DOI:10.1111/j.1365-2125.2005.02521.x

Editors' view

Prescribing statins

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'Be not the first by whom the New are try'd,
Nor yet the last to lay the Old aside'.
Alexander Pope, *An Essay on Criticism*.

These lines by Alexander Pope, or variants of them, are often cited in relation to the use of medications. But Pope was writing specifically about the use of language in poetry; the lines that precede the quotation above are:

'In Words, as Fashions, the same Rule will hold;
Alike Fantastick, if too New, or Old'.

Just as certain comments in Aristotle's *Poetics* have come to be misinterpreted as describing features of drama that are important to its structure – the so-called dramatic unities [1], so Pope's comments on poetic structure have been taken to have a wider meaning than he originally intended. Nevertheless, the exhortation to be careful about prescribing new medications is not a bad one. Someone has to be first, but don't let it be you, unless you're an expert, one who thoroughly understands the pathophysiology of the disease, the mechanism of action of the drug, and how the two can be married to produce appropriate drug therapy [2]. On the other hand, when enough information has accrued from use of the drug by others to show that it is worth prescribing, don't wait until everyone else has used it before giving your patients the benefit.

It is not clear, however, what factors actually induce practitioners to prescribe. Take the statins, which I have discussed before in relation to over-the-counter availability [3]. The statins, competitive inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A reductase, were introduced only about 20 years ago [4] and were first used to treat patients with familial hypercholesterolaemia. But before long their potential in reducing the risks of cardiovascular disease in the general population were recognized, culminating in the Polypill hypothesis in 2003, which stated that a combination of four different varieties of medication (aspirin, a statin, folic acid, and three different types of antihypertensive drugs in subtherapeutic doses), if used in appropriate people, would reduce the risk of cardiovascular disease in the population by over 80% [5]. The electronic responses to this suggestion in the *British Medical Journal* [6] were as rabid as they were rapid. However, with time and increasing evidence the Polypill idea has come to be accepted, albeit perhaps grudgingly in some quarters [7].

The principle as far as statins are concerned is simple. The serum cholesterol concentration is a poor screening test for the risk of cardiovascular disease, since only 10% of those who get a heart attack or a stroke have a serum cholesterol concentration above the usual reference range. Age over 55 years and a previous history of cardiovascular disease are much better screening tests. Those who fall into those categories are at increased risk and should be treated. If you fill the bill, don't bother measuring your cholesterol: whatever it is, it's better if it's lower. This principle is supported by the latest evidence, a meta-analysis of data from 90 056 individuals in 14 randomized trials: statin therapy produced a 12% proportional reduction in all-cause mortality per mmol/l reduction in LDL cholesterol [8]. The authors of this analysis have been quoted as saying that 'statin drugs could be beneficial in a much wider range of patients than is currently considered for treatment' (Colin Baigent) and that 'statins are very safe' (Rory Collins) [9].

In this issue of the *Journal*, Walley *et al.* show that during 1997–2003 there has been a huge increase in the use of lipid-lowering drugs in the nine European countries that they studied [10]. The median increase was 36% per year, greatest in Ireland (54% per year) and least in France (14% per year). The increases were entirely attributable to increased prescribing of statins, partly by an increase in the prescribed daily dose, but mostly by an increase in the number of patient treatment days. This is encouraging. However, we have previously published evidence that the statins are still being underprescribed [11]. Furthermore, there is evidence that, when they *are* prescribed, insufficient attention is paid to the dosage and to the choice of statin in patients who are taking other drugs that inhibit CYP3A4 (when pravastatin or fluvastatin should be preferred) [12].

Walley *et al.* point out that there is no correlation between the use of statins and deaths from ischaemic heart disease [10]. This is disappointing, but it is probably too soon to expect such changes to be detectable, and underprescribing militates against such an association. There may also be selective prescribing in individuals with variable risks of cardiovascular disease. For example, elsewhere in this issue Thomsen *et al.* show that there is a socioeconomic gradient in the use of statins in Denmark, at least among men [13]; those of higher socioeconomic classes, who are less likely to have cardiovascular disease, were more likely to be given a statin.

If we knew more about the factors that cause practitioners to prescribe (or not to prescribe) drugs such as statins, in the face of overwhelming evidence of their efficacy and a highly favourable benefit to harm balance, we might be in a position to encourage appropriate prescribing. However, the factors are elusive. For example, in this issue of the *Journal*, Dybdahl *et al.* report that they found no support for their reasonable hypothesis that general practitioners who prescribe certain drugs a lot will be more likely to prescribe new drugs in the same therapeutic group [14].

I suspect that the factors that induce practitioners to prescribe are so complex and variable across different populations that we shall never fully understand them in a way that will allow us to manipulate them. But, given the evidence, we should be educating and encouraging practitioners to prescribe statins for those who are likely to have cardiovascular disease in the future. Stand up all those over 55.

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