



## Homocysteine — differing conclusions

From a funding perspective we are told that there is an increasing demand to spend money on pharmacological vascular risk reduction. Guidelines for hypertension, dyslipidaemia and type 2 diabetes are therefore advocating ever-decreasing optimal target levels for blood pressure, lipid and glucose control, which commonly require combination therapy rather than monotherapy. The list of medicines to reduce long-term vascular morbidity and mortality is growing and the advocated doses of such drugs are increasing. Such medication can be very expensive, and there are also associated costs: for example, the BHF rates for homocysteine tests are R87.70 (random) and R103.70 after methionine loading. Should we test for plasma homocysteine, and what is the evidence for intervention when the levels are raised? Two reviews in this issue illustrate the folly of relying on reports, which may be biased in favour of intervention without adequate proof.

Jacobs and Wood (p. 191) review the pathophysiology of homocysteine and the vascular endothelium and find it inexplicable that controversy persists regarding treatment. They speculate that 'perhaps this is because, for primary prevention, proof of benefit is not yet sufficient to justify worldwide supplementation although preliminary results are expected to reach statistical significance within 3 years'. Despite the uncertain evidence the authors go on to state 'rationally it is recognised that local authority or government need to add at least folate to some widely consumed food staple'. They conclude that the argument is compelling and 'needs to be widely acknowledged and responded to by doctors and nurses as well as third party payers in South Africa — as it is elsewhere in the world'.

The review by Mbewu, Nogoduka and Taylor (p. 192) examines both sides of the argument of plasma homocysteine and arterial thromboembolic disease and comes to conclusions that differ from the above. The traditional risk factors for coronary heart disease (CHD) — cigarette smoking, hypertension, diabetes mellitus, age, raised total cholesterol, low high-density lipoprotein — may be insufficient to account for all cases of CHD. Novel risk factors such as homocysteine have therefore gained popularity as potential independent risk factors for CHD. High serum homocysteine concentrations are associated *inter alia* with genetically determined enzyme dysfunction, methionine-rich diets, excessive coffee consumption, high alcohol intake, smoking and lack of physical activity. Although homocysteine appears to be positively associated with vascular events, it remains to be seen whether it is an independent, and furthermore causal risk factor for thromboembolic disease. No results of prospective randomised trials are as yet available to establish the effects on cardiovascular outcomes of lowering homocysteine, or to ascertain the effect of folate and vitamin B<sub>6</sub> supplementation on such events. It is therefore premature to advocate screening and intervention programmes for elevated homocysteine levels.

Most importantly, the health benefits of prudent living and eating, rather than relying on hopeful enthusiasm for yet another pill, are reinforced!

## Does calcium supplementation prevent pre-eclampsia?

Public health interventions such as vaccination against infectious diseases and the fluoridation of drinking water have strongly beneficial effects, particularly in poorer communities. Does calcium supplementation in an attempt to prevent pre-eclampsia fall into this category?

High blood pressure with or without proteinuria is a major cause of both maternal and perinatal death and morbidity worldwide. Preterm birth, commonly associated with hypertensive disorders, is the leading cause of early neonatal death and infant mortality, particularly in low-income countries. For these reasons, strategies to reduce the risk of hypertensive disorders of pregnancy have received considerable attention. Hofmeyr *et al.* (p. 224) therefore undertook a systematic review of randomised trials that compared supplementation with at least 1 g calcium daily during pregnancy with placebo.

They found that there was a modest reduction of risk of pre-eclampsia with calcium supplementation. The effect was greatest for women at high risk of hypertension and those with low baseline calcium intake. Since these benefits were confined to several small trials and not found in the largest trial conducted in a low-risk population, further research is required.

## Rheumatic fever — a jab is better than a swallow

Rheumatic fever (RF) is the most important cause of acquired heart disease in children and young adults worldwide. The prevalence of RF and rheumatic heart disease is high in areas with poor socioeconomic conditions, overcrowding and limited access to medical care. The severity and prognosis of rheumatic heart disease depend on the extent of the carditis and the frequency of recurrent attacks. Secondary prevention is particularly important since even an asymptomatic or optimally treated group A streptococcal throat infection can still trigger RF recurrence.

Manyemba and Mayosi (p. 212) provide a systematic review assessing the effects of different penicillin regimens and formulations for preventing streptococcal infection and RF recurrence. They conclude that intramuscular penicillin is more effective than oral penicillin in preventing RF recurrence and streptococcal throat infections. Two-weekly or 3-weekly injections appeared to be more effective than 4-weekly injections. They caution that the evidence is based on poor-quality trials and the use of outdated formulations of penicillin.

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