Current Treatment Strategies for Rheumatoid Arthritis

ERIC L. MATTESON, MD, MPH

The management of rheumatoid arthritis has changed considerably during the past 15 years. Current strategies emphasize the need for early diagnosis and therapeutic intervention based on the use of disease-modifying antirheumatic drugs. The advent of agents that are more tailored to inhibit the specific disease processes will profoundly affect management. Immunogenetic studies may eventually assist in identifying subgroups of patients with rheumatoid arthritis who have more aggressive disease and who require a more aggressive treatment approach.

Rheumatoid arthritis (RA) is a common disease that affects about 1% of the population worldwide. Women are affected almost 3 times as often as men. The prevalence increases with advancing age, and 4% to 6% of the white population older than 65 years may have RA. Although the cause is unknown, evidence suggests an association between severe RA and HLA, particularly to alleles coding for a shared epitope on the HLA-DRB1 molecule.

Major features of active disease include symmetrical polyarthritis with joint swelling and tenderness and morning stiffness lasting for an hour or longer. Subcutaneous nodules, presence of rheumatoid factor (in about 80% of patients with RA), and radiographically evident erosions or juxta-articular osteoporosis in or adjacent to the involved joints are further characteristics of RA.

The onset and clinical course of RA are variable. Gradual onset is most common. About 20% of patients will have a monocyclic course, which will abate within 2 years, whereas the rest will have a polycyclic or progressive course. The long-term prognosis of patients with abrupt onset of disease is similar to that for patients with gradual onset of disease.

Rheumatoid arthritis is one of the most common causes of disability. After 12 years of disease, more than 80% of patients with RA are partially disabled, and 16% are completely disabled. Life expectancy is shortened by an average of 7 years in men and 3 years in women, an outcome equivalent to the increased mortality of patients with Hodgkin disease, diabetes, and stroke. Factors contributing to the poor prognosis include the presence of extraarticular disease and infections, as well as complications of treatment such as gastrointestinal (GI) toxic effects of nonsteroidal anti-inflammatory drugs (NSAIDs).

MANAGEMENT PRINCIPLES

The goals of therapy for RA are to alleviate pain, control inflammation, preserve the ability of the patient to function in activities of daily living and work, and prevent joint destruction. Appropriate and timely therapeutic intervention after accurate diagnosis diminishes not only the symptoms but also the progress of RA. The primary care physician has a crucial role in this process by early recognition of the symptoms of RA, leading to its diagnosis and use of the resources necessary to establish a successful treatment program to achieve these goals, and by participating in the ongoing management of the patient with RA.

Early in the course of RA, education on the disease and vocational, lifestyle, and family counseling must be provided. Patients are best served by a multidisciplinary team that includes a rheumatologist and other specially trained medical personnel, including nurses and occupational and physical therapists skilled and knowledgeable about RA.

Physical modalities such as joint protection, orthotics and other adaptive devices, and exercises improve the symptoms, function, and well-being of the patient. Adequate rest reduces the fatigue associated with active RA, and resting the involved joints lessens the symptoms of inflammation.

THERAPY

Nonsteroidal anti-inflammatory drugs reduce inflammation and help relieve pain but seldom completely eliminate signs and symptoms of active arthritis. They inhibit 1 or both types of cyclooxygenase (COX). Cyclooxygenase-1 is...
constitutively expressed in the GI mucosa, kidneys, platelets, and vascular endothelium. Cyclooxygenase-2 is functionally expressed and promotes the elaboration of prostaglandins in inflamed tissues.

Selective blockage of COX-2 may lead to an improved safety profile for these agents. Celecoxib and rofecoxib are the first such agents available in the United States that selectively block COX-2. Of importance, the efficacy of these COX-2 inhibitors does not differ substantially from that of conventional NSAIDs. Their putative advantage is principally because of a reduced rate of adverse events, especially upper GI bleeding. Cyclooxygenase-2 inhibitors should be considered in patients at high risk of GI bleeding, including those older than 65 years and those with a previous history of GI bleeding. Despite advantages, these drugs may be associated with important adverse reactions, including allergy and fluid retention, and like other NSAIDs should be used with caution in patients with renal insufficiency.

Glucocorticoids are the most potent suppressors of inflammation and may be needed to control severe polyarticular disease until disease-modifying antirheumatic drugs (DMARDs) have been added and become effective. At that point, the glucocorticoids should be tapered and discontinued. Glucocorticoids should not be used alone in the management of RA. Oral prednisone or an equivalent is given in dosages typically ranging between 2 and 15 mg/d, often in divided doses (eg, 2 mg twice a day). A splitting regimen is frequently necessary because the anti-inflammatory effect is relatively short. It is preferable, but often not possible, to avoid long-term glucocorticoid therapy in patients with RA because of the well-appreciated adverse effects of these drugs. Systemic extra-articular manifestations such as rheumatoid vasculitis may require treatment with initial prednisone dosages of 40 to 60 mg/d, tapering according to response. Intra-articular injection of glucocorticoids is an effective means for reducing pain and inflammation in individual recalcitrant joints.

Disease-modifying antirheumatic drug therapy is associated with reduced morbidity and mortality in patients with RA. It should be used when the diagnosis of RA has been established and before erosive change appears. Disease-modifying antirheumatic drugs are usually given with NSAIDs and glucocorticoids, if needed. The DMARDs currently in use are listed in Table 1. The mechanism of action of most of these agents is diverse and to a variable extent overlapping. For many of the agents, the mechanism of action is defined incompletely, whereas for some, including the new class of tumor necrosis factor (TNF) blockers, it is better understood.

For patients with mild disease, hydroxychloroquine is often the first drug of choice because of ease of use and its favorable toxicity profile. Retinopathy due to hydroxychloroquine rarely develops when appropriate dosages are used. The onset of antirheumatic disease activity occurs in about 3 to 4 months in almost 50% of patients, although 6 months may be needed for the full benefit to be realized. For patients with moderately active or severe newly diagnosed disease, methotrexate or sometimes sulfasalazine is a preferred initial choice. In patients with continuing active established disease, methotrexate may be used in combination with other agents including hydroxychloroquine, sulfasalazine, or both or cyclosporine, azathioprine, and the more recently available DMARDs. For patients with acute and severe disease, a combination of DMARDs, prednisone, and an NSAID may be initiated; the dose of prednisone should be tapered during the ensuing weeks to months as disease control improves.

Because of its favorable efficacy and toxicity profile, methotrexate is regarded by many rheumatologists as the anchor therapy for RA. The initial dosage is usually 7.5 to 10.0 mg/wk, titrated upward to an average dosage of 12.5 to 15.0 mg/wk, although dosages of 20 to 30 mg/wk (if tolerated) may be necessary to realize this drug’s therapeutic potential before the response is deemed “inadequate.” Methotrexate may be given in tablet or liquid form; the liquid form is substantially less expensive than tablets, and injection may be associated with less stomatitis and GI upset. Appropriately managed, methotrexate can be used effectively for long periods to control RA. Although generally well tolerated, methotrexate can cause GI upset and hepatotoxicity including liver fibrosis and cirrhosis. Concomitant alcohol use is an important risk factor for methotrexate-related hepatotoxicity, and thus alcohol should not be used by patients taking this drug. Methotrexate can also cause a syndrome of pulmonary hypersensitivity manifested by dyspnea, cough, and fever and should not be used in patients with hepatic or renal insufficiency or severe lung disease. Supplemental folate (usually 1 mg/d) seems to reduce the occurrence of other adverse effects, including stomatitis, hair thinning, and bone marrow suppression. In patients taking methotrexate, physicians should avoid prescribing antifolate drugs such as sulfamethoxazole for sinusitis or cystitis, which may precipitate pancytopenia.

Use of DMARDs has substantially improved disease control and the long-term outlook for patients with RA. Their use may be associated with a lower incidence of extra-articular disease manifestations such as systemic vasculitis. In a series of more than 3000 patients monitored for up to 20 years, patients who had received DMARD therapy had a 30% reduction in long-term disability and improvement in survival compared with patients who had received NSAIDs alone. Despite these successes, major challenges exist. For example, DMARDs are becoming...
Table 1. DMARD Therapy for Rheumatoid Arthritis*

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Dosage</th>
<th>Toxic effects requiring follow-up</th>
<th>Monitoring studies†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azathioprine</td>
<td>50-150 mg/d in 1-3 doses, based on body weight; take with food</td>
<td>Myelosuppression, hepatotoxicity, lymphoproliferative disorders, malignancy</td>
<td>CBC and platelet count every 1-2 wk with changes in dosage, every 1-3 mo thereafter</td>
</tr>
<tr>
<td>Chlorambucil§</td>
<td>0.05-0.10 mg/kg/d; maintenance dosage generally 4-6 mg/d in 1-2 doses</td>
<td>Myelosuppression, myeloproliferative disorders, malignancy</td>
<td>CBC and platelet count every 1-2 wk with changes in dosage, every 1-3 mo thereafter</td>
</tr>
<tr>
<td>Corticosteroids (oral prednisone, others)</td>
<td>For synovial disease, 2-15 mg/d in 1-4 doses; for extra-articular disease (vasculitis), 20-60 mg/d according to response</td>
<td>Hypertension, hyperglycemia, osteoporosis</td>
<td>Baseline blood pressure, chemistry panel, lipid profile, bone densitometry in high-risk patients; follow-up tests including glucose and lipids as indicated</td>
</tr>
<tr>
<td>Cyclophosphamide§/</td>
<td>50-150 mg/d orally in a single morning dose</td>
<td>Myelosuppression, myeloproliferative disorders, malignancy, hemorrhagic cystitis</td>
<td>CBC and platelet count every 1-2 wk with changes in dosage, every 1-3 mo thereafter</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>2.5-5 mg/kg/d in 1 or 2 doses</td>
<td>Renal insufficiency, anemia, hypertension, hirsutism</td>
<td>Creatinine every 2 wk until dose is stable, then monthly; then periodic CBC, potassium, liver function tests‡</td>
</tr>
<tr>
<td>Penicillamine§</td>
<td>125-250 mg/d in a single initial dose, increased to not more than 1500 mg/d in 3 doses; take on an empty stomach</td>
<td>Myelosuppression, proteinuria</td>
<td>CBC and urine dipstick for protein every 2 wk until dosage is stable, then every 1-2 mo</td>
</tr>
<tr>
<td>Etanercept</td>
<td>25 mg subcutaneously 2 times a week</td>
<td>Reactions at injection site, influenza-like symptoms</td>
<td>Not defined</td>
</tr>
<tr>
<td>Gold# (intramuscularly)</td>
<td>10 mg in a single dose the first week, 25 mg the following week, then 25-50 mg/wk thereafter; frequency may be reduced after total dose of 1 g administered</td>
<td>Myelosuppression, proteinuria</td>
<td>CBC, platelet count, urine dipstick every 1-2 wk for first 20 wk, then at the time of each (or every other) injection</td>
</tr>
<tr>
<td>Gold (oral)</td>
<td>3-9 mg/d in 1-3 doses</td>
<td>Myelosuppression, proteinuria</td>
<td>CBC, platelet count, urine dipstick for protein every 4-12 wk</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>200-600 mg/d in 1 or 2 doses; take with food</td>
<td>Macular damage</td>
<td>Yearly ophthalmologic examination</td>
</tr>
<tr>
<td>Infliximab</td>
<td>3 mg/kg intravenously every 8 wk</td>
<td>Influenza-like symptoms, development of autoantibodies</td>
<td>Not defined</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>100 mg/d for 3 days, then 10-20 mg/d</td>
<td>Thrombocytopenia, hepatotoxicity, diarrhea</td>
<td>CBC and AST every 4-8 wk</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Single dose of 7.5-25 mg orally, subcutaneously, or intra-muscularly per week</td>
<td>Myelosuppression, hepatic fibrosis, cirrhosis, pulmonary infiltrates or fibrosis</td>
<td>CBC, platelet count, AST, albumin every 4-8 wk‡</td>
</tr>
<tr>
<td>Minocycline</td>
<td>200 mg/d in 2 doses; take on an empty stomach</td>
<td>Photosensitivity, skin discoloration, gastrointestinal upset, drug-induced hepatitis, dizziness</td>
<td>Not defined</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>2-3 g/d in 2-4 doses</td>
<td>Myelosuppression</td>
<td>CBC, AST, creatinine every 2-4 wk for first 3 mo, then every 3 mo**</td>
</tr>
</tbody>
</table>

*AST = aspartate aminotransferase; CBC = complete blood cell count; DMARD = disease-modifying antirheumatic drug.
†Suggested laboratory studies; complete guidelines have been previously published.§
‡When chemotherapeutic agents are initiated, obtain a baseline chest radiograph (current within 6-12 mo), hepatitis B and C, CBC, platelet count, creatinine, and AST value.
§Chlorambucil and cyclophosphamide are not generally very effective for the treatment of synovitis, although they can be useful in treating extra-articular disease, specifically rheumatoid vasculitis.
¶Fluid intake should be 2-3 L/d, and bladder should be emptied before bedtime.
∥Although this drug is considered a DMARD, I do not use it in patients with rheumatoid arthritis because of its limited therapeutic benefit and its high incidence of adverse effects.
¶¶Rarely use gold in the treatment of rheumatoid arthritis; however, I continue to prescribe it to a few patients who have taken it for years and have done well. In my opinion, the therapeutic benefit-toxicity ratio of gold is poor.
**Baseline glucose-6-phosphate dehydrogenase in susceptible population.
more accepted among practicing physicians and their patients, however, adverse effects or failure of the drug to produce long-term disease control often leads to a change in DMARD therapy.

To improve disease control, therapies that contain combinations of DMARDs are often used. About 50% of patients with RA treated by rheumatologists are prescribed combination therapies with either 2 or 3 DMARDs. The combination of methotrexate, hydroxychloroquine, and sulfasalazine is among the most popular regimens. Methotrexate is often combined with other DMARDs including cyclosporine, but many other combinations of DMARDs have also been used.

In addition to hydroxychloroquine and methotrexate, other traditional DMARDs include penicillamine, gold, and sulfasalazine. Sulfasalazine was among the first drugs to be developed for the treatment of RA and may be chosen as the initial DMARD for patients with no allergy to sulfa, rather than hydroxychloroquine or methotrexate. I seldom recommend gold or penicillamine because of the limited efficacy and the pronounced incidence of adverse effects associated with these drugs.

Three to 6 months may be needed before agents such as gold, hydroxychloroquine, and even sulfasalazine are effective. If the response is inadequate after 6 months of treatment, a second DMARD should be added or the DMARD regimen should be changed.

In the past year, 3 new DMARDs, etanercept, infliximab, and leflunomide, have been approved for the treatment of patients with RA. Etanercept and infliximab are TNF-α antagonists that have powerful anti-inflammatory effects in patients with RA. Tumor necrosis factor is a potent inflammatory cytokine expressed in increased amounts in the serum and synovial fluid of patients with RA. It promotes the release of other proinflammatory cytokines, particularly interleukin (IL) 1, IL-6, and IL-8 and stimulates protease production. Etanercept consists of fusion monoclonal antibody composed of 2 identical chains of recombinant human TNF-α receptor fused with the Fc portion of human IgG1. In vitro it binds to soluble TNF. About 70% of patients receiving subcutaneous etanercept at dosages of 25 mg twice a week have substantial improvement in the extent of joint inflammation, often within 1 to 2 weeks after initiation of therapy. This improvement can be enhanced by combination with methotrexate. Adverse effects of etanercept are influenza-like symptoms and reactions at the injection site, which usually abate after the first few injections. The efficacy of infliximab, a recombinant TNF receptor fusion protein, seems to be roughly equivalent to that of etanercept. Infliximab is given intravenously once every 8 weeks, a regimen that may be more convenient for some patients.

Potential long-term risks of these TNF-α antagonists have not been established. Infliximab may be associated with development of autoantibodies such as antinuclear antibodies. To date, neither drug has an increased risk of malignancy, autoimmune disease, or infection, issues that are the subject of ongoing postmarketing surveillance. The cost of these drugs is about $10,000 to $12,000 a year, generally higher for etanercept than infliximab. The available TNF-α antagonists should be considered in patients with recalcitrant disease not controlled by methotrexate.

Leflunomide is a pyrimidine synthesis inhibitor with clinical efficacy generally equivalent to methotrexate. Adverse effects reported include rash, alopecia, allergy, weight loss, thrombocytopenia, and diarrhea. Diarrhea often occurs early in the course of treatment and may abate, but discontinuation of the drug is necessary when diarrhea cannot be ameliorated with dose reduction or concomitant use of antidiarrheal agents.

Serious extra-articular disease manifestations including vasculitis, scleritis, and recalcitrant serositis generally require systemic glucocorticoids and may necessitate the use of immunosuppressive agents such as cyclophosphamide. In my opinion, the only indication for cyclophosphamide in the treatment of RA is severe extra-articular disease, especially vasculitis.

Of importance, the decision about the use and aggressiveness of DMARD therapy should not be based solely on the presence or absence of the rheumatoid factor. Early in the course of RA, the rheumatoid factor may be absent, whereas in patients with established polyarticular arthritis, absence of the rheumatoid factor is not invariably associated with mild disease and good disease outcome. Treatment must be tailored to the disease manifestations and needs of the individual patient. Consultation with a rheumatologist is helpful for patients who are pregnant or considering pregnancy because many antirheumatic drugs have severe fetal toxic effects including teratogenicity.

Management suggestions for several clinical scenarios involving patients with RA are listed in Table 2.

When the symptoms of RA are well controlled, the glucocorticoids should be tapered, and the NSAIDs may also be tapered or used as needed. As a generalization, DMARD therapy should be continued indefinitely; however, if the patient does well and has no signs of active disease for at least 1 year, DMARD therapy could be carefully tapered. With combination DMARD therapy, one of the DMARDs could be tapered if the patient has been in remission for at least 6 months. I consider methotrexate an “anchor” therapy and generally continue this drug for the longest period. Of note, less than 5% of patients with bona fide seropositive RA remain in long-term disease-free remission.
<table>
<thead>
<tr>
<th>Scenario</th>
<th>Therapeutic strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Newly diagnosed RA in a young patient with presence of rheumatoid factor and mild disease (few joints involved and sedimentation rate &lt;30 mm/h)</td>
<td>1. Hydroxychloroquine, 400 mg/d, with or without an NSAID, and prednisone, 3-5 mg/d over a 1- to 3-mo period; sulfasalazine, up to 3 g/d in 2 divided doses, is an acceptable alternative</td>
</tr>
<tr>
<td>2. Patient with new-onset RA with pronounced symptoms including fatigue, low-grade fever, weight loss, and polyarticular disease†</td>
<td>2. Methotrexate, with an NSAID, and prednisone, 5-15 mg/d; taper prednisone over a 3- or 4-mo period if possible. If adequate control cannot be achieved after the initial 6-8 wk of therapy, consider adding hydroxychloroquine, sulfasalazine, or both to this regimen; a frequent cause of “methotrexate failure” is an inadequate dose of methotrexate (providing that the patient is able to tolerate the higher doses)</td>
</tr>
<tr>
<td>3. Patient with established mild disease</td>
<td>3. Hydroxychloroquine, 400 mg/d, with or without an NSAID, and prednisone, 3-5 mg/d over a 1- to 3-mo period; sulfasalazine, up to 3 g/d in 2 divided doses is an acceptable alternative</td>
</tr>
<tr>
<td>4. Patient with established RA in whom optimal dose of methotrexate is partially effective†</td>
<td>4. NSAIDs if they add measurably to symptom control; prednisone, 5-15 mg/d</td>
</tr>
<tr>
<td>a. Initiate combination therapy</td>
<td>a. Add hydroxychloroquine, sulfasalazine, or both</td>
</tr>
<tr>
<td>b. Combination therapy with hydroxychloroquine, sulfasalazine, or both is ineffective (many rheumatologists may not use any of these combinations but would add a tumor necrosis factor α antagonist)</td>
<td>b. Continue methotrexate but discontinue the combination drug and add etanercept or infliximab. TNF-α antagonists should be avoided in patients with chronic infections, draining nodules, or history of TB or TB exposure: I suggest discontinuation of these agents 7-10 d before and after major surgery</td>
</tr>
<tr>
<td>c. Combination therapy with methotrexate and cyclosporine, leflunomide, or azathioprine is poorly tolerated or ineffective (many rheumatologists may not use any of these combinations but would add a tumor necrosis factor α antagonist)</td>
<td>c. Continue methotrexate but discontinue the combination drug and add etanercept or infliximab. TNF-α antagonists should be avoided in patients with chronic infections, draining nodules, or history of TB or TB exposure: I suggest discontinuation of these agents 7-10 d before and after major surgery</td>
</tr>
<tr>
<td>5. Patient with established RA in whom methotrexate is ineffective, not tolerated, or contraindicated†</td>
<td>5. Mild disease: leflunomide, sulfasalazine, and azathioprine. Severe disease: cyclosporine and combinations of DMARDs such as sulfasalazine, hydroxychloroquine, and others, or etanercept or infliximab; gold may be considered, particularly in combination with any of these therapies, although in my experience it is rarely tolerated or useful</td>
</tr>
<tr>
<td>6. Patient with established seronegative RA</td>
<td>6. Of importance, decision about use and aggressiveness of DMARD therapy should not be based solely on the presence or absence of the rheumatoid factor. Early in RA, rheumatoid factor may be absent, whereas in established polyarticular arthritis, absence of rheumatoid factor is not invariably associated with mild disease and good disease outcome; treatment must be tailored to the disease manifestations in the individual patient</td>
</tr>
</tbody>
</table>

*Rheumatoid arthritis is a serious disease. Follow-up early in the course of disease and in patients with poorly controlled disease should be every 2 to 6 weeks. Patients with well-controlled disease may be seen every 3 to 6 months. The primary care physician has an important role in the management of RA and can effectively guide and monitor routine therapy, with periodic consultation by a rheumatologist as needed. Assessment of disease activity and treatment efficacy is enhanced substantially with serial use of standard outcome measures, including duration of morning stiffness, severity of fatigue, presence and degree of joint pain and stiffness including joint counts, global and disease-specific health assessment instruments such as the modified Health Assessment Questionnaire, erythrocyte sedimentation rate, and radiographs of involved joints. Appropriate medical care for patients with RA includes immunization and prompt treatment of infections. Patients with RA have a high risk of infections even if they are not taking DMARDs but particularly when they are taking immunosuppressive drugs. Several medications used to manage RA, including NSAIDs, cyclosporine, and glucocorticoids, may cause or exacerbate hypertension. Rheumatoid arthritis is associated with an increased incidence of pulmonary disease, and patients who smoke have an especially high rate of lung disease. In patients at high risk of GI bleeding, including elderly women and those with a previous history of GI bleeding, prophylaxis is achieved with |

*DMARD = disease-modifying antirheumatic drug; NSAID = nonsteroidal anti-inflammatory drug; RA = rheumatoid arthritis; TB = tuberculosis; TNF-α = tumor necrosis factor α.†The role of the TNF-α antagonists is evolving; some rheumatologists may institute therapy with these agents in several of these scenarios.
agents such as proton pump inhibitors and misoprostol. As a general principle, use of NSAIDs should be avoided when possible and certainly discontinued when symptoms diminish. Virtually all patients with RA have or develop osteoporosis as a complication of the disease or its treatment. Adequate intake of calcium (1200-1500 mg/d) and vitamin D (400 IU/d) is important. In all patients receiving long-term corticosteroid therapy, including men, an antiresorptive agent such as bisphosphonates or calcitonin should be considered. In postmenopausal women, estrogen replacement therapy or agents such as raloxifene may be considered. Finally, mouth and eye moisturization is necessary for patients with sicca complex symptoms.

Understanding the relationship of disease susceptibility and severity with genetic factors may provide an avenue for individualized treatment of patients with RA in the future. It may be possible to treat patients lacking genetic markers of severe disease with milder agents, while those with markers of severe disease may be treated more aggressively. More than 80 drugs are currently being developed for treatment of RA; thus, further advances in the management of the disease are forthcoming.

REFERENCES

Questions About Treatment of RA

1. Which one of the following would be an acceptable therapeutic program for a patient with early mild RA?
   a. Hydroxychloroquine with an NSAID
   b. Hydroxychloroquine, methotrexate, and an NSAID
   c. Methotrexate and prednisone at 5 to 15 mg/d
   d. Etanercept and prednisone
   e. Leflunomide and sulfasalazine

2. Which one of the following regimens would be appropriate for a patient with RA and new-onset systemic vasculitis?
   a. Azathioprine, hydroxychloroquine, and prednisone at 10 to 15 mg/d
   b. Prednisone, 20 mg/d, and methotrexate, 25 mg/wk
   c. Prednisone, 40 to 60 mg/d, and cyclophosphamide
d. Cyclosporine and prednisone at 20 to 30 mg/d
e. Prednisone, 40 to 60 mg/d, and immunosuppression column treatment

3. Which one of the following situations is not a relative contraindication to the use of etanercept?
   a. Patient with history of tuberculosis exposure
   b. Patient with history of lymphoma
   c. Patient with active chronic infection
   d. Patient with newly diagnosed RA
   e. Patient with established RA receiving hydroxychloroquine and methotrexate

4. Which one of the following statements about the clinical course of RA is false?
   a. The median life expectancy of patients with RA is the same as that for the general population
   b. Most patients with RA have some disability after 12 years of disease
   c. Predictors of poor outcome in patients with RA include the extent of radiographic erosions, female sex, and functional class
   d. Patients in whom the rheumatoid factor is present have a worse prognosis than those with seronegative disease
   e. Disease-free remission is unusual

5. Which one of the following statements about COX is true?
   a. Cyclooxygenase-1 is constitutively expressed in the gastric mucosa, kidney, and platelets
   b. Use of the currently available selective COX-2 inhibitors is safe in patients with renal failure
   c. Currently available selective COX-2 inhibitors have been proved in multiple clinical trials to be safe in patients who are taking warfarin
d. Cyclooxygenase-1 is functionally expressed and promotes the elaboration of prostaglandins important in the inflammatory cascade
e. Selective COX-2 inhibitors are not associated with risk of GI bleeding

Correct answers:
1. a, 2, c, 3, e, 4, a, 5, a