may be the end result of a variety of injuries to the lung. Chronic GVHD is thought to be a prime cause for its development in bone marrow transplant recipients.

Educational objective: To be familiar with the clinical presentation of chronic graft-versus-host disease.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical manifestations and diagnosis of chronic graft-versus-host disease
2. Renal failure following bone marrow transplantation

Answer to Question 130
Answer: B

The patient's clinical picture of an acute mononeuropathy, subacute polyneuropathy, and systemic complaints of fever and weight loss are consistent with a diagnosis of a systemic vasculitis. These include polyarteritis nodosa (PAN), Wegener's granulomatosis (WG), and Churg-Strauss syndrome (CSS). The striking eosinophilia is suggestive, though not diagnostic for CSS; milder degrees of eosinophilia are seen in some patients with WG. However, the respiratory tract findings of wheezing and transient pulmonary infiltrates are more consistent with CSS than PAN or WG. Asthma, eosinophilia, mononeuropathy, and the pulmonary infiltrates are four of the six criteria for the diagnosis of CSS established by the American College of Rheumatology. (The presence of four or more criteria establishes the diagnosis with an 85 percent sensitivity and 99.7 percent specificity.) A fifth criteria for CSS, tissue biopsy, is met in this case as well. The biopsy demonstrates a necrotizing granulomatous vasculitis with marked extravascular eosinophilia.

Although peripheral eosinophilia and neuropathy may be features of the hypereosinophilia syndrome, asthma is not a typical pulmonary manifestation. In addition, the biopsy demonstrates a vasculitis.

L-tryptophan use has been associated with the development of the eosinophilia-myalgia syndrome, characterized by intense myalgias and peripheral eosinophilia. The patient's clinical features and biopsy are not consistent with this diagnosis.

Educational objective: To recognize the clinical features of vasculitis and review the diagnostic criteria for vasculitis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Classification of and approach to the vasculitides
2. Idiopathic hypereosinophilic syndrome
3. Churg-Strauss syndrome (allergic granulomatosis and angiitis)
4. Clinical manifestations and diagnosis of Wegener's granulomatosis and microscopic polyangiitis

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Answer to Question 131
Answer: B

This patient has developed an acute auricular inflammation characteristic of relapsing polychondritis. Additional clinical clues include the relapsing/remitting nature of the symptoms, the polyarthralgias, and the nonspecific laboratory findings of inflammation. Next to the auricular inflammation, peripheral joint involvement (usually arthralgias or a mild arthritis) is the most commonly observed clinical feature, which was noted in one series to be present in two-thirds of 645 patients.

Internal ear involvement, more commonly auditory than vestibular, was seen in approximately one third of patients. Laryngotracheobronchial or eye disease was seen in one-half of patients with polychondritis. A vasculitis involving the medium-sized vessels is far less common, observed in about one sixth of patients.

Educational objective: To review diagnostic priorities in evaluation of relapsing polychondritis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical manifestations of relapsing polychondritis
2. Diagnostic evaluation of relapsing polychondritis

Answer to Question 132
Answer: D

Patients with SLE may develop renal abnormalities, low complement levels, and anti-dsDNA antibodies. These abnormalities are observed less commonly in drug-induced lupus. However, both disorders are associated with antibodies directed against histone. Such antibodies are found in up to 80 percent of patients with SLE, and in more than 90 percent of those with drug-induced lupus, particularly those taking procainamide, hydralazine, chlorpromazine, and quinidine.

The autoantibodies in drug-induced lupus are primarily formed against a complex of the histone dimer H2A-H2B and DNA, and with hydralazine, to the H1 and H3-H4 complex. DNA is required either to stabilize the complex or to contribute part of the antigenic epitope. In contrast, the antihistone antibodies in idiopathic lupus are primarily directed against the H1 and H2B histone subunits.

Educational objective: To understand the laboratory abnormalities associated with SLE and drug-induced lupus.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Drug-induced lupus

Answer to Question 133
Answer: C

Neurologic symptoms due to spinal column involvement and spinal cord compression can occur because of several potential complications of AS. This may occur at the level of the cervical, thoracic, or lumbar spine. This patient has motor and sensory features involving all four limbs, suggesting an upper motor neuron problem. Similar to patients with longstanding rheumatoid arthritis, patients with AS may develop atlantoaxial subluxation that may present insidiously and without neck pain. Atlantoaxial subluxation can cause neurologic symptoms and signs similar to those seen in this patient. Thus, choice C is correct.

The other choices are less appropriate:

- A herniated cervical disc is a very unusual occurrence in ankylosing spondylitis as disc height is usually maintained and disc herniation does not occur.

- A fracture of a syndesmophyte can occur with minor trauma. Although this patient had no history of trauma, very minor trauma could have been overlooked. With this possibility, however, there should be significant localized tenderness over the affected spine. The most common site for this to occur is the C5-6 interspace, which would more likely have produced hyporeflexia in the upper extremities.

- A compression fracture with propulsion of a (cervical) vertebral fragment into the spinal canal causing upper motor neuron findings would be unusual without prior trauma or the presence of localized spinal tenderness.

- The cauda equina syndrome is a rare complication in patients with longstanding AS. It is caused by an arachnoiditis of the lumbosacral nerve roots and would result in lower rather than upper motor neuron signs in the lower extremities; it would not explain the upper extremity findings in this patient.

Educational objective: Be able to interpret neurologic findings in the setting of ankylosing spondylitis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical manifestations and diagnosis of ankylosing spondylitis

Answer to Question 134
Answer: E

Hydroxychloroquine is the most commonly used antimalarial drug in the United States for the treatment of rheumatic diseases including RA, SLE, and juvenile rheumatoid arthritis. It is a 4-aminoquinoline derivative, structurally similar to chloroquine, differing only by replacement of an ethyl group in chloroquine with a hydroxyethyl group in HCQ.

An inability to focus is the most common ophthalmologic effect early in the course of antimalarial therapy. This is due to muscle dysfunction and generally resolves without changing the medication or dosage.

Antimalarial drugs used in the treatment of RA and SLE have been reported to cause a toxic neuropathy, myopathy, and cardiomyopathy. The neuromyopathy is thought to be due to the accumulation of the drug in lysosomes and the subsequent inhibition of lysosomal enzymes. Phospholipid and glycogen then accumulate in the lysosomes, producing characteristic myeloid and curvilinear bodies seen on biopsy. Affected patients present with painless proximal muscle weakness. Peripheral sensory abnormalities, including decreased vibratory sense and absent deep tendon reflexes, may also be present. In addition, a cardiomyopathy may develop, which presents as a conduction system abnormality or as congestive heart failure. Endomyocardial biopsy shows changes similar to those in skeletal muscle.

HCQ lowers the serum cholesterol concentration, probably due to its effects upon receptor recycling. It is also a mild anticoagulant, causing inhibition of platelet aggregation and adhesion.

Although gastrointestinal upset is the most common side effect resulting in the discontinuation of the drug, HCQ does not cause ulcer formation or life-threatening gastrointestinal complications.

Educational objective: To recognize the potential toxicities associated with the use of hydroxychloroquine.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Antimalarial drugs in the treatment of rheumatic disease

Answer to Question 135
Answer: E

Substantial therapeutic benefits using sulfasalazine for the treatment of rheumatoid arthritis have been demonstrated in multiple well-designed studies, as well as meta-analyses. Studies from two major centers have found beneficial effect with sulfasalazine on the rate of new erosion development in the first three years of disease, along with concurrent findings of decreased erythrocyte sedimentation rate and serum C-reactive protein. The patient's reluctance to consider methotrexate and her age and child bearing potential make sulfasalazine a reasonable choice for treatment of her RA.

Although some men treated with sulfasalazine experience oligospermia and infertility, the drug has no effect on a woman's fertility. Most clinicians feel that sulfasalazine is safe in women who may become pregnant.

Adverse reactions are common with sulfasalazine. Approximately 20 to 25 percent of patients withdraw from clinical trials because of intolerable side effects. Two-thirds of such withdrawals result from symptoms due to gastrointestinal and central nervous system toxicity; approximately 4 to 5 percent withdraw because of rash.

Therapy with sulfasalazine is possible despite her history of allergy to sulfonamide antibiotics. Among patients with potential sensitivity to sulfasalazine, desensitization can be accomplished using a slowly escalating dose.

Educational objective: Understand the evidence supporting the therapeutic benefit of sulfasalazine in rheumatoid arthritis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Sulfasalazine in the treatment of rheumatoid arthritis

Answer to Question 136
Answer: C

This patient with refractory RA has evidence for ongoing joint destruction. Thus, it would be appropriate to consider the use of one of the newer biological therapies. Having failed infliximab, additional therapeutic choices may include etanercept or recombinant human IL-1ra (rHuIL-1ra). IL-1ra is a naturally occurring glycoprotein inhibitor of IL-1 that binds the high affinity cell surface IL-1 receptor but has no receptor activation activity. Thus, the agonist effects of IL-1 are partially regulated by IL-1ra.

IL-1ra is released primarily by monocyte and tissue macrophages. It inhibits prostaglandin production by synovial cells and chondrocytes and matrix metalloproteinase production by activated synovial cells and articular chondrocytes. This agent (rHuIL-1ra) can be used concomitantly with NSAIDs.

Because this is a fully humanized protein, it differs from infliximab, which is chimeric, part-mouse and part-human. It can therefore be used in patients who were previously allergic to infliximab.

The most common adverse reaction noted in clinical trials is the development of transient injection site reactions. Retardation of radiographic progression as assessed by erosions and joint space narrowing is evident as early as 24 weeks of therapy.

Educational objective: To be familiar with the use of newer therapies for the treatment of patients with moderate-severe rheumatoid arthritis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Role of cytokines in rheumatic diseases
2. Anticytokine therapies in rheumatoid arthritis

Answer to Question 137
Answer: A

The alkylating agent cyclophosphamide is metabolized in the liver; both active and inactive metabolites are primarily excreted unchanged in the urine. Although the half-life of the active metabolites may not be prolonged by renal insufficiency, it is suggested that the initial dose of the drug should be reduced from the standard dose (0.75 g/m2) by one third, in patients with renal insufficiency such as the individual described above.

The other choices are incorrect:

- Alkylating drugs such as cyclophosphamide are the best documented and most potent at inducing ovarian failure. They alter base pairs, leading to DNA cross-links, and introduce single-strand DNA breaks. As a result, they can theoretically affect both resting cells, such as oocytes, and dividing cells. The effects are age-, dose-, and drug-dependent. Younger women are affected less often than older women, presumably because they have more remaining oocytes.

- Bladder cancer has not been described in patients treated exclusively with intravenous pulse cyclophosphamide. However, it has been reported in patients treated with oral regimens of the drug. In the absence of proof of new onset or worsening glomerulonephritis, it is recommended that patients with new microscopic hematuria undergo cystoscopy.

- Marked lymphopenia is common during cyclophosphamide therapy and is not a major cause for concern. The dose should be reduced or held if leukopenia occurs.

Educational objective: To be familiar with the use of cyclophosphamide therapy.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. General principles of the use of cyclophosphamide in rheumatic and renal disease

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Answer to Question 138
Answer: E

This patient presents with features highly suggestive of GCA. These include age greater than 50, the new onset of a localized headache, an ESR greater than 50 mm/hr, and tenderness over the temporal and facial arteries.

A tender or swollen segment of the temporal artery should be chosen for biopsy if present, since inflammatory involvement may be focal. However, biopsy of the temporal artery in this patient did not reveal evidence for GCA. Thus, the right occipital artery should be biopsied since it is likely to be abnormal. The left temporal artery, which is clinically normal, is less likely to reveal a vasculitis. Thus, choice E is correct.

The other choices are incorrect:

- A temporal artery biopsy performed following the initiation of corticosteroid therapy may still show evidence of persistent arteritis even several weeks later. In one study, the incidence of a positive biopsy was similar in those patients who had and who had not been treated with corticosteroids.

- Discontinuing or decreasing the dose of prednisone should not be performed in a patient with a high clinical likelihood of having GCA.

Educational objective: To be familiar with issues related to the diagnosis and management of GCA.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical manifestations and diagnosis of giant cell (temporal) arteritis
2. Treatment of giant cell (temporal) arteritis
3. Pathogenesis of giant cell (temporal) arteritis

Answer to Question 139
Answer: B

Primary or isolated vasculitis of the central nervous system (ICNSV) affects the small arteries of the cerebrum and spinal cord resulting in neurologic signs and symptoms. There are no features to suggest a systemic vasculitis, and the cause is unknown. Clinical features include headache, confusion, personality changes, paresis, and cranial neuropathies. The ESR is elevated in most cases and the CSF findings include an increased opening pressure, a lymphocytic pleocytosis, and raised total protein.

The diagnosis may be suggested based on cerebral angiographic findings; however, these may be nonspecific. Angiography alone is not sufficient to diagnose vasculitis since there are many processes that "mimic" the vascular changes on angiography that are compatible with vasculitis. Biopsy is the crucial step in making a firm diagnosis of ICNSV. A combined cortical and leptomeningeal biopsy is most likely to be diagnostic, with results from angiography identifying an affected area. The likelihood of a positive biopsy is increased if the tissue is taken from an area in which there was contrast enhancement.

The other choices are incorrect:

- Temporal artery biopsy is of no value in evaluating a patient with possible ICNSV.

- There is insufficient experience with PET scanning to recommend a specific role for this modality.

- A serum or CSF ANCA antibody is not useful diagnostically, since it has not been noted to be elevated in patients with ICNSV.

- Therapy should not be initiated until the diagnosis has been firmly established.

Educational objective: To be familiar with the appropriate evaluation of patients with central nervous system vasculitis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Isolated central nervous system vasculitis

Answer to Question 140
Answer: C

Leflunomide can cause fetal harm when administered to a pregnant woman and is contraindicated in women who are or may become pregnant. If it is taken during pregnancy or if the patient becomes pregnant while taking leflunomide, the patient should be apprised of the potential hazard to the fetus. To accelerate elimination of the drug in such women, administration of cholestyramine (8 g PO TID for 11 days) is recommended.

Although many of the NSAIDs have not been individually studied, current recommendations are to avoid these medications, especially in the second and third trimesters because of the potential risk of premature closure of the ductus and for their interference with uterine contractions and parturition.

There is no data about the use of etanercept during pregnancy. Nevertheless, etanercept is contraindicated in women who are pregnant or nursing.

Educational objective: To be familiar with the teratogenicity of leflunomide.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Rheumatoid arthritis and pregnancy
2. Leflunomide in the treatment of rheumatoid arthritis

Answer to Question 141
Answer: B

This patient has features suggesting the diagnosis of a connective tissue disease. Sclerodactyly, Raynaud's phenomenon, and puffy hands can be seen in SLE and other connective tissue diseases. However the presence of tendon friction rubs are highly specific for scleroderma. Her symptoms of progressive dyspnea, along with marked hypertension, renal insufficiency, anemia, and thrombocytopenia are most consistent with the diagnosis of scleroderma renal crisis. The limited findings of sclerodactyly without proximal scleroderma should not dissuade the examiner from a diagnosis of early diffuse scleroderma. In fact, the skin findings have clearly evolved from those described only a few weeks earlier. The moderate elevation of blood pressure can be seen in scleroderma renal crisis. The hematologic findings consisting of anemia (presumably with microangiopathic hemolysis) and thrombocytopenia are also features of scleroderma renal crisis. Prednisone use at any dosage, but particularly at a dosage of 15 mg or more per day, may increase the risk of renal crisis.

TTP and HUS could present with renal and hematologic findings but could not explain the other clinical features such as sclerodactyly, Raynaud's, and puffy hands.

The patient's dyspnea is almost certainly the consequence of acute left ventricular failure due to the sudden rise in blood pressure. Interstitial lung disease, presumably related to her scleroderma, would be unlikely to progress this rapidly and would not explain the renal insufficiency or anemia.

Educational objective: To review the manifestations of scleroderma renal crisis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Scleroderma renal disease
2. Causes of thrombotic thrombocytopenic purpura-hemolytic uremic syndrome
3. Pulmonary manifestations of systemic lupus erythematosus

Answer to Question 142
Answer: A

The interferons may have marked immunomodulatory effects. Thus, the possibility of either inducing or exacerbating an underlying autoimmune disorder should always be considered when using this agent. Interferon alpha-2a is

commonly used to treat patients with hepatitis C. The major autoimmune syndromes encountered during interferon therapy for liver disease involve the thyroid gland and the liver. In particular, hypothyroidism due to the development of a painless thyroiditis can occur. The patients at greatest risk for this complication include women with circulating thyroid peroxidase antibodies.

Worsening hepatic disease could possibly explain this patient's fatigue; however, this should be associated with a worsening of the liver function studies, rather than the normalization, which was reported.

Cryoglobulinemia per se is not a typical cause of fatigue unless there is deposition of the cryoglobulins in the peripheral nerves. However, this should be associated with additional complaints such as pain and/or dysesthesia. To date, an interferon-associated myopathy has not been described.

Although certain illicit drugs might cause fatigue, it is important to first consider the possibility of occult thyroid disease, as noted above.

Educational objective: To recognize the complications related to interferon therapy.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Principles of interferon therapy in liver disease and the induction of autoimmunity

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Answer to Question 143
Answer: E

This patient has a polyarthritis resembling rheumatoid arthritis, however there are two uncommon features to his condition, namely the positive ANA and the neutropenia. In addition, the blood smear demonstrates the presence of large granular lymphocytes (LGL). Generally, these cells comprise 5 percent of the population of peripheral blood mononuclear cells. There may be the development of a chronic lymphoproliferative disease related to the clonal or reactive expansion of LGLs.

The LGL syndrome is characterized by a mild to moderate lymphocytosis, bone marrow infiltration by LGLs, splenomegaly, anemia, and neutropenia. Infection is a leading cause of morbidity and mortality. About one-third of patients have a polyarthritis resembling RA. These patients may be labeled as having Felty's syndrome. Similar to those with Felty's syndrome, they may be ANA positive; however, unlike patients with Felty's syndrome, up to one-third of patients with LGL syndrome can be seronegative for RF.

There is an increased frequency of HLA-DR4 in this disorder. The presence of arthritis does not seem to affect the course of the hematologic disorder.

Educational objective: To be able to identify the large granular lymphocyte syndrome in patients with rheumatoid arthritis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Large granular lymphocyte syndrome in rheumatoid arthritis

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Answer to Question 144
Answer: C

This patient presents with features suggesting the diagnosis of primary biliary cirrhosis (PBC). These include the onset of fatigue, itch, and hyperpigmentation, which is thought to be due to excess melanin deposition. The elevation of the serum alkaline phosphatase and normal serum transaminase levels are consistent with the diagnosis. The presence of a positive ANA may sometimes be observed, but in this situation, it more likely relates to her underlying Sjögren's syndrome. Antimitochondrial antibodies are highly sensitive and specific for the diagnosis of PBC; the sensitivity and specificity of this antibody is 95 and 98 percent, respectively. However, their role in the pathogenesis of PBC is unclear and antibody titers do not correlate with disease severity or rate of progression.

The presence of cirrhosis, regardless of the etiology, is a risk factor for the development of hepatocellular carcinoma.

In one study, patients with later stages of PBC had a 6 percent incidence of this malignancy.

Patients with early PBC have mild elevations of low-density and very-low-density lipoproteins (LDL and VLDL) and striking elevations of high-density lipoproteins (HDL). This may explain why these patients, despite striking hypercholesterolemia, are not at increased risk of death from atherosclerosis.

Although asymptomatic patients have a longer life expectancy, those with features of thyroiditis, sicca symptoms, or scleroderma, have reduced survival rates.

PBC is unique among the autoimmune diseases in that it never occurs in childhood and is rarely found before age 30.

Educational objective: To recognize the clinical presentation of primary biliary cirrhosis in patients with underlying connective tissue diseases.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical manifestations and diagnosis of autoimmune hepatitis
2. Clinical manifestations and diagnosis of primary biliary cirrhosis
3. Pathogenesis of primary biliary cirrhosis

Answer to Question 145
Answer: C

Paget's disease of bone, also known as osteitis deformans, is a focal skeletal disorder characterized by an accelerated rate of bone turnover. The excessive resorption and formation of bone results in a "mosaic" pattern of lamellar bone associated with increases in local bone blood flow and in fibrous tissue in adjacent marrow. It is more common in areas of the world with large concentrations of people of Anglo-Saxon origin, and is rare in Asia, India, and Scandinavia.

This patient's radiograph shows enlargement of the skull associated with a "cotton wool" appearance due to disruption of the normal bone architecture. The 8th nerve can be compressed in the skull, resulting in hearing loss. This is one of the more common complaints, being present in 37 percent of respondents in one survey of 2000 patients with Paget's disease. Pagetic involvement of the middle ear ossicles, which dampens the motion of these ossicles can also result in hearing loss.

There may be compression of the 2nd, 5th, and 7th nerves by new pagetic bone formation, resulting in visual disturbance and facial palsy. Primary hyperparathyroidism has been reported in as many as 15 to 20 percent of patients with Paget's disease

Paget's disease is not responsive to radiation therapy.

Educational objective: Understand the evaluation and treatment of Paget's disease of the bone.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Treatment of Paget's disease of bone
2. Clinical manifestations and diagnosis of Paget's disease of bone

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Answer to Question 146
Answer: E

Infliximab is a chimeric (human-murine) IgG1 monoclonal antibody to TNFa. The development of a HACA response that recognizes the murine component of infliximab is detected in approximately 40 percent of patients when the drug is used alone. Concomitant methotrexate use reduces the development of these antibodies. In clinical trials, the development of HACA responses was inversely related to the dose of infliximab administered; in one study, 53 percent of patients receiving 1 mg/kg of infliximab developed antibodies, compared to only 7 percent of patients receiving 10 mg/kg.

It does not appear that a HACA response has any clinical significance. Data from the ATTRACT trial does not demonstrate any effect of these antibodies on either clinical efficacy or safety.

Educational objective: To be familiar with the relevance of anti-HACA antibodies in patients treated with infliximab.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Anticytokine therapies in rheumatoid arthritis

Answer to Question 147
Answer: A

This patient's skin lesion is consistent with lupus profundus, a disorder presumably due to an immune complex arteriolitis. Lupus profundus presents as a firm nodular lesion with or without an overlying cutaneous lesion. The nodules, which are often painful, may appear in the mid-dermal, deep-dermal, or subcutaneous layers. When the nodules occur without skin lesions, they are called lupus panniculitis. They consist of perivascular infiltrates of mononuclear cells plus panniculitis, manifested as hyaline fat necrosis with mononuclear cell infiltration and lymphocytic vasculitis.

The nodules may appear on the scalp, face, arms, chest, back, thighs, and buttocks. They usually resolve, but may leave a depressed area.

Some patients with lupus profundus exhibit no other manifestations of SLE. Only 10 to 25 percent of such patients eventually develop SLE. Thus, in the absence of features suggesting an underlying connective tissue disease, there is no indication to initiate treatment with immunosuppressive agents. Therapy should remain symptomatic. Localized morphea can sometimes have a similar appearance to lupus profundus.

There is no association between this lesion and HIV. Similarly, there is no benefit from the initiation of antibiotic therapy.

Educational objective: Recognize the presentation of lupus profundus.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. General symptomatology and diagnosis of systemic lupus erythematosus
2. Weber-Christian disease and other forms of panniculitis

Answer to Question 148
Answer: D

This patient has the "shoulder pad" sign, which is caused by soft tissue swelling due to a nodular hypertrophied synovium directly infiltrated by amyloid. Primary (AL) amyloidosis involves the tissue deposition of fragments of monoclonal light chains rather than fragments of secondary amyloidosis (SAA). The arthropathy in AL amyloid is low-grade, subacute, progressive, and symmetric, with a predilection for the shoulders, knees, wrists, metacarpophalangeal, and proximal interphalangeal joints, and to a lesser degree the elbows and hips. The joints are mildly tender or nontender, and there is usually little morning stiffness. Erosions and joint space narrowing are prominently absent, and there may even be widening of the joint space radiographically. Aspirated joint fluid is usually noninflammatory, with a good mucin clot and consists of predominantly mononuclear cells; the fluid may appear cloudy due to the presence of synovial fragments, which can be shown to contain amyloid by Congo red staining of the spun sediment. These characteristics help to distinguish this disorder from RA.

A potentially misleading finding is the presence of whitish subcutaneous nodules in about 60 percent of cases; these nodules are typically in and around the joint, on the extensor surfaces of the forearms, and elsewhere. Biopsy will clearly distinguish these lesions from rheumatoid nodules and demonstrate them to be composed of congo red birefringent material typical of amyloidosis.

AL amyloid should be considered in the differential diagnosis of jaw claudication along with giant cell

arteritis/polymyalgia rheumatica. Jaw claudication is due to predominantly vascular amyloid that compromises the lumina of the facial branches of the external carotid artery. The presence of a monoclonal gammopathy and lack of response to corticosteroids suggest the diagnosis of AL amyloid.

Educational objective: To be able to identify the presentation of AL amyloidosis and to distinguish this condition from rheumatic diseases.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Diagnosis of primary (AL) and secondary (AA) amyloidosis
2. Causes of secondary (AA) amyloidosis and relation to rheumatic diseases
3. Clinical manifestations and diagnosis of giant cell (temporal) arteritis

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Answer to Question 149
Answer: A

Coccidiodes immitis is a dimorphic fungus that inhabits soils of the desert in southwestern United States. Infection begins after inhalation of spores, and disseminated infection occurs in about 1 percent of patients, either as skin lesions, meningitis, or bone and joint infections. Almost one-half of patients with disseminated infection have bone or joint involvement. Coccidioidal septic arthritis is seen in the weight-bearing joints, most commonly knees and ankles, as well as hands and wrists, usually in a mono- or oligoarticular pattern. Synovial tissue or bone biopsy cultures are necessary to establish a definitive diagnosis.

The other choices are incorrect:

- Histoplasmosis does not typically affect joints.

- The clinical features of this patient's illness, in particular the systemic complaints, are not consistent with either spondyloarthropathy or Lyme disease. Furthermore, Arizona is not a region endemic for Lyme disease.

- Mycobacteria marinarum can cause an indolent bone or soft tissue infection. It is acquired through exposure to a contaminated marine source.

Educational objective: To be familiar with the presentation and treatment of disseminated Coccidiomycosis.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Disseminated Coccidiomycosis
2. Musculoskeletal manifestations of Lyme disease
3. Epidemiology of nontuberculous mycobacterial infections
4. Diagnosis and treatment of disseminated histoplasmosis

Answer to Question 150
Answer: E

This patient has polyarteritis nodosa (PAN). Patients with PAN typically present with systemic symptoms such as fatigue, weakness, fever, arthralgias, and signs of multisystem involvement including hypertension, renal insufficiency, neurologic dysfunction, and abdominal pain. The diagnosis must be confirmed by biopsy of a clinically affected organ, such as peripheral nerve (eg, sural nerve), testis, skin, or kidney. In view of his rapidly worsening renal status, a renal biopsy would be appropriate.

Renal biopsy in classic polyarteritis nodosa may reveal pathognomonic inflammation of the medium-sized arteries. However, affected arteries are often not seen due to sampling error or to primary involvement of the smaller vessels in microscopic polyarteritis. The most prominent finding in this setting is a focal necrotizing glomerulonephritis, often with prominent crescent formation. Among patients with glomerulonephritis, the urinalysis typically reveals mild to moderate proteinuria, with an active sediment containing red cells and cellular and granular casts. In some patients, however, the urinalysis may be normal or near normal, with the sediment containing only a few cells or casts. Thus, awaiting further changes on the urinalysis would be incorrect.

A sural nerve biopsy would not be helpful since this patient does not have neurologic signs or symptoms, an abnormal EMG, or nerve conduction study.

The ANCA is typically negative in PAN. Although this patient could have SLE, awaiting the results of the ANA and complement levels would not be helpful since the major concern at present is to characterize the cause and the extent of the patient's renal disease.

Educational objective: Recognize the presentation of polyarteritis nodosa in comparison to other rheumatic diseases.

For more information see the following UpToDate topic review(s) in the RSAP2001 program:
1. Clinical manifestations and diagnosis of Wegener's granulomatosis and microscopic polyangiitis
2. Classification of and approach to the vasculitides
3. Polyarteritis nodosa

RSAP2001: Rheumatology Self-Assessment Program

Answer Key

1. Answer E
2. Answer D
3. Answer C
4. Answer C
5. Answer B
6. Answer D
7. Answer D
8. Answer D
9. Answer B
10. Answer C
11. Answer C
12. Answer B
13. Answer E
14. Answer C
15. Answer D
16. Answer B
17. Answer B
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27. Answer B
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30. Answer B
31. Answer B
32. Answer A
33. Answer C
34. Answer B
35. Answer C
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103. Answer C
104. Answer C
105. Answer D
106. Answer C
107. Answer B
108. Answer C
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110. Answer B
111. Answer E
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117. Answer B
118. Answer D
119. Answer A
120. Answer D
121. Answer B
122. Answer E
123. Answer E
124. Answer C
125. Answer E
126. Answer B
127. Answer C
128. Answer B
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130. Answer B
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132. Answer D
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145. Answer C
146. Answer E
147. Answer A
148. Answer D
149. Answer A
150. Answer E