

glucose levels is frequently seen. The incidence of this occurrence is variously reported between 0-100 percent of the time.

This discrepancy in the incidence of altered blood glucose levels seems to result from 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 that is used by the investigator, the higher will be 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 over the next 3 or 4 hours are 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 have been the highest. In one cross-sectional study 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 percent. Third, the types of subjects given the oral contraceptive is extremely 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 who have delivered a large number of babies, (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 infants weighing more than 9 pounds at birth.

The type of oral contraceptive also seems important. Again, it 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 there are fewer studies performed on this group. 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.

Senator NELSON. What do you mean by the type of steroid hormone?

Dr. SPELLACY. I will point out a little later, Senator, that the type of progestin used has a particular meaning as far as metabolic changes. There are some progestins that are virtually free of any metabolic changes, and there are some that produce very definite changes. So if a particular preparation contains a progestin that does not cause the changes that we are looking at here, then whether it is in the combined or the sequentially administered oral contraceptive, there will be fewer problems in that group of subjects.

Senator NELSON. So you are saying in the formulation of the progestin, synthetic progestin, there is a difference in the physiological consequences of the change, is that correct?

Dr. SPELLACY. Yes.

Senator NELSON. Can you identify or have those progestins been identified in their differences? Do we know what they are?

Dr. SPELLACY. Some have. They have not all been investigated, however.