

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. Dr. Wynn has reviewed the studies of his own group and has noted elevated levels of blood pyruvate in 12 of 55 subjects—22 percent—studied who were taking the oral contraceptives. We first noted elevated blood insulin levels in women taking oral contraceptives and subsequently many others have confirmed this finding. 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 affect 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.

Senator NELSON. What is the significance of increasing the level of growth hormone in the blood?

Dr. SPELLACY. We began these investigations in an attempt to elucidate the mechanisms by which the blood glucose was being changed. It is known that if one has abnormally high levels of growth hormone, as in such diseases as giantism, there is a significant elevation of blood glucose, so that this hormone can raise blood glucose levels. It has also been shown that estrogen can raise the levels of this hormone. If the estrogen is given to men or postmenopausal women or premenopausal women, their levels of growth hormone accordingly goes up. Whether or not this elevated level that we measure in women taking estrogen is biologically active or whether it is inactive is not known.

The remaining questions are two in number: first, are these changes reversible, and, two, are they harmful?

There are no complete studies available as to the reversibility of these changes. In short-term investigations of only 1 to 4 months duration of treatment, the changes are usually reversible. For the longer duration studies, the data is 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. 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 medically.

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