argument we need more, not fewer, new drugs.

Perhaps this relative paucity reflects the limitations of our old methods for drug discovery. However, the relative paucity of solutions demands new solutions and new technologies, not a retreat.

During the last 20 years new indications have emerged for older drugs, for example ACE inhibitors in acute myocardial infarction and (with indapamide) in prevention of secondary stroke, aldosterone antagonists and beta blockers to reduce mortality in heart failure, and the use of antibiotics to treat peptic ulcer. When a drug is first developed its ultimate indications (and degree of innovation) may not be recognised. At the same time, we have seen, frighteningly rapidly, the emergence of antibacterial, antimalarial and antiviral drug resistance, making some old drugs progressively less effective.

The need for new drugs is obvious – for old and new infections, as well as for the chronic diseases mentioned by Burnet – and there is enormous potential for the development of new drugs. According to the WHO Report on Genomics and World Health:

> It has been estimated that successful drug therapy currently is directed at fewer than 500 targets. Considering that the human genome contains some 30 000 genes, it is possible that its study could lead to at least 3000 to 5000 potential new targets for therapy. Currently, predominant candidates include G protein-coupled receptor families and other receptors and related molecules, a wide range of enzymes including proteases, kinases and phosphatases, hormones, growth factors, chemokines, soluble receptors and related molecules, and many others. Exactly the same principles are being applied to the search for agents to interfere with key biochemical pathways in pathogens, based on information which is being obtained from the pathogen genome project.[4]

Just as discoveries in the old disciplines of chemistry and biochemistry in the early 20th century took many years to translate into new drugs, so it will take time to learn how to realise the potential of the new discipline of genomics. But learn we must.

If a potential drug discovery/innovation/invention is not patented, it will never find its way into practice. With new drugs said to cost around $1 billion to bring to market, investment will only be made if patent protection is assured. If the degree of 'real innovation' must be predetermined, based on previous experience, valuable therapies may be lost. Whatever our differences of emphasis, the ultimate goal is the same: effective, accessible, affordable medicines for all.

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Conflict of interest: none declared

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.

Quality use of medicines – prescribing for manufacturers or patients?

Editor, – I refer to the editorial 'Quality use of generic medicines' (Aust Prescr 2004;27:80–1).

Confusion resulting from the availability of multi-sourced brands of medications is predictable within our rapidly changing prescribing and dispensing environments.

For decades, prescribing by manufacturers' brand names was manageable when most medications were available as a single brand. It should also be noted that brand names are required for all products as part of Therapeutic Goods Administration (TGA) regulatory requirements.

Australia has a growing generics segment. This is synonymous with growing numbers of brands of the same medications and it is time for current prescribing practices to be reviewed to determine better ways to manage multi-sourced brands.

An Australian Pharmaceutical Advisory Council (APAC) subcommittee has concluded that Australia should move towards increased use of active ingredient names. In the UK, this has served to educate the public and health professionals to identify medications, primarily, by their international (approved) active ingredient names and not by local, brand names.

As per the authors' comments, increased prominence of active ingredient names is being recommended by various health committees to assist patients and professionals.

An APAC subcommittee will shortly deliver a report on the management of these issues. This report will address concerns about confusion related to over-reliance by all stakeholders on brand names. The process has begun to make some simple but essential improvements to the management of all medications by speaking and writing more in the language of medicine and less in the language of marketing.

Mike Hobbs
Director, Sales and Marketing
Hexal Australia
Pyrmont, NSW

Thiazolidinediones

Editor, – The article 'Thiazolidinediones – mechanisms of action' (Aust Prescr 2004;27:67–70), states that 'hepatotoxicity does not seem to be associated with the other two compounds (pioglitazone, rosiglitazone)'. Although admittedly this may be referring to the rare but fatal cases of hepatotoxicity associated with troglitazone, it does seem somewhat at odds with the ADRAC Bulletin. This reported on 16 cases of hepatic adverse reactions including elevated liver function tests, jaundice, hepatitis and hepatocellular damage. Although it does add the rider that 'liver enzyme levels may be elevated with diabetes or obesity'.[1]

Derek Grubb
Pharmacy Department
Bunbury Regional Hospital
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Reference

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Dr J.R. Greenfield and Professor D.J. Chisholm, the authors of the article, comment:

In contrast to troglitazone, which was withdrawn because of rare but fatal liver failure, placebo-controlled trials show that the risk of liver function abnormalities (reversible elevations of alanine transferase greater than three times the upper limit of normal) in patients treated with pioglitazone or rosiglitazone is 0.2–0.3% and not different from placebo-treated patients.[1] While rare case reports of hepatocellular injury and hepatic failure have been described in patients treated with these newer drugs[2], whether liver dysfunction can be definitively attributed to the thiazolidinedione has been challenged.[3] As Mr Grubb acknowledges, liver function may be abnormal in patients with diabetes and/or obesity, particularly due to non-alcoholic fatty liver disease. Furthermore, liver function may actually improve following treatment with these drugs, due to a reduction in hepatic lipid content.[4] As stated in our article, and the accompanying paper (Aust Prescr 2004;27:70–4), and by the Adverse Drug Reactions Advisory Committee, pharmacovigilance with periodic tests of liver function is recommended, despite the safety of pioglitazone and rosiglitazone.

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3. Freid J, Everitt D, Boscia J. Rosiglitazone and hepatic failure. Ann Intern Med 2000;132:164.
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Warfarin: balancing the benefits and harms

Editor, – As an eye surgeon I was surprised to read that warfarin was contraindicated when eye surgery was contemplated (Aust Prescr 2004;27:88–92). Given that cataract surgery is one of the most common elective surgical procedures performed in this country and most patients are aged over 65, this advice was somewhat at odds with accepted practice. A number of papers have looked at this issue and a study from New Zealand suggested that there was no greater risk of adverse events in patients undergoing surgery being maintained on warfarin, provided their INR was between 2.0 and 2.5.[1]

T. Hodson
Ophthalmologist
Mount Gambier, SA

Reference

1. Morris A, Elder MJ. Warfarin therapy and cataract surgery. Clin Experiment Ophthalmol 2000;28:419-22.

Dr M. Borosak, Ms S. Choo and Professor A. Street, the authors of the article, comment:

The contraindications to warfarin indicated in the article were obtained primarily from the product information. The relevant paragraph indicates that any circumstance where the 'hazard of haemorrhage might be greater than the potential clinical benefit of anticoagulation' may constitute a contraindication. It goes on to say that examples of these circumstances **may** be haemorrhagic tendencies and blood dyscrasias, recent or contemplated surgery of the central nervous system, the eye or traumatic surgery resulting in large open surfaces. The

risk:benefit analysis is the key to the decision making related to what is considered a contraindication.

This view is also supported by a study of the management of anticoagulation before and after elective surgery, which presented figures pertaining to such a risk:benefit analysis. The absolute risk of thromboembolism associated with a few days of perioperative subtherapeutic anticoagulation is generally very low while the risk of bleeding if anticoagulated may be relatively high.[1]

The study quoted by Dr Hodson describes a retrospective review of 28 cataract patients being treated with warfarin (outcomes were available for 23 eyes) who had INRs ranging from 1.0 to 2.4 (median 1.5). There were four haemorrhages, all of which were visually not significant, and there were no thromboembolic phenomena. The conclusion was that with modern techniques cataract extraction can safely and effectively be performed in patients taking warfarin who have an INR of approximately 2.0.

It is our opinion that in all perioperative circumstances the patient's individual risk factors for thrombosis and haemorrhage should be considered before a decision is made to maintain warfarin therapy and the INR level above 2.0.

Reference

1. Kearon C, Hirsch J. Management of anticoagulation before and after elective surgery. N Engl J Med 1997;336:1506-11.

Antibiotic prescribing

Editor, – In the article 'Antibiotic prescribing: how can emergence of antibiotic resistance be delayed?' (Aust Prescr 2004;27:39–42) I note the emphasis on using these drugs for the shortest time possible. Is it time to change our advice to patients to 'make sure you complete the course, even if you feel better after a few days'?

The reason for this advice appears to be twofold. Firstly, the infection will recur if incompletely treated. Secondly, the emergence of resistance is facilitated by shorter courses of antibiotics, presumably because relatively resistant strains of the pathogenic bacteria may still be viable at the end of such a course. However, is complete eradication of the pathogen desirable or necessary in the clinical world of bacterial tonsillitis, severe otitis media, bacterial sinusitis, bacterial gastroenteritis, urinary tract infection, impetigo and chest infection? Do we actually have any evidence relating duration of antibiotic courses, emergence of resistant pathogens, and clinical 'cure' in these conditions?

Nancy Sturman
General practitioner
Indooroopilly, Qld

Dr J. Ferguson, the author of the article, comments:

The situation is complex and varies according to the infected site. With infections such as otitis media, when antibiotics are used, the counsel is now to use 'short and sharp' – an adequate dose to eradicate the pneumococcus and short duration to avoid extended selective pressure. Generally, the longer the course, the greater the selective pressure. This is facilitated by the number of bacteria present – an undrained abscess with pseudomonas will see quick emergence of resistance whereas a patient with streptococcal endocarditis will not have resistance emerge despite several weeks of therapy (the bacterial count is much lower and the intrinsic character of the organism less liable to mutational or other resistance acquisition).

Insulin glargine

Editor, – I would like to draw your attention to the review of insulin glargine (Aust Prescr 2004;27:50–1), particularly the statement that insulin glargine is not suitable for use in patients with type 2 diabetes.

Insulin glargine has an indication for use in type 2 patients in its approved product information. The use of insulin glargine in this patient group continues to be supported by a large body of clinical trial evidence, as well as postmarketing experience in many countries where it has been used in clinical trials or commercially available for almost five years.

The review, which referred to guidelines prepared by the National Institute for Clinical Excellence (NICE) in the UK, has omitted the important qualifying information which NICE made to its general advice on the use of insulin glargine. These guidelines in fact specify quite distinct groups of patients in which insulin glargine should be considered, which taken together account for a significant proportion of all patients with type 2 diabetes.[1]

In addition, the claim that 'long-term effectiveness of insulin glargine is currently unknown' is, we believe, out of date. There are several published studies involving insulin glargine lasting up to 52 weeks in duration. There is no evidence to date that the effectiveness of insulin glargine diminishes with time.

James Robertson
Senior Medical Advisor
Aventis Pharma
Lane Cove, NSW

Reference

1. National Institute for Clinical Excellence. Guidance on the use of long-acting insulin analogues for the treatment of diabetes – insulin glargine. London: NICE; 2002. http://www.nice.org.uk/pdf/53_Insulin_analogues_full_guidance.pdf [cited 2004 Nov 8]

Editorial comment:

The *Australian Prescriber* comment accurately reflected the conclusion of the National Institute for Clinical Excellence (NICE) that insulin glargine 'is not recommended for routine

use for people with type 2 diabetes who require insulin therapy'. The NICE recommended that insulin glargine should only be considered, in type 2 diabetes, for patients:

- who require assistance from a carer or healthcare professional to administer their insulin injections
- whose lifestyle is significantly restricted by recurrent symptomatic hypoglycaemic episodes
- who would otherwise need twice-daily basal insulin injections in combination with oral antidiabetic drugs.

Medicines Australia Code of Conduct: breaches

Medicines Australia (formerly the Australian Pharmaceutical Manufacturers Association) has a code of conduct to guide the promotion of prescription drugs in Australia.[1,2] The annual report of the Code of Conduct Committee for 2004 is now available on the Medicines Australia web site.[3] Since the previous summary in *Australian Prescriber*[4] the Code of Conduct Committee has resolved 17 complaints. In nine cases there was at least one breach of the Code (Table 1).

Only three complaints were made by healthcare professionals. Most of the complaints were made by companies about their rivals' promotional materials. These promotional materials have to be withdrawn if they are in breach of the Code, however by the time a complaint is resolved the advertising campaigns may have concluded.

There seems to be a growing concern about the promotion of prescription medicines to the general public. Several complaints involved the connection between companies' products and the information on web sites about related topics. There was also a complaint about a television advertisement, but this was not upheld. More details about the complaints can be found in the annual report.[3]

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1. Roughead EE. The Australian Pharmaceutical Manufacturers Association Code of Conduct: guiding the promotion of prescription medicines. Aust Prescr 1999;22:78-80.
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Table 1

Breaches of the Code of Conduct January – June 2004

Company	Drug involved in complaint		Sanction imposed by Code of Conduct Committee
	Brand name	Generic name	
AstraZeneca	Nexium	esomeprazole	withdrawal of promotional material $10 000 fine
Eli Lilly	Cialis web site	tadalafil	withdrawal of reference to prescription-only drug
GlaxoSmithKline	Seretide	fluticasone/salmeterol	withdrawal of promotional material $5000 fine
Merck Sharp & Dohme	starter packs supplied to a member of the public		$30 000 fine
Novo Nordisk	NovoSeven	eptacog alfa	withdrawal of promotional material corrective letter to specialists $20 000 fine
Pfizer	Viagra web site	sildenafil	withdrawal of reference to prescription-only drug
Sanofi-Synthelabo	Panadeine Forte	paracetamol/codeine	withdrawal of promotional material $10 000 fine
Schering Plough	Caelyx	doxorubicin	withdrawal of promotional material corrective letter to specialists $10 000 fine
Schering Plough	Pegatron media release	peginterferon alfa-2b	withdrawal of promotional material corrective letter to specialists $30 000 fine