

is a mixture of results with some causing elevations of blood glucose and others having little or no effect. Finally of those with an effect, it is again related to the dosage of progestin used. For example, both Geshberg et al. and Spellacy et al. have demonstrated that medoxyprogesterone acetate causes an elevation of the blood glucose levels (45, 46). In contrast to this ethynodiol diacetate (44), progesterone (44, 47) and chlormadinone acetate (48, 49) have been shown to not significantly alter blood glucose. Thus, the dose of estrogen and the type and dose of progestin used in the oral contraceptive would certainly affect the incidence of abnormal glucose results produced in the users.

In addition to the blood glucose levels, other parameters of carbohydrate metabolism have been studied. Wynn and Doar have noted elevated levels of blood pyruvate in 12 of 55 subjects (22%) studied who were taking the oral contraceptives (16). Spellacy and co-workers first noted elevated blood insulin levels in women taking oral contraceptives and subsequently many others have confirmed this finding (37). Since we previously discussed the fact that insulin can increase the production of the blood lipid triglycerides, and since the levels of insulin are elevated in oral contraceptive users, we again can see how one area of metabolism being altered can several others. Spellacy et al. reported that levels of growth hormone in the blood are also elevated in women taking the oral contraceptive and this, too, has been confirmed (37). Therefore, the fact that carbohydrate metabolism has been altered in women using these drugs is no longer doubted. The important remaining questions are (1) are these changes reversible and (2) are they harmful?

There are no complete studies available as to the reversibility of these changes. In short, term investigations of only one to four months duration of treatment, the changes are usually reversible. For the longer duration studies the data is even more meager. This is because of several factors. The subjects discontinue from the studies for a variety of reasons and they can therefore not be located for followup testing, or they refuse to discontinue the drugs so that the reversibility of the alterations can be tested.

Probably the most significant question concerns itself with the possible medical hazards resulting from these alterations in carbohydrate metabolism. This question should be looked at in two parts. First, the patient who has a slightly abnormal carbohydrate metabolism when not taking oral contraceptives may be converted from a latent disease to overt insulin requiring diabetes mellitus if given these drugs (37, 42, 46). There is little controversy about giving the overt diabetic patient the oral contraceptive. The control of her disease may be slightly more difficult with the oral contraceptive, but it can be handled (37, 39).

The final problem concerns the normal subject who is given the oral contraceptive. One clinical finding which may be encountered is the development of a vaginal yeast infection (*candida albicans*). This problem is significantly more common in oral contraceptive users and probably results from the alterations in carbohydrate metabolism that are produced (37). This is a medical nuisance but not a serious health hazard. The production of diabetes mellitus would be a health hazard. No reliable information is available on this question at this time. Wynn and Doar noted that 13% of their subjects developed a chemical diabetes while taking the oral contraceptive and have warned of this complication as have others (17, 37). Since again we are discussing a theoretical disease occurrence which probably requires many years to develop, there is no answer at this date. An awareness of the problem, persistence of observation, and close followup of the treated patients is obviously necessary.

In conclusion, the data that I have reviewed for you today lends itself into two general areas. First, the scientific area. There are several important points. It should be immediately striking that the conclusions we are drawing come from very small sample sizes. For example, more than 18 million women are presumably using these drugs whereas the liver biopsy reports and the long term carbohydrate studies are based upon 31 women each. Most of the metabolic processes seem to be interrelated as with the liver-lipids and carbohydrates. A primary alteration in one may lead to significant alterations in the others. These alterations have to be considered for two types of populations. The one group are those with an already latent disease status, such as the women with a history of jaundice of pregnancy, abnormally high blood lipids or high levels of blood glucose. This group, although small in number, is particularly prone to develop serious medical complications from the use of the oral contraceptive. The prescribing physicians must be made aware of these facts and they must recognize