#### EDITORIAL

# Professor Barrie Vernon-Roberts, AO, MD, BSc, PhD, FRCPath, FRCPA, FAOrthA (Hon), FRS.SA

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Abstract This issue of Inflammopharmacology contains papers that have been submitted to commemorate the life and work of Professor Barrie Vernon-Roberts, an outstanding clinical scientist in the field of bone pathology and its pharmacological regulation. This review briefly summarizes his major works and achievements as well as a list of his publications.

This issue of Inflammopharmacology is dedicated to Professor Barrie Vernon-Roberts, one of the leading founding members of the Editorial Board of the Journal.

Indeed, he and Professor Michael Whitehouse were authors in the first issue of the journal in 1991 (Figs. 1, 2, 3) of a key article that featured significant and pioneering observations on the concept of "Conditional Pharmacology". To quote this concept concerns "the action and potency of a drug within the context of the whole syndrome to be treated. Endogenous factors (substances) are considered that might permit and/or augment the desired action of a drug (or even occasionally impede it). Such substances

Special issue: dedicated to the "Life and work of Professor Barrie Vernon-Roberts".

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Discipline of Anatomy and Pathology School of Medical Sciences Division of Health Sciences, University of Adelaide, Frome Road, Adelaide, SA 5005, Australia e-mail: david.haynes@adelaide.edu.au may be absent in healthy subjects or present in lower concentrations". (Whitehouse and Vernon-Roberts 1991). Thus, Conditional Pharmacology embraces the disease-> drug->disease interactions that may underlay a whole range of actions of drugs.

In a like manner Professor Vernon-Roberts has been a leading authority on many aspects of the mechanisms of inflammation and the drugs used to treat inflammatory conditions and cancer. His major speciality is recognized internationally as being in the pathology of bone, and notably the spine. Recognition of Professor Vernon-Roberts's outstanding contributions to spinal research was the



Fig. 1 Prof. Barrie Vernon-Roberts. Photograph kindly provided by Mr. Dale Caville (Discipline of Anatomy and Pathology, University of Adelaide)



Fig. 2 A recent photograph of Prof. Vernon Roberts (*left*) with Assoc. Prof. David Haynes his long-standing collaborator and coeditor of this special issue

award in 2005 of the Inaugural Allan Dwyer Medal for a lifetime of excellence in spinal research awarded by the Spine Society of Australia (Prof Nigel Jones, www.spinesociety.org.au/node/119, downloaded 10/5/2013). He had previously been awarded the International Volvo Award in 1986 Low Back Pain Research. This award was for fundamental research examining degenerative disc changes in sheep in which discrete tears of the outer annulus of lumbar discs were shown to be important in degeneration of the intravertebral joint complex (Osti et al. 1990a). Some 26 additional awards that Professor Vernon-Roberts has received include recognition of his widespread research interests, notably studies on low back pain and lumbar inflammation and disc degeneration. He has also made major contributions to understanding of the pharmacological control of chronic inflammation in inflammatory cells and in the adjuvant arthritis animal model in vivo. His groundbreaking work on hip prosthesis loosening in identifying the role of macrophages causing bone loss and prosthesis failure due to wear particles from the prosthesis has had a significant impact on the field of Orthopaedics (Evans et al. 1974 and B. Vernon-Roberts, and M.A.R. Freeman, "The Tissue Response to Total Joint Replacement Prostheses", in The Scientific Basis of Joint Replacement, S.A.V Swanson, M.A.R. Freeman (eds.), Pitman Medical Publishing, Tunbridge Wells, Kent, UK, 1977, pp. 86–129). The extensive research in experimental models and elegant histopathological investigations of clinical material has demonstrated an extraordinary understanding of the pathogenesis of many diseases. These valuable observations and data on basic pathological processes give insight into the underlying inflammatory and immunological changes involved in joint destruction in a variety of conditions.

The ultimate accolade was the award to Professor Vernon-Roberts of the Officer of the Order of Australia (AO) in the General Discussion in the Queen's Birthday Honours in 2005. This award was given "for service to medicine as a researcher, education and administrator, particularly in the areas of disorders of the bones and joints and pathology of the spine".

Professor Vernon-Roberts was born in North Wales and educated at Ruthin School (established as a private school for boys in 1284) at Ruthin, Clwyd (near Wrexham in North Wales). He studied medicine at the Charing Cross Hospital Medical School and received the MB, BS degree of the University of London in 1960. He received several undergraduate prizes and was awarded the Llewellyn Scholarship as an outstanding medical graduate. After internships at Charing Cross Hospital he had a Lectureship at King's College, University of London. He undertook research on sex and other hormonal regulation of macrophages for which he received a PhD in 1965 and an MD in 1966. He was then invited by Cambridge University Press on the basis of this.

Research on macrophages to write a major book on the macrophage which was published in 1972 (242 pp, ISBN: 0521084814). He was appointed a Senior Lecturer and Consultant Pathologist at the Royal London Hospital Medical College in 1974. Then he established a collaborative research centre, the Arthritis and Rheumatism Council's Bone and Joint Research Unit, of which he became its Director. In 1976 he was appointed to the prestigious post of the George Richard Marks Professor of Pathology at the University of Adelaide Medical School, Adelaide, South Australia, as well as Head of the Division of Tissue Pathology at the Institute of Medical and Veterinary Science (IMVS) and Senior Visiting Pathologist at the Royal Adelaide Hospital (RAH). In 1997 he was appointed Deputy Director and Chief Pathologist at the IMVS and in 1998 was appointed Director and Chief Executive of the IMVS. This institute was originally founded in 1938 by an eminent physician, Sir Trent Champion de Crespigny who had been Medical Superintendent of the RAH and Dean of Medicine at the University of Adelaide in the period from 1929 to 1947 (Kearney 1997). He had the inspired vision for an institute combining laboratory services with teaching and research. The IMVS became a world-renown clinically based medical and veterinary research institution and has been known for many major discoveries of clinically important diseases and their treatment. Prof Vernon-Roberts was instrumental in redefining the focus and development of the IMVS including the establishment in 1991 of the Hanson Institute (formerly the Hanson Centre for Cancer Research funded originally by the South Australian Anticancer Foundation). This became the research division of the IMVS housed in superb Fig. 3 Front page of article on conditional pharmacology by Whitehouse and Vernon-Roberts (1991)

# CONDITIONAL PHARMACOLOGY: EXPRESSION OF ANTI-INFLAMMATORY ACTIVITY MAY REQUIRE PRE-EXISTENT INFLAMMATORY MEDIATORS AND/OR HORMONES

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#### ABSTRACT

Whitehouse MW, Vernon-Roberts B. Conditional pharmacology: expression of anti-inflammatory activity may require pre-existent inflammatory mediators and/or hormones. Inflammopharmacology. 1991;1: 61-68

Aspirin, aminopyrine, azapropazone, bufexamac (100 mg/kg), and even high doses of copper acetate (50 mg/kg p.o.) showed no acute anti-inflammatory activity in the standard assay based on the carrageenan-induced rat paw oedema in healthy, normal rats. Repeating the assays in animals with pre-established inflammation revealed that these drugs are effective anti-oedemic agents. The acceptability of these agents in clinical practice may therefore rest on the fact that certain inflammatory mediators can support and/or induce the expression of an anti-inflammatory activity of agents, that are ineffective in animals not affected by additional inflammations. If misoprostol (a prostaglandin- $E_1$  analogue) is given p.o. together with the above test-drugs to healthy rats, the anti-oedemic properties of these drugs are revealed, suggesting that prostanoids may potentiate some of the NSAIDs which do not inhibit prostanoid synthesis *per se*.

Keywords: Copper, aspirin, aminopyrine, azapropazone, anti-oedemic, bufexamac, misoprostol

## INTRODUCTION

Several drugs continue to be used clinically to treat inflammatory disorders and associated pain, even though they show little or no significant anti-inflammatory activity in some 'acute' pharmacological assays. Examples include aminopyrine (4-dimethylamino-phenazone), also known as amidopyrine or pyramidone [1], azapropazone [2], bufexamac [3] and the simple salicylates [4]. One explanation is that the pharmacological assays used may be too blunt, or even inappropriate, for detecting a response to these drugs (assuming they are indeed anti-inflammatory). Another explanation might be that such drugs are merely analgesics, and it is this property which sustains patient demand and their extensive usage. This report indicates that these particular drugs probably possess anti-inflammatory properties and that one traditional 'rapid' pharmacological assay, utilizing suppression of carrageenan-induced paw oedema in rats, can be readily adapted to reveal the effects of drugs hitherto found to be inactive. This has important ramifications for preclinical testing and for an understanding of ways in which a disease process may work with, or against, a drug [5].

laboratories with world-class researchers in Centres for Cancer Research, Bone and Joint Research, Clinical Research, Neurological Diseases and Biomedical Research (www.hansoninstitute.sa.gov/aboutus/history.phr; downloaded 12/5/2013). The Adelaide Centre for Spinal Research was one of the research centres of the Hanson Institute whose development was actively supported by Prof. Vernon-Roberts whose pioneering research on spinal conditions has formed the basis of major contributions to research by this centre.

His research has been supported by leading competitive grant agencies (e.g. including the Australian National Health and Medical Research Council) to the extent of over \$AU15 m over the years. He was an active member of a large number of peer-reviewing grant committees and agencies in Australia and was a senior administrative officer of the University of Adelaide including being Pro-Vice Chancellor, Vice-Dean of the Faculty of Medicine. He was also an executive member of several Boards, Foundations and Councils involved in public health, medical research and professional bodies in Australia. He retired from the University of Adelaide and the IMVS in 2005 after completing his term as Director of the IMVS and is currently Senior Consultant Pathologist at the Adelaide Centre for Spinal Research and an Emeritus Professor of the University of Adelaide.

Professor Vernon-Roberts also inspired and educated a large number of research students and researchers that now make important impacts in their field. The publications in this special issue are contributions from some of Professor Vernon-Roberts' collaborators and past students that cover the wide spectrum of his interests. The Editors are most grateful to these authors for their valuable contributions.

# Appendix: A personal appreciation of Professor Barrie Vernon-Roberts

Professor Vernon-Roberts was an early supporter of neuropathology as a specialty at the Institute of Medical and Veterinary Science (now part of SA Pathology), the major provider of public and private pathology services in the state of South Australia. Since neuropathology has been my longstanding research interest, I have benefited greatly from this support. He also founded the Hanson Institute Centre for Neurological Diseases at this institution in 2004 and, under the leadership of Professor Peter Blumbergs, the Centre has become the major focus for diagnostic pathology and research in this field in the State. One of the Centre's main strengths is traumatic brain injury (TBI) and Professor Vernon-Roberts helped to foster this activity from the early stages. I have had a long association with the Centre, principally assisting with the development of animal models of TBI. Using his dual appointment as Professor of Pathology at the University of Adelaide and Head of Tissue Pathology (and later Director) at IMVS, Barrie strengthened the nexus between these institutions and many postgraduate students have benefited as a result. He facilitated, for example, my interest in ultrastructural pathology, which led to a higher degree in this area. A tangible legacy of Professor Vernon-Robert's support for neurological disease research is the continuing close relationship between the University's School of Medical Sciences (under Professor Robert Vink) and the Centre for Neurological Diseases. He also recognised the important role of veterinary services in a biomedical research institution such as the IMVS and this support allowed me to pursue my interest in veterinary diagnostic and investigative pathology. Barrie was always available to discuss bone and joint pathology over a double-head microscope and share his vast knowledge in this specialised field. His tenure as Director of the IMVS is widely recognised as being one of the most productive and innovative periods in its long history.

Dr John Finnie Senior Veterinary Pathologist SA Pathology

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- Listed below are the published works of Professor Vernon-Roberts based on available information. The inclusion of these is intended to be a comprehensive account of his research work. An interesting compilation of biographical cutting and references in media referring to reports of his activities and articles can be found in a book at the National Library of Australia details of which are as follows:
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- Citation: http://catalogue.nla.gov.au/Record/553876 [downloaded 10/5/ 2013]
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