ORAL CONTRACEPTIVE STUDY—EPIDEMIOLOGICAL PRINCIPLES*

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Epidemiology is defined as "... study of the distribution and determinants of the prevalence of disease in human societies". Use of the term 'prevalence' implies concern with duration as well as incidence of disease and clearly recognizes the epidemiological relevance of the study of programmes adopted as public measures for the containment as well as the prevention of ill-health.

Excessive fertility

An important cause of the incidence of ill-health in women, as well as of its continuation where established, has for many centuries been excessive fertility. By 'excessive', we mean beyond that desired in the relevant context. Thus, the concept of individual fertility control (the 'fifth freedom') has become as important an argument for contraception as the more general need for population control.

Fertility control

Contraceptive methods capable of providing a measure of population control have been desired throughout the centuries and practised by many societies. But fertility control at the individual level has only recently become a secure reality with the introduction of oral contraceptives. Despite considerable interest in their possible harmful effects it has only been after more than twelve years use that certain toxic hazards have been reported. The occurrence of these at far from negligible levels has been associated with considerable alarm among the medical profession (although less so among the public) and calculations relating the hazards of contraception to those of pregnancy have been bewildering and diversely presented and interpreted. It seems clear that in respect of the major hazard specifically involved, the risk is lower than in pregnancy but the comparison is not altogether valid since pregnancy is not the only alternative to pill taking. Another comparison might be with riding a motor cycle or smoking cigarettes both of which are many times more dangerous than pill taking and for which—like pill taking—those who engage in them claim there is no equally satisfactory alternative.

So far, no large-scale prospective study has attempted to provide a reasonable balance sheet of advantage and disadvantage based on intensive scrutiny of the health of two groups of women distinguished only by the

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fact of one group being pill takers and the other not. The reasons for this have partly lain in the extreme difficulties of effecting such a comparison and some of the principal of these deserve consideration.

The major difficulty is that any group of women taking the pill seems likely to differ from a group not taking the pill in respects which many be either consequences or causes of the difference under examination.

The consequences of pill taking seem to be now well demonstrated in terms of the primary intended effect—viz., the control of fertility. Pill takers become pregnant less often than non pill takers if similarly sexually exposed. Since morbidity arises quite commonly from pregnancy and childbirth, and also possibly from anxiety related to the risk of pregnancy, we should expect an excess of morbidity in non-takers which might mask or modify the obviousness of any morbidity associated with the pill. It is possible, on the other hand, that pregnancy protects against certain kinds of morbidity such as breast cancer and hypertension. The principal issues here are, however, relatively clear and we may return to them later.

So far as antecedent differences are concerned two kinds may be distinguished; those which may have precipitated the decision to go 'on the pill' (e.g. complications of pregnancy actually experienced or potential), and those which may be particular to the class of women that select the pill as a method of contraception. For example, since pill takers are self selected to at least a certain extent, they may include disproportionate numbers of smokers, drinkers, promiscuous persons, libidinous or precocious persons. Or they may include disproportionate numbers of women who make use of general practitioners for degrees of morbidity which do not enforce medical consultation. In any of these cases we might expect to record a higher morbidity level among takers than among non-takers.

An important difference seemed a priori a possibility, viz., that previous obstetric experience might be different. Pill takers might include a higher proportion of nulliparous and multiparous women. Just as the class of women most at risk of pregnancy per unit time consists of young married women with one child, so the likelihood that a rigorously effective contraceptive is selected is greater in the residual classes still within the fecund period.

It is, of course, quite impracticable and possibly unethical to mount a rigorous study based on random allocation between pill and placebo. Even if pill and placebo were additional to a standardized additional contraceptive device the trial would lose much of its relevance to real life situations.

In short, it was considered necessary to mount a longitudinal study of the natural history of health, sickness and reproduction in two groups of women who differed chiefly in respect of their use or non-use of the pill, and to seek to record such additional factors as seemed to be relevant so as to minimize, so far as possible, extraneous sources of differential experience. In fact, this is a detailed study of two groups of women with sources of differences carefully considered rather than a rigorous experiment on lines appropriate to laboratory animals.
However, the major trial now being mounted is not an unconsidered voyage on wholly uncharted seas. It has been carefully designed on the basis of two previous trials specifically designed to yield data relevant to the design. In these, attempts have been made to isolate important differences between takers and controls so that control selection can be suitably undertaken and eventual analysis suitably controlled.

The main trial was designed to assess the practicability of the projected method of recruitment of takers and controls; to check the efficiency of the information recording methods; to assess the workload and acceptability of the trial among participating doctors, but most importantly to look for major differences between takers and controls.

Age

Previous experience had suggested that takers are younger than the related population of women. Controls were therefore matched for age within three years either way. Comparison showed that this device had succeeded in producing a control group with age distribution very close to that of the takers, although the controls had a marginally older age distribution. In both takers and controls the age distribution was markedly different from that of all married women at the 1961 Census. Takers and controls were much more markedly concentrated into the age range 20–29 where fertility is maximal.

Social class

Distributions by social class were also—and perhaps surprisingly closely similar for takers and controls. Although in respect of more traditional methods marked social class preponderances have been recorded, little reliable data has so far been recorded on the social class of pill takers. To some extent, any potential differences between takers and controls have probably been minimized by selection of controls from the lists of the same general practitioners as the takers. This imposed tendency to homogeneity may also operate in respect of other potentially troublesome variables.

Medical history

Past medical history was also similar in takers and controls, and the similarity was maintained at each parity. This suggests that past morbidity is relatively unrelated to childbearing and that morbidity arising from childbearing is not an important determinant of the decision to go ‘on the pill’.

Past fertility

In contrast there was a statistically highly-significant difference between the previous fertility of pill takers and controls. Pill takers have been appreciably more fertile. This, taken in conjunction with the similar age and social class distributions and the similar morbidity history, suggests the outstanding importance of fertility based on fecundity as a reason for the adoption of the pill as a contraceptive, and the relative unimportance of other selective processes.

These findings tend to justify our confidence that potential extraneous differences will not be too great to control in the analysis but we remain
convinced of the need to record as many such findings as are practicable.

It is important to state that the design of the enquiry is intended to create a register of two distinguishable groups of women whose contraceptive practice, fertility and significant morbidity has been carefully recorded, as well as providing narrative data. Additional data may more readily be obtained if desired.

The size of the study (about 60,000 women years will be scrutinized) will permit the detection of relatively small increases in relatively uncommon conditions. Complete elucidation of the relationships of such increases to oral contraceptive practice may then require the mounting of special ad hoc studies. However, the posing of hypotheses in relation to specific complications is considered a prime and very valuable function of the study.

In addition to comparisons between cases and controls, the size of the enquiry will permit comparisons of the amount and severity (measured by hospitalization) of morbidity between takers of different preparations or at different dosage levels. Analysis of intragroup and intergroup differences will often be helpful in explaining sources of differences.

One important consideration in respect of which initial decisions have been left open, concerns the desirability of regular recall of controls at intervals corresponding to those at which prescriptions are given to takers. Although there are arguments for such a procedure in terms of the possibility of casually reported morbidity in the taker group when prescriptions are issued, there is an equal possibility that arranged contacts between general practitioners and controls will produce more casually reported morbidity than will prescription visits. At present such control contacts have not been incorporated but consideration of this issue continues and trials may well be instituted to clarify the question.

Not the least important epidemiological consideration is the methodological one represented by the whole concept of such a mass study based on the Royal College of General Practitioners. The opportunity to place the natural history of so large a population under so intensive and prolonged a scrutiny would be effectively unattainable by any other feasible technique of contemporary epidemiology.

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A COMPARISON OF TWO METHODS OF DETERMINING SOCIAL STATUS

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THE ATTEMPT TO CLASSIFY THE almost infinite variety of Man's social habits must always result in an uneasy compromise. When no single method can be perfect, different criteria tend to be used for different purposes, but the