

disease has increased with time since the introduction of these compounds.¹ The most frequent serious complication associated with the oral contraceptives is peripheral venous thrombosis with or without the complication of pulmonary infarction.

This report focuses on occlusive disorders of the cerebral vasculature because they are the most common arterial complications reported from the use of these compounds and because they also allow consideration of intrinsic vascular alterations as an etiologic mechanism.

CLINICAL REPORTS OF CEREBROVASCULAR ACCIDENTS IN WOMEN USING ORAL CONTRACEPTIVES

From the time of the first report of an unexplained cerebrovascular accident in a young woman using an oral contraceptive by Lorentz (22) until the report by Walsh and colleagues (31), a total of 10 cases were described. Two of them were included as cases No. 10 and No. 20 in the Proceedings of a Conference on Thromboembolic Phenomena in Women Using the Oral Contraceptives (29) and the other eight, including three deaths, appeared in isolated reports in the British literature. Walsh (31) reviewed the latter eight cases and collected 61 additional ones from numerous colleagues following publication of an Editorial by Cogan (6) requesting that such cases be sent to Dr. Walsh. The available data on the 69 cases were analyzed according to age of onset, duration of oral contraceptive usage, and type of central nervous system involvement.

In 63 patients, the mean age at onset of illness of 28.9 years was older than the mean age of American married women using hormonal contraceptives (26). The average duration of usage was 9.7 months, but 60 per cent were using the drugs six months or less at the time of the incident. Some of the reported cases had a predisposing condition. The temporal relations between the onset and course of the disorder and the starting and discontinuation of the oral contraceptive suggested an etiologic role.

Pseudotumor cerebri was reported in four cases who were the youngest and had the longest duration of use. Stroke was reported in 17 cases, two of whom succumbed. Ocular involvement occurred in 20 cases; eight had optic neuritis and the remainder had retinal vascular involvement. Migraine was reported in only 10 cases. Finally ten other cases with neurologic syndromes had incomplete information. The authors concluded that the evidence warranted further study.

Illis and coworkers (17) from the National Hospital, Queen Square, London, compared the frequency of cerebral arterial occlusion among women aged 18-45 years before and after 1961. Only arteriographically proven cases were considered. Although the overall yearly admission rate from January, 1955 to July, 1965 seemed stable, four (22%) of 18 patients admitted since 1961 were known to be using hormonal contraceptives. This proportion of users is probably a conservative one. Nevertheless, of the 18 cases admitted from 1961 to July 1965, the number who might have been expected to be using oral contraceptives according to the estimates of the Family Planning Association would be less than one (0.375) as compared with the four observed. Although this difference is significant statistically, no definite conclusion is possible because of uncertainty as to the use of the drugs in the population from whom the series was drawn.

Shafey and Sheinberg (28) described a variety of neurological syndromes including occlusive cerebral artery disease (five cases), thrombosis of cortical veins (one case) and vascular headaches (28 cases). This series contained no patients with a previous history of migraine attacks before starting oral contraceptives. Three of their six "stroke" patients, including a fatality, were included among the 17 stroke patients reported by Walsh (31). Each of the four patients who had angiographic studies showed "beading" of the vessels supplying the infarcted area of brain. Similar angiographic changes were evident in the case shown to have thrombosis of cortical veins. The authors did not place great weight on this finding because of a paucity of degenerative or inflammatory changes in the vascular system of the brain or of the rest of the body.

¹ See Appendix 2C, Greene.