

Spotlight on musculoskeletal conditions

Anti-inflammatory drugs following hip replacement surgery could harm rather than help

The use of anti-inflammatory drugs following hip replacement surgery could do more harm than good, according to a new study co-ordinated by The George Institute for International Health in association with orthopedic centres throughout Australia and New Zealand.

The results of the study, designed to determine the risks and long-term benefits and risks of anti-inflammatory drugs in patients undergoing hip replacement surgery were recently published in the *British Medical Journal*. The project specifically measured the effects of a short post-operative course of anti-inflammatories on the development of 'ectopic' bone formation related pain and disability, six to twelve months after surgery.

"Ectopic bone is abnormal bone that can form in the soft tissues around the operated hip. This occurs in more than one third of all patients in the months after hip replacement surgery," explained, Dr Marlene Fransen Head, Musculoskeletal Program within the Injury and Musculoskeletal Division at the Institute and Principal Investigator of this study. Research within the Musculoskeletal Program at The George Institute focuses on the prevention and treatment of chronic conditions such as osteoarthritis.

Many surgeons prescribe anti-inflammatory drugs in the immediate post-operative period for pain management or to reduce the risk of developing ectopic bone. While the researchers found the use of post-operative ibuprofen, a common anti-inflammatory drug, did indeed greatly reduce the risk of ectopic bone formation,



patients reported no greater reductions in hip pain or physical disability six to twelve months after surgery, compared with those not taking the drug. However, they also found evidence suggesting there may be an increased risk of major bleeding events in those taking the drug.

"For this reason, our study shows that recommending a routine course of an anti-inflammatory drug, following hip replacement surgery, is not justified," said Dr Fransen.

Chronic osteoarthritis of the hip is common among Australians aged 60 years or older and total hip replacement surgery is a well-established and highly effective treatment. Chronic musculoskeletal conditions are important global causes of disability. By 2020, osteoarthritis is projected to become the fourth leading cause of disability worldwide, consistent with changing

demographic patterns. In Australia, osteoarthritis is ranked the leading health problem.

Whilst joint replacement surgery greatly reduces chronic hip pain and improves physical function in most, residual symptoms are common. Over 900 patients from 20 orthopedic surgery centres across Australia and New Zealand participated in this study, half of whom were allocated to receive ibuprofen, a common anti-inflammatory drug, for 14 days commencing immediately after surgery.

"These results provide further evidence that guidelines for routine clinical care in surgery must be based on clinically important outcomes. Without such evidence, the widespread use of routine anti-inflammatory-based treatment after major orthopaedic surgery may well result in harm rather than benefit," Dr Fransen added.

This study was funded by NHMRC and the Medical Benefits Fund of Australia Limited.

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Chronic diseases - the new challenge for India

In this issue of George Research, Professor Bruce Neal, Senior Director at The George Institute, contributes his thoughts on the current climate of chronic disease in rural India.



The last century saw huge advances in the health of the Indian population. Life expectancy trebled and rates of childhood and maternal mortality plummeted. But with these successes has come a significant new challenge. Chronic diseases are on the rise and the Indian health system is ill-equipped to deal with them.

Disease is in a state of rapid transition in India. Just how rapid, is highlighted by the findings of a large new study of 20 developing rural villages in Andhra Pradesh conducted by the Institute in collaboration with The University of Queensland, Australia, the Byrraju Foundation, the Centre for Chronic Disease Control (CCDC) and the CARE Foundation in India. Results recently published in the journal *Diabetes Care* showed diabetes at levels usually found in developed, Western societies. 13% of those aged 30 or over were found to have diabetes and as many again showed signs of pre-diabetes.



The reasons for this transition to Western disease patterns in the developing rural sector of India are simple. Reasonable sanitation, a reliable food supply and basic health services reduce life-threatening malnutrition and fatal disease in childhood. More births progress to adulthood and most deaths occur in middle and older age. And, even in developing regions, the majority of deaths in middle and older age are attributable to chronic conditions like diabetes, smoking and high blood pressure.

Delaying death from childhood to older age is a major step in the right direction but a huge burden of chronic diseases results. In developing countries like India, conditions such as diabetes, blood pressure and cholesterol are often untreated. Complications occur years earlier than in developed countries. A much larger proportion of the population is afflicted at an economically-productive, younger age and the social and fiscal consequences are enormous. By 2015 it is anticipated that cardiovascular diseases alone will trim more than 1% from the gross domestic product of India.

The high levels of diabetes reported in this study from Andhra Pradesh are fortunately not representative of the whole of rural India. Villages surveyed were more developed than the average and had progressed further down the path of 'western' diseases than most. However, these villages provide a clear indication of what is looming for other parts of India. The next decade will see large sections of rural India reach comparable stages of development.

Soaring rates of cardiovascular diseases, cancers and injuries will almost inevitably ensue.

Fortunately, India is not without options by which it can address the new challenge presented by

chronic diseases. Health care in many areas is limited, both in terms of the services available and the capacity to pay for them. However, a basic, effective and nationwide primary health care infrastructure is in place. In part, the reason why modern India has to deal with chronic diseases is the success with which this service has addressed major infectious and maternal causes of ill health. Expanding the capacity of this largely non-physician service may be the best hope for an immediate low-cost assault on chronic conditions.

What India must not do is try and emulate the chronic disease care mechanisms of high-income countries. Western, physician-driven programs could provide a high cost solution for a wealthy few, but it will do little to contain the epidemic of chronic disease threatening the country. Novel low-tech and low-cost solutions that use only the most cost-effective and broadly applicable components of proven treatment and prevention strategies are both plausible and feasible.

In the case of diabetes and vascular disease, the results of decades of research in the West provide clear guidance about the form that such intervention programs might take. One strategy advocated by The World Health Organisation, for example, recommends simple, low-cost diagnostic techniques to identify high-risk individuals. With subsequent treatment using a range of safe, inexpensive and highly effective drug therapies. The key to this, and other such programs, is that they could be implemented by non-physician health care workers. This would ensure widespread and equitable access across India's social and economic strata.

One further significant asset in the battle against chronic diseases in India is the country's world-leading generic pharmaceutical industry. Generic drug treatments for cardiovascular

disease can dramatically cut the risks of heart attacks and strokes. There is ongoing innovation in generic treatment strategies such as the so-called 'polypill' for cardiovascular prevention (whereby several highly effective treatments are combined in one tablet). This promises further simplification of dosing regimens and three quarter reductions in the risk of premature death for just a few dollars a month.

The Government of India has a clear leadership role to play in the control of chronic diseases in India. Already, the government has at its disposal data that provide excellent insight into the extent, and principal causes, of chronic disease in the country. Likewise there is a wealth of data about ways that the causes of disease can be modified. What is missing is robust information about how the course of chronic diseases can be changed in very low income settings. While research findings about the determinants of disease transfer fairly well across societies, evidence about the practicalities of health service delivery does not.

The Indian Council of Medical Research and other local organisations can do much to aid the generation of sound evidence on which cost-effective health policy can be formulated. However, local access to resources for translational and operational research is limited and a pending epidemic of this magnitude requires a major response. Philanthropic organisations such as Gates, Rockefeller and Wellcome have enabled tremendous advances in the delivery of health care in developing regions. However, almost all of their investment has been on infectious, childhood and maternal conditions, the traditional scourges of less affluent countries.

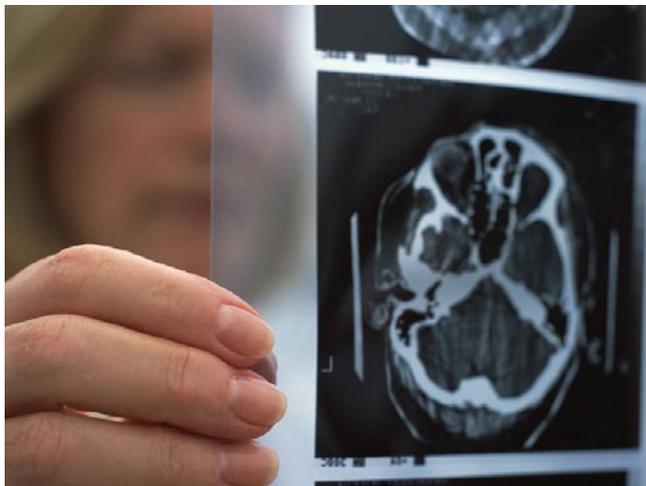
Billionaire Warren Buffet recently announced that he would donate much of his personal fortune towards global health initiatives. Mr Buffet showed tremendous vision in directing his donation through the Gates Foundation with its established and respected track record in the dissemination of philanthropic dollars. It can only be hoped that at least some of this new resource will be used to tackle the massive burden of chronic disease now afflicting developing countries.



Bruce Neal

The George Institute for International Health

Hard to predict depression after stroke



Researchers at The George Institute, in conjunction with The University of Auckland, New Zealand, have shown that predicting who will experience a mood disorder following stroke is extremely difficult.

Emphasizing the complex nature of abnormal mood or depression following stroke, the results of the study conducted in New Zealand found that "a simple, clinically applicable, predictive model appears difficult to develop" as published in *Stroke*.

Further studies by the same authors have indicated that at least one third of patients experience abnormal mood, or depression, after the onset of stroke. It is therefore vital to implement preventative strategies targeted at those patients most at risk.

Of the 739 patients involved in this aspect of the Auckland Regional Community Stroke (ARCOS) study, 27% met the criteria for abnormal mood six months after having a stroke. Researchers noted important predictors of mood disorders were increased disability and a history of depression. However, the sex and age of patients were not found to be predictors of abnormal mood following a stroke. These are key indicators of abnormal mood in otherwise well populations.

"Clearly numerous factors are likely to contribute to mood disorders," says lead author Dr Maree Hackett, Senior Research Fellow at The George Institute.

"Depression is a complex condition, which may explain why we were unable to reliably predict who experienced changes in mood after stroke. If we are not able to identify those at the greatest risk, we need to develop simple and safe preventative strategies that can be delivered to all stroke survivors"

"We also found two-thirds of patients who were experiencing abnormal mood in this study were not receiving any treatment. This presents a significant problem, and may reflect uncertainty among clinicians concerning the most appropriate treatment, inadequate follow-up of patients, insufficient access to healthcare services and unwillingness to receive a diagnosis or medication."

The role of the Neurological and Mental Health Division at The George Institute is to help bridge the gap between neurological conditions and mental disorders. Further work is planned to effectively develop preventative strategies for abnormal mood in stroke patients.

FOCUS ON CHINA

China Health Policy Roundtable Series III – ‘Access to Basic Health Care

The China Health Policy Roundtable on ‘Access to Basic Health Care Services’ took place on the 11 and 12 May 2006 in Beijing. This meeting was the final in a series of three Roundtables established under the auspices of a Memorandum of Understanding between the China Ministry of Health and the George Institute for International Health.

Around fifty participants from the public, private and non-profit sector, including senior delegates from the Chinese Government dedicated the meeting to discussing the key components of basic health care services in China. Notable delegates included HAN Qide, the President of Peking University, and Vice Chairman of the Standing Committee for the National People’s Congress. Jim Tulloch, the Principal Health Advisor to AusAID, officially opened the 2006 Roundtable meeting.

The Roundtable series aims to bring international health experts from the public and private sectors together with senior representatives from the Chinese Ministry of Health and other government departments to discuss and examine health policy issues relevant to China with the aid of international case-studies and research.

The 2006 Roundtable meeting included bilingual discussions and simultaneous interpretation for all participants throughout the two-day discussion. The four main sessions centered on:

- Financing for Basic Health Care Services in China:
 - The Role of the Government; and
 - The Role of the Insurance;
- Delivery of Basic Health Care Services in China:
 - The Role of Health Service Providers; and



International delegates gather in Beijing, May 2006 for the third annual China Health Policy Roundtable

“The Roundtable series aims to bring International health experts together.”

- The Management of Pharmaceuticals.

These sessions were followed by a key, final interactive ‘policy forum’, in which policy recommendations were distilled from the debate so far and drafted together in the group.

The meeting this year generated an intense debate on the challenges facing China in relation to basic health care services and delegates spent much of the time between sessions also discussing the issues. The key discussion areas of the meeting included:

- A ‘Whole of Government’ Approach to Health Reform
- Challenges for Financing Basic Health Care Services;

- Options for a Basic Health Care Package;
- Developing a National Drug Policy;
- Resource Allocation for Basic Health Care Services; and
- A Framework for Safe and Cost-effective Basic Health Care Services.

Following the Roundtable meeting, The George Institute, working in collaboration with members of an International Reference Group, prepared a policy report and recommendations based on the meeting outcomes. The report will be presented to the Ministry of Health for their consideration, and it is hoped to positively influence the health policy reform agenda in China.

Following the 2005 Roundtable meeting on ‘Health Care Safety in China’ and the presentation of the policy report to the Ministry of Health, the State Council of China established a National Safety Council to coordinate the national health care safety agenda. The Institute believes that this is evidence of the positive effect on health reform in China. Similarly it provides evidence to support the approach taken in



Services'

“This is evidence of the positive effect the Health Policy Roundtables have had and will continue to have on health reform in China.”

these discussions of providing international case-studies and practical experience for Chinese health-policy makers to consider and then apply and implement themselves in a way which will be most effective for the situation currently facing China.

Finally, The George Institute would like to acknowledge the generous sponsors of this year's Roundtable:

- AusAID, Australia
- The George Foundation, Australia
- HLSP Ltd, United Kingdom
- Merck Sharp & Dohme Ltd, China
- QANTAS Airways, Australia
- Joint Commission International, USA
- World Health Organization, Switzerland
- UnitedHealthcare International, Asia

A report from the 2005 Roundtable on 'Health Care Safety in China' can be found at www.thegeorgeinstitute.org. Further information on the Roundtable Series, the program for this year's meeting or official attendees list can be requested from amcdonald@george.org.au.



HAN Qide, Vice-Chairman of the Standing Committee of the China National People's Congress, China



Drivers distracted every six minutes

New results on driver distraction show that, on average, drivers engage in a distracting activity once every six minutes, frequently resulting in driving errors and road crashes. The George Institute study published in the international journal, *Injury Prevention*, shows that driver distraction causes one in five crashes reported by drivers.

The research, conducted by The George Institute and The University of Western Australia found that during a driving trip:

- 72% of drivers will display a lack of concentration,
- 69% will adjust in-vehicle equipment,
- 58% are distracted by outside events, objects or people, and
- 40% talk to passengers.

The survey involved more than 1300 drivers aged between 18 and 65 in New South Wales and Western Australia.

While driver distraction is extremely common, the rate of driver error following a distraction is of particular concern. Chief Investigator of the



study and Senior Research Fellow at The George Institute, Dr Suzanne McEvoy, said "These errors included braking suddenly, failing to see road signs and taking wrong turns. Most importantly, such errors can lead to crashes and this is a critical issue facing road safety authorities."

Young drivers, aged 18-30, were also found to be significantly more frequently distracted while driving. While this group perceived distracting behaviours to be less hazardous than older drivers, they were significantly more likely to crash as a result of being distracted.

Professor Mark Stevenson, Senior Director at The George Institute, Chair of the Australasian

College of Road Safety (Sydney), and co-author of the study, stressed the need for a strategy to minimise distracting activities while driving, with a strong focus on young drivers, "The exposure to distracting activities is high and action to reduce crashes caused by this behaviour is urgently needed. Policies that include driver education and innovative enforcement practices are essential to decrease the prevalence of these behaviours and thereby, reduce the adverse outcomes."

This study was funded by the Motor Accidents Authority of New South Wales (MAA).

Staff Profile



DR ANDRÉ PASCAL KENGNE

Clinical End-point Adjudicator, ADVANCE* Project,
MD, University of Yaounde in Cameroon

André Pascal joined The George Institute after leaving Cameroon in 2005, bringing a wealth of enthusiasm and knowledge of non-communicable diseases to the Cardiovascular Division.

André Pascal says the opportunity to work at "The George" came as a timely solution for his wish to dedicate more of his time to cardiovascular research, "Water always finds a way out is an African proverb, which best summarizes my journey to The George Institute."

Following his honor roll graduation as MD from the University of Yaounde in Cameroon, André Pascal immediately worked as a GP, and at the same time became involved in a number of research activities focusing on non-communicable diseases.

"Soon after, I decided to join the medical school. As I received my specialist training, it became obvious that research must be essential in any attempt to address the most prevalent medical problems in my field. At the end of 2002, I decided to expand on the research component of my activities."

After developing a strong interest in cardiology and a desire to contribute to high quality and high impact research, André Pascal knew he would have to leave Cameroon to explore the field further. Before departing however, "I worked in setting up the National Obesity Center in Yaounde to support the national cardiovascular prevention initiatives and lectured in a private University in Cameroon called Université des Montagnes, training junior colleagues."

His concern for the growing problems of cardiovascular disease and in particular the impact on people with diabetes is a perfect fit for his current role at The George Institute. As End-Point Adjudicator for the ADVANCE* project, André Pascal's major focus "is around cardiovascular risk evaluation in people with diabetes. The project will provide new evidence about widely practical treatment strategies for the prevention of the vascular complications of diabetes".

Also currently enrolled as a student at The University of Sydney, André Pascal's time is spent working on his PhD "Cardiovascular risk evaluation in people with diabetes on a global perspective"

"My challenge is to be sure that I am useful to myself and to those who may need my service. It is my dream to be able to contribute to raising the awareness of cardiovascular diseases as a high priority in developing countries, with particular reference to Africa."

*See www.thegeorgeinstitute.org for details.

The John Chalmers Oration

Before joining The George Institute for International Health, Professor John Chalmers served at Flinders University School of Medicine and Flinders Medical Centre with great distinction.

The John Chalmers Oration was established to honour John's achievements during 21 years of service to Flinders Medical Centre and Flinders University School of Medicine between 1975-1996.

Each year, speakers at The John Chalmers Oration are reminded of John's combination of enormous energy, intellectual capacity and outstanding administrative and research skills. The Oration plaque reads "His pursuit of excellence and his professional achievements as the Inaugural Professor of Medicine laid the foundations for the impressive reputation

of both the School and Medical centre. As an innovator in Undergraduate and Postgraduate Medical Education, adviser and mentor to outstanding young graduates shaping their future careers, he has produced a lasting impact on the Australian health environment."

Staff at The George Institute and Flinders University know John as an engaging personality, with his direct approach and incisive mind. Recognised as an inspirational leader, he generates enormous loyalty, cohesion and commitment from those who work with him. The George Institute is proud to benefit from his tireless efforts as a Senior Director and Head of the Research Advisory Unit, which sees him contributing to the strategic planning of research and development in the Institute.



A portrait of John Chalmers displayed at Flinders University Medical Centre honours the oration

The John Chalmers Award

In acknowledging John's many successes and in appreciation for his time and encouragement of young researchers at The Institute, The John Chalmers Award was established in 2002.

The Award recognises outstanding research undertaken by doctoral students and post-doctoral fellows of The Institute. The annual award is given to the best original paper published in a scientific journal during the previous calendar year.



John Chalmers congratulates Suzanne McEvoy, Alex Martiniuk and Fiona Turnbull at the John Chalmers Award Ceremony on 23 August 2006

2006 Winners

The John Chalmers Post-Doctoral Award:

Alex Martiniuk - The fraction of ischaemic heart disease and stroke attributable to smoking in the WHO Western Pacific and South-East Asian regions, published in *Tobacco Control*.

Joint winners of The John Chalmers Doctoral Award:

Suzanne McEvoy - Role of mobile phones in motor vehicle crashes resulting in hospital attendance: a case-crossover study, published in the *British Medical Journal*.

Fiona Turnbull - Effects of Different Blood Pressure-Lowering Regimens on Major Cardiovascular Events in Individuals With and Without Diabetes Mellitus, published in the *Archives Internal Medicine*.

THE JOHN CHALMERS ORATION PRESENTERS:

1998 PROFESSOR JOHN FUNDER AO

1999 DR NEIL BLEWETT AC

2000 DR LOWITJA O'DONOHUE AC

2001 THE RT HON MALCOLM FRASER AC

2002 PROFESSOR PETER DOHERTY AC

2003 THE HON DR BRENDAN NELSON

2004 PROFESSOR FIONA STANLEY AC

2005 EMERITUS PROFESSOR
SIR GUSTAV NOSSAL AC

2006 PROFESSOR SIR MICHAEL MARMOT

Staff Profile



MR. LAURENT BILLOT
Head, Statistical Services
MSc

Before joining The George Institute as Head of Statistical Services earlier this year, Laurent said goodbye to friends and family in France and travelled 'down under' to Australia and New Zealand in October 2005 for some 'R&R'. A keen hiker and nature-lover, what Laurent likes best about Sydney and Australia is "The natural environment, the warm climate, and the fauna and flora."

In addition to the new and diverse landscape of Australia, Laurent was enthusiastic about working for The George Institute. "I was attracted to the not-for-profit status of the Institute and the mix of academic and commercial work. Compared to the pharmaceutical industry, I felt like the Institute would provide me with more diversity and a richer career perspective."

Laurent's role in Statistical Services is to coordinate the statistical resources across the different projects conducted by the Institute. "My task is to develop standards and procedures for good clinical practice and quality control, and obviously provide statistical support. I am currently involved in a number of projects with the Institute (such as ADVANCE, Interact, INIT2, NICE, BPLTTC*)." "I also love SAS programming," says Laurent. "This is widely used statistical software based on a specific programming language. It is used by The George Institute to produce statistical analyses."

Whilst studying his Masters of Statistics and Computer Science at the University of South-Brittany, Vannes, in France, and after work placement as a statistical consultant at Statistics Collaborative in the US, Laurent decided to complete a degree at University Rene Descartes, Paris, France focusing on biostatistics and epidemiology.

Laurent then joined the School of Public Health as a Statistician in Nancy, France (1999-2001) before returning to Statistics Collaborative in the US as a biostatistician.

In the future, Laurent would like to "Expand my experience in statistics and medical research, and possibly do some teaching."

In the meantime, Laurent will continue to enjoy regular hiking trips. "Sydney is great. I enjoy being near the ocean and having access to several national parks. I am thinking of joining a bushwalking club in the spring."

*Further information on these projects can be found at www.thegeorgeinstitute.org.

The George, Berman and Julius form 'The Academic Alliance for Clinical Trials'

BERMAN CENTER
FOR OUTCOMES AND CLINICAL RESEARCH


THE GEORGE INSTITUTE
for International Health

Julius Center
Health Sciences and Primary Care

In a move to assemble a diverse range of expertise, The George Institute for International Health has formed a world-first, academic research alliance. Through a single umbrella organisation, the Academic Alliance for Clinical Trials (AACT) brings together a broad spectrum of services, and the capacity to deliver high impact research on a global basis.

The AACT coordinates resources of three major international clinical research centres and affiliated academic institutions. These include the MMRF Berman Centre for Outcomes and Clinical Research/ Coordinating Centre for Biometric Research (University of Minnesota, USA), The George Institute for International Health, (University of Sydney and Peking University, Australasia) and The Julius Centre for Health Sciences and Primary Care (University Medical Centre Utrecht, Europe).

The Alliance is focused on reducing the incidence and impact of global disease through high-calibre research, exploring new approaches to preventing and treating chronic disease, and advancing evidence-based improvements and innovation in health practice and policy.

Together, the partners share an extensive track record in clinical research, and have established reputations as key thought and opinion leaders in their respective research fields and in the wider academic community. The AACT's collaboration of clinical and academic resources offers both public and private organisations access to good science and quality research conduct on a global, coordinated basis.

The Alliance has established primary and specialty care research networks that extend across the globe, and include over 1000 collaborating centres in five continents. Selected based on quality performance and alignment with AACT's mission, the networks include centres in highly-developed regions such as the US, Western Europe and Australasia plus culturally competent centres, researchers and staff in emerging regions such as India, China, South East Asia and Eastern Europe.

The AACT is likely to attract increased research funding from potential sponsors of large-scale international research, and thus promises to strengthen the research capacity of The George Institute, and increase its impact on health policy and clinical practice. Joining forces with both The Berman Centre and Julius Centre will help raise the bar in the conduct of world-class clinical research and reinforce the Institute's commitment to improving health where it is most needed.



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