

rate from all forms of thromboembolism including stroke, greater than 1.5:100,000 in young women users to 3.9:100,000 in older users. Similar rates for non users are 0.2 to 0.5:100,000. Since deep vein thrombophlebitis and pulmonary embolism are much more common than stroke, in women in the child-bearing years, whether they take oral contraceptives or not, it is obvious that the death rate from stroke which could be attributed to the use of "The Pill" is quite small.

In the absence of clearer epidemiological evidence, it is worthwhile to look more closely at the strokes themselves. There are some suggestions that the strokes occurring in women taking "The Pill" may be different in their form and in their method of development from more common forms.

First, their onset is often prolonged, for days or even weeks, marked by premonitory migrainous headache, attacks of double vision, transitory weakness which recovers for a time, giddiness and syncopal attacks, which eventually develop into a full-blown stroke. This sort of onset is fairly common in older patients, where it is apparent due to the breaking off of small emboli from plaques of arteriosclerosis. The young pill users, however, often do not have arteriosclerosis at all.

Second, in a few autopsied cases, there is microscopic evidence that a slow process of thrombosis and then healing has been going on in several parts of the brain for some time before a major vessel was involved.

Third, the vertebral and basilar arteries, at the base of the brain, seem to be involved more often than one would expect, especially in the quite young women who have never had any hypertension and have no arteriosclerosis at all.

Fourth, the age incidence is of course unusual. In 59 cases now being analyzed, some my own, many from the literature, this was as follows:

20-24:	13
25-29:	14
30-34:	16
35-39:	11
40-44:	3
45+ :	2

This certainly reflects the childbearing years, but it does not show the steady increase one would expect if the strokes were simply due to the increasing incidence of hypertension, arteriosclerosis, and other medical diseases which could lead to stroke. It may simply reflect the incidence of use of "The Pill" in various age groups—though older child bearing women are often quite anxious to avoid further pregnancy.

Fifth, although mortality is fairly high, eight of fifty-nine, or 15.7% in this group, the survivors seem in most cases to make surprisingly good recoveries; about two thirds of the fifty-one in this group made good to complete recoveries.

Sixth, although coronary artery disease is a common concomitant of strokes as known in older people, there is as yet no good evidence that there is a concomitant increase in coronary disease in women on the pill.

These differences suggest a search for a different mechanism for the strokes and thromboembolic effects of "The Pill". This may be found in the changes in constituents and clotting mechanisms in the blood. It is known that synthetic steroids alter the lipoprotein pattern of blood plasma toward the male one, increasing the low density lipoproteins, triglycerides, cholesterol, and high density lipoproteins. They may cause an increase in alpha and beta globulins, and C-reactive protein, while decreasing serum chloesterinase and albumin. They increase serum iron, iron-binding capacity, prothrombin time, fibrinogen, and profoundly effect fibrinolytic activity and the Factor VII-X complex of the clotting system. Mechanism, at least, for alterations in normal clotting behavior are certainly present.

The steroid drugs used produce in their recipients a state which to some degree resembles pregnancy, a condition known to be accompanied by an increased incidence of disorders of blood vessels and blood clotting. There is evidence that blood clotting mechanisms, constituents of the blood, and carbohydrate metabolism are significantly altered by contraceptive steroids. There is further, the conviction on the part of many cautious and experienced clinicians that such cerebral accidents are now more frequently seen. It seems safe to conclude the following:

(1) There does seem to be a relationship between the taking of currently used oral contraceptives—"The Pill"—and the evolution of a stroke like syndrome or a frank stroke.