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Advances In Treatment For Rheumatoid Arthritis

Robert J Moots, MD, PhD

Rheumatoid arthritis (RA) is the most common autoimmune disease and causes considerable morbidity and a reduced life expectancy. Sadly, therapy for RA in the past has been inadequate-with ineffective drugs used, or effective drugs withheld until joint damage and disability had already occurred. Over recent years, however, the treatment of RA has advanced significantly and this is set to continue, even more dramatically, in the future. The first major advance was the appreciation that early and aggressive treatment with conventional disease modifying anti-rheumatic drugs, typified by methotrexate, can significantly suppress disease activity and improve outcome. The second major development, the biologic drugs, resulted from breakthroughs in understanding the pathological mechanisms that underlie RA, heralding an exciting new era for therapy.

Many pathological processes are involved in the inflammation of RA. These range from cellular mechanisms, typified by the T-lymphocyte, through to cytokines-of which TNF-(and IL-1(appear to be the most important. Targeting T cells for therapy was theoretically attractive, but has yet to fulfil its promise in the clinic. Anti-cytokine drugs, typified by the anti-TNF-(agents (the soluble receptor, etanercept and monoclonal antibodies, infliximab and adalimumab) have, in contrast, proven to be highly effective in RA and provide fresh hope for patients with previously refractory disease. Pivotal trials have confirmed the efficacy of anti-TNF-(therapy in RA and this is borne out by clinical experience. However, these drugs differ in adverse effect profile (infliximab is associated with reactivation of tuberculosis and other infections), in disease indication (infliximab is effective in Crohn's disease and etanercept is not) and potentially in efficacy in RA (with open label studies and meta-analyses favouring etanercept). In addition, these drugs provide new and powerful tools to investigate the pathophysiological

* Professor of Rheumatology University Hospital Aintree Liverpool, UK

processes in RA in the clinical situation.

The current biologics are the first of what is likely to be a range of new and exciting therapies for RA. Research is currently underway to identify newer generations of anti-rheumatic drugs, targeting a whole variety of cytokines, including IL-1β, IL-6, -15 and -18. In addition, strategies to target other immune cells, from B cells to neutrophils are being considered with some considerable promise. The biologic drugs available today, and the promise of further developments in the future mean that the outlook for a patient with RA has never been healthier and there has been no better time to be a rheumatologist.