

In April 1965, the Johns Hopkins neurophthalmologist, Frank Walsh, asked his fellow specialists (via the *Archives of Ophthalmology*) to report to him any cases they had seen with visual troubles similar to those he had observed in women on oral contraceptives. By November he had assembled some sixty cases in this way—seventeen with strokes, twenty-one with eye troubles, and twenty-three with other symptoms, including migraine. Without claiming a cause-and-effect relationship, he nevertheless wished to put the experience on the record and to ask for further study.

Meanwhile other physicians continued to report deaths as a result of compromise of the blood supply to the nervous system. One twenty-six-year-old Englishwoman died of a clot in her vertebral artery after a seven-week illness during which she had paralysis of all four extremities. In Ireland, a twenty-five-year-old patient expired with a large dead area in her brain caused by a clot in the carotid artery.

Dr. Sherif Shafey in Miami was at the same time accumulating his own series of thirty-four women, ranging in age from twenty to thirty-nine years and all receiving some form of oral contraceptive, who developed various sorts of neurologic complications, including migraine headache and clots in the arteries and veins of the brain.

Next, effects on the heart were reported. In January of 1965 a Norwegian pathologist described the sudden death of a thirty-two-year-old woman who had been taking oral contraceptives for five months. Postmortem examination revealed that the smaller branches of the coronary arteries were plugged with clots of various ages, with resulting death of the heart tissue. This was followed by a fatal case from England with clots in all of the major arteries of the heart; others have since been noted.

Why have these cases been put on record by physicians from various parts of the world? All the complications described are known to occur in people who do not use oral contraceptives. No new diseases have been seen. Why, then, the concern over the possibility of a cause-and-effect relationship?

It must be remembered that the suspicion of alert physicians is almost always the first indicator of pharmacotherapeutic mischief. Rarely can the doctor do more than suspect a cause-in-effect relation between drug and toxic effect, since hardly any drug's side effects are unique to that drug. Further, massive pulmonary embolism, strokes, and heart attacks are relatively rare in young women. This is a recurrent theme in the statements of concerned physicians, such as the British doctor who wrote:

"This cause of death [pulmonary embolism in a twenty-two-year-old woman on oral contraceptives for a few months] . . . in young people is extremely rare. In the few cases I have seen in young women there has always been some underlying explanation. . . . It is this feature which has been worrying me in my examination of an otherwise perfectly healthy woman. My own feeling is that [it] is just too much to be a coincidence. I have never seen a similar case . . . and I have seen many unexpected deaths in young people. This does not amount to proof."

Supporting this sentiment was a letter from a Cambridge scientist who disclosed the following information:

"From 9,280 consecutive autopsy reports . . . covering 1946-63, we have collected 27 cases [of massive pulmonary embolism] under the age of 70. Of 21 . . . females, only 3 women were under the age of 45, and they were either pregnant or had recently been pregnant. Thus we have no examples of non-pregnant women. . . ."

Other studies are in agreement. The coroner's records of Cuyahoga County in Ohio were reviewed in 1964 to see how often pulmonary embolism and unexpected sudden death occurred in supposedly normal persons between fifteen and forty-five years of age. Sixteen females had died in this manner during an eleven-year period. Five of these were pregnant at the time of fatal embolism, and eight of the eleven non-pregnant females were over forty. Thus, while such unexplained deaths are not unheard of in young women, they are decidedly rare.

In Hamburg, Germany, a study was made of fatal pulmonary embolism in a series of 5,200 autopsied cases. Of 500 consecutive cases of pulmonary embol-