

Senator NELSON. But in most cases, I take it, then, they are temporary side effects without permanent injury to the patient.

Dr. LEVINE. In most cases this is so. Of course, in the case of agranulosis it is a dangerous side effect.

Senator NELSON. Of which drug?

Dr. LEVINE. Chlorpromazine in particular has been shown to give rise to agranulosis but other drugs in the phenothiazine class also give rise to this side effect.

With regard to the extrapyramidal symptoms—this is rigidity of muscles and tremor, masklike facies which are the symptoms of Parkinson's disease—we can treat these with anti-Parkinsonian agents.

Senator NELSON. You can?

Dr. LEVINE. Yes, we can treat these symptoms with anti-Parkinsonian agents or with reduction in level of the psychotropic medication and this leads to a relief of these symptoms. When phenothiazine drugs are given in large amounts for prolonged periods of time, another neurological manifestation which has been called tardive dyskinesia and which is shown by unusual movements of the mouth and tongue and choreiform-type movements of the fingers are seen. They are thought to be related to large and continued phenothiazine usage and they are not as reversible or controllable as the extrapyramidal symptoms.

The symptoms of Parkinsonian, I might mention, Senator, are less often seen on an outpatient basis, since the amount of drug that is given is much lower than that given in a hospital. It is much more common in hospitals to see the extrapyramidal side effects and the other side effects that I discussed.

Mr. GORDON. I have a public health monograph called "Facts Needed To Assess Public Health and Social Problems in the Widespread Use of Tranquilizing Drugs." It is quite old. This was in a publication that came out in 1957 or 1958, and on chlorpromazine it says, "A large variety of toxic effects produced by chlorpromazine in man are well known. Among these are severe hypotension, dermatitis, Parkinsonism, jaundice, and agranulosis, to name only a few. Because of the way many of the results are reported, it is difficult to compare incidence of complications between studies by age, sex, type of disorder, and so on."

Dr. LEVINE. Yes, Mr. Gordon, if I can interrupt here, I think those are precisely the effects I mentioned, orthostatic hypotension, lowering of the blood pressure, increased pigmentation, liver damage, and agranulosis, so I think that older document in fact picked up the same kind of side effects that we know about today.

Mr. GORDON. Do you use reserpine or rauwolfia today?

Dr. LEVINE. No, not to any great extent. Reserpine came out about the same time chlorpromazine did and was found to be effective in reducing the symptomatology associated with major psychoses, but over the years it has been found that the phenothiazine-type drugs are more effective and have fewer side effects than reserpine. If a patient shows an allergic reaction to phenothiazine-type drugs, fortunately we have the reserpine drugs to fall back on as well as some newer classes of drugs that have been developed, the thioxanthine category of drugs and the butyrophenone category of drugs.