ARCHIVES OF OTOLARYNGOLOGY

VOLUME 49 JANUARY 1949 NUMBER 1

MÉNIÈRE'S SYMPTOM COMPLEX

Its Relation to Chemistry; an Etiologic Study

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THE CAUSE of Ménière's disease is unknown; so say the wise men of the medical profession. It has been variously ascribed to: disturbances of endocrine glands; infection; syphilis; low and high blood pressure; disturbances of the metabolism of salt, potassium, magnesium, iodine and calcium; deficiencies of certain vitamins (those responsible for spasm of blood vessels, as deficiency of thiamine, nicotinic acid or choline compounds); allergy; creatine-creatinine metabolism, and the action of the nondecarboxylated fraction of histidine-histamine. No one, so far as I know, has attempted to relate the disease to disturbances of nutrition and thus to body chemistry. This is the purpose in this paper.

VITAMIN DEFICIENCIES RELATED TO MÉNIÈRE'S DISEASE

Since the appearance of the first edition of the work of Williams and Spies [1] on thiamine, in 1938, biologic and medical research have shown not only that degenerative changes occur in peripheral nerves but that, as Sure [2] aptly expressed it, "The Little Things in Life" have proved to be the big things in life and are helping to solve many of the complex problems with which man is beset today. In nothing has this been found more important than in Ménière's disease.

Covell,[3] studying the eighth nerve and the cochlea in rats, guinea pigs and chicks, showed that histologic changes of the nerve and its ganglion cells (both cochlear and vestibular) resulted from deficiencies of the vitamin B complex and that they sometimes occurred in lesser degrees in other deficiencies. Covell's studies were made at my suggestion when I was investigating the subject of nerve and conduction

1. Williams, R. R., and Spies, T. D.: Vitamine B, (Thiamin) and Its Use in Medicine, New York, The Macmillan Company, 1938.

2. Sure, B.: The Little Things in Life, New York, D. Appleton-Century Company, Inc., 1937.

3. Covell, W. P.: Pathological Changes in the Peripheral Auditory Mechanism Due to Avitaminosis, Laryngoscope **50**:632-647 (April) 1941; Vitamins and the Ear, ibid. **51**:683-691 (July) 1941.

deafness. Himwich [4] divided the vitamins into two groups: those demonstrated to be necessary for the prevention of degenerative changes of the central nervous system and those not required for the maintenance of nervous structures. In the first group he included thiamine (vitamin B_1), nicotinamide, riboflavin, pantothenic acid and pyridoxine (vitamin B_6); in the second, ascorbic acid and vitamins A, D and E. Mellanby,[5] however, reported that definite degenerative changes were produced by vitamin A–deficient diets not only in the central nervous system but also in the eighth nerve and that these changes in the nerve were not, in the early stages, due to pressure of new bone in the modiolus or elsewhere in the internal auditory meatus. Gladys Emerson,[6] of Evans' Laboratory, stated that the latter and his co-workers have found that changes occur in certain peripheral nerves in vitamin E–deficient guinea pigs. As another bit of evidence that vitamin deficiencies play an important role in the degenerative changes of the nervous system, Wolbach [7] stated, "No one vitamin is concerned with the maintenance of myelin." Morsch [8] presented histories of 4 patients with typical symptoms of Ménière's disease who also had symptoms of deficiencies of both vitamin A and ascorbic acid. He reported that an improvement was noted in the vertigo, tinnitus and deafness after intensive vitamin treatment.

The relationship of the vitamin B complex and Ménière's disease has been widely reported in the recent literature. Harris and Moore [9] were the first to report. They were impressed with the peculiar dietary habits of people with this disease, who were almost all addicted to diets in which vegetables or carbohydrates were preponderant and had an inadequate intake of protein. They treated 20 patients with large doses of thiamine hydrochloride. No result was observed. Then they used nicotinic acid. Again there was no result. Finally they combined both treatments, giving thiamine hydrochloride, 10 mg., night and morning, and nicotinic acid, 50 mg., five times a day. With this treatment there was entire relief of tinnitus in 10 cases and almost

4. Himwich, H. E.: The Role of Vitamins in Brain Metabolism, A Research Nerv. & Ment. Dis., Proc. (1943) **22**:33-41, 1943.

5. Mellanby, E. J.: The Experimental Production of Deafness in Young Animals by Diet, J. Physiol. **94**:380 (Dec. 14) 1938.

6. Emerson, G.: Personal communication to the author.

7. Wolbach, S. B.: Pathological Changes Resulting from Vitamin Deficiencies, J. A. M. A. **108**:7-13 (Jan. 3) 1937.

8. Morsch, P.: Vitamin Therapy of Ménière's Disease and Other Disorders Accompanied by Tinnitus and Vertigo, Acta oto-laryng. **27**:629-637, 1938.

9. Harris, H. E., and Moore, P. M., Jr.: The Use of Nicotinic Acid and Thiamin Chloride in the Treatment of Ménière's Syndrome, M. Clin. North America **24**:533-542 (March) 1940.

entire relief in the other 10. Seventeen patients were entirely relieved of vertigo, and the other 3 had sufficient relief to be able to return to their work. Harris,[10] in a letter dated Feb. 28, 1944, stated:

. . . We are still using thiamine hydrochloride, 10 mg., three times a day, and nicotinic acid, 100 mg., three times a day, for an initial period of five months. I find the vast majority are relieved of their dizzy spells in from two to six weeks, and as the vertigo subsides, the tinnitus decreases in intensity. As our series of cases progresses, and we now have over 500, I believe that the nicotinic acid with the marked peripheral vasodilatation caused by it, is the chief factor of their relief.

Guggenheim,[11] referring briefly to Ménière's syndrome, cited the finding of Somyngi that in allergic states there is depletion of potassium salts in the cells and increase of these salts in the body fluid and that the depletion is corrected through administration of potassium and insulin. He also mentioned a case in which petechial hemorrhages and presence of blood in urine and stool suggested the possibility that permeability of the stria vascularis, increased through deficiency of ascorbic acid, was a cause of Ménière's disease. He stated further that the most important agent in the prevention of neural degeneration in Ménière's disease is the vitamin B complex, i. e., thiamine and nicotinic acid.

Atkinson [12] contributed a thorough and satisfactory review of the subject. He concluded that allergy and histamine sensitivity accounted for 20 per cent of his cases and that the remaining 80 per cent, cases in which the patient was nonsensitive, were related to lack of nicotinic acid. In 69 of 108 cases data were available for analysis. Relief of vertigo was reported in 32 cases. He considered the disease the result of a constriction of the vascular supply. In a letter dated Feb. 14, 1944, he wrote:

I have just completed another paper on my results in 110 patients treated with nicotinic acid. In this series the tinnitus was removed entirely in 13 cases (12 per cent) and improved in 42 (40 per cent). Thus, in half the cases one can achieve an appreciable improvement in this symptom.

Cooper [13] emphasized the effects of choline compounds, which cause dilatation of the vessels supplying the viscera in mammals, and referred to Starr's report of relief of vertigo in 1 patient, suggesting that choline

10. Harris, H. E.: Personal communication to the author.

11. Guggenheim, L.: Treatment of Deafness, Laryngoscope **50**:773-783 (Aug.) 1940.

12. Atkinson, M.: Diagnosis and Treatment of Ménière's Disease, Arch. Otolaryng. **37**:40-53 (Jan.) 1943.

13. Cooper, M. J.: Clinical Observations on the Effect of Choline Compounds in Neurological Disorders with Special Reference to Ménière's Syndrome, Am. J. M. Sc. **195**:83-88 (Jan.) 1938.

compounds might be of value in the treatment of Ménière's disease. He reported that 6 patients who had taken methacholine chloride U. S. P. by mouth showed definite improvement or complete disappearance of tinnitus and vertigo, especially if the drugs were taken prophylactically or during the period of attack.

Adams [14] related deficiency of ascorbic acid to asthenia and Ménière's disease, in both of which there are apt to be autonomic imbalance and vasomotor disturbances. He observed several cases in which ascorbic acid was absent from the urine, probably because of lack of this vitamin in the diet, and in which the condition was improved or entirely relieved by an increased intake of fruit and food containing ascorbic acid. He referred to O'Dell's suggestion that lack of this vitamin was a frequent cause of Ménière's syndrome. In several cases Adams used some of the factors of the B complex in addition to ascorbic acid.

Because the lack of sufficient amounts of the vitamins, particularly of thiamine, nicotinic acid, riboflavin, pantothenic acid and pyridoxine, plays an important role in the aging process, one is justified in stating that Ménière's disease is a function of the aging process. Talbott and associates,[15] in a tabulation of 33 cases, showed that the patients were all 50 years old or older. In my studies, all the patients with eighth nerve deafness who were 40 years of age and over showed definite loss of high tones, severe in most of them. In all the cases the urine showed thiamine and nicotinic acid definitely low; in half the cases it showed porphyrin increased. When the eyes were checked for dark adaptation by Dr. Evelyn Blanchard with her "reginometer," the results were out of line in nearly all cases.[15a] Many of the patients were 60 years of age and over. It should not be forgotten that the aging process frequently begins in early childhood and not infrequently before birth. Stieglitz [16] made the comment that premature development of the changes of senescence in one or more organs might well be caused by particular dietary deficiencies of the parents and that the geriatric, anatomic and functional changes of the thyroid, pituitary and adrenal glands may be influenced by heredity, by the nutrition of the parents at the time of conception and by the nutrition of the mother before and after birth. The far reaching effect of nicotinic acid deficiency, for instance, has

14. Adams, J.: Ménière's Syndrome and Avitaminosis, J. Laryng. & Otol. **54**:256-258 (May) 1939.

15. Talbott, J. H.; Brown, M. R.; Coombs, F. S., and Consolazio, W. V.: Electrolyte Balance of Blood in Ménière's Disease, Proc. Soc. Exper. Biol. & Med. **38**:421-422 (April) 1938.

15a. The "reginometer" is thought to be an improvement over the biophotometer in use at that time.

16. Stieglitz, E. J.: Geriatric Medicine, Philadelphia, W. B. Saunders Company, 1943.

been depicted graphically by Frostig and Spies [17] and others. Sebrill, of the United States Public Health Service, in his histologic study of Jukes's rats, deficient in pantothenic acid, stated that both the adrenal cortex and the gonads showed beginning atrophy of cells. It is interesting that a few human subjects whom two genitourinary specialists of San Francisco treated with large doses of pantothenic acid (100 mg. daily intravenously) appeared to experience restorative effects in their flagging sex life.

The experimental dog, Benny, of Morgan and Simms [18] (fig. 1) shows an aging process induced by dietary measures that may have a definite analogy to that of human life. At the age of 6 weeks this dog was restricted to a diet deficient in pantothenic acid, nicotinic acid and some other factors, unknown. He showed considerable irregularity of gait, especially in the hindlegs, suggesting some disturbance of the

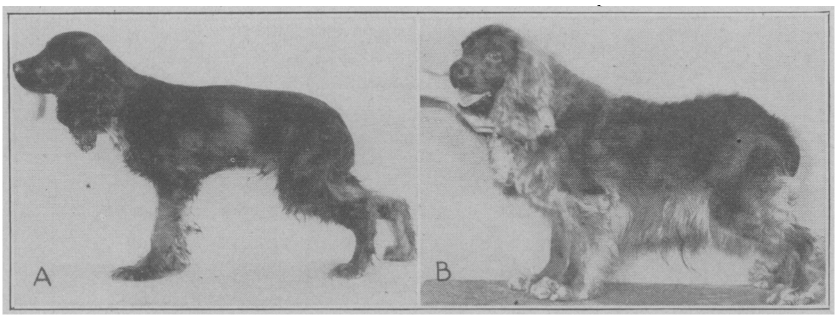

Fig. 1.—This dog shows the aging effect of a deficiency of pantothenic acid, nicotinic acid and other factors of the vitamin B complex. The experiment was reported by Morgan and Simms.[18]

vestibular apparatus. The aging process was evidenced by changes of posture, increasing grayness of hair, increasing ptosis of belly muscles and finally inability to stand erect. The dog died at the age of only 3 years; the average life span of a cocker spaniel varies from 8 to 12 years. Inasmuch as this dog's diet was normal except for the lack of pantothenic acid, nicotinic acid and some other factors, unknown, it seems obvious that the aging appearance and the pathologic changes are related to the missing factors. The autopsy report showed that the principal organ involved was the adrenal cortex.

17. Frostig, J. P., and Spies, T. D.: The Initial Nervous Syndrome of Pellagra and Associated Deficiency Diseases, Am. J. M. Sc. **199**:268-274 (Feb.) 1940.

18. Morgan, A. F., and Simms, H. D.: Graying of Fur and Other Disturbances in Several Species Due to Vitamin Deficiency, J. Nutrition **19**:233-250 (March) 1940.

This brings to mind the relation of pantothenic acid deficiency and fatty infiltrations and the possibility that the fatty substance may be cholesterol. Oakey [19] has already demonstrated that pantothenic acid is related to cholesterol in the production of dietary gallstones. It is known that choline is related to fatty livers and is a vasodilator substance, as is also nicotinic acid; hence these three substances may be definitely related to Ménière's disease, and perhaps to certain cardiovascular diseases. Certainly, these substances are present in inadequate amounts in some of the aging people whom I have observed in my studies of eighth nerve deafness.

ALLERGY AS A CAUSE OF MÉNIÈRE'S SYNDROME

Grove [20] has given the impression that most cases of Ménière's disease can be classified as cases of allergy. He stated that many patients present extra-aural symptoms, headaches, vasomotor rhinitis, chilly sensations, gastrointestinal symptoms, fatigability, insomnia and loss of memory and often have urticarias.

Dean [21] has shown a definite leaning toward allergy. He reported 2 cases. One patient was sensitive to several foods, which were removed from his diet. While this improved the vertigo, more complete relief was not obtained until the infected tonsils were removed. His second patient was sensitive to staphylococcus. Injections were helpful, but it was necessary to remove an infected adenoid and to correct a low basal metabolic rate with thyroid before a satisfactory result could be obtained.

AMINO ACIDS

Histamine is a noncarboxylated fraction of the amino acid histidine. Abandoned by its principal sponsors, Longcope, Haskin and Dwyer, of New York, it was resurrected, after nearly twenty-five years, by Horton [22] before the Clinical Congress of the American College of Surgeons in Chicago, in 1940, and has been written about favorably, especially by Grove [20] and Atkinson,[12] in relation to Ménière's disease.

Recently Horton and associates [23] stated that they had used histamine successfully in a large series of cases of multiple sclerosis. It is their

19. Oakey, R.: Gallstone Formation and Intake of B-Vitamins in Cholesterin Fed Guinea Pigs, Proc. Soc. Exper. Biol. & Med. **51**:349, 1942.

20. Grove, W. E.: Evaluation of Ménière Syndrome, Ann. Otol., Rhin. & Laryng. **50**:55-69 (March) 1941.

21. Dean, L. W., Jr.: Ménière's Syndrome, Internat. Clin. **3**:231-234 (Sept.) 1941.

22. Horton, B. T.: The Use of Histamin in Mènière's Disease, Surg., Gynec. & Obst. **72**:417-420 (Feb.) 1941.

23. Horton, B. T., and others: Treatment of Multiple Sclerosis by Intravenous Administration of Histamine, J. A. M. A. **124**:800-801 (March 18) 1944.

opinion that the prompt improvement that follows histamine therapy probably results from the vasodilatation produced in the central nervous system. In the discussion of this paper, Wagener apparently questioned the findings, saying that the cases were followed for only fifteen months and that it would take at least five years to evaluate fully the effects of this treatment. Squier expressed the belief that with most allergic conditions histamine therapy would prove disappointing. He stated that he had seen 2 patients who had been given intravenous injections of histamine phosphate elsewhere and who had relapses during such therapy. These discussions show that medical opinions as to the value of histamine vary greatly but that the majority of physicians who have reported on the use of histamine do not consider that it tells the whole story.

Cordes [24] has shown that histamine can cause both arterial spasm and increased permeability of capillaries. He stated that histamine or histamine-like bodies circulating in the blood and their action on hypersensitive arterioles and capillaries can account for all the lesions usually attributed to cold, focal infection and allergy, that the pathologic changes are all due to spasm of smooth muscle and increased permeability of capillaries with resultant anoxia of capillaries and tissues. This constitutes further evidence that the reactions observed in the various allergies have fundamental causes other than protein sensitivity, which still remain to be identified.

INFLUENCE OF THE ELECTROLYTES

Mygind and Dederding [25] have advanced the theory that the symptoms of Ménière's disease, including tinnitus, are due to disturbance of the metabolism of water and that relief may be obtained by eliminating salt and water through perspiration and urination, stimulated by the use of pilocarpine or mersalyl. Tinnitus was not much affected. Cawthorne and Fawcett [26] reported that tinnitus, vertigo and, to a lesser extent, deafness were improved by diminishing the intake of fluids and that vertigo and deafness were made worse immediately when the intake of fluids was increased but were not greatly influenced by increasing the salt in the diet.

24. Cordes, F. C.: The Use of Vasodilators in Acute Fundus Disease, Am. J. Ophth. **26**:916-927 (Sept.) 1943.

25. Mygind, S. H., and Dederding, D.: Clinical Experiments with Reference to the Influence of Water Balance on the Ear, Ann. Otol., Rhin. & Laryng. **47**: 360-369 (June) 1938.

26. Cawthorne, T., and Fawcett, J.: Fluid Balance in Ménière's Disease, Lancet **2**:1404-1409 (Dec. 17) 1938.

Talbott, Brown, Coombs and Consolagio,[15] and in a later report Talbott and Brown,[27] presented a careful laboratory study of the concentration of the acid-base constitution of the blood serum, including total fixed base, sodium, potassium, calcium, chloride, total carbon dioxide, phosphate, protein and nonprotein nitrogen. They expressed the belief that potassium salts are of far greater importance than sodium salts, which are implicated in the theory of Furstenberg, and that neither hydration nor alkalosis nor elevated serum sodium is a necessary accompaniment of Ménière's disease. Their chart indicates that the sodium-potassium ratio is definitely out of line, which should furnish a reason for their choice of therapy. They intimated that if the present laboratory methods of microbiologic and other studies of the blood for the members of the vitamin B complex (thiamine, riboflavin, nicotinic acid, nicotinamide, pantothenic acid, pyridoxine, biotin, inositol, para-aminobenzoic acid, adenylic acid, choline and folic acid), as well as for ascorbic acid and the tocopherols, were available much more would be known of the body chemistry.

Yoshiza treated tinnitus with magnesium sulfate. He made no mention of Ménière's disease, but Shick [29] stated that these salts have a diuretic effect and exert an influence on the entire central and peripheral nervous system, affecting the vasomotor mechanism, especially in the vestibular area. According to Sherman,[30] magnesium salts enhance the activity of the enzymes known as phosphatases and assist at certain stages in the metabolism of carbohydrates.

Little mention has been made of calcium being used in the treatment of Ménière's disease. Brunner [31] mentioned the use of calcium and iodine. In a letter dated Feb. 16, 1944 he said that he still used them in tinnitus and thought he obtained results; however, he seemed somewhat doubtful. Apparently his use of these substances has been empiric and not based on any laboratory studies. The constant shifting of the electrolytes is such that many determinations would be necessary over a period of weeks before the true picture would be known.

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27. Talbott, J. H., and Brown, M. D.: Ménière's Syndrome: Acid-Base Constituents of the Blood; Treatment with Potassium Chloride, J. A. M. A. **114**:125-130 (Jan. 13) 1940.

28. Footnote deleted by the author.

29. Schick, A.: Treatment of Ménière's Syndrome with Magnesium Salt, Ann. Otol., Rhin. & Laryng. **52**:45-51 (March) 1943.

30. (*a*) Sherman, H. C.: Chemistry of Food and Nutrition, New York, The Macmillan Company, 1941. (*b*) McCance, R. A., and Widdowson, E. M.: The Chemical Composition of Foods, Medical Research Council, Special Report Series, no. 235, London, His Majesty's Stationery Office, 1940.

31. Brunner, H.: Ménière's Syndrome, Laryngoscope **49**:877-911 (Oct.) 1939.

THE ENDOCRINE GLANDS

Drury[32] observed in 568 cases of Ménière's syndrome that the pituitary gland was disturbed in 289, the thyroid gland in 148, the gonads in 119 and the adrenal cortex in 12. In the detailed study of 4 cases, classified as cases of Ménière's disease due to hypothyroidism, he gives an excellent exposition of the accompanying symptoms.

Werner[33] simply mentioned that tinnitus and vertigo may occur without causative lesions (no cardiovascular lesion). This is not an uncommon situation at the approach of, during and after the menopause.

Lisser,[34] in a letter dated March 28, 1944, stated:

> I have had a good friend, a man of 60 years, under observation in the last two years, who had had three characteristic attacks of Ménière's disease prior to getting established on a proper maintenance dose of thyroid. He had a low basal metabolic rate, although he had no obvious symptoms or signs of hypothyroidism. He required 5 grains [0.32 Gm.] daily to maintain his rate at a normal level, and now for fully one and one-half years he has had no further attacks.

Selfridge[35] studied basal metabolic rates, hemoglobin content, intake of vitamin B complex, excretion of porphyrin (in urine), type of tinnitus and nature of catamenia in a series of patients with Ménière's syndrome. The basal metabolic rate was out of line in most of them. Most of the patients were markedly improved by the use of several vitamins, estrogenic substances and thyroid when these were indicated. A recent review of the subject indicates that pseudo Ménière's disease is not uncommon in younger persons, that it is often present in women during the menopause and that in the treatment of the latter the use of multiple tocopherols, as suggested by Spies, particularly in cases of nonorganic tinnitus, is not to be forgotten.

Little has been said on the subject of amino acids and their importance in the general metabolic picture, but Holt,[36] in a paper presented at the Cleveland meeting of the American Chemical Society, in 1944, emphasized the importance of tryptophane, arginine, valine and methionine in warding off certain signs of senility, i. e., baldness, decay of teeth, anemia, cataract, permanent bloodshot appearance of the eyes, degeneration of the gonads in the male and reproductive failure in the female.

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32. Drury, D. R.: Syndrome Complex, New England J. Med. **220**:170-173 (Jan. 24) 1939.

33. Werner, A. A.: Ovarian Hypofunction and Afunction, in Endocrinology: Clinical Application and Treatment, Philadelphia, Lea & Febiger, 1937, pp. 239-240.

34. Lisser, H.: Personal communication to the author.

35. Selfridge, G.: Chronic Progressive Deafness with Special Reference to Estrogenic Substances, Ann. Otol., Rhin. & Laryng. **49**:52-55 (Aug.) 1940.

36. Holt, L. E., Jr.: Elixir of Youth in Protein, Science News-Letter, April 15, 1944, pp. 252-253.

It has already been shown that the active chemical agents of the endocrine glands are proteins—amino acids—but the chemical formulas of the six active fractions of the anterior lobe of the pituitary gland are unknown. Much studying has been done but it may continue for generations before the formulas are worked out. The formulas of most of the amino acids and of the vitamins have been published, and the chemical setups of all foods and beverages have been published by Sherman [30a] and McCance and Widdowson.[30b]

It is agreed that the chemical actions, reactions and interactions occurring in the human body are controlled by the endocrine glands and that the pituitary gland, especially the anterior lobe with its six known fractions, controls all the other glands. The thyroid gland ranks first in the control of the metabolic processes, including that concerned with water, and the adrenal cortex appears to have a controlling action on most of the electrolytes and also on several of the vitamins. The gonads should not be ruled out, especially as the menopause approaches and emotional factors appear. Even at other ages of life tinnitus and sensations of dizziness are influenced by estrogens and also by androgens.

Carbohydrate when converted to dextrose is the most important chemical substance in cerebral metabolism. The first studies of this conversion, by Peters,[37] of Oxford, England, implicated thiamine as the principal factor in the process by which dextrose is converted through the intermediary of pyruvic acid to lactic acid, but it is now considered that thiamine, riboflavin, nicotinic acid and ascorbic acid are the principal factors in carbohydrate metabolism, and this combination, especially with choline added, is believed to influence fat metabolism also. In addition to this action on carbohydrates and fats, investigators are beginning to believe that these substances have an important influence on the vasomotor system. Long,[38] in his discussion of carbohydrate metabolism and its relation to the endocrine gland system, gave the definite impression that while the anterior lobe of the pituitary gland is the great controller, all the glands are involved in the process of carbohydrate metabolism. Elvehjem [39] pointed out that thiamine, as such, inhibits the action of cholinesterase, especially when the dosage of thiamine is at high levels. Thus, some of the symptoms associated with thiamine deficiency may be correlated with a decreased acetylcholine content of certain tissues of the body as well as with an increased pyruvic acid content.

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37. Peters, R. A.: The Biochemical Lesion in Vitamin B Deficiency, Lancet **1**:1161-1164 (May 23) 1936.

38. Long, C. N. H., in Duncan, G. G.: Diseases of Metabolism, Philadelphia, W. B. Saunders Company, 1942, pp. 19-71.

39. Elvehjem, C.: Relationship of Enzymes to Deficiency: Nutritional Deficiencies, Baltimore, Williams & Wilkins Company, 1943.

WATER METABOLISM

This subject apparently is confusing, since Dederding and Furstenberg, and their groups, have held that Ménière's disease is linked with water binding and sodium chloride, while Talbott and his co-workers have concluded that it is related to potassium salts. Goldzieher [40] pointed out that the actual requirements of the body and the amount of water retained are almost independent of the intake of water and yet are subject to both environmental and endocrine influences, and that the presence of such ordinary cell constituents as sodium salts, certain chlorides and carbohydrates is known to increase the avidity of the tissues for water. The posterior lobe of the pituitary gland plays a definite role in the control of water metabolism in cases of diabetes insipidus, and the thyroid gland has a definite part in the control of water and salt metabolism, especially in cases of myxedema. Likewise, the adrenal cortex, often called the gland vital for life, has an important role to fulfil not only as a controller of water balance but also as the probable controller of several of the electrolytes—sodium, potassium and perhaps others. In addition, it has some influence on the members of the vitamin B complex and on ascorbic acid. Deficiency of pantothenic acid definitely influences the adrenal cortex, and Sebrell noted atrophy of the cortical cells as well as of the gonads. Gower [41] linked riboflavin, pantothenic acid and possibly some other vitamins of the B complex to water metabolism. Dr. Marjorie M. Nelson, of the department of biological research of the University of California, told me that animals deficient in pantothenic or in nicotinic acid showed definite evidences of dehydration, and Lepkovsky, of the department of poultry research of the University of California, told me that animals deficient in pyridoxine were avid for water. These various findings are but suggestions that in Dederding's and especially in Furstenberg's cases the symptoms might have been controlled by other means than ammonium chloride and salt-free diets.

Tobey [42] closed an excellent review of the medical treatment of Ménière's disease with these words:

> . . . It is apparent that studies in water and mineral metabolism have yielded definite results, and still offer a fertile field for investigation. Development in our knowledge of vitamins shows promise of increasing influence in the treatment of Ménière's disease.

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40. Goldzieher, M.: Biological Aspect of Constitution, A. Research Nerv. & Ment. Dis., Proc. (1933) **14**:122-137, 1934.

41. Gower, S.: Water Metabolism, Proc. Soc. Exper. Biol. & Med. **49**: 691-692 (April) 1942.

42. Tobey, H. G.: Medical Treatment of Ménière's Disease, Surg., Gynec. & Obst. **72**:425-430 (Feb.) 1941.

PSYCHOSOMATIC AND WEATHER PROBLEMS

Psychosomatic conditions and physical stresses imposed by changes of weather have a bearing on the subject of tinnitus, whether this occurs singly or as a symptom of Ménière's disease, and are mentioned by Fowler in his recent study of tinnitus, but with not enough emphasis, in my opinion, on the psychosomatic picture. Apparently, little attention has been paid to emotional factors in pseudo Ménière's and real Ménière's disease. Weiss and English [43] related tinnitus to anxiety states, sexual tension and disease of blood vessels, and stated that the tinnitus is vastly increased if there is any degenerative involvement of the eighth nerve, and that suggestive treatment is in order.

Kerr,[44] since World War I, has written at some length on anxiety states. He mentioned that patients suffering from anxieties presented symptoms and signs of tetany associated with hyperventilation. In a recent conversation he mentioned having seen several more cases of Ménière's disease since publishing his first article, and emphasized the need of a study of the acid-base balance in all cases. He expressed the belief that a large proportion of people consulting physicians since World War I and during the present world crisis are victims of anxiety states with symptoms that simulate those of serious organic diseases. Hence the study of psychosomatic medicine and geriatrics should be followed intensively by those really interested in improving the health and well-being of patients consulting otolaryngologists.

Another factor, and a potent one, influencing these psychosomatic conditions has been set forth in a convincing maner by Peterson and Mills. In 1934 Peterson [45] discussed at some length the season of the year and the effects of cold, and mentioned that in Ménière's original case the first episode occurred on Dec. 28, 1860, and another on February 6, during the winter months. He considered further the relation of abnormal water balance and defective vasomotor function, hearing as affected by heat and cold and the close integration of Ménière's syndrome, migraine, epilepsy and psychoses. He seemed to think Ménière's syndrome is frequently initiated with meteorologically induced vascular spasm and that the acute attacks have a tendency to occur in the later winter and early spring months, when polar infalls (cyclonic types of weather) are apt to occur. The type of arterial

43. Weiss, E., and English, O.: Psychosomatic Medicine, Philadelphia, W. B. Saunders Company, 1943, p. 475.

44. Kerr, W. J.: Some Physical Phenomena Associated with the Anxiety States and Their Relation to Hyperventilation, Ann. Int. Med. **11**:961-992 (Dec.) 1937; Treatment of the Anxiety States, J. A. M. A. **113**:637-641 (Aug. 19) 1939.

45. Peterson, W. F.: The Patient and the Weather, Ann Arbor, Mich., Edwards Brothers, 1934, vol. 2, p. 489.

spasm referred to by Selfridge in two recent articles [46] is similar to the type due to polar infalls.

Mills [47] told a fascinating story of the life of man as affected by climate and meteorologic factors and showed that the Chinese, because of the lack of cyclonic weather and because of a diet consisting largely of soybeans, do not have arteriosclerosis and coronary disease. He pointed out the various factors involving, in particular, the peoples of the United States. He stressed the observation that many symptoms in people, and bad moods and many actions of both animals and human beings are definitely related to "falling barometers." He stated that the exact mechanism by which such weather changes affect human beings in so many ways is not yet known; then he added:

> . . . Peterson believes it is all due to a shifting chemical balance in the blood and body tissues. . . . Other preliminary findings indicate that our tissues take up more water at such times, and a resulting slight swelling of the brain may upset us emotionally.

SUMMARY

I have repeatedly pointed out that deafness (and this includes Ménière's disease) is not caused by any one thing but is related to all the factors involved in growth, i. e., endocrine products, electrolytes, amino acids and vitamins, including vitamin A. Guggenheim,[11] while he advocated that vitamins D and A be used along with ascorbic acid and the vitamins of the B complex in the treatment of other forms of deafness, did not advise that they be used in the treatment of eighth nerve involvement. Gladys Emerson [6] stated that Evans and his co-workers have shown that guinea pigs born of parents slightly deficient in tocopherol (vitamin E) and themselves quite deficient at birth apparently made a complete recovery, provided this factor was administered within fifteen days. In my experience, patients with eighth nerve deafness who had only a slight loss of high tones recovered the loss in a few weeks with the use of thiamine and nicotinic acid, whereas patients who had an abrupt loss in the audiometric curve did not show any recovery. Babbitt emphasized the well known fact that when the nerve is badly damaged the pathologic process cannot possibly be reversed by any use of endocrine substances, vitamins, electrolytes or amino acids. He mentioned the brilliant studies of Crowe and associates on the loss of perception of the higher tones in children due to tubal stenosis and stressed the importance of preventive measures (radium treatment of adenoid remnants); failure to treat such conditions in

46. Selfridge, G.: Arterial Spasm and Fat Metabolism: Their Relation to Certain Diseases and to Certain Members of the Vitamin B Complex, California & West. Med. **62**:163 (April) 1945; Ann. Otol., Rhin. & Laryng. **54**:384-389 (June) 1945.

47. Mills, C.: Climate Makes the Man, New York, Harper & Brothers, 1942.

48. Footnote deleted by author.

children may mean high tone deafness in the aging period of life. Babbitt made the statement that in the management of aging ears the three most troublesome conditions are deafness, vertigo and tinnitus, inevitably present in the complex Ménière's syndrome. To all this I subscribe, bearing in mind, however, that all aged patients are not the victims of pseudo or real Ménière's disease and that a small percentage of those who suffer from these diseases can be relieved when the proper chemical therapy is worked out. To determine deficiencies of the diet one must have a complete list of the foods eaten each day in a period of one week, detailing the quality and the quantity of each food. In addition, a thorough physical examination should be made, and the usual laboratory studies, including determinations of the blood levels of all vitamins, electrolytes and some amino acids. A large part, or even the whole, of the etiologic problem, including the role of the adenoids, is definitely related to dietary deficiencies, which can explain the continued infection of this tissue. Blockage caused by tubotympanic tissue is definitely related in many cases to riboflavin deficiency. Covell[3]

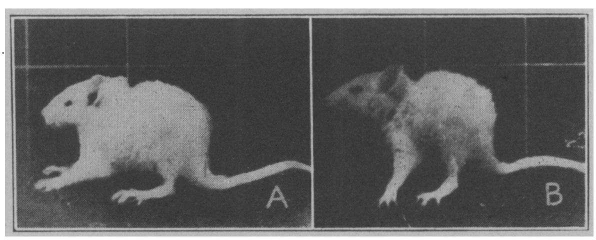

Fig. 2.—These rats are about to have a definite attack of vertigo, the cause of which is a deficiency of thiamine.

has shown that this blockage is present just at the point where the eustachian tube enters the middle ear. I have noticed that in patients with this type of ear who also complained of stuffy nose and postnasal drip, mucoid in character, with no pus present, improvement followed administration of riboflavin (30 mg. daily) or a vitamin B complex preparation with vitamin A and ascorbic acid added.

Crowe, discussing an article by Altman and Fowler Jr.,[49] mentioned having observed 1,000 cases of Ménière's disease, and wrote, in an article in *Medicine,* that patients with this disease are extraordinarily free from general systemic disorders, such as cardiorenal disease, arteriosclerosis, focal infections and allergies. He did not obtain satisfactory results with histamine and nicotinic acid and concluded that surgical division of the labyrinthine branch of the eighth nerve was the only procedure that offered relief from the terrible vertigo. However, Talbott,[15] of the Massachusetts General Hospital, has not advocated

49. Altman, F., and Fowler, E. P., Jr.: Histological Findings in Ménière's Symptom Complex, in Bothman, L., and others: The 1943 Yearbook of Eye, Ear, Nose, and Throat, Chicago, The Year Book Publishers, Inc., 1943, p. 403.

surgical procedures since his adoption of the use of potassium chloride, and Davis, of the Cleveland Clinic, said in a letter of recent date that the neurologic surgeons of that clinic have not divided the nerve since the decision to try diets and administer thiamine hydrochloride and nicotinic acid in large doses over periods of months. Five hundred cases have been studied since their first 20 cases in which such treatment was given were reported in 1940.

In the laboratory studies of blood chemical and dietary deficiencies, pantothenic acid was determined by the method of Strong, Feeney and Earle,[50] riboflavin by the method of Snell and Strong,[51] and nicotinic acid by the method of Krehl, Strong and Elvehjem.[52] Other suggested laboratory procedures are the determination of the basal metabolic rate, the complete blood sedimentation rate, vitamin A and carotene, ascorbic acid, cholesterol, sulfobromophthalein sodium, chlorides, sodium, potassium, calcium, phosphorus, blood sugar, urea nitrogen and, when possible, choline-tocopherols, trace minerals, special amino acids and acid-base balance.

COMMENT

The principal treatments advocated for Ménière's disease are:

1. Surgical section of the labyrinthine branch of the eighth nerve.
2. Those related to the metabolism of salt and water.
3. Those related to the metabolism of potassium.
4. Those related to the use of certain vitamins, especially thiamine and nicotinic acid, nicotinic acid alone, and a member of the group of choline compounds (choline is now known as a fraction of the B complex).
5. Those related to the use of histamine.

A review of the recent literature gives the impression that the most favorable results have followed the use of several of the vitamins. Apparently, since the use of electrolytes, vitamins or endocrine substances began, surgical intervention has lost its popularity. Since the vitamins and the endocrine substances are so closely allied, as shown by their chemical formulas, it hardly seems preposterous to make the claim that Ménière's disease is a chemical problem still requiring further study if and when more is known of the rare minerals and the recent, almost unknown factors added to the list of vitamins, and that it is related to nutritional and environmental factors.

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50. Strong, F. M.; Feeney, R. E., and Earle, A.: Pantothenic Acid, Indust. & Engin. Chem. (Anal. Ed.) **13**:561, 1941.

51. Snell, E. E., and Strong, F. M.: Riboflavin, Indust. & Engin. Chem. (Anal. Ed.) **11**:346, 1939.

52. Snell, E. E., and Wright, L. D.: Microbiological Method for Determination of Nicotinic Acid, J. Biol. Chem. **139**:675-686 (June) 1941.