

cidence of such accidents in healthy women not on the drugs, nor the actual number of women in a given population on drugs, and being in doubt as to the accuracy of detection, diagnosis, and reporting of cases in women on the drug, it was impossible to interpret the earlier reports as anything more than a cause for concern. We were dealing with a fraction, of which we knew with certainty neither numerator nor denominator.

Between 1965 and 1968 several investigators published reports in which they attempted to meet these difficulties. These reports were of two general kinds. Some were studies from stroke centers, to which patients with stroke were referred in considerable numbers. With such clinical material, it was possible to compare numbers of cases in young women occurring before and after the time when oral contraceptives became available. Others were studies of strokes occurring in the population of large teaching hospitals, again using numbers of cases and incidences before and after The Pill came into use. In both of these approaches, and especially the latter, the absolute number of cases were very small, and in both it was impossible to relate strokes to a well-defined population of women taking the drugs.

These reports brought out the interesting point that strokes in young healthy women are quite possibly more common than was realized, but they were hampered by being drawn of necessity, from centers for study of such disorders, whose case load would normally increase with time, and by the fact that the case load could not easily be related to a population base. Their results are conflicting as in the following example :

STROKES IN WOMEN (15 TO 45 YEARS OF AGE)

	Bickerstaff—50 cases			Jennet—65 cases		
	No O.C.	O.C.	T	Pregnant	Nonpregnant	T
1954.....	2		2			
1955.....	1		1			
1956.....	2		2	0	4	4
1957.....	4		4	3	2	5
1958.....	3		3	5	2	7
1959.....	2		2	2	3	5
1960.....	1		1	2	5	7
1961.....	2		2	1	1	2
1962.....	4		4	4	4	8
1963.....	4		4	2	5	7
1964.....	2	4	6	0	6	6
1965.....	2	4	6	4	10	14
1966.....	3	10	13			
Total.....	32	18	50	23	42	65

Bickerstaff, drawing his patients from the Midlands, seems to have seen a clear increase in patients in the 1960's, and notes that of the 25 patients seen 1964-66, 18 were on oral contraceptives. Jennet, in Glasgow, felt there had been no increase in such accidents, and noted that of the twenty-six non-pregnant women in his 1961-65 group, 24 had never taken such drugs, one had discontinued them three months before her accident, and the last gave no information. Similarly conflicting reports were made by various American centers, among others those reported from Duke University and the Mayo Clinic.

In the last two years two carefully controlled studies were reported, one from England by Inman, Vessey, and Doll, and one from the United States by Sartwell and his associates. These again were retrospective studies in which cases of thrombophlebitis, pulmonary embolism, stroke, and in the British series, coronary occlusion were identified through hospital and physicians records. These were analyzed for presence or absence of possible contributing causes such as trauma hypertension, obesity, infections, etc., and suitable matched controls were selected and similarly analyzed. Cases and controls were then interviewed personally.

The results of these two studies were similar. Both indicate an increased risk of thromboembolism and stroke in the users of oral contraceptives. The British study suggested that the increased risk may be as high as eight or nine times, the American that it was of the order of four and one-half times that of the risk to non-users.

Though the risk is evidently greater, the absolute numbers remain small. The British figures, rather the higher of the two, do not suggest a range of death