Mr. WINN. Dr. Rosen.

Dr. ROSEN. I just wanted to answer the question about the alcoholism if you wanted to know about the withdrawal from that.

Withdrawal from alcohol is much more life-threatening. If you have a patient who has experienced that once, you can expect that in the next withdrawal from alcohol they would again have at least that much in terms of convulsions and delirium tremens.

In my experience, and among that I have had about seven, I would say, who have had previous delirium tremens and convulsions in alcoholic withdrawal, and each one of those went through the withdrawal without even the shakes, which was unbelievable to me.

Mr. WINN. Dr. Davidson, you have had no experience with alcoholism?

Dr. DAVIDSON. No.

Mr. WINN. Thank you, Mr. Chairman.

Chairman PEPPER. Is that all?

Mr. Sandman.

Mr. SANDMAN. No questions.

Mr. BLOMMER. No questions.

Mr. RANGEL. No questions.

Chairman PEPPER. Mr. Davidson, we are very much indebted to you for coming and giving us the benefit of your experience as a man of thought in the profession and what you have had to say is of great interest.

(The study previously referred to follows:)

[Exhibit No. 15]

RESULTS OF PRELIMINARY PERSE STUDY

In the past few months Dr. Davidson, associate director of the Boston City Hospital Drug Abuse Clinic, has sent approximately 30 people to New York to undergo withdrawal from heroin and/or methadone with Perse, a new, non-addictive drug. The patients were given a series of daily injections and oral dosages of Perse by its inventor, Dr. Emanuel Revici. The treatment lasted approximately 5 days with varied, but overall encouraging results. Upon their return to Boston those patients that could be reached were asked to fill out a questionnaire involving the effect of Perse on various withdrawal symptoms and the overall success of the new "cure" for opiate addiction.

Out of all the subjects involved in this particular study only 12 filled out this form. Ten of these had undergone drug withdrawal before. Four were addicted to heroin only at the time. (One patient underwent Perse therapy twice—the first time withdrawing from methadone, the second from heroin—and filled out a form for each experience.) Eight patients were on both heroin and methadone, methadone only, or another similar opiate. The majority of the patients recorded "slight" or "moderate" overall withdrawal symptoms experienced with Perse; only three recorded that the symptoms were "bad."

The following is a runthrough of the individual responses to the specific symptoms experienced both with and without Perse recorded in the questionnaires:

The "runnning nose" withdrawal characteristic was quite diminished with Perse, and recorded by most as "bad" without Perse.

"Diarrhea" varied from "none" to "moderate" with Perse (with only one exception in which it was noted as "bad") and from "moderate" to "bad" without (with only one exception in which there was "none").

"Vomiting" was recorded by four patients as being "moderate," by the rest as "none" with Perse; by three as "bad" or "moderate," and the rest as "none" without Perse.

Four patients found "leg pain" "bad," three "moderate," and the rest "none" with Perse; five found it "bad" and the rest mostly "moderate" or "slight" without Perse.

"Stomach cramps" were found to be generally "slight" with only one "bad" with Perse; and "moderate" or "bad" with one "none" without it.

The "no sleep" symptom varied a lot with Perse—three "bad." three "none," the rest "moderate"; without Perse—generally "bad" or "moderate."

The sympton of "irritability" varied also with about six patients recording "none," two "bad," the others "slight" or "moderate" with Perse; while the majority noted the symptom as "bad," with the rest "moderate' or "slight," without.

With Perse "tension and nerviousness" was recorded by most as "bad" with some "moderate" or "slight" and one "none." Without Perse, all put down "bad" with the exception of one "slight."

"Craving" seemed notably diminished with Perse, the majority recording "none." Without it, the symptom was noted by most as "bad."

In answer to the last symptom, "tiredness," seven recorded it as "bad" with three "slight" or "none" and two "moderate" with Perse; while eight noted it as "bad," the rest "moderate" or "slight" and one "none" without Perse.

All patients, with the exception of two, recorded that Perse made their withdrawal symptoms better. The two that differed said that Perse had "no effect" and were, incidentally, addicted to rather high daily dosages of methadone. Methadone addicts have been found to require a longer period to withdraw than do heroin addicts. Most likely the chances of a successful withdrawal for these people would have been greater if the perse therapy had been continued over a longer period of time.

In response to the question involving the overall success of withdrawal on Perse the majority of the patients said that it was indeed "successful," with two stating that it was "partially" so and two that it was "not successful." Again, these last two were addicted to methadone and probably needed more time which this particular study was not set up to give.

Many of the users involved remarked verbally as well as in the questionnaire that they were struck by the fact that they experienced "no craving" for dope on Perse. One girl mentioned that she "forgot what it was like to be stoned." That perse seems to block off the craving for drugs in most people is an important attribute. This craving or the desire to return to drugs after experiencing the usual withdrawal distress and being clean is the result of "complex rationalizations which are difficult for the nonaddict to understand." [1]

A person assumes several different attitudes as he becomes addicted to drugs: He sees himself as an addict: he desires to increase his dosage; he is constantly dependent on the drug; and he sees the drug as a kind of panacea and various moral taboos wear off as the immediate beneficial effects of the drug become realized. Inherent in all this is a "reversal of effects" [2] in which the opiate "originally foreign to the body, becomes intrinsic" [3] as the union between it and the brain cells grows stronger. It becomes a nutritive element—a "means of carrying out the business of the entire organism." [4] This reversal occurs gradually and permiates deeply.

Drug addiction itself and the accompanying attitudes are all the result of the user's awareness and fear of withdrawal distress. Even after "successful" withdrawal these attitudes, although formed as a result of withdrawal distress, persists independent of it. Therefore the fact that perse seems to block off the desire for opiates is of considerable value in the face of the deep seated, somewhat irreversible nature of drug addiction.

There were problems encountered in the study which revealed the need to "tease out" psychological from physical withdrawal symptoms. Strangely enough, withdrawal symptoms have been known to reoccur in some after a year of abstainence from narcotics. Perhaps a double-blind study would solve some of the problem in separating the psychological from the physical and help evaluate perse.

Certain patients involved in this pioneer study were not psychologically ready to withdraw from their addiction. Obviously a study of this kind can only be useful to addicts who are ready for it. Perhaps a preliminary preparation of patients involved in further perse studies would somewhat insure their readiness to undergo withdrawal and to respond as objectively as possible.

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[1] Alfred R. Lindesmith, "Opiate Addiction"; (Principia Press of Illinois, Inc., 1957) p. 123.
[2] Ibid., p. 29.
[3] Ibid., p. 29.
[4] Ibid., p. 29.

The Perse experiment also revealed the need for a standardized environment conducive to drug withdrawal. Some patients were placed together and left on a "ward" with nothing to do but dwell on their symptoms; while others had to find their own accommodations outside and report to Dr. Revici daily. Withdrawal patients need people around them. Patients left alone have been known to suffer longer distress. A supportive staff would help to guide and encourage the patients in their individual interests and activities; to maintain a therapeutic atomisphere conducive to both psychological withdrawal from the whole drug milieu and physical withdrawal from the drug itself.

Again, in order to receive pertinent, cogent results from a study like this the environment must be standardized and rehabilitative. The dosages of the Perse administered must also be standardized according to the extent of the individual patient's addiction. Because of the preliminary nature of this experiment these things were not fully accomplished. Different dosages were given to different patients, the extent of whose addiction was not often clear. Some people needed more than the allotted time for withdrawal as has been pointed out. A fixed potentcy and a definite schedule should be maintained in relation to each patient.

Enough followup information on each subject involved is also important if there are accurate, cumulative results to be gained. All of the patients were not able to be located following the study and less than half filled out the questionnaire needed in this evaluation.

That there is a definite need for a more solid, clear method to be followed for future studies with Perse is obvious. Preliminary preparation of patients, a rehabilitative environment, a supportive staff, standardized dosages of Perse, and extensive followups of each subject would all help in revealing more clearly the merits of Perse. But regardless of the beginning nature of this study and its often varied results, it is obvious that Perse causes a definite altering of withdrawal distress. Indeed, many heroin addicts reported complete success with Perse; and the overall effect of the drug on those addicted to methadone —a notoriously difficult drug to kick—were encouraging enough to warrant more extensive study. Methadone itself has been proven to be a very beneficial tranquilizer to heroin addicts of certain temperaments. Its only drawback is that it is addictive. If Perse could solve this problem methadone could be used more freely in drug therapy.

This preliminary study with Perse has revealed the strong possibility that a nonaddictive cure for narcotics addiction has been discovered. The dilemma of addiction becomes more urgent every day and this new medication could possibly be a cure. This in itself is enough to warrant more extensive tests of Perse.

PERSE STUDY

Name _____

Date of treatment _____

Date of this report _____

Have you ever withdrawn before? Yes _____ No _____

Drugs used when Perse started:

Heroin _____ How much _____

Methadone _____ How much _____

Other _____ How much _____

Symptoms during withdrawal:

1. None _____ 2. Slight _____ 3. Moderate _____ 4. Bad _____

	With perse				Other times			
Running nose	1	2	3	4	1	2	3	4
Diarrhea	1	2	3	4	1	2	3	4
Vomiting	1	2	3	4	1	2	3	4
Leg pain	1	2	3	4	1	2	3	4
Stomach cramps	1	2	3	4	1	2	3	4
No sleep	1	2	3	4	1	2	3	4
Irritability	1	2	3	4	1	2	3	4
Tension, nervousness	1	2	3	4	1	2	3	4
Craving	1	2	3	4	1	2	3	4
Fatigue tiredness	1	2	3	4	1	2	3	4

Perse injections made symptoms Better_____ Worse_____ No effect_____

Withdrawal Successful_____ Partially_____ Not_____

Chairman PEPPER. That concludes the hearing for the day and we wish to thank all the witnesses and the members of the committee for the patience they have shown.

We will recess until 10 a.m., June 2, in room 2325.

(The following statement was received for the record.)

[Exhibit No. 16]

STATEMENT OF WILLIAM T. BEAVER, M.D., ASSOCIATE PROFESSOR, DEPARTMENT OF PHARMACOLOGY, GEORGETOWN UNIVERSITY, SCHOOLS OF MEDICINE AND DENTISTRY

It has come to my attention that the Select Committee on Crime has solicited testimony regarding the impact on medical practice of banning all imports of opium and opium alkaloids into the United States and the feasibility of completely substituting synthetic narcotic analgestics for those opium alkaloids and their semisynthetic derivatives currently in medical use. Because such a move would have a very substantial impact in certain areas of the practice of medicine and the conduct of medical research, and because you re contemplating making certain very widely used and long accepted drugs totally unavailable for the treatment of pain and other illness, it is, of course, fundamental that you consider a broad sampling of medical opinion and practice.

For the past 8 years I have been engaged in extensive controlled trials of analgesics in cancer patients and patients with postoperative pain to compare the therapeutic efficacy and side effect liability of a large number of naturally occurring and synthetic analgesics. I have published both the results of these studies and general review articles on the clinical pharmacology and relative therapeutic merit of these drugs. Simultaneously, I have been involved either directly or on a consulting basis in the day-to-day management of pain problems in thousands of patients with severe pain, predominantly due to advanced cancer. I have lectured extensively to medical students, hospital house staffs, and groups of medical practitioners on the optimal use of analgesics in the management of pain. In addition, I have served as a consultant to many governmental and nongovernmental agencies in this subject area, and am a member of the Panel on Drugs for the Relief of Pain of the NAS–NRS Drug Efficacy Study. I am therefore deeply interested in the substance and outcome of these hearings.

After reading several statements presented to your committee in April, I feel that insufficient emphasis has been placed on the significance, indeed the present indespensability, of some of the opium derivatives in the optimal therapy of patients with particular types of painful and nonpainful conditions. While it is true that the development of a variety of totally synthetic analgesics and antitussives over the course of the last 30 years has freed us from a total dependence on opium imports in the event of a national emergency, and while it is true that certain of these totally synthtetic compounds may be freely substituted for naturally occurring compounds in specific clinical situations and may in fact be drugs of choice in preference to naturally occurring compounds of some of these situations, it is by no means the case that such a substitution can be made in all clinical situations without patients suffering some or perhaps even serious detriment.

Among analgesics, none have properties which are entirely identical. They very in their potency, in the maximal analgesia obtainable by doses which have been proven safe, and in the speed of onset and duration of their action. Some are very much more effective than others when administered by mouth, while a tendency to irritate tissues sets practical limits to the size of the dose of certain drugs which may be injected hypodermically. The potent analgesics differ in their effect on mood, their tendency to produce sedation, their abuse liability and the pattern of their side effect profiles. Many of the newer synthetic agents have never been used to an adequate extent in certain special patient populations (e.g., children, women in early pregnancy, tolerant patients requiring very high doses of narcotics or patients concurrently receiving certain potentially interacting medications) to establish their relative safety under these circumstances. Likewise, there are certain clinical situations where only a single drug seems ever to have been given a careful therapeutic trial. For example, morphine is so extensively and universally used in acute pulmonary edema that there is little evidence to indicate whether other narcotics would prove effective in this condi-