



AUSTRALIAN AND NEW ZEALAND
SOCIETY OF THE HISTORY OF MEDICINE

10th Biennial
Conference

Medicine in Context

Tuesday 3 July – Friday 6 July 2007

Manning Clark Centre, The Australian National University, Canberra

www.anzshmconf.com.au

Arthritis Workshop: building the evidence for health practice

*Presented by the Australian and New Zealand Society of the History of
Medicine with the Bone and Joint Decade 2000-2010*

Thursday 5 July 2007

ANZSHM/BJD Arthritis Workshop report

Compiled by Prue Deacon



Australian and New Zealand Society of the History of Medicine

www.anzshm.org.au

- Our aim is to promote the academic study of the history of health sciences within the Australasian region.
- This national society was founded in 1986 and is incorporated in Victoria.
- Membership of the society is open to anyone with an interest in the history of medicine.

This is a learned Society whose terms of reference include the sharing of all aspects of the history of health - including the professions of dentistry, medicine, nursing, pharmacology and health themes within history itself.

The Society consists of a collegiate group with members who are both amateur and professional historians, clinicians with an interest in the history of their disciplines and those simply with a love of the progression of health practice down through the ages.

There is an emphasis on medicine and health in the Australia Pacific region, but many members also have major interests in European, Oriental, Middle Eastern and Classical Medicine as well.

The Society's biannual journal, *Health and History*, is a peer reviewed publication of original papers and research. There is also a quarterly newsletter and a major conference is held at exciting venues every two years. Local state/territory country groups of medical history are also encouraged.

Bone and Joint Decade 2000-2010

www.bjd.org.au

What is the BJD

The Bone and Joint Decade 2000-2010 (BJD) is an umbrella organisation for professional societies, governments, patient advocacy groups, industry and researchers who work together to make bone and joint health the business of every Australian.

Aim of BJD

- Raise awareness of the growing burden on society of musculoskeletal disorders caused by poor bone and joint health
- Promote care and prevention being better than surgical or medical cure
- Empower patients to participate in care of their own bones and joints
- To advance research on cost-effective prevention, diagnosis and treatment of musculoskeletal disorders

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Introduction

The Arthritis Workshop was held as part of “Medicine in Context: the 10th Biennial Conference of the Australian and New Zealand Society of the History of Medicine, Canberra 3-6 July 2007”. It was presented with the Bone and Joint Decade 2000-2010.

The workshop looked at changes in the management of arthritis, sharing the perspectives of different groups (historians, health professionals, patients and others). Arthritis was also considered as a case study, for reflection on historical aspects of broader topics such as evidence-based medicine, chronic disease, drug development and patient participation. The workshop aimed to provide background in the methods of history and show how historical perspectives may give some guidance for current attitudes and practice in healthcare.

The keynote paper was an overview of the history of arthritis and its treatment presented by Professor Peter Brooks. Dr John Quintner then talked about viscosupplementation, a therapy for osteoarthritis. Next Dr Richard Travers, Dr John Dowden and Dr John McEwen tackled drug therapy, looking at both efficacy and the problems of side effects. Mick Hoare provided the population health context: policy, priorities and funding. Finally Ben Horgan presented a patient's perspective.

Conference proceedings are not prepared for ANZSHM conferences. Hence it was decided to use the speakers' notes in dot point format for this report. These notes have either been supplied by speakers or taken from their PowerPoint slides to provide a format that was easier to read. Illustrations have not been included.

Workshop participants received a kit which included information about arthritis, sourced from the websites of Health*Insite* information partners. Details are provided in the Background section.

On behalf of the ANZSHM and the Conference Committee, I would like to thank the speakers and the Bone and Joint Decade 2000-2010 for its support and participation.

Prue Deacon
November 2007

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Workshop Program

Arthritis Workshop: building the evidence for health practice

Thursday 5 July 2.30-5.30pm

Chair: Prue Deacon, Health*Insite*, Australian Government Department of Health and Ageing

2.30 – 3.30

Peter Brooks, Executive Dean, Faculty of Health Sciences, University of Queensland
Keynote paper: Historical aspects of arthritis and its treatment

John Quintner, Consultant Physician in Rheumatology and Pain Medicine
The long road to viscosupplementation

Richard Travers, Rheumatologist and Historian
The development of DMARDS for rheumatoid arthritis

3.30 – 4.00 (approximately) – Afternoon tea

4.00 – 5.30

John Dowden, Editor-in-Chief, Australian Prescriber
What a COX up! Australian Prescriber and the end of a blockbuster

John McEwen, former Principal Medical Adviser, Therapeutic Goods Administration
Not the first time – safety issues with phenylbutazone and benoxaprofen

Mick Hoare, Director, Asthma and Arthritis Section, Australian Government
Department of Health and Ageing
A history... national health priority areas with a focus on arthritis

Ben Horgan, National Coordinator/Ambassador, Bone and Joint Decade 2000-2010
Rheumatoid arthritis: a patient's perspective

Abstracts

Brooks, Peter

Historical aspects of arthritis and its treatment

Musculoskeletal diseases, particularly arthritis, are one of the major causes of disability around the world. In Australia, the burden of arthritis is significant with over 3 million sufferers and costs in excess of \$11 billion. Rheumatic diseases (arthritis) have been described through the ages and in many prehistoric animals including dinosaurs and camels. Gouty tissue was reported in Egyptian mummies long before the birth of Christ and treatment with crocus and saffron prescriptions are documented in the Ebers Papyrus. Hippocrates spent much time thinking of arthritic conditions and commented on their aetiologies and risk-factors in his writings. He noted for example “eunuchs do not take the gout or become bald” and described associations of the conditions with “drunkenness and sexual activity”. The great physicians of the first centuries AD such as Celsus and Galen often wrote of arthritic conditions describing treatments with colchicine and other more exotic concoctions including dragon’s blood. Physical treatments such as hydrotherapy and manipulation were used throughout the centuries particularly by the Chinese, and arthritis is also often mentioned in literary works as diverse as the Bible and in Shakespeare’s plays. The great English physicians, Heberden in particular, noted the use of bark and pain killers such as opium but it was the observation of the Reverend Mr Edmond Stone in 1763 that the bark of the willow cured arthritis that led eventually to the development of the salicylates. This development and the appreciation of their side effects was probably one of the factors that drove the pharmaceutical industry for a significant part of the last century. Development of true anti-rheumatic drugs such as gold, D-Penicillamine and salazopyrine dominated the latter 1900’s but the real revolution in therapeutics has occurred with the development of the biologic agents. These drugs, although expensive, can very significantly alter inflammatory rheumatic diseases and may eventually lead to a cure for these deforming diseases. It is likely that in this century, treatment of rheumatic diseases will be dominated by specific biological agents, a more targeted approach to pain control and the use of new bio-materials that can re-create cartilage and bone to their almost natural state.

Quintner, John

The long road to viscosupplementation

Although its mode of action is still to be elucidated, the injection of hyaluronic acid is now evidenced-based therapy for painful osteoarthritic knee joints. This paper, which draws upon ancient and other historical writings, traces the evolving understanding of the structure and function of synovial fluid, as well as the changes it undergoes in joint disease, culminating in the theoretical basis for viscosupplementation in today’s practice of rheumatology.

Travers, Richard

The development of DMARDs for rheumatoid arthritis

The medications given for rheumatoid arthritis and other causes of idiopathic inflammation of the joint lining (synovitis) are the analgesic drugs, the anti-inflammatory drugs and the disease-modifying anti-rheumatic drugs (DMARDs). These latter agents are given to make the disease less active and thus cause less pain and stiffness and less joint destruction. The stories behind the introduction of several

examples (intramuscular gold injections, hydroxychloroquine, sulfasalazine, penicillamine, methotrexate) will be told, emphasizing the difficulty in planning the treatment of a condition whose cause is unknown. The recent introduction of biological therapy with TNF- α inhibitors has more logic behind it, but it is still only palliative.

Dowden, John

What a COX up! Australian Prescriber and the end of a blockbuster

Australian Prescriber is the national journal of drugs and drug therapy. It was originally published by the Commonwealth Department of Health, but is now published by the National Prescribing Service. The journal is popular with health professionals for its independent reviews of new medicines. Since its first edition in 1975, Australian Prescriber has regularly reviewed treatments for diseases of the bones and joints. Although the first volume contained articles on gout and Paget's disease, it was not until 1978 that there was a feature on arthritis. The first new drug for arthritis reviewed by Australian Prescriber in 1978 was naproxen. By the 1990s the adverse effects of naproxen and similar drugs were well known. This led to the launch, in 1999, of apparently safer drugs called COX-2 inhibitors. These new drugs were enthusiastically prescribed, but in 2004 one was suddenly withdrawn from the market. What went wrong with these 'blockbusters'?

McEwen, John

Not the first time: safety issues with phenylbutazone and benoxaprofen

Phenylbutazone (Butazolidin) was patented in 1951. In Question Time in November 1953, the Australian Minister for Health was asked if he would have it placed upon the Pharmaceutical Benefits (PB) list. The Australian Scheme for reporting adverse reactions was initiated in August 1964. By March 1966, a "reminder/warning" was published in the Medical Journal of Australia about hazards, especially blood disorders. Increasingly severe steps to limit its indications and PB subsidisation continued until the late 1980's. Pre-marketing hype created great expectations in Australia for benoxaprofen. Approval was denied in March 1982 because of photosensitivity reactions in clinical trials – an action disputed by practising doctors. Worldwide withdrawal occurred in August 1982.

Hoare, Mick

A history... national health priority areas, with a focus on arthritis

Population health has its foundation in antiquity, with a revival in the developed world, including in Australia, only in the last hundred or so years. The Australian Government's National Health Priority Areas approach of 1996 was a national consultation and agreed strategy to improve the prevention, care and management of chronic conditions. The concept ultimately stemmed from Australia's signing of the international WHO-led Alma Ata agreement in Russia in 1981. In November 2005, all Australian Health Ministers (Federal, state and territory ministers) signed off on the Chronic Disease Strategy, five National Service Improvement Frameworks and the Blueprint for nation-wide surveillance of chronic diseases and associated determinants. Six National Health Priority Areas (cardiovascular disease, asthma, diabetes mellitus, cancer, mental health and injury prevention) became seven in 2002 with the addition of arthritis and musculoskeletal conditions. This led to a total of eight years of committed funding to improve prevention, care and management of osteoarthritis, rheumatoid arthritis, juvenile idiopathic arthritis and osteoporosis with

the Better Arthritis Care initiative 2002-03 to 2005-06 and the current Better Arthritis and Osteoporosis Care initiative 2006-07 to 2009-10.

Horgan, Ben

Rheumatoid arthritis: a patient's perspective

Ben Horgan was diagnosed with Juvenile Rheumatoid Arthritis in 1973 aged 2. The disease quickly consumed every joint in his body changing his and his family's lives forever. Not expected to live past the age of 10, Ben's story is one of determination and courage. He has not only enabled himself to survive but he has also helped hundreds of families to live with Juvenile Arthritis. He was instrumental in starting camps for kids with the disease and has travelled the world inspiring people to make the most out of any situation. Ben is currently working for the Arthritis Foundation of WA. He was the world's first patient representative to be inducted as an Ambassador to the International Bone and Joint Decade 2000 – 2010 and recently was appointed Chair of the National Action Network which coordinates the Bone and Joint Decade activities in Australia. Ben has travelled the globe advocating for people with arthritis, and other chronic conditions, to play a much greater role in the treatment of their disease and to spread the message that arthritis is not just 'a fact of life'.

Biographical statements

Brooks, Peter

Professor Peter Brooks is the Executive Dean of the Faculty of Health Sciences at The University of Queensland. His postgraduate work with Professor Watson Buchanan in Glasgow in the 1970's stimulated his initial interest in the history of the treatment of rheumatic diseases. He was the Foundation Professor of Rheumatology at the University of Sydney from 1983 until 1991 and retains a significant research interest in treatment and epidemiology of rheumatic diseases.

Quintner, John

Dr John Quintner is a Consultant Physician in Rheumatology and Pain Medicine. He is interested in the historical and theoretical basis for current practice within his speciality and is a regular contributor to the Annals column of *Medical Observer*.

Travers, Richard

Dr Richard Travers is a rheumatologist in private practice in the western suburbs of Melbourne. He directed the Rheumatology Unit at Western Hospital from 1979 to 2007 and was also at the Royal Melbourne Hospital for that time. He gained the DHMSA (London) in 1978 and has continued his interest in medical history with membership of the Medical History Society of Victoria and the ANZSHM.

Dowden, John

Dr John Dowden is the Editor-in-Chief of *Australian Prescriber*, Australia's national journal of drugs and therapeutics. Dr Dowden has worked in hospital medicine and general practice in several countries. Before joining *Australian Prescriber* he was in rural practice in South Australia. Dr Dowden currently works in the Canberra office of the National Prescribing Service.

McEwen, John

Dr John McEwen PSM retired as the Principal Medical Adviser, Therapeutic Goods Administration (TGA) in July 2005. He is currently documenting the history of the Commonwealth's regulation of therapeutic goods on behalf of the TGA.

Mick Hoare

Mick Hoare took over the position of Director of the Asthma and Arthritis Section in the Chronic Disease and Palliative Care Branch in the Australian Government's Department of Health and Ageing early in May 2007. Since completing 23 years as a uniformed member in the Executive Department of the Royal Australian Navy in various shore and sea postings in 2001, Mick's work has included three Director positions at the Centre for Research Management and Policy in the National Health and Medical Research Council (NHMRC). His expertise and experience include program and project management, human and resource management, instruction and training policy and IT Systems management.

Horgan, Ben

Ben Horgan is currently working for the Arthritis Foundation of WA. He was the world's first patient representative to be inducted as an Ambassador to the International Bone and Joint Decade 2000 – 2010 and recently was appointed Chair of the National Action Network which coordinates the Bone and Joint Decade activities in Australia

Deacon, Prue

Prue Deacon is a librarian with the Internet gateway site *HealthInsite*, within the Australian Government Department of Health and Ageing. She is a foundation member of ANZSHM with a particular interest in the science behind the development of medicine.

Historical aspects of arthritis and its treatment

Peter Brooks

Please note: These notes make references to slides which are not included here.

- The first thing to remember is that there are many forms of arthritis, the most common of course being osteoarthritis which is the largest single cause of movement impairment in the world. Low back pain is a major cause of disability in both the young and the old and rheumatoid arthritis affects 1% - 2% of the population.
- Rheumatism really came from the idea of a humour that would descend into the joints causing redness and swelling. This is little different from the terms that Hippocrates used for catarrh.
- Arthritis has been found in fossil remains of dinosaurs, crocodiles and camels and was first described in humans in the Egyptian Mummies. This is both spondylitis deformans, a form of osteoarthritis, and of course gout.
- Gouty material has been found in mummified skeletons from Egypt both as tophus and urinary calculi. The Ebers Papyrus, part of which is shown in this next slide, describes arthritis of the toes and prescriptions of both crocus and saffron which were used to good effect. This next slide shows a tophus around the joints of the foot in an Egyptian Mummy and the next slide shows the clinical features of gout as we know it today with that pain, redness and swelling.
- Hippocrates, often considered the father of medicine, described a number of clinical associations of gout. He noted that women did not take the gout until they were much older and that young men needed to reach puberty before they developed gout and also noted that eunuchs did not get gout. He also noted even in those early days (next slide) that gout was associated with hard drinking and lechery although one would have to wonder if that was not other forms of arthritis such as gonorrhoea. This print from the 1800's shows the typical features of gout associated with good living and heavy drinking. And this of course has been the butt of artists and writers over the years.
- Hippocrates also described rheumatic fever again commenting on the severe pain and noticing that it occurred in younger patients. It was not until the 1600's however that a French doctor, Guillaume de Baillou, described rheumatic fever in his book on rheumatism.
- Other great physicians of the 1st Century, Celsus, Galen and Aretaeus, noted things such as variation of symptoms with temperature and (next slide) Galen also described an innovative way of treating arthritis (possibly Gout) by putting the feet into a cool stone. In the middle of the first millennium the great Arabian physicians, Aetius and Alexander of Tralles, described treatments such as colchicine. Colchicine comes from the autumn crocus which grew in the ancient Kingdom of Colchis which was around the Black Sea.

- Paul of Aegina described a very interesting form of treatment [Very old and acrid cheese pounded and applied with a decoction of fat swine's flesh; Dragons blood; Whole wolves or hyaenas in oil] - often wonder how he got the dragons blood.
- This next Arabian woodcut shows a patient receiving traction on the spine.
- The Arabian, Avicenna, who lived between 980 and 1036 described gout and sciatica and Ballonius in 1570 wrote a very extensive critique on rheumatic aches and pains and coined the term rheumatism.
- Many famous people have had arthritis – the Medicis Cosimo and Piero both described illnesses with fever, arthritis of back and feet and at post mortem was shown to have fused sacro iliac joints consistent with ankylosing spondylitis.
- Chinese physicians also described treatments for arthritis – this ancient Chinese painting showing some physiotherapy to the shoulder.
- Descriptions in literature and paintings of arthritis also abound. Shakespeare often talked of arthritis particularly gout in his plays – Falstaff suffering from gout in the toes; Prospero complaining of aged cramps.
- Posthumous and Cymbeline described gout but also interestingly noted that it was probably wiser to stay away from one's physician.
- Titania in Midsummer Nights Dream described the association of rheumatic diseases with dampness.
- Arthritis is shown in paintings through the ages but one has to be careful because many early painters did not necessarily paint what was there but provided portraits that were “pure”. This painting from the Flemish School shows a family portrait and on high power (next slide) clearly shows arthritis affecting the hands of what seems to be a relatively young lady.
- In the 1600's, Thomas Sydenham the famous English physician described chronic rheumatism and lumbago and acute rheumatic fever. He made the observation that it was common in the autumn and chiefly affected the young and the vigorous – probably referring to rheumatic fever.
- Treatment using fresh cow dung and bruised snail shells.
- This next slide of a piece of Meissen pottery shows a street seller of theriac, a potion usually made up by that individual seller that was supposed to relieve aches and pains.
- William Heberden the Elder, a famous English physician after whom Heberden's nodes are named, described gout and its many clinical presentations. And also rheumatism, again noting it occurring in the young and its response to Peruvian bark.
- The great describers of rheumatic conditions remain: Hippocrates – rheumatic fever and gout; Londre Bauvais from Paris; Ankylosing

Spondylitis - Von Bechterew; Reactive Arthritis – Brodie in 1818, and Hans Reiter in 1916 describing its occurrence during the First World War.

- One of the most fascinating watersheds in rheumatology was that of the observation by Edmund Stone written in a letter to the President of the Royal Society in 1763 – “An account of the success of the bark of the willow in the cure of the agues”. Stone had noticed the association between rheumatic aches and pains and dampness and the fact that willows grew in these areas. He then used willow bark or an extraction thereof and showed that it often produced relief. This next slide shows the willow tree which is the emblem of the Australian Rheumatology Association. Stone’s observation led really to the development of the modern pharmaceutical industry.
- Salicylic acid was synthesised in the mid-1800’s and was put into commercial production in 1874. Osler, a father of modern medicine, did not think very much of salicylates and felt that the most beneficial forms of treatment for arthritis were massage, climate and hydrotherapy. Use of salicylates was quickly associated with indigestion and this led to the development of the modern pharmaceutical industry with the non-salicylate analgesics – phenylbutazone, indomethacin and, in the 1970’s, proprionic acids.
- Gold salts will be described by one of my colleagues but again were used after the observation that patients receiving gold for tuberculosis noted a lessening of their rheumatic symptoms. Forestier and Simpson carried out clinical trials which led to its widespread use in the mid-1900’s.
- In the 1990’s there was a renaissance in therapeutics of arthritis particularly rheumatoid arthritis. The biologic agents offer real hope for those with rheumatoid arthritis and the development of these agents will continue to burgeon. New anti-inflammatory drugs with the COX-II inhibitors were also developed and their demise will be discussed by John Dowden. New biomaterials are being developed all the time and of course the total joint replacement of both the hip and the knee remain probably the most successful surgical procedure that there is. These exciting advances augur well for rheumatology but it should be remembered that there are still many patients around the world who do not have access to these therapies and there is still much to be done. This has led to the designation of the first decade of this millennium as the Decade of Bone and Joint Disease, an international organisation with some 60 affiliated nations including Australia. Increased evidence of the burden produced by musculoskeletal conditions has led the Australian Government to designate arthritis and musculoskeletal disease as Australia’s 7th National Health Priority.

The long road to viscosupplementation

John Quintner

Osteoarthritis of the knee

Prevalence:

- 10% of adults age 55 and over – pain due to OA
- of those, 25% severely disabled
- Two out of every 3 women > 80years will require a total knee replacement

Management

The standard approach

- Paracetamol
- NSAIDs
- Exercise
- Braces, footwear etc
- Knee surgery

Other approaches

- Nutraceuticals
- *Viscosupplementation*
- Chondroplasty

Viscosupplementation

The intra-articular instillation of synthetic hyaluronan preparations aiming to restore normal synovial fluid properties and function (viscosity and elasticity).

Hyaluronan

- Component of synovial fluid
- Type B synoviocytes or fibroblasts
- Responsible for its viscoelasticity
- In OA reduced concentration & molecular weight of the hylan polymers

The Ancients

“Firstly, she has covered the two bones with cartilage, then she has poured a slippery viscous humour on these cartilages, resembling a kind of oil, such that all the junctures of the bones can move freely and without danger of being eroded.”

Galen: *On the Function of the Parts of the Human Body*

The Renaissance

SYNOVIA: [*syn*-(together) & *oon*-(egg)] = Name for any body fluid resembling white of an egg

Paracelsus, 1520

Dawn of scientific era

Synovia produced by “a particular sort of Glands seated in the Joynts” ... the *glandulae mucilaginosea*.

Clopton Havers: *Osteologia Nova* (1691)

First intra-articular injection

Two patients - severe knee inflammation - failed to respond to application of emollient cataplasms (poultice or plaster) and a vesicant - aspirated large quantity of colourless, transparent fluid and then injected *eau de Goulard* and a twelfth of camphorated tafia (rum). These injections were discontinued after a few days, by which time both patients were considerably improved
Jean Gay [1792]

Injectables

- Lipiodol - iodized poppy seed oil [1920s]
- Acids: lactic acid [1938]; phosphoric acid [1944]
- Human fat [1939]
- Corticosteroids [1950]
- Mineral oils - silicone oil [1971]
- Hyaluronic acid - hylan G-F 20 (Synvisc) [1971]

Hylan GF-20 Protocol

Weekly intra-articular injection Hylan GF-20 (Synvisc) for 3 weeks
Cost = \$440 per course

Possible mechanisms

- lubricating effect [Grecomoro et al., 2001]
- analgesic effect - joint nociceptors [Ghosh, 1994; Gomis et al., 2006]
- promote endogenous HA production by stimulating synovial fibroblasts [Akmal et al., 2005; Bagga et al., 2006]
- anti-inflammatory effect on leukocyte function [Forrester & Balazs, 1980; Håkansson et al., 1980]

Cochrane review of HA for knee OA 2005

- The HA class superior to placebo
- Synvisc significantly better than placebo
- Synvisc significantly improved pain & function better than IA corticosteroids & similar to continuous NSAIDs at 5-13 & 14-26 weeks after treatment
- The majority of Synvisc studies in the class analysis had more robust effect sizes than studies with other HA products

Local treatment for local disease?

“... the clinician should still view viscosupplementation as a more costly and labour intensive option for patients refractory to corticosteroid injection, oral medications, or physical rehabilitation.”

[Cochrane Database of Systematic Reviews 2005]

Are we there yet?

“In the balance of benefit to harm, the trade-off is probable benefit with respect to pain reduction and physical function improvement with low risk of harm.”

[Campbell et al., 2007]

The development of DMARDS for rheumatoid arthritis

Richard Travers

Note: This paper began with images of Rheumatoid Arthritis (RA) affecting the hands, illustrating “the *progression* we hope to stop, or at least slow down, with the use of Disease-Modifying Anti-Rheumatic Drugs (DMARDS)”.

Gold injections - chrysotherapy

Parenteral gold therapy I

- 1890 – Koch demonstrates that gold cyanide is bacteriostatic for TB
- 1913 – Bruck and Glück; gold in lupus vulgaris
- 1913 – Feldt – gold in pulmonary TB
- 1927 – Landé – ATG (Solganol) in SBE, Rh Fever
- 1929 – Forestier’s report with gold thiopropanol (Allochrysine) in RA [Jacques Forestier (1890-1978): War hero, Olympian, rheumatologist *extraordinaire*]

Jacques Forestier (read by Georges-Louis Faroy). L’aurothérapie dans les rhumatismes chroniques. *Bull. et Mém de la Soc. Méd. des Hôp. de Paris*, 1929, 323-327.

...L’analogie de l’évolution clinique de certaines formes graves de rhumatisme chronique avec celle de la maladie tuberculeuse: évolution fébrile, avec poussées fluxionnaires ou fièvre continue, atteinte de l’état général, anémie, leucocytose, etc., nous ont fait penser que les sels d’or employés dans la tuberculose pourraient rendre de très grands services aux rhumatisants...

(page 324)

Forestier – first use of gold salts in RA, May 1928

- Aurothiopropanol sulphionate (Allochrysine) 250 mg IM, 10-12 times (max 24, min 2) at 5-7 day intervals. Some patients had a second course a month later.
- 15 cases (11 F, 4 M) mean age 42 years; established RA, resistant to treatment.
- Results: 5 were improved so much that one would hope for a cure; 5 were markedly improved, and walked well, instead of slowly; 2 had made progress, but one felt they had not had enough injections; 3 cases we haven’t been able to get news of the patient. As far as we know, no one was made worse by the treatment
- Unwanted effects : injection reactions 8 (fever 4, fever + vomiting, diarrhoea and desquamating rash nodes 4), toxic reactions 3 (prolonged rash, severe mouth ulcers and, in 1 patient, a flare of furunculosis and reactivation of malaria)
- *Small numbers, no control group, poor definition of patients and of response*

Parenteral gold therapy II

- 1938 – Empire Rheumatism Council trial started, then stopped
- 1939 – Snyder RG, Traeger C and Kelly L – RA, OA, & “mixed”

- 1940 – Ellman P and Lawrence JS – RA
- 1945 – Fraser, TN – ATM (Myocrisin) in RA (part of ERC trial)
- 1961 – Empire Rheumatism Council trial published.
- 1962 – ERC follow-up trial

Empire Rheumatism Council trial (1960) – summary

“Gold therapy undoubtedly improved the average clinical condition of the majority of patients in the gold-treated group over a period of 18 months. A further assessment in one year’s time will show if this improvement is being maintained.”

- 1970s – Aurothiomalate (Myocrisin) was joined in Australia by aurothioglucose (Gold-50) and the oral preparation auranofen (Ridaura)
- 1980s – gold eventually succumbed to methotrexate

Sulfasalazine (Salazopyrin®)

Nanna Svartz (1890-1986) Med. Lic. Stockholm (1918)

Sulfasalazine : II. Some notes on the discovery and development of Salazopyrine.

American Journal of Gastroenterology, Vol. 83 (5), 1988 : 497-503

“Munk’s Roll” Vol. VIII, p. 488-490

- MD thesis (1927) on intestinal bacteria in ulcerative colitis (UC)
- The granulation tissue of RA very similar to that of UC
- Streptococci found in intestine and nose of RA patients – probably the cause of the RA
- Sulfapyridine effective against streptococci (LEH Whitby, *Lancet*, 1938)
- Sulfapyridine helpful in UC but not RA – probably because it did not get into the connective tissue, like aspirin (which is also anti-inflammatory)
- After a year of unsuccessful attempts to combine sulfapyridine and salicylic acid, she asked Pharmacia to do so. Willstedt produced several compounds, one of which was salicylazosulfapyridine (abbreviated to salazopyrine, later called azusulphidine or sulfasalazine)
- SSZ ‘excellent’ in UC but unpredictable in RA – some early cases responded (results published in *Acta Med. Scand.* Vol. 110, 1942 : 577-598)

Sinclair & Duthie – SSZ trial (1949)

- RJG Sinclair and JJR Duthie. Salazopyrin in the treatment of rheumatoid arthritis. *Annals of the Rheumatic Diseases*, Vol. 8: 226-231 (1949)
- “Salazopyrin does not appear to be of any specific value in the treatment of this disease.”

d-Penicillamine as DMARD

Jaffe IA. Penicillamine treatment of rheumatoid arthritis – rationale, pattern of clinical response, etc. cology and toxicology. *In Penicillamine Research in Rheumatoid Disease*, Oslo, 1976, p. 11-24.

- 1942 – a penicillin metabolite; Chain described chemical structure in 1949
- 1958 – Heimer & Frederico showed d-Pen dissociates Rh Factor *in vitro*
- 1962 – Jaffe showed intra-articular dissociation of Rh Factor

- 1963 – Jaffe removed Rh Factor from a patient by plasmapheresis without benefit, compared with d-Pen, which helped clinically
- 1970 – Jaffe treats rheumatoid vasculitis
- 1973 – (*Lancet*) Multi-Centre Trial Group found d-Pen effective in severe RA

“If it had not been for the skill and perseverance of these investigators, penicillamine would still be awaiting recognition as a valid therapy for RA.”

Jaffe, 1976

Treatment of Lupus Erythematosus with Mepacrine.

Francis Page, M.D Lond., MRCP; Medical Registrar, Middlesex Hospital

Lancet, Oct. 27 (1951), 755-758

Chronic Discoid Lupus Erythematosus with Rheumatoid Arthritis

Case 3 – A woman, aged 40, had had lupus erythematosus on her face and hands for five years. In the past three years she had been given many courses of bismuth and carbon dioxide snow...Quinine and vitamin E were given without effect. For two years before treatment with mepacrine was started the patient had had rheumatoid arthritis of wrists, elbows, shoulders, fingers, knees, and ankles, with swelling, diminished movement, and weakness.

Effect of Mepacrine. – A month after mepacrine treatment began the physiotherapy department reported : "*there has been amazing improvement in the rheumatoid arthritis and the skin.*" This improvement in the joints continued and, four months later, the joints were normal. The skin disease, although better controlled for a longer period than with any other treatment, has always shown some activity.

1948 – the annus mirabilis for rheumatology

(EGL Bywaters, 1-4)

1. Hench, Kendall *et al* synthesise Compound E (cortisone)
2. Rose and Waaler discover rheumatoid factor
3. Hargreaves discovers the LE Cell phenomenon
4. Probenecid is introduced for treatment of gout
5. Farber introduces the folic acid antagonist aminopterin (methotrexate) for the treatment of acute leukaemia

Aminopterin

Gubner R, August S, Ginsberg V. Therapeutic suppression of tissue reactivity II.

Effect of aminopterin in rheumatoid arthritis and psoriasis. *Am. J. Med. Sci.* Vol. 221 (2): 176-182 (1951)

- Cortisone – does it inhibit connective tissue formation by a specific hormonal regulatory influence, or is it a non-specific effect?
- Aminopterin is a potent inhibitor of connective tissue.
- Aminopterin 1-2 mg daily to 7 patients with RA, for only 1-3 weeks – 6 responded, all of them relapsed.
- Case 2 (M, 36) had RA 3 months and psoriasis 20 years – joints *and* skin improved a great deal.

- Hence, aminopterin also given to 5 patients with psoriasis + associated arthritis and 3 patients with uncomplicated psoriasis. Good results with 1.5 to 2 mg daily to total dose 19 to 120 mg.
- Result overlooked because of the preoccupation with cortisone?

Methotrexate use : the rise to the top

JR O'Dell – *Rheum Dis Clin North Am* 23 (4) : 779-796 (1997) – Table 3

- 1972-1983 Reports of significant efficacy in open studies
- 1984-1985 Four placebo-controlled studies demonstrate efficacy
- 1989-1995 Long-term efficacy and tolerability shown to be superior to other DMARDs
- 1990-1994 Recognition that folate replacement therapy can be given without affecting efficacy.
- 1994 Liver toxicity monitored primarily with blood test, routine liver biopsies not recommended.
- 1995-1996 Methotrexate shown to work well in combination with other DMARDs.

Leflunomide

- Developed in the early 1990s to stop tumour rejection; its active metabolite (AT 1726) inhibits purine synthesis. An anti-inflammatory action in autoimmune disease was also noted.
- 1999 – J Smolen and the European Leflunomide Study Group. Efficacy and safety of leflunomide compared with placebo and sulphasalazine in active rheumatoid arthritis: a double-blind, randomised, multicentre trial. *Lancet*. Jan 23; 353 :259-66.
- 1999 – V Strand and the Leflunomide Rheumatoid Arthritis Investigators Group. Treatment of active rheumatoid arthritis with leflunomide compared with placebo and methotrexate. *Arch Intern Med*. 1999 Nov 22;159(21):2542-50.

The development of DMARDS

- After 80 years, treatment is still palliative
- Based on the perceived causes of RA
 - Infection, tuberculous (gold) or streptococcal (SSZ)
 - Malignancy (AZA, MTX)
 - B-cell dysfunction (d-Pen)
 - T-cell dysfunction (Leflunomide, TNF α inhibitors)
 - Serendipity (antimalarials)
- Early investigation would probably not have survived modern ethics committees or experimental design
- We use the same drugs still, but in different ways – we start them earlier, we use them in combinations, we make fuller use of them and we have the TNF- α inhibitors if necessary.

What a COX up! Australian Prescriber and the end of a blockbuster

John S. Dowden

History of Australian Prescriber

- Founded in 1975
- Replaced British Prescribers' Journal
- Published by the Commonwealth Department of Health
- Quarterly
- First [arthritis-related] article on gout in 1978
- Phenylbutazone was a recommended treatment
- Immunosuppressant drugs in rheumatoid arthritis
- New arthritis drug 1978
- Naproxen approved for rheumatoid arthritis
- AP verdict: in most cases aspirin is still the drug of first choice for the management of rheumatoid arthritis; not a replacement for gold
- Journal evolves over time
- Arthritis articles reflect changing practice

The rise of NSAIDS

- 1978 – sulindac; 1979 – fenoprofen; 1980 – diflunisal; 1981 – diclofenac; ketoprofen; 1982 – comprehensive review of NSAIDS by Peter Brooks

Disease modifying drugs

- *Disease modifying drugs in adult rheumatoid arthritis*. Anita T.Y. Lee and Kevin Pile. Australian Prescriber Vol 26 No 2 2003

Biological therapies for arthritis

- *Experimental and Clinical Pharmacology: Tumour necrosis factor alpha inhibitors for the treatment of adult rheumatoid arthritis*. Geoff McColl. Australian Prescriber Vol 27 No 2 2004

New technology in publishing

- 1994 development of an electronic version
- 1996 Australian Prescriber becomes one of the first medical journals in the world to provide free access to full text
- www.australianprescriber.com

Internet expands the audience

- Consumer comments 1997
- International accreditation 2002

Problems with NSAIDS

- Indigestion, heartburn (9%)
- Nausea (5%)
- Abdominal pain (26%)
- Serious adverse effects include: stomach ulcers, bleeding from the gut, high blood pressure, heart failure, kidney failure

- Gastrointestinal side effects: serious complications in 1.5% of patients per year, five-fold increased risk of bleeding ulcer
- increase risk of hospitalization: (NSAIDs account for 4-10% of drug-related hospital admissions), possibly 400 deaths per year

Cyclo-oxygenase inhibitors

- *Experimental and Clinical Pharmacology: COX-2 inhibitors*. Peter M. Brooks. Australian Prescriber Vol 23 no 2 2000
- Arachidonic acid → COX-1 → Prostaglandins (gastric and kidney function); Thromboxanes (platelet function)
- Arachidonic acid → COX-2 → Prostaglandins (inflammation)

A question of balance

- NSAIDs inhibit COX-1 and COX-2 – reduce inflammation in joints, but increase risk of ulcers
- COX-2 inhibitors only inhibit COX-2 – less risk of ulcers

Race to develop COX-2 inhibitors

- Searle versus Merck – celecoxib (Celebrex) versus rofecoxib (Vioxx)
- USA approval: celecoxib January 1999, rofecoxib May 1999
- Australian Pharmaceutical Benefits Scheme: celecoxib August 2000, rofecoxib February 2001 (osteoarthritis only)

Australian Prescriber's verdict

- 1999 “The COX-2 inhibitors have the potential to replace NSAIDs for the relief of arthritic symptoms. Whether or not they fulfil this potential will depend on their long-term safety.”
- 2000: “Although rofecoxib is more selective it may not be safer. Until evidence of long-term safety and efficacy is available the choice of treatment will be influenced by the cost of the drugs.”

Questions about COX-2 inhibitors

- VIGOR Study (Compared rofecoxib and naproxen)
- Mortality - 0.5% rofecoxib, 0.4% naproxen
- Myocardial infarctions - 0.4% rofecoxib, 0.1% naproxen. Was this an effect of naproxen? aspirin?
- COX-1 involved in production of prostaglandins
- Prostaglandins help to prevent the stomach ulcers, but also have other functions

A question of balance

- NSAIDs inhibit COX-1 and COX-2
- COX-2 inhibitors only inhibit COX-2 - upset the balance of thromboxane and prostacyclin – increasing constriction of blood vessels and platelet stickiness

October 2004

- Rofecoxib withdrawn from the market
- Bowel cancer study found: increased heart attacks, increased strokes

- Rofecoxib 3.5% v Placebo 1.9%
- If 63 people are treated one will have a heart attack or stroke

Australian Prescriber December 2004

The vascular effects of COX-2 selective inhibitors. Richard O. Day and Garry G. Graham. Australian Prescriber Vol 27 No 6 Dec 2004

“The risk of myocardial infarction and stroke after 18 months was high enough to prompt the removal of rofecoxib from the market.”

Impact of rofecoxib withdrawal

- An estimated 250,000-300,000 Australians were affected by the withdrawal of rofecoxib
- How many heart attacks?
- How many people died?
- Could this have been foreseen?

COX-2 inhibitors caution

- *Editorial: The changing treatment of arthritis.* Lesley G. Cleland, Susanna M. Proudman, Michael J. James and Peter Penglis. Australian Prescriber Vol 23 No 2 Apr 2000
- “A major unresolved question is the impact that COX-2 inhibitors may have on the risk of thrombotic vascular events. This risk is unlikely to be seen in short term efficacy trials or early post-marketing surveillance...”

Why did this happen?

- COX-2 inhibitors being prescribed: for people who could not take NSAIDs; for unapproved conditions (injuries; tendonitis; gout)
- Marketing: Australian spending unknown. USA direct-to-consumer advertising (US dollars): Campbell’s Soup \$58 million; Nike sports shoes \$78 million; PepsiCola \$125 million; Budweiser beer \$146 million; Vioxx \$160 million. (NIHCM Foundation)

Conclusion

- Australian Prescriber is the national journal of drugs and therapeutics
- Read Australian Prescriber for independent analysis
- Today’s breakthrough could be tomorrow’s disaster
- Australian Prescriber is living history

Not the first time - safety issues with phenylbutazone and benoxaprofen

John McEwen

Some of the information presented has been collected while the author has been undertaking a project for the Therapeutic Goods Administration.

Medicines to treat arthritis

- The various forms of arthritis include common diseases;
- Several forms of arthritis are chronic diseases;
- Even today, at least theoretically, a new medicine to treat chronic diseases like arthritis can achieve registration based on clinical trials with few patients taking it for long periods;
- Not surprising that serious adverse effects may emerge only after a medicine has been registered and used widely;
- Often great “hype” for new drugs to treat chronic diseases, pre-registration and before PBS listing.

Phenylbutazone

- Patented in USA to Geigy in 1951
- Geigy brand name was Butazolidin

- Question in House of Representatives - 27 November 1953: Mr Haworth: “Will the Minister inform the House whether any new clinical history is known about butazolidine and has the drug been found to be effective in the treatment of rheumatoid arthritis? If so, will the Minister have it placed upon the list under the Pharmaceutical Benefits Act?”
- Reply from the Minister (Sir Earle Page): “Several suggestions have been made to me regarding the use of butazolidine, and the matter has been submitted on several occasions to the Pharmaceutical Benefits Advisory Committee. Each time that committee has rejected the drug from inclusion in the list of life-saving drugs.”

- Generally thought to be an effective analgesic and anti-inflammatory.
- With use, a number of serious adverse effects emerged – especially the blood disorder aplastic anaemia.
- Also the innovator company marketed a related drug oxyphenbutazone (Tanderil)

- Notes on Current Drugs – Medical Journal of Australia, March 5, 1966: 422- “published at the request of the Director-General of Health”: “At its fourteenth meeting, the Australian Drug Evaluation Committee recommended that a reminder/warning of the hazards involved in the use of phenylbutazone, incorporating information available from the Registry of Adverse Drug Reactions, should be communicated to the medical profession.”

- “Since August 1964 (when reporting was first solicited in Australia), 18 reports of serious adverse reactions with one death have been notified to the Registry in patients treated with phenylbutazone.”
- “Of these, 12 patients developed blood dyscrasias, two suffered liver damage and two developed peptic ulceration.”
- “The total use of phenylbutazone is not accurately known, though more than 1,250,000 prescriptions were written during 1965, indicating that this drug is widely used” (Also observed that reactions may be under-reported)
- “Over a similar period, 50 reports of serious complications with 18 deaths were reported to the Committee on the Safety of Drugs in the UK, associated with the use of phenylbutazone.”
- 1969 – ADEC noted 89 reports received.
- 1977 – British Medical Journal – Inman WHW, 1:1500-1505. Study of 269 deaths in UK in 12 months from 1 October 1974. 83 deaths probably caused by drugs, most commonly aplastic anaemia while being treated with phenylbutazone (28) and oxyphenbutazone (11). Phenylbutazone mortality rates varied up to 6 per 100,000 exposed for women aged > 64 years.
- Adverse Drug Reactions Advisory Committee (ADRAC) established in 1970 as subcommittee of ADEC.
- Case studies and warnings published: 1975 (234 reports - 13 fatal blood disorders); 1979 – letter to teaching hospitals; 1979 – case study (MJA); 1980 – case study – fever, rash, salivary swelling (MJA)
- In 1980, Australian Rheumatism Association (ARA) recommended to PBAC that the drug be limited as a PB item to the sero-negative spondyloarthropathies, gout and rheumatoid arthritis not responding to other NSAIDs.
- In 1983, ADRAC and ADEC recommended to PBAC that the ARA recommendations should be implemented.
- Also June 1983, ADRAC published a further Bulletin item - observing that in only 2 of 11 reports of blood disorders received since January 1980 had use clearly fallen within ARA guidelines.
- Subsequently in 1983, PBAC recommended an Authority Required listing and only for conditions as recommended by ARA;
- 1984 – Innovator (Ciba Geigy) proposed severe restrictions to indications and duration of use.
- 1985 - Innovator restricted use internationally and withdrew oxyphenbutazone
- 1986 – action to bring generic products into line with the innovator
- Difficult to track ultimate withdrawal in Australia
- No longer registered in Australia
- Some sponsors did not transfer to the new registration system in 1991?
- Occasional adulterant in imported herbal medicines.

Benoxaprofen

- Early 1980's – new product publicised before registration as “the arthritis medicine to use when others fail”. See Smith R, Medical journals and pharmaceutical companies: uneasy bedfellows. *BMJ* 2003;326: 1202-5.
- Marketed in UK March 1980.
- March 1982 – ADEC considered application to market in Australia. Australian evaluator of clinical information drew attention to high frequency of photosensitivity reactions in clinical trials.
- Additional information confirmed high incidence in UK – company was recommending use of sunscreen. Also noted in small number of patients who had individual approval for use in Australia.
- ADEC recommended that it not be approved in Australia.
- Therapeutics Subcommittee of ARA proposed a monitored release in Australia, with use of sunscreens, gradual exposure to the sun.
- ADEC confirmed its rejection (May 1982)
- Worldwide withdrawal – 8 August 1982
- In UK, photosensitivity reactions more common in the South. Severe liver toxicity more common in the North.

A history... national health priority areas, with a focus on arthritis

Mick Hoare

Population health in antiquity

- Population health - an approach that aims to improve the health of an entire population. It is not a modern concept.
- Holistic health concepts were present in China over 4,000 years ago.
- In ancient Greece, physical fitness was just as important as knowledge and learning.

Hippocrates (BC c. 460-377)

- The “Father of Medicine”- was the first physician to separate health from superstition.
- Disease prevention through cleanliness, rest, a good diet, fresh air, and suitable construction of towns and houses for a healthy environment.
- Individual differences - the ability of some individuals to cope with their disease and illness better than others. (‘Weak’ and ‘strong’ constitutions of 1940s and 50s.)
- It was to take over 2000 years, until the Renaissance, before this connection between lifestyle management and health was rediscovered.
- [Historical note... Hygieia was the Greek goddess of cleanliness, sanitation, prevention of sickness and the continuation of good health. Hence the term hygiene.]
- Hippocrates recommended that people burn their clothes and boil the water before they drank it.

Claudius Galen (AD c. 129-210)

- “Is it not disgraceful, that a person should, by reason of that extraordinary arthritis, be unable to use his hands and should need somebody else to bring food to his mouth and to perform his toilet necessities for him?” (Galen)
- Galen - the maintenance of health by control of hygiene, diet and physical fitness.
- In Greek and Roman times, the preservation and promotion of health was just as much a part of the doctor's business as the treatment of disease.
- Physical exercise was considered to be as important as cleanliness.
- Ancient Rome’s aqueducts, built between 312 BC and 226 AD, supplied the city with clean water. The longest aqueduct was 59 miles long. Over one cubic metre of water per day was available for each inhabitant in Rome for cleanliness and sewerage purposes.

Epidemiology and population health – the beginnings

- The science of epidemiology - a branch of medicine dealing with the incidence and prevalence of disease in large populations.

- The Chinese practiced inoculation against small pox by 1000BC.
- Modern epidemiology was founded in London by Dr John Snow -1854 cholera outbreak.
- Modern concepts of population health in the 1880s - Robert Koch's germ theory and Louis Pasteur's production of artificial vaccines.

Population health in the 20th century...

- A dramatic increase in average life span through large scale vaccination programs and infectious diseases control.
- Australian programs to: reduce smoking, increase the number of adults doing physical exercise, and increase the uptake of population-based screening programs, e.g. mammography and Pap smear testing.
- Other programs: motor vehicle and worker safety, family planning, and fluoridation of drinking water.
- Population health focus shifted to an ageing population, and programs to decrease chronic diseases, such as cancer, heart disease and stroke, which reduced the quality of life (sometimes, shortening it).

20th Century international population health movements

Australia was a signatory to the World Health Organization's first international health declaration, the 1978 Declaration of Alma-Ata, promoting "Health for All" through primary health care.

- All governments, health and development workers, and the world community must protect and promote the health of all the people of the world...
- Health and access to health care are fundamental human rights.
- Gross inequality in the health status of different peoples is unacceptable.
- Sustained economic, social development and world peace depend on promotion and protection of health.
- National policies and strategies must provide: primary health care, health education, nutrition, safe water and sanitation, maternal and child health, and immunisation.

Ancient history was informing the second half of the 20th century!

Social determinants of health

- Ottawa Charter for Health Promotion in 1986 - the first international conference on health promotion.
- Broadening focus of population health from individual behaviours and risk factors to population-level issues.
- Canadian research [(Raphael, D. (Ed.). (2004). *Social determinants of health: Canadian perspectives*. Toronto: Canadian Scholars')]: social determinants of health have a large impact on health outcomes, and medicine and health care have a relatively minor impact on improving health overall.
- The Canadian 11 social determinants of health: Aboriginal status; early life; education; employment and working conditions; food security; health care services; housing; income and its distribution; social safety net; social exclusion; unemployment and employment security.

- In Australia: 17-year gap in life expectancy between Australian Aboriginal and Torres Strait Islander peoples, and the Australian average!
- Status and social stratification can lead to stress, and stress-related conditions, including chronic conditions.
- Economic inequality is bad for everyone's health (both the privileged and under-privileged).

Hippocrates foreshadowed this knowledge that individual differences in human circumstances and reactions affect health prospects.

The Australian Government's 1996 National Health Priority Areas...

- The National Health Priority Areas policy - a national consultation strategy.
- WHO's Alma-Ata agreement in the world-wide trend to national health outcomes.
- Australia's National Health Goals and Targets of 1994.
- The next challenge was to identify and implement some nationally coordinated strategies.
- Australia focuses on health service funding, promoting quality of health care and population health improvement.
- Australians health was generally among the best in the world and continuing to improve but: cancer - still one of the nation's biggest killers; diabetes - rising death rate particularly in the Indigenous Australian population; mental illness – common.

National Health Priority Areas (NHPA) initiative

- An excellent opportunity to close the gap in health outcomes between population groups.
- Collaboration between: Commonwealth and state and territory governments, non-government organisations, health experts, clinicians, and consumers.
- Continuum of care from prevention through to treatment, management and maintenance, based on evidence-based research and data sources.
- The Australian Bureau of Statistics National Health Surveys conducted since 1975.
- Australian Institute of Health and Welfare reporting progress in population health since 1988.
- Statistics were highly relevant to the choice of national health priority areas.
- Target specific health areas that imposed high social and financial costs on Australian society.
- Chosen diseases and conditions targeted under the NHPA initiative to achieve significant gains in the health of Australia's population.
- By the end of 1996, there were six proclaimed national health priority areas: cardiovascular health; cancer control; mental health; diabetes mellitus; injury prevention and control; and asthma.

For each of the NHPAs, the future work program would include:

- National action plans;
- Identification of gaps in our understanding of good practice in the prevention, and evidence-based best practice in treatment and management to fill these gaps;

- Development of primary care clinical guidelines;
- Designing, validation and refinement of indicators for reporting outcomes; and
- The non-government sector including peak bodies, experts and consumers included in the decision-making.

Six National Health Priority Areas become 7 in 2002...

- The National Health Priority Action Council was established as a sub-committee of the Australian Health Ministers' Advisory Council.
- The Arthritis Foundation of Australia requested the Council to consider musculoskeletal disease and arthritis for national health priority status.
- An Access Economics report (in support) estimated costs as \$9 billion in 2000.
- The Bone and Joint Decade 2000-2010 supported the application.
- Support from all states and territories
- July 2002, Australian health ministers announced arthritis and musculoskeletal disorders as a new national health priority area.
- Six National Health Priority Areas (cardiovascular disease, asthma, diabetes mellitus, cancer, mental health and injury prevention) were now 7.
- 8 years of committed Australian Government funding: Better Arthritis Care (BAC) initiative 2002-03 to 2005 06 (\$11.5m); and Better Arthritis and Osteoporosis Care (BAOC) initiative 2006-07 to 2009-10 (\$14.8m).

The Australian Government's 2005 National Health Priority Area achievements...

In November 2005, all Australian health Ministers (Federal, state and territory) endorsed a Chronic Disease Strategy, five National Service Improvement Frameworks and the *Blueprint for nation-wide surveillance of chronic diseases and associated determinants*.

Three complementary components:

- Agreed policies (WHY do it?)
- Agreed actions (WHAT to do?)
- Agreed evaluation strategies (IS IT WORKING?)

Achievements of the BAC and BAOC initiatives (2002 to 2010)...

- Australian health Ministers endorsed a National Action Plan to guide strategic activity for osteoarthritis, rheumatoid arthritis and osteoporosis + a National Service Improvement Framework.
- These documents guide prevention and improved care and management for people with the conditions and their carers.
- Two influential reports - Australian Institute of Health and Welfare's: *Arthritis and musculoskeletal conditions in Australia 2005*; *National indicators for monitoring osteoarthritis, rheumatoid arthritis and osteoporosis, October 2006*.

BAOC

The BAOC initiative is now implementing national programs to:

- Improve national awareness;
- Improve self management of arthritis and osteoporosis;

- Provide core competencies in universities;
- Produce primary care clinical guidelines and decision support materials; and
- Advance data monitoring of the conditions.

The Department receives advice on the BAOC initiative from the Arthritis and Osteoporosis Expert Advisory Group's range of experts: Professor Nicholas Bellamy, Dr Julien de Jager, Assoc. Professor Lyn March, Dr Richard Osborne, Dr Neil Hearnden, Ms Ainslie Cahill, Ms Judy Stenmark, Professor Ric Day, Mr Mick Hoare and Professor Peter Brooks (Co-chair), Professor John Eisman (Co-Chair)

Key activities include working with Arthritis Australia (AA) and Osteoporosis Australia (OA).

- AA runs educational camps for children with juvenile arthritis.
- OA has developed community guides - educational kits – Fact Sheets.

The National Centre for Monitoring Arthritis and Musculoskeletal Conditions at the AIHW was launched in October 2005 and continues with data monitoring.

Other key organisations involved: RACGP, RACP, AOA, University of Melbourne, University of South Australia

The arthritis awareness workplace pilot is:

- Promoting awareness of the prevalence of arthritis in the working community;
- Giving workplace-based healthy lifestyle education; and
- Supporting the needs of people with arthritis in the workplace.

BAOC initiatives for the future...

- Up-datable clinical decision support materials and professional education modules for each of the conditions;
- A national osteoporosis fracture register and recall program;
- A next fracture prevention program; and
- Progressive evaluation.

The history of arthritis and population health in Australia is still in the making...

Rheumatoid arthritis: a patient's perspective

Ben Horgan

In January 1973, as a 2-½ year old, my life was about to change forever. I was waking up in the middle of the night with a very swollen knee and elbow and a temperature of 103. I would scream in agony until I was finally able to fall back to sleep. Then I would wake the next morning feeling as normal as I did when I went to bed the night before. Over a period of months I gradually got worse, until I was hospitalised with the hope of finding a diagnosis. At one stage there was a thought that I might have had leukemia, as my symptoms of spiking fevers and painfully swollen joints matched the patient in the bed next to me who had already been diagnosed. Eventually after about 3 months they diagnosed me with Juvenile Rheumatoid Arthritis. After 12 months the disease had moved throughout my entire body and I was forced to take 50 milligrams of prednisone twice daily, as well as massive amounts of aspirin.

Along with this it was suggested to my parents that I stay in bed for as long as I was in pain and only to get up if I really wanted to. All of this for a 3 year old who only 12 months earlier was as healthy and happy as any toddler could be. None of this was fair or even understandable, but with the help of 2 wonderfully brave and determined parents, I have survived and flourished to be the successful person I am today.

Nothing about juvenile arthritis for me has been easy. In fact at times as a child I would have rather been dead than go through some of the torture I was faced with. I'm talking about much more than the treatments that I had to endure, and much closer to home. The pain I endured just walking from my bed to the toilet was indescribable, yet the indignity of having to use a bottle or pan when the toilet is less than 10 meters from my bed was soul destroying.

I find it quite fascinating that the pain I remember is always the times when I felt that my life had been cut short and everyone else around me was fulfilling their hopes and dreams while I sat in my chair and watched it happen. This is the worst hurt because this is the pain that can be remembered. From my experience, and those who I have spoken to with similar chronic pain, you can't remember what physical pain felt like after the fact. You might be able to describe what it felt like but you can't ever bring that pain back through memories. The physical pain just disappears forever, but the heartache is with you forever.

Being forced to live a life of pain and suffering is nothing compared to losing that chance to have a normal life. It's not the pain that hurts, it's the inability to live that can eventually destroy you. This is where I believe the saying "you don't treat the disease you treat the patient" comes from. As a small child it is very hard to be anything other than 'the kid with arthritis'. Ben Horgan was just the name at the top of my hospital bed. I could have changed my name to Arthur I Tis because that was who I was for a very long time. My whole existence, and my family's, revolved around arthritis.

I would be at physio 3 times a week, plus hour long exercising twice daily. I would do hydrotherapy twice a week. See a G.P. once a week for a check up and have a visit

with my specialist once a month. It would not be surprising for me to need to take over 30 tablets a day to control the disease. I would wear hand splints through the day and resting splints at night. I would use leg traction while I slept and wear calipers when I went to school. Due to the frequent hospital visits and missing so much school, I ended up finding it very hard to associate with any of my peers. It was much easier for me to converse with adults than kids my own age.

I have always liked to focus on the positive side of things and believe it or not there have been plenty of positives to come out of my arthritis.

Such as, academically I was travelling very well even though I missed a lot of school because I found learning easy to do when I was hurting, and even a good way to get my mind off things. That was until my HSC year when my arthritis was in full remission and I had just got my driver's license. I finally managed to fit into a peer group and I was the true rebel without a cause. Hence my final marks weren't anywhere near what they should have been, but I still feel that was the time when I really started learning about life. Life's lessons can't be learnt in a hospital or a doctor's waiting room.

After I left school, I started training to be a radio announcer. Through a lot of hard work and some good fortune I have been in the industry ever since. Radio announcers are getting younger and younger, even in the city. Through my experience in the industry it has always been the older 'jocs', as we are called, that make the better announcers. It's not because their voices have matured and they sound more resonant. It's not because they have had more years in the industry. It's because they have had more "life experience" and are better equipped to relate to their audience.

This has got to be our number 1 aim in treating a person with arthritis. To give them their lives back and enable them to be an integral part of society. Especially if it gives them a chance to have a family of their own as I have been lucky enough to have. We have been blessed with some remarkable advancement in the treatment of arthritis in recent years. If I were to be diagnosed today I would not endure the problems that I have had in my life, I am confident of that. However, for the most severe cases, as mine has been, the real solutions are out of reach. We must have a PBS system that keeps up with our advancing treatment programs. We must have the ability to offer people their lives to live as they choose. Whether they want to have a career in commercial radio or just have a family, or both. This is too important an issue. This is about people's lives. As I said earlier, there were times that I would have rather died than deal with my disease. But you don't die from arthritis. You have to live with it. That is where the tragedy of this disease lies. I can tell you. It's time we made a difference. Pardon me for finishing on a 'retro' note, but, "we have the technology" so lets make sure that the people who need it can use it. Let's keep moving forward, because we never want to go back from where I've come.

Concluding comments

At the end of the workshop, speakers were asked to identify lessons from history relevant to the current treatment of arthritis.

Not surprisingly, after listening to Ben as the last speaker, a central theme was the patient: “Learn by listening to patients”, “Honour the patient’s story”, “Use an individual approach, including being aware of differences in the way that patients fight the disease”, “The importance of the whole healthcare team, including family”. As shown by Ben’s story, with chronic disease individual patients personally experience the history of the development of therapy.

A related theme was that we can learn from what the early physicians observed and recorded, even if we disagree with the diagnosis and treatment of the time.

Thirdly was the need for circumspection about treatments because of possible long-term effects: “There will be more false dawns in the future for drugs – many won’t stand the test of time”. Indeed the efficacy of a treatment for arthritis can only be established by long-term outcomes. Breakthrough research may take years to get to clinical trials, may then not work as hoped or may have unacceptable side effects. This poses a problem for the pharmaceutical industry, and is not much fun for the patient either.

The last theme was the importance of public policy with its population health approach to prevention, funding, regulation and equity.

Looking back over the last 50 years, there have been major advances in the treatment of arthritis. Standing out are: the development of DMARDS for rheumatoid arthritis; the development of joint replacement surgery for osteoarthritis; and the better evaluation of the efficacy and side effects of treatments. As Ben indicated, no child diagnosed with juvenile rheumatoid arthritis today would need to endure the problems that he faced in the 1970s. Yet, as Mick Hoare said, the history of arthritis is still in the making. Much treatment is still palliative, the cause of rheumatoid arthritis is unknown and the rising prevalence of obesity may lead to an epidemic of osteoarthritis.

The history of arthritis treatment is a very broad subject and the workshop barely touched on many important areas such as joint surgery, rheumatology as a specialty and physiotherapy. There is plenty of scope for papers at future ANZSHM conferences!

Prue Deacon

Background on arthritis

Participants at the workshop received a kit which included information about arthritis, sourced from the websites of Health*Insite* Information partners. The partner URLs are provided below with additional useful links.

HealthInsite. Your gateway to reliable health information online.

www.healthinsite.gov.au

Arthritis topic page

www.healthinsite.gov.au/topics/Arthritis

Australian Government Department of Health and Ageing. Better health and active ageing for all Australians

www.health.gov.au

Arthritis and musculoskeletal conditions

www.health.gov.au/internet/wcms/publishing.nsf/Content/pq-arthritis

Australian Institute of Health and Welfare. Australia's national agency for health and welfare statistics

www.aihw.gov.au

Arthritis series

www.aihw.gov.au/publications/index.cfm/series/381

Australian Prescriber online. Free, rapid access to independent peer reviewed information on drugs and therapeutics.

www.australianprescriber.com

Better Health Channel. Health and medical information for consumers, quality assured by the Victorian Government.

www.betterhealth.vic.gov.au

Arthritis factsheet

www.betterhealth.vic.gov.au/bhcv2/bhcarticles.nsf/pages/Arthritis

myDr. An Australian healthcare website dedicated to providing Australian consumers with comprehensive and relevant health information.

www.mydr.com.au

Arthritis Centre

www.mydr.com.au/default.asp?Section=arthritis

The Cochrane Collaboration, Cochrane Reviews. Cochrane Reviews explore the evidence for and against the effectiveness and appropriateness of treatments. Free access in Australia.

<http://www.cochrane.org/reviews/index.htm>

Virtual Medical Centre. Australia's online medical information news resource for personal healthcare information by professional medical specialists.

www.virtualmedicalcentre.com

Joints Centre

www.virtualmedicalcentre.com/default.asp?centre=rhe