# Introduction

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All clinical encounters include assessment of benefit/risk by clinicians and patients in decisions about therapies. Historically, the consequences of rheumatoid arthritis (RA) have been underestimated by the medical community, the general public, and even by rheumatologists. Increased awareness in the 1980s of the long-term consequences of this disease, with recognition that most patients experience radiographic progression, functional declines, work disability, and premature mortality, has led to reappraisal of the "risks" of disease. Recognition of these risks has led to advocacy of more aggressive treatment strategies, using therapies earlier in the disease in order to halt or reverse inflammatory activity as effectively as possible, and thereby slow or prevent joint damage.

Several important new agents have been introduced in recent years, notably methotrexate (aggressively-dosed), cyclosporine, leflunomide, targeted anti-TNFα biological agents – infliximab, etanercept and adalimumab, and the IL1-receptor antagonist, anakinra. These new agents are associated with extraordinary potential benefit, but also with potential new risks. It is therefore appropriate to summarize the current state-of-the-art concerning benefit/risk of these new agents in RA.

We have been privileged to assemble this Supplement, the sixth in a series of annual supplements of *Clinical and Experimental Rheumatology* on contemporary topics in rheumatology, concerning the current status of benefit/risk of new agents for RA. We are fortunate that many leading rheumatology investigators have contributed outstanding summaries of their recent research findings.

The supplement is divided into four sections. The initial section presents clinical considerations, with an expanded discussion of the introductory paragraph above, a summary of the excellent studies of early undifferentiated arthritis in the Netherlands by Verpoort, van Dongen, Allaart, Toes, Breedveld, and Huizinga, analysis of innovative approaches to imaging early inflammatory arthritis by Brown, Wakefield, Conaghan, Karim, O'Connor, and Emery, use of patient questionnaires by Pincus, Sokka and Kavanaugh, novel programs for internet monitoring of patients by Lee, Lenert, and Kavanaugh, a pharmacosurveillance program involving industry and government in Canada by Barr, Marin, Chung, and Maksymowych, and pioneering observations concerning healing of radiographic erosions by Rau, Herborn, and Wassenberg.

The second section reviews benefits of therapies, including a discussion of possible absolute goals for therapies rather than statistically significant ACR 20 or 50 responses compared to a placebo, evidence of new long-term benefits on radiographic damage and physical function by Strand, analyses of cost effectiveness of anti-tumor necrosis factor agents by Wong, and a discussion of the benefit/risk of combination therapies by Zerkak and Dougados.

The third section reviews small molecules, including glucocorticoids by Townsend and Saag, methotrexate by Rau and Herborn, leflunomide by Kremer and Cannon, and cyclosporine by Gremese and Ferraccioli.

The fourth section reviews the benefit and risks of biological agents, with an overview presented by Imperato, Bingham, and Abramson, early analyses of switching between biological agents by van Vollenhoven, followed by up-to-date summaries concerning lymphomas by van Vollenhoven, tuberculosis and opportunistic infections by Bieber and Kavanaugh, demyelination by Magnano, Robinson, and Genovese, heart failure and drug-induced lupus by Cush, and safety issues concerning emerging therapies by Keystone.

We thank the contributors for their outstanding, timely efforts, and the sponsors for their unrestricted, generous support. We hope this Supplement will serve an important need for the worldwide community of rheumatologists, and will contribute to improved outcomes for millions of people with rheumatoid arthritis.