

His hearings are expected to explore the possibility that the Pill is doing or can do damage to genes which would not show up until future generations.

The Wynn-Doar research deals with how the body handles carbohydrates and fats and the changes in blood levels of these substances when The Pill is used. They interpret the changes they find as like those which precede diabetes and circulatory disease which leads to heart attacks—and therefore frightening.

Wynn rejects the argument that The Pill is just a relatively small dose of hormones natural to women in child-bearing years. "The Pills are not hormones," he says. "They are synthetic drugs with hormonal action . . . and their effects are equivalent to the last trimester of pregnancy and more."

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ORAL CONTRACEPTION AND DEPRESSION

Delay in the recognition of serious side-effects of new drugs is commonplace in psychiatry. The addictive potential of barbiturates and amphetamines and the hypertensive crises found with monoamine oxidase inhibitors are three examples, and it was a long time before serious depression caused by long-term medication with chlorpromazine was seen to be a much commoner and more troublesome side-effect than either jaundice or agranulocytosis.

It is no surprise, therefore, in a different context to find that the effect on mood of oestrogen—progestogen mixtures is displacing thromboembolic episodes at the focus of disquiet about oral contraceptives. Though as far back as 1961 T. B. Leberherz and C. D. Fobes (1) noted that 7 out of 112 patients being treated for endometriosis showed emotional distress, and that two of them became severely depressed, the general tenor of impressionistic reports until recently has been sanguine. From 5-30% of women complain of such symptoms as irritability, tension, and depression, but many have had premenstrual symptoms before they started on the pill, and in any case those who complain are balanced by the 10-20% who experience relief of premenstrual tension and an increased sense of well-being. High rates of depression appear to be associated with pills with a high progestogen content (2, 3), and depression diminishes with change to a more oestrogenic pill. When massive doses of the progestogen norethynodrel were given to 20 patients with endometriosis J. W. Scott and P. Brass (4) reported mood changes in all of them. Three developed depression of moderate severity, but it responded to antidepressant drugs.

A. Lewis and M. Hoghughi (5) have recently compared the depressive side-effects in 50 women taking oral contraceptives with 50 well-matched controls from the same group practice. Of the "pill" group 13 were mildly and 6 severely depressed, compared with only 2 and 1 respectively of the controls. Two of the severely depressed women had made suicidal attempts unknown to their general practitioners. The patients with a previous depressive history were significantly more depressed than those who had not—a finding that confirms earlier reports (6, 7). Two other trends emerged but did not reach the level of "significance": there was more depression with the more strongly progestogenic pills: and the longer a patient had been on the pill the more likely she was to be depressed. This last observation has been made before (8).

It seems, then, that the pill can precipitate depression in predisposed women of child-bearing age. But need these women, and others who become depressed out of the blue on such medication, be denied the undoubted benefits of oral contraception? Recent work suggests that prevention of this iatrogenic depression may be possible. Steroids, including cortisol and oral contraceptives, appear to influence tryptophan metabolism (9-12). The net effect seems to be to create a functional deficiency of pyridoxine, a coenzyme in the conversion of tryptophan both to nicotinic acid ribonucleotide and to 5-hydroxytryptamine. There is evidence that premedication with pyridoxine prevents the disturbance of tryptophan metabolism by cortisol (12), and some evidence, too, that a very few cases of "pill"-induced depression have responded to pyridoxine (13). A contraceptive pill incorporating pyridoxine has already been marketed in Spain (14).

NOTE.—Numbered references at end of article.