SPECIAL ARTICLE

Seven wonders in the world of rheumatology: a short story of romance, reminiscences and renaissance

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Abstract

Genesis and evolution of contemporary rheumatology is many centuries old. The lessons of medical history, its triumphs and failures, its twists and turns, have all facilitated today’s science. Even in the ancient era some rheumatic diseases have been described with vivid accuracy. Among these are gout, spinal afflictions, osteoporosis and rheumatoid arthritis, as we recognize them today. Ancient systems of medicine such as Ayurveda in India led to the introduction of gold salts. Invention of the microscope paved the way to the birth of microbiology, unfolding infective, and later inflammatory diseases, cellular pathology and immunology. Progress in therapeutics was slow and physicians and rheumatologists had to borrow drugs from other medical disciplines, for example antimalarials and cytotoxics. The Nobel Prize-winning discovery and development of cortisone was a major landmark in medicine, while also treating rheumatoid arthritis. Thanks to the advent of molecular medicine, rapid strides have been accomplished, and we now have new agents of biotechnology research. Orthopedics with computer-assisted and robotic surgeries, are becoming almost fail-safe for specific indications. The nature of chronic rheumatic diseases, necessitating long-term treatments, have led to the popularity of alternative medicines. Seven significant episodes are essayed herein. Rheumatology is on the threshold of exciting medical progress, enabling the majority of rheumatic patients to enjoy enhanced quality of life.

Key words: alternative medicines, Ayurveda, rheumatic diseases

INTRODUCTION

Since time immemorial, man’s quest for happiness and health is as ancient as mankind itself. The saga of medicine is saturated with human endeavors to subdue ill health and disease. A few months ago, the world reflected on the seven wonders of the world:

Ancient

• The Great Pyramid of Giza
• The Colossus of Rhodes, Greece

Contemporary

• Taj Mahal, India
• Christ the Redeemer, Brazil

But what of the seven wonders in our world of rheumatology? This narration is an invitation for a brief tour of seven wonderful developments which have shaped rheumatology and rheumatologists into what
they are today, knocking on the door of exciting new dimensions to combat rheumatic diseases.

SEVEN WONDERS IN THE WORLD OF RHEUMATOLOGY

1 The ancient times: lasting lessons
2 Microbe hunters and the genesis of immunology
3 The age of investigations and ‘borrowed’ drugs
4 Aspirin the wonder drug
5 Nobel during World War II
6 The brave new world of molecular medicine
7 The wonderland of orthotics/alternative medicine

1 The ancient times: lasting lessons

Medicine was thought to be an offshoot of religious beliefs. Not surprisingly, those who professed to know medicine treated patients in environs of temples and other places of worship. It happened in Greece, in Rome, and in ancient lands such as Egypt, India and China. The birth and growth of Ayurveda was significant. Charaka (500 BC, India), the famous ayurvedic physician described many remedies (Fig. 1). Oxidized gold salts were commonly used for the treatment of arthritis. Until recently, many of us have used gold preparations such as Myochrysine with good results, essentially an original Indian contribution since ancient times.

Hippocrates, the father of modern medicine, made invaluable contributions, for example, gout was described vividly:

‘Eunuchs do not take gout, nor become bald
A woman does not take gout unless her menses are stopped
A young man does not take gout unless he indulges in coitus
In gouty affection inflammation subsides in 40 days.’
Hippocrates (5th century BC, Greece)

Later, famous painters largely described arthritic manifestations accurately. Amazingly, the portraits and pictures of famous painters make excellent teaching slides. Look at Picasso on Renoir, renowned painter who himself suffered from rheumatoid arthritis (RA) (Fig. 2).

The history of osteoarthritis-osteoarthrosis is nicely outlined by J Dequekar and FP Luyten in a recent issue of the Eular Journal.1

2 Microbe hunters and the genesis of immunology

Rene Laennec, the inventor of the stethoscope had the most authentic description of pulmonary rheumatological signs and symptoms, including, tuberculosis (TB) and what we recognize as cor pulmonale/interstitial lung disease. Laennec himself died of TB at young age of 45 years.

Antonius van Leeuwenhoek, so as to confirm postulated germ theory, tried to locate germs by putting up

Figure 1 Charaka: famous ayurvedic physician, India 500 BC.

Figure 2 Photograph of Renoir (left), his portrait by Picasso (right). Notice RA hands with ulnar deviation.
Seven wonders in the world of rheumatology

The man–microbe relationship is as old as mankind itself. Yet it is only over the last 150 years we have seen the beginning of germ warfare.

Serendipity climaxed Röntgen’s work, resulting in the first X-ray picture of the hand of his wife who had RA! (Fig. 5).

3 The age of investigations and ‘borrowed’ drugs

Rose and Waaler working independently, evolved the first diagnostic test for rheumatoid factor using its ability to agglutinate red cells. Blood of some patients with RA produced agglutination of sheep red blood cells sensitized to rabbit anti-sheep red cell serum. 1948 was significant. The lupus erythematosus (LE) phenomenon became a simple test to diagnose systemic lupus erythematosus (SLE). Then, the hypothesis of autoantibodies in diseases became real by the demonstration of antinuclear antibodies. In the mid-1950s, Charles Plotz developed the Latex Fixation Test for RA, used universally. Other immunological tests such as antineutrophil cytoplasmic antibody (ANCA) held much promise. Anti-citrilitated cytoplasmic protein (anti-CCP) is a useful addition to the latex fixation test for RA. Significant demonstration of anticardiolipin antibodies correlating with antiphospholipid syndrome was the landmark work of Graham Hughes et al. Yet, so much more needs to be done in the realm of investigations for early detection and diagnosis of rheumatic diseases.
Although clinical descriptions of osteoporosis, RA, rheumatic fever, Reiter’s disease and ankylosing spondylitis have been well known for over a century, rheumatologists until recently had to borrow drugs from other medical disciplines. Gold salts came from the treatment of TB (phthisis). Antimalarials for RA were used for nearly a century. Sulfasalazine (sulfanilamide + acetyl salicylic acid) though initially developed for RA, forgotten and gifted to gastroenterology for ulcerative colitis, was then brought back into rheumatology! Cytotoxic drugs were borrowed from oncology, azathioprine in RA was written up in 1969, cyclophosphamide in the 1970s and methotrexate in 1985 by Wienblatt et al. Nearly all disease-modifying antirheumatic drugs (DMARDs) were ‘borrowed’ in that sense.

4 Aspirin the wonder drug

Relief of pain is the motto of every patient and every doctor. Willow bark and its extracts were said to be the analgesic since the time of Hippocrates. But it required Felix Hoffman, a young chemist, to synthesize the molecule with the urge to relieve the agonies of his father who had RA. The result was aspirin (Fig. 6).

After many decades indomethacin was introduced in the US and many analgesics such as pheniatric, phenylbutazone, oxyphenylbutazone and others came from the Rhine Valley, a bastion of organic chemistry. It required John Vane, UK a pharmacologist, to work out the pathway of pain and inflammation and define the role of prostaglandins. This then paved the way for newer nonsteroidal anti-inflammatory drugs (NSAIDs) such as Cox-1 and Cox-2 inhibitors. Vane won the Nobel Prize for his efforts, and was knighted as well!

NSAIDs are one of the top prescription items as ‘pain killers’ but not without ‘headaches’ (side-effects) and not without controversy. It is now predicted that cannabis (LSD 25) will be the analgesic of the future sans addictive properties.

5 Nobel during World War II

Philip Hench a rheumatologist in the US was gifted with astute observational powers. He noticed that his younger RA patients went into remission when they developed jaundice. He also observed that when his younger RA patients became pregnant, they went into remission. Hench proposed, isolated and then synthesized Compound E, that is, cortisone (together with Kendall and Reichstein). World War II led to rumors that German Luftwaffe pilots were able to fly higher without oxygen to evade radars, thanks to the ingestion of a ‘mysterious powder’ rendition of ‘Compound E’. President Roosevelt from the White House, with liberal funding, encouraged and expedited steroid development as a response.

The first RA crippled patient who received Compound E at the Mayo Clinic, Rochester, MN, US, reportedly went shopping within a couple of days. When the case was presented at the Mayo Clinic by Hench, there was excitement and word went round of this ‘miracle cure for arthritis’. Incidentally, patient No. 5, a French painter who was crippled, improved and painted bouquets of flowers and presented these to the three Nobel laureates (Fig. 7). Curiously, as he took aspirin and steroids together continuously for 5 years, he died of gastric...
herniation. Hench was embarrassed about the abuse of steroids, went into depression and reportedly committed suicide. Perhaps the greatest contribution to medical therapeutics was the discovery of cortisol and the invention of steroid compounds so useful in every discipline of medicine. A Nobel prize well won, but a precious life lost!

6 Brave new world of molecular medicine

Signalling between cells has been the function of cytokines. Tumor necrosis factor (TNF) became known as the pivotal culprit of cytokines in the induction of inflammatory arthritis, thanks to the classical ‘bench-to-bedside’ work of Feldmann and Maini. Development of specific monoclonal antibodies against TNF resulted in dramatic remission. Rheumatologists of today are confident of inducing remission rapidly, preventing deformities.

‘Superman’ Christopher Reeve was accidentally grounded, funded stem cell research, and thus stimulating it. The concept of tissue repair and reconstruction will dramatically change prognosis of osteoarthritis and osteoporosis. Osteoarthritis may not always require joint replacement. Osteoporosis may well be treated not by pharmaceuticals, but by regeneration of bone mass by inducing osteoblast growth in vitro/in vivo (Fig. 5). What is more, emerging strategies of bone and joint repair will be practical: Tissue factories to repair and replace joint structures are on the anvil. Pharmacogenetics will guide us to prescribe drugs without side-effects, genetic engineering will help predict and prevent joint diseases. Nanotechnology will enable diagnosis and therapy with mini-imaging devices and drug delivery systems at targeting rogue cells. Are we ready for it? ‘Magic bullets’ predicted by Aldous Huxley in 1928 are here today. More is on the anvil. Are we ready for this brave new world of molecular medicine?

7 The Wonderland of Orthotics/Alternative Medicine

Orthotics and prosthetics have already made patients with deformities mobile with near total success rates. Many deformed joints besides knees and hips will be replaced. Spinal surgery, once dreaded, will be made easier by simpler specific procedures and devices, thanks to kyphoplasty, vertebroplasty with minimum surgery and computer-assisted robotic surgery, with enhanced success ratios.

In ancient lands such as India and China, and even in the West, alternative medicines are growing in popularity; even if there are no proven or significant contributions in decades or even centuries; lack of side-effects have an appeal, even if there may be no effects. At times, it may be hard for a patient to differentiate between a practitioner of complementary medicine, different alternative medicines, and a quack, however soothing may be his ways, confusing the patient. (Fig. 9). Alternative medicine defies definition and may take the form of Ayurveda, traditional Chinese medicine, homeopathy, and newer procedures such as aroma therapy, music therapy, flower therapy, hydrotherapy, hypnotherapy, magic ray therapy, gland therapy, magnetotherapy, megavitamin therapy, to name just a few. These are usually outside the control of regulatory authorities. Due to lack of sufficient investments into their studies, most of them do not fit into our norms of evidence-based medicine; thus gullible patients may become victims of quackery. Positive placebo reactors may be benefited, for example,
by faith healing. In a well-studied cover story, Newsweek concluded,\textsuperscript{10} that after all, the best placebo is the qualified doctor.

**EPILOGUE**

Practicing rheumatology, which has never been attractive, save for the diehard, has won the grudging respect of doctors and patients alike. The wonderland of rheumatology has many brilliant accomplishments that one can be proud of, and the challenge to explore and conquer makes it a gratifying discipline. Relieving pain and mobilizing the crippled is becoming realistic. Classical research will yield better, logical therapeutics. Historical events have lessons for us to enhance observational powers and look for serendipity which may unexpectedly provide therapeutic advances. After all, Pasteur did say that ‘chance favours the prepared mind.’ Yet, mere errors, as in the case of Fleming for penicillin and Röntgen for X-rays cannot be relied upon as the only way toward discoveries:

‘Errors are fine
but only some time (s).
Not everyone heading for India
discovers America\textsuperscript{11}

The world of rheumatology is a wonderful treasure trove of inspiring discoveries and inventions. Indeed a wonderful science, rheumatology is the promise of the future whose time has come. Let us prepare for a spectacular take off, the count down has begun.

**REFERENCES**