abortion are not known, it often results from a cytogenetic defect in the embryo. These cases would, therefore, not benefit from steroid therapy. Clearly those synthetic progestogens that are known to have androgenic properties should be avoided in the therapy of threatened abortion or hibitual abortion.

G. Miscellaneous Uses

The value of oral contraceptives in the treatment of conditions such as "menopausal syndrome", acne, chronic vulvar infections, and psychiatric disorders could not be ascertained because of the preliminary nature of the available reports.

recommendations

In making the following recommendations, the Committee has given careful consideration to this problem, which is unique because of the large number of healthy women taking the oral contraceptives over very long periods of time, the low incidence of serious side effects, the metabolic changes induced, the paucity of requisite statistical and scientific data, and finally, the health and social benefits to be derived. These factors have imposed the requirement for unprecedented standards of safety; they have demanded the detection of sequelae that are often remote and infrequent; they have opened to question the existing methods of surveillance and retrieval of data; and they have required the design of highly refined epidemiological experiments.

As our case is new and unique in the history of therapeutics, so have we had to think anew in framing these recommendations.

I. A large case-control (retrospective) study of the possible relation of oral contraceptives to Thromboembolism.

This study should follow the methods developed in a pilot trial described in appendix 7 (p. 71) to this report. In view of the results of the pilot trial, such a study becomes mandatory. This study must include a considerable number of hospitals, which should be of large size and high clinical standards and quality of medical records. The potential contributions of operations already existing in the Food and Drug Administration to maintain systematic, unified collaboration with such hospitals should be explored. Most important, the investigation should be under competent epidemiologic supervision.

II. Continuation and support of studies such as the ones being carried out by the Kaiser Permanente group in California and the University of Pittsburgh group in Lawrence County, Pa.

III. Support of additional controlled population-based prospective studies utilizing groups of subjects that are especially amendable to long-term followup, such as married female employees of certain large industries, and graduate nurses.

Although such prospective studies are difficult and require large populations, they may provide the only feasible method to answer the question of a relationship between the oral contraceptives and carcinoma, as well as the effect of these compounds on the growth and development of subsequent offspring.

IV. Continuation and strengthening of the present surveillance system of the FDA.

V. Review of the mechanism of storage, retrieval, and analysis of surveillance data.

If this system is to serve its prime purpose; namely, that of early warning, a much more efficient system of "feedback" will have to be instituted.

VI. A conference be held between FDA and the respective drug firms concerning uniformity and increased efficiency of reporting.

There is every evidence that the drug firms are willing and anxious to cooperate with FDA and with each other to achieve more efficient surveillance and more meaningful data.

VII. Priority be given to support laboratory investigations concerning all aspects of the hormonal contraceptive compounds.

VIII. Uniformity in labeling of contraceptive drugs.