

Mr. GORDON. But this is conducive to cancer in beagles, is that it?

Dr. SPELLACY. I have not read that report. Beagles spontaneously can develop cancer of the breast.

Senator NELSON. Thank you very much, Doctor. We appreciate your testimony. It has been very useful to us as that of Dr. Corfman, too, and we appreciate your patience.

(The complete prepared statement and supplemental information submitted by Dr. Spellacy follows:)

STATEMENT OF WILLIAM N. SPELLACY, M.D., ASSOCIATE PROFESSOR, DEPARTMENT OF OBSTETRICS AND GYNECOLOGY, UNIVERSITY OF MIAMI SCHOOL OF MEDICINE

EFFECTS OF THE ORAL CONTRACEPTIVES ON THE LIVER, LIPIDS, AND CARBOHYDRATES

I have been asked by this committee to review for them the effects of the oral contraceptives upon three aspects of metabolism; the liver, lipids, and carbohydrates. It is an honor and a privilege for me to come here and attempt to do this.

Before reviewing these three areas, let me point out the difficulties and dangers of such generalizations. It would appear that investigations of these problems would be easy. Careful thought, however, will show that this is not true. The medical literature on the oral contraceptives is expanding at a fantastic rate. However, this does not mean that all of the experimental and clinical data can be related into a central theme. Quite the opposite. Since there are so many synthetic estrogens and progestins used in oral contraceptives, and since the dosage of each is likely to vary considerably in each commercial product, and since the duration of treatment also seems to be important as well as the characteristics of the subject taking the drugs, the task of interpreting the literature is enormous. In addition, many reports do not deal with information on a pure drug-dosage-duration group, but rather upon a group of heterogenous subjects taking a variety of drugs for varying lengths of time. As a consequence, these results are virtually uninterpretable.

Cross-sectional studies, where women are investigated only while taking the drugs, do not guarantee that any changes noted were not existing prior to beginning the oral contraceptives. Isolated case reports of complications may point out areas of concern to receive special study, but they do not reveal incidence figures because the size of the total treated group is unknown. Finally where animal experimental data exists, its application and relevance to humans is not always known. As a consequence, a review of this large experimental literature does not answer all of our questions, and perhaps it raises more problems than it resolves. To find these answers will require large in-depth prospective studies of each organ system for all synthetic steroids at many dosages and drug combinations carried out for any years in a variety of different environments on many types of people. This is not practical. With this ideal in mind I will attempt then to review the existing medical knowledge in each of these three areas and to show any interrelationships and central themes that may exist.

A. Liver

The liver carries on many functions within the body.

The anatomic structure of the liver in women taking oral contraceptives is difficult to evaluate because of the inaccessability of the organ. Whereas Kleiner and associates found normal patterns on two biopsies studied with the light and electron microscope (1), three more recent reports dealing with thirty-one women who had liver biopsies performed while they were using oral contraceptives found changes. Although the light microscope could not demonstrate consistent changes, there were structural alterations within the liver cells involving the mitochondria particularly, which were seen with the electron microscope (2-4). Whether these alterations existed before the drugs were used, their frequency of occurrence, and whether they are progressive or reversible is not known.

The biochemical effects of the sex hormones on the liver are legion. It is well recognized for example that the liver produces most of the plasma proteins, and that this production is influenced at the cellular level by these hormones. Thus, giving estrogens to animals, including humans, results in an alteration in liver

NOTE.—Numbered references at end of statement.