

Dr. PILLARD. Well, the grandfather of the lot is chlorpromazine, which was developed in France, I believe, in 1954, by two French scientists—1948, Dr. Freedman tells me. It was first used extensively in this country in 1954 and 1955, but it was developed in 1948.

Senator NELSON. By two French scientists?

Dr. PILLARD. Deniker and Delay.

Mr. GORDON. May I ask a question at this point?

You just mentioned a VA study.

Dr. PILLARD. Yes.

Mr. GORDON. Was that made known to the medical profession; the fact that these drugs are essentially the same?

Dr. PILLARD. The studies were published, and been cited in subsequent reviews. So they have been made known in the sense that they have appeared in the medical literature.

Mr. GORDON. Does the average practicing physician know about this?

Dr. PILLARD. I am not sure he knows that study by name, but I think that most of them realize that the different phenothiazines are approximately equal. There are some exceptions to that which I will go into, but I think most people recognize this.

Senator NELSON. But the basic drug was developed by two French scientists?

Dr. PILLARD. Yes.

Senator NELSON. And then the other drugs that you have named here are of the same compound, are they?

Dr. PILLARD. Well, they are the same chemical family, phenothiazine, but they are slightly different, there are molecular alterations.

Let Dr. Freedman comment on this, he is an expert on it.

Dr. FREEDMAN. These were developed originally from antihistamines. I think the first synthesized antihistamine is the one that we would know as diphenylhydramine or Benadryl. And they were used in anesthesia to help stabilize the patient's temperature and bodily functions. And they first accidentally discovered or tried by Delay and Deniker to see if they would also calm patients who were agitated. The chemical developments we are speaking of, these phenothiazine compounds with slight molecular alterations can become an anti-pruritic agent. Each one of them is concentrated in different parts of the brain. So they do differ.

They differ mostly, I am sure you would agree, in terms of side effects, and somewhat drastically in terms of side effects. All you have to do is start playing games with a molecule and you get drugs that may have different biological effects and uses. The ones that are available for psychoses, in terms of efficacy, as proven by those studies, are similarly efficacious, but they may not be similarly advantageous.

Mr. GORDON. Concerning these molecular modifications—would an organic chemist or a person skilled in the art know exactly how to do these things?

Dr. FREEDMAN. Yes. Synthetic chemists are the people who rearrange these molecules.

We can already group them into several different kinds. Some have what we call a P. periliro tail on the nucleus. They have a different range of subjective effects, and tend to be more alerting or less drowsiness-producing.