

as it occurs in relatively young age groups is overwhelming. The atherosclerotic lesion itself is not usually the cause of the final obstructive event. Most commonly, this is brought about by a clot forming in the blood and adhering to the vessel wall where it is damaged by the atherosclerotic process, thus obstructing the flow of blood through the vessel. It can be seen, therefore, that in many women taking oral contraceptive medication, the following potential risk factors may be operating, either singly or in combination, namely, abnormal glucose and insulin levels, abnormal serum lipid levels and abnormal blood clotting. Some have developed blood pressure as well. As far as we know, risk factors are additive in their effect. To give the Committee some indication of the importance attached to the metabolic (carbohydrate and lipid) abnormalities in the development of atherosclerosis, I have prepared a list of references (Appendix I) mainly from the literature published during the past three years. The list is by no means complete, and of course does not consider the clotting mechanism at all.

At this point, two important questions need to be examined. First, if these risks exist, why has occlusive vascular disease not become more of a problem than it is known to be at the present time? The answer is that atherosclerosis, in most instances, is a very slowly developing disease and it may take ten, twenty or thirty years of exposure to the metabolic abnormalities listed above before clinical manifestations of the disease appear. Those women who have already developed venous or arterial occlusions while taking oral contraceptives have usually done so through the operation of the abnormal clotting factor which may have been the only identifiable cause of their illness. It is still far too early to expect the major clinical manifestations of atherosclerotic vascular disease to manifest themselves as the result of oral contraceptive usage.

The second question is, are the metabolic abnormalities less important in the case of women than in man? I have already referred to the fact that in women before the menopause diseases such as coronary thrombosis are unusual compared to men. But this does not mean that young women possess a natural immunity which will protect them against the influence of untoward metabolic changes. Indeed, Dr. Michael Oliver, giving the G. A. Gibson lecture entitled "Ischaemic Heart Disease in the Young Adult" in October 1969 at the Edinburgh Royal College of Physicians, reported that in 135 women under the age of 45 with coronary artery disease the majority had abnormalities of lipid or carbohydrate metabolism. Whenever relatively young people with occlusive vascular disease are examined the incidence of abnormal carbohydrate and lipid metabolism is invariably high. One searching enquiry recently found such an association in 95% of the subjects tested ("Lipid and carbohydrate abnormalities in patients with angiographically documented coronary artery disease" by R. A. Heinle, R. I. Levy, D. S. Fredericksen and R. Gorlin, *American Journal of Cardiology*, Volume 24, August 1969, p. 178).

I conclude, therefore, that the carbohydrate and lipid abnormalities produced by the oestrogen-progestagen oral contraceptive constitute an atherogenic risk. How many subjects will be affected and what period of exposure to the medication is needed to produce the disease are questions which cannot be answered at the present time. But the number at risk is large and the dangers inherent in the medication are therefore correspondingly great. This hazard is not one which can continue to be overlooked.

I should like to consider now very briefly the problem of diabetes mellitus in relation to oral contraceptive steroids. The clinical condition generally understood by the term "symptomatic diabetes" falls naturally into two categories although there is considerable overlap. An acute, usually severe disease is the type characteristically seen in young people below the age of 40. Insulin is required for its management in most cases. A more common form of the disease is that which occurs in older people and is called maturity-onset diabetes. Women are more affected than men, and these patients are often overweight and even frankly obese. This disease is usually insidious in its onset and may have existed for many years without causing symptoms until some precipitating factor such as an illness or surgical operation brings it to light. The disorder can often be treated by diet alone, or by oral hypoglycaemic drugs. Oral contraceptive steroids commonly exacerbate diabetes mellitus in both its forms when the condition is already established, or present in a latent but still symptomless stage. This is not surprising considering the fact that earlier I described the diabetogenic effect of the oestrogen-progestagen contraceptives. But whether or not these steroids can actually cause symptomatic diabetes (as opposed to symptomless