TABLE 77-3 DISEASE-MODIFYING ANTIRHEUMATIC DRUGS

CONVENTIONAL AGENTS	TOXICITIES
Hydroxychloroquine	Retinal toxicity, requires ophthalmologic monitoring
Sulfasalazine	Nausea, bone marrow suppression
Methotrexate	Oral ulcers, nausea, bone marrow suppression, pneumonitis; contraindicated in pregnancy and coexistent lung disease
Leflunomide	Bone marrow and hepatic toxicity; cholestyramine washout if toxic; contraindicated in pregnancy
Tofacitinib (oral DMARD)	Infection rate similar to biologic DMARDs; bone marrow and hepatic toxicity, hyperlipidemia
BIOLOGIC AGENTS	**MECHANISMS**
Adalimumab, certolizumab, etanercept, golimumab, infliximab	Cytokine directed, anti-TNF-α
Tocilizumab	Cytokine directed, anti-IL-6
Anakinra	Cytokine directed, anti-IL-1
Abatacept	T-cell directed, inhibits costimulation
Rituximab	B-cell directed, anti-CD20

DMARDs, Disease-modifying antirheumatic drugs; IL, interleukin; TNF, tumor necrosis factor.

Administration (FDA) for the treatment of RA (Table 77-3). Five TNF-α–directed therapies are available. The TNF-α inhibitors are the most widely used biologic agents because of the rapid improvement they produce in patients resistant to methotrexate therapy. They are recommended in addition to methotrexate after methotrexate failure (level A evidence).

Most biologic DMARDs are given by intravenous or subcutaneous injection and are quite expensive. Some have an increased risk of infection, including risk of reactivation of tuberculosis. Other cytokine-directed therapies include the IL-6 receptor antagonist tocilizumab and the IL-1 receptor antagonist anakinra. Biologic DMARDs also include an inhibitor of T-cell costimulation, abatacept; and a B-cell–depleting agent, rituximab

For a deeper discussion of these topics, please see Chapter 36, "Biologic Agents," in Goldman-Cecil Medicine, *25th Edition.*

Medical Care Specialized for Rheumatoid Arthritis

RA is a chronic disease that requires focused care for comorbidities. DMARDs themselves require frequent laboratory monitoring for toxicities, including bone marrow suppression, hepatotoxicity, and renal dysfunction. Opportunistic infections can occur in patients receiving biologic therapies and DMARDs. In the setting of acute infection, DMARDs and biologic therapies should be withheld. Prophylactically, all RA patients should be vaccinated for pneumococcal, influenza, and hepatitis B infection. Herpes zoster vaccine to prevent shingles should be given prior to biological agents because the vaccine is live.

RA itself is a risk factor for osteoporosis, and combined with glucocorticoid use, it can lead to severe osteoporosis and subsequent morbidity. In every RA patient, bone health should be addressed to prevent development of osteoporosis. RA is also a risk factor for cardiovascular disease due to chronic inflammation and should be aggressively monitored.

Caution should be taken preoperatively when the RA patient is being anesthetized to avoid C1-C2 subluxation and spinal cord compression. Joint replacement surgery plays an important role for patients who have had severe, destructive joint disease, particularly in the knees and hips.

PROGNOSIS

Although the underlying cause of RA is unknown, advances in cell biology, immunology, and molecular biology have led to dramatic therapeutic advancements for this disease. Conventional and biologic DMARDs improve short- and long-term outcomes. Bone erosions occur within 1 to 2 years of disease onset, and early initiation of DMARDs is essential to prevent further morbidity.

RF positivity, CCP positivity, and extra-articular features are characteristic of severe disease. The incidence of lymphoma and other malignancies is increased among patients with RA, and the overall mortality rate is increased by coexisting cardiovascular disease and infection.

Although up to 15% of patients can go into drug-free remission, long-term disability is significant. Fifty percent of patients with RA are not working after 10 years, approximately 10 times the rate in the normal population. Most patients fall between these extremes with various levels of disability. Some have a waxing and waning course over a period of years, with acute episodes of single- or multiple-joint exacerbations.

Future developments will include guidelines about when to institute biologic DMARDS, novel targeted biologic agents, and personalized approaches based on an understanding of individual disease pathogenesis.

SUGGESTED READINGS

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