

peutic effects will be found, sooner or later, under the right combination of circumstances, to have undesirable, serious or fatal effects as well. To a degree at least, this is a hazard of all drug therapy.

One of the effects of oral contraceptives is to simulate, to some extent, a pregnancy or at least the earlier portion of a pregnancy. There are obviously many points of difference, but in several biological respects the woman on "The Pill" is pregnant, though the state lasts only a month, and no products of conception are present. Pregnancy is itself not a completely benign state; in 1965 the maternal mortality in this country was 2.4 per 10,000 for whites under optimal conditions of care, and 9.7 for non-whites under less than optimal conditions. It seems fair to assume then, that to the degree that the biological condition of the woman taking "The Pill" resembles pregnancy, she must be expected also to be exposed to the inherent medical hazards of pregnancy.

One great difference, of course, is the much shorter duration of each cycle on the pill. If one accepts the duration of pregnancy as 280 days, plus an anovulatory post partum period of about 30 days, one natural pregnancy exposes a woman to its medical hazards for 310 days. If on "The Pill" she will have had at least 10 pill cycles in that time. If natural pregnancy and the state induced by oral contraceptives were identical in risk, (and we have no reason to assume that they are identical) the woman on "The Pill" would have had ten times as many chances of developing a pregnancy-associated complication as would the woman naturally pregnant.

I emphasize—this is in no sense numerically exact or even medically proven. I mention it only to point out that there is reason to suspect that some of the natural hazards of pregnancy might occur in patients taking oral contraceptive agents; there is reason to suspect that they might seem to occur more frequently, since the state induced by the pill is so much shorter and more frequently repeated than is natural pregnancy.

Natural pregnancy has been recognized for decades to be attended occasionally by neurological complications. Migrainous headache often worsens, rarely improves, during pregnancy. Thromboses of arteries, or of the large intracranial veins were recognized as complications of the pregnant state decades before The Pill was available. Some authorities believe that intracranial aneurysms—congenital dilatations of arteries of the brain—are more liable to rupture during late pregnancy than at other times, and there is a clear and inescapable association between pregnancy and aneurysm of arteries of the upper abdomen.

All of these as complications of pregnancy are rare. Only the consultant—in the case of the nervous system, the neurologist—is apt to see any number of them and even he does not see many. Since spontaneous cerebral vascular accidents have for years been thought to be very rare in healthy, non-pregnant women, especially younger ones, it is not surprising that the question of a relationship between oral contraceptives and strokes should have been suggested at first largely by neurologists, who would naturally tend to see a concentration of such problems.

The first suggestive case report appeared in 1962. In the ensuing eight years, rather better than 100 cases have been reported in the world medical literature in varying detail, in which an association between the taking of oral contraceptives and the occurrence of a stroke has been suspected. In this time, an often bitter controversy developed over the relationship, if any, of the strokes to the taking of the drugs.

The reasons for this difference of opinion are simple. In the first place, the earlier cases were necessarily observed as sporadic events; their numbers were small. The physicians, usually neurologists or ophthalmologists, who became interested in them had no way of knowing how many women were taking such drugs. There was and is no reliable and continuing system of reporting, and there was therefore no way to know the total number of cases, or to relate this number reliably to the number of patients at risk.

Further, it was rapidly found that physicians had no really accurate idea of the incidence of spontaneous cerebral vascular accidents in young, healthy, non-pregnant women. Available data suggested a very low rate; Johnson and Walker, for example, found a preponderance of males over females of 4:1 in the below forty age group, and Gurdjian only seven of both sexes below that age, in a series of 258 cases. This sort of evidence, however, tells us only something of comparable frequencies between males and females, and nothing of actual incidence of spontaneous strokes in young healthy women. Knowing neither the expected in-