Optimizing Disease Control to Manage RA-Associated Pain in Adults

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Goal

To review the pathophysiology of rheumatoid arthritis (RA) and discuss pharmacologic and non-pharmacologic options for managing pain associated with RA in adults.

Objectives

After completing this activity, the participant should be able to:

- **Explain** the pathophysiology of RA.
- **Discuss** nonbiologic disease-modifying anti-rheumatic drugs (DMARDs) and biologic DMARD therapies.
- **Identify** the potential adverse effects of pharmacologic therapies used for treating pain associated with RA.
- **Evaluate** nonpharmacologic options for managing pain associated with RA.

Rheumatoid arthritis (RA) is a chronic auto-immune disease that affects more that 1.3 million people in the United States. (1) More commonly diagnosed in women, RA usually presents between 40 and 60 years of age, but it can develop at any age. (1) The disease can be difficult to diagnose because the symptoms often are subtle and may mimic other illnesses. Patients may complain of morni ng joint stiffness, fatigue, loss of energy, loss of appetite, or low-grade fevers. (1) Referral to a rheumatologist is important, particularly early in the course of the disease, to establish the diagnosis and promptly begin treatment. (1)

Typically, a diagnosis of RA is made through physical examination, x-rays, and laboratory evaluation. On physical examination, patients with RA have painful joints that are warm, tender to the touch, and swollen (Figure 1). Rheumatoid nodules – firm lumps found just below the skin in areas such as the elbow and hands – also are consistent with a diagnosis of RA. (1) Radiographs of the affected joints taken at presentation may not show structural damage, but they are important for monitoring how the disease progresses or responds to treatment. (1)

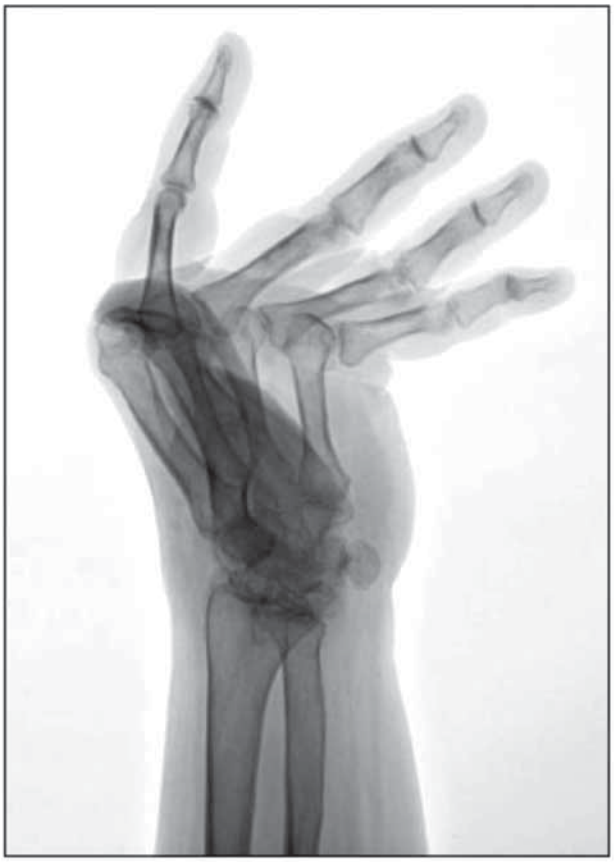

FIGURE 1. *Radiograph of the hand and wrist joints in a patient witb RA. Photo courtesy of the NIH/DHHS*

Sursa: US Pharmacist.

Baseline laboratory evaluation typically includes a CBC to assess for anemia, rheumatoid factor (RF), and erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP). Most patients with RA have a positive RF and an elevated ESR or CRP (non-specific indicators of inflammation). (1,2) Additionally, renal and hepatic function should be checked to help determine which drug therapy is safest for treatment. (2)

Patients with RA typically experience pain during the course of the disease. Despite adequate treatment, in some patients the disease will progress to the point of joint destruction, deformity, and disability. (2) Pain management is crucial for improving the quality of life of RA patients and reducing the debilitating effect of the disease.

Pathophysiology

Although RA is classified as an autoimmune disorder, its exact cause remains unknown. (1,3) The current consensus is that, most likely, some sort of stimulus – such as an infection – triggers the release of inflammatory mediators that ultimately results in inflammation of the synovium. (1) More specifically, a peripheral stimulus binds to receptors on dendritic cells, which are a type of immune cell. (3) These cells then move into the lymph nodes, where they present antigen to T lymphocytes (T cells), thus activating the immune system. (3) Once activated, the T cells proliferate and migrate to the joint and synovial tissue. (3) T cells produce interferon-gamma and other proinflammatory substances, called cytokines, that stimulate the production of macrophages, fibroblasts, monocytes, chondrocytes, and B cells. (3,4) Macrophages, fibroblasts, and monocytes generate cytokines such as tumor necrosis factor alpha (TNF-alpha), interleukin (IL)-1, and IL-6 in the synovial tissue. (4) These cytokines produce matrix metalloproteinases and osteoclasts, which eventually leads to inflammation and irreversible damage to soft tissue and bone. (4)

The single most important step in managing the pain associated with RA is to control the disease. Although nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroids provide symptomatic relief, they do not induce disease remission. (2) Drugs that target the immunologic mechanisms known to cause joint destruction are a fairly recent development in the treatment of RA and are important for preventing disease progression, joint damage, and pain. (4)

Pharmacologic therapies

NSAIDs

While disease-modifying antirheumatic drug (DMARD) therapy (discussed later) is an essential consideration for patients with RA, NSAIDs (including salicylates) are used initially to help treat pain and swelling and to improve joint function. (2) These drugs should not be used as monotherapy for RA since they do not change the course of the disease or prevent disease progression. (2) All NSAIDs have similar effectiveness at equipotent doses; however, patient response may vary depending on the drug. (5) It is impossible to predict response, so a patient should receive at least 2 weeks of NSAID therapy at full doses before a particular drug is deemed ineffective. If the patient does not experience relief, then subsequent trials of different NSAIDs at maximum doses are the next step. (5)

NSAID therapy is typically well tolerated for short periods of time. (6) Patients with RA, however, may require a longer duration of treatment given the chronic nature of the disease. Close monitoring for adverse effects associated with these drugs is important. Patients with RA are almost twice as likely as those with osteoarthritis to experience a serious adverse effect resulting from NSAID therapy. (7) Blood pressure and weight should be closely monitored to check for fluid retention that may worsen hypertension or exacerbate congestive heart failure. NSAID therapy also may precipitate renal impairment, particularly in patients with underlying kidney disease, so monitoring of serum creatinine values is important. (6)

Gastrointestinal (GI) side effects are another concern with NSAID use. The risk of NSAID-induced gastroduodenal ulcers increases with age (≥75 years), preexisting history of ulcers, concomitant use of corticosteroids or anticoagulants, use of high doses of NSAIDs, use of multiple NSAIDs, and the presence of serious underlying health issues. (8) Use of protective medications, such as high-dose H_2 antagonists, proton-pump inhibitors, and prostaglandin analogs (misoprostol), may reduce the incidence of NSAID-induced gastropathy. (9-12) Selective cyclo-oxygenase 2 inhibitors were found to have a better side-effect profile compared with traditional NSAIDs with regard to GI toxicity; however, all but celecoxib were removed from the U.S. market because of an associated higher risk of cardiovascular events. (13) This same warning about the increased risk of cardiovascular problems was later extended to all traditional NSAIDs. (13) Before any type of NSAID

therapy is initiated, health care professionals and patients should discuss cardiovascular risk factors and review the potential risks and benefits of treatment. (2)

Corticosteroids

Corticosteroids (steroids) are potent immunosuppressants that benefit RA patients by suppressing the inflammatory response. (6) Whether given systemically or by intra-articular injection, steroids remain an important tool for relieving the symptoms of RA, particularly as a bridge to the often delayed response of DMARD therapy. Low-dose oral steroid therapy (equivalent of <10 mg prednisone daily) may produce significant pain relief and improvement in functional status in a matter of days. (2) Studies suggest that the use of low-dose steroid therapy slows the rate of joint damage. (14) Additionally, radiographic evidence shows that disease progression increases when steroid therapy is discontinued. (15) Typically, steroids are used not as monotherapy, but rather in conjunction with DMARD therapy. (6) Use of the lowest dose and duration helps minimize the predictable side effects of steroids. (6)

Intra-articular injection of a steroid is safe and effective in patients experiencing a high degree of inflammation in one or two joints. (2) With this method, patients experience pain relief that allows them to participate in rehabilitation that improves lost joint function. (2) Injections in the same joint ideally should be limited to no more than every 3 months, with the need for more frequent injections triggering a reevaluation of the current treatment plan. (2) Recurrent severe pain in the same joint may not be a flare of RA, but rather may be an infection or microcrystalline arthritis. (2) It is important to rule out infection as the source of pain prior to giving an intra-articular steroid injection. (2)

The adverse effects of steroid therapy limit their use not only in RA, but in other disease states as well. Long-term treatment with steroid therapy is associated with osteoporosis, hypertension, weight gain, skin thinning, cataracts, fluid retention, and potential premature atherosclerosis. (2,6) Patients should be counseled about the risks associated with steroids prior to initiation of therapy. Bone-density assessment and aggressive management of cardiovascular risk factors can help reduce complications that result from steroid therapy. (2,6) The use of bisphosphonates with concomitant calcium and vitamin D supplementation should be considered at the time of steroid initiation to prevent steroid-induced osteoporosis. (2,6)

DMARDs

DMARDs manage pain associated with RA through the prevention of disease progression and joint damage. Since there is no cure for RA, the ultimate goal of DMARD therapy is early disease remission. (6) DMARD therapies are categorized as nonbiologic or biologic. Nonbiologic therapies – the first DMARDs that were available for treatment – include such agents as methotrexate, sulfasalazine, and hydroxychloroquine. The newest nonbiologic medication is leflunomide. (6,16) Biologic agents such as infliximab, etanercept, and rituximab represent newer, novel therapies that target specific cytokines known to play a role in the pathophysiology of RA.

Although most patients use nonbiologic DMARDs, the number of patients treated with biologic DMARDs is rising. (16) The number of new biologic agents approved for treating RA continues to steadily increase as well. The newest biologic drug, tocilizumab, was approved by the FDA in January 2010 for the treatment of RA in adult patients who have had an inadequate response to or are intolerant to other DMARDs. (17) Tocilizumab works by blocking the effects of IL-6 in the body, which helps reduce the inflammatory response and structural damage associated with RA. (17) Table 1 compares the indications, dosing, and adverse-effect profiles of commonly used nonbiologic and biologic agents.

For patients who fail monotherapy, combination DMARD therapy may be considered. Evidence best supports the use of the following nonbiologic combinations: 1) methotrexate plus hydroxychloroquine; 2) methotrexate plus sulfasalazine; 3) methotrexate plus leflunomide; 4) sulfasalazine plus hydroxychloroquine; and 5) sulfasalazine plus methotrexate plus hydroxychloroquine. (16) The American College of Rheumatology (ACR) last published guidelines for the use of nonbiologic and biologic DMARD therapies in 2008. In these guidelines, the ACR did not recommend combination biologic therapies because of the increased risk of adverse events; however, combining a biologic product with a nonbiologic medication may be efficacious.[16] Most biologic drugs are FDA-approved for combination therapy with nonbiologic DMARDs such as methotrexate. (16)

Before starting any DMARD therapy for RA, a patient should be assessed for contraindications to treatment. DMARD treatment should be held or suspended in the setting of an active infection until the infection has been successfully treated. (16) Latent infections such as latent tuberculosis (TB) are not a contraindication to DMARD therapy, but

TABLE 1. *Disease-Modifying Antirheumatic Drugs*

MEDICATION	INDICATION	DOSING	ADVERSE EFFECTS	ADDITIONAL INFORMATION
Nonbiologic Agents				
Azathioprine (Imuran)	Monotherapy for active RA	Max 2.5mg/kg/day	Myelosuppression, N/V/D, rash, fever, ↑LFTs	Consider alternative tx in pts deficient in TPMT activity
Cyclosporine (modified) (Neoral, Gengraf)	Monotherapy for early RA or in combination with methotrexate for severe, unresponsive dz	Max 4 mg/kg/day	↑SCr/BUN, N/V/D, HTN, rash, gingival hyperplasia	Keep trough level between 100-200 ng/mL
Gold (Myochrysine)	Monotherapy for active RA	Max 9 mg/day po; titrate up to max 100 mg IM/wk	Dermatitis, pruritus, stomatitis, N/V/D, HA, anaphylaxis	Max cumulative dose 1 g; most AEs occur with cumulative doses between 400-800 mg
Hydroxy-chloroquine (Plaquenil)	Monotherapy for RA or in combination with methotrexate alone or methotrexate/ sulfasalazinetriple therapy	400-600 mg/day, then reduce to 200-400 mg/day	Urticaria, HA, dizziness, N/V/D, myelosuppression	Ocular toxicity a concern
Leflunomide (Arava)	Monotherapy for all dz activity levels or in combination with methotrexate	100 mg po for 3 days, then 20 mg/ day	N/V/D, alopecia, HA, rash, ↑LFTs, HTN, anaphylactoid reactions	Long half-life; to quickly remove drug, use cholestyramine 8 g po tid for 11 days
Methotrexate (Rheumatrex)	Monotherapy or in combination with abatacept, adalimumab, anakinra, etanercept, golimumab, hydroxychloroquine, infliximab, leflunomide, rituximab, sulfasalazine, or sulfasalazine/ hydrox-ychloroquine	7.5-20 mg/wk po	N/V/D, ↑LFTs, stomatitis, rash, myelosuppression, pruritus, PF	May change to IM or SC for inadequate response or noncompliance
Sulfasalazine (Azulfidine)	Monotherapy or in combination with hydroxychloroquine, methotrexate, or methotrexate/ hydrox-ychloroquine	Max 2,000 mg/day	N/V/D, HA, rash, pruritus, anorexia, dyspepsia, oligospermia	Contraindicated in pts with sulfa allergy
Biologic Agents				
Abatacept (Orencia)	Monotherapy for M/S RA or in combination with other DMARDs	500-1,000 mg IV q2w, then q4w starting at wk 8	HA, URI, HTN, nausea, pyrexia, dizziness, serious infection	Modulates T-cell activation; do not combine with TNF-alpha antagonist
Adalimumab (Humira)	M/S RA	40 mg SC q2w	Myositis, HA, rash, nausea, ISR, HTN, hyperlipidemia, ↑LFTs	TNF-alpha antagonist
Anakinra (Kineret)	Monotherapy for M/S RA in pts who failed ≥1 DMARD or in combination with other DMARDs	100 mg/day SC	Abdominal pain, diarrhea, HA, ISR, infection, flulike sx	IL-1 antagonist; do not combine with TNF-alpha antagonist
Certolizumab (Cimzia)	M/S RA	400 mg SC q2w, then 200 mg SC q2w	Rash, HA, HTN, arthralgias, serious infections, fatigue, pyrexia	TNF-alpha antagonist
Etanercept (Enbrel)	Monotherapy for M/S RA or in combination with methotrexate	50 mg/wk SC	Injection-site pain, infection, HA, rash, dizziness, asthenia, abdominal pain	TNF-alpha antagonist
Golimumab (Simponi)	M/S RA, in combination with methotrexate	50 mg/mo SC	HTN, ↑LFTs, ISR, dizziness, nasopharyngitis	TNF-alpha antagonist
Infliximab (Remicade)	M/S RA, in combination with methotrexate	3 mg/kg IV once, repeat at wk 2 and 6, then q8w	Fever, chills, HA, rash, myalgias, fatigue, ↑LFTs, dyspnea, infection	TNF-alpha antagonist
Rituximab (Rituxan)	M/S RA, in combination with methotrexate in pts with inadequate response to ≥1 TNF-alpha antagonist	1,000 mg IV days 1 and 15, then q24w	Infusion reaction, HA, fever, nausea, hypotension, angioedema, pruritus, myelo-suppression, bronchospasm	Modulates B-cell activation

AE: adverse event; BUN: blood urea nitrogen; DMARD: disease-modifying antirheumatic drug; dz: disease; HA: headache; HTN: hypertension; IL: interleukin; IM: intramuscularly; ISR: injection-site reaction; LFT: liver-function test; max: maximum; M/S: moderate-to-severe; N/V/D: nausea, vomiting, diarrhea; PF: pulmonary fibrosis; pt: patient; SC: subcutaneously; SCr: serum creatinine; sx: symptoms; TNF: tumor URI: upper respiratory infection. Source: References 19, 27.

patients should receive appropriate preventive treatment prior to initiating DMARD therapy. (16)

Chronic hepatitis B or C presents more of a challenge in that the degree of underlying liver injury may not be compatible with the use of certain DMARDs. For example, the ACR recommends not using biologic therapy in patients with significant liver injury (defined as Child-Pugh classes B and C). (16) The ACR further recommends that methotrexate be avoided in patients with a creatinine clearanc e less than 30 mL/min, and that TNF-alpha antagonists not be used in patients who have multiple sclerosis or severe heart failure. (16)

Once the decision is made to start either non-biologic or biologic treatment, an initial evaluation should be performed to provide baseline data that are useful for comparison as part of an ongoing monitoring plan. Table 2 presents recommendations for baseline and ongoing monitoring of DMARD medications. As a part of the baseline evaluation for DMARD treatment, patients should be assessed for vaccination status against pneumococcal disease, influenza, and hepatitis B. (16) Live vaccines should not be administered to patients receiving biologic medications. (16) Patients with risk factors for TB should be screened prior to starting biologic therapy. Treatment of latent TB infection should be completed prior to beginning biologic therapy. (16)

In the past few years, the FDA has required manufacturers to make changes to the prescribing information that pertain to the safety of several biologic drugs. The class most affected by these labeling changes is the TNF-alpha blockers. The FDA mandated that manufacturers of TNF-alpha antagonists add to the labeling a warning for health care professionals to be particularly vigilant about recognizing serious bacterial or fungal infections, TB, and sepsis in patients treated with this class of drugs.[18] More recently, manufacturers of TNF-alpha antagonists were required to add information to the labeling that discusses new safety concerns about the increased risk of lymphoma and other cancers in

TABLE 2. *Recommended Monitoring for Adverse Effects of DMARDs*

MEDICATION	ADVERSE EFFECTS	INITIAL MONITORING	CONTINUED MONITORING[a]
Nonbiologic Agents			
Azathioprine (Imuran)	Myelosuppression	CBC,[b] SCr, LFTs	CBC[b]; watch for fever, bruising, pallor
Cyclosporine (modified) (Neoral, Gengraf)	HTN, anemia, renal insufficiency	CBC,[b] SCr, BP	CBC,[b] SCr, BP; watch for edema
Gold (Myochrysine)	Proteinuria, myelosuppression	Urine dipstick for protein, CBC,[b] SCr	Urine dipstick for protein, CBC[b]; watch for fever, bruising, rash, pallor, stomatitis
Hydroxychloroquine (Plaquenil)	Macular damage	CBC,[b] SCr, LFTs	Monitor for changes in vision; annual fundoscopic and visual-field exam
Leflunomide (Arava)	Myelosuppression, HF	CBC,[b] SCr, LFTs, hep B/C testing, albumin	CBC,[b] LFTs, albumin; watch for HTN, diarrhea, weight loss
Methotrexate (Rheumatrex)	Myelosuppression, HF, pneumonitis	CBC,[b] CXR, LFTs, SCr, albumin, hep B/C testing	CBC,[b] LFTs, SCr, albumin; watch for cough, SOB, stomatitis, nausea
Sulfasalazine (Azulfidine)	Myelosuppression, neutropenia	CBC, LFTs, SCr, consider G6PD testing	CBC[b]; watch for fever, bruising, pallor
Biologic Agents			
Abatacept (Orencia)	Infection, HTN	CBC,[b] LFTs, SCr, BP, PPD	Watch for signs of infection, HTN
Adalimumab (Humira)	Infection	CBC,[b] LFTs, SCr, PPD	Watch for signs of infection, sx of CHF and demyelinating dz
Anakinra (Kineret)	Pneumonia, neutropenia	CBC,[b] LFTs, SCr, PPD, screen for asthma	CBC[b]; watch for signs of infection
Certolizumab (Cimzia)	Infection	CBC,[b] LFTs, SCr, PPD, BP	Watch for signs of infection, HTN, sx of CHF and demyelinating dz
Etanercept (Enbrel)	Infection	CBC,[b] LFTs, SCr, PPD	Watch for signs of infection, sx of CHF and demyelinating dz
Golimumab (Simponi)	Infection	CBC,[b] LFTs, SCr, PPD, BP	LFTs; watch for signs of infection, sx of CHF and demyelinating dz, and HTN
Infliximab (Remicade)	Infection	CBC,[b] LFTs, SCr, PPD	LFTs; watch for signs of infection, sx of CHF and demyelinating disease
Rituximab (Rituxan)	Myelosuppression	CBC,[b] LFTs, SCr, PPD	CBC[b]; watch for signs of infection

[a] Continued monitoring also includes regular pain, joint function, and radiographic assessments to determine response to treatment.
[b] Including platelets.
BP: blood pressure; CHF: congestive heart failure; CXR: chest x-ray; dz: disease; DMARD: disease-modifying antirheumatic drug; G6PD: glucose-6- phosphate dehydrogenase; hep B/C: hepatitis B and C; HF: hepatic fibrosis; HTN: hypertension; LFT: liver-function test; PPD: purified protein derivative skin test for tuberculosis; SCr: serum creatinine; SOB: shortness of breath; sx: symptoms.
Source: References 6, 16, 27.

children and adolescents treated with these medications. Additionally, an existing warning about the risk of malignancies was required to be updated to reflect leukemia as a potential risk associated with therapy. (18) The manufacturer of rituximab was asked to modify the prescribing information to warn about cases of progressive multifocal leukoencephalopathy – a rare demyelinating disease of the central nervous system caused by activation of the JC virus – that occurred in patients treated with rituximab. (18) A warning about an increased risk of opportunistic infections was added to the prescribing information for cyclosporine. Of specific concern is the activation of latent viral infections, including the BK virus, which may cause an associated nephropathy. (18)

Any medication taken for the purpose of immunomodulation is not without risk. Prior to starting DMARD therapy, patients – particularly women of childbearing age – should be counseled extensively about the risks and benefits. The newest DMARD, tocilizumab, was approved with the requirement of a Risk Evaluation and Mitigation Strategy (REMS) to ensure that prescribers are informed about appropriate monitoring parameters for the hepatic and GI side effects that are possible with this medication. Additionally, the REMS includes a medication guide for patients that provides information about the risks and benefits of therapy. (17)

Nonpharmacologic interventions

A comprehensive plan for treating the pain associated with RA includes not only pharmacologic interventions, but also nonpharmacologic measures. Patient education about RA, the course of the disease, and treatment options is an integral part of optimizing patient care. (19) Providing patients with information about cognitive-behavioral techniques such as activity pacing, relaxation techniques, activity scheduling and goal setting, distraction techniques, and mental imagery gives patients additional tools to effectively manage pain. (19) Stress contributes to poor pain control; therefore, training patients to identify stressors and develop new coping skills can help them adapt to changes in social relationships, emotional responses, and other life changes associated with a diagnosis of RA. (19) Identification of barriers to pain control, such as patient concerns about medication side effects, addiction, and pill burden, facilitates dialogue between patients and health care providers and ultimately leads to better pain management. (20) One recent study found that higher numbers of reported barriers to pain management were associated with poor pain control in patients with RA. (20)

Smoking cessation may reduce disease progression, and maintaining an appropriate body weight helps patients stay active and protect their functional status. (21,22) Practice guidelines are an important resource in evaluating the role of exercise and nutrition in treating pain associated with RA. (19,23) Although avoiding obesity through good nutrition ultimately helps control pain, special diets and the use of nutritional supplements are not currently recommended for the treatment of RA pain because the evidence to support such interventions is limited. (19,23)

Exercise programs should be designed under the guidance of a provider knowledgeable in the care of patients with RA. While participation in exercise and sports is advisable in early RA, modifications may be required for patients with more advanced disease. (23) Exercises that build muscle strength and improve flexibility are most beneficial for helping control RA pain. (19,23) Joint-protection programs are sometimes prescribed, but these have little effect on pain. (23) Patients with more severe impairment may benefit from occupational and physical therapy to assess the need for adaptive devices, transcutaneous electrical nerve stimulation, or other measures necessary to increase their range of motion and pain control. (19)

Surgical procedures such as total joint arthroplasty and synovectomy are options to relieve pain in some patients. Referral for a surgical evaluation should be made when the patient's disease and pain are unresponsive to noninvasive treatments and function is impaired. (19) Early referral before contracture, severe deformity, muscle wasting, and deconditioning occur is preferred and yields better patient outcomes. (19) Surgical intervention may be considered in patients whose disease causes pain that limits their functional status and prevents them from attaining physical-activity goals. (19)

Role of the pharmacist

Pharmacists in all practice settings have numerous opportunities to improve the care and pain control of patients with RA. Because they are easily accessible, pharmacists can take the lead in educating patients about their disease and available treatments. Table 3 lists some available online resources to assist pharmacists in providing patient education.

The use of DMARD therapies affords pharmacists many points of possible intervention. Examples

TABLE 3. *Resources for Patient Education*

National Library of Medicine/National Institutes of Health (MedlinePlus) *www.nlm.nih.gov/medlineplus/tutorials*
Arthritis Foundation *www.arthritis.org*
American College of Rheumatology *www.rheumatology.org*
Mayo Clinic *www.mayoclinic.com*
Cleveland Clinic *http://my.clevelandclinic.org*

include ensuring appropriate drug monitoring; assessing patients for immunization status prior to treatment initiation; educating patients with regard to expected onset of symptom relief; discussing the risks and benefits of steroid therapy as a bridge with DMARDs; evaluating the need for effective contraception when using certain DMARDs; and recommending bisphosphonate and calcium and/or vitamin D as appropriate for patients taking steroids.

Pharmacists also can address with patients the various barriers associated with poor pain control and provide information and solutions that facilitate optimal treatment of RA and, thus, better pain management.

Conclusion

RA is a progressive autoimmune disease that leads to joint inflammation, joint destruction, pain, and debility. (24) Studies suggest that RA may decrease life expectancy and increase mortality, particularly in elderly women. (25,26) Although treatment of the disease has improved in recent years, there remains no cure for RA. Patients with RA benefit greatly from coordinated, collaborative care that includes both pharmacologic and nonpharmacologic therapies that are designed ideally to induce disease remission or halt disease progression and provide optimal pain control.

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