

problem is significantly more common in oral contraceptive users, but it can be medically handled and although a nuisance, it is not a serious health hazard.

The production of diabetes mellitus would be a health hazard. No reliable information is available on this question at this time. Wynn and Doar noted that 13 percent of their subjects developed a chemical diabetes while taking the oral contraceptive and have warned of this complication as have others. There is no confirmed data at this point. Since again we are discussing a theoretical disease occurrence which probably requires many years to develop, there is no answer now. An awareness of the problem, persistence of observation, and close followup of the treated patients is obviously necessary.

In conclusion, the data that I have reviewed for you today lends itself, I think, into two general areas. First, in the scientific area there are several important points that can be made. It should be immediately striking that the conclusions we are drawing come from very small sample sizes. For example, more than 18 million women are presumably using these drugs whereas the liver biopsy reports and the long-term carbohydrate studies are based upon 31 women each. Most of the metabolic processes seem to be interrelated as with the liver-lipids-and carbohydrates. A primary alteration in one may lead to significant alterations in the others. These alterations have to be considered for two types of populations. The one group are those with an already latent disease status, such as the women with a history of jaundice of pregnancy, abnormally high blood lipids or high levels of blood glucose. This group, although small in number, is particularly prone to develop serious medical complications from the use of oral contraceptive. The prescribing physicians must be made aware of these facts and they must recognize these women so that they can be given some other form of conception control. The larger population will be presumably normal and for them the potential production of serious complications such as liver disease, vascular disease, or diabetes mellitus are only a theoretical speculation at this time.

For the philosophical area of conclusions there are significant lessons to be learned from the past. As new modalities of conception control are introduced into medicine for normal subjects, it is important that ongoing prospective in-depth studies of their toxicity be carried out. In December 1969 Dr. Edward Tyler and others of Los Angeles published their long-term followup of one of the first groups of women in the United States to be given the oral contraceptives. Now after 12 years of use and with a current population of more than 8 million women taking these drugs in this country, they can report on but 176 women using the same drug, but at varying dosages, for only 4 to 10 years. The maintenance of a large core group for followup is not easy nor inexpensive, but it must be done to insure the safety of future generations. The studies must follow a pure research design utilizing selected drugs and isolated component steroids at the minimum dosages needed for effectiveness, then in future reviews we will no longer need to refer to "oral contraceptive studies" but to specifics such as the progestin α study of 17 women taking the drug for 36 months' time. Only this kind of information will be particularly meaningful.

Practicing physicians must be kept aware of the recent advances in our knowledge of fertility control so that their patients receive the