ON THE POSSIBLE EFFECT UPON THE AUDITORY
LABYRINTH OF THE EHRLICH-HATA REMEDY
IN THE TREATMENT OF SYPHILIS.*

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Professor Finger recently reported three cases of syphilis in which there appeared peculiar and somewhat serious symptoms affecting the organs of hearing. It must, therefore, be our most diligent study to determine as early and as surely as possible, whether, in the presence of such symptoms, we have to do with poisonous action of the arsenobenzol upon the auditory nerve or not. I may be able to contribute some material which will aid in the clearing up of this question. For a period of six years I have constantly collected clinical and, as far as it was possible, anatomic material for the study of syphilitic diseases of the ear, and this material is for the most part already prepared for publication in the "Handbook of Genital Diseases."

Up to the year 1907 my material consisted of all those cases of syphilis which for purposes of diagnosis were sent from the two dermatologic clinics of the Vienna General Hospital to the Ear Clinic. Through the kindness of my colleagues of the Policlinic, privatdocent Dr. Nobl and privatdocent Dr. Brandweiner, I have had the opportunity to observe all the cases of syphilis appearing there since 1907. During the years 1907-1908 I also had the opportunity of examining the material from the clinic of Professor Finger. This gave me the opportunity to observe and diagnose those forms of disease of the ear, and especially of the auditory nerve, which give so few symptoms, and these so rapidly disappearing, that the patient

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does not usually apply for treatment. For this reason such ear symptoms are easily overlooked. Finally, my material consists also of those cases in which the patient complained of trouble in the ear either at the time of or since the syphilitic infection that have applied for treatment at the ear department of the Policlinic since 1907.

A short time before the paper of Professor Finger was published he asked me the following important question, "Before we had the Ehrlich-Hata remedy '606' you had for a long time the opportunity to observe, and to methodically examine, my clinical material. Have you seen during this time any cases similar to those which I observed after the use of the injection?" This question I now answer. My observed material of syphilis of the ear, excluding those cases of diseases of the ear metaluetic in character (i. e., of tabes and paralysis), consist of sixty-eight cases. These have all been thoroughly examined and observed for quite a long time so that I am able to draw conclusions of both diagnostic and prognostic significance. In the course of the last six years I have seen twelve cases of ear disease appearing in the early stages of syphilis. Three of these cases showed disease of the external and middle ear, but in comparison with the cases reported by Professor Finger and Professor Urbantschitsch they show less severe affections of the auditory nerve and are, therefore, to be excluded. Comparing, now, my remaining nine cases with the three of Professor Finger, I obtain the following results: My nine cases represent a period of observation of six years; the three cases of Professor Finger of six months. In one of Professor Finger's cases the syphilis was of six weeks' duration; in the other two it was of three months' duration. Among my nine cases I can find only one in which the ear disturbance developed after thirteen weeks. In all the other cases in which the disturbance of hearing came during the early stage of the syphilis, it did not appear earlier than the fourth, fifth or sixth month.

We will now compare them as regards severity. Four of the cases showed a very slight degree of disturbance of the auditory nerve, slight dizziness or a slight degree of deafness, with subjective noises and a rapid favorable result. Serious or severe ear disease, as in Professor Finger's cases, I have observed in only five of my cases. One of them was treated

with atoxyl; in the other four the symptoms appeared after the ordinary forms of mercurial treatment by inunction or injection. From this it follows that acute syphilitic neuritis of the auditory nerve, whether localized in the cochlear or vestibular portion of the nerve, is, in the early stages of syphilis, very rare. During a period of six years, and with a much larger material, I have seen only one case more (5) with vestibular symptoms than has Professor Ffinger with his arsenobenzol-treated material during six months. In the literature up to the present time, cases of labyrinth syphilis, i. e., syphilitic inflammation of the auditory nerve in the early stages of syphilis, have been almost unknown. In his book on Ménière's symptom-complex, von Frankl-Hochwart surveys forty cases of syphilis. The symptom-complex of Ménière is nothing else than a disease of the labyrinth or the vestibular nerve, and the entire forty cases of von Frankl-Hochwart are those of chronic or latent syphilis. Professor v. Frankl-Hochwart has told me that he has never observed the Ménière symptom-complex in an early stage of syphilis. Politzer has reported the appearance of labyrinth syphilis in one case of syphilis of seven days' duration. This observation was made in 1878 and is, up to the present time, unique.

From the foregoing it is certain that the cases reported by Professor Ffinger, in so far as they are cases of disease of the auditory nerve in an early stage of syphilis, must be considered to have an etiologic relation to the arsenobenzol. It is not yet possible to assume with absolute certainty if during antisyphilitic treatment severe labyrinthine symptoms appear, that such symptoms are of necessity due to the treatment. Should one, however, defend this assumption, he must admit that it is possible to have, as Professor Riehl has rightly pointed out, severe cases of Ménière's symptoms, the severe acute forms of auditory nerve disturbance, even absolute deafness after or during the usual mercurial treatment. Among my material I recall two such cases, in both of which severe Ménière's symptom-complex appeared during the usual mercurial treatment. Both were, however, as are the other cases in the literature, cases of long-standing syphilis.

I now come to the consideration of my own observations on patients treated with arsenobenzol. These observations are based on the cases of syphilis treated by privatdocent Dr. Nobl.,

with arsenobenzol, seventy-two in number. Regarding the other peculiarities of his observations he has already spoken. Of the seventy-two cases, there was only one in which, after the injection, symptoms of disease appeared in the organ of hearing.

The patient was a seamstress thirty years of age who acquired syphilis in the spring of 1910 and had injections of mercury. At the end of July disturbances of hearing appeared in the right ear. She complained of deafness and disagreeable tinnitus, increased by movements of the head. Dizziness was also produced by movements of the head and she had the feeling as though something was turning inside the head; she staggered toward the right side but did not observe any turning of herself or apparent rotation of the surroundings. She had neither nausea nor vomiting. There was at this time some disturbance of vision in the right eye. The patient came to my clinic early in August. Examination showed disease of the right auditory nerve in the cochlear as well as the vestibular portion. At this time the left ear was absolutely normal. Under treatment by Dr. von Zumbusch in the Rudolphshospital the right-sided ear affection completely healed. She heard perfectly well in each ear and remained free of all symptoms until Oct. 2. On Oct. 16 she came to the clinic with the history that the right ear had remained completely healed but that on the afternoon of the 2d of October she suddenly noticed that she heard badly in the left ear and at the same time severe noises appeared. Examination at this time showed the right ear to be normal in every way while the hearing power of the left ear was greatly diminished (cochlear affection), but there were no vestibular symptoms to be attributed to the left side. The same day, Oct. 16, she received from Dr. Nobl an injection of the Ehrlich-Hata "606." After the injection the noises in the left ear stopped; she thought also that she heard better in the left side. Several days later sharp pains in the left ear came on, these extended down the neck and on to the back of the head and have continued up to the present time (Dec. 6) almost unchanged. On rising on November 10 she noticed that she heard very badly in the left ear, and the noises were as bad as in the beginning. On her way to the Polyclinic she had a severe attack of dizziness so that she very nearly fell to the ground; articles about her seemed to turn to the right and

she has had more or less dizziness since. On this date there was also some fever. Since Nov. 11 she has vomited two or three times daily. The dizziness is increased by changes of position, the attacks becoming paroxysmal on standing up or lying down, while during complete rest there is occasional freedom from the dizziness. Examination of the ear on Nov. 11 showed that the originally diseased right ear remained absolutely normal; on the other hand, the left ear had completely lost its function and the vestibular apparatus and the vestibular nerve did not react. This condition remains now, Dec. 6, unchanged. Since the middle of November there is also present a paralysis of the left facial nerve in all three branches. The paralysis is not complete, and the reaction to the faradic current still remains.

We have here a clinical picture under observation from the very beginning, as the patient before the Ehrlich-Hata injection had already, in the early stage of the syphilis, symptoms of disease in the inner ear of the right side. These symptoms affected the right ear only, and after treatment by mercury they entirely disappeared and complete healing took place.

Later, however, although still in the early stage of the syphilis, similar symptoms appeared in the left ear and became very much worse after the Ehrlich-Hata injection. Following this injection the disease extended itself over the entire area of the left auditory nerve and finally resulted in deafness and complete loss of function in the labyrinth of that side.

I think this case is suitable for bringing to our understanding the part which the arsenobenzol played as the etiologic factor in the production of the ear disease. It is important to notice that the arsenobenzol was given at the time when the left auditory nerve was acutely diseased. In my opinion the previously existing disease of the vestibular nerve presented a point of weakened resistance to the action of the arsenobenzol. The right auditory nerve, which was healed at the time, was not affected, but the left, already diseased ear was made much worse after the injection; hence we come to the conclusion that in cases of recent syphilis where there is already disease of the auditory nerve there is danger that the disease of the nerve will be made much worse by the use of the arsenobenzol.

Further observations will be necessary to determine whether

this danger exists only in the presence of already existing syphilitic disease of the auditory nerve, as in my case, or whether an already existing nonsyphilitic disease of the auditory nerve affords a predisposition or probability that the disease of the nerve will be made worse by the use of the arsenobenzol.

When one considers the experiments made with arsazetin, it seems probable that there is some danger of making the condition worse in every case in which at the time of the arsenobenzol injection there is already present disease of the auditory nerve, whether syphilitic or otherwise.

Ehrlich produced, by injecting white mice with arsazetin, phenomena similar to those of the true Japanese dancing mouse. Röthig has examined the central nervous system of the arsazetin-injected mouse after the plan of the work of Kreidel and myself on the ear of the Japanese dancing mouse. As an anatomic basis for the dancing movements of the arsazetin-injected mouse he found degeneration of the central fibers of the vestibular nerve. In order to answer the question why, apart from the optic nerve, the arsazetin finds its point of attack in the vestibular nerve in the white mouse, he examined the vestibular nerve in a larger number of normal white mice. He found that in the white mouse there was already beginning a certain amount of vestibular degeneration. The arsazetin finds, therefore, in the vestibular nerve of the ordinary white mouse, a point of lessened resistance. This explains, according to Röthig, why, after the arsazetin injection, there appears at once in the white mouse a severe degeneration in the vestibular nerve and at the same time a disturbance in the turning movements. From these conclusions we come to the following theory. It is not to be expected that a previously sound auditory nerve will be destroyed by the arsenobenzol injection. On the other hand, an unfavorable action from the arsenobenzol is to be feared whenever the auditory nerve is diseased previous to the use of the arsenobenzol.

Finally, I wish to state my own standpoint as an otologist with reference to the manner of the action of arsenobenzol upon syphilitic ear patients. More and more often is the question asked whether, in a case of syphilitic ear disease, the Ehrlich-Hata injection is indicated or not. After the preced-

ing observations, which naturally do not give an absolute finding, it is to be recommended to use caution in cases of acute syphilitic disease of the auditory nerve. Especially is caution in the use of the remedy to be recommended in the presence of acute or chronic disease of the auditory nerve in cases of recent syphilis, as here it is to be feared that the ear symptoms will be made worse. It appears to make no difference whether the disease of the auditory nerve is of itself of syphilitic origin or not.

An unfavorable influence is also to be feared in cases of acute syphilitic affection of the auditory nerve in old cases of syphilis or latent chronic syphilis. In cases of hereditary syphilis it is also to be recommended in the presence of acute manifestations of trouble with the auditory nerve to wait before giving the Ehrlich-Hata injection.

On the other hand, there are a large number of cases of ear disease in which the previously described dangers from the arsenobenzol injection cannot be considered as dependent upon it. Here belong the cases of chronic syphilitic affection of the auditory nerve with slight diminution of hearing power and considerable tinnitus, as well as the cases of chronic labyrinth dizziness. I would only mention that in these cases we had good results from treatment before the time when "606" achieved good results.

Finally, the Ehrlich-Hata has a good effect in cases of chronic labyrinth disease in chronic syphilis. The good results reported by Professor Urbantschitsch in one case of hereditary syphilis and in two cases of cochlear disease and chronic syphilis encourage us to proceed farther along the path already laid out.

NOTES BY THE TRANSLATOR.

The three cases of Professor Finger to which reference is made were those cases out of 170 treated with "606" which showed ear symptoms after the injection.

CASE I, male, twenty-two years, came to the clinic Aug. 20, 1910, with cutaneous syphilis and osteoperiostitis of the tibia. Aug. 24, 0.5 neutral Ehrlich-Hata injected. Aug. 25, nystagmus, dizziness, typical falling symptoms, but with intact hearing. Diagnosis by the Ear Clinic: Isolated disturbance in function of the vestibular nerve. Complete recovery in a few days.

CASE II, male, twenty-five years of age, syphilis six weeks. Aug. 27, 1910, 0.45 Ehrlich-Hata, method of Wechselmann, injected. Sept. 8, initial lesion healed, patient discharged. No sign of secondary syphilis up to Nov. 2, and Wassermann negative. On this date, nine weeks after the injection, and three months after the infection, dizziness and deafness appeared. At the Ear Clinic the diagnosis of bilateral labyrinthine deafness was made. The condition remains unchanged.

CASE III, female, eighteen years, came Aug. 1 for macular type of syphilis of three months' duration. Aug. 5, 0.45 neutral Ehrlich-Hata, method of Wechselmann, injected. Aug. 17, all signs of syphilis had disappeared and she was discharged cured. On Nov. 3 she was free from syphilis. Wassermann reaction negative. Nov. 3, complained of dizziness, headache, and the Ear Clinic made a diagnosis of labyrinthine deafness, dizziness and spontaneous nystagmus. There is no improvement at time of reporting, Nov. 27, 1910. (Wien. klin. Wochenschr., No. 47 and No. 51, 1910.)

At a subsequent meeting of the Gesellschaft für Aerzte in Vienna, before which Professor Finger's paper was read, some other cases in addition to those of Professor Alexander were reported where ear disease had appeared as late manifestations after the use of the Ehrlich-Hata.

v. Zumbusch had found in the literature, among 7,000 cases from twenty-five clinics, 9 cases of auditory nerve disturbance, all being cases with secondary manifestations from second to seventh month, and in most cases the Wassermann was negative.

Dr. H. Frey reported a patient injected on Aug. 9 with 0.5 arsenobenzol who returned late in October with deafness and some vestibular nystagmus. This case later showed the exanthemata of syphilis so that Dr. Frey was not certain that these manifestations could be laid to the arsenobenzol. (Wien. klin. Wochenschr., No. 50, 1910.)

Through the kindness of Dr. Daniel Kaufmann, I was given the opportunity of seeing two cases, each of whom had deafness and labyrinthine symptoms some time after the Ehrlich-Hata injection. At the time of the appearance of these symptoms the Wassermann reaction was positive. Both patients were given mercury by injection, and when I saw them all symptoms were improving. Here it might be difficult to say

whether the ear symptoms were due to the arsenobenzol or to the uncured syphilis. In Dr. Kaufmann's opinion they were due to the arsenobenzol.

Professor Rille, of Leipzig, has recently reported (Berl. klin. Wochenschr, Dec. 12, 1910) three cases of ear involvement which may be briefly referred to:

CASE I, female, twenty-one years old, with no previous ear symptoms, maculopapular syphilide with involvement of the tonsil, was given an injection of Ehrlich-Hata, July 7, 1910. Four weeks after the injection, 0.45 gr., there appeared dizziness, noises in ear and deafness located largely in the right ear, where both air and bone conduction were lost. Later there appeared a partial facial paralysis and symptoms of choked disk in the right eye. Up to Nov. 15 there had been some improvement, there is some bone conduction, but conversation speech is not heard. The left ear is normal.

CASE II, female, eighteen years old. Ehrlich-Hata injection, 0.45, on July 10. On Oct. 10 pain in head and dizziness appeared and on the following day right-sided facial paralysis, followed in three days by optic neuritis. Under treatment with mercurial ointment the facial paralysis and other symptoms disappeared. Nov. 17, discharged cured.

CASE III, male, thirty-three years old. Injection of 0.7 Ehrlich-Hata, July 7. In middle of October there suddenly appeared a high degree of double-sided labyrinthine deafness at which his previous occupation, that of blacksmith, may have predisposed.