3. Case-Control Surveillance

It is proposed that an organized system be established to monitor the effects of oral contraceptives in case-control retrospective studies. Such investigations will be used to determine the possible relationship between oral contraceptives and such illnesses as diabetes, cardiovascular disease, cancer, and congenital malformations. Primary sources for data will be hospitals and reporting systems already in existence. Two studies on breast cancer have been approved by NIH and await the FY 1970 appropriation. Another is being developed on the possible effect of these agents on children conceived after the interruption of oral contraceptive use. Two or three additional studies should be initiated in each of the next few years.

4. Specially Designed Prospective Studies

Research problems in oral contraceptives are similar to those encountered in studying the relation between smoking and various diseases but the problems with oral contraceptives are considerably more complicated. Both retrospective and prospective studies are often required to convince all parties concerned that a positive relationship exists; it should be pointed out that comparable difficulty may also occur in proving that a positive relationship does not exist.

One specially designed prospective study is now underway at the Kaiser Permanente Hospital in Walnut Creek, California. This important project should be expanded and one more parallel facility established, preferably one serving a different socio-economic group than does the project at Walnut Creek.

NEW STUDIES

5. Metabolism of Oral Contraceptives

There is little information on how the body actually handles the synthetic hormones in contraceptive steroids. Such ignorance is remarkable considering the widespread use of these agents. Elucidation of these processes will undoubtedly clarify the understanding of the mechanisms of action and side effects of these agents and may lead to technological improvements in steroid contraceptives.

Studies of this type will require about three years and will cost approximately $500,000 for each combination of drugs. The studies require the development of radiolabelled drugs at a cost of approximately $50,000 each and the administration of the labelled drugs to experimental subjects. These studies should then be extended to the longer term examination of the biological effect of the metabolites identified.

6. Dose Response Studies

For oral contraceptives, as for other drugs, it is important that the lowest possible dose to be used. A considerable decrease in the amount of progestogens in oral contraceptives has occurred over time but no comparable decrease in the amount of estrogens has taken place. Carefully designed studies are needed to determine the lowest possible dose which can be employed and still maintain the efficacy which has made oral contraceptives such a valuable method of fertility regulation.

To date, essentially no work of this type has been undertaken by Federal agencies or non-profit groups. Such work may have been undertaken by the drug industry but, if so, information is not available. One major difficulty with such investigation is the real risk of unwanted pregnancies in the experimental subjects.

Dose response studies are relatively short-term and inexpensive. It would cost approximately $100,000 to determine the most effective dose for any particular combination.

7. Data From Family Planning Clinics

In addition to specially designed prospective studies, oral contraceptive research should include the monitoring of data derived from family planning clinics. Such a system would be analogous to the successful Cooperative Statistical Program on intrauterine devices conducted by the Population Council. Data should be obtained on such endpoints as cervical cytology, subsequent fertility, weight gain, and depression. Some of this information is already gathered as part of routine care and more could be obtained through special design.

This data collection system could be supported through contracts or become a direct Departmental operation. The National Center for Health Statistics is now developing a nationwide record system for Federally supported family planning clinics and it is possible that the required data on oral contraceptive use could be derived from this facility.