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FIBROLYSIN IN OTOLOGY.

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So large a literature has already accumulated upon the uses in otology of thiosinamin and its derivative fibrolysin that I have felt some hesitation in adding thereto. But since opinions, both in Great Britain and on the Continent, appear to be very much divided, I have thought that the publication of further experiences might be of some possible value, and I therefore offer for consideration the results of its use in the twenty cases which I selected for trial.

Before entering upon these experiences, however, it will be well to review those published by other observers, and to describe briefly the nature of the remedy.

Thiosinamin, known chemically as allyl-sulpho-urea, is obtained by the action of ammonia on essence of mustard, and occurs in colourless monoclinic or rhombic crystals, with a bitter taste and garlic odour. These crystals dissolve well in alcohol, very badly in water, and slightly better in hot water. It was first prepared by Berzelius, of Stockholm, in 1828. Its derivative, fibrolysin, we owe to F. Mendel (1), who succeeded in improving the aqueous solubility of thiosinamin by the addition of salicylate of soda in

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the proportion of one molecule of the former to half a molecule of the latter, whereby the painful nature of injections of the alcoholic solution of thiosinamin has been abolished by the substitution of the aqueous solution of fibrolysin. This solution has been further improved by Michel, of Paris, by using one molecule of thiosinamin with half a molecule of antipyrin, thus forming a syrupy liquid at ordinary temperature, more soluble in water than fibrolysin. This solution has been made use of in otology by Lermoyez and Mahu (2), who give its composition as—

Thiosinamin	15·0 grm.
Antipyrin	7·50 „
Distilled water . . .	100·0 „

Thiosinamin appears to possess the peculiar property of softening cicatricial tissue, and this selective action has been explained by Glas (3), quoted by Lermoyez and Mahu. The drug causes an œdema in cicatrices, their limits become less marked, and it is impossible to distinguish them from the tissue immediately adjoining them. The nodules appear to be separated, the fibres swell up and are dissociated. The action of thiosinamin is comparable to that of venous stasis as produced by Bier's method. There is produced interstitial œdema and softening. This "lymphagogue" action is not produced in healthy tissues provided that therapeutic doses are not exceeded. In toxic doses thiosinamin produces in frogs, according to Lange (4), a persistent anasarca. Besides this, it provokes (Doliker), as early as four hours after its administration, a very marked leucocytosis, and, influenced by a kind of positive chemiotaxis, the leucocytes travel towards the cicatrix and act as phagocytes upon the cicatricial tissue (Sugar [5]). Thiosinamin softens cicatricial tissue, but does not destroy it. Its effect is rapid, frequently demonstrable at the end of four hours, but is often of a passing character, and the benefit disappears some days after the cessation of treatment. Thiosinamin can thus only be an auxiliary to mechanical treatment, which should in its turn be used to extend definitely cicatrices which have become distensible under its use (Teleky [6]).

According to Lermoyez and Mahu, thiosinamin is a non-toxic, inoffensive agent. They quote van Horn as carrying out treatment upon two female patients, over a course of fifteen months, by injections two or three times weekly of a 15 per cent. alcoholic solution, a dose which produced at length a slight loss of appetite and feeling of fatigue, which disappeared rapidly on stopping the treatment.

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In spite of the assertion that thiosinamin is an inoffensive agent, certain published cases show that it can be dangerous. Thus Teleky quotes the case of a young man who had undergone a gastrostomy for cicatricial contraction of the œsophagus. Fibrolysin was used after some weeks, and, whilst it was possible easily to dilate the stenosis, the patient's death was caused by rupture of the gastric cicatrix. Hebra has observed old caries to light up again in tuberculous persons, and afebrile tubercle to become febrile. Stocker (7) has collected a number of instances in which the use of thiosinamin has been attended with untoward results.

Thiosinamin was introduced into therapeutics by von Hebra (8), who communicated his first experiences to the Congress of Dermatology at Vienna, in 1892. In 1893, Latzka (9) published his results. Hance next applied it successfully to the treatment of urethral strictures, but Richter (10), who did not use it in conjunction with mechanical methods, failed in similar cases. Other investigators followed, until Teleky improved the technique and obtained good results by applying it methodically in cases of fibrous stenosis of the œsophagus.

The first person to experiment with thiosinamin in otology was Sinclair Tousey (11), in 1897, who improved a case of long-standing deafness by its means. Lermoyez and Mahu, inspired by Teleky and ignorant of Tousey's case, next made trial of it in their clinic at the Hôpital St. Antoine. They treated twelve cases of deafness due to chronic affections of the ear, without selection, by a series of twenty injections of $\frac{1}{2}$ to 1 cm. of a 15 per cent. alcoholic solution of thiosinamin, given by the arm. Six cases were put also under local treatment, the rest were left to the action of the drug. Results were *nil*. About the same time Robinson and Beck had satisfactory results in adhesive cases by associating with the injections otomassage and inflation, and Sugar began to use the drug successfully in adhesive otitis, carefully eliminating otosclerosis, by hypodermic injection and intra-tympanic injections by catheter of a glycerinated 10 per cent. solution of thiosinamin. Lermoyez and Mahu then returned to their researches with a different technique. They used ear-baths of warm solution, according to the formula given above, for five minutes every night, otomassage being employed twice weekly. From this trial they describe thiosinamin as "a new remedy rich in promise," and state that failures in this method are due to two causes—faulty technique and faulty diagnosis, and that the only cases of deafness in which the treatment is justified are those of adhesive otitis due

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to a healed suppuration or a non-suppurative catarrh, but they add that cases must be carefully selected, and those with secondary labyrinthine complication or ankylosis of the stapes refused.

Maupetit and Coltart (12), quoting Lermoyez and Mahu, say that thiosinamin "has not fallen short of its promises, and that it is probable that otology can expect help from it." Among the authors mentioned by them as obtaining good results are Hirschland (13), Kassel, Tapia, Horeau, and Baratoux, who all combine to insist upon the necessity of associated mechanical treatment. Maupetit and Coltart used the same solution and technique as Lermoyez and Mahu, viz. local baths, with associated mechanical treatment, controlling their observations by using the latter alone, or in conjunction with baths of a 1 per cent. solution of iodide of potassium in sterile water. They give details of their results thus: "We consider this new treatment not only as useless as regards improving the condition of the patient, but more than that, hurtful. Therefore we renounce it completely. *Primo non nocere.*" In all, or nearly all their cases, the treatment set up discharge.

Poutchowsky (14) published ten personal observations treated by injecting fibrolysin. He selected patients whose labyrinthine functions were intact, and who had no trace of arterio-sclerosis nor any chronic affection of the lungs. He concluded that mechanical treatment must accompany the use of the drug, and that, although the latter has an incontestable influence on cicatricial tissue, treatment therewith alone does not give very important results.

Austerlitz (15) reports his statistics, and concludes that a severe control of the cases justified by careful functional examination for treatment must be practised during and long after employing thiosinamin.

Bichaton (16) reported twelve cases treated by thiosinamin. Seven showed no change, one was made worse, two were improved, and two preferred to discontinue. In four cases discharge followed. He concludes "that thiosinamin does not appear to us to have justified the hope founded upon it as concerns the treatment of adhesive otitis, and that in every case it is a drug to handle with caution, and the employment of which should be watched very narrowly if one does not wish to be exposed to disappointment."

Gay French (17) last year published his results with fibrolysin in this country. He reported 68 cases, of which 21 were suffering from post-suppurative conditions and 47 from chronic dry middle-

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ear catarrh. Of 52 cases of deafness and tinnitus the hearing improved and noises diminished in 16; hearing alone improved in 14, and 15 gave no result. In 16 cases of deafness without tinnitus, 10 showed improvement. The method employed was hypodermic injection in the upper arm of 30 minims of fibrolysin and the intra-tympanic injection of 5 minims into each ear. This was followed in fifteen minutes by otomassage. The treatment lasted twice a week for six weeks. The cases were controlled by six weeks' catheter and otomassage treatment before the fibrolysin was used. French concluded that the method was more successful in the non-suppurative than in the post-suppurative cases, although the latter showed greater amounts of improvement. He thought that "in cases of non-suppurative middle-ear catarrh this method gives much better chances of improvement than any other," except in those cases which showed a thinned and stretched tympanic membrane. Results in otosclerosis were practically *nil*. In one case of non-suppurative middle-ear catarrh the treatment had to be abandoned owing to marked vertigo after each injection.

Skrypta (18) and Knowles Renshaw (19) have also published good reports, whilst Hirschland (*loc. cit.*) and Urbantschitsch (20) have considered it, the former as a means of cure, the latter as a means of obtaining results which are otherwise unattainable in otology.

My own results have not been sufficiently good to justify a continuation of this method of treatment, vaunted by some and condemned by others, in my practice. I have used it, with some slight variation of technique, in 20 cases, 7 males and 13 females, with the meagre result that three, or 15 per cent., were improved, sixteen, or 80 per cent., were unimproved, whilst in one, or 5 per cent., the improvement was doubtful. The following gives the histories of these cases in detail:

Case I.—Female, aged eleven. Deaf three years, no tinnitus. Adenoids removed in June, 1909. Right tympanic membrane thickened. Left tympanic membrane thickened and showing calcareous plaques. *Tests:* Weber—R. positive; Rinne—R. and L. double negative. Bone-conduction—R. + 15 sec., L. + 10 sec. Low tones—R. and L. C16 to C128 lost. Acoumeter—R. 2 ft. 6 in., L. 1 ft. 3 in. Voice—R. 10 in., L. 5 in. Whisper—R. 5 in., L. 3 in. As the hearing did not improve after the removal of the adenoids catheterisation and otomassage were used every second day for four weeks, but gave no results. On November 13, 1909, fibro-

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lysin injections, hypodermic and by the Eustachian tubes, were employed every second day (thirty-five injections in all), with continuation of the mechanical treatment, until February 1, 1910. The tests gave similar results on three occasions, the last being taken the second week in February. Improvement was *nil.*

Case II.—Female, aged thirty-seven. Deaf since scarlet fever at ten years of age. No tinnitus. The discharge lasted for "some years," and tends to return when she has a cold. Nasal septum deflected to right, with enlargement of right middle turbinate. Left tympanic membrane: Perforation in anterior inferior quadrant. Right tympanic membrane: Healed perforation in anterior segment. A submucous resection of the nasal septum, with reduction of the right middle turbinate, was performed July 16, 1909. She returned home before she was tested, and was treated by catheter and massage by her own doctor until September, when she returned to the clinic, and her *tests* gave Weber—L. positive, Rinne—R. and L. double negative. Bone-conduction—normal, or slight loss on both sides. Acoumeter—R. 2 in., L. $\frac{1}{4}$ in. Voice—R. 2 ft., L. 4 ft. Whisper—R. 3 ft., L. 1 ft. 6 in. Low tones—R. and L. C16 to C64 lost. She was then treated with fibrolysin injections (hypodermic and intra-tympanic) every second day, with daily inflation and otomassage. After ten injections her tests gave: Acoumeter—R. and L. 1 ft. 4 inches. Voice—R. 8 ft., L. 6 ft. Whisper—R. 1 ft., L. 9 in. She returned to hospital on November 10, 1909, and remained until December 8, during which time treatment was resumed, and she had a further twenty injections, making thirty in all. Tests at close of treatment: Acoumeter—R. 2 ft. 4 in., L. 1 ft. 6 in. Voice—R. 3 ft. 1 in., L. 2 ft. 4 in. Whisper—R. 1 ft., L. 1 ft. 8 in. Low tones as before treatment. These results appeared to be contradictory, as her voice hearing, at first improved, deteriorated later, whilst that for acoumeter and whisper improved. This improvement was maintained.

Case III.—Male, aged twenty-six. Deaf twelve years, constant tinnitus, paracusis Willisii. Maternal uncle and aunt and younger brother deaf. R. and L. tympanic membranes normal in texture, indrawn, mallei mobile. Chronic pharyngitis, slight septum deflection, but no obstruction. *Tests:* Rinne R. and L. double negative. Bone-conduction—R. + 5 sec., L. + 6 sec. Low tones—R. and L. C16 to C128 lost. Acoumeter—R. 4 in., L. *nil.* Voice—R. 5 in., L. 3 in. Whisper—*nil.* He was treated from

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September 15 to October 6, 1909, by daily inflation and otomassage, strychnine internally, and a nasal alkaline douche. On the latter date his tests gave: Acoumeter—R 3 in., L. 1 in. Voice—R. 1 ft. 6 in., L. 8 in. Whisper—R. 1 ft., L. *nil.* Tinnitus not improved. On October 14 fibrolysin was commenced, as in Cases 1 and 2, with catheter and otomassage, and continued every day for two months, making thirty injections in all. On December 22 tests gave: Acoumeter—R. 5 in., L. 1 in. Voice—R. 1 ft. 8 in., L. 1 ft. 1 in. Whisper—R. 1 ft., L. 8 in. Tinnitus slightly improved. This slight improvement was not maintained for more than one month, and the case is, therefore, not counted as successful.

Case IV.—Male, aged twenty-one. Deaf one and a half to two years. Five years ago had discharge from both, due to acute otitis following bathing. When seven years old had earache and "inflammation of the ears." Paracusis Willisii. No tinnitus. Worse with colds. Left ear shows anterior and posterior ivory exostoses, but with sufficient passage to obtain a good view of the membrane. R. and L. tympanic membranes dull and thickened. R. and L. mallei mobile. Nasal septum deflected to left, enlargement of R. and L. middle turbinates. *Tests:* Rinne—R. and L. double negative. Bone-conduction—R. and L. normal. Gelle—R. and L. negative. Low tones—R. C16 lost, L. C16 to C64 lost. High tones—well heard. Acoumeter—R. and L. 15 ft. Voice—R. 3 ft., L. 2 ft. 10 in. Whisper—R. 16 in., L. 12 in. Catheter improved voice to R. 4 ft. 3 in., L. 3 ft. 11 in. On May 22, 1907, a submucous resection operation was performed, with removal of the anterior ends of the middle and posterior ends of the inferior turbinates. From June 17 to 29 he underwent a course of daily catheterisation and otomassage and at the end of that time he heard voice—R. 7 ft. 3 in., L. 7 ft. 2 in. Whisper—R. 21 in., L. 19 in. This improvement was maintained for fourteen days after the cessation of treatment, but then gradually went back until, on October 12, he only heard voice—R. 6 ft., L. 2 ft. 9 in. Whisper—R. 14 in., L. 7 in. Otomassage improved him to some extent, but then failed to help him. As it was concluded that the deterioration was due to the recontraction of adhesions in the middle ear, left by the earlier suppuration and stretched by the treatment, fibrolysin was tried, with otomassage, for fourteen injections (hypodermic only), without result. The patient refused to persist further with the treatment.

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Case V.—Male, aged thirty. Deaf twelve to thirteen years, from "colds." Variable hissing tinnitus, not continuous. Paracusis Willisii. R. and L. tympanic membranes dull and indrawn, mallei mobile. L. vomerine crest. Hypertrophic pharyngitis. *Tests*: Weber—R. posterior. Rinne—R. and L. double negative. Bone-conduction—R. + 10 sec., L. − 5 sec. Gelle—R. and L. negative. High tones—well heard. Low tones—R. C16 and C32 lost, L. C16 to C64 lost. Acoumeter—R. 1 in., L. *nil*. Voice—R. 13 in., L. 8 in. Whisper—*nil*. He was treated by daily catheter and massage for seven days without result, then, as he was anxious to return to New Zealand and his time was limited, fibrolysin was tried at his own request. He had twenty-six injections (hypodermic only), from June 29 to July 29, 1908, with the following results: (1) After the fifteenth injection he volunteered that he could no longer hear better in a noise, and this symptom has, so far, not returned. (2) His tinnitus, in his own words, was "greatly improved." (3) On July 25 his tests gave: Weber—not lateralised. Acoumeter—R. 6 ft. 9 in., L. 3 ft. 4 in. Voice—R. 6 ft. 7 in., L. 5 ft. 5 in. Whisper—R. 1 ft. 6 in., L. 6 in. Rinne—R. and L. double negative. Bone-conduction—R. + 8 sec., L. normal. Gelle—doubtful. Low tones—R. and L. C16 only lost. One year later he wrote saying that the improvement was maintained.

Case VI.—Female, aged twenty-six. Deaf eight years; worse since a bad cold at Christmas, 1907. Subject to colds. Tinnitus very seldom, then only faint buzzing. Paracusis Willisii since July, 1907. No family history. Never any treatment. R. tympanic membrane slightly indrawn, texture normal; L. tympanic membrane slightly indrawn, texture normal, promontorial blush. Mallei mobile. A definite pad of adenoids, with deep sulci, and adhesions in Rosenmüller's fossæ, seen by posterior rhinoscopy. *Tests*: Weber—not lateralised. Rinne—R. and L. double negative. Bone-conduction—R. − 10 sec., L. −8 sec. Galton—R. 25,000 d.v., L. 26,000 d.v. Gelle—doubtful. Low tones—R. C16 to C64 lost, L. C16 and C32 lost. Acoumeter—R. 5 in., L. 8 ft. Voice—R. 11 in., L. 30 in. Whisper—R. *nil*, L. 6 in. On March 12, 1908, her adenoids were removed and the adhesions cleared, and from March 18 to 26 she had regular daily catheterisation, with oto-massage. On March 24 she heard acoumeter—R. 13 in., left 8 ft. Voice—R. 17 in., L. 8 ft. Whisper—R. doubtful, L. 15 in. Bone-conduction—R. and L. −7 sec. Low tones—R. C16 and C32 lost, L. C16 only lost; other tests as before. She returned home,

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where treatment was continued by her own doctor. On January 13, 1909, she heard voice—R. 20 in., L. 41 in. Fibrolysin, by hypodermic injection only, was tried, in addition to the other treatment, her own doctor giving her twenty injections. One month after she heard voice—R. 17 in., L. 36 in. only. There was no change in the membrane, save that the blush on the left side was no longer visible. Ten further injections were given, but without result.

Case VII.—Female, aged twenty-nine. Deaf three years, L. worse. Worse past twelve months, and with colds. Pulsating tinnitus, not continuous. No paracusis Willisii. Tonsils and adenoids removed in 1908. R. and L. tympanic membranes indrawn and thickened. Nasal septum deflected to L. *Tests:* Rinne—R. and L. negative to C128, positive to C512. Bone-conduction—R. — 8 sec., L. — 10 sec. Gelle—R. and L. positive. Low tones—R. and L. C16 and C32 lost. High tones heard well. Acoumeter—R. 4½ in., L. 3 in. Voice—R. 1 ft. 7 in., L. 1 ft. 3 in. Whisper—*nil.* She was treated by inflation by her own doctor without result. In the summer of 1909 a submucous resection was performed with excellent result as to nasal breathing and colds, and this was followed by regular catheterisation and otomassage, which improved her hearing for voice 1 ft. R. and L. On September 16 she was found to have gone back to—voice, R. 29 in., L. 12 in., and fibrolysin was tried by hypodermic and Eustachian injection. Only a few injections were given by her own medical man (Dr. Lascelles, who took much trouble with the case), as the patient objected to the length of time the fluid remained in the Eustachian tubes. Improvement *nil.*

Case VIII.—Female, aged thirty-five. Deafness four to five years, R. first affected. Worse past two years with colds and damp weather. Continuous rushing tinnitus R. and L. No paracusis Willisii. Was first conscious of her deafness after her first confinement at age of thirty. Has had four children, and was worse after each one. One brother deaf. R. and L. tympanic membranes slight indrawing, mallei mobile. Nose, throat, and post-nasal space *nil.* *Tests:* Rinne—R. and L. double negative. Bone-conduction—R. — 9 sec., L. — 13 sec. Gelle—R. and L. negative. High tones well heard, low tones—R. and L. C16 and C32 lost. Acoumeter—R. 12 ft., L. 1 ft. 1 in. Voice—R. 8 ft., L. 10 in. Whisper—R. 15 in., L. 21 in. From January 18 to February 2,

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1909, she was treated regularly by catheterisation and otomassage, strychnine in increasing doses, nasal alkaline syringing, and counter-irritation. On January 30 her tests gave: voice—R. and L. 10 ft., whisper—R. and L. 3 ft., and aërial perception for C32 had returned. A bad attack of influenza occurred, and when she returned to me on October 4, 1909, her tests gave: Weber—L. positive; acoumeter—R. 8 ft., L. 46 in; voice—R. 17 in., L. 5 ft; whisper—R. 10 in., L. 5 in., and she had again lost aërial perception for C32. Fibrolysin was then tried, and she had thirty injections, with otomassage and occasional catheterisation. The first sixteen injections were partly hypodermic and partly by the Eustachian tubes, but, owing to the discomfort and increased deafness from the latter, they were discontinued. On February 28, 1910, her tests gave: Acoumeter—R. 5 ft., L. 46 in. Voice—R. 32 in., L. 57 in. Whisper—R. 12 in., L. 33 in. Weber not lateralised. Low tones—R. and L. C16 to C64 lost. The result here was doubtful, as it was impossible to eliminate the possible effects of the mechanical treatment. Moreover, she had again become pregnant.

Case IX.—Female, aged thirty-two. First seen in 1897 for deafness with colds, and was treated by her own doctor by catheterisation, without result. When next seen (November 16, 1908) she had been married for seven years. Still deaf, with occasional tinnitus and paracusis Willisii. R. and L. tympanic membranes dull, thickened, and indrawn, mallei mobile. Nasal septum irregular, old chronic hypertrophic rhinitis passing to atrophy. Chronic pharyngitis. *Tests:* Rinne—R. and L. double negative. Bone-conduction—R. and L. + 7 sec. Gelle—R. and L. negative. High tones well heard. Low tones—R. and L. C16 to C128 lost. Acoumeter R. 13 in., L. 14 in. Voice—R. 15 in., L. 8 in. Whisper *nil*. She was treated from November 17 to December 23, 1908, by regular catheterisation and otomassage without appreciable result. From December 28 to March 29, 1909, she had thirty-three injections of fibrolysin (hypodermic only), with catheterisation and otomassage. Result *nil*.

Case X.—Female, aged forty. Deaf, L. eleven to twelve years. R. slightly deaf past year. Singing tinnitus, continuous, but varying in intensity, worse in L. No paracusis Willisii. R. tympanic membrane dull and indrawn. L. tympanic membrane markedly indrawn and thickened. L. malleus restricted in movement. Chronic

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pharyngitis. Nose *nil*. *Tests*: Weber—L. positive. Rinne—R. negative to C128, positive to C512. L. double negative. Bone-conduction—R. and L. + 10 sec. High tones heard well. Low tones—R. and L. C16 lost. Acoumeter—R. 10 ft., L. 4 in. Voice—R. 10 ft., L. 2 in. Whisper—R. 19 in. L. *nil*. From June 15 to July 28 she was treated by regular catheterisation and otomassage, strychnine and an alkaline nasal douche. On the latter date she heard voice—R. 12 ft., L. 5 ft. Whisper—R. and L. 8 ft. Tinnitus less noticeable. On October 17 she had gone back to voice—R. 10 ft., L. 9 in. Whisper—R. 8 ft. L. *nil*. She then had forty injections of fibrolysin (hypodermic only) carried out by her own doctor, with otomassage. She improved to R. 12 ft., L. 17 in. Whisper—R. 12 ft., the left malleus moved normally, and the tinnitus had disappeared. When tested again on February 17, 1910, she heard acoumeter—R. 12 ft., L. 6 in.; voice—R. 12 ft., L. 21 in.; whisper—R. 10 ft.; L. *nil*, so that her improvement was maintained.

Case XI.—Female, aged forty. Deaf two to three years, worse with colds. Continuous buzzing and whistling tinnitus. Paracusis Willisii. R. and L. tympanic membranes indrawn, with stretching of the posterior superior quadrant on the L. side. Mallei mobile. Chronic pharyngitis and rhinitis. *Tests*: Weber—R. positive. Rinne—R. and L. double negative. Bone-conduction—R + 5 sec., L. + 9 sec. Low tones—R. C16 to C128 lost, L. C16 to C64 lost. Gelle—R. and L. negative. Acoumeter—R. 18 in., L. 29 in. Voice—R. 7 in., L. 11 in. Whisper—*nil*. She was treated by regular catheterisation and oto-massage, with an alkaline nasal douche, from May 20 to June 12, 1908, with no practical result. On December 10 she again presented herself, when her tests gave: Acoumeter—R. 14 in., L. 19 in. Voice—R. 12 in., L. 15 in. Whisper—R. and L. *nil*. Other tests as before. From that date until March 30 she had thirty injections of fibrolysin (hypodermic only), with catheterisation and otomassage. The catheterisation was discontinued after the first fifteen injections, but the otomassage was persisted with. On March 30 her hearing was: Acoumeter—R. 3 ft. 6 in., L. 3 ft. 9 in. Voice—R. and L. 2 ft. 4 in. Whisper *nil*. The fibrolysin was then stopped, but otomassage continued for one month, when she stated that she could hear the clock and the household bells better, but her hearing had deteriorated for the voice to—R. 16 in., L. 2 ft.

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Case XII.—Female, aged fifty-four. Deaf over seventeen years, chiefly L. Pulsating tinnitus, constant, in L. only; causes insomnia. Paracusis Willisii. R. and L. tympanic membranes dull and indrawn. Mallei mobile. Chronic pharyngitis and rhinitis. *Tests:* Weber—L. positive. Rinne—R. positive, L. double negative. Bone-conduction—R. − 5 sec., L. + 10 sec. Gelle—R. positive, L. doubtful. High sounds—heard well. Low tones—R. C16 lost, L. C16 to C128 lost. Acoumeter—R. 10 ft., L. 28 in. Voice—R. and L. 10 ft. Whisper—R. 10 in., L. 14 in. She sought treatment rather for her tinnitus than for her deafness. Regular catheterisation and otomassage, with alkaline nasal douching, counter-irritation, and constitutional treatment were carried out from October until mid-December without any result. From May to July, 1909, she underwent a course of fibrolysin (thirty injections, hypodermic and by catheter), with the usual mechanical treatment. On July 10 her tests gave the same results as those previously noted. Tinnitus was in no way improved.

Case XIII.—Female, aged forty-one. Deaf L. "several years." Hissing and pulsating tinnitus. Worse with colds. No paracusis Willisii. Cerumen removed from L. L. tympanic membrane normal in texture and indrawn. R. tympanic membrane thickened and more indrawn than L. Mallei mobile. Septum deflected slightly to L., no obstruction. *Tests:* Weber—L. positive. Rinne—R. positive, L. double negative. Bone-conduction—R. + 7 sec., L. + 5 sec. Gelle—R. positive, L. negative. High tones heard well. Low tones—R. C16 lost, L. C16 to C64 lost. Acoumeter—R. 12 ft., L. 5 in. Voice—R. 12 ft., L. 20 in. Whisper—R. 12 ft., L. *nil* For one month she was treated by catheterisation, otomassage, counter-irritation, nasal alkaline douche, and strychnine, but without improvement. She then had a full course of thirty injections (hypodermic) of fibrolysin, mechanical treatment by catheter and otomassage being continued. Improvement, either in hearing or tinnitus, *nil*.

Case XIV.—Female, aged twenty-nine. Deaf thirteen years, worse past three to six months. "Rumbling" tinnitus. Began with colds. Paracusis Willisii. R. and L. tympanic membranes indrawn. Mallei somewhat restricted in movement. Chronic pharyngitis. No marked nasal obstruction, but remains of adenoids and adhesions in Rosenmüller's fossæ. *Tests:* Weber not lateralised. Rinne—R. and L. double negative. Bone-conduction—R. and L.

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— 12 sec. Gelle—R. and L. negative. Slight loss of high tones. Low tones lost R. and L. up to and including C1024. Acoumeter —R. 5 in., L. 3 in. Voice—only raised through a conversation tube. Whisper—*nil.* A bad prognosis was given and lip-reading advised, but as the patient begged for treatment the post-nasal adhesions were cleared and a course of catheter and otomassage tried for three weeks, without result. Thirty injections (hypodermic and by catheter) of fibrolysin were then administered, in addition to mechanical treatment. Results — *nil.* Restriction of malleolar movement in this case was uninfluenced.

Case XV.—Male, aged fifty-two. Deaf twenty-five years, with tinnitus, which has lately become "unbearable." Paracusis Willisii. Mother and brother deaf. R. and L. tympanic membranes indrawn. Mallei mobile. Irregular septum and chronic pharyngitis. *Tests:* Weber not lateralised. Rinne—R. and L. double negative. Bone-conduction—R. and L. + 7 sec. Gelle—R. and L. negative. High tones—slight loss. Low tones—R. C16 to C64 lost, L. C16 and C32 lost. Acoumeter—R. 3 in., L. 6 in. Voice—R. 8 in., L. 14 in. Whisper—*nil.* As this patient had already undergone several long courses of careful treatment at the hands of other specialists, he was, after having had the situation explained to him, at once put through a course of fibrolysin. He had thirty injections (hypodermic), and two injections by catheter. The latter were discontinued, as they made his tinnitus worse. Result at end of course and one month later, *nil.*

Case XVI.—Female, aged thirty-four. Deaf, L. several years, R. six months; "rushing" tinnitus. L., no paracusis Willisii. R. and L. tympanic membranes dull and indrawn, mallei restricted in movement. Chronic rhinitis and pharyngitis. *Tests:* Weber—not lateralised. Rinne—R. negative to C128, positive to C512, L. double negative. Bone-conduction—R. and L.—5 sec. Gelle—R. and L. negative. High tones—heard well. Low tones—R. C16 and C64 lost, L. C16 to C128 lost. From June 24 to July 8, 1908, treatment by regular catheterisation and otomassage, with nasal douching, Mandl's pigment and strychnine was carried out, without obtaining any improvement. From July 9 to 28, fourteen injections (hypodermic) of fibrolysin were given in addition, but as no alteration in either hearing or tinnitus occurred the patient abandoned further treatment.

Case XVII.—Female, aged forty-nine. Deaf sixteen years, due

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to colds. Paracusis Willisii. Occasional tinnitus. Sixteen years back "went the round of the aurists," but gave up treatment until one year ago, when she took a course of "high-frequency currents" under a notorious quack, which improved her subjective symptoms, probably by suggestion. She had been told of the "wonderful cures" effected by fibrolysin and insisted upon trying it. R. and L. tympanic membranes thickened and indrawn. Nasal septum irregular, but no obstruction. *Tests:* Rinne—R. and L. double negative. Bone-conduction—R. + 5 sec., L. — 8 sec. Gelle—R. and L. negative. High tones—heard well. Low tones—R. and L. C16 to C128 lost. Acoumeter—R. and L. concha. Voice—R. 4 in., L. 6 in. Whisper—*nil.* A course of thirty injections was carried out, with mechanical treatment by catheter and otomassage. Result—*nil.*

Case XVIII.—Male, aged twenty. Deaf three years, from frequent colds. L. buzzing tinnitus. No paracusis Willisii. Mother deaf ("catarrhal"). R. and L. tympanic membranes indrawn and dull. Septum badly deflected to R. inferiorly and to L. superiorly, with pressure on enlarged middle turbinates. *Tests:* Weber—L. positive. Rinne—R. and L. double negative. Bone-conduction—R. and L. + 5 sec. Gelle—R. and L. posterior. High tones—well heard. Low tones—R. C16 to C64 lost. L. C16 to C12 lost. Acoumeter—R. 10 ft., L. 6 in. Voice—R. 27 in., L. 18 in. Whisper—R. 3 in., L. 1 in. Nasal operation, followed by a course of treatment, was the advice given, but, beyond using a nasal douche, the patient procrastinated. He returned two months later much worse, having had several bad colds. Hearing for the voice had decreased to R. 18 in., L. 10 in. He then submitted to a submucous resection, which greatly improved his nasal airway and tendency to colds. A month's treatment by catheter and otomassage failed, however, to improve the hearing, and as he was anxious to try fibrolysin he was put upon a course. After thirty hypodermic injections tests gave voice R. 20 in., L. 12 in.—a result which amounted practically to *nil.*

Case XIX.—Male, aged forty-one; deaf twenty years, with attacks of "roaring" tinnitus and occasional vertigo of a general character. Paracusis Willisii. Had undergone numerous treatments by inflation, electricity, iodide of potassium, bromides, strychnine (hypodermically), etc., without result. R. and L. tympanic membranes indrawn and thickened, mallei immobile.

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Nares narrow, inferior turbinals much scarred by galvano-cautery. *Tests :* Weber—not lateralised. Rinne—R. and L. double negative. Bone-conduction—R. and L. doubtful, repeated tests giving variable results. Gelle—R. negative, L. doubtful. High tones—slight loss. Low tones—R. and L. C16 to C128 lost. Acoumeter—R. 48 in., L. 7 in. Voice—R. 14 in., L. *nil.* Whisper—R. 7 in., L. *nil.* There was much difficulty in passing the catheter, especially on the right side, but the patient underwent a course of catheterisation and bougie, with otomassage, without appreciable result, and then decided to try a course of treatment at Mont Dore. Although better whilst at sea he was as deaf as ever at Mont Dore and on his return. After further courses of treatment he asked to be treated by fibrolysin, but after twenty injections, with persistent mechanical treatment, he abandoned it, result being *nil.*

Case XX.—Male, aged twenty-four. Deaf seven years, for which he had seen four otologists of repute, had had two operations for adenoids, and had undergone several courses of inflation and otomassage with galvano-cautery to the throat and nose. Paracusis Willisii. Some tinnitus. Used to have frequent colds, during which he was worse. R. and L. tympanic membranes thickened and indrawn. Mallei mobile. Distinct adhesions in Rosenmüller's fossæ, nasal septum irregular and thick. *Tests :* Rinne—R. and L. double negative. Bone-conduction—R. + 12 sec., L. + 10 sec. Gelle—R. and L. negative. High tones—reduced. Low tones—R. and L. C16 to C128 lost. Acoumeter—R. 3 in., L. 1 in. Voice—R. 8 in., L. 5 in. Whisper *nil.* A bad prognosis was given, but at his own request the post-nasal adhesions were cleared, and a course of thirty injections (hypodermic and by catheter) of fibrolysin were given, with mechanical treatment by catheter and otomassage. The result was absolutely *nil.*

I have given these cases very fully, and it will be noted that II and V were instances of post-suppurative adhesions, VI was one of otosclerosis mixed with catarrh, whilst the remainder were cases of late stages of chronic middle-ear catarrh or of post-catarrhal adhesions. In every case other treatment had been tried before fibrolysin was used, whilst in a few the latter drug was employed at the patient's own request. In three cases improvement was noted (Cases II, V, X). The first of these was one of post-suppurative adhesions, whilst in Case IV, in which there were probably also fibrous

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adhesions about the stapes, no amelioration took place. The first case in which I used this treatment was No. V, and the result was so surprising and so gratifying that I believed the remedy likely to prove valuable. A very interesting point in this case was that, after the fifteenth injection, the patient volunteered that his paracusis Willisii had disappeared. In this case, too, improvement was maintained. In the third case (Case X) also there was a continuance of the good result. In one case (Case VIII) the result was doubtful, as the occurrence of pregnancy may have prevented improvement. In none of the others was there any appreciable result, or, if a slight amelioration occurred, it was not maintained. In Case VI, one of mixed otosclerosis and catarrh, it is noteworthy that the characteristic promontorial blush disappeared, but this may have been coincidental, as I have noted this to happen in other otosclerotics in the course of the condition. In three cases (Cases X, XIV, and XIX) impairment of malleus mobility was noted; in only one of these (Case X) was this condition modified by the treatment.

As regards the question of tinnitus, this symptom was noted in seventeen of the twenty cases, and in one (Case XII) it was on account of its distressing nature that fibrolysin was tried, without result. In only two (Cases V and X) was the symptom improved by the treatment.

The injections were given in the arm, and although two cases stated that the administration was followed by pain, not of a lasting character, it was never attended by any ill-effects. In no case did I use "ear baths," as advocated by some other investigators, as they appear to have set up discharge in certain of the reported cases.

I would like to point out here that I am not absolutely satisfied in my own mind that the improvement in the three cases was due to the action of the fibrolysin, in spite of the fact that preliminary mechanical treatment had taken place. I have seen cases decidedly benefited by prolonged treatment, and therefore I do not think that this possibility can be excluded here.

I would further point out that, judging by what has been said as to the action of fibrolysin upon cicatrices, it should, from the swelling and œdema of the pathological fibrous tissue in the middle ear, cause the patient to be more deaf during its repeated administration. Such a result seems only logical. Tympanic membranes which are thickened by the development of pathological fibrosis ought to soften, become pink and œdematous, just as surface scars

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are said to do under the influence of thiosinamin or fibrolysin. Throughout my cases I have constantly watched for such manifestations of the action of the drug, but in no case have I succeeded in detecting it. I feel, therefore, bound to think that, whatever may be its effects on cicatricial tissue elsewhere, it has no action upon pathological fibrosis in the middle ear occurring as the result of chronic catarrhal inflammation.

Finally, it will be noted that the stapes was fixed in a large proportion of my cases. I am aware that this condition is regarded by some investigators as a contra-indication for the use of fibrolysin, and rightly so when that fixation is due to new bone, as in otosclerosis, but it appears to me that when the ankylosis is a fibrous one, as it often is in old catarrhal cases, it is the very condition in which the treatment ought to do good, especially as it is one which is less likely to yield to other methods.

My results were, therefore, very disappointing, and I have now abandoned further trials. I think, however, that in a limited number of cases it might prove of use, but such cases would require to be very carefully selected. I cannot agree, from my own experiences, that fibrolysin merits the eulogies that some observers have lavished upon it.

References.

(1) Mendel, F.—*Therap. Monatsch.*, February and April, 1905; *Therap. d. Gegenw.*, August, 1905; *Berliner Klinik*, October, 1907.

(2) Lermoyez and Mahu.—*La Presse Médicale*, June 22, 1907.

(3) Glas.—*Deut. med. Woch.*, 1903, No. 40.

(4) Lange.—*Ibid.*, 1907, No. 48.

(5) Sugar.—*Arch. f. Ohrenheilk.*, Bd. lxxiii (Festschrift).

(6) Teleky.—*Centralbl. f. d. Grenzgeb. d. Med. u. Chir.*, No. 1, 1901.

(7) Stocker.—*Corresp.-Blatt. f. Schweiz-Aertze*, Year 39, No. 24.

(8) von Hebra.—*Intern. klin. Rundschau*, September 11, 1892.

(9) Latzko.—*Wiener klin. Woch.*, No. 6, 1893.

(10) Richter.—*Wiener med. Woch.*, No. 43, 1893.

(11) Tousey.—*New York Med. Journ.*, vol. v, No. 2, 1892, and vol. xi, No. 6, 1897.

(12) Maupetit and Coltart.—*Rev. Hebd. d'Otol.*, etc., May 1, 1909.

(13) Hirschland.—*Arch. f. Ohrenheilk.*, Bd. lxiv, Heft 2 and 3.

(14) Poutchowsky.—*Arch. d'Otologie*, December, 1909.

(15) Austerlitz.—*Centralbl. f. Ohrenheilk.*, August, 1908.

(16) Bichaton.—*Bull. et Mém. de la Société Franç. d'Oto-Rhino-Laryng.*, 1909, p. 504.

(17) French, Gay.—*Lancet*, July 24, 1909.

(18) Skrypta.—*Münchener med. Woch.*, 1909, p. 876.

(19) Renshaw, Knowles.—*Lancet*, 1909, vol. ii, p. 473.

(20) Urbantschitsch.—*Monatschr. f. Ohrenheilk.*, No. 2, 1907.

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