Reminiscences, Romance and Renaissance in Rheumatology

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There is no greater saga in the history of mankind than the epic of medicine. There are vague descriptions of rheumatic diseases in literature of ancient civilisations. Medical sciences have registered rapid strides. Progress in rheumatology was perhaps relatively slow until recently.

Initial descriptions of rheumatoid arthritis (RA) made depressing reading indeed. Sir William Osler wrote :

"ARTHRITIS DEFORMANS

Once established, the disease is rarely curable. Too often it is a slow, but progressive crippling of the joints, with a disability that makes the disease one of the most terrible of human afflictions."

- W. Osler, 1909

The Principles and Practice of Medicine

Podagra (gout) was said to be a disease of kings, infective arthritis especially tuberculous, probably of the masses. Reiter's disease was first described in the late 1800s; seronegative arthropathies today have specific subsets. The HLA B27 story of Professor Brewerton and others in the 1970s was a landmark. Professor H. Behcet described trisymptom complex in 1935.

In the field of diagnostics, following Rose Waller test, rheumatoid factor latex fixation test came up in late 1950s, by Professor Charles Plotz et al. Another landmark discovery of ANA made diagnosis of SLE facile. ANCA and APLA detection paved the way to better diagnosis of vasculitis and antiphospholipid syndrome. Yet, so many rheumatic diseases defy early diagnosis. Are we making sufficient investment of research in diagnostics?

Progress in pharmacology gave us many antirheumatics. From aspirin in 1897 to NSAIDs with COX-2 inhibitors have taken a century. Precise description of the mechanism of action of NSAIDs by Nobel Laureate John Vane stimulated development of better NSAIDs.

Since eighty years early rheumatologists have been attacking disease pathology. In 1935 Professor Jacques Forestier introduced Gold injections inducing remission in RA. With the advent of sulphonamide and aspirin came sulphasalazine in 1930s. For over seventy years this drug is still in vogue. Antimalarials and cytotoxic drugs were borrowed from other disciplines of medicines. Professor Wienblatt's paper in 1983 paved the way for worldwide methotrexate usage in RA. We don't see often florid crippling deformities that made us depressed in yesteryears. The first tailormade leflunomide has most interesting pharmacokinetics. A line extension may yield us an even better DMARD.

Let's never forget the serendipitious discovery of glucocorticoids by Nobel Laureates Hench and Kendall. Perhaps the most dramatic and useful drug mankind ever knows with such salutary results in so many disciplines of medicines. A contribution emanating from rheumatology.

Late Professor Eric Bywaters, a brilliant physician together with the legendary late Professor Barbara Ansell, trained a generation of paediatric rheumatologists in Taplow and London.

The story of TNF alpha has again changed our mindset, thanks to classical research from bedside to bench to bedside by Professor Maini and Professor Feldmann. So much more on the anvil: with more cytokines into focus such as IL-1, IL-6, IL-15, IL-17, IL-18, BAFF, defensins, G proteins, metalloproteinases, B-Cell therapy with retuximab, angiogenesis inhibitors, and prospect of small proteins implicated in pathogenesis of RA, the scenario will change. Extending indications for remission in ankylosing spondylitis and psoriasis have enthused new optimism in physicians and patients alike, that most of rheumatic diseases will be controlled in our lifetime. Although TNF alpha blockade has become a reality, the following questions are pertinent :

" What do we have yet to learn ?
Is there a fundamental difference between the good responders to TNF
Blockade and the low or nonresponders? If so, is it genetic or is it acquired ?

Why are there no cures ?

What are the mechanisms of side effects, such as induction of antibody response against double-stranded DNA (frequent), severe infections (less frequent) or possible demyelination (rare) ?

What can be safely added to TNF blockade to augment the therapeutic benefit but not the side effects ?

Is it possible to block TNF production specifically in the disease tissue?

Why are multiple anticytokine therapies blocking TNF, IL-1, IL-6 or IL-15 effective, whereas anti-immune therapy (against CD4, CD7, CD5 or CD52) is marginal or ineffective ? "

- Marc Feldmann and Ravinder N Maini

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Another landmark contemporary discovery was the antiphospholipid syndrome by Graham RV Hughes and his team (Hughes' syndrome). To cite his original vivid description:

"In the 15 years since our description of the antiphospholipid syndrome, it has become recognised as an important disease, not only in the world of lupus but in the broader areas of obstetrics, neurology and vascular disease.

Although advances have been made in the understanding of the interactions of antibodies, protein co-factors, clotting molecules, endothelium and platelets, much still needs to be learnt about management where strokes, in particular, continue to cause significant morbidity. "

- Graham RV Hughes
Lupus (1998) 7, Suppl 2, S1-S4

Last winter 2003, celebrations were held to commemorate 20th Anniversary of the first description of antiphospholipid syndrome.

Gazing in a crystal ball, imaging modalities know no limits. Nanotechnology may enable recognition of early erosions by the bedside. We shall then speak of cell traps, cell orienters and movement stimulators, collagen aligners, biosensors and nano drug delivery systems and nanorobotics. Likewise, pharmacogenomics and stem cell research seem promising. Stem cells yielding chondrocyte cell lines may be implanted in OA joints.

In ancient lands of APLAR, is alternate medicine complementary or competitive? An ongoing debate! Medicine is a graveyard of ideas. Let us open up our minds, albeit with the bottom-line of evidence-based medicine. Can the patient community be educated to safeguard themselves from zealots and quacks?

After three decades of being with APLAR, I find rheumatology ever so exciting. With the spirit of investigation and sound education, a new generation of rheumatologists is on the anvil. While we shall experiment with the new, we must not forget the old.

"*Be not the first when the new is tried*
Nor yet the last to lay the old aside"

- Alexander Pope

As bold and beautiful minds herald our brave new world of rheumatology, yet with

all humility we must not forget what Hippocrates the father of medicine said philosophically :

"Art is long
Time is short
Experience is fallacious
And judgement difficult "

Therefore, while reminiscing, let us romanticise our science as its humble pupils and deliberate towards renaissance in rheumatology.