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The third generation pill controversy ("continued")

The risks are still small compared with those of pregnancy

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The debate about the safety of third generation oral contraceptives shows no sign of fading away. Since it began in 1995 the main participants have been epidemiologists and clinical pharmacologists. There has been little input from the clinicians who prescribe oral contraceptives or from the women who use them.

About 80% of British women use the pill at some time between the ages of 16 and 24.[1] It was this age group that paid the price of the October 1995 scare, prompted by the publicity surrounding the announcement of the Committee on Safety of Medicines that third generation oral contraceptives had a higher risk of inducing venous thromboembolism. In the first quarter of 1996 in England and Wales there were 6198 more abortions than in the previous quarter (a 16% rise), and the increase continued more slowly until 1998.[2] Doctors who counsel women with unplanned pregnancy are still angry about the amount of human misery caused by information mismanagement.

The 1995 scare arose from three studies that reported that the risk of venous thromboembolism among users of pills containing levonorgestrel was half that of pills containing desogestrel or gestodene—the so called "third generation" progestogens. Over the following five years, 16 studies compared second and third generation pills.[2] Three found no difference in the risk of thromboembolism, but the others found higher risks with third generation pills, the increase varying from 1.4 to 4.

This week a meta-analysis by Kemmeren et al of 13 of the studies (p 131) concludes that the risk with third generation pills is 1.7 times that with second generation pills.[3] When the original 1995 studies appeared critics suggested that their findings might be due to bias or confounding. For example, the risk of thromboembolism is higher among women who have just started the pill. Such "new users" may have tended to use the newer formulations. Kemmeren et al have systematically checked for such biases and conclude that they are insufficient to explain the observed difference.

Clinicians will ask whether there is now a consensus among the experts. Over the past year, editorials and reviews have advised that second generation pills are the preparation of first choice.[4–6] Official advice is less specific. Guidelines from the Faculty of Family Planning of the Royal College of Obstetricians and Gynaecologists do not specify a first choice, but they point out that there is a higher risk of venous thromboembolism with third generation pills which "has not been satisfactorily explained by bias or confounding."[7] The Department of Health advises that third generation pills may be offered as first choice provided that the slightly increased risk is explained to the woman.[8]

But how does a clinician explain all this? The *British National Formulary* sets out the figures: the baseline risk of deep venous thrombosis among young women without risk factors is about 5 per 100 000 person-years for non-users, 15 for users of the second generation pill, and 25 for users of the third generation pill. If a woman asks about her chance of dying she is usually told that the mortality of deep venous thrombosis is 1-2%, which means mortality is about 2 per million users. This figure seems low enough to be reassuring.

This view was challenged by a New Zealand study which calculated a fatality rate of 10.5 per million users and suggested that this should not be glossed over during counselling.[9] Others, however, estimate that the number of excess deaths from venous and arterial disease among young pill users is 2-6 per million per year.[4] Indeed, an editorial accompanying the New Zealand study stated that the risk of fatal embolism is "much less than that associated with pregnancy."[6] We know from the UK Confidential Enquiries into Maternal Deaths that the risk of fatal venous thromboembolism can be as low as 12 per million pregnancies.[10]

Prescribers and their clients have become used to commentators "talking up" or "talking down" the pill's risks. In the past such biases reflected underlying views on sex, but now they may also reflect attitudes to the pharmaceutical industry. Writers have compared the results of studies with and without pharmaceutical funding,[5] and there have even been accusations that the industry has kept unpalatable results secret.[11] Kemmeren et al conclude that studies funded by pill manufacturers produce more favourable results than independent studies.

It is fashionable to portray global companies as villains. It is worth asking, however, whether prejudice against the pharmaceutical industry might also introduce bias into independent studies. It is entirely possible that both biases are unconscious. What is becoming clear is that, despite efforts to make published evidence entirely objective, "science is not a dispassionate activity."[12] Clinicians know this and are generally shrewd enough to allow for bias when interpreting papers. They already understand the risks of thromboembolism. They should also know that neither

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second nor third generation pills increase the risk of myocardial infarction among young women,[13] and that the risk of stroke is increased by 1 in 24 000 among pill users[14] irrespective of the type of pill.[15]

Prescribers still await a consensus on risk factors for thromboembolism. According to one review, "obesity is not considered a contraindication to the use of oral contraceptives,"[4] but the *British National Formulary* states that the pill should be avoided if the body mass index is above 39, and the faculty guideline gives no clear advice.[7] Doctors would also be helped—and lives might be saved—by clearer guidance on asking about a family or personal history of thromboembolism with a view to thrombophilia screening.

Finally, while debating whether risks are 1 or 10 in a million, we should remember that in most of the world the risk of death associated with pregnancy is at least a hundred times higher than this. Many thousands of lives could be saved each year if contraception were more widely available in the developing world.

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JOD has received research funding in the past from Schering UK, an oral contraceptive manufacturer, though the research was not on contraception.

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Poverty reduction strategy papers

It's too soon to say whether this new approach to aid will improve health

See also *Papers* p 139 and *Education and debate* p 152

A path out of abject poverty is currently being beaten by many low income countries which are developing poverty reduction strategy papers (PRSPs) as a condition for debt relief. This new acronym in the alphabet soup of international aid is the latest lifeline being offered by the World Bank and the International Monetary Fund after what many regard as the failure of its predecessor, the structural adjustment programme (SAP). By May, 33 interim and four full poverty reduction strategy papers had been developed: do they offer genuine hope to low income countries or are they the same old approaches under a new name?

Structural adjustment was characterised by economic policies such as devaluation and public expenditure reduction coupled with longer term structural reforms such as privatisation and trade liberalisation. It has been blamed for rising food prices, closed schools, and massive lay offs and for delivering the final blow to creaking health systems. Poverty reduction strategies instead offer good intentions such as "national ownership," "less dictation from Washington," "civil society participation," and "a focus on poverty." But the money, or the stick of withholding it, is still in the hands of the World Bank and the International Monetary Fund, since poverty reduction strategy papers are a condition for further cheap loans. They are therefore crucial to the future of 78 developing countries where poverty is by far the most important cause of ill health. According to Oxfam, 3.4 million children under 5 die in the highly indebted poor countries each year from easily preventable diseases.[1]

An investigation by the London based Overseas Development Institute was cautiously optimistic about the process of developing poverty reduction strategy papers in eight African countries.[2] The siting of poverty reduction in finance ministries (traditionally the most powerful parts of government) was seen as a sign of the importance many governments are giving to poverty. There are signs too of the benefits of increased civil participation. In Tanzania a poverty reduction strategy regional workshop was seen as contributing to the abolition of primary school fees. Yet the enormous difficulties encountered during the preparation of poverty reduction strategy papers cannot be ignored. Systems to collect data to monitor poverty reduction are crude, government policies fragmented, and public servants demoralised. Countries such as Rwanda do not have their own technical capacity to collect and analyse data, while the scant national budgets of Benin or Mali offer little real prospect of reform. Civil society may give its voice on the poverty strategies, but it remains excluded from discussions on the macroeconomic framework of the poverty reduction strategies.

Doubts have also been cast on the "revolution in thinking" that the World Bank and International Monetary Fund claimed had happened when they launched poverty reduction strategies two years ago. A

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