Musculoskeletal disorders (MSD) are likely as old as the homosapiens. The first recorded evidence of MSD appears in Ebers Papyrus written around 1500 BC. It describes what appears to be arthritis deformans (probably rheumatoid arthritis - RA). Paleopathological studies of Egyptian mummies suggest existence of RA in Egyptians. G. Elliot based on his studies, concluded that RA was par excellence the disease of Egyptians. 2
Many authorities, however, do not agree and consider RA to be a modern disease.

In the Indian literature, Charak Samhita (approx 300 – 200 BC) describes pain, joint swelling and loss of function. 3 In a recent reappraisal Aceves-Avila et al – claim that RA is an old disease. 4
Hippocrates described arthritis 2400 years back (400 BC). For a long time the term arthritis was used loosely without reference to any specific form of arthritis.
Galen (129-216 AD) introduced the term rheumatismus. Camroe (1940) coined the term rheumatologist while the word rheumatology appears for the first time in the text book by Hollander (1949). 5
Rheumatic disorders were attributed to humors (rheuma). It was postulated that a substance i.e. humor, flows, settles in joints, and causes arthritis. Paracelsus (1493-1511) postulated that substances that could not be passed in urine accumulated, got precipitated in joints, and caused arthritis. Ayurveda considered arthritis as one of the Vata.
Sydenham recognized it as a separate form of arthritis (1665). Since then, rheumatology has come a long-long way. It is no more an “also branch” of medicine. No more is a rheumatologist questioned “what can you do?” There is today virtually no branch of internal medicine that probably does not interact with rheumatology. The present article attempts a brief review of evolution (history) of rheumatology up to the present time and peeps into (read dreams) the future.

The Rheumatic Diseases

“A disease is born when named”
Slowly but surely from the all pervasive diagnosis of arthritis individual disease entities have been recognized. Presently more than 100 specific rheumatic diseases are known. There surely are more to be defined.
Box 1: Rheumatic diseases with eponyms

- Schönlein: 1874 Henoch (1837) (Henoch Schönlein purpura)
- Charcot’s joints (1868)
- Jaccoud’s arthropathy (1869)
- Paget’s disease of bone (1877)
- Pott’s disease (spine) (1882)
- Weber – Christian disease (1892)
- DeQuervain’s tenosynovitis (1895)
- Poncet’s disease (1897)
- Still’s disease (1897)
- Reiter’s syndrome (now called reactive arthritis) (1916)
- Tietze’s syndrome (1921)
- Libman Sachs endocarditis (1923)
- Sjogren’s syndrome (1933)

(DeQuervain’s tenosynovitis is named after the discoverer, DeQuervain (1895).)

Box 2: Landmark developments

- Leuwenhoek – microscopic appearance of urate crystals in a tophus (1634)
- X-rays of rheumatoid joints – Bannatyne (1896)
- Calorimetric measurement of uric acid - Folin Wu (1912)
- Antistreptolysin antibodies – Todd (1932)
- Rheumatoid factor - Rose and Waaler (1940)
- LE cell-Hargraves (an interesting story of serendipity) (1948)
- Lupus anticoagulant – Conley (1952)
- Antinuclear antibodies - Fritou (1958)
- Bone densitometry – Cameron (1960)
- Radioimmunoassy for 25 (OH) D3 – Haddad (1971)
- Association of HLA B 27 with AS - Schlosstein and Brewerton (1973)
- ANCA – Davis (1982)

(Despite the increasing availability and use of diagnostics, rheumatology remains a clinical specialty par excellence.)

Clinical practice. Disease activity indices have empowered rheumatologists to tailor/modify treatment(s) to achieve maximum disease control in an objective way and not based on mere impressions.

These activities have been formulated by national and international associations including Indian Rheumatology Association. With all these inputs the practice of rheumatology has become more scientific and objective.

Guidelines

Guidelines of management have also been developed for most of the rheumatic diseases. These too are updated periodically.

International initiatives

Ongoing COPCORD (Community Oriented Programme for Control of Rheumatic Diseases) and the just completed, bone and joint decade (2000-2010) have been two recent major international initiatives. COPCORD was launched in late 1980’s by WHO and International League Against Rheumatism (ILAR) to collect epidemiologic data (of pain and disability), to impart health education and control the risk factors with improved health care in developing countries (grass root developing economies). World-wide, several countries have participated in this programme. These studies have highlighted the very significant burden of musculoskeletal disorders (MSD), emphasizing MSDs as measure of public health problems.

Bone and Joint Decade (2000-2010) was supported by WHO and United Nations. Its agenda included trauma, arthritis and osteoporosis as target conditions. The aim was to create awareness and empower patients. India has been an active participant in both the initiatives.

Diagnostics

Microbiology, including serology, biochemistry, imaging modalities, radioimmuno and other assays, genetics have been an integral part of rheumatology. Some of the important/landmark developments are listed in (Box 2)

Molecular Biology

The edifice of modern rheumatology is based on advances in molecular biology. It is beyond the scope of this article to elaborate the immense contributions of molecular biology to rheumatology. Briefly, molecular biology has revealed that
i. Molecular and genetic events shape diseases, their progression, and response to therapy.

ii. Immune dysfunction (autoimmunity) forms the basis of many rheumatic diseases.

iii. HLA and other gene polymorphisms play a role in autoimmune diseases

iv. Immune cells, cytokines, signalling pathways and mediators of inflammation are important therapeutic targets.

Therapeutic Milestones

Rheumatology has directly or indirectly contributed to the development of some of the most important therapeutic agents, such as NSAIDs, cortisone, sulfasalazine, and biologics.

- NSAID\textsuperscript{13,14}

  The earlier therapies involved use of plant extracts of Willow bark and leaves; most contained salicin. Hippocrates, Galen, and others used Willow extracts to treat pain of rheumatic disorders. Madhav nidan (7 century AD) subclassified arthritic disorders. Chakradatta in the 11\textsuperscript{th} century fine tuned pharmacologic and nonpharmacologic Ayurvedic therapy. It included diet, local treatments, bowel cleansing and medicated enemas, depending upon the type of arthritis. Salicylic acid was identified as the active substance by Leroux in 1929. In 1853, acetyl salicylic acid (aspirin) was synthesized by Gerhardt. The first nonaspirin, nonsteroidal anti-inflammatory drug, phenylbutazone became available in 1949 and was followed by a host of NSAIDs. Though effective, NSAIDs have significant toxicity profile, especially gastrointestinal ulcers and bleeding, renal toxicity, hypertension and oedema. Vane (1971) demonstrated that NSAIDs inhibit prostaglandin synthesis by acting on the enzyme cyclooxygenase (COX). In 1991 COX-2 (the inducible form) was discovered by Simmons and the next generation of NSAIDS (selective COX-2 inhibitors) were developed.

- Colchicine\textsuperscript{2}

  Extracted from Autumn crocus, colchicine was used to treat acute gout as far back as 6\textsuperscript{th} century AD. A B Garrod established its use for the diagnosis and therapy of gout.

- Cortisone\textsuperscript{2}

  - 1930 - Kendall isolated 6 different compounds (A-F) from adrenal gland
  - 1948 - Compound E was found to have anti-rheumatic properties (Kendall)
  - 1948 - Hench treated the first case of rheumatoid arthritis with compound E

Today cortisone is an integral part of treatment of many inflammatory rheumatic and non rheumatic disorders (despite the love and hate relationship it generates).

- Methotrexate \textsuperscript{14}

  - Methotrexate (MTX) was synthesized in 1950’s as a folate antagonist to treat leukemia.
  - Double-blind placebo controlled trials were carried out in 1980’s. These established its role in the treatment of rheumatoid arthritis
  - In 1990’s the role of folic acid supplementation to reduce methotrexate toxicity was realized
  - Presently MTX is the sheetanchor of treatment of RA either as monotherapy or in combination with other agents (DMARDs and biologics)

- Biologics\textsuperscript{15}

  1975 – Monocyte derived tumour necrosis (TNF) factor was identified its role in orchestrating inflammation appreciated (1988)
  1993 – Anti-TNF antibodies were shown to be effective in the treatment of patients with RA (1993). Presently there is an explosion of biologic agents that act against the many components of immune response such as cells, cytokines, and signaling pathways. While highly effective, danger of infection especially tuberculosis soon became apparent leading to the (modified) concept of diagnosis and treatment of latent tuberculosis.

  Cost remains an important consideration while considering their use. Most biologics work better in combination with methotrexate.

- Antimalarials\textsuperscript{14,16}

  Payne (1895), first suggested the use of quinine to treat lupus erythematosus and rheumatic diseases. In 1951 Page demonstrated efficacy of quinacrine (mepacrine) in lupus erythematosus. This was followed by the use of chloroquine (Baguall 1957) and now hydroxychloroquine (HCQ). HCQ today is used extensively in many rheumatic diseases because of its multiple benefits, low toxicity, and low cost.

- Gold\textsuperscript{17}

  As far as back 2000 BC, Egyptians and Chinese used gold for medicinal purposes. In 1927 Landre had recommended its use to treat rheumatic fever.

  Gold salts were first used to treat rheumatoid arthritis by Forestier (1925) on the wrong assumption of tuberculosis as its aetiological factor and gold was then used to treat tuberculosis. In the 1970’s and 80’s gold was the most commonly used DMARD. Presently gold salts are rarely used to treat RA because of the availability of better and safer drugs.

  Steroids, methotrexate, chloroquine/hydroxychloroquine, leflunomide, sulfasalazine, mycofenolate, biologics and others (cyclosporine, azathioprine etc.) have revolutionized the outcome of rheumatic diseases.

Change in Therapeutic Perception

Early action and aggression is the new ‘Mantra’ of rheumatology, especially in case of R.A. The change is -

- RA is not a benign disease
- Joint damage starts early
- The best chance to control the disease effectively is as near the disease onset as possible. The previous go slow, go low paradigm is not acceptable.
- Combination therapy is effective and not more toxic
- Complete remission is possible, (albeit at present in a small proportion of patients)

Pulse therapy

Some examples are -

- Methotrexate in weekly pulse doses (effective and less toxic)
- Pulse cyclophosphamide treatment (Austin 1986). It has had a significant impact on the management of SLE, systemic vasculitidis, and other systemic rheumatic diseases.
- Steroid pulse therapy for rheumatic emergencies
Surgery

Before the advent of joint replacement therapy surgical interventions consisted mainly of synovectomy and arthrodesis for synovitis and osteotomies for osteoarthritis of knee and hip.

Hip joint replacement, developed by Charnley, (1961) changed it all. Joint replacement has proven to be a boon to patients with advanced joint disease, unbearable pain, and disability. Newer models have increased the range of joint motion, improved function (squatting and negotiating stairs is possible with modern prosthesis) and longevity of the prosthesis.

Historically Gluck (1853-1942) had suggested knee replacement with implants made of ivory and metal and carried out joint replacement in joint tuberculosis and tumours (of hip, knee, shoulder, elbow and wrist)!

Support service

Ever improving orthotics, physiotherapy, nutrition and formation of support groups have in no small measure contributed to improved patient care (especially in the more advanced countries).

Future – Crystal-ball Gazing

The wish list is large. A few expectations are

- Effective preventive measures
- Vaccination
- Preclinical diagnosis of rheumatic diseases
- Magic bullets

There is great hope that most if not all can be achieved in the present century itself –

Specifically for India one hopes

- Availability of rheumatologist (at least one) in each district
- Availability of cheap and effective therapeutic agents including surgical implants
- Scientific evaluation of systems of medicine especially Ayurveda
- Public education and awareness. Today there is unfortunately a plethora of misconceptions and blind faith

References

3. Dr. Ashwinkumar Raut (personal communication)