introduction

THE oral contraceptives present society with problems unique in the history of human therapeutics. Never will so many people have taken such potent drugs voluntarily over such a protracted period for an objective other than for the control of disease. These compounds, furthermore, furnish almost completely effective contraception, for the first time available to the medically indigent as well as the socially privileged. These factors render the usual standards for safety and surveillance inadequate. Their necessary revision must be carefully planned and tested, lest the health and social benefits derived from these contraceptives be seriously reduced. Probably no substance, even common table salt, and certainly no effective drug can be taken over a long period of time without some risk, albeit minimal. There will always be a sensitive individual who may react adversely to any drug, and the oral contraceptives cannot be made free of such adverse potentials, which must be recognized and kept under continual surveillance. The potential dangers must also be carefully balanced against the health and social benefits that effective contraceptives provide for the individual woman and society.

The oral contraceptives currently in use are probably not those that will be employed 10 or even 5 years hence. Drugs with even less potentially adverse effect, utilizable in smaller dosage, will undoubtedly be developed through continuing research. At present several such promising compounds are under investigation. The research essential to the development and testing of these compounds is carried out by the drug industry working in close cooperation with the medical profession. It would be indeed unfortunate were such research and testing to be stifled by unnecessarily complicated, unscientifically harsh, and inelastic administrative procedures. It is axiomatic that all drugs must be carefully tested on several species of laboratory animals under comparable conditions before they can be given to human volunteers. It is equally important that the results of such experimentation be appropriately interpreted in extending their application to human beings. Particularly in reproductive functions man differs from experimental animals and other primates. To deprive a population of drugs of great benefit by overattention to adverse effects based on animal data without due consideration of clinical experience is unjustifiable. Throughout this report various types of adverse experience will be discussed. Most of them, however, occur naturally, with a definite though low incidence in our population. The data necessary to demonstrate an increase in these naturally occurring phenomena among users of oral contraceptives are not available. Most adverse reactions, including deaths, have been reported as individual cases or small series. Except in carefully controlled studies, neither the total number of people exposed to the oral contraceptives nor the number of adverse reactions in any locality is known. The crucial data are the numerator (adverse reactions) and the denominator (users) and a control made up of nonusers having the same or a different number of adverse reactions. The difficulty of obtaining such data for the oral contraceptives makes unreliable any assumptions regarding a cause and effect relationship of drug and adverse reaction.

There are, however, several epidemiological approaches which can shed light on the problem. The simplest and most obvious method is a system of surveillance leading to the reporting by physicians of suspicious illness in their patients who are taking the drug. Such a system is essential because it can give the earliest warning of trouble in a situation where quick action may be imperative. It should, however, be recognized that when the physician reports a suspected adverse reaction to a drug he usually cannot know with any certainty that what he has seen is in fact an adverse reaction and not a coincidental happening. The major deficiencies of this system are:

(*a*) Incomplete reporting by physicians of adverse experience for medico-legal rea-