

ference was held in Boston to enumerate and discuss the metabolic¹ effects of the contraceptive steroids. Approximately 75 persons participated in that conference, including representatives of various foundations and Federal agencies of the United States. Most of what I have to say is derived from proceedings of that conference and, in a general sense, is summarized in the preface to the book, "Metabolic Effects of Gonadal Hormones and Contraceptive Steroids."

These alterations, which have been demonstrated, include changes in carbohydrate metabolism, fat metabolism, protein metabolism, and the endocrine, liver, nervous and vascular system, among others. The findings are straightforward and reproducible. The implications and interpretations of the laboratory and clinical findings, however, are not yet resolved.

Certain facts are clear. First, the contraceptive steroids are not natural substances and should not be identified as such. They are unique, synthetic compounds, each with its own spectrum of activity, and regardless of dose, route, and frequency of administration, their effects cannot be equated with pregnancy, pseudopregnancy, or various phases of the normal menstrual cycle. I believe that the semantic oversimplification which equates the pharmacological state induced by the contraceptive steroids with biological states such as pregnancy should be abandoned.

Second, contraceptive steroids are not "equal." They are not all the same.

Senator NELSON. May I interrupt a moment?

Dr. SALHANICK. Yes, sir.

Senator NELSON. In your sentence, "I believe that the semantic oversimplification which equates the pharmacological state induced by the contraceptive steroids with biological states such as pregnancy should be abandoned," in what ways are they different?

Dr. SALHANICK. Well, they differ in some hormonal levels which occur. They differ in some of the biological responses which occur. They differ in the ratios of the estrogenic and progestational substances and in many of the fine descriptions of the chemical changes in the blood.

The contraceptive steroids are not "equal." They differ both in chemical structure and in biological function. Modern chemistry has synthesized a vast array of steroid molecules and has produced a comparatively thorough understanding of their metabolic functions. The limited structure-activity data available appear to indicate that it may be possible to separate some of the metabolic effects from the contraceptive activity. To my knowledge, however, no steroid with contraceptive action has been demonstrated to be of all metabolic effects. I see the development of such a substance as one of the very difficult challenges of the future.

Not only do the contraceptive steroids differ qualitatively, but there are probably different dose-response relationships. This is an important aspect of the problem if we anticipate the development of new steroids with minimal side effects. It is of interest that after more than 10 years of use, the dose-response curve for contraceptive effective-

¹ Metabolism: The sum of all the physical and chemical processes by which living organized substance is produced and maintained * * *, and also the transformation by which energy is made available for the uses of the organism * * *. Dorland's Medical Dictionary, 23d ed.