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President—GAVIN YOUNG, M.C., M.B., F.R.F.P.S.(Glas.).

DISCUSSION ON THE MEDICAL TREATMENT OF AURAL VERTIGO.

The Medical Treatment of Ménière's Disease

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MR. G. H. BATEMAN: The work on which this contribution is based has been done at St. Thomas's Hospital and Mr. L. R. S. Taylor and Mr. J. Kodicek have been largely responsible for it. Mr. Taylor will give details of the cases treated and the results obtained in our series.

There are two conceptions of Ménière's disease, firstly that it is a primary affection of the vestibular apparatus and, secondly, that it is a vestibular manifestation of a constitutional disorder. We think that most would agree that the second hypothesis is correct and this opinion is supported by the various medical treatments that have been discussed and tried in the past few years, e.g. Mygind and Dederding's restriction of fluid intake and salt-free diet, treatment with urea to aid excretion of sodium, and also by Wright's focal sepsis and the Scandinavian intestinal intoxication theories. Incidentally we may be wrong in ascribing this latter to Scandinavia as it has been the basis of the spa treatment of Ménière's disease, and other diseases, for a long time. Histamine therapy is based on a vasoconstriction theory of the causation of the disease and it appears that Miles Atkinson's theory grew out of this. It is very difficult to trace the origin of the various theories as they soon get distorted. Miles Atkinson's latest paper read at the Fourth International Congress in London in July, 1949, emphasizes vitamins, and histamine is mentioned only as a convenient method of differentiating between the various vitamin-B deficiencies.

Results of treatment are very diverse, but the varied habits of living and perhaps climate of many countries may provide different causes of labyrinthine pathology, and therefore the results of treatment found in one country cannot always be comparable with those in another.

On analysing the results of the treatment we have followed at St. Thomas's Hospital we feel that, while not curing all patients of their symptoms, we have succeeded in providing them with a *modus vivendi*, free from the fear of sudden crippling attacks of giddiness.

This treatment is our interpretation of one advocated by Miles Atkinson in 1946 in a paper read to this Section at Torquay (*Proc. roy. Soc. Med.*, xxxix,

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807). His theory was that the vertigo is caused by a vascular disorder of the small vessels of the labyrinth resulting in excessive formation of endolymph. This disorder may be primary vasodilatation with excessive transudation supposedly through the stria vascularis of the scala media, or a primary vasoconstriction of the arterioles which leads to an anoxia of the capillaries and this in turn leads to excessive transudation through the capillaries when the vasoconstriction passes off. This may be likened to Raynaud's disease. The two groups may be distinguished by a histamine skin test. 0·05 c.c. of a 1 : 10,000 solution of histamine (0·275 mg. of histamine diphosphate in 1 c.c.) is injected intradermally in the flexor aspect of the forearm 2 in. below the bend of the elbow. The result is read fifteen minutes after the injection. A negative reaction is a central circular wheal of about $\frac{1}{3}$ to $\frac{1}{2}$ in. in diameter surrounded by an areola of $1\frac{1}{2}$ to 2 in. in diameter. A positive reaction gives an irregular central wheal of 1 to $1\frac{1}{2}$ in. in diameter with centripetal pseudopodia and a bigger areola round it of 2 to 3 in. in diameter. There are some intermediate results which should be retested with a double dose of histamine and those which are not definitely positive should be considered negative. There are difficulties in interpretation of this test and errors of classification became obvious in failure of response to treatment. When wrongly classified cases are often made worse by therapy and improved when the other treatment is substituted.

Negative cases are treated by vasodilatation; this controls the vasoconstriction and so prevents the anoxia which causes the increased permeability of the capillaries. Nicotinic acid is the vasodilator we have used and big doses must be given. 100 mg. t.i.d. is a moderate dose and doses up to 250 mg. t.i.d. have been necessary to relieve the symptoms in some cases. Intramuscular injection of 35 or 50 mg. of nicotinic acid are sometimes needed in the early stages. If the symptoms are controlled, dosage must be continued indefinitely though it can often be reduced.

Positive cases are treated by histamine desensitization. 0·05 c.c. of a 1 : 10,000 solution of histamine is first injected subcutaneously and the treatment is continued by repeating the injections on alternate days, increasing the dose by one-half on each occasion. The dose is taken up to about 0·4 c.c. of a 1 : 1,000 solution. It is rarely possible to take up the dosage at this rate throughout the course and if the reaction, flushing, palpitation and headache, is severe, the previous dose should be repeated and the rate of increase reduced. A course thus lasts about four weeks.

Miles Atkinson now advocates the use of enormous doses of riboflavin for positive cases, such as 90 mg. t.i.d. but the price is prohibitive in this country.

MR. L. R. S. TAYLOR: Cases have been selected which fulfil the criteria laid down as constituting Ménière's disease: perceptive deafness, tinnitus and vertigo occurring in bouts. Headache or head pains have been found in nearly every case, and these have often been previously diagnosed as migrainous and have been centred on the ear.

Caloric reactions were tested after the method of Cawthorne, Fitzgerald and Hallpike, using water at 44° C. and 30° C., delivered for 40 seconds from a suspended douche can. Time was taken from the start of stimulation until

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nystagmus ceased as estimated by the observer using reflected light, and confirmed where possible by the patient. Fifteen minutes were allowed between each test, the whole test taking over an hour to complete.

Cases were divided into positives and negatives by an intradermal skin test made by injection of histamine 2 ins. below the bend of the elbow in the centre of the flexor aspect of the forearm. The reason for this choice of injection site is to facilitate readings in doubtful cases and to aid in standardization. The grouping is dependent on the anatomy of the lymphatic system and therefore, for comparison, the same site must be chosen in each patient. Results are read fifteen minutes after injection. Straightforward cases have already been described. The doubtful cases show small serrations or even centrifugal pseudopodia, but these must be ignored. Any pseudopodium extending upwards, if associated with a good erythema and bleb, should be read as positive. If the injection is made subcutaneously the result will always be negative, hence the necessity for accurate placing of the needle. Unfortunately the easiest way of learning to read these tests is the hard way of experience, which may be uncomfortable to the patient and disheartening to the physician. The results obtained have, however, justified the time spent.

The treatment of the negative group will be considered first. The patient is told to take 100 mgm. of nicotinic acid three times a day before meals, and to expect a warm flush in the face, neck and forearms ten minutes later, lasting for about ten minutes. If no flushing occurs the patient is told to chew up the tablets before swallowing.

After a week the patient is seen again and, if nothing untoward has occurred, 100 mg. t.s.d. a.c., are given for a month before he is seen again. In severe cases intramuscular injections of 50 mg. or 100 mg. once or twice weekly, or even daily at first, have been given. A few cases were bedridden when first seen. These were admitted to hospital and treated with larger doses; injections of 75 mg. intramuscularly were given to one man three times a week at first. It is exceedingly important to stress the necessity of the continuation of a small maintenance dose when the symptoms are controlled. This will vary from patient to patient, but we have found 100 mg. t.d.s. to be an adequate dosage, although individuals often require a greater amount. This is a continuous treatment and makes no pretence of curing the underlying cause of the disease. The natural history is one of irregular bouts of attacks. These must still be expected by the physician and patient and, at the first warning sign, for example increase in tinnitus, an intramuscular dose is given of 50 to 100 mg. and an extra 100 mg. daily should be taken by mouth for a few days. In women, we have found an intramuscular injection of 50 mg. 48 hours before the expected menstrual period to be very effective in warding off an attack. Thorne and his co-workers have shown that in women there is a considerable sodium retention in the immediate premenstrual period with consequent cerebral œdema. Any tendency towards labyrinthine hydrops will therefore be accentuated at this time. The onset of acute coryza is another indication for increasing the dosage temporarily.

The histamine positives present a simpler group clinically for treatment, though in our hands results have not been so satisfactory as for the negatives. This is contrary to Atkinson's experience. Cases after completion of histamine

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desensitization have remained well for varying periods up to 18 months, but all have required a second course, and it would seem that maintenance dosage fortnightly or monthly is necessary.

The dangers associated with this form of therapy are few. Excess nicotinic acid is said to cause imbalance in vitamin B complex absorption. Two cases on very high daily dosage (800 to 1,000 mg. daily) have indeed shown such symptoms (emotional instability, feeling of fullness of head and photophobia) and both have been relieved of their complaints within a week by reducing their doses. A third case exhibited nausea, vomiting and water brash signifying a severe gastritis and a fourth constant diarrhœa, until the nicotinic acid was rested on the former, and dose reduced in the latter. These symptoms should be controlled by giving a compound vitamin B capsule.

Subcutaneous injection of histamine if given slowly will be without reaction, but if given too deeply into the muscles, or intravenously, produces alarming temporary symptoms of histamine shock (correctable by adrenaline (1 : 1,000 solution) min. v. intramuscularly, or intravenously) and in elderly hypertensives would not be without danger.

A total of 53 patients has been treated by the Miles Atkinson method. In none of these was there any doubt as to the diagnosis. All the patients attended a special clinic and were supervised by the same team of clinicians throughout. Caloric vestibular reactions have been studied in 37. The remaining 16 cases had no caloric tests for various reasons.

Age and sex distribution. Of the 53 patients 23 were men and 30 women. The ages varied between 21 and 75, but practically half the patients were between 40 and 60 years of age.

TABLE I.

AGE AND SEX DISTRIBUTION (53 PATIENTS).

Age in years	20-29	30-39	40-49	50-59	60-69	70-79
Male ..	—	8	4	6	5	—
Female ..	1	4	7	9	7	2

Histamine skin reaction. Fifteen patients were "positive" (28 per cent.). This figure is rather higher than Atkinson's. Eleven of these were females and 4 males. No special age incidence was noticed. The remaining 38 patients were histamine "negative" (72 per cent.) and both sexes were equally represented.

A number of errors in the histamine grouping were made early in the series, mainly through incorrect reading of the reaction and through subcutaneous injection of histamine. A marked increase in the severity of symptoms was noted in these cases, sometimes with remarkable suddenness. Repetition of the test and the institution of appropriate treatment resulted in rapid improvement and none showed any permanent ill-effects (e.g. increased deafness).

Effect of treatment. Vertigo responded extremely well, being relieved in 32 (60 per cent.) cases and improved in another 20 (38 per cent.).

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Tinnitus. Relief was obtained in 12 (23 per cent.) and improvement in another 22 (42 per cent.). In the latter group the musical component was usually lost, leaving the pulsatile (vascular) tinnitus.

Deafness. Both subjective and objective improvement in hearing was noted in 10 cases (19 per cent.), the average gain in the speech range being about 10 decibels.

Headaches were noted as a marked feature in 25 cases (47 per cent.). Relief was obtained in 17 of these and improvement in duration and severity in a further 6 cases.

TABLE II.
RESULTS OF TREATMENT.

	Vertigo	Tinnitus	Deafness	Headache
Relieved ..	32	12	—	17
Improved ..	20	22	10	6
No change ..	1	19	43	2

The cases have been followed up for a period of 18-30 months. The number of favourable results far exceeded that resulting from any other non-operative treatment we have tried. Furthermore the inconveniences to the patients of special dieting and restriction of water intake are avoided, while at the same time they are allowed to return to an active and useful life.

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MR. I. A. M. MACLEOD, *General Hospital, Nottingham.* In June, 1946, there was a group of 7 patients attending the Aural Department of the General Hospital, Nottingham, suffering from such severe symptoms of Ménière's disease that they were completely incapacitated. They had undergone practically all the recognized courses of medical treatment, and in three instances surgical measures had also been carried out. Unable to work, their symptoms unrelieved, they had abandoned all hope of being able to live useful lives again. Following the Address given to this Section that summer by Dr. Miles Atkinson[1], it was decided to try his methods of treatment on this group. The results of the decision, which was virtually one of despair, were so encouraging that in order to study the method more thoroughly it was extended to further cases and has now become a routine in the Department.

The series analysed here is of the first 50 consecutive cases. More cases have occurred but they are either still undergoing treatment or the time elapsing since the cessation of therapy has been too short for purposes of review. Twenty-eight cases have been male and 22 female. All have been unilateral in type and have exhibited the triad of acute vertigo, tinnitus and deafness in varying degrees of severity. It is interesting to note that 26 of the patients

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have been wakened from sleep by the onset of vertigo—some on more than one occasion.

Treatment has been carried our according to the results obtained from the histamine skin test described by Atkinson.[2] The salt used for skin testing and therapy has been histamine acid phosphate. This has been prepared in the research laboratory of a large drug firm in Nottingham who produce ampoules of a sterile 1 : 10,000 solution calculated in terms of histamine base, and I should like to acknowledge our gratitude to Sir Jack Drummond for his great help in this connection.

In the interpretation of the skin test at the beginning of the series two independent judgments of the results were exercised lest one observer might be erroneous in his conclusions. Using normal saline, and in some cases horse serum as a control in the " untested " arm and counting no reaction as sensitive, unless one or more " pseudopodia " developed, it soon became evident that reactions were clear-cut and definite and gave rise to no uncertainty. Viewing the reaction by oblique light gave greater relief to the edges of the wheal and pseudopodia. Further, by using an intradermal injection of 0·1 c.c. of a 1 : 10,000 solution of histamine base, instead of 0·1 c.c. of a 1 : 20,000, it was found that wheals and pseudopodia in sensitive cases became more sharply defined, but not larger or longer than when the weaker solution was employed. Similarly, in insensitive cases the edges of the wheals were more raised and sharp, but there was no tendency to develop pseudopodia, nor was the reaction time prolonged.

Of the series, 32 cases gave an initial sensitive reaction, 14 were insensitive, and the remaining 4 were intermediate, i.e. the wheals were approximate to a positive reaction in size and duration but presented a scalloped or budded periphery without the formation of true pseudopodia. I do not think there is any significance in this initial large number of sensitive cases, as the proportion of sensitive to insensitive and intermediate reactions is tending to even out, the larger the series grows.

The sensitive group. The cases in this group were treated by weekly subcutaneous injections of histamine. The initial dose was 0·1 c.c. of a 1 : 10,000 solution of histamine base. This was increased by 0·1 c.c. weekly, working up to a concentration of 1 : 1,000 solution of histamine base until a reaction was shown by the patient in the form of flushing and headache following the injection. This dose was repeated or increased thereafter on three occasions so that four consecutive reactions were produced. Treatment was then discontinued. This reaction point varied from 0·3 c.c. of the 1 : 10,000 solution to 0·4 c.c. of 1 : 1,000 solution, but so far no patient has required a greater dose than 0·5 c.c. of a 1 : 1,000 solution of histamine base.

On the average most patients felt better by the time they had received 0·3 c.c. of 1 : 10,000 solution, in that their attacks of vertigo had decreased in number, intensity and duration, and in some cases the vertigo had ceased altogether. A striking point was the sense of well-being and return of confidence they exhibited.

Regarding the results of therapy to date, I am aware of the shortness of the time factor involved, but without trying to offer any definite conclusions I think that so far they appear to be encouraging.

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Of the 32 histamine-sensitive cases 23 have remained free from vertigo since the end of their course of therapy, the time factor being a minimum of six months and a maximum of two years and eleven months. Six cases have relapsed and had further attacks of vertigo, 3 of these after 6 months' freedom, 1 after 9 months, and 2 after 1 year. Three of these cases on retesting had become histamine-insensitive and responded to nicotinic acid after histamine made their symptoms worse. The other 3 were still sensitive and responded to further histamine therapy. All have now remained free for periods of over 6 months.

Three cases have not shown improvement in that they are still subject to attacks of vertigo at intervals of less than 2 months.

The histamine-insensitive group. This group has been treated by nicotinic acid. Initially intramuscular injections of 25 mg. to 30 mg. were given daily combined with oral administration of 50 mg. to 200 mg. The balance between individual tolerance and freedom from symptoms has varied greatly, but most patients have been stabilized on oral dosage only, ranging from 50 mg. to 400 mg. daily.

Of the 14 cases thus treated 9 have remained free from vertigo. Four cases relapsed; 2 of these responded to increased dosage and 2 became worse. According to the skin reaction, these 2 cases had become histamine-sensitive and were relieved of their vertigo by a course of histamine injections.

One case has not improved though apparently remaining in the histamine-insensitive group.

The intermediate group. In this group of 4 cases 2 have remained symptom free on nicotinic acid therapy and 2 have been unrelieved.

SUMMARY OF RESULTS.

Group	Histamine sensitive	Histamine insensitive	Inter-mediate	Total	%
Vertigo-free ..	23	9	2	34	68
Relapsed ..	6	4	0	10	20
Unimproved ..	3	1	2	6	12

Freedom from vertigo, with its accompanying nausea and vomiting, has been taken as the criterion of improvement in this series. It has been found, however, that improvement in tinnitus and deafness did not take place nearly so frequently.

In 11 cases tinnitus disappeared completely, whilst in a further 9 cases it became less intense though still present. In 30 cases it was unimproved.

Improvement in hearing has been least frequent and only 9 cases have shown as appreciable increase in the hearing level, as checked by audiometry before and after treatment; 41 cases being unaffected.

	No. abolished	%	No. improved	%	No. unaffected	%
Tinnitus	11	22	9	18	30	60
Deafness	Nil	0	9	18	41	82

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MR. C. S. HALLPIKE said he was glad to hear Mr. Bateman use the term Ménière's *disease* of the labyrinth. In his view the use of the term Ménière's *disease* was justified and represented a clarification of their ideas on the fundamentals of the disorder.

Ménière's disease was in some ways a very satisfactory condition to treat, but in other ways less so. In the majority of cases satisfactory results could be obtained with judicious sedation with luminal, and nothing else. This meant that anyone who knew this and was capable of diagnosing the condition could treat it with success, and it was in fact so treated by neurologists, general practitioners and others. But when they came to the group of patients who did not do well on this very easy treatment, special chemical methods had to be employed, and again, in his experience, a high proportion did well.

Here the unsatisfying feature was that the patients seemed to do well whichever of these special treatments was selected, and here arose the difficult question of their rationale. If they reverted to the early history of this subject in particular histamine therapy, they had been told that histamine sensitivity, as shown by skin tests meant that the patient was suffering from a labyrinthine manifestation of histamine of which he could be relieved if his resistance to histamine were increased by means of histamine injections. From the point of view of theoretical immunology that had always seemed an unsound notion. Sometimes an allergic basis for Ménière's disease had been suggested, but the manifestations of allergy were multiple, while, on the whole, other allergic phenomena were not seen in Ménière's disease. Further, allergic patients always had their first allergic manifestations early in life, whereas in Ménière's disease the symptoms appeared later. Finally, in allergy there was nearly always a family history of the condition, which was not seen in Ménière's disease.

As regards skin tests, they had been told that if the patients were sensitive to histamine on skin tests, histamine should be given in such cases, but if they were insensitive, they must have nicotinic acid. But the experience of himself and his colleagues at Queen Square did not seem to bear that out (Harrison, M. E. S., 1945, *St. Thomas's Hosp. Gaz.*, xliii, 88). If subjects were negative to histamine with skin tests, this did not seem to forbid successful treatment with histamine, and *vice versa*. Histamine and nicotinic acid were chemically quite different, but they had this in common that they probably produced an increase of the circulatory rate in the labyrinth. It did not seem to matter very much which was given.

In the cases in which he had been concerned, histamine or nicotinic acid was used in accordance with this principle, not much notice being taken of skin tests, and the dose was regulated to produce the maximum circulatory effect. He hoped that further work would be done on the circulation of the fluids in the internal ear, since until more was known of this he did not think there could be any sound basis for either the treatment or the prognosis of this disorder.

MR. H. V. FORSTER said that about the year 1910, as a junior physiologist he had been interested in a certain type of intermittent inner-ear deafness, characterized by low tone loss, though exacerbations might occur with a sensation of fullness in the ear, clonus of one or other of the intratympanic muscles, and a sense of disorientation, aggravated by movement of the head.

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It was not until the publication of S. H. Mygind's researches that he felt that a reasonable explanation of these cases of bass inner-ear deafness had been offered.

The development of successful medical treatment for morbus Ménière, quite apart from the relief of the symptom of vertigo, might preserve the function of the cochlea if such cases of deafness were recognized in the early stages. He had been informed by an American colleague that "dramamine" the now well-known seasickness remedy, was useful in Ménière's disease. He understood that this preparation was a theophyllinate of benadryl and the formula of the Canadian preparation "gravol" had been given to him as follows: Beta-dimethyl-amino-ethyl-benzohydryl ether : 8-chlorotheophyllinate.

He had consulted the medical superintendent of one of the great liner companies, and understood that theophyllin compounds of the anti-histamine drugs available in this country were being tried out for seasickness, with hopeful results from phenergan theophyllinate. He, Mr. Forster, had recently attempted the treatment of a few cases of tinnitus from a small supply of "dramamine". He would be very interested to hear from members of the Section of any experience they might have in the use of these newer modifications of the anti-histamine drugs in morbus Ménière.

Mr. I. Simson Hall said that a similar investigation had been in progress in Edinburgh and he was, therefore, well acquainted with the painstaking and time-consuming character of the work which had been described by the openers.

Mr. Hallpike had already referred to the difficulties in ascertaining the rationale of treatment. He himself had been interested in this subject for a good many years, and on looking through some of the older cases he found that he had tried each routine as it was brought to his notice and that in the case of the salt-free diet system and again in the early histamine treatment, each claimed approximately the same proportion of success. Now there had been added to this the nicotinic acid therapy and a higher percentage of success was reached. Certainly in the series of cases observed in Edinburgh, the observations extending to one year or more, the success as measured in the relief of the vertigo approached 83 per cent. This was for 40 cases.

The difficulty was to assess the value of each treatment as it was introduced. A much greater time would be required before the success of any of these newer treatments could be judged. In an attempt to assess the progress which had been made he had examined the records regarding the references to operative treatment. It seemed to him that instead of accepting the fact that a patient had been free from attack for two years it would be well to see how many cases had been complete failures. Out of a series of 150 to 200 cases he discovered that 20 per cent. had been referred for surgical treatment—in other words, they were complete failures. In the last series of cases, from 1946 to a year ago, 15 per cent. were complete failures in the sense that they had been referred for operation. In this respect he thought a definite advance in the treatment of Ménière's disease could be claimed for the new methods.

Mr. E. J. Gilroy Glass said that from his own observations he could say that results with Miles Atkinson's treatment had been better than anything he

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had seen before. He had been particularly struck by the sense of well-being and confidence of the patient.

There were two cases in Mr. Macleod's series which he had not mentioned. They were very alarming at the time though very suggestive in retrospect. Owing to an error in dispensing a batch of histamine, it was made up to 1 : 10 instead of 1 : 10,000, or, in other words, 0·79 gm. instead of 1 mg. Two patients received this injection. Both dropped completely unconscious, with very severe shock, and one was thought to have expired. They both recovered, however, and the interesting thing was that neither of those patients had had any vertigo since. An even more significant thing was that both those patients, who had been extremely deaf, had normal hearing when they recovered consciousness. In one case the normal hearing was maintained for 6 months and in the other for one month. It was not an experiment to be repeated, but something happened with the histamine which restored the hearing, at least temporarily.

MR. TERENCE CAWTHORNE desired to associate himself with what Mr. Hallpike had said. He was interested in Mr. Simson Hall's figures, because, in their own series of cases, he had found that whatever medical treatment was advised about 50 per cent. seemed to be benefited. If one carried on from one medical treatment to another a further 25 per cent. came into the satisfactory group—the group, that is to say, in which the attacks were perhaps not cured but were kept at bay. There remained the 25 per cent. for which surgical treatment might be required.

There was one aspect of Ménière's disease or hydrops of the labyrinth which deserved consideration. It was sometimes forgotten that this was a disease of the cochlea as well as the vestibule, and he had been struck by the variation of the hearing in these cases of fluctuating hydrops of the labyrinth. One day the hearing was down, particularly in the low tones, and on another day it was up. One could measure the progress not only by the symptom of vertigo but actually by the change in the hearing which was often easily demonstrable with the audiogram.

From what they had already heard it was quite clear that in many cases medical treatment would give moderately good results, but when it came to the rationale underlying these forms of treatment it was very difficult to be precise or convincing. From time to time further theories might be brought forward ; he was quite sure they had by no means got to the end of the story. The advent of dramamine and other histamine products had been mentioned. He had had the opportunity of trying dramamine and another product, phenergan, but it was much too early yet to give the results as he had been using these compounds only for the past 3 months. In some cases they might produce useful results, while in others the patients said that the cure was almost worse than the disease.

DR. M. G. GOOD, speaking from the point of view of a physician, said that he found many a patient suffering from vertigo which was not dependent on an ear condition. The cause was an " idiopathic myalgia ", a functional disease of the skeletal muscles. An article on this subject was published in the *Lancet* (1940 (ii), 326) claiming that idiopathic myalgia may simulate visceral,

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neurological (neuralgia, neuritis) diseases and also vertigo. This " muscular vertigo " is often associated with headache localized by the patient in the occiput—occipital headache. The characteristic " myalgic spots " are regularly found and can be objectively located in one or both trapezius muscles. On appropriate injection of 1-2 ml. of procaine into each myalgic area the complaints disappear very rapidly and permanently.

The concept developed by the speakers that Ménière's disease arises from a disturbance of circulation in the labyrinth appealed to him as a basis of further research. It might, in his opinion, be due either to vasoconstriction—diminished inflow—or vasodilatation, leading to stagnation of the blood and diminished outflow. The common denominator is diminished blood flow, i.e. quantity of blood passing through the unit of tissue per minute, which of necessity leads to a relatively diminished oxygen supply or hypoxia. The relative oxygen deficiency may cause noises by irritation or interference in hearing by hypofunction of the acoustic nerve fibres : it is known that nerves and brain have the highest oxygen consumption.

Dr. Good suggested that the concept of disturbed circulation could be tested experimentally : if nitrites, femergin or other vasodilators produced a relief, even of a temporary nature, the complaints were likely to be caused by vasoconstriction. On the other hand if some of the patients were improved by ephedrine, methedrine, the therapeutic effect would certainly favour the assumption of vasodilatation as the basis of the disease. The discussion had clearly shown that two types of Ménière could be distinguished. It appeared possible to the speaker that the distinction was due to vasoconstriction or dilatation respectively.

MR. BATEMAN, in reply, said he did not altogether agree with Mr. Hallpike that most of these patients could be relieved by sedation. Some could be relieved in that way, but he did not think that sedation would put many cases into the " satisfactory " group though it might be that a number would go into the group labelled " improved ". As for allergy, he thought they would get into great complications if they started discussing that subject. He did not think, however, that allergy entered into the ætiology of this disease in any appreciable number of cases, but he disagreed with Mr. Hallpike when he said that it did not matter if one failed to differentiate the two groups, positive and negative to the histamine skin test. If therapy were started without carrying out the histamine test one could predict with great accuracy what the histamine test would have shown.

He had seen one or two cases who had been given dramamine for their Ménière's disease. This therapy seemed to come into the same category as sedation. It would produce more relief than most sedatives but it would not produce complete relief such as could often be brought about over a long period with the treatment described in the opening papers. He should have stressed a little more the feeling of well-being of these patients ; it was quite remarkable how they would comment on their feeling that they could now do things which they did not attempt before. In other words, they had lost their nervousness and they were able to go back to work and to enjoy it in very many cases.

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Observations on the Pathological Mechanism of Conductive Deafness in Certain Cases of Neuroma of the VIIIth Nerve.

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UNTIL recently it has been our impression that the tuning-fork tests in cases of unilateral deafness due to VIIIth nerve neuroma conform to the classical pattern of so-called " nerve deafness ". That is to say, the sound of the fork with Weber's test is typically referred to the normal ear, Rinne's test is positive, and perception with the absolute bone conduction test is reduced. Should the Rinne be negative it is a false negative ; that is to say, the apparently good perception by bone conduction with the affected ear is due to the transfer of the vibrations to the opposite cochlea, through which it is in fact perceived. This well-known fallacy is recognizable and can be excluded by abolishing the perception by the normal ear of this bone-conducted sound by means of an air-conducted masking sound.

In the course of a previous communication made to this Section (*Proc. roy. Soc. Med.*, 1949, xlii, 527), we said that there were some exceptions to this rule, in which a true negative Rinne appeared to be present in the ear affected by the neurofibroma and it is this point to which we return to-day.

So far as we know, all writers who have published their observations upon the tuning-fork tests in the deafness of VIIIth nerve neuroma are in agreement that they conform to the classical pattern of nerve deafness and they have little more to say on the subject. All observers except one, T. H. Just, who, in an excellent paper published in 1930 (*Proc. roy. Soc. Med.*, xxiii, 722) insisted that in certain cases of VIIIth nerve neuroma the negative Rinne is no artefact, but a true and, as he described it, " disturbing phenomenon ".

In our own experience at Queen Square we have encountered a number of cases of this kind. In 2 of these death followed surgical intervention carried out soon after our examination and we were able, through the good offices of Dr. Greenfield, to carry out a histological examination of the temporal bones.

It is the purpose of this communication to describe our findings, and explain how we think they account for this interesting, and as Just described it " disturbing " anomaly—the negative Rinne—in the tuning-fork test results.

The first of our subjects was a man of 57, and the second a woman of 47. They were under the care of our colleagues at Queen Square, Drs. Walshe and Carmichael, to whom we are greatly indebted for permission to investigate the cases and to make use of the clinical notes. The findings in both were characteristic of an VIIIth nerve neuroma.

CASE I. A.E., male, aged 57, under the care of Dr. F. M. R. Walshe.

Complaint : pain behind the left ear and deafness, left ear, four years. Numbness left side of face and unsteadiness in walking, seven months. He had recently experienced difficulty in winking his left eye, and in tasting things on the left side of his tongue.

The pain behind the left ear had been intermittent, never very severe, and never lasted for more than a few hours at a time. The deafness had never been accompanied by tinnitus and in the patient's opinion was quite slight. The difficulty in walking was constant but not severe. He tended to run into things

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on his left side and was unable to turn round quickly without losing balance. He had never actually fallen or needed support, and there had never been any giddiness.

Neurological findings. General condition : alert and co-operative.

Visual fields full, fundi normal. Pupils normal. External ocular movements full. Corneal reflexes : right brisk, left absent.

Diminished sensation to cotton-wool, pin-prick and cold over the whole distribution of the left Vth nerve, including the tongue and hard palate. Some weakness of the left temporal muscle. Slight weakness of the left side of the face of the lower motor neurone type, with impairment of taste over the anterior two-thirds of the tongue on the left. IXth, Xth, XIth and XIIth cranial nerves normal.

Motor system : normal except for very slight inco-ordination with the heel/knee test on left side.

Neurological diagnosis (Dr. F. M. R. Walshe). Left VIIIth nerve neuroma.

X-rays : normal skull. No evidence of enlargement of the internal auditory meatuses. Ventriculography : slight, symmetrical hydrocephalus. The aqueduct was lengthened and bowed slightly backwards. The fourth ventricle was displaced to the left, and the anterior border rotated to the right. *Conclusion.* A left cerebello-pontine angle expanding process (Dr. J. W. D. Bull).

C.S.F. lumbar puncture : pressure 160 mm. Cells : white nil. Red 5 per c.mm. Protein 260 mg. per 100 c.c.

Otolaryngological examination. Hypo-æsthesia to pin-prick on left side of soft palate, left side of tongue and left inferior turbinate. Tympanic membranes normal. Other findings normal.

Cochlear function. Whisper (normal 30 ft.) : Left, at meatus. Right > 20 ft. Weber (512 c.p.s.) referred to left. Rinne, Left : Negative with masking of right ear. (The masking procedure was carried out by means of a speaking tube through which an assistant applied to the right ear a continuous sh-sh-ing sound.)

Pure tone audiometry (air conduction only). With the left ear there was an approximately uniform loss (50 db.) for all tones up to 2,048 c.p.s. Above this frequency the loss increased and 8,192 cycles could not be heard at the maximum output of the audiometer (90 db.). There was also a slight loss of hearing in the right ear (Fig. 1A).

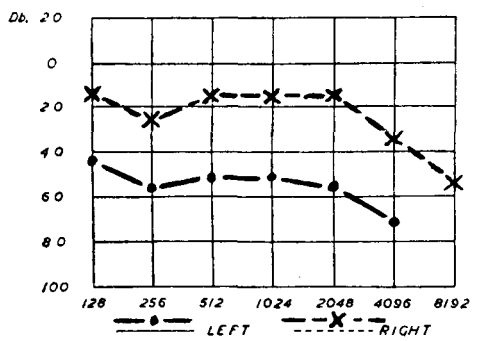


FIG. 1A.—Case I.

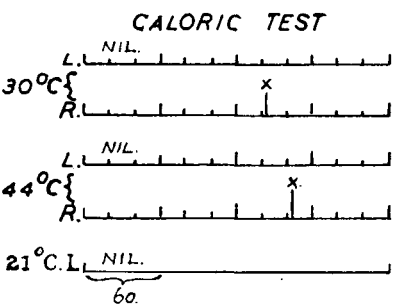


FIG. 1B.—Case I.

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Vestibular function. Posture and gait : a marked tendency to drift to the left when standing or walking with the eyes closed.

Spontaneous nystagmus : with the head erect, first degree vestibular nystagmus was present both to the left and to the right, that to the left being of greater amplitude than that to the right.

Positional nystagmus : in the supine position with the head back and to the left second-degree positional nystagmus of the central type was present to the right. Optokinetic nystagmus : this was markedly diminished to the left, particularly at higher speeds of the drum.

Caloric responses : complete abolition of the left responses with some directional preponderance to the right of the right responses (Fig. 1B).

Summary of otological findings. Cochlear function : partial deafness of the left ear ; conductive type. *Vestibular function :* spontaneous nystagmus. Positional nystagmus of the central type and abnormality of optokinetic nystagmus. Complete loss of the left caloric responses.

Otological diagnosis. Left VIIIth nerve neuroma.

Operation. The left cerebello-pontine angle was explored on *28.10.46* by Mr. Wylie McKissock. The left cerebellar hemisphere was lifted and retracted medially to reveal a small typical acoustic neuroma lying in the cerebello-pontine angle. A complete extracapsular removal was carried out.

Following the operation the patient recovered partial consciousness but became drowsy two hours later and died in coma on the following day.

Post-mortem. The tumour cavity lay between the upper and lower halves of the cerebellum and indented the left side of the pons in its lower half. The tumour had been completely removed. Histological examination showed it to be a neurofibroma of rather unusual histology. Examination of the pons showed almost complete hæmorrhagic destruction of the tegmentum passing inwards as far as the mid-line against the ependymal lining and extending backwards along a line running from the central fovea of the ventricle to the outermost part of the ventral surface.

The temporal bones were removed and on superficial examination appeared normal apart from a moderate degree of enlargement of the left internal auditory meatus.

CASE II. G.B., female, aged 47, under the care of Dr. E. A. Carmichael.

Complaint. Deafness in the right ear three years. Suboccipital headaches six months. Attacks of vomiting with nausea three months.

The deafness was of gradual onset. Recently it had become progressively worse and had been accompanied by " a noise like a railway engine " all over the head. For a short time before admission she had been rather unsteady with a tendency to deviate to the right. No history of giddiness, although objects sometimes tended to " sway up and down ".

Neurological findings. Alert and well orientated in space and time. No impairment of memory. Visual fields full. Mr. Williamson-Noble reports : " Slight blurring of both discs but within physiological limits." Pupils normal. External ocular movements full. Corneal reflexes : left present, right absent. Loss of sensation to pin-prick and cotton-wool over the facial distribution of all three divisions of the right Vth nerve but no motor weakness. Slight weakness

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of the right side of the face of the lower motor neurone type, and slight fibrillation of the right side of the tongue with deviation to the right. Motor system: upper limbs—some loss of tone and inco-ordination of the right hand and right leg. Loss of sensation to pin-prick over the second cervical segment. Reflexes: right K.J. > left K.J.

X-rays (including Towne's projection): normal skull. Ventriculography: the fourth ventricle was dilated and displaced upwards and to the left, the displacement being most marked at its lower end. The appearances were those of a space-occupying lesion in the posterior fossa on the right side.

Neurological diagnosis. ? Right VIIIth nerve neuroma, C.S.F.: pressure 80 mm. clear and colourless. Cells: 1 lymphocyte per c.mm. Protein 300 mg. per 100 c.c.

Otolaryngological examination. Tongue, palate, pharynx and larynx normal. Nose and nasopharynx normal. Tympanic membranes: left—imperforate, marked atrophic changes. Right—imperforate, slight atrophic changes.

Cochlear function. Whisper (normal 30 ft.). Left: > 20 ft. Right: at the meatus. Weber (512 c.p.s.) referred to left. Rinne: left positive. Right negative, with masking of the left ear. (Masking as in Case I.) Absolute bone conduction: right slightly reduced.

Pure tone audiometry (air conduction only). Left normal. Right: there was a severe loss chiefly affecting hearing for the highest and lowest frequencies (Fig. 2A).

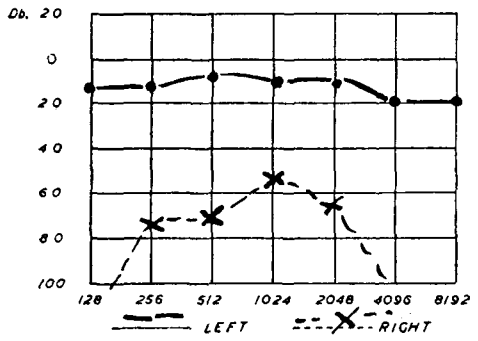


FIG. 2A.—Case II.

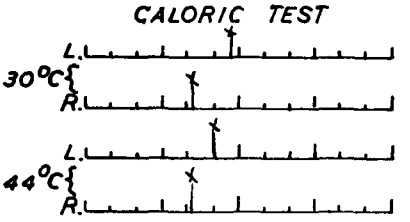


FIG. 2B.—Case II.

Vestibular function. Spontaneous nystagmus: with the head erect, first-degree vestibular nystagmus was present both to the left and right, that to the right being slower than that to the left. Positional nystagmus: in the supine position, second-degree positional nystagmus to the left was present with the head back and to the right. Optokinetic nystagmus: the response to the left was abolished. Caloric responses: a well-marked diminution of the right responses to both cold and hot stimulation. No directional preponderance was present (Fig. 2B).

Summary of otological findings. Cochlear function: partial deafness of the right ear. The deafness was, in some respects, characteristic of a conductive lesion.

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Vestibular function: spontaneous nystagmus, positional nystagmus and abnormality of optokinetic nystagmus. Reduction of the right caloric responses.

Otological diagnosis. Right VIIIth nerve neuroma.

Operation. The right cerebello-pontine angle was explored on *7.3.46* by Mr. Wylie McKissock. On retraction of the right cerebellar hemisphere a typical and fairly soft acoustic neuroma was exposed. The surface was coagulated and a considerable amount of tissue removed with the aid of a scoop and suction. Extracapsular removal was then completed.

The patient died on the following day. At post-mortem, hæmorrhagic changes were found in the right side of the pons with flattening of the right middle cerebellar peduncle. A small nodule of tumour remained in the right auditory meatus which was not enlarged. Histological examination of the tumour removed revealed a typical acoustic neurofibroma. The temporal bones were removed and on superficial examination appeared normal.

Pathological Examination of Temporal Bones

The temporal bones of both subjects were fixed in 10 per cent formalin and embedded in celloidin. Serial sections were then cut in the usual way.

In the course of this procedure it is normally possible to see a great deal of the finer labyrinthine structures through the clear medium of the celloidin. With the affected temporal bones of these two subjects, however, the labyrinthine structures were obscured by a fine " coagulum " or gel formation which was evenly distributed throughout and completely filled all the perilymph and endolymph spaces. It was much less dense than that found in labyrinthitis and much more even in its texture and distribution than the exudation which commonly occurs in this condition and indeed in any pathological condition of the labyrinth that we have previously examined. The nature of the abnormality is illustrated in Figs. 3 and 4. These are photographs of two celloidin blocks taken during the course of section cutting. Fig. 3 shows a normal temporal bone in which the normal cavities and membranes of the labyrinth can be clearly seen. Fig. 4 shows the affected temporal bone of a patient with an VIIIth nerve neuroma in which the naked-eye appearances closely resembled those seen in the two cases which form the subject of this paper. The obscuration of the membranes and labyrinth spaces is very evident.

When the sections had been cut and stained in the usual way, with hæmatoxylin and eosin, we were further interested to observe that no sign of the " coagulum " so evident during the process of section cutting could be observed. The histological features of the two cases are shown in Figs. 5 and 6. In both, the external auditory meatuses and the middle ears are normal. The internal auditory meatuses are distorted and occupied by the remains of the neuromata. In the cochleae, higher magnifications reveal degenerative changes in the nerve fibres and cells of the spiral ganglia. In neither of the sections shown, however, is it possible to appreciate that all the labyrinthine cavities are completely occupied by the homogeneous " coagulum " to which reference has been made. The appearance of the sections was next studied without staining and with dark ground illumination. Under these conditions the presence of the " coagulum " could be readily seen. Figs. 7 and 8 are photo-micrographs of

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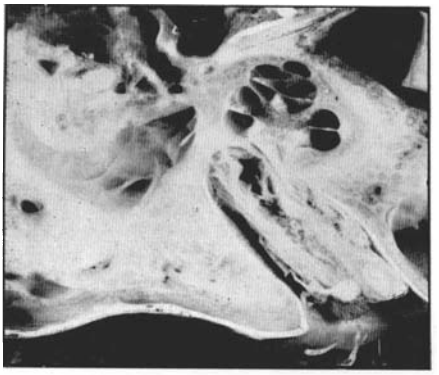


Fig. 3.

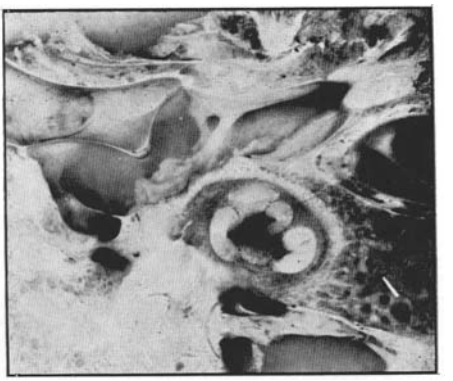


Fig. 4.

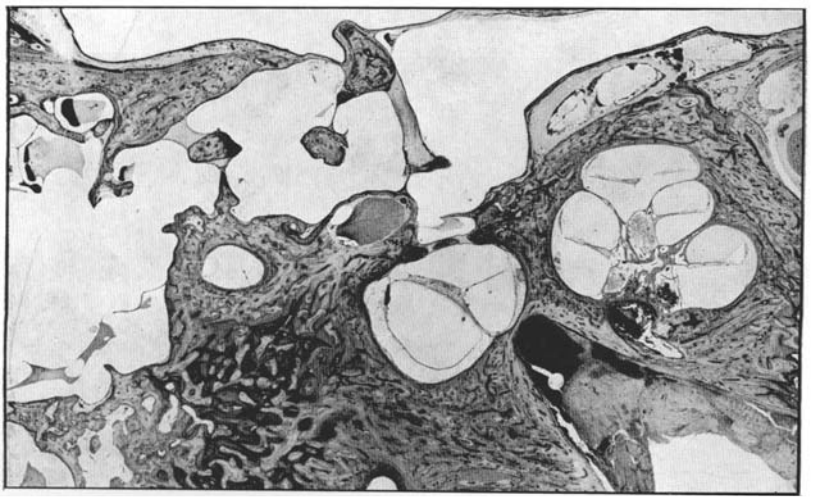


Fig. 5.

M. R. Dix and C. S. Hallpike : Observations on the Pathological Mechanism of Conductive Deafness in Certain Cases of Neuroma of the VIIIth Nerve.

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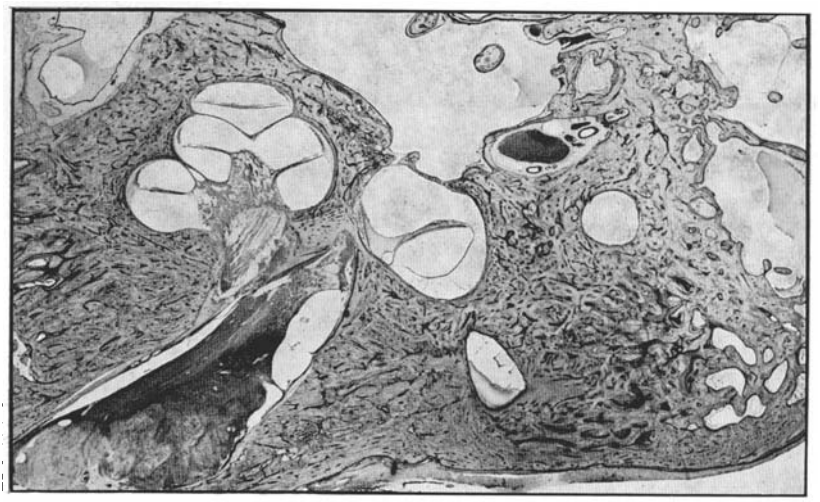


FIG. 6.

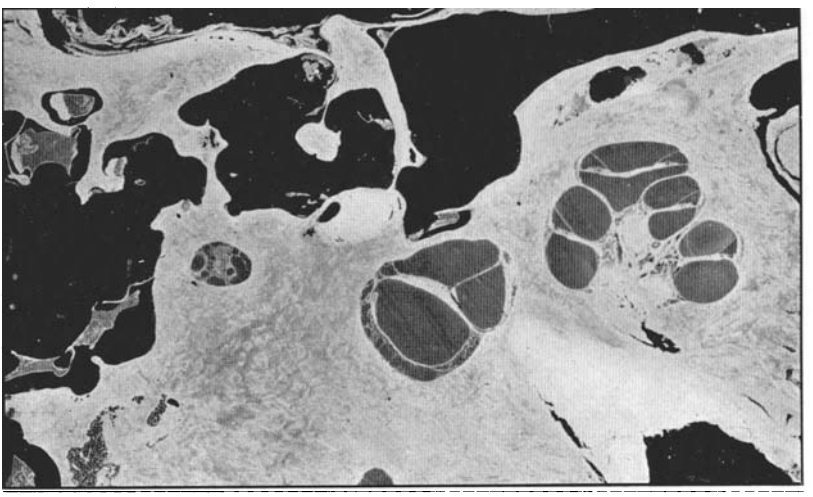


FIG. 7.

M. R. Dix and C. S. Hallpike : Observations on the Pathological Mechanism of Conductive Deafness in Certain Cases of Neuroma of the VIIIth Nerve.

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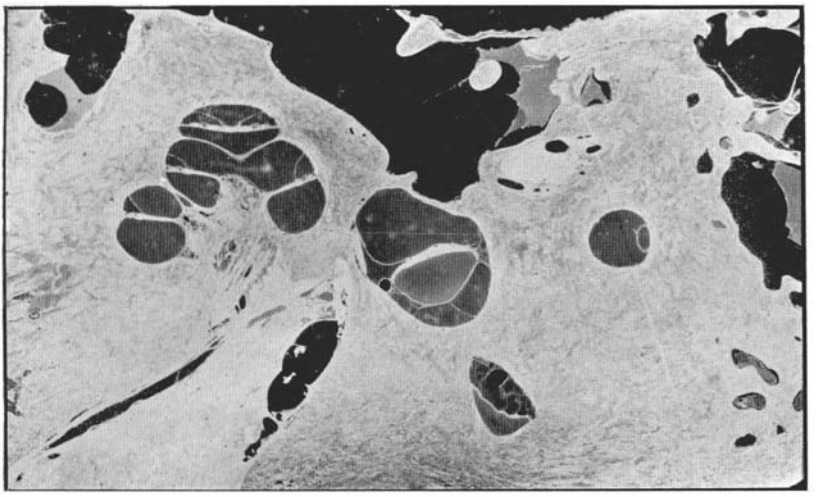


FIG. 8.

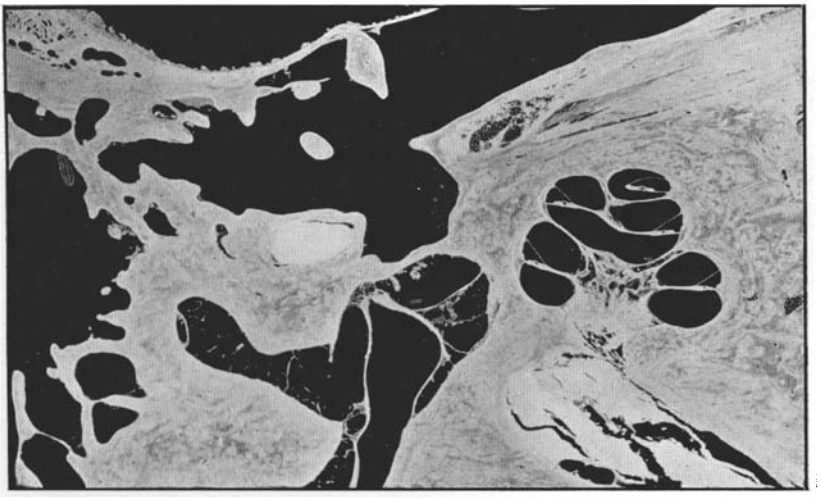


FIG. 9.

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unstained sections serially consecutive with those shown in Figs 5 and 6. They are photographed at the same magnification and with dark ground illumination. In both, the fine " coagulum " can be seen uniformly filling every part of the labyrinthine spaces. The abnormality of this appearance is illustrated by comparison with Fig. 9 which shows the appearance of a normal labyrinth prepared and photographed under identical condition.

Discussion

It is well known that the labyrinthine spaces are the site of a variety of exudates and transudates, resulting not only from VIIIth nerve tumours but from many other pathological conditions. Nearly always, however, the distribution and texture of the resulting " coagula ", if this term be permissible, are much more irregular than that revealed in the present two cases. In addition, it is usually demonstrable quite readily with hæmatoxylin stain. It is justifiable, therefore, to regard the present findings as quite unusual and our next task is to consider how they could be applied to the explanation of the equally unusual but clinically important finding of deafness of the so-called conductive type.

The physical problems concerned with hearing by air and bone conduction, though complex, still seem capable of explanation, in their essentials, in terms which can have changed very little since the days of Bezold. It is known, for instance, that in hearing by air conduction by far the greater proportion of the sound energy reaches the basilar membrane by way of the conducting mechanism which includes not only the tympanic membrane and ossicles but also the fluid contents of the labyrinth. In the case of hearing by bone conduction, while a proportion of the sound energy still reaches the basilar membrane by way of the conducting mechanism, other and more direct pathways through the bony cochlear walls are available.

It follows, therefore, that lesions which disturb the conducting mechanism will have their chief effect on hearing by air conduction ; hearing by bone conduction will be affected to a similar extent. In this way we have the poor hearing by air conduction and the relatively good hearing by bone conduction which are typical of conductive deafness and underlie its characteristic tuning-fork reactions, in particular the negative Rinne. The mechanical characteristics of the middle-ear mechanism are, of course, bound up with its function of overcoming, by virtue of its impedance-matching properties, the severe attenuation which normally occurs when airborne sound enters a fluid medium. The efficiency of this function, however, is necessarily dependent upon normal physical conditions of the labyrinthine fluid, and we think it likely in this connexion that the abnormal histological appearances of this fluid described in our two cases connote the existence during life, if not of an actual coagulum, at any rate of some considerable change of its density. The suggestion is therefore made that this density change brings about in turn a mechanical change in this, the terminal component of the conductive mechanism, which disturbs its performance as a whole in a manner which is essentially comparable to that brought about by better-known lesions of its other components, as, for example, middle-ear disease or otosclerosis. As a result, the consequent deafness is of

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the same conductive type. Loss of hearing by air conduction is severe, hearing by bone conduction relatively good and the Rinne test negative.

If this suggestion be acceptable, then it follows that a conductive element would also be likely to occur in the deafness which results from other forms of labyrinthine disease which are characterized by similar changes in the labyrinthine fluid. Of these, neuro-labyrinthitis, in particular that secondary to meningitis, may be taken as a likely example. In the majority of such subjects the deafness, which is due in large part to the destruction of the nervous elements, is extreme both by air and bone conduction, and no qualitative tests are therefore possible. We have, however, encountered some cases of this kind with partial deafness in whom the tuning-fork tests could be carried out with reasonable accuracy, and in a few of these we have been interested to note the presence of a true negative Rinne. A summary of the clinical features of three such cases is appended.

P.I., aged 10.

History. Meningitis aged 3. Deafness in left ear noticed at age of 8.

Examination. Tympanic membranes normal. Rinne (512 c.p.s.): left negative with masking of right: right positive. Absolute bone conduction (left) much reduced with masking of right.

Audiograms. (Tests of left ear carried out with masking of right ear, see below, Figs. 10A and 10B.)

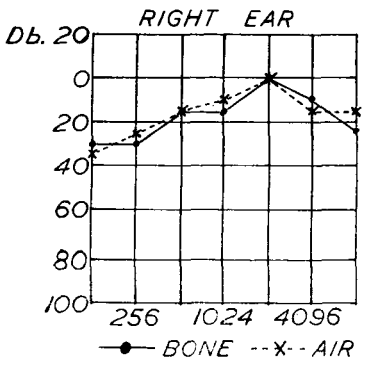


FIG. 10A.

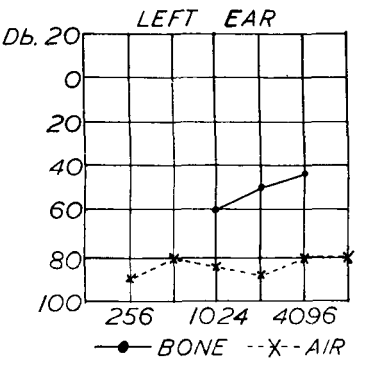


FIG. 10B.

A.P., aged 32.

History. Deaf since meningitis aged 2.

Examination. Tympanic membranes normal. Rinne (512 c.p.s.): left negative; right false negative. Absolute bone conduction (left) much reduced. (See Fig. 11.)

R.T., aged 8.

History. Maternal rubella at second month. Deafness noticed at age of 5.

Examination. Tympanic membranes normal. Rinne (512 c.p.s.): left negative; right negative. Absolute bone conduction grossly reduced left and right. (See Fig. 12.)

A clinical feature of all three cases, and one of importance in clarifying the

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diagnosis, was the reduction of perception with the absolute bone conduction test, a finding to which we attach clinical importance in the diagnosis of disease of the cochlear nervous elements. In two of the three cases also (P.I. and A.P.) a gross abnormality of the caloric responses was also present. In the third case (R.T.) the caloric tests were not carried out. It seems, therefore, necessary to stress the clinical value in these difficult cases, both of the absolute bone conduction and the caloric tests, since they make so plain that co-existent with the conductive element of the deafness a perceptive element is also present.

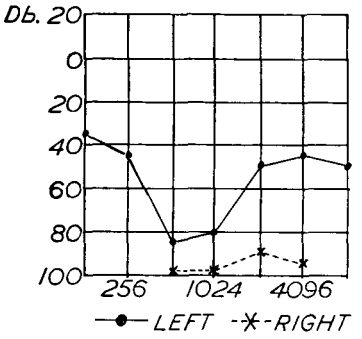


FIG. 11.
Audiogram of Case A.P. (air conduction).

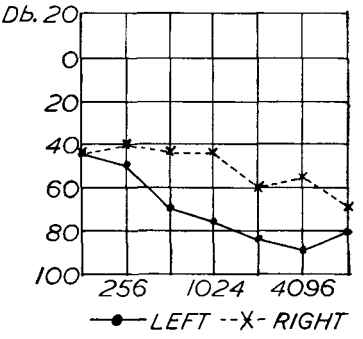


FIG. 12.
Audiogram of Case R.T. (air conduction).

In conclusion, it may be said that although the conception of the labyrinthine fluid as constituting an element of the conductive mechanism is not a new one, this would appear to be the first occasion on which it has been possible to give it the support of direct anatomical and clinical observations.

MR. F. C. ORMEROD recalled a discussion on acoustic nerve tumours by this Section in 1923 when the negative results of the Rinne test were mentioned but not discussed at any length. In 1929, T. H. Just definitely described the true negative Rinne and in 1934 Albert Gray described the histology of the temporal bones of two cases of bilateral acusticus nerve tumours (*Proc. roy. Soc. Med.*, xxvii, 1179). Both patients, one under the care of the late Professor de Kleijn and the other under the care of the speaker, showed a negative Rinne test. In both cases Gray demonstrated otosclerotic changes in the neighbourhood of the oval window and he felt that this explained the negative Rinne. He felt also that the occurrence of otosclerotic changes following acusticus tumours confirmed his theory as to the vasomotor origin of otosclerosis. The findings were illustrated in the second volume of Gray's Atlas of Otology.

MR. T. A. CLARKE asked Mr. Hallpike how the coagulum found in cases of VIIIth nerve tumour with apparent negative Rinne differed from that found in similar cases with the usual finding of a positive Rinne. It was agreed that perfect masking of the good ear had still to be achieved in testing bone conduction on the diseased side. Could any failure in masking account for the apparent negative response described in the Rinne test in these cases?

MR. I. SIMSON HALL said that Mr. Hallpike's findings had interested him enormously. On one occasion during the fenestration operation, in a case of fairly extreme deafness, he opened the labyrinth and found a condition he

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could not understand. The bone surrounding the canal was rather soft and the outlines were blurred completely. He supposed that the patient must have had a labyrinthitis, but it now occurred to him that Mr. Hallpike's explanation might have been the correct one. The operation was a complete failure.

MR. PHILIP SCOTT said that he was stimulated, on getting notice of this Paper, to refer to some of his notes, and now he was stimulated again to go back and look at his sections. In the sections at which he had had an opportunity of looking he was dissatisfied in one particular case with the negative Rinne. That case did have a noticeable coagulum throughout the section. He now intended to re-examine the section in the light of the observations of Mr. Hallpike and of some others.

MR. HALLPIKE, in reply, said that when they began to encounter these cases with evidence of conductive deafness they used to think of the likelihood of an associated otosclerosis, but as they had the opportunity of examining further material they never found otosclerosis, and in the cases shown that day the stapes footplates and middle ears were normal.

Mr. Clarke had asked how this particular coagulum compared with the coagulum which occurred not uncommonly in other conditions of the labyrinth. Generally speaking, such coagulum was much more scattered and less homogeneous than that found in the two cases under discussion. As to guaranteeing the efficiency of masking, this it was difficult to do.

He had been very much interested in what Mr. Simson Hall had told them, because in some cases of deafness in children of 5 to 10 years of age the diagnosis of juvenile otosclerosis was sometimes made with some confidence on the basis chiefly of a negative Rinne test. It seemed to him that had caloric and absolute bone conduction tests been done in Mr. Simson Hall's case a different view might have been taken of the diagnosis.

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