

novobiocin, the novobiocin blood level in the patient who receives the combination is less than the blood level observed in the patient who received the same amount of novobiocin alone. It is markedly depressed.

Senator NELSON. The language here is that in that test the novobiocin serum levels went to subtherapeutic levels.

Dr. LEY. In all fairness I must say that I would have phrased this somewhat differently. Our knowledge at this time, Senator, of the exact relationship between a blood level and a therapeutic result in a patient is very, very poor. So that I would have qualified that to apparently subtherapeutic levels. It is a minor point. But I think it is important to make it for the record. The fact is that the level decreased markedly, to the degree that there is reasonable doubt that the novobiocin in the combination was therapeutically effective in the patient. With that I would certainly agree.

Senator NELSON. Then this continues:

This report of one crossover study dated November 14, 1960 comparing novobiocin and tetracycline serum levels alone and levels of both after Panalba, reconfirmed the marked depression of novobiocin levels and moderate lowering of tetracycline serum levels with the combination drug compared with each component drug given separately.

He concludes, as I understand it, then, that it reduces the level of the tetracycline too.

Dr. LEY. To a much lesser degree, I would agree with that one qualification.

Senator NELSON. Now, quoting further:

This is a report of a double blind clinical study submitted by Bennett W. Billow, M.D., using tetracycline alone and the Panalba combination. There were 25 cases in each group, each stated to be moderately to severely ill with a pneumonia treatable with tetracycline.

Now Dr. McQueen is quoting from the Upjohn Co.'s report of its own investigator:

Results of our investigation and laboratory studies unequivocally prove to us that there is no difference between—

And this is the code number—

58M and 57M clinically and laboratory-wise. There were no toxic reactions in either group, and reactions as well as therapeutic results were practically the same in both studies.

So as to this study, I take it they are concluding that there was no difference between the combination and its therapeutic effect and tetracycline administered alone, is that correct?

Dr. LEY. That is exactly correct.

Senator NELSON. Quoting again from Dr. McQueen's report:

This report concerns a crossover study of some subjects given two capsules containing 200 million grams each of tetracycline phosphate and novobiocin the first dose, and five days later the subjects were crossed over and given four capsules containing 5 million grams each of the two drugs. Comment: Both tetracycline and novobiocin serum levels are depressed.

What does that mean?

Dr. LEY. That means that neither the tetracycline nor the novobiocin absorb or produce as high blood levels when given in combination as when given individually.