



– Physics, University of Cambridge) in 1997 appears to continue to hold ground: ‘Simple-minded analysis may suggest that water, being a fluid, cannot have a structure of the kind that such a picture would demand. But cases such as that of liquid crystals, which while flowing like an ordinary fluid can maintain an ordered structure over macroscopic distances, show the limitations of such ways of thinking. There have not, to the best of my knowledge, been any refutations of homeopathy that remain valid after this particular point is taken into account.’

Perhaps then, the only end that can and should be sought is the end of poorly substantiated conclusions resulting in unnecessary worldwide sensationalism.

For the complete HSA response visit [www.hsa.org.za](http://www.hsa.org.za)

**Brenda Saunders**

**Neil Gower**

Homeopathic Association of South Africa  
Suite 293  
Private Bag X11  
Craighall  
2024

1. Linde K, Clausius N, Ramirez G, *et al.* Are the clinical effects of homeopathy placebo effects? A meta-analysis of placebo-controlled trials. *Lancet* 1997; 350: 834-843 (Erratum in: *Lancet* 1998; 351: 220).
2. Shang A, Huwiler-Muntern K, Nartey L, *et al.* Are the clinical effects of homeopathy placebo effects? Comparative study of placebo-controlled trials of homeopathy and allopathy. *Lancet* 2005; 366: 726-732.

**Bridget Farham replies:** Predictably enough those who practise homeopathy have responded both to my summary<sup>1</sup> of the article on homeopathy in the *Lancet* and to the *Lancet* themselves. While those who use homeopathy in their practice have every right to do so, as long as it doesn't compromise patient care, I feel compelled to answer some of the points in their response that serve only to emphasise just how unscientific their approach is.

The first and most important point is the complaint that the *Lancet* article was based on only 8 trials of homeopathy. The whole point of the analysis was to try to tease out whether or not the effects of homeopathy can be ascribed more to the placebo effect than to a specific effect. In order to do this, the authors of the *Lancet* article could only use certain types of trials that met the rigorous criteria demanded of fully randomised, placebo-controlled trials – that left only 8 trials of homeopathic medication. The authors took bias into account, for both trials of conventional medicine and homeopathic medicine. That is precisely what makes the analysis so scientifically rigorous.

The comments by others in the homeopathic field serve only further to emphasise the lack of a scientific approach. Studies of the effect of penicillin should be designed precisely to ignore the preconceived idea that penicillin has an intrinsically beneficial nature. That is how scientific hypothesis should

work. I am not qualified to comment on the comments made by materials scientists. But I would still, on the basis of a rigorous scientific training (not obtained during my medical degree, I hasten to add), question whether changes that are too small to detect can have a clinical effect in the human body. What a scientist tries to avoid is the idea encapsulated in the phrase, ‘if I hadn't believed it, I wouldn't have seen it.’

1. Farham B. The start of reason (Forum). *S Afr Med J* 2005; 95: 764.

## Dangers of DDT

**To the Editor:** Your comments on the use of DDT and Rachel Carson's book *Silent Spring* in a recent issue of the *Journal*<sup>1</sup> cannot go unchallenged. Carson's book highlighted a phenomenon that had been troubling environmentalists, namely the decline in a number of species, particularly some bird species.

The implication that the only organisms affected by DDT were the mosquito and possibly ‘certain species of aquatic invertebrates’ is fatuous. This is documented by the effectiveness of DDT in combating agricultural pests across a number of families, such as the codling moth, cotton boll weevil and corn borer. In 1959, 35 771 tons of DDT were used in the USA.<sup>2</sup> Such a volume would inevitably have had a profound effect on a number of food chains. Anecdotally, I visited the Okavango Delta during the tsetse fly eradication campaign involving use of Dieldrin (a related compound). A notable feature of the trip was the masses of fish floating belly up, interspersed with a fair number of birds of different species. There is nothing specific about the action of DDT on mosquitoes.

Granted some of the claims may have been exaggerated, but there is fieldwork backed by laboratory studies to substantiate the toxicity of DDT and its metabolites on a number of species. In addition, a novel and unexpected effect on eggshell thickness has been demonstrated. This had the effect of birds laying fragile eggs, easily damaged and resulting in a high mortality among the chicks. This was particularly pronounced in species such as birds of prey at the top of a food chain.<sup>3</sup> The decline in a number of species has been attributed in part to this effect. The fact that some species have shown an increase in numbers following the ban on DDT could be taken as further evidence for this effect.

Although the evidence for carcinogenicity among humans is not conclusive there are good experimental data to show a carcinogenic effect in both rodents and non-human primates.<sup>2,4</sup> There is concern that DDT and its metabolites could have an effect on reproduction and pregnancy.<sup>4</sup>

Contrary to the comments in your Editor's Choice<sup>1</sup> a recent review<sup>2</sup> concluded that there was sufficient evidence of



environmental damage and experimental evidence suggesting a carcinogenic effect in non-human primates to warrant continuation of the ban, and that alternatives should be urgently sought.

Attitudes to DDT have changed and it is no longer sprayed indiscriminately into the environment. Despite limiting its use to indoors, concerns remain. A review in the *Lancet*<sup>4</sup> concluded that 'indoor spraying will unavoidably expose women to amounts of DDT that are associated with forms of toxic effects that might increase infant mortality'. To blandly state that it is quite innocuous to humans is to ignore the evidence.

Finally, to assume that the dramatic decline in malaria cases, as described by Marahaj *et al.*,<sup>5</sup> is entirely due to the reintroduction of DDT should be viewed cautiously. Rainfall patterns have a significant effect on malaria and 2000 was a singularly wet year, as noted by the authors.

Your comments do not add to the topic, which needs to be debated and not shrugged off with a glib comment.

#### Dave Whitelaw

Department of Medicine  
Stellenbosch University and  
Tygerberg Hospital  
Tygerberg, W Cape

1. Ncayiyana D. Valuing human life above that of aquatic invertebrates (Editor's choice). *S Afr Med J* 2005; **95**: 811.
2. Turusov V, Rakitsky V, Tomatis I. Dichlorodiphenylchloroethane (DDT) ubiquity, persistence and risks. *Environ Health Perspect* 2002; **110**: 125-128.
3. Radcliffe DA. Decrease in eggshell weight in certain birds of prey. *Nature* 1967; **215**: 208-210.
4. Rogan WJ, Chen A. Health risks and benefits of bis (4-chlorophenyl)-1,1,1 trichloroethane (DDT). *Lancet* 2005; **366**: 763-773.
5. Maharaj R, Mithembu DJ, Sharp BL. Impact of DDT re-introduction on malaria transmission in KwaZulu-Natal. *S Afr Med J* 2005; **95**: 871-874.

## Concurrent use of clopidogrel (Plavix) and atorvasatin (Lipitor) is contraindicated

**To the Editor:** After a recent discussion with two family physicians in Lenasia, south of Johannesburg, it has come to our attention that it is common practice for cardiologists in the area to prescribe both clopidogrel (Plavix) and atorvasatin (Lipitor) simultaneously after a coronary event. Clopidogrel induces irreversible alterations of the platelet adenosine diphosphate (ADP) receptor P2Y<sub>12</sub> mediating inhibition of stimulated adrenal cyclase activity by ADP.<sup>1</sup> Permanent modification of the platelet ADP receptor by thienopyridines is consistent with time-dependent, cumulative inhibition of ADP-induced platelet aggression upon repeated daily dosing with ticlopidine or clopidogrel and with slow recovery of platelet aggression function after drug withdrawal.<sup>2</sup>

Clopidogrel is a prodrug, requiring hepatic metabolism by cytochrome P450 isoform 3A4 in order to generate the active metabolite, a transient intermediate that covalently modifies

and inactivates the receptor.<sup>3</sup>

When clopidogrel and atorvasatin, a CYP3A4 substrate, are present at equimolar concentrations *in vitro*, clopidogrel metabolism is inhibited by more than 90%.<sup>3</sup> Three separate studies<sup>4-6</sup> suggest that concurrent treatment with lipophilic strains that are substrates of CYP3A4 (e.g. atorvasatin and simvastatin) may interfere with the inhibitory effects of clopidogrel on platelet function. In the study by Lau *et al.*<sup>5</sup> atorvasatin, but not pravastatin, attenuated the antiplatelet effect of clopidogrel in a dose-dependent manner.

It would therefore seem that the concomitant use of atorvasatin and clopidogrel is contraindicated.<sup>7</sup>

We welcome comments from cardiologists and the drug companies (Pfizer and Sanofi-Synthelabo).

#### N Chetty

#### N H Naran

Platelet Research Unit  
National Health Laboratory Service/  
University of the the Witwatersrand  
Johannesburg

#### M Munster

Haemostasis and Thrombosis  
National Health Laboratory Service/  
University of the Witwatersrand  
Johannesburg

1. Hollopeter G, Jantzen HM, Vincent D, *et al.* Identification of the platelet ADP receptor targeted by antithrombotic drugs. *Nature* 2001; **409**: 202-207.
2. Patrono C, Collier B, Fitzgerald GA, Hirsh J, Roth G. Platelet-active drugs: the relationships among dose, effectiveness, and side effects. *Chest* 2004; **126**: 234S-264S.
3. Clarke TA, Waskell LA. The metabolism of clopidogrel is catalysed by human cytochrome P450 3A and is inhibited by atorvastatin. *Drug Metab Dispos* 2003; **31**: 53-59.
4. Jaremo P, Lindahl TL, Fransson SG, Ritche A. Individual variations of platelet inhibition after loading doses of clopidogrel. *J Intern Med* 2002; **252**: 233-238.
5. Lau WC, Waskell LA, Watkins PB, *et al.* Atorvastatin reduces the ability of clopidogrel to inhibit platelet aggregation: a new drug-drug interaction. *Circulation* 2003; **107**: 32-37.
6. Neubauer H, Günesdogan B, Hanefeld C, Spiecker M, Mügge A. Lipophilic statins interfere with the inhibitory effects of clopidogrel on platelet function – a flow cytometry study. *Eur Heart J* 2003; **24**: 1744-1749.
7. Phillips DR, Conley PB, Sinha U, Andre P. Therapeutic approach in arterial thrombosis. *J Thromb Haemost* 2005; **3**: 1577-1589.

## Emergency medicine

**To the Editor:** Congratulations on two counts to those involved in the advancement of emergency medicine in South Africa.

First and foremost for the establishment of emergency medicine as a separate specialist discipline.<sup>1</sup>

Secondly (and perhaps somewhat pedantically) for adhering to the correct terminology. In the USA there is a tendency to interchange the term 'emergency', meaning sudden, urgent, usually unexpected occurrence or occasion requiring immediate action,<sup>2</sup> with the term 'emergent'.

The primary meaning of the word 'emergent' relates to its derivation from 'emerge', meaning coming into view or notice or rising from a liquid or other surrounding medium.<sup>2</sup> Use of the term emergent to replace emergency represents a