

position in this controversy. I have no view on what should or should not be included in the package insert for their product. I do, of course, have a view of what conclusions can reasonably be drawn from the evidence provided by the Sartwell report.

*Summary of my position*

I should say first that I think that the study reported by Sartwell and his colleagues appears to have been done with great care and thoroughness and that it appears to be representative of the best work of this kind. The reporting is especially careful and meticulous, both in respect of the description of methods and in detailed reporting of the results. The study, standing alone, or taken together with the British studies, raises serious questions about the possibility of a casual relationship between the use of oral contraceptives and thrombo-embolic phenomena.

At the same time, this study is subject to the same kinds of limitations which afflict the British studies, and these limitations, which are mostly unavoidable, are of a kind which are not mitigated by replication of more studies of a similar kind. On account of the meticulous reporting in the present study it is possible to document some of these limitations from the evidence provided in the report itself.

I hold that none of these reports, nor all of them taken together, can be considered to provide conclusive evidence on the possibility of a casual relationship between the use of oral contraceptives and thrombo-embolic phenomena. Even less do they provide a satisfactory basis for discriminating degrees of risk due to different products.

*Retrospective studies*

Before I deal with the evidence of the report itself, let me mention by way of hypothetical examples the kinds of difficulties which arise in retrospective studies. Because the population at risk is dealt with only indirectly, it is entirely possible for important subgroups of afflicted individuals to escape observation altogether, or for incidental associations between use of a drug and exceptional incidence of the affliction in some particular stratum of the population to emerge as an apparent increased risk due to the drug. It is ordinarily far easier to recognize such situations in prospective studies and to correct for their effects. It is frequently difficult even to recognize them in retrospective studies, and often impossible to correct for such effects, even if they can be recognized.

As an example of a case in which an important segment may be entirely unavailable for observation in a retrospective study, consider an affliction which in an appreciable fraction of cases results in sudden death. A study which depends on post hospitalization interview must necessarily miss this segment entirely. If the effect of the drug is to modify such cases in a helpful way, so that they survive to be diagnosed and treated, the result of a retrospective study would be a finding of increased risk due to the drug—the exact opposite of the situation that would in fact obtain.

A second example is the following. Suppose we are dealing with an illness which tends to afflict those who engage in sedentary occupations and that the drug is expensive and used for minor conditions. It might happen, then, that professional individuals would tend to have a higher frequency of drug use, and a higher incidence of the disease. In a retrospective study where occupation was not one of the matching variables, the result would be to show an increased risk associated with the drug. There is, in fact, no great problem when the relevant characteristic is recognized and used as a matching variable in setting up the study. The problem is serious when, as is usually the case, there are many possible relevant variables, and matching is possible only for a few of those recognized—not to mention those of which we are unaware.

*Aspects of the Sartwell study—data acquisition*

As is clearly set forth in table 1, p. 66, over 2600 records of patients with thrombo-embolic phenomena were abstracted, but over 85 per cent of these were eliminated because of possibly predisposing conditions. The report makes the valid point that the concern is with the population of subjects for whom prescription of oral contraceptives would be expected. Despite the claim, however, that few women actually using oral contraceptives would be subject to