ticularly in women who are in a "high-risk" group. To safeguard their health in later years, we must try to see today with the eyes of tomorrow.

Thank you.

Senator NELSON. Thank you very much, Doctor.

Is there any—are you aware of any studies, or do you have them with you, about the potential difference from physiological effect, such as you have mentioned here between, say, the 100 micrograms and a 75 or 50 microgram estrogen or lower? In other words, is the amount of the dosage a factor?

Dr. LEWISON. Senator Nelson, the amount of the dosage is a factor. We have reasonably good clinical evidence to indicate this.

For instance, in my own practice, in my own clinic, we will see women with breast cancer. Now, these are women who actually have breast cancer. By giving them massive doses of estrogen, unphysiologic high doses of estrogen, we can actually suppress or cause a regression of their disease. By giving them small doses, physiologic doses of estrogen, we can cause an acceleration of this same disease. So that it is perfectly obvious that there is a dose-time relationship.

Senator NELSON. Are there any studies that indicate the kind of dilemma that occurs when high dosages are used? Dr. Wynn's studies and some U.S. studies indicate that the high dosage of estrogens increase the incidence of thromboembolism. Are you suggesting that for, say, a patient who as a predisposition in one of the categories you listed or a recurring benign breast disease, that the higher the dosage of estrogen, the less the chance they will develop carcinoma?

Dr. LEWISON. I think these time-dose relationships have to be very carefully worked out in future research. We do know that the very small dose will stimulate or aggravate a breast cancer that is already in existence. We do know that the larger dose of this same estrogen presumably, according to the testimony of Dr. Wynn and others, will aggravate thromboembolic disease. But I am talking about therapeutic doses of estrogen for breast cancer that are in the very, very high range. For instance, doses that may be 100 to 200 times the dosage that you are talking about. This is therapy for advanced breast cancer.

Senator NELSON. So we do not know whether or not, in that woman with some predisposition, that in fact 100 or 75 micrograms of estrogen are more serious in terms of inducing carcinoma than 50 or 25 micrograms of estrogen?

Dr. LEWISON. In that range, we do not know. That is correct.

Senator NELSON. Mr. Duffy, do you have questions?

Mr. DUFFY. Yes, thank you.

Doctor, just one question, if I may. You indicated earlier that the risk of breast cancer increases with age, is that right?

Dr. LEWISON. Yes, many cancers show a downturn after the menopause, but unfortunately, breast cancer is ever increasing with each decade of life.

Mr. DUFFY. You would feel, then, that as a woman ages, she should be more careful if she chooses to use the pill?

Dr. LEWISON. Yes, I certainly agree with this. And since breast cancer also occurs at the ages of 50, 60, and 70, I would be even