EDITOR'S VIEW

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J. K. Aronson, Chairman of the Editorial Board, British Journal of Clinical Pharmacology

University Department of Clinical Pharmacology, Radcliffe Infirmary, Woodstock Road, Oxford OX2 6HE, UK

Preventing heart attacks and strokes

Current evidence shows that whatever your serum cholesterol concentration is, it can always be beneficially lower. For example, for every 1.8 mmol l⁻¹ reduction in low density lipoprotein (LDL) cholesterol, from any starting point, the risk of an ischaemic heart disease event is reduced by 61%. Furthermore, the serum cholesterol concentration is not a good screening test for the risk of stroke or myocardial infarction, because at any age those in the top few percent of the serum cholesterol distribution suffer only a small percentage of all vascular events. However, the risks of the complications of a raised serum cholesterol increase with age, and so age is a much better screening test than serum cholesterol. This implies that anyone with hyperlipidaemia and everyone over the age of 55 years, whatever their serum cholesterol, should be given a lipid-lowering drug.¹ However, when Yang *et al.* (pp. 288–298 of this issue), studied 25 331 patients of UK GPs who were taking lipid-lowering drugs and 16 287 patients who were not, they found that the former were more likely to be elderly smokers with more concomitant severe cardiovascular comorbidity. Treatment of this sort needs to be more eclectic. Of course, giving a statin to everyone over the age of 55 years would be expensive, but the large resultant reduction in mortality would be cheap at the price.

Similarly, if everyone over 55 years took a 75-mg aspirin each day, the risk of ischaemic heart disease events would be reduced by 34%. So, using these two strategies together, in other words giving everyone over 55 years both a statin and an aspirin, would reduce the risk of ischaemic heart disease events by about 74%.² However, the major downside of this is that some patients would develop gastrointestinal bleeding from the aspirin (the risk of adverse effects from the statin being much lower). So how do you know in which patients aspirin is safe? Well, Loke *et al.* (pp. 282–287) show that it is possible to calculate the benefit-to-harm ratio for individual patients, using estimates of the baseline risks for cardiovascular events and gastrointestinal haemorrhage, combined with estimates of the relative risks of these events with treatment.

This strategy of giving everyone over 55 years a statin and an aspirin a day is so simple and effective that it

should be implemented as soon as possible. In addition, adding folic acid, to reduce the serum homocysteine concentration, would improve the reduction in ischaemic heart disease events to 78%. Furthermore, if one could also reduce the blood pressure a bit (lowering the diastolic pressure to 75 mmHg), even in those who are not hypertensive, the benefits would be even greater; up to an 85% or so reduction in ischaemic heart disease events overall.² For patients in whom the risk of gastrointestinal bleeding is unacceptably high, aspirin can be withheld; the benefit from using the other drugs is still about 80%. This type of multifactorial attack on the factors that cause heart attacks (and strokes, for which the benefits are also great) is the coming thing.³

Complementary medicines

Meanwhile, the consumption of complementary medicines continues to rise, some would say unacceptably. For example, in a study of all the patients who attended a US emergency department,⁴ 43% had used at least one such therapy at some time and 24% were current users. All complementary treatments were considered to be safe by 16%, and 33% failed to tell their physicians they were taking them. Furthermore, 15% of the women and 7% of the men believed that complementary therapies do not interact with other medications. However, if in the future many people are going to be taking a combination of a statin, aspirin, folic acid, and antihypertensive drugs, interactions with other medications, including herbal remedies and other complementary treatments, will be important. For example, in 16 healthy men, St John's wort reduced the plasma concentrations of simvastatin and its main metabolite.⁵ For these and other reasons, we have commissioned two reviews on complementary medicines, the first of which appears in this issue of the *Journal* (pp. 226–233). The accompanying commentary (p. 225) sets the scene.

Genetic testing

I was interested recently to read a consultation paper, issued by the Nuffield Council on Bioethics, entitled 'Pharmacogenetics: ethical issues'. One of the questions raised in the paper was whether pharmacogenetic tests

might allow patients to be grouped racially or ethnically. Three papers in this issue add to the growing corpus of information on the distributions of drug-metabolizing enzymes in different populations. Two deal with CYP3A, the activity of which was normally distributed in a Chinese population, with higher activity in women than in men (pp. 264–269), while in Asian patients with and without cancer the activity of CYP3A was similar to that in other populations (pp. 270–277). In other studies, CYP3A activity was slightly lower in Japanese men than European-Americans, but not when corrected for body weight,⁶ and Vietnamese and Caucasian subjects did not differ.⁷ In the other genetic study in this issue, a study of *NAT2* alleles, 64% of a Thai population were rapid acetylators and 36% slow acetylators, a pattern similar to those found in many Asian populations, although the frequency of *NAT2**4 was significantly lower and the frequency of *NAT2**7 higher than in Oriental populations (pp. 278–281).

When the Gileadites wanted to identify their enemies, the Ephraimites, they asked them to pronounce the word *shibboleth*, since the Ephraimites could not pronounce the *sh* sound (Judges xii, 5–6); 42 000 Ephraimites perished. But the current evidence suggests that either there are no interethnic pharmacogenetic differences in particular

phenotypes, or that when there are, there is too much variability within and between populations to make pharmacogenetic testing a biochemical shibboleth. Which is just as well.

References

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