1945 - 1946

CHAPTER 43
THE VIPERIN - DREAM.

Now to something else. Since I had now a good position in the hospital and also some income from my private practice, which although small kept growing, my greatest desire was to for my Viperin. get contact with one of the large American drug companies.

Through friends, whom we knew from Cuba, refugees from France, who were now also in New York, a family Weil, I was introduced to a Dr. Dreyfus, who had connections to the big drug company Hoffman-LaRoche. He made an appointment for me and I went out one day with all my material to Nutley in New Jersey, where I met a director, Dr. Furter, and explained the whole subject to him. He was very impressed and interested, and after further conferences a meeting with the president of the company, whose name I have forgotten, was arranged for the conclusion of a so-

called optional contract. That was in the home of that president on 5th Avenue. We agreed that the company would have two years to decide, whether it would produce the product and put it on the market or not. I would do all the necessary experiments in the laboratory, for which I would be paid a small salary of \$250.- per month, in preparation for the definitive product. I was not bound to work a certain number of hours, could come or go whenever I wanted. My royalties were causing some difficulties in our discussion, but I had finally to give in, as the president appeared to be a hard bargainer, and we settled for 3%.

We received samples of different snake venoms from Butantan in Brazil, and I had to try them out. I had again to experiment with white mice to ascertain the strength of the venoms, made then at first small amounts of ointment with the venom of the same I had used in Havana, which had come from Costa Rica. It turned out, when I used the ointment on myself and also on some of my patients in my office, that it was very effective, so that I did not have to try out venoms from other snake species anymore. I produced very soon bigger amounts of ointment, which were filled into tubes and sent out to different clinics. It took some time, till reports came in, which were very favorable, and Dr. Furter was very pleased. Every month I presented my bill of \$ 250.-, which was paid promptly. It was pleasant for me to work there, in that elegant, modern laboratory, where everybody was friendly and nice.

But it was a difficult time for me, as I had 3 jobs, the one in the hospital, the other one in my office and the one in the laboratory of Hoffman-LaRoche, and I had a very tight sche-

dule. On the three days a week that I was in the laboratory, I had to cancel my office rours, and so I was only 3 times a week in my office. But it worked out allright, only that I never got enough sleep, was always sleepy, slept also in the bus to New Jersey, which was not much, since I had to change busses in Passaic in New Jersey.

Toward the end of the second year a mishap occurred, which spoiled all my endeavours. It was partially my fault. To prove a point, I had prepared two batches of ointment, one which was very effective and another one, which was ineffective, since I had added some Wintergreen oil, which is chemically Methyl Salicylate, to the ointment. As I said, I wanted to prove a point and the ointment should have been used in 2 clinics, without the doctors, who tried them out, knowing, that they were using an ineffective ointment. On the jar, which contained that ineffective ointment, I had put a big label, which said clearly that it was ineffective. But the medical director disregarded this label and used only that ointment, sending it out to different clinics. The jar with the effective ointment was not used at all. The result was that very unfavorable reports started to come in. The medical director, a Dr. Sevringhouse, was fired on account of that, since Dr. Furter knew that he had made that mistake. But nothing could be done anymore, and I fell through with my contract.

I said that I wanted to prove a point when I made that ineffective ointment. I should not have done that. It was unnecessary to prove anything. I had a wonderful ointment, which was used with great success in Europe and then also in Cuba. I should not have changed the formula. But as I have

said before, I was always sleepy when I went to New Jersey, after a sleepless night and continuous service for 16 hours in the hospital.

In that sleepy condition I planned to make two kinds of cintment, an effective one and an ineffective one. It was unnecessary and foolish to do that. I was at that time sure that the company Hoffmann-LaRoche will put the product on the market. We were close to the end of the 2-year period when they had to decide wether they will put the product on the market of not, and they decided not to bring it out. When Dr. Furter revealed that to me, I was consternated, shocked. He showed me, when I saw him the last time, a big jar full of capsules of Benadryl, a medicine which was newly invented in France, the first antihistamine, supposed to be very effective in cases of head cold, hayfever. That new medicine put my Viperin apparently in the shadow, as they say in German. Very soon other antihistamines came out, Pyribenzamine, and others.

Looking back now, many years later, I can say that none of these medicines, antihistamines and combinations with Aspirin, whith which the market was flooded, were as effective as Viperin. First of all, they caused unpleasant side effects, especially drowsiness, so that people, who had for instance to drive a car, could not use them. And the effect of the antihistamines was of short duration, so that the medicines had to be taken 3 or 4 times a day. And finally, the effect was less good than that of Viperin, much less good.

The state I was in was more than sleepiness. It was general exhaustion. I had not had a vacation for many years. Behind me were 5 years in the subtropical climate of Cuba

and half a year of exhausting studying in preparation for the state board examination, and the last 2 years of the combination of hospital work at night, laboratory work at Hoffmann-LaRoche and private practice on some afternoons. I was constantly on the run. The nights in the hospital were the worst part of my work. It was, as I said before, a maternity hospital. There were nights, which were relatively quiet, and I could lie down in my room for an hour or two till I was called for a delivery. But there were other nights, when we had up to 8 deliveries and I could not move away for a moment, had to keep track of everything that happened.

After such a night, when I went out to New Jersey, I was exhausted and slept on the bus, first to the 41st Street in Manhattan to catch the bus to Passaic, New Jersey, and there I had to change to the bus to Nutley, where the Laboratory of Hoffmann-LaRoche was. I was not used to that kind of continuous work with little sleep, and that went on for months. I often fell asleep while working on the white mice.

My work in the laboratory consisted primarily in the preparation of the ointment, usually in amounts of 1 - 2 kg., which was then filled into tubes and sent out to different clinics for trials on patients. I had to determine the strength of the snake venom by injecting small well-measured amounts into mice. When I arrived at the laboratory in the forenoon, there was ready prepared a small container with 40 mice and a long wire container with 20 separate compartments. I had a list prepared, had to weigh each mouse, and after the injection of a small amount of the venom, I put the mouse into the first compartment wrote on my list the amount I had injected and the exact time. The next mouse — received the same amount of venom as the

first mouse. Again I put down on my list the weight, the time and the amount of venom. I continued in that way till all the 40 mice were injected. I then had to observe the time when the mice died. The mouse which died first within one hour gave me the exact strength of the venom and I could the proceed to prepare a big amount of ointment, which I usually did at my next visit to the laboratory, 2 or 3 days later. That was my main job. But I did many other things, so for instance experiments on rabbits, which were suffering from a disease called Pasteurella pestis, caused by bacilli, which cause pague in humans. bubonic Plague and plague pneumonia. The carriers of the disease are always rodents, like rats, rabbits, etc. and starts with bites of humans, and the disease is transmitted from man to man by flies or other insects. Anyway, laboratory animals have often symptoms of the disease, recognizable in rabbits by sniffels, for instance by sniffles and secretion from the nose. which is thencovered by crusts. It is in these animals usually a more or less chronic disease.

I used my Viperin ointment on these animals, after clipping the hair on their backs and rubbing in the ointment. There were always good results: disappearing of the secretion and diminished or disappearing crusts. There was no cure of the disease, of course, which is deep-seated.

I conducted other experiments on mice. They had there a strain of mice, which were almost naked, had no hair or only very fine hair. I clipped off the fine hair on one side of the back and rubbed in the ointment. To my astonishment, dense hair grew back after a few days in the treated area, which led me to believe that snake venom has a hair-growing effect. I reported my observation to Dr. Furter, but he was sceptical.

There were other experiments which I did under the guidance of Dr. Schnitzer, in whose department I worked. He was an immunologist and biochemist, and had quite a reputation in these fields. I had to immunize 10 rabbits against typhoid fever by injecting typhoid bacilli into the veins, increasing the amounts in short intervals. I vill not describe the whole experiment, as it would be difficult to understand it without going into great details. The purpose of these experiments was to prove that after rubbing in the Viperin ointment into the skin of the rabbits the degree of immunity against typhoid fever changed, which proved that the snake venom was absorbed from the skin and had gone into the circulation.

There was one chemist there, a German, whose name I have forgotten. He became interested in my work and gave me often advice. I did not trust him and had the feeling that he wanted me to do something wrong. There was much jealousy among the chemists in laboratory work. Once he told me about an interesting article he had read about an enzyme, a so-called spreading Hyaluronidase factor, which accelerated the spread of substances in the body. I followed his advice and went down to the library in the same building to read that article. There was also mentioned Wintergreen Oil, chemically Methyl Salicylate, which is being mauch used as Spearmint in foods. It also accelerates, according to this article the spread of substances through the skin. Slow

absorption is what I regarded as important, as it meant prolonged effect. Still, when I returned from the library, I could not resist his suggestion that I add some Wintergreen Oil to my ointment. I had just finished the preparation of a large amount of cintment, about 2 kg., and I added to one jar a small amount of Wintergreen Oil. I knew that I had ruined that cintment and I put a big label on that jar, which said that it was a less effective cintment. I found out later in my office in Brooklyn that the cintment was ineffective. I was before always very careful and had resisted suggestions that I add something to the base like Salicylic Acid or Boric Acid or that I use another base and not only simple Lanclin. And here I gave in and ruined everything, all my work of many years, as if hypnotized.

The whole thing was caused by my constant sleepiness. I was only 3 nights per week at home in bed and the other 3 nights I was in the hospital, where I had little chance to sleep. In such a condition I was hardly able to do any work and that was such a moment when I mixed some Wintergreen Wil into the ointment.

It was not an easy job for Dr. Furter to tell me that the company had decided not to put the ointment on the market. He had prepared himself quite well forthat, had a big jar full of Benadryl capsules on hand to show them to me. He knew that the medical director, Dr. Sevringhouse had committed an error, when he used that ointment witha big label, which said that the ointment had little effect, and had sent it out to different clinics. Dr. Furter told me that on account of that Dr. Sevringhouse was fired. That was of little solace to me. Dr. Furter knew that the ointment was for many years on the market in Europe and was very successful. He also had already some very enthusiastic reports

from doctors here in the U.S. These didn't seem to count, as there were a great number of negative results, and there was the Benadryl. And there was to be expected the foreseeable difficulty with the Food- and Drug Administration, which was against every new discovery in Medicine. There was probably the fear that critics would have used the fact that 'Snake Venom' should be used for the fight against the common cold, a relatively harmless disease, or hay fever, and thereby make the propaganda for snake venom ointment more difficult and more costly.

Viperin, of course, was an ideal medicine and would have been a great success, as in Europe, where people immediately used it by the thousands. Benadryl, like many other antihistamines, with which the market was swamped, was much less effective and until now no other really effective medicine was found. There are hundreds of antihistamines on the market, also combinations of antihistamines with other medicines like Aspirin, Ephedrine etc, also in form of nasal sprays.

Dr, Furter gave up too soon and thereby deprived the American public of a really great medicine. I am partially responsible too, as I explained before, when I worked in a state of exhaustion, without sleep for 30 hours or more, and made the mistake in changing the formula of the ointment.

I mentioned the word 'hypnotized' and ever since then the idea that I may have been hypnotized, kept coming back. It is the only logical explanation for that what I have done, why I had followed the 'advice' of that man, that chemist whose name I have forgotten. I was in a state of exhaustion and he had an easy object to work on. I am now convinced that he had hypnotized me and made me ruin my work. That explains everything that happened in

those days. Under normal circumstances I would not have done it.

I had made the ointment many times and it was routine work. And

I would not have done anything to change the formula. Here I ordered a small amount of Wintergreen Oil and mixed it in. It somehow neutralized the snake venom, made it ineffective.

I am now sure that I was hypnotized by that man. It was foul play, a rare type of foul play, a type I had never heard of before. Why he chose me to play his tricks, I can not imagine. Perhaps only to have fun. I was a newcomer in this country, did not know that foul play was quite common here. Did not know much about hypnosis. I know now that a trained hypnotist has no difficulty to hypnotize a victim and I have seen hypnotists do their work with great ease. It must be very easy when the person is not aware of it, tired and exhausted and sleepy, as it was the case with me.

For me it meant the end of my Viperin-dream. I was shocked and did not want to talk about it anymore, not think about it.

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There was, as I mentioned already, the offer of Dr.Schnitzer to connect me with another group of people and to do the Viperin business with them. I should have followed his advice, but I was so disgusted that I did not do anything. I was busy with my patients and that was what I wanted to do.

Looking back now, many years later, I see everything in a different light. My mistake to make an ineffective ointment was the cause that the company Hoffmann-LaRoche decided against putting out the product on the market. But that was not the only cause. More important was the fact that the antihistamines appeared on the market, a new medicine for head colds, hayfever, etc., which had to be taken in the usual way, by mouth, in the form of capsules or tablets.

In the case of Viperin an entirely new way had to be used, the rubbing of an ointment into the skin. And there was the snake venom, not used then for medical purposes.

There was always the difficulty with the Food and Drug Administration, which was antagonistic to everything new in medicine. Here many explanations would have been necessary and a rejection had to be anticipated. They would have asked for proof that the medicine is not harmful and it would have taken years, before a approval would have come from them, if ever. It would have been a long struggle.

When Dr. Furter showed me the big jar with the capsules of Benadryl, put on the market by the also very big company Parke Davis, he probably had already made up his mind and decided against Viperin. He must have been very impressed by the appearance of the antihistamines on the market, the first medicine for the treatment of the common cold, which was regarded as incurable in those days. The whole medical world was very impressed. The same would have been the case if Viperin would have come out first, before the antihistamines.

When I left the laboratory for the last time, the director of that part of the laboratory, where I had worked, told me that

he knew people who would be very interested in bringing out the product and he handed me a little note with a telephone number. He told me that there was plenty of money.

I never called these people. I was terribly disappointed and so disgusted that I gave up the whole thing and did not try anymore to negotiate with another company. I had a family to support and since my practice had grown in the meantime, I did not want and could not afford to lose time with other things. I also gave up my job in the hospital in order to dedicate myself completely to my private practice and to earn money. That was the right thing to do.

I have found an old letter, which I had written to Dr. Furter early in 1946. The letter is not dated. With this letter I can bring the chapter 'Viperin' to a conclusion. It shows the obstacles I had to confront in my work, when foreinstance a man, Dr. Floody, whom I had not known, wrote a report about my preparation and presented it in a board meeting, neglecting to separate results of treatment with an ointment which was marked as worthless, from other results. Disregarded were the good results and the positive clinical reports from Europe.

My letter shows the whole mixup and how badly I was treated with my medicine, which was called a wonderdrug by many, who had used it, or a miracle drug!. Till now - and we are now in the year 1981 - no really good medicine for head cold, hay fever, sinisitis, etc. had been found.

Now to the letter:

Dear Dr. Furter:

I am still missing your answer to my letter of February 4, 1946. On February 25, I spoke by phone to your secretary and asked her to remind you that you had not answered that letter. On March 18, I asked you by another letter for your answer, and on April 3, Mr. Steindecker, whom I had requested to talk to you, had called you up, and you promised him to look for the missing 100 individual case reports, and to answer me soon. But so far, I did not get anything.

Nevertheless, I am making another attempt, and ask you again to do something in that matter. Not answering letters can not be the right way to settle this problem. After all, I am entitled to get the investigational material, according to our contract, article 2, which says that you will promptly place at my disposal all experimental data and the results collected in your laboratories and during the clinical investigations for my unlimited use. In case you do not exercise the option,

The explanation, which you gave to Mr. Stein-decker, that you cannot find the missing 100 individual reports, and that the medical director, who was in charge of the clinical investigations and who has been dismissed since, must have mislaid these reports or so, is surely not sufficient. First of all, you could have given this explanation to me directly by answering my letters. And then, you have to assume the responsibility for your personnel.

It is now exactly two years, since I got in contact with your firm. I have lost two valuable years, but as I felt sure all the time that I would get the whole investigational material in case that you would not accept my preparation, I was patient and accepted your proposal for another extension of our contract for six months last June. My confidence was too great, I did not get the material, and I don't even get an answer when I ask for it.

This is an ropportunity for ime to show you how badly I have been treated already before, although I realize that most of the facts are known to you. Last

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December, I got your negative answer, and I was, as you remember, very surprised and disappointed, after all the excellent results, which you had had with my preparation. You told me then that you had to come to a negative decision in spite of 77% positive results in common cold and 54% positive results in hay-fever.

The main reason for the negative decision was, as you told me, the skepticism of the doctors regarding the action of the preparation, and the high cost of the preparation, as the price for the public would be about β 2.80 per tube. I told you, that this was already taken into consideration $1\frac{1}{2}$ years ago, when we negotiated about the contract, that Dr. Barrell and I had calculated the price of the preparation then, and that we did not come to such a high price. Anyway, this was not the real reason for the refusal of the preparation, nor was it the skepticism of the doctors. Doctors are mostly skeptical before they use a new preparation.

The real reason was the memorandum, which Dr. Floody wrote about the preparation on December 21, 1945. This report was prepared for the meeting of the mamagement, which was held 1 or 2 days later, and which had to come to a final decision about the preparation. It is difficult to find the right words for that what Dr. Floody did in this report. One may classify it as carelessness, but it may be something else. I don't think that it was done with the intention to mislead the board of directors, but it certainly could not have another result.

There were two different preparations, NU-602-1 and N-60M-1, which had to be tested, and which Dr. Floody confused in his report. You will remember how I asked you time and again to be careful about that, and you assured me that it would not happen.

But it did happen and in the following way: Last June, I told you that I would like to make an experiment with a preparation, which would benunch weaker than the old one, and to which I would add Methyl Salicylate, which is supposed to improve the absorption of chemical substances and toxins through the skin. Itold you that

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I would like to see the effect of such an ointment in experiments on a large scale in order to compare the results. You had started some time ago with experiments in a number of factories in New Jersey. I asked you to the new ointment too in one or two factories, but to be very careful, so that no confusion may occur.

On July 11, I prepared a few pounds of this ointment, and went then over to your office, where I asked one of the ladies to make arrangements the next day for the filling of the ointment into tubes. She madeea note on a piece of paper that the ointment was only half as strong as the normal ointment and that it contained 5% Methyl Salicylate.

I had found out very soon that the new ointment was almost worthless. It seemed that the admixed Methyl Salicylate had impaired the action of the drug. Whenever I saw you afterwards, I reminded you that this ointment was much weaker than the old one, and that the results should be valued accordingly. This was for instance the case last November, when I was at your office, and Dr. Floody had told you over the phone that Dr. Urbach had submitted a completely negative report about the ointment. Your answer was always that I should not worry about a confusion of the ointments.

When I got the final report of Dr. Floody, I saw that this bad ointment N-60M-l had been sent for experiments to two investigators, who are outstanding allergists and whose opinion had to be considered as very important for the final decision about the preparation. These were Dr. Erich Urbach of Philadelphia, and Dr. Maxwell Gelfand, director of the allergy Clinic at Bellevue.

Dr. Floody found it necessary to emphasise in his report the bad results, which these two investigators had with the ointment, but he did not mention that a weak ointment was used. Why did he not say that other investigators had sent very enthusiastic reports? Why did he not say that there were 100% negative results with the ointment N-60M=1? And why did he mix up these results with the results obtained with the ointment

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NU-602-1, when calculating the percentage?

As far as I can find out, 22 cases of hay-fever had been treated by the two above mentioned investigators. These 22 cases should be subtracted from the total number of 117 cases of shay-fever, if we want to correct the calculation of Dr. Floody, leaving only 95 cases of which 63 (66%) were benefitted, and 32 (34%) not improved. Dr. Floody calculated 54% positive and 45% negative results.

How many of the 113 cases of common cold had been treated with the bad preparation, can not be found out, as you did not send me the complete individual reports. Though 77% positive results calculated by Dr. Floody can already be considered as very satisfying, the percentage would again be higher, if the cases which have been treated with the bad ointment would not have been added.

Most disgusting is the last paragraph in the report of Dr. Floody, expressing his opinion "that despite the encouraging figures, the beneficial results, being entirely subjective, are largely psychogenic in origin and might well be duplicated by a placebo preparation."

It is not worth while to argue with Dr. Floody. Acute rhinitis, vasomotor rhinitis, hay-fever, and sinusitis are well defined conditions, and the average doctor is able to see whether a patient is benefitted by a certain treatment or not, whether the condition has disappeared or is still present. Beneficial results in these conditions are certainly not "entirely subjective". The papers, which I got from you, contain a great number of very enthusiastic reports, in many instances disappearance of all symptoms of bad colds within 24 hours, quick relief in vasomotor rhinitis and chronic sinus conditions. Dr. Floody is boasting in his report that the beneficial results might well be duplicated by a placebo preparation. Placebo is defined in Gould's Medical Dictionary as: an inert drug to satisfy patients. If Dr. Floody can really get 77% beneficial results in common cold and 66% beneficial results in hay-fever with a placebo preparation, he should rather do that than scientific work, and millions of people in the U.S.A. would be thankful to him.

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This extensive description was necessary to show you, how the success of many years of my work has been frustrated by carelessness and by a misleading report. This report was the main reason of the refusal of the preparation by the board of directors, and not the high price nor the skepticism of the doctors.

It is really not necessary that you, dear Dr. Furter, cause even more hardship to me by keeping back 100 individual reports, and by not answering my letters. These reports contain a great number of positive results, and I need them urgently for the continuation of my work.

Hoping that I have not written again in vain, I am,

very sincerely yours.