

I might say parenthetically again, and with respect to the national magazine that Senator Nelson just referred to, physicians are not able to distinguish susceptible and individuals except in special circumstances, when the patient is not in good health. And this, in my view, is an exception. Most of the patients that utilize these agents are in good health and there is no way in the world that a doctor can tell which one will suffer from thrombophlebitis, for example, which is the condition I am talking about now, and undoubtedly others as well.

Going directly now to the question of blood-clotting in the veins, there are several lines of evidence that imply a definite risk of blood-clotting with use of oral contraceptive agents (1). First, a number of cases of thrombophlebitis with pulmonary embolism have been described in young women who did not have vein disease and who were not pregnant but who were taking oral contraceptive agents.

This kind of evidence is pertinent in that it would be considered extremely unusual for such a person to suffer this sequence of events. Thrombophlebitis ordinarily is seen in older patients who are bedridden, obese, suffering from cancer, suffering from heart failure, or in patients following surgery.

The second line of evidence is simply that of quantitative evaluation of the above general observation. It is the British studies which have already been referred to frequently in these hearings. Thus, careful studies of population groups have indicated that women taking oral contraceptive agents are eight times, or in fact more, depending on how you look at the data—are eight times more likely to suffer thrombophlebitis and pulmonary embolism than are comparable young women not taking these agents (2, 3).

Again parenthetically, many early studies neglected the fact that the instance of thrombophlebitis gradually increases with age and usually involves some other disorder. So we failed to compare completely normal young women taking the pill with completely normal young women not taking the pill.

A third line of evidence has to do with mechanisms whereby this unfortunate side effect of oral contraceptive therapy might take place. It is important to realize that in establishing a cause and effect relationship between an agent and a disorder, simple demonstration of association between the two is not enough. It is essential that some rational mechanism whereby the cause could lead to the effect be demonstrated.

The mechanism for causation of spontaneous thrombophlebitis—occurring independently of oral contraceptive agents—is not fully understood. However, a combination of data achieved through study of the kinds of patients described above, as well as data obtained in the laboratory, lead to several general conclusions.

First, one of the major contributing causes of thrombosis in veins appears to be that of reduced velocity of flow of blood in the veins or relative stagnation or stasis of flow in the veins.

A second factor of great importance in reproducing this disorder in animals, but very poorly understood in man, is that of the changes in

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NOTE.—Numbered references at end of statement.