

## In this issue ...

Whenever the new millennium begins, the end of 1999 was a time for reflection. This is also a time of looking forward and in this issue the members of the Executive Editorial Board of *Australian Prescriber* speculate on the future of their specialties.

In the past century the management of wounds has dramatically improved. Donald MacLellan updates us on the new approach to chronic wounds. Some wounds require surgery, but there are particular problems if the patient is anticoagulated. Rohini Sridhar and Andrew Grigg provide helpful advice on how to manage patients taking warfarin when they need surgery.

In addition to advances in treatment there have also been developments in diagnostic tests. Michael Pain reviews some of the respiratory function tests which were once research tools, but are now used in everyday practice.

One of the problems of everyday practice is remembering all the effects drugs can have on normal physiological functions. Barry Saker reminds us of some of the commonly prescribed drugs which can affect the kidneys. Patients with renal problems may be interested in the work of the Australian Kidney Foundation which has provided the information on page 20.

The electronic version of *Australian Prescriber* has greatly increased the journal's international readership. Apart from the title, the previous cover had no distinctive features identifying Australia. To correct this anomaly, the Executive Editorial Board has selected a new cover with Aboriginal art as its focus. The painting was created for National Medicines Week in 1998 and tells a story of the quality use of medicines. This story is best told by the artist herself, Jennifer Summerfield (see page 19).

## EDITORIALS

# A century of progress in cardiovascular medicine

*P. J. Fletcher, Professor of Cardiovascular Medicine, and Director, Cardiovascular Department, John Hunter Hospital, Newcastle, N.S.W.*

*(Aust Prescr 2000;23:2)*

Cardiovascular medicine is fortunate to have a wealth of clinical trials providing a solid evidence base from which the clinician can make an informed choice of appropriate, efficacious and cost-effective therapies. This trend will continue because of the growing commitment worldwide to the principles of evidence-based medicine.

The progressive fall in age-adjusted cardiovascular mortality, which has been one of the remarkable success stories of the last 25 years, will continue in this millennium. However, even with this improvement, because of the ageing of the population, the total burden of cardiovascular disease on the health care system and on society will continue to increase.

Nowhere will this be more evident than with cardiac failure. Clinical trials will continue to provide evidence of therapies which reduce mortality and need for hospitalisation. However, producing a clinically meaningful improvement in quality of life in this terrible disease may remain an elusive goal. This is

because none of our therapies, other than heart transplantation, has so far managed to influence the fundamental problem of loss of myocardium.

There is the potential for molecular biological techniques to address this issue. Myocardial cells have always been considered as terminally differentiated, from shortly after birth. By unlocking the secrets of the processes which control cell differentiation and division, scientists will soon be able to produce new myocardial cells. This will be the first step in a process which has the potential, in the longer term, to repair the damaged heart.

However, it is in the area of pathogenesis and pathophysiology of disease that these molecular approaches will have their greatest impact. Scientists are just starting to reap the rewards from studying animals with either selective deletions or selective over-expression of specific genes. This allows them to test hypotheses about the role of the gene and its product in the pathogenesis of particular diseases.

# Drug therapies for children at the end of this century

*Noel Cranswick, Clinical Pharmacologist, Royal Children's Hospital, Melbourne*

*(Aust Prescr 2000;23:3)*

It is only in the 20th century, that we (society) have recognised that children are different to adults. Previous generations would dress children up as adults and often send them out to work at an early age, unable to recognise their social and developmental vulnerability.

Our knowledge of therapeutics in children is languishing, even though many influences on our current use of drugs are based upon mistakes made which affected children (e.g. thalidomide). The end of the 20th century has brought with it a renewed interest in the uniqueness of children and their treatment.

Initial attempts by the American Food and Drug Administration to address the 'vulnerable child' resulted in legislation to ensure that only studies of the highest quality were performed in children. The unfortunate result was that even fewer trials were performed in the young. Children have been identified as

therapeutic orphans (only 20% of drugs licensed in Australia have paediatric information). There are now incentives, such as extension of marketing exclusivity, to perform studies in children. I hope that this will result in children having full access to the medicines that they need.

This century will further encourage the safe and efficacious use of medicines in children and adults. The human genome project will have defined many of the differences that currently confound our use of drugs. Drugs and doses will be individualised depending upon individual genotype and phenotype (defined by simple bedside testing). The 'numbers needed to treat' statistic will be a thing of the past. No longer will evidence-based medicine meta-analysis be required for treatment of a population – appropriate therapy will be aimed at individuals based upon their unique characteristics. By the start of the 22nd century, many of the therapeutic approaches in current practice will be considered as antiquated as we now consider the widespread therapeutic use of arsenic.

## Ageing in the millennium

*S. Kanagarajah, Head, Geriatric Medicine, Illawarra Area Health Service, Warrawong, N.S.W.*

*(Aust Prescr 2000;23:3)*

The 20th century has seen a huge change in both longevity as well as social attitudes to ageing. The increase in life expectancy has been due to dramatic improvements in public health, and the application of medical science. The rate of knowledge increase in molecular biology and genetics, in particular, has meant that it is extremely difficult to predict the impact of this on 'healthy ageing'. While cardiovascular disease remains the main cause of mortality and morbidity<sup>1</sup>, current treatment options are likely to change dramatically, even within the foreseeable future.

There is much concern that we will survive longer, only to be disabled and therefore dependent on the rest of society. We therefore face very complex questions about how evolving medical advances as well as social changes will impact on the ever-increasing proportion of elderly people. Australia has been a world leader in developing effective and efficient

community-based support and rehabilitation for the disabled elderly. However the costs of social support and residential care continue to spiral.

What then will be the role of the doctor and prescriber in this ageing society in the future? While advances will reduce the proportion of disability due to disease, it is likely that there will be a significant (and probably increasing) group of vulnerable elderly people who are dependent, especially on their doctors. These people may not be 'curable', but their lives will be enriched immensely by an empathetic relationship with their doctor which allows them to maintain their autonomy and dignity, have access to wisely applied scientific advances and retain their position as valued members of society.

#### REFERENCE

1. Kelly DT. 1996 Paul Dudley White International Lecture. Our future society. a global challenge. *Circulation* 1997;95:2459-64.

## Interesting times

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*John Marley, Professor, Department of General Practice, University of Adelaide, Royal Adelaide Hospital, Adelaide*

*(Aust Prescr 2000;23:4)*

There is an ancient curse, 'may you live in interesting times'. For the latter half of the 20th century it seems that general practice has been its victim. In most countries general practice has gone through multiple re-organisations, profound lows and some major highs. Eventually, governments that have to pay for the delivery of medical care, come round to support for general practice. This is not out of altruism, but a recognition that general practice provides care, which is extremely cost-effective.

The therapeutics revolution following World War II has seen many infectious diseases virtually disappear and conditions which required surgery, such as peptic ulcer disease, as well as others such as hypertension, become almost exclusively treated in general practice.

In prescribing, the uptake of computerised prescription writing is bound to become universal. With it, will come much better decision support systems. These will cope with the uncertainties of general practice in a way that hard line evidence-based medicine currently does not.

General practitioners will work in teams, with other health professionals doing tasks that medical practitioners do not need to do. This already happens in many other countries such as Canada and Holland, and is a liberation rather than a threat. In rural practice, the only viable way to deal with the shortage of rural practitioners is to restructure the way in which medical care is delivered.

In Australia, one of the most highly sought after postgraduate trainings is now general practice. This century is beginning as the last century did, with the bulk of medical care being delivered in general practice.

## Whither psychiatry: what might the future hold?

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*John W. G. Tiller, Associate Professor and Reader, University of Melbourne, Royal Melbourne Hospital, and Director, Academic Psychiatry Unit, Albert Road Clinic, Melbourne*

*(Aust Prescr 2000;23:4)*

Mental illness should be a health priority as it is the major cause of community morbidity and untreated illness is a major community cost.

Effective medicines have allowed the community management of patients who previously required prolonged hospitalisation. This process is dependent on developments in psychopharmacology, improved community support and changed attitudes regarding the role of hospitalisation which is now predominantly used for crisis intervention. There has been a major change from the past of shamanism through to alienists and humane therapy with few effective treatments, to a better understanding of the biology of

mental illness and its treatment. There is hope for major improvements in treatment with the results of gene studies and the human genome project, better understanding of molecular biology, more effective drug design and improved drug evaluation. However, in the immediate future there is no indication that newer medicines will have greater efficacy than those currently available. Better community awareness and more widespread psychological and social interventions may improve outcomes with available treatments.

Psychiatry is a part of medicine. It can integrate knowledge from psychology and sociology with the new biology. This will lead to a better understanding of the processes of disease and recovery and ultimately improved treatments.

# Conquering chemotherapy

*J. S. Dowden, Editor*

*(Aust Prescr 2000;23:5)*

Few reading this journal in 2000 will live to see the next century; death for all is inevitable. There should be an increased focus on how we die. As great advances have been made in reducing cardiovascular mortality, the relative importance of cancer will increase.

Chemotherapy can cure certain cancers. Unfortunately, in advanced cancers chemotherapy often merely delays the inevitable, sometimes only for a few weeks. In that short time the patient may have to endure unpleasant adverse effects. Chemotherapy aims to destroy all dividing cells, in the hope that normal cells will recover faster than cancer cells.

Patients are poisoned to the edge of their existence and products such as G-CSF allow us to push them even closer to the precipice. Some patients will fall because of their treatment rather than the disease.

The ability to destroy abnormal cells while sparing normal tissues has a strong appeal. Although it is still in its infancy, immunotherapy could be the way forward. There have been attempts to put the theory into practice, but there is a need to find antigens which are more specific for tumour cells.

I hope that by the end of the next century, we will be able to use the body's own immune system to fight cancer. This would allow us to consign aggressive chemotherapy to the list of twentieth century treatments, which already seem medieval.

## Letters

Letters, which may not necessarily be published in full, should be restricted to not more than 250 words. When relevant, comment on the letter is sought from the author. Due to production schedules, it is normally not possible to publish letters received in response to material appearing in a particular issue earlier than the second or third subsequent issue.

### St. John's wort

Editor, – I enjoyed reading Professor Mitchell's article on *Hypericum perforatum*, 'St. John's wort – quack medicine or novel antidepressant treatment?' (Aust Prescr 1999;23: 112–3). It is nice to see some openness about herbal medicine in the medical profession. I would like to comment on hyperforin, one of the active ingredients in hypericum. It is true that studies have confirmed the antidepressant activity of hyperforin, however, this compound is very unstable, especially during the drying process of the herb, hence it is unlikely that the extracts which have been shown to be effective in many different clinical trials contained any hyperforin. Yet they worked. The hypericums may not have antidepressant activity in their isolated form, however one study has shown that oligomeric procyanidins (OPCs) are necessary for the bioavailability of hypericum. Hypericum extracts are now being marketed which are standardised to both hypericum and hyperforin, however these are only marker compounds for quality control. When the whole herb extract is used, St. John's wort is a safe and effective medicine for depression, anxiety and tension.

Michael Thomsen  
Medical Herbalist  
South Hobart, Tas.

### Antidepressants

Editor, – I refer to the articles on the new antidepressants (Aust Prescr 1999;22:106–8, 108–11). I have read elsewhere that antidepressants have not been shown to work better than an active placebo such as bextropine mesylate. Active means a placebo that makes you feel as though you are taking something by producing adverse effects such as a dry mouth.

Could one of the authors of your recent antidepressant articles comment?

Kevin O'Dempsey  
General Practitioner  
Kallangur, Qld.

*Associate Professor T.R. Norman, the author of 'The new antidepressants – mechanisms of action', comments:*

'Active placebos' have been employed occasionally in controlled evaluations of antidepressant drugs. Most often these have been used in tricyclic antidepressant trials to maintain the 'blind' as these drugs are well known for their anticholinergic effects and can often be distinguished from placebo on this basis. Over the course of evaluation of new antidepressants some trials will show no significant difference from placebo, but the weight of clinical evidence is that the new antidepressants are clearly more effective than placebo. Several reasons for the failure to distinguish a psychotropic medication from placebo can be recognised, such as inclusion of incorrect diagnostic groups, mild forms of depressive illness, failure to include a placebo washout period prior to commencing trial medication, and non-compliance with the study drug. Non-specific factors in treatment are also important and the psychotherapeutic aspect of a patient regularly consulting with someone willing to listen to their problems cannot be ignored. Furthermore, it should be recognised that the natural history of depression is for recovery to eventually take place, without treatment. (Medications can considerably shorten the period to recovery.) Clearly, if patients are at the point of recovery then any treatment, active drug or placebo, will apparently be 'successful'.