Chloroquine-induced retinal toxicity

To the Editor: Dr Rivett's letter on chloroquine-induced retinal toxicity[1] requires comment.

For Dr Rivett to state that 'many patients develop profound visual loss every year as a result of chloroquine toxicity' is misleading. We comment on three aspects:

1. Data referring to choloroquine alone are scant, as many authors deal with antimalarials as a group. MacKenzie[2] was probably the first to examine the issue after it became accepted that retinopathy had been identified as a potential problem. He quotes data clearly establishing a dose-related effect. Of 928 patients treated with between 2.0 and 3.7 mg/kg/d of chloroquine 'for years', none developed retinopathy. The incidence of pigmentary degeneration *without scotoma or visual loss* increased to 6% at doses above 4.6 mg/kg/d. At doses estimated to range from 11 to 33 mg/kg/d, chloroquine is associated with a sharply rising incidence of scotomas and decreasing visual acuity. Despite these findings there are widely quoted figures for visual loss in the literature, ranging from 0.001% to 40%.[3] Easterbrook,[4] a leading ophthalmologist, concludes that 'the incidence of retinopathy is very low at doses of less than 6.5 mg/kg/day of hydroxychloroqine or less than 3.0 mg/kg/day chloroquine . . .', and this probably sums up our current state of knowledge on this subject.

This matter has received considerable attention in the dermatology and rheumatology literature, and we would assume that most of our colleagues follow the published guidelines (as published in Dr Rivett's letter.)

2. Chloroquine appears to be a more effective drug than hydroxychloroquine.[5] Removing the drug from the market and replacing it with one that is less potent only risks exposing our patients to potentially more toxic alternatives.

3. While both hydroxychloroquine and chloroquine induce retinal damage, it is generally accepted that the former is less toxic. The general opinion is that patients on either drug require monitoring. The debate at the moment is the most cost effective manner to achieve this.[4]

It is unfortunate that the contents of Dr Rivett's letter were reported in a local paper, which could only have generated anxiety in any patient taking this generally very safe drug.

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1. Rivett K. Chloroquine-induced retinal toxicity (Scientific letter). *S Afr Med J* 2004; **94:** 41.
2. McKenzie AH. An appraisal of chloroquine. *Arthr Rheum* 1970; **13:** 280-287.
3. Easterbrook M. Ocular effects and safety of antimalarial agents. *Am J Med* 1988; **85:** suppl 4A, 23-29.
4. Easterbrook M. Screening for antimalarial toxicity: current concepts. *Can J Ophthalmol* 2002; **37:** 325-328.
5. Felson DT, Anderson JJ, Meenan RF. The comparative efficacy and toxicity of second line drugs in rheumatoid arthritis. *Arthr Rheum* 1990; **33:** 1449-1461.

Prescribed minimum benefits or minimum prescribed benefits?

To the Editor: Discovery Health notes the contents of Professor Rayner's submission to the *SAMJ*.[1]

If we had had the opportunity to reply before publication, we would have been able to confirm that the medication prescribed for the patient mentioned in the article was approved within our appeals process on 5 July 2004, before publication of the *SAMJ*. We take umbrage that we were not afforded the opportunity to address and comment on Professor Rayner's concerns before publication. It is unfortunate that we have had to write this letter retrospectively, especially as it may not reach the readership/audience of the August 2004 journal.

In relation to this article, allow us to clarify further.

1. Discovery Health has always been fully compliant with the legal requirements of Act 101 and its requirements. In point of fact, during 2003 Discovery Health was an integral partner in assisting the Council for Medical Schemes in drafting treatment algorithms. The regulations permitted the creation of formularies related to the Chronic Disease List (CDL) conditions, in order that this benefit could be included in lower premium plans, promoting affordability and thus allowing more people to access cover.

2. With specific reference to hypertension, the drug formulary that we offered was fully compliant with the Council's guidelines and requirements and was also in accordance with the most recent Hypertension Guideline update. The formulary applied to specific benefit options, and was not a general feature of all options.

3. Members who purchased an ancillary benefit have access to an enhanced chronic benefit and are not limited to a formulary. Those who do have the ancillary benefit qualify for basic chronic cover as stipulated by the Prescribed Minimum Benefits. The choice of drugs included within the formulary on these plans was based on their cost effectiveness, related either to their list price or to the discount price offered to Discovery Health members.

For drugs prescribed outside of the formulary, the scheme allows members to fund their therapy with a monthly medical allowance set at a similar level to that of items included in the formulary.

Since legislation has now been implemented with regard to single exit prices and the discontinuation of mark-ups related to drugs, Discovery Health can now afford to expand its formulary, enabling members to access as many drugs as is clinically appropriate and cost-effective to the Scheme.

As regulations also require consideration of other drugs not on the formulary for 'ineffective' care and for 'adverse effects', an appeal process was created to facilitate this. It is important to note that this is not an open 'loophole' to bypass the formulary,

upon which the premium of the plan was based, but a mechanism to permit consideration of other costlier drugs, which become cost-effective because they specifically address a more serious clinical situation.

Applications for non-formulary drugs for patients with mild or newly diagnosed conditions not included in this definition will not be accepted, consistent with good and cost-effective clinical practice.

E Gottlich

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1. Rayner B. Prescribed minimum benefits or minimum prescribed benefits? *S Afr Med J* 2004; **94:** 623-624.

Brian Rayner replies: I would like to thank Dr Gottlich, Principal Clinical Specialist, Discovery Health for replying to my article in the *Journal*. It is a very sad state of affairs that I had to place my viewpoint in the *Journal* to get his attention. Over the past year I have made several motivations to Discovery Health and I have never received a reply. This complete lack of recognition of my (and other doctors') professional standing is certainly cause for umbrage.

It seems that Dr Gottlich has also missed several key points in my article. Firstly, as I clearly stated, I am in favour of the use of affordable and cost-effective medication for hypertension. I also have no issue with the use of formularies by medical funders provided that these are based on recognised clinical standards, preferably the Southern African Guidelines for Hypertention.[1] I see many patients who are members of Discovery Health, and I can usually manage their hypertention effectively with the use of their formulary. Yet as a prominent specialist in this field I am referred complicated hypertensive patients, who just cannot be managed within the confines of a very basic formulary or algorithm.

Secondly, Dr Gottlich is incorrect in stating that patients on prescribed *minimum* benefits (PMBs) are only entitled to receive benefits within the Council for Medical Schemes algorithm, or Discovery Health formulary. Apart from the fact that the PMBs constitute the standard care to be afforded to members on the lowest options, and should not be construed as to become the maximum, the regulations to the Medical Schemes Act of 1998 (Act No. 131 of 1998) clearly state that '. . . provision must be made for appropriate exceptions where the protocol has been ineffective or causes or would cause harm to the beneficiary *without penalty to the beneficiary*. Furthermore if managed health care entails use of a formulary or restricted list of drugs such formulary or restricted list must be developed on the basis of evidence-based medicine taking into account considerations of cost-effectiveness and affordability, but must make provision for appropriate substitution of drugs where a formulary drug has been ineffective or causes or would cause harm to the beneficiary *without penalty to the beneficiary.*'

Thirdly, despite protestations, Discovery Health's compliance with the hypertension algorithm is selective. It does not allow the use of angiotensin receptor blockers in patients with type 2 diabetes and microalbuminuria.

Fourthly, regarding the specific patient who prompted my communication, it is simply a distortion of the truth to state that Discovery Health changed their mind on review. This occurred because I lodged a formal complaint with the Council for Medical Schemes. Sadly, most patients are unaware of their rights in this regard. This leaves medical practitioners with no option but to face time-consuming administrative hurdles, including difficulty in accessing clinical peers in such cases as the one I described.

1. FJ Milne and VJ Pinkney-Atkinson for the Southern African Hypertension Society Hypertension Guideline Working Groups 2000 and 2003. Hypertension guideline 2003 update. *S Afr Med J* 2004; **94:** Part 2, 209-226.

A tale of two industries

To the Editor: On 30 September, Merck voluntarily stopped selling its arthritis drug rofecoxib (Vioxx) because new data found that it doubled patients' risk of heart attack and stroke.

Vioxx was a bestseller, with global annual sales of R16 billion. Merck could have continued marketing the drug with appropriate health warnings, but it decided that it was in the best interests of its patients to withdraw the medication.

Cigarettes, too, double the risk of heart attacks and stroke. In addition, smokers are 10 times more likely to die of emphysema or lung cancer. In fact, smoking is linked to 50 diseases, from blindness to foot amputations.

So what have cigarette manufacturers done to protect their customers? Did they warn of the dangers and prepare to phase out cigarette sales? Well, no. Actually they did exactly the opposite. They hid the facts and tried to sell more cigarettes.

The US Justice Department has charged the companies with behaving like an organised crime syndicate. In a current court case, US cigarette makers are accused of conspiracy to defraud consumers by denying the dangers of smoking and passive smoking; of sponsoring junk science by funding sympathetic scientists to carry out research to cloud the issue; of manipulating nicotine levels to keep smokers hooked; of intentionally marketing to youth; of promoting low-tar cigarettes as less harmful knowing that this is not true; and of destroying and concealing documents to hide their illegal activities.

The truth is that the cigarette companies have lost touch with reality and what is responsible behaviour. British American Tobacco, for instance, blathers that government proposals for new picture-based health warnings to better inform the public of