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Oral contraceptives and cardiovascular disease: some questions and answers

Since the mid-1960s a vast amount of epidemiological, clinical, and laboratory evidence has linked the use of combined oral contraceptives with certain types of cardiovascular disease, especially venous thromboembolism, thrombotic stroke, and myocardial infarction.¹⁻³ Despite this, some research workers have remained unconvinced by the data, and many of their major criticisms have recently been brought together in an article by Shearman.⁴

Firstly, several authors suggest that national trends in cardiovascular mortality (which have been generally downward) are incompatible with the estimates of risk attributable to the pill derived from case-control and cohort studies.⁵⁻⁷ Mann and Vessey,⁸ however, have pointed out that a proper analysis of mortality trends must take into account all the relevant facts and not just selected ones. Such an analysis should, for example, recognise that use of the contraceptive pill has been shown to be related only to certain forms of cardiovascular disease; that use of oral contraceptives is concentrated in young women while pill-associated mortality is concentrated in those aged 35 years or more; that cardiovascular disorders have a complex multifactorial aetiology (and hence a favourable change in one risk factor could easily counteract an unfavourable change in another); and that there have been many changes over the years in the formulation of the pill and in the way in which it is used.⁹ Casual examination of national trends in cardiovascular mortality and oral contraceptive use is therefore too simple; and the observed patterns are, in fact, compatible with a wide range of possible risks attributable to the pill.

Secondly, the excess deaths in those women using the pill have been said to be almost entirely attributable to smoking.⁴ This assertion is not in keeping with the facts. An excess risk of fatal and non-fatal cardiovascular events associated with use of the pill has been observed both in non-smokers and in comparisons of users and non-users of oral contraceptives smoking similar numbers of cigarettes a day.¹⁰⁻¹² None the less, the risk of suffering a fatal arterial event attributable to use of the pill is heavily concentrated in smokers. As for venous thromboembolism, this condition does not appear to be related to smoking at all.¹³

Thirdly, Goldzieher¹⁴ has discounted the studies showing a relationship between use of the pill and venous thromboembolism because the clinical diagnosis of deep venous thrombosis is unreliable and potentially subject to bias. He quotes a paper by Barnes *et al*¹⁵ in support of his view. These authors studied a group of women referred to them as possible cases of venous thrombosis. This diagnosis was confirmed by ultrasonography in 31% of non-users of the pill but only 17% of users ($p \approx 0.05$). A substantial proportion of the 54 users, however, had no physical signs; thus only 26 had leg tenderness and only eight had oedema. It seems reasonable to conclude that in this particular study patients taking the pill were being referred for investigation on the merest suspicion of trouble, and it seems important not to draw far-reaching conclusions from the findings. Tibbut, for example, confirmed a diagnosis of venous thrombosis by phlebography in equal proportions of users and non-users of the pill referred to him in routine hospital practice.¹⁶ Moreover, Vessey and Doll^{17 18} found the relation between use of the pill and venous thromboembolism to strengthen the more conclusive the evidence of disease.

Finally, Shearman⁴ has drawn attention to two major topics of controversy which remain to be resolved—the extent to which use of the pill is related to subarachnoid haemorrhage and whether or not there is a residual excess risk of cardiovascular disease in ex-users of oral contraceptives. With regard to the first of these questions, the Royal College of General Practitioners¹² has found as strong an association between use of the pill and subarachnoid haemorrhage in its cohort study (20 deaths in total; relative risk users:non-users 4.0:1) as between use of the pill and ischaemic heart disease (17 deaths in total; relative risk users:non-users 3.9:1). Most others have found a much weaker association, with relative risks of the order of 1.5:1.¹⁹⁻²¹ As to the second question, all were agreed until the appearance of a recent publication by Slone *et al*²² that the excess risk of myocardial infarction and venous thromboembolism was probably confined to current users of the pill. The paper by Slone *et al* now suggests that there may be some residual excess risk of myocardial infarction in women aged over 40 with five or more years' use of the pill in the past. The major controversy, however, concerns the risk of stroke in ex-users of oral contraceptives, some studies suggesting that there is an excess risk^{12 23} and others not.^{19 24} Vessey *et al*²⁴ have pointed out the difficulty in assessing mortality rates in ex-users of the pill—"the increased risk in former users could result from the development of ultimately fatal illnesses in some women while they were current users which led to them stopping the pill."

Shearman⁴ has questioned whether results obtained in one country may be extrapolated to another. If this is done it should be with great caution, since the background risk of the different cardiovascular disorders and the distribution of factors predisposing to them vary appreciably in different parts of the world. It seems reasonable, however, to extrapolate from one developed country to others which are closely similar—for example, from Britain to the United States, Canada, or Australia.

Perhaps we should not demand too much in the way of fine detail from the epidemiological studies. Their consensus is that fatal cardiovascular events are most likely when high-dose pills are used by older women, especially those who smoke or who have other risk factors. These observations have led to the development of modern oral contraceptives containing very small amounts of oestrogen and progestogen which are prescribed mainly for young women at low risk of cardio-

vascular disease. In aggregate, these changes seem likely to have resulted in a substantial decrease in mortality attributable to use of the pill during the past few years.

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The General Medical Council and postgraduate education

It was fitting that Sir John Walton's first task as president of the General Medical Council should have been to chair an important conference on postgraduate medical education in London last week. The Medical Act of 1978 gave the General Medical Council's Education Committee the task of co-ordinating all stages of medical education, but while responsibilities for undergraduate training and the preregistration year were precisely defined the committee's role in postgraduate education was less clear. The purpose of the conference, attended by over 250 delegates representing educational interests, the BMA, the Health Departments, and research councils was to consider what steps the General Medical Council might take in this crucial area.

The consensus that emerged was that the education committee should have a function in overseeing and monitoring postgraduate education, perhaps in the same way as it now does with undergraduate training, leaving the Royal Colleges and Faculties (as with the medical schools) to supervise the content and standards of education. At present the main source of dissatisfaction is at senior house officer level, where posts may be used for general or specialist professional training, for vocational programmes in general practice, or for overseas doctors, depending on the different criteria used by the approving bodies. Informed observers believe that many posts fall short of expectations and that others are inappropriate at such an early stage in a doctor's career. Doubts about the wisdom of commitment to specialisation so soon after registration and the difficulty of moving between the specialties have led to calls for a common general professional training lasting perhaps one or two years (though Sir Douglas Black warned against what he called "compulsory flexibility"), and the conference suggested

that the General Medical Council might examine this aspect in detail as its first task.

While coordination of medical education from undergraduate to senior house officer might resolve what some speakers see as the present chaos, there are also problems in specialist training. Much of the difficulty is caused by each approving body functioning differently. Some hold their examinations at entry to specialist training, others at its completion; some grant specialist accreditation, others do not. Sir John made it clear that the General Medical Council had no intention of setting up a compulsory specialist register, but he would like to see an improvement in the present haphazard arrangements for registration of higher qualifications.

Some speakers thought that training needed to be more closely monitored; consultants should be prepared, for example, to have their educational programmes reviewed by their peers in the same way that general practice trainers do theirs. More detailed information about opportunities was demanded by trainees, though Sir Henry Yellowlees pointed out that much of it was already available centrally. Unfortunately the conference had no time to consider the important topic of continuing education, and it side-stepped the issue of financing yet another body concerned with postgraduate education. And before the General Medical Council's Education Committee takes on its new role it might care to look critically at the present bureaucratic machinery, which many believe is already top-heavy.

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