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FIBROLYSIN IN THE TREATMENT OF  
MIDDLE EAR DEAFNESS.

Thesis for the degree of M. D.,

by

H U G H J. M O R E,

M.B., Ch.B.

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FIBROLYSIN IN THE TREATMENT OF  
MIDDLE EAR DEAFNESS.

Thiosinamine is a substance known in organic Chemistry as an allyl - sulpho - carbamide. It is prepared by the action of ammonia, upon the essence of mustard and occurs in colourless monoclinic crystals, which have a bitter taste and an odour like garlic. Those crystals dissolve very little in cold water and they are more soluble in hot water and dissolve well in alcohol.

Thiosinamine was prepared for the first time in 1828 by Berzlius, a chemist of Stockholm. It was first introduced into Therapeutics by Von Hebra, who in 1892 communicated his researches on the subject to the Congress of Dermatology of Vienna. He used the substance for the purpose of softening the cicatrices following lupus and used hypodermic injections of 15 per cent solution.

In the following year Latzko obtained good results from its use, and after that it was used by different observers in the treatment of conditions such as urethral stricture (Hane), Reloids (Unna), pelvic peritonitis and by Teleky in the treatment of fibrous stenosis/

stenosis of oesophagus.

Before going on to consider the application of Thiosinamine to disease of the middle ear, let us consider the action which the drug has been found to exert upon cicatricial tissue, and upon the system generally.

The specific action, which is claimed for Thiosinamine, is that which it exerts upon cicatricial tissue; and upon this action its therapeutic application is founded, that is, its property of softening and dissolving these cicatrices. It is also claimed, that this action can take place at a distance, and that this action is exerted upon pathological fibrous alone.

This elective action upon cicatricial tissue has been described by Glas, as follows ;- "This body causes oedema in the cicatrices. Histologically the cicatrices lose their usual aspect, their limits become less marked and it is impossible to distinguish them from the tissues immediately adjoining them. The cells appear to be separated; the fibres are swollen up and dissociated." As an illustration of this cedematous condition he instances a case of fibrous stenosis of the larynx, following upon syphilitic ulceration, where four injections of Thiosinamine/

Thiosinamine caused such a degree of swelling that tracheotomy had to be performed.

The action of thiosinamine is comparable to that of venous stasis, which is produced in Bier's congestion, that is, it produces an interstitial oedema and softening of the cicatricial tissues - it does not destroy such tissue. This condition is not permanent, but passes off after a few days, if the injections are discontinued - the drug is thus to be used as an auxiliary to mechanical measures; these are employed to definitely stretch cicatrices, which have become distensible by its use (Teleky).

"Thiosinamine acts as a sensitiser of cicatricial tissue, which obliges such tissue to yield to mechanical influences which it would have resisted otherwise." (Lermoyez and Mahu).

Tyrode, one of the most recent observers, however, has noted that in animals, to which large doses had been given, no histological alteration could be found in the fibrous tissue of the heart and kidneys, but against this it can be urged that such fibrous tissue has not a pathological origin.

Another beneficent action claimed for thiosinamine, is that it produces a marked leucocytosis; this, it is/

is said, occurs as early as four hours after administration of the drug.

"Influenced by a kind of positive chemiotaxis the leucocytes travel towards the cicatrices and act as phagocytes upon the cicatricial tissue". (Sugar)

Löwitt, Richter and Offergeld studied the action of the drug on the blood, and agreed that it first lowers, and then increases, the number of leucocytes, and also that it does not increase the haemoglobin.

Leonards states that he found a marked leucocytosis in dogs.

These findings are unfavourably criticised by Charteris in the Lancet of August 1909. He writes - "Leonards, Wolf and others believe that thiosinamine is an energetic lymphagogue, which attracts leucocytes and produces local hyperaemia. During the past few months I have made many observations of the effect of thiosinamine upon the blood of persons receiving the drug.

First of all I attempted to discover if it had any chemiotactic influence. Thus, sterile glass capillary tubes were partially filled with the drug, in solid form and in solution and introduced into the peritoneal cavity of pithed frogs.

At/

At the end of twenty-four hours the tubes were withdrawn and examined under the microscope to determine whether there was any accumulation of leucocytes in the tubes. In no instance could the presence of leucocytes be demonstrated inside the tube. This finding is quite in accord with that of Winternitz who found that thiosinamine caused no focal necrosis or accumulation of leucocytes at the site of injection.

In an attempt to determine whether the drug has the power of causing any marked leucocytosis, I have made numerous counts upon patients and upon healthy men. As a rule, after the injection of considerable doses no leucocytosis could be demonstrated. Sometimes there was a trifling increase in the number of white cells, and in a single instance an increase of 100 per cent was recorded.

The counts were made at first at intervals of forty minutes, and counting in some cases was continued for forty-eight hours."

This writer also finds that his own experience has not substantiated the favourable results reported by others following upon the use of thiosinamine as a therapeutic agent.

Other experimental works have been done upon thiosinamine/

thiosinamine but none of these have succeeded in really establishing the general pharmacological action of the drug.

Lange and later Döleken obtained general oedema in frogs, and vomiting, salivation, sleeplessness, and diminution in the number of respirations in dogs, and practically the same symptoms in rabbits.

The most recent and exhaustive researches have, however been carried out by Tyrode, and were published in the Boston Medical and Surgical Journal of January 1909. In the course of this article he reviews the work done by other observers upon the subject, and mentions a case reported by Gross of a man who received in fourteen days four injections of 0.2 grammes of thiosinamine. This man exhibited the following symptoms; marked general malaise nausea and violent vomiting, rise of temperature, weakness of the heart and anuria. He also mentions that Forster and Van Hovin had demonstrated an antiseptic action in vitro, and that Von Froschauer had found animals were less susceptible to bacterial infection after injections with thiosinamine.

Tyrode's observations were carried out upon frogs, rabbits and guinea pigs and were undertaken rather for the/

the purpose of demonstrating the general action of the drug upon the system, than for establishing its action upon scar tissue.

One series of observations was made upon temperature changes, another with regard to the local action upon rabbits' ears and a third upon the influence on general metabolism.

He summarises the results of his observations as follows.

- (1). "Marked depression of respiration, which causes death in wain-blooded animals.

This depression is sometimes accompanied by oedema of the lungs and marked congestion, especially if the process of dying has been prolonged.

- (2). No influence on blood pressure, heart still very strong when the respiration stops in acute experiments on rabbits. The heart is only weakened and stopped by very large amounts applied directly to the organ in frogs.

- (3) Profound changes in the metabolism, consisting in rapid loss of weight, with increased proteid combustion and general fatty degeneration of the different parenchymatous organs, especially of the heart and kidneys. The heart was so fatty in some/



some instances that its weakness may explain some of the oedema and congestion seen in animals, dead after several days poisoning."

Clinically we find that although in some cases thiosinamine exercises a bad effect on the patient's health, as a rule no general evil effects are produced by its use.

Patients have been treated for months with large doses of thiosinamine, and at worst have only experienced a slight loss of appetite and feeling of fatigue, which ceased at once on stopping the treatment.

Urbantschitch treats patients with twenty or thirty injections carried out every second day, without any ill effect.

Sometimes at the point of injection, the skin takes on a yellowish coloration which takes some weeks to disappear, and occasionally small nodules have been observed in the vicinity of the needle puncture, which although painless, have taken some months to disappear.

These are due to crystallisation of a small part of the fluid injected - the crystals acting as aseptic foreign/

foreign bodies.

However, although in most cases the drug is inoffensive, a certain degree of care must be exercised in selecting the cases, to which it is to be applied; especially as regards the existence of cicatrices which it would be unwise to meddle with.

Thus Teleky cites an example - "A gastrostomy was practised upon a young man, affected by cicatricial contraction of the oesophagus. At the end of some weeks, fibrolysin was used. Now, whilst the stenosis became soon dilatable, the patient's death was caused by rupture of the gastric cicatrix."

We should therefore refuse the use of thiosinamine to those who have had abdominal operations.

Hebra considers that it should not be used in tuberculous people as under its influence he has observed old caries light up afresh, and afebrile tubercule become febrile. It also should not be used where the existence of a malignant tumour is suspected, as it opens up the lymph channels and favours metastasis.

In the treatment of diseases of the middle ear, where we are particularly studying its use, the drug is not in some cases absolutely free from risk, as regards the condition of the ears themselves.

In/

In the Revue Hebdomadaire d'otologie etc. Bichaton describes twelve cases and in four of these he finds, that the use of the drug determined the return of former evils. In these cases there was a setting up of aural discharge due, sometimes to an otitis externa, a myringitis or sometimes to the stirring up of an old otorrhoea, which had been cured for a certain time.

In the Archives d'Otologie, December 1909, H. Poutchovoky of Smolensh, using the drug in the treatment of middle ear disease, noticed that some patients complained of vertigo and tinnitus for two or three days after the injection.

In one patient, he found that the injection was followed by epistaxis, and the appearance of acne on the face.

He considers the drug contra-indicated in arterio-sclerosis and in lung disease.

Gay French in reviewing 68 cases treated with Fibrolysin, writes -

"In only one of my cases were there any bad symptoms produced by the injections. This was a case of a young woman, aged 25 years, with double non-suppurative middle ear catarrh of two years duration. She was/

was put on the fibrolysin course, but this had to be stopped owing to her developing marked vertigo after each injection. A number of other cases in which bad symptoms have followed the injections have been reported from time to time but the above was the only one in my personal experience."

In the few cases which I have had the opportunity of treating with the drug, I have experienced none of these evils before referred to; although the patients were treated for periods varying from six weeks to three months with injections given every second day.

In none of the cases was increased tinnitus, vertigo or loss of appetite, complained of.

Let us now consider the various forms in which thiosinamine can be used.

On account of the sparing solubility in water, and ready solution in alcohol, the alcoholic solution was first used; and it was with a 15 per cent alcoholic solution that Von Hebra made his first observations.

The injection of this alcoholic solution was however found to be exceedingly painful; and to obviate this disadvantage, the solution of thiosinamine known as Fibrolysin and that which is now generally used was elaborated.

It/

It was invented in 1905 by Dr. Felix Mendel of Essen who discovered that the solubility of thiosinamine could be increased by the addition of another body, which formed with it a double salt. Thus by combining two molecules of thiosinamine, with one molecule of salicylate of soda a white crystalline powder was obtained; to which he gave the name of Fibrolysin.

This combination dissolves readily in water up to the proportion of fifteen per cent. The fibrolysin, prepared by Merch is generally used in this country and is prepared in the above manner.

Lermozy and Mahu, writing in La Presse Medicale, June 1907 criticise this preparation of the drug, on the ground that the solution prepared by Merch decomposes readily on exposure to air and light, and they assert that the odour of garlic, which is perceptible when the solution is emptied out of the glass ampullae in which it is made up is an evidence of its decomposition.

They also raise the objection that it crystallises out so rapidly as to obstruct the needles by which it is injected.

As against the German solution, these writers extol /

extol a solution prepared by Michel of Paris. This firm has found that of all the substances which favour the solution of thiosinamine in cold water, antipyrin is the best.

One half molecule of antipyrin, united to one molecule of thiosinamine forms a syrupy liquid at an ordinary temperature. This liquid is colourless odourless and more soluble in water than is fibrolysin.

This combination also has the advantage of keeping better, in air and light.

The formula for this preparation is :-

Thiosinamine	15 grammes.
Antipyrin	7 " 50
Distilled water	100 "

Lermoyez and Mahu use a 15 per cent solution of this preparation.

In their article in La Presse Medicale these preface their description of its actions and results in the treatment of ear disease by saying.

"At last we possess the means of making not all deaf people hear but certain of such people. In such matters prolonged doubt is prudent. So many forms of treatment for deafness have seen their decline prematurely succeed to their rise, that our confidence is/

is not given unreservedly to all forms of therapeutics. However it seems that thiosinamine which is already fifteen years old has not fallen short of its promises and that it is probable that otology can expect some assistance from it."

It will be my object in this thesis to determine how far this assertion holds true.

Let us now pass on to consider the use of Fibrolysin in ear disease. We can at once, I think, exclude oto-sclerosis, from the conditions in which its use is justifiable. In this affection the labyrinth is as a rule affected along with the middle ear; the labyrinth lesion consisting in an osteitis of the long capsule of the labyrinth, which causes hyperostoses destroying the nerve terminations in the interior of the labyrinth. Local treatment as a rule only seems to aggravate this condition and hasten the advent of tinnitus.

Of this condition Dr. S. W. Syme writes in an article in the British Medical Journal of December 21, 1908.

"In oto-sclerosis, except perhaps in the early stage, one would not expect any benefit."

Gay French in Lancet, July 24th, 1909 writes. -

"In/

"In true oto-sclerosis the results obtained with fibrolysin were very poor; only two out of fifteen cases showed any improvement and that very slight."

It is in cases of adhesive otitis media, that we would expect the use of fibrolysin to be followed by benefit, to the patients hearing. We would also expect it to be of some use in treating the cicatricial changes which follow up an acute otitis media or a chronic otitis media.

"Chronic catarrhal otitis media - otitis media chronica adhesiva vel hypertrophica - is a progressive insidious, and subinflammatory affection of the middle ear, consequent upon extension of the so-called catarrhal inflammation from the mucosa of the naso-pharyngeal space, which involves firstly the Eustachian tube, and eventually the middle ear." (Lake. )

The incidence of the disease is very frequently connected with the presence of adenoid vegetations, in the naso-pharynx. And also the existence of some form of nasal obstruction. The onset is gradual and the affection may at first be unilateral; although with the lapse of time it as a rule tends to become bi-lateral. Certain general conditions of the system also favour the development of this condition, such/



such as anaemia, gout, malarial poisoning, dyspepsia and constipation.

The results of this sub-inflammatory condition of the middle ear, are the formation of adhesions and thickening of the tympanic mucosa. A progressive plastic condition is set up, which deforms the middle ear and binds down the ossicles.

The tympanic membrane in this condition is thickened, either in whole or in parts; and calcareous patches may be found and also patches of local atrophy. In most cases, the membrane is much retracted, and in some cases adherent to the inner tympanic wall.

The handle of the malleus, as a rule occupies an abnormal position, being retracted either directly inwards or upwards; in some of the former cases, the tip of the handle is adherent to the promontory. In almost all cases, the mobility of the malleus as tested by means of the pneumatic speculum is either abolished or very markedly diminished.

In many cases, the stapes becomes antylosed by formation of cicatricial tissue; this is evidenced by Gelle's test, and the following signs " A shortened bone -conduction, a markedly negative Rinne, together with an extensive defect in air conduction at the lower/

lower end of the scale." (Lake. )

It is in such cases that we would expect the use of Fibrolysin, combined with mechanical treatment to be of service. In the Handbook of Diseases of the Ear 1910, Lake writes :-

"Thiosinamine and Fibrolysin should certainly be tried when the malleus is immobile or when there is reason to expect the presence of cicatricial tissue in the cavum tympani."

Also in the adhesions left of old suppuration, we would expect good results; and it is perhaps in this class of cases that the most successful results have been obtained.

In both these sets of cases it is claimed that Fibrolysin by reason of its solvent action upon cicatricial tissue softens the indurated and thickened tympanic membrane, and relaxes the adhesions binding down the ossicles which can then be mobilised by means of mechanical treatment. The latter consists of inflation of the tympanum by means of the Eustachian catheter or oto massage by means of the oto masseur or pneumatic speculum.

In the Lancet July 24th 1909 J. Gay French writes -

"The cases in which I have systematically carried out/  
out/

cut this treatment as those of deafness and tinnitus resulting from -

(1) Post-suppurative middle ear catarrh, when there has been a cessation of discharge with formation of scar tissue and destruction or ankylosis of the ossicles; and (2) Chronic dry middle ear catarrh, i.e. non-suppurative catarrh - retracted membranes, with or without ankylosis of the ossicles.

"From the results obtained it would appear that this form of treatment was more successful in the non-suppurative than in the post-suppurative cases ; but whilst this was so in regard to the percentage of cases showing improvement in hearing and diminution in tinnitus, yet when taken from the point of view of the amount of improvement produced, the post-suppurative cases gave far better results; and I arrived at the conclusion that the fibrolysin treatment is by far the best treatment in this class of case - the earlier the case is treated after cessation of the discharge and formation of the scar tissue the better the prognosis. I think that from the results obtained it will be seen that in cases of non-suppurative middle ear catarrh this method of treatment gives better chances of improvement than any other."

Maupetit and Colat in their article in the Revue Hebdomadaire/

Hebomadaire d'Otologie write as follows :-

"According to the promoters of this treatment the cases which should be treated by means of thiosinamine are above all those whose deafness is provoked by those affections which we have called by the names of cicatricial otitis or chronic dry adhesive ctitis media but chiefly the first. Moreover the affection should not have reached the labyrinth and the chain of ossicles should have retained its mobility."

Lermoyez and Mahu, in their article in La Presse Medicale June 1907, lay claim to having been among the first to make use of fibrolysin in the treatment of middle ear disease. They write as follows :-

"The works of Teleky gave us the idea about five years ago, i.e. 1902 of using thiosinamine for softening the cicatrices of the middle ear, following upon cured otorrhoeas and thus to relieve the deafness and the tinnitus which accompanied them.

We did not know that Sinclair Tousey in 1897 had in this way improved a case of long standing deafness."

These observers at this time, treated twelve patients at the Hospital of St. Antoine, who were affected with chronic conditions of the ear; but however without very good results, as the cases were not/

not selected as experience has since dictated, but included as many cases of oto-sclerosis as of adhesive otitis.

In 1902 Beck published the results of the use of the drug in deafness. In five cases of chronic catarrhal otitis media, thiosinamine was administered by subcutaneous injection over a period of three months. No noteworthy improvement was remarked. In nine cases he added to the thiosinamine treatment electrolysis of the Eustachian tubes with oto-massage and inflation of the tympanum.

He arrived at the following conclusions -

- (1) The injections of thiosinamine improve the condition only in that sometimes they diminish tinnitus.
- (2) With the help of electrolysis and injections he considers that it facilitates the passage of the elastic bougie.

Other otologists who have written on the subject, are Dr. Hirschland, who in 1905 recorded results of treatment with Fibrolysin and Thiosinamine and since then numerous others have experimented and written upon the subject.

Let us now consider the various ways in which the/  
the/

the drug Fibrolysin can be employed in the treatment of chronic middle ear disease and the histological sequence of the various methods. It was at first used as before stated in the form of the 15 % alcoholic solution, and was given in this form by subcutaneous injection.

Lermoyez and Mahu treated their series of ten cases in this way,  $\frac{1}{2}$  to 1 cubic centimetre being injected into the arm.

Dr. Martin Sugar who was amongst the first to use the drug in 1905 used the method of subcutaneous injection but along with the injections he also employed extra-tympanic injection of a 10 % glycerinated solution of thiosinamine - the solution being insufflated into the middle ear by means of the Eustachian catheter.

In 1905 Kassel gave the results of his observations in four patients affected by cicatricial otitis, whom he had treated by means of subcutaneous injections using the 15 per cent alcoholic solution. He found an improvement in hearing without any change in the tinnitus.

In 1906 Tapia found no result produced in certain cases of otc-sclerosis whom he treated by means of a 10 per cent glycerine solution.

In/

In 1906 Lermoyez and Mahu recommenced their experiments which they abandoned in 1902 and now gave up the use of hypodermic injections and used thiosinamine locally either as in the form of instillations via the Eustachian tube or as baths applied via the external auditory meatus.

In La Presse Medicale they write -

"Our technique is of extreme simplicity. The patient gives himself every night before going to bed an ear bath lasting five minutes of a warm solution of thiosinamine antipyrin.

Twice a week he goes to see his medical man who gives him oto-massage.

Only in cases of failure do we proceed to injections by the tubes. This procedure demands a more strict surveillance but it does not however seem to be more effective than the simple baths."

They consider that thiosinamine or fibrolysin can diffuse through the drum and soften the adhesions situated in the interior of the middle ear.

In 1907 André Horeau in his Thèse de Paris advocated the use of ear baths of thiosinamine, combined with injections into the Eustachian tube and assisted by massage of the tympanic membrane, the treatment being/

being given twice a week. In this thesis he gives observations of ten patients treated by this method. In every case he found that a more or less marked improvement had been produced, and he never observed the presence of any inflammatory complications. He used the solution prepared by Michel of Paris. This method was also used by Bichaton in the twelve cases which he published in the *Revue Hebdomadaire d' Otologie* etc. of November 1909. Bichaton however seems to have preferred the use of ear baths alone, as only in three of the twelve cases were tubal injections practised.

In 1904, Dr. Martin Sugar suggested the injection of fibrolysin into the periostium of <sup>the</sup> tympanic cavity, in order to obtain its local effect.

Another method which I think seems to be the most likely to be effective is the combination of subcutaneous injection of Fibrolysin, with injections via the Eustachian tube. This is the method employed by Mr. J. Gay French in the series of cases which he publishes in the *Lancet* of July 24th 1909. In this article he writes :-

"In my first series of cases the results were not generally satisfactory; some cases certainly showed/



showed fair improvement but the greater majority were in no way benefited. At this time I had been giving the injections once a fortnight and I determined to increase them to twice a week, and at the same time to apply it locally to the middle ear through an Eustachian Catheter - a method employed with success by André Horean in connexion with thiosinamine. The results immediately improved. The method which I employ is to use one ampulla of fibrolysin containing 2.3 cubic centimetres, roughly 40 minims, as follows ; - 30 minims are injected subcutaneously into the upper arm and 5 minims are insufflated through an Eustachian Catheter into each middle ear.

After an interval of fifteen minutes massage is applied on each side for from three to five minutes by means of an oto-masseur.

This routine is gone through twice a week for six weeks; if at the end of that time there is no definite improvement my experience is that the case is a hopeless one and that it is useless to persevere with the treatment."

The method which I myself have used <sup>in</sup> the few cases which I have had the opportunity of treating is that employed by Mr. Macleod Yearsley to whose clinique at/

at the Royal Ear Hospital, Scho, the cases belonged.

This method is practically identical to that advocated by Gay French - that is 25 to 30 minims are injected into the arm and about 5 minims are insufflated into <sup>the</sup> Eustachian tube by means of the catheter. The treatment was moreover given more frequently, as a rule every second day and for a longer period, as no case was considered to be hopeless, till a full series of thirty injections and insufflations had been given.

In none of the cases did this frequently repeated, and long continued treatment, appear to have a detrimental action upon the patient's health; either locally as regards the aural condition, or generally in causing any constitutional disturbance.

The following is the detailed report of the cases treated by me at the Royal Ear Hospital, Soho.

## Case I.

E. D. (Male)                      Musician - Age 26.

Deaf twelve years. Deafness was gradual in onset.

Continual tinnitus of a rushing character. Mother, brother and sister deaf.

Right membrane, normal in texture, slightly congested, cone of light small, membrane mobile.

Left membrane, normal in texture, cone of light broken, membrane mobile.

Chronic Pharyngitis present.

Nasal septum deflected to the right, not markedly so however.

15 : 9 : 09. Functional examination.

Right		Left.
4 inches	Acoumeter	0 inches.
5 "	Voice	3 "
0 "	Whisper	0 "
Negative	Rinne	Negative.
+ 5 sec.	C mastoid	+ 6 sec.

Low tones lost up to and including C. 128.

After inflation with Eustachian catheter, some improvement.

Acoumeter Right = 6 inches      Left = 1 inch.

Daily/

Daily catheterisation and inflation ordered.

Strychnine and Collunaria Potass. Chlor. also given.

6 : 10 : 09.

Right		Left.
3 inches	Acoumeter	1 inch
1 ft. 6 in.	Voice	8 "
1 ft.	Whisper	0

13 : 10 : 09.

Fibrolysin treatment commenced by injection into arm and by insufflation into Eustachian tube by means of the catheter as before described.

27 : 12 : 09.

After patient had received thirty injections.

Right		Left.
5 inches	Acoumeter	3 inches.
1ft. 8 in.	Voice	1 ft. 1 in.
1 foot	Whisper	8 inches.

Strychnine was administered during the whole course of the treatment.

In this case tinnitus was on the whole improved although it was heard much worse at some times than at others during the course of the treatment.

## Case II.

S. P. (Female)      Age 37.

Deaf in both ears since age of ten when she had scarlet fever. Discharge from both ears at that time which lasted some years and then ceased, tending however to recur when the patient had a cold in the head.

Nasal Septum deflected to the left.

Right middle turbinal enlarged.

Right membrane - healed perforation.

Left membrane - perforation anterior inferior quadrant.

16 : 7 : 09.

Submucous resection. Anterior end of right middle turbinal removed.

22 : 9 : 09.

Right		Left.
2 inches	Accoumeter	$\frac{1}{4}$ inch
6 feet	Voice	4 feet
3 feet	Whisper	1 ft. 6 in.
Negative	Rinne	Negative.
	Weber	positive.

1 C. 2 C. 3 C. not heard on either side.

Patient was taken into hospital on this date  
for/

for treatment. Fibrolysin by subcutaneous injection and by Eustachian catheter, administered every second day. Daily catheterisation and oto-massage also given.

15 : 10 : 09.

Right		Left
1 ft. 4 in.	Acoumeter	1 ft. 4 inches.
8 ft.	Voice	6 feet.
1 ft.	Whisper	9 inches.

3 C. not heard on either side. Left hospital to-day after having had ten injections.

10 : 11 : 09.

Returned to Hospital. Fibrolysin continued along with inflation and oto-massage as before.

Right		Left
2 ft. 5 in.	Acoumeter	1 ft. 2 in.
4 ft. 2 in.	Voice	1 ft. 4 in.
10 in.	Whisper	11 in.

from 3 C. to C. 4 heard on both sides.

8 : 12 : 09.

Right		Left.
2 ft. 4 in.	Acoumeter	1 ft. 6 in.
3 ft. 1 in.	Voice	2 ft. 4 in.
12 in.	Whisper	1 ft. 8 in.

from 3 C. to C.4 all heard on both sides.

During this stay in Hospital twenty injections were given making thirty in all.

## Case III.

C. W. (Female)      Age 11.

Has been deaf for three years.    Adenoids removed  
June 1909.

Right membrane thickened.

Left membrane thickened and shows the presence of  
placques.

Catheter and oto-massage given every second day for  
four weeks with no result.

Fibrolysin injections and insufflations given every  
second day in all fifteen injections with no result  
however.

## Functional examination.

Right		Left.
2 ft. 6 in.	Accumeter	1 ft. 3 in.
10 in.	Voice	5 in.
5 in.	Whisper	3 in.
Negative	Rinne C. C <sup>2</sup>	negative.
+ 20 secs.	C. mastoid	+ 10 secs.

As no perceptible improvement had been produced,  
the patient decided to discontinue the treatment.

## Case IV.

A. H. (Female) Age 40.

May 6th 1908.

Has been deaf on the right side for two or three years  
Left side becoming affected. Constant tinnitus of  
a buzzing character, sometimes whistling. Is subject  
to colds in the head.

Right membrane tympani indrawn, cone of light not  
broken but widened and diffused. Mobility fair.

Left membrane tympani, indrawn and atrophic. Posterior  
superior segment ballooned out. Chronic pharyngitis  
present. Chronic hypertrophic rhinitis going on to  
atrophy. Septum straight. Treated with catheter  
and oto-massage from May 20th to June 12th 1908  
almost daily. This improved some slight improvement  
as at the beginning the functional tests were as  
follows :-

Right		Left
18 inches	Accumeter	29 inches.
7 "	Voice	11 "

After treatment.

Right		Left
14 inches	Accumeter	33 inches
16 "	Voice	10 "

Seen again on December 12th 1909.

Functional/



Functional tests then gave following results.

Right		Left.
14 inches	Accumeter	19 inches.
12 "	Voice	15 "
8 "	Whisper	7 "
+ 6 seconds	C. mastoid	+ 5 seconds.

Weber lateralised to right (uncertain)

Rinne C. and C.<sup>2</sup> negative on both sides 3C. 16, 2 C. 32, 1 C. 64, C. 128 not heard on either side.

Fibrolysin treatment was then started three times a week. The method employed was that of subcutaneous injection accompanied by the insufflation of a few minims into the middle ear by means of the Eustachian catheter. Inflated and oto-massage being carried out at the same time.

On February 2nd 1910. After fifteen such injections had been carried out the functional tests were :-

Right		Left
9 inches	Accumeter	28 inches.
10 "	Voice	5 "
3 "	Whisper	4 "
+ 5 seconds	C. mastoid	+ 9 seconds.

Rinne C. and C<sup>2</sup> negative on both sides. Weber lateralised to the left(uncertain).

3 C. 16, 2 C. 32, 1 C. 64, C. 128 not heard on the right.

3 C., 16, 2 C. 32, 1 C. 64, not heard on the left.

Fibrolysin treatment continued in order to complete the course of thirty injections.

The remaining fifteen treatments consisted in the injection of the whole ampulla of fibrolysin without the intra-tubal insufflations.

Inflation and oto-massage continued.

On March 23rd 1910 immediately after receiving the last treatment the functional tests were as follows :-

Right.		Left.
40 inches	Acoumeter	48 inches.
28 "	Voice	26 "
12 "	Whisper	13 "
+4 seconds	C. Mastoid	+5 seconds.

Rinne C. and C.<sup>2</sup> negative.

Weber lateralised to the left (uncertain).

3 C. 16, 2 C. 32, 1 C. 64 not heard on either side.

It must be noted that the former examinations were made just after the patient received treatment.

On March 30th the tests taken immediately before inflation and oto-massage gave almost precisely the same results as those recorded on March 23rd.

There was thus a certain small degree of improvement.

The following are seven hitherto unpublished cases which Mr. Macleod Yearsley has kindly permitted me to add to my other cases. They were treated by Mr. Yearsley himself.

## Case V.

R. S. (Male) age 21 years.

Deaf  $1\frac{1}{2}$  to 2 years. Discharge five years ago, after bathing. Used to have earache and "inflammation of ears" at seven years of age. Paracusis Willisii present. No tinnitus. Is worse with colds.

Right membrane - thickened and dull - malleus mobile.

Left membrane - view obscured by two ivory exostoses, but what is seen of it is thickened. Septum nasi deflected to the left. Both middle turbinals hypertrophied. Posterior ends large.

## Functional examination.

Right.		Left
15 inches	Acoumeter	15 inches
36 "	Voice	34 "
16 "	Whisper	12 "
Negative	Rinne C & C. <sup>2</sup>	negative.

Bone conduction normal or slightly plus on both sides.

High tones well heard. Gellé negative on both sides.

Low tones 3 C. 16 lost on Right.

3 C. 16 to 64 lost on Left.

After/

After inflation with catheter -

Voice Right = 51 inches. Left = 47 inches.

22 : 5 : 07.

Septum straightened, posterior ends removed, also anterior ends of both middle turbinals.

17 : 6 : 07.

Course of daily catheterisation with intra-tympanic injections and massage at end of course.

87 inches          Voice          86 inches.

21    "            Whisper    19        "

The improvement was maintained for 14 days, after which he went back. Oto-massage daily, improved him again.

As I had concluded that his deafness was largely due to the contraction of adhesions left in the middle ear by previous inflammatory attacks, and that improvement had resulted from their stretching and that the relapse was due to their contracting again, I advised fibrolysin and massage. He was given 14 injections by his family doctor, who then gave up the treatment as useless.

Case VI. /

Case VI.,

R. G. C. (Male) Age 30 years.

Deaf on both sides for 12 to 13 years. Deafness began with colds. Is subject to colds. Hissing tinmitus, Variable and not continuous. No discharge. Paracusis Willisii "nearly always".

Both membranes tympani, dull and indrawn. Mallei mobile.

Left posterior vomerine crest. Hypertrophic pharyngitis.

Functional tests.

Right		Left.
1 inch	Accoumeter	0
13 inches	Voice	8 inches
0	Whisper	0
Negative	Rinne C C. <sup>2</sup>	Negative.
+ 10 sec.	C. mastoid	- 5 sec.
positive	Weber	

High tones well heard.

Low tones Right : 3 C. 16 and 2 C. 32 lost

Left : 3 C. 16 to 1 C. 64 lost.

Gelle negative on both sides.

He was treated by daily catheter and massage for seven days without any result.

As/

As he was obliged to return to New Zealand and his time was limited to a few weeks, he urged me to try Fibrolysin and was injected daily. He had in all 26 injections between June 29th and July 29th 1908 with oto-massage and occasional catheterisation.

The results observable were -

- (1) That by the fifteenth injection he volunteered that the paracusis Willisii was much less.
- (2) The tinnitus was greatly improved.
- (3) His functional tests on July 25th gave

Right	Left
6 ft. 9 inches Accumeter	40 inches.
6 ft. 7 " Voice	5 ft. 5 inches.
18 inches Whisper	6 inches.
Negative Rinne C. C. <sup>2</sup>	negative
+ 8 sec. C. Mastoid	normal.

Weber not lateralised. Gelle's test doubtful.

Low tones, only 3 C. 16 not perceived on either side.

One year later he wrote from New Zealand that the improvement had been maintained.

#### Case VII.

W. M. A. (Female) Age 26 years.

Deaf for eight years, worse since December 1907, after having a bad cold. Subject to colds. Very gradual onset/

onset. Tinnitus very seldom, then only faint buzzing. Left side better than right. Otomyasthenia. No family history.

Right membrane : normal texture, slightly indrawn, no blush.

Left membrane : slight indrawing, normal texture, blush over promontory.

Mallei mobile. Nose nil. Posterior rhinitis.

Definite pad of adenoids with deep sulci. Adhesions in Rosenmüller's fossae.

March 12th 1908.

Adenoids removed and adhesions broken down.

From March 18th to 26th regular daily catheter and oto-massage. Returned home and treatment continued by her own doctor.

January 13th 1909.

Right		Left
20 inches	Voice	41 inches.

Fibrolysin ordered. Up to May 4th had twenty injections by her own medical man along with oto-massage, none now for a month.

May 4th 1909.

Right		Left.
17 inches	Voice	36 inches.

No/

No change in membranes except that the blush had gone. Injections continued in order to complete the full course of thirty. No improvement.

## Case VIII.

J. M. (Female) Age 29.

24 : 2 : 09.

Deaf on both sides. Duration three years. Left side worse. Condition worse with colds. Thumping tinnitus. Worse on stooping, not continuous. occasional vertigo.

Deafness worse for last twelve months. No headaches. Both membranes indrawn and thickened. Mallei mobile. Tonsils and adenoids removed last year. Nasal septum deflected to the left.

18 : 3 : 09.

Politzerisation tried by Doctor - no result. In Summer submucous resection done with excellent results as regards nasal breathing and colds. This was followed by regular catheterisation and oto-massage.

16 : 9 : 09.

Has gone back in hearing.

Right		Left
29 inches	Voice	12 inches.
Fibrolysin/		



Fibrolysin tried and abandoned. In this case half an ampulla was insufflated into the two tubes by means of the catheter, the other half injected hypodermically. The patient objected to the length of time it remained in Eustachian tube.

Improvement slight, if any.

Functional examination. 24 : 2 : 09.

Right		Left.
$4\frac{1}{2}$ inches	Acoumeter	3 inches.
1 ft. 7 in.	Voice	1 ft. 3 in.
0	Whisper	0
negative	Rinne C	negative.
positive	Rinne C <sup>2</sup>	positive.
- 8 seconds	C mastoid	- 10 seconds
positive	Gelle	positive.
35000	Galton	33000.
3 C. 16 and 2 C. 32 lost on both sides.		

Case IX.

D. M. (Female) Age 35.

14 : 1 : 09. Deaf on both sides. Right side first affected, now both equally affected. Duration four to five years, worse past two years. Worse with colds, patient not however subject to colds.

Deafness/

Deafness worse in damp weather. Continuous rushing tinnitus. No vertigo. No. P. W.. Was first conscious of deafness after first confinement at age of thirty.

She has had four children, deafness worse after each child.

One brother deaf.

Both membranes fairly normal, very slight indrawing, Mallei mobile.

Throat, nose and post-nasal space - nil.

Functional examination.

Right		Left
12 ft.	Acoumeter	49 inches.
8 ft.	Voice	10 feet
15 inches	Whisper	21 feet
negative	Rinne C & C <sup>2</sup>	negative.
- 9 seconds	C. Mastoid	- 13 seconds.
41000	Galton's whistle	43000
negative	Gelle	negative.

Air 3 C 16, and 2 C 32 lost on both sides.

From January 18th to February 2nd regularly treated with catheter and oto-massage. Increasing doses of Strychnine also given. Coll. Sodii and Pigment.

Iodi. et Capsici.

30 : 1 : 09/

30 : 1 : 09.

Right		Left
10 feet	Voice	10 feet
36 inches	Whisper	36 inches.

Hearing for 2 C 32 returned on both sides.

An attack of influenza intervened and the deafness became worse again.

4 : 10 : 09. She returned and the tests were.

Right		Left
8 feet	Acoumeter	46 inches.
17 inches	Voice	5 feet
10 inches	Whisper	5 inches
negative	Rinne C. C <sup>2</sup>	negative.
- 8 seconds	C. Mastoid	- 10 seconds.
	Weber	lateralised.
41000	Galton	45000.

Air3 C 16 and 2 C 32 lost on both sides.

From that date i.e., October 4th to February 21st she had 30 injections of Fibrolysin with oto-massage and catheter. The first sixteen injections were made partly by the catheter, partly by hypodermic injection, but owing to their discomfort and increasing deafness they were discontinued.

Tests 20 : 2 : 10.

Right/

Right		Left
5 ft.	Acoumeter	46 inches
32 inches	Voice	57 inches
12 "	Whisper	33 inches
Negative	Rinne C.	Negative
positive	Rinne C <sup>2</sup>	Negative
- 6 seconds	C. Mastoid	- 7 seconds
41000	Galton	41000

Air 3 C 16 to 1 C 64 lost on both sides.

Result here is doubtful, as she again became pregnant.

#### Case X.

Mrs. S.                      Age 32 years.

First consulted Mr. Yearsley in 1897 and was treated by catheter by her medical man with however no result.

16 : 11 08

Has been married seven years.      Still deaf, occasional tinnitus.      Has fewer colds than formerly.

Paracusis Willisii.

Both membranes dull white and thickened indrawn, mallei mobile.

Nasal septum irregular.      Old chronic hypertrophic rhinitis, showing signs of atrophying.

Chronic pharyngitis present.

Functional examination.

Right/

Left

Right		Left
13 inches	Acoumeter	14 inches
15 "	Voice	8 "
0	Whisper	0
negative	Rinne C. C <sup>2</sup>	negative
+7 seconds	C. Mastoid	+ 8 seconds.
negative	Gelle	negative.

Low tones lost up to and including C on both sides.

Treated from November 17th 1908 to December 23rd by regular catheterisation and oto-massage with no result.

From December 28th to March 29th 1909 had thirty-three injections of Fibrolysin - none given by catheter with inflation and oto-massage. No result.

#### Case XI.

Mrs. J. S.            Age 40 years.

26 : 3 : 08.

Deaf on left side for eleven to twelve years. Right ear becoming deaf during past year. Singing tinnitus, worse on the left side, varying in intensity continuous. No colds in head. No paracusis Willisii. No family history. Breast removed for carcinoma eight years ago.

Right/

Right membrane dull and indrawn.

Left membrane markedly indrawn and thickened.

Left Malleus restricted in movement.

Chronic pharyngitis. Nose nil.

Functional examination.

Right		Left
10 ft.	Acoumeter	4 inches
10 ft.	Voice	2 inches
19 inches	Whisper	0
Negative	Rinne C.	Negative
positive	Rinne C. <sup>2</sup>	negative.
+ 10 seconds	C. Mastoid	+ 10 seconds.
40,000	Galton	36,000

Air : 3 C 16 lost both sides only.

From June 15th to July 29th treated by regular catheterisation and oto-massage with Strychnine internally and Coll. Sodii.

29 : 7 ♯ 08.

Right		Left
12 ft.	Voice	5 feet
8 ft.	Whisper	8 "

17 : 10 ; 08. Gone back.

Right		Left
10 feet	Voice	9 inches
8 "	Whisper	0

Patient/

Patient then had forty injections of fibrolysin with oto-massage given by hypodermic injection by her own medical man. Improvement.

Seen and tested on February 17th 1910, and showed improvement fully maintained.

Right		Left
12 feet	Accoumeter	6 inches
12 feet	Voice	21 inches
10 feet	Whisper	0

In addition to those unpublished cases I wish also to insert in this thesis some cases recorded by Maupetit and Colat in the Revue Hebdomadaire d'otologie of May 1909 and which I have translated from that periodical. In this article they endeavour to discover what the true value of thiosinamine is as a therapeutic agent and take certain precautions in using it which render the results more precise.

They employ the method advocated by Lermoyez and Mahu, that is ear baths associated with mechanical treatment.

In their article they write as follows :-

"We find ourselves in presence of three different therapeutic elements acting at the same time.

- (1) The insufflations and massage.
- (2) Cold baths applied to the membrana tympani.
- (3) Thiosinamine.

It is most important to be able to define precisely the action of the drug itself. For this reason we have acted as follows.

- (1) Every time a patient was recognised as suitable for this treatment, we submitted him first of all to a series of insufflations of air by the Eustachian tube, with oto-massage, until the maximum of improvement had/



had been attained.

Then, whilst continuing this mechanical treatment we used thiosinamine. If an improvement then took place, we knew that the local bath had participated a good deal in its production.

(2) Along with this medicament we used local baths of a 1 per cent solution of Iodide of Potassium and sterile water. This constituted a kind of control treatment. When for instance a patient had both ears affected, we used thiosinamine on one side and the control solution on the other; and the latter solution was always applied to the more affected ear. In this manner we could satisfy ourselves that the improvement was not produced merely by the cold baths but by the thiosinamine itself."

I. Marie C. 27 years.

For several years double cicatricial otitis with perforation of the right membrane. Right ear more deaf than the left.

We practised on both sides catheterisation and massage; after one month, the patient had gained as regards hearing the watch, two centimetres on the right, and three centimetres on the left. We then started treatment/

treatment by means of iodide of potassium on the right, and thiosinamine on the left as before described.

After eight treatments the patient complained of pain in the left ear; she had already felt some passing itching sensations chiefly on the left side.

Hearing on the right side had remained the same; on the left side it had sensibly diminished. On objective examination we remarked that the left drum was a little reddened. We stopped the treatment on the left side and continued it on the right, replacing the iodide by thiosinamine. After four treatments a slight purulent non fetid discharge appeared on the right side, which became of an offensive odour after a few days; this discharge continued for twenty days in spite of assiduous treatment. The patient did not wish to go on with the treatment.

II. Marie F . . . . . 33 years.

Double cicatricial otitis with perforations on both sides due to previous otorrhoea.

For five years we practised inflation of the Eustachian catheter without much improvement. The left ear was the worse.

We then started thiosinamine on the right, and iodide of potash on the left.

Between/

Between the treatments the patient complained of itching especially on the right side. After the tenth the hearing seemed to be slightly improved.

After five other treatments, both ears began to discharge, but more profusely from the right than from the left side.

We treated the discharge, which continued for two months on the right side, but only two weeks on the left side. The patient refused to resume treatment.

III. Rose R . . . 37 years.

Double chronic dry otitis media, which started three years ago.

The left ear was the worse.

In the nasal fossa we removed a septal spur on the left side, and posterior end of inferior turbinal on the right; after this we carried out inflation and oto-massage on both sides.

At the end of one month the patient had gained five centimetres on both sides as regards hearing the watch.

We then started thiosinamine on the right side with iodide on the left.

Slight itching especially on the right. After the/

the eleventh treatment, very slight improvement on both sides.

We stopped the treatment, for six days and then started it again.

After the sixth treatment, the patient complained of marked itching in the right ear, accompanied by slight pain.

The membrane was found to be very red, as also was the deepest part of the meatus. We left the ear alone that day, and the following day a slight sero-purulent discharge made its appearance which was odourless; it lasted for a couple of weeks.

The patient at the end of this time was unwilling to resume treatment.

IV. Sister X. 32.

Double cicatricial otitis; the commencement of which seemed to date from twenty years ago, as the result of repeated discharges.

She had been treated for five years by means of the Eustachian catheter.

We resumed this treatment without benefit. The right ear was more deaf than the left. We started baths of potassium iodide on the right side and thiosinamine on the left.

The/

The patient frequently complained of itching in the left ear.

After the treatments, without any improvement, there appeared from the left ear an abundant odourless muco-purulent discharge. This discharge lasted two months in spite of all treatment.

V. Joseph G . . . 38 years.

Double cicatricial otitis media, treated for one month without improvement.

Thiosinamine started on the right Iodide on the left. After the fifteenth treatment slight improvement on both sides. The patient however complained of itching, chiefly on the right side. Finding also that the results were not sufficiently marked, and noticing moreover the re-appearance of discharges in the other patients treated in the same manner as himself, he refused to continue the treatment.

VI. Catherine C . . . 44 years.

Double cicatricial otitis media, duration about eight years. Mechanical treatment brought about no improvement.

Thiosinamine on the left side and distilled water on the/

the right side commenced.

After the seventh treatment, an otitis externa appeared on the left side. Treatment stopped.

VII. X . . . . 18 years.

Double dry adhesive otitis media.

Posterior ends of inferior turbinals and adenoid vegetations removed.

After one month and a half of mechanical treatment there was very slight improvement on both sides. The left ear remained somewhat more deaf than the right. Thiosinamine on the right, and distilled water on the left commenced.

After eight treatments, itching and myringitis on the right side.

Treatment stopped for five days, it was then started again using thiosinamine on the left and distilled water on the right. After ten treatments, slight otitis externa on the left.

No improvement being produced the local baths were stopped.

Mechanical treatment was then carried out alone without any fresh change in hearing power.

VIII. Louise G . . . . . 25 years

Double/

Double cicatricial otitis media with persistence of a perforation on the left side. After one month of mechanical treatment slight improvement on both sides. The right ear was the better of the two.

Thiosinamine on the right and distilled water on the left commenced. After fifteen treatments a very slight improvement, whose presence was however denied by the patient, seemed to be produced on both sides. Pain and myringitis however appeared on the right side. The patient was unwilling to continue the treatment.

IX. Odette D . . . . 15 years.

Right cicatricial otitis media with persistence of a perforation.

After two months and a half of mechanical treatment there was a well marked improvement.

Baths of thiosinamine started. Patient complained after each treatment.

After the tenth treatment a slight non fetid muco-purulent discharge made its appearance, which lasted eighteen days and brought with it an increase in deafness.

We stopped the thiosinamine and resumed inflation and massage which restored the hearing to its condition before the appearance of the discharge./

discharge.

X. Armand T. . . . . 30 years.

Left cicatricial otitis media, lasting 14 years.

Inflation and massage at the beginning brought about a slight improvement.

Thiosinamine treatment was started but this produced no fresh improvement ; after ten treatments, myringitis with otitis externa made its appearance.

Three other patients had started to submit to the treatment; after three or four visits however they were unwilling to continue as they said they had pain after each treatment.

I shall now add twelve cases of adhesive catarrhal otitis treated by means of fibrolysin by Dr. Bichaten of Rheims and translated from the Revue Hebdomadaire d'otologie of November 27th 1909 in which they were published.

These cases were treated by means of warm baths of fibrolysin associated with the usual mechanical treatment.

Only in three cases were insufflations made into the middle ear by means of the Eustachian catheter.

The/



The following is the summary of the twelve cases .

L. M. A.            25 years.

Bi-lateral adhesive otitis for the last two years.

On the right tympanic membrane adherent to promontory.

On the left a reniform perforation in the lower segment of the membrane.    Watch heard at 2 centimetres on the right.    Only on contact on the left.

Bone conduction good on both sides.

Weber not lateralised.

After having employed the usual therapeutic measures without success, daily baths of fibrolysin were prescribed and twice a week these were followed by the use of Delstanche's masseur.

On June 18th after a month's treatment, hearing for the watch was six centimetres on the right and three centimetres on the left.

The patient was seen three months after this; the improvement had persisted on the left but had almost entirely disappeared on the right side.

II.    M. A. . . .            20 years.

Deafness due to bi-lateral tubo-tympanic catarrh lasting ten months.    Voluminous adenoid vegetations and hypertrophic rhinitis on the right side.

Membranes very slightly movable with Siegle's speculum.

The/



## Functional examination.

	Watch :	Bone :	Good.
Right.	"	Air :	2 centimetres.
		Rinne	negative.
	Watch :	Bone :	Not very good.
Left.		Air :	on contact.
		Rinne	negative.

Weber not lateralised.

Ordinary mechanical treatment produced no change.

In September Fibrolysin with mechanical treatment was started. At the beginning of October however treatment had to be stopped as the patient complained of pain in the ear and appearance of a slight sero-purulent discharge. The treatment was resumed fifteen days after on both sides without incident.

Towards the end of November, the watch was heard at 15 centimetres on the right side and at 5 centimetres on the left.

The patient was seen again in March 1909, the improvement had not been maintained on the left, but persisted on the right side.

IV. Mme. B. . . . . 45 years.

Formerly had adenoids, adhesive otitis on the left for the last fifteen years.

Functional examination :-

Watch :	Bone :	Good.
	Air :	Contact/

Watch : Bone : Good.  
 Left. Air : Contact.  
 Rinne negative

Weber not lateralised. Right ear normal. Four treatments with fibrolysin accompanied by fibrolysin were carried out without benefit. The patient was unwilling to go on with the treatment.

V. Maurice B. 17 years.

Suppurative otitis media lasting eight years.

Adhesive otitis on the right.

Membrane on the right side adherent to the promontory and immobile with Siegle's speculum.

Functional examination. October 10th 1907.

Right. Watch Bone : Middling.  
 " Air : Contact.

Rinne negative.

Daily baths of fibrolysin were prescribed with massage and catheterisation three times a week. As this proved unsuccessful some drops of the solution were injected at five different times into the Eustachian tube by means of the catheter, and on February 17th a slight improvement was produced.

The watch was perceived at 3 centimetres and loud voice/

voice was well heard. Whispered voice, which had formerly not been heard was heard at 30 centimetres. From the patient's account the intra-tympanic injections were always painful.

VI. Marcel H. . . . 18 years.

Seen February 10th 1908.

Double cicatricial otitis lasting three or four years. On the left side there was destruction of the anterior half of the membrane owing to an otitis which had been cured for the last two months.

Functional examination.

	Watch	:	Bone	:	Good.
Right	"	:	Air	:	20 centimetres.

Rinne negative.

	Watch	:	Bone	:	Good
Left.	"	:	Air	:	Contact

Rinne negative.

Weber lateralised to the left side.

A first attempt at treatment with fibrolysin was made, but after two treatments the discharge re-appeared from both sides.

This was cured in about three weeks and the patient was sent off for three months. At the end of this time the treatment was commenced again, but as on the first occasion the use of fibrolysin was followed by suppuration. The patient got tired of the treatment and was lost sight of.

VII. Mlle. M. . . . . 21 years.

Examined March 4th 1908.

Adhesive catarrh on the right side and a large perforation involving anterior part of the membrane on the left.

Bi-lateral atrophic rhinitis. No ozena.

Functional examination.

	Watch	:	Bone	:	Good.
Right	"	:	Air	:	Good.
			Rinne		negative.
	Watch	:	Bone	:	Good
Left.	"	:	Air	:	Contact.

Rinne negative. Weber not lateralised.

Mechanical treatment commenced. At the end of six treatments the watch was heard at 15 centimetres on the right, with however no improvement on the left. Treatment continued, but no further improvement took place.

Baths of fibrolysin was then applied to the ear whilst continuing the mechanical treatment. At the end of one month the watch was heard at 30 centimetres on the right. The left ear showed no improvement.

VIII. George P . . . . . 12 years.

Examined April 15th 1908.

Deafness/

Deafness due to a bi-lateral adhesive otitis.

Siegle's speculum moves the anterior part of the right membrane, the left is immobile.

Adenoids present.

Functional examination.

	Watch	:	Bone	:	Good.
Right.	"	:	Air	:	6 centimetres.

Rinne negative.

	Watch	:	Bone	:	Good.
Left.			Air	:	Contact.

Rinne negative. Weber lateralised to left.

Mechanical treatment alone gave watch at 25 centimetres on the right, and at 3 centimetres on the left. Baths of fibrolysin were then prescribed, no benefit however followed their use. Then whilst continuing the instillations of fibrolysin mechanical treatment was re-commenced, i.e. massage and catheterisation and by the end of July the results were as follows.

Right	Watch	:	Air	:	50 centimetres.
Left	"	:	"	:	12 "

IX. Madame L . . . . . 25 years.

Examined June 1908. Complaining of tinnitus and deafness in the left ear lasting one year.

Membrana/

Membrana tympani retracted with a hyperaemic zone in the postero-superior quadrant. Maleus immobile.

Functional examination.

Left	Watch	:	Bone	:	Good.
	"	:	Air	:	contact.

Rinne negative. Weber lateralised to the left.

Fibrolysin and massage employed; after two treatments the patient complained of itching in the ear and a slight discharge commenced.

Treatment was stopped and commenced again at the end of a fortnight with the same result as before after three days. The treatment was then abandoned. No improvement had taken place.

X. M. B. . . . . 18 years.

Examined November 1908.

Complaining of deafness which had lasted several months.

Right membrane completely destroyed, left membrane markedly retracted and absolutely immobile to Siegle's speculum.

Functional examination.

Left	Watch	:	Air	:	Nil
			Bone	:	passable.

Rinne negative.

Catheterisation/



Catheterisation and massage three times a week for a month; the postero superior part of the membrane tympani alone became mobilised. The watch was then perceived on contact but no further improvement was seen.

Baths of fibrolysin followed by massage were then prescribed. At the end of five weeks no change had been produced. At the end of this time fibrolysin was instilled into the middle ear via the Eustachian tube on two occasions. Immediately after this treatment, however, the patient experienced such severe pain that she was unwilling to continue. No benefit had been derived from the treatment.

XI. Mlle. S. . . . . 18 years.

Seen at beginning of February 1909 suffering from a bi-lateral adhesive otitis following catarrh of the naso-pharynx. Treated at first without favourable result.

Bone conduction good on both sides.

	Air	-	contact on right.
Watch	"	-	1 centimetre on the left.

Rinne negative.

After three weeks of thiosinamine slight improvement. In fact the watch was perceived at 8 centimetres on/

on the right, and at 3 centimetres on the left.

Treatment was continued with catheterisation super-added. Hearing was not modified further.

XII. M. L. . . . 39 years.

Adhesive otitis media on the right dating one a half years.

Tympanic membrane little movable with Siegle's speculum.

	Watch	-	Air : Contact
Right	"	-	Bone - fair.

Rinne negative.

After some years of mechanical treatment the watch was perceived at one centimetre. We then started baths of thiosinamine with massage. At the eighth sitting the patient felt a sensation of itching in the ear and at the ninth a slight sero-purulent discharge made its appearance as well as an inflammation of the meatus.

The patient was seen again a fortnight later and the hearing was found to be, if anything, rather diminished.

In the Lancet of July 24th 1909, J. Gay French publishes the results of his investigations into the actions and uses of fibrolysin in the treatment of middle ear deafness, and I think it would be useful to consider the results which he experienced in the cases which he treated in this manner.

The cases in which he used this treatment were those of deafness and tinnitus resulting from post-suppurative middle ear catarrh, and chronic dry middle ear catarrh.

He summarises his results as follows :-

"The number of cases that have had the six weeks treatment have been 68. Of these 21 were cases of post-suppurative middle ear catarrh and 47 were cases of chronic dry middle ear catarrh. Of the 21 cases of post-suppurative middle ear catarrh, 16 had tinnitus and five had no tinnitus.

Of the 16 with tinnitus, four were complete failures; there was no improvement in hearing or diminution in the noises - indeed, one patient stated that she was much worse in both respects. Six had no improvement in hearing, but stated that the noises were less; two of these stated that the noises had completely ceased, and they thought they could hear a little/

little better (this, however was not borne out by the tests). Six showed good improvement in hearing to the tests, and stated that the noises were diminished in three, completely ceased in two, and no better in one. Of the five cases with deafness and no tinnitus two showed no improvement and three showed improvement. Of the 47 cases of dry middle ear catarrh, 36 had tinnitus and 11 had no tinnitus. Of the 36 with tinnitus, 11 were complete failures; eight showed no improvement in hearing to the tests, but stated that the noises were diminished (completely ceased in two); and 17 showed improvement in hearing to the tests, and of these, six stated that there was no diminution in the noises (although in one they had become intermittent instead of being constant), eight stated the noises to be diminished, and three reported the noises to have quite ceased. Of the 11 without tinnitus, seven showed improvement to the tests, and four no improvement.

In order to prove that it was the fibrolysin, and not the Eustachian catheter and the oto-masseur which brought about the improvement, 15 of the above cases - all with tinnitus as well as deafness - were first treated by the catheter and massage for six weeks without/

without having any fibrolysin, and their tests taken; they were then put on the fibrolysin course, and at the end of the six weeks of fibrolysin treatment their tests were again taken and the three sets of tests were compared.

It was found that in seven out of the fifteen there was no improvement in hearing, though two out of these seven reported diminution in the tinnitus.

I turn next to the question of the permanency of the results obtained. Of the 16 cases showing improvement in hearing and diminution in tinnitus, ten were treated a year ago or over and have had no treatment since; four were cases of post-suppurative middle ear catarrh.

Of these one only had a relapse in both hearing and tinnitus; in two the improvement in hearing is maintained, but the noises slightly returned; and in one the improvement is maintained and there has been no return of the tinnitus. Six were cases of the dry catarrhal type. Of these two have relapsed ( one patient states she is just as bad as ever, the other has had a return of the tinnitus and there is a slight diminution in the hearing power); four have retained their improvement in hearing, but in two of these there has been, in one, in whom the noises had quite disappeared, an occasional return of the tinnitus, and in the/

in the other in whom the noises had considerably diminished there has been a slight increase.

Two have retained their improvement in both respects.

All the above cases were treated by means of subcutaneous injection of Fibrolysin combined with insufflation of the solution into the middle ear by means of the Eustachian catheter. Mechanical treatment was also given along with the Fibrolysin treatment."

In trying to form an estimate of the value of Fibrolysin in the treatment of middle ear disease, one is faced by the difficulty that none of the results published by the different individuals who have used the treatment, seem to show any marked degree of correspondence with cachotter.

It is thus a matter of great difficulty, even after having examined the records of a number of cases, to lay down any rule as to which class of cases is the most likely to benefit by the treatment; or even to say definitely, that any cases of deafness do really benefit by the use of Fibrolysin.

One/

One fact I think stands out clearly, and that is the fact that the more recent reports, are not nearly so enthusiastic as were those, published at the time when the use of the drug was first advocated. Another point is, I think, that if any benefit is to be expected it is in the class of cases, formed by those suffering from post-suppurative cicatricial changes in the middle ear.

As to the favourable reports published by the earlier writers such as Horean and others, one can only assume that the results which they experienced, were in a large measure brought about by a more systematic use of the mechanical measures, than was practised, when the latter were used alone without fibrolysin.

Added to this, these favourable results were perhaps the outcome of the optimistic reception of a new method of treatment, which seemed to hold out a rational expectation of success; when the results claimed for it in the treatment of cicatricial conditions in other parts of the body are taken into account.

In any case the users of the drug become less and less enthusiastic about it, and it is gradually being/

being set aside as useless by many of them.

In my series of cases the results have been rather discouraging, as only three out of eleven showed any appreciable improvement as the result of treatment.

All these cases were carefully treated both as regards fibrolysin and as regards mechanical means. The drug had, I think, a fair trial given to it, as the majority of the cases were treated with a course of thirty injections extending over a period of from six weeks to two months.

In case II. in which there was a degree of improvement which was appreciated by the patient herself, I was unfortunately unable to give a preliminary course of mechanical treatment, as she lived in the country and was only able to stay in Hospital for a limited period.

In this case, which was one of cicatricial otitis media, hearing was quite markedly improved - as will be seen by reference to the tests - after the first ten injections. On returning to Hospital after a month's absence, the improvement had been lost, and was not regained, after completing the course of thirty injections.

One/



One is driven to conclude that the marked initial improvement must have been due to regular mechanical treatment.

In case IV. - This patient who was treated with a full course of thirty injections, accompanied by the usual mechanical treatment over a period of about three months shows a small degree of improvement.

It will be noticed that the first fifteen treatments were followed by practically no benefit. At this point the intra tubal injections were suspended and the Fibrolysin administered by hypodermic injection alone.

At the end of the thirty treatments hearing for the voice had risen from 10 inches on the right and five inches on the left; to 28 inches on the right, and 26 inches on the left - See tests.

The patient however still remained for all practical purposes very deaf indeed, but was conscious of some slight improvement, declaring that she could hear sounds, such as the ticking of a clock much more clearly than before the treatment was commenced.

In case VI., which was probably one of adhesive otitis of naso-pharyngeal origin, there was quite a marked improvement which seems moreover to have been maintained/

maintained.

In this case - as will be seen on referring to the tests - hearing for the voice rose, from approximately one foot on each side to six feet, and this was accompanied by lessened tinnitus, and improvement in paracusis Willisii. In this case as the patient's time was limited mechanical treatment did not have a fair preliminary trial, as the patient was only treated with catheter and massage for one week. We are thus left in doubt as to which agent brought <sup>about</sup> the improvement in hearing.

In all the other cases, the improvement was so slight, as to be unworthy of mention or absolutely nil.

In the series of ten cases, published by Maupetit and Colat, the results of treatment by means of baths of fibrolysin seem to have been almost nil; and the treatment by means of baths of a weak solution of potassium iodide, seem to have been much more efficacious. These writers seem to have found fibrolysin worse than useless, in that it caused in almost all the cases, either irritation of the meatus, or a recurrence of discharge. They sum up their results as follows :-

"In consideration of such results, Thiosinamine has been definitely put aside, and has not since been used/

used in the Otological Clinique of the Faculty of Medicine of Bordeaux."

They go on to explain that they had intended to treat a second series of cases by means of instillations via the Eustachian tube but that the results produced by the other method - that of ear baths - and the accidents following upon its use had cooled their experimental zeal.

They go on to say- "We have noticed that all the complications which supervened, during the treatment by means of the aqueous solution, were the same as those which Horeau himself demonstrated, when at the commencement of his experiments, he made use of the alcoholic solution; he at that time attributed them to the action of the alcohol. For ourselves, after obtaining the same results with the aqueous solution we attribute these results to the thiosinamine itself.

We regard this new treatment not only as useless as regards improving the condition of the patient; but more than that, hurtful. We therefore renounce it completely. *Primo non nocere* ".

In the series of twelve cases published by Bichaton the results of treatment are not by any means encouraging. In only two cases - that is No. VII and No. VIII./

No. VIII - was any real degree of improvement shown. In the first Case No. VII the watch was heard at 30 centimetres at the end of the course of treatment instead of at 15 centimetres, at which distance it was audible at the beginning of treatment. In Case No. VIII the perception for the watch passed from 25 centimetres on the right and 3 centimetres on the left, to 50 centimetres on the right and 12 centimetres as will be seen on reference to the tests.

Several of the other cases gained a few centimetres as regards hearing the watch but this very slight improvement was speedily lost.

In Case No. XII hearing was, if anything, diminished as the result of treatment and in four patients Cases, III. V. IX. and XII. the baths of fibrolysin caused the appearance of discharges which had been absent at the commencement of the treatment.

In Gay French's series of sixty eight the results are much better and the tests which he publishes in his article show in every case a well marked improvement as regards hearing the watch and whisper.

In only one of these cases was any bad result produced by the injections and this showed itself not in the setting up of discharge but in the production of/  
of/

of vertigo. This notwithstanding the fact that the whole 68 cases were treated by intra-tympanic insufflations of the drug.

In all the cases which I have treated I also have never met with any such unfavourable accidents, although all the cases were treated by means of intra-tympanic insufflations.

This I think indicates strongly that the method of ear baths employed by the French writers is a bad one; and that the solution containing antipyrin which they use, is much more irritating than that which is employed in this country, and which contains salicylate of soda.

In such a condition as middle ear deafness we must, I think, submit any promising treatment to a very searching examination before we finally reject it, as ever a slight improvement is always valuable to those suffering from the condition.

My experience, though rather limited, has been somewhat discouraging; and it, taken along with the examination of the numerous recorded cases, make me rather apt to consider that the maximum of improvement can be produced by mechanical treatment alone, and to make me feel unwilling to submit a patient to a long and arduous series of injections of fibrolysin.

I think then that the use of Fibrolysin may be practically discarded as a therapeutic measure in the treatment of middle ear disease. It would however be quite legitimate to try a certain number of injections along with the usual mechanical treatment, after having explained to the patient that the treatment was entirely of an experimental character and that he must not necessarily expect to derive any farther improvement from it.

Of course a very careful supervision must also be exercised to guard against the inflammatory complications of which the published cases record numerous examples. It is not however on account of the occurrence of these complications that I should condemn the employment of Fibrolysin in the treatment of middle ear deafness - as I do not think that they are a necessary consequence of the use of the drug. It is rather on account of the results, as regards improvement in hearing, that I should condemn it; as I do not think that the results are sufficiently favourable to justify its use.