

drug goes on for many, many years before perhaps an important finding like this is revealed.

Senator DOLE. Thank you.

Senator NELSON. Of those three who had hypertension when they were taking the pill and it disappeared upon return to normal afterward, had any of those had a history of hypertension?

Dr. LARAGH. No. None of those did.

The rechallenge experiment is what made us most suspicious of the cause and effect relationship. I think what supports it most strongly is the fact that since our reports, groups all over the world—I do not have exact figures, but I can say that perhaps at least 50 such experiences have been reported in the literature by other medical groups. So I do not think there is any question about the fact that in certain rare situations, fortunately rare, this can be a side effect or a consequence or a toxic effect of the use of these hormones.

Our next step, since I am, as I indicated, not a gynecologist, but a physician who studies high blood pressure, our next step was to measure certain components of the kidney adrenal hormonal system which we are interested in, and which we have found to have an important connection with the causes of all high blood pressure. We found that when you feed or administer oral contraceptive agents to these women, you produce in all of them an enormous increase in a chemical known as the renin substrate which circulates in the blood. This substance has the capacity to release angiotensin, a hormone which is the most powerful of all hormones in its capacity to raise the blood pressure.

The observations, then, revealed that the use of oral contraceptive agents produced a striking deformity of this blood pressure hormone system involving the kidneys and adrenal glands, a hormonal system which regulates the blood pressure in all of us and which regulates the blood pressure through regulating the amount of salt in the body—you all know that there is a well-known connection between salt and blood pressure and these hormones which cause salt retention and are implicating other kinds of high blood pressure.

It is also well known that women taking these oral contraceptives—some of them, at least—swell up and accumulate salt and water. Probably this occurs through activation of the renin angiotensin hormonal system which regulates the amount of salt in the body of all of us.

So that we have some chemical explanation or basis for why the oral contraceptives might cause hypertension in certain women. The observations of this sort, I think, are given increasing relevance by, first of all, what Senator Dole indicated that it may provide us with an analog of the experience during natural pregnancy, where hypertension is well known to occur.

Secondly, there may be other situations in which hormones, female hormones, are used, such as in the treatment of prostatic cancer, where hypertension may also have been induced, or even in the treatment of the menopause. So that this effect has, is expressed or is fulfilled in other areas where estrogens are used.

I would express, however, that while we do not have accurate epidemiological figures, and as you have heard from many speakers, these are indeed hard or almost impossible to come by. This effect of the oral contraceptives is a rare one and it does not occur in a large majority of women who are taking the pill.