Rheumatology in the 21st century: Progress, promise and challenges

Dr. Mihir D. Wechalekar trained in Internal Medicine at the Mahatma Gandhi Institute prior to migrating to Australia where he underwent specialist training in rheumatology. He then went on to join a full time PhD as a National Health and Medical Research Council (NH and MRC) Scholar. He is also one of the 10 world-wide multinational fellows of the “3e” (evidence, expertise, exchange), a global multinational program that aims to create worldwide guidelines for rheumatological diseases. His areas of interest include early rheumatoid arthritis, arthroscopic synovial biopsy and synovial pathology in health and disease and markers of disease activity and remission. Dr. Wechalekar has been the recipient for several awards including recipient of gold and silver medals in medicine and grants and awards including from the NH and MRC, Arthritis Australia and Australian Rheumatology Association and the Flinders Centre for Clinical Change and Health Care Research. In addition to research, he currently practices as a part time Consultant Rheumatologist in Adelaide, Australia.

This is the decade of the bone and joint[1] (its mandate was renewed in 2010) and fittingly results of the Global Burden of Disease 2010 study[2] were recently published. This largest-ever systematic effort to describe the global burden of a wide range of diseases, injuries and health risk factors was funded by the Bill and Melinda Gates Foundation and involved nearly 500 researchers in over 300 institutions in 50 countries. The study highlights a continuing global shift from communicable to non-communicable diseases as a cause of disability; among the latter, musculoskeletal disorders show a very significant increase — by 45% - over the last 20 years.[2] Epidemiological data from the developing world is sparse and a World Health Organization (WHO)-International League Against Rheumatism Community (ILAR) Community Oriented Program for Control of Rheumatic Diseases (COPCORD) study, designed to collect community data on pain and disability in developing economies suggests that the spectrum of musculoskeletal diseases in terms of their severity and range are not very different compared to the developed world, but the impact and burden of disease, mainly owing to the very limited rheumatology services, is far greater.[3]

The practice of rheumatology itself has seen a major change over the last several years; this has been underpinned by explosive growth in understanding the basic biology of underlying immunological mechanisms by molecular techniques and the development of rational therapies based on a new understanding of immunopathology. The successful application of these new therapies (monoclonal antibodies), often referred to as “biologics,” against tumor necrosis factor alpha (TNF-α), interleukin-6, interleukin-1, CD20, T-cell co-stimulation and soluble human B lymphocyte stimulator (BLyS) protein among others and better understanding of disease pathophysiology has led to very different outcomes than in the years past.

There is increasing recognition of disease subsets and disease heterogeneity and a trend to early treatment. Rheumatoid arthritis (RA), for example, given the heterogeneous clinical presentation, disease course and propensity to long term joint damage, can almost be considered an umbrella term embracing multiple disease subtypes with different phenotypes correlating to different genotypes.[4] Remission definitions have become more stringent over the years.[5,6] It is now recognized that there is a “window of opportunity” (when the disease has a distinct and different cytokine profile and responds better to treatment) and a push to early[7] and combination[8,9] therapy, with a treat-to-target approach[10] aiming for remission which is now considered an achievable goal. The biologics have only partially lived up to their promise and despite the lack of head-to-head trials and fair control arms,[11] recent studies comparing targeted conventional disease modifying anti-rheumatic drugs (DMARD) therapy have shown that long-term clinical outcomes with

Access this article online

Quick Response Code:  
Website: www.jmgims.co.in  
DOI: 10.4103/0971-9903.126224
targeted combination DMARD and biologic therapy are similar;\(^8,12\) this finding may be of particular relevance in developing economies with cost-limitations to accessing biologic DMARD therapy.

The spondyloarthritides (SpA) have seen a new classification scheme\(^13\) and recognition of non-radiographic SpA; non-steroidal anti-inflammatory drugs (NSAIDs) have been shown to have a disease modifying effect,\(^14\) albeit with continuous rather than on-demand use.\(^15\) It remains to be definitively seen whether TNF-α inhibitors will live up to being disease modifying,\(^16\) although they probably are so in early disease.\(^17\) There have been advances in understanding pathophysiology in SpA, especially the role of the Th17 and Th22 cell pathways;\(^18,19\) these have led to therapeutic advances in ankylosing spondylitis\(^20\) and psoriatic arthritis\(^21\) with a promise of more to come.

In the area of the inflammatory myositis, inflammatory connective tissue diseases and vasculitis, there have been significant advances as well. Autoantibody profiling using myositis specific antibodies (these are antibodies directed against cytoplasmic antigens, ribonucleoprotein and certain nuclear antigens) can now identify several clinical, histologic and prognostic subsets in the inflammatory myopathies.\(^22\)

Statin associated immune necrotizing inflammatory myopathy\(^23\) is now increasingly recognized. In systemic lupus erythematosus (SLE), a new drug - Belimumab (an anti-BLyS monoclonal antibody) - has been approved in over 50 years;\(^24\) Rituximab (a B-cell-depleting monoclonal anti-CD20 antibody) has emerged as an important therapeutic option in renal, non-renal and conventional-treatment-resistant systemic vasculitis.\(^25,26\)

Overarching these individual rheumatological problems is the recognition of the cardiovascular risk engendered by ongoing inflammation and effects of therapy (especially glucocorticoids), particularly in RA\(^27\) (where the risk of mortality due to coronary artery disease can be up to 59% higher compared with the general population), SLE\(^28\) and psoriatic arthritis.\(^29\) There have been renewed concerns over the cardiovascular safety of both conventional and COX-2 selective NSAIDs.\(^30\)

The bounds of this editorial scope preclude comprehensive enumeration of advances in various areas of rheumatology, though an attempt has been made above to enumerate a few. The advances in RA have recently been reviewed in *The Journal* and in this issue of *The Journal*, authors from across the country have written on a range of rheumatological topics including the anti-phospholipid syndrome, monoarthritis and advances in SLE.

Despite rapid advances in the specialty as a whole, individualized therapy remains tantalizingly close and yet distant; in the backdrop of individual biologic variability, the redundancies and intricacies of immune pathways add to the complexity. Pathophysiologic, diagnostic and therapeutic advances apart, an individual’s autoimmune disease remains their very own, including clinical presentation, laboratory markers of disease activity and severity and response to therapy; the challenge remains to maximize therapeutic response by developing biomarkers of disease activity and treatment response which are applicable to the patient as a biologically distinct individual rather than an extrapolation from a clinical trial.

Mihir D. Wechalekar\(^1,2\)

*Rheumatology Research Unit, Repatriation General Hospital, Australia and \(^1\)Flinders University School of Medicine, South Australia, Australia*

**Address for correspondence:** Mihir D. Wechalekar, E-mail: mihir.w@gmail.com

**References**

7. Bosello S, Fedele AL, Peluso G, Gremese E, Tolusso B, Ferraccioli G. Very early rheumatoid arthritis is the major predictor of...


Source of Support: Dr. Mihir D. Wechalekar is supported by a National Health and Medical Research Council Medical and Dental Postgraduate Research Scholarship, APP1018009 (as a NH&MRC Scholar) and additional grants from Arthritis Australia.

Conflict of Interest: None declared.