

Senator NELSON. And is it any problem altering the formula to create the progestin that causes this problem?

Dr. SPELLACY. No, this would seem to be one logical approach to this whole general problem. Picking out the steroids that have the fewest metabolic effects and using those in the oral contraceptives.

Senator NELSON. What studies have been done to identify this?

Dr. SPELLACY. I am only familiar with the few that are mentioned in this text dealing with particular lipids and carbohydrates. I am not familiar with other studies as for example those dealing with blood clotting or changes in cervical epithelium. I think it is a great danger in using labels such as oral contraceptives because we have such a large variety of drugs and now have it is very clearly shown, that certain of the steroids cause many more adverse changes than do the others, and to lump them all into a group under one label makes it very difficult to assess any of the existing data or to predict for the future.

Senator NELSON. Are these different steroids patented? Is it possible that some of the progestins that would cause a different kind of a problem physiologically and the one that may cause the problem in one place may cause different problems some place else?

Dr. SPELLACY. In general, when a steroid alters one area of metabolism there are alterations demonstrated in other areas. Conversely, one that is free of metabolic effect in one area is usually free in the other areas, too.

Senator NELSON. Do you know how much research is being done to identify the differences in the metabolic effects of the different groups of progestins that are being used?

Dr. SPELLACY. No, I could not give you exact figures as to the total amount of work. Perhaps Dr. Corfman could.

Senator NELSON. Dr. Corfman, does NIH have figures or studies on that problem?

Dr. CORFMAN. We could develop a list of projects, if you wish, on this subject supported by a variety of agencies. It would not be just NIH. We could do that.

Senator NELSON. There are studies identifying the difference between metabolic effects of various synthetic progestins?

Dr. CORFMAN. Well, yes.

Senator NELSON. We will go back to you then.

Go ahead.

Dr. SPELLACY. Several investigators have recently studied the estrogens and progestins separately. Although the data is still sparse, the results show that several of the estrogens alone can elevate blood glucose levels. When the progestins are investigated, there 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 the progestin used. For example, two studies have shown that one progestin, medroxyprogesterone, will elevate, and in contrast three other commonly used progestins (ethynodiol diacetate, progesterone, and chlormadinone acetate) show little or no change in glucose or plasma insulin. We have been investigating in a limited way some of these effects in dogs and in humans and are able to confirm most of these reports.