

The second concern is for those women who are normal before receiving the oral contraceptive. This area again is only open to speculation as no definite scientific data are available to draw upon. Theoretically, if coronary artery and vascular disease is found in association with elevated blood cholesterol and triglyceride levels, then the production of higher blood cholesterol and triglyceride levels in normal women by use of the oral contraceptive may produce or predispose to vascular disease. Although several investigating groups have warned of this problem (22, 29, 36), it has not been documented to occur. A note of caution should be raised however, in that a requirement of time may be necessary before any permanent structural alteration is manifest. Should ten to twenty years of "hyperlipidemia" be necessary, then the clinical diseases should not be expected at this date.

C. Carbohydrates

In 1963 Waive, Frieden and Caplan reported in an abstract in an obscure medical journal that several of the women they were treating with oral contraceptives for rheumatoid arthritis demonstrated an abnormal blood glucose tolerance test (37). Since that report there have been more than 33 published articles in the world dealing with carbohydrate metabolism in more than 1,633 women using the oral contraceptive for periods ranging from 19 days to more than 8 years. Although an attempt will be made to summarize these data, the same problems are encountered, that is, the reports include many different drugs, dosages, durations of treatment and types of tests. Nevertheless, certain information is available and some generalizations can be made.

In prospective studies where the women are tested before taking the drugs and then serially thereafter, the development of elevated blood glucose levels is frequently seen. The incidence of this occurrence is variously reported between 0-100% of the time (37, 38-42).

This discrepancy in the incidence of altered blood glucose levels seems to be dependent upon several factors, and each should be studied in some detail. First, the type of testing that is done is important and in general the more elaborate and sensitive the test, the higher is the reported incidence of abnormal findings. Accordingly, the cortisone stimulated oral glucose tolerance test gave more abnormal results than did the plain oral glucose tolerance test or the intravenous glucose tolerance test. In general, for the group studies of short duration, the fasting blood glucose values are generally normal whereas the tolerance curve becomes abnormal. Second, the duration of time that the oral contraceptive had been taken seems to be important. In those studies where the duration of treatment with the oral contraceptive was several years, the incidence of abnormal results was the highest. In one cross-sectional study by Spellacy and associates of 31 women who had used the oral contraceptive continuously for more than 100 cycles, the incidence of abnormal oral glucose tolerance tests was more than 75% (37). Thirdly, the types of subjects given the oral contraceptive is important. In a presumably normal group of women there are certain characteristics which predispose them to a statistically greater likelihood of developing an abnormal blood glucose level while using the oral contraceptives. These characteristics included: (1) women of older age, (2) those of high parity, (3) those who gain excessive amounts of weight while taking the drugs or those that are obese prior to beginning the drugs; (4) those with a positive family history of diabetes mellitus; and (5) those women who had delivered excessively large infants, for example greater than nine pounds at birth. Fourth, the type of oral contraceptive used seems to be important. Again, this is difficult to evaluate but several points are worth mentioning.

The sequentially administered drugs have a somewhat lower incidence of abnormalities than do the combination type drugs. Admittedly the sequential preparations have been used for a shorter duration of time and the studies of them are fewer in number. Probably of more importance than the way the drugs are combined is the type and dosage of the steroid hormone contained in the oral contraceptive. Clinch and colleagues have recently reiterated the importance of dosage of steroids used in relation to the incidence of abnormal glucose results developing (43). Generally the lower the dose the fewer the side effects as was seen with the previous discussions on the liver and lipids. Of even greater interest to the future of contraception is the type steroid used. Several investigators have recently studied the estrogens and progestins separately. Although the data is still sparse, the results show that several of the estrogens above can elevate blood glucose levels (37, 44). When the progestins are investigated there