

52. Wallgren, A.: *Beitr. zur Klin. der Tuberk.*, **69**, 641, 1928.
53. Warner, W. P., and Graham, D.: *Arch. Int. Med.*, **52**, 888, 1933.
54. Meyer, W.: *Trans. Am. Surg. Assn.*, **32**, 592, 1914.
55. Graham, E. A.: *Arch. Surg.*, **6**, 321, 1923.
56. Coryllos, P. N.: *Ibid.*, **20**, 767, 1930.
57. James, R. M.: *British J. Surg.*, **21**, 257, 1933.
58. Roberts, J. E. H., and Nelson, H. P.: *Ibid.*, p. 277.
59. Brunn, H.: *Arch. Surg.*, **18**, 490, 1929.
60. Graham, E. A., and Singer, J. J.: *Ibid.*, **19**, 1560, 1929.
61. Whittemore, W.: *Ibid.*, **86**, 219, 1927.
62. Mumford, J. G., and Robinson, S. D.: *Trans. Am. Surg. Assn.*, **32**, 688, 1914.
63. Körte, W.: *Arch. Klin. Chir.*, **85**, 1, 1907.
64. Archibald, E., and Brown, A. L.: *Arch. Surg.*, **16**, 322, 1928.
65. Ballou, D. H.: *J. Thoracic Surg.*, **3**, 267, 1933.
66. Jackson, C., Tucker, G., Clerf, L. H., Lukens, R. M., and Moore, W. F.: *J. Am. Med. Assn.*, **84**, 97, 1925.
67. Roles, F. C., and Todd, G. S.: *British Med. J.*, **2**, 639, 1933.
68. Beaumont, G. E.: *Ibid.*, p. 708.
69. Hefferman, P.: *Ibid.*, p. 708.
70. Chandler, F. G.: *Ibid.*, p. 795.

OPHTHALMOLOGY

UNDER THE CHARGE OF

WILLIAM L. BENEDICT, M.D.,

HEAD OF THE SECTION OF OPHTHALMOLOGY, MAYO CLINIC, ROCHESTER, MINN.,

AND

H. P. WAGENER, M.D.,

ASSISTANT PROFESSOR OF OPHTHALMOLOGY, MAYO FOUNDATION, ROCHESTER, MINN.

NUTRITIONAL DISEASES AND THE EYE. THE RÔLE OF VITAMIN B.

IN the February, 1934, number of this JOURNAL, Benedict reviewed the subject of nutritional diseases and the eye with special reference to the effects of deprivation of vitamin A. Brief mention was made of the report by Day, Langston and O'Brien on the development of cataracts in experimental animals on a diet low in vitamin G (B₂). Further studies on the ocular lesions produced by experimental deprivation of vitamin G have been carried on by O'Brien, by Langston, Day and Cosgrove,¹ and by Yudkin and his associates.² Langston, Day and Cosgrove reported the findings in a series of young albino mice which were placed on a diet entirely adequate except for the total absence of vitamin G. Seventy-nine per cent of the animals showed keratitis after an average of 43 days of the diet, 96% developed cataracts after an average of 48 days, and 57% developed general ophthalmia after an average of 50 days of the diet. These cataracts were primarily of cortical type but went on to complete, mature opacity of the lens if the animal lived long enough. Yudkin noted lenticular changes in 6 of 8 young rats kept for 10 weeks on a diet free from vitamin G. The lens changes developed completely in 7 days. He stated, however, that lens changes had not developed in older animals that had been kept for 3 months on a diet deficient in vitamin G, and

he was not sure that these experiments could be interpreted as indicating a cause of cataract in the human. He brought out the fact that the incidence of cataract in human pellagra was not especially high. O'Brien³ was able to arrest the progress of lenticular changes in experimental animals by adding vitamin G to the diet, and in one of Yudkin's² rats an early opacity of the lens absorbed after feeding with vitamin G. Cosgrove⁵ studied a series of patients with senile cataracts from the standpoint of vitamin G deficiency. He found that the majority of them ate only small amounts of food rich in vitamin G and that persons of similar age on a balanced diet did not develop cataracts to maturity during a 6-year period of observation.

In a further study of experimental cataract, Yudkin and Arnold⁴ were able to produce cortical cataract in young rats after 70 to 94 days on a diet containing 70% lactose. Nuclear cataracts developed in young rats after 11 to 14 days on a diet containing 50% galactose, after 10 to 14 days with 35% galactose, and after 14 to 20 days with 25% galactose. In older rats, cortical cataracts developed after 21 days on a diet containing 50% galactose. Yudkin suggests that these cataracts may be caused by the disturbance of calcium metabolism induced by lactose and galactose or by the direct action on the lens of increased percentages of those sugars in the aqueous. The theory of faulty calcium metabolism is supported by the known clinical association of cataract with endemic and postoperative tetany, with rickets, and with spontaneous hypoparathyroidism.

In this country, at least, the association of ocular lesions with the vitamin G deficiency of primary pellagra has not received particular attention. The occurrence of pellagra-like syndromes secondary to gastro-intestinal disturbances and chronic alcoholism has been rather generally recognized. In 1934, Levine⁶ reported a case of bilateral acute optic neuritis in "alcoholic pellagra." The neuritis cleared up with return of the vision to normal after several months on a balanced diet with added amounts of vitamin B₂. Levine stated that Quagliano had observed pellagrins with hemeralopia; that Bietti had seen optic neuritis in many cases of pellagra; that Krylov, in Russia, among 36 cases of pellagra, saw cataract formation even in children, paleness of the nerve heads, sluggish pupils, narrow vessels, scotomas for red and green in advanced cases, diplopia, hemeralopia and hallucinations, and that Kandelaki observed diplopia, cataracts and hemeralopia. These findings might be considered to indicate general nutritional deficiency rather than specific effects of vitamin G deprivation. Bristow⁷ stated that routine and special examinations of the pellagrins admitted to the South Carolina State Hospital for the Insane had failed to reveal any very characteristic ocular lesions. A number of years ago the author had the opportunity of seeing quite a few cases of pellagra of varying degrees of severity. The only striking ocular complication noted was ulceration of the cornea in some of the more advanced cases. The eyes showed, as a rule, little inflammatory reaction, the ulcers responded very poorly to treatment and progressed to complete sloughing of the cornea in several instances.

The occurrence of ocular lesions in association with deficiencies of vitamin B₁ seems to be more definitely established than in the case

of vitamin B₂. It is true that primary beriberi is probably rare in this country. In other countries, retrobulbar optic neuritis has been reported in beriberi by Fernando,⁸ by Shimazono, and by Katajama.⁹ Katajama was able to demonstrate degeneration in the medullary sheaths and axis-cylinders of the optic nerves in experimental deprivation of vitamin B₁. Moore¹⁰ reported a high percentage of visual defects apparently on the basis of retrobulbar neuritis occurring in a group of native South African students who lived largely on a diet of cooked manioc or cassava which contains a high percentage of starch. He noted that in the early phases of the disease, vision could be restored to normal by proper additions to the diet. In the more advanced stages, the visual defects were permanent. Moore was uncertain whether the optic nerve lesion was due to a vitamin deficiency or to a direct toxic effect of the manioc. He considered the vitamin deficiency the more likely cause. In this connection the case reported by Kepler¹¹ is of considerable interest. He found bilateral optic neuritis with secondary optic atrophy associated with a beriberi-like syndrome in a colored woman who had lived for some time on a diet consisting mainly of raw laundry starch.

In this country, however, more importance attaches to the types of deficiency neuritis which occur in association with dietary deficiencies resulting from gastro-intestinal disturbances of varying sorts. Christopher, Paskind and Snorf¹² reported 2 cases in which multiple neuritis developed after operations on the biliary tract. They expressed the opinion that the neuritis was due to avitaminosis resulting from prolonged postoperative vomiting which had lasted for 41 days in the first case and 43 days in the second case. Wechsler¹³ reported 8 cases of multiple neuritis which he thought were caused by avitaminosis resulting from prolonged vomiting, gastro-intestinal disturbance, or restriction in diet. Recently, Wagener and Weir reported 2 cases of rapid loss of vision associated with nystagmus, ocular muscle paralysis, and mental confusion which occurred as complications of prolonged postoperative vomiting. The loss of vision was due in the first case to optic neuritis and in the second case to retrobulbar neuritis. The symptoms in both patients improved rapidly after the cessation of the vomiting and the addition of intramuscular doses of liver extract to a balanced diet.

Jolliffe, Colbert and Joffe¹⁴ have confirmed the belief of Strauss that the peripheral polyneuritis of the alcohol addict is attributable to the deficiency of vitamin B₁ and not to the toxic effect of alcohol. It seems probable from the observations of Shastid,¹⁵ Keefer¹⁶ and others that the deficiency of vitamin B₁ resulting from restricted diet may be at least partially responsible for the retrobulbar optic neuritis or toxic amblyopia usually ascribed to the overuse of alcohol and tobacco. Addition of vitamin A (Yudkin²) or vitamin B₁ (Shastid¹⁵) to the diet is said to hasten recovery in these cases as well as in cases of optic neuritis of indeterminate origin. It has been suggested also by Keefer¹⁶ that the retrobulbar optic neuritis seen at times in nursing mothers and spoken of hitherto as "lactation optic neuritis" may really be due to avitaminosis.

Winans and Perry¹⁷ expressed the opinion that the polyneuritis associated with pernicious vomiting of pregnancy is a deficiency disease. They found that the disease responded favorably to the intramuscular administration of liver extract and they considered the deficiency to be largely one of vitamin B₁. Optic neuritis occurs at times in pernicious vomiting of pregnancy, often in association with polyneuritis or neuronitis as reported by Berkwitz and Laufkin.¹⁸ In these cases the optic neuritis is most probably also due to deprivation of vitamin B₁. It seems probable that the hemorrhages in the retina which are seen in some severe cases of pernicious vomiting of pregnancy as reported by Stander¹⁹ are also manifestations of vitamin deficiency, whether of vitamin B₁ or vitamin C it is difficult to say. However, in a case recently reported by Wagener and Weir, the hemorrhages disappeared rapidly under intramuscular administration of liver extract.

While clinical reports of ocular lesions dependent on or associated with deficiencies of vitamin B₁ and B₂ are rather scattered as yet, in this country at least, it would seem that enough experimental and clinical data are accumulating to indicate that deficiencies of these vitamins may play a more important rôle than is generally appreciated in the causation of acute and chronic affections of the optic nerve and perhaps of the ocular muscles and of hemorrhagic lesions of the retina. The words of Winans and Perry¹⁷ might well be applied to optic neuritis and retrobulbar optic neuritis: "The nutritional background of a considerable portion of the population is such as to provide for the development of deficiency polyneuritis under a variety of conditions. Marked changes in the diet may decrease the intake of the vitamin B complex below the necessary minimum. Alcoholism, intestinal operations, and prolonged gastro-intestinal upsets, including the vomiting of pregnancy, may all serve to develop this disease. In any continued illness associated with loss of appetite, the possibility of the development of polyneuritis must be borne in mind."

H. P. WAGENER, M.D.

REFERENCES.

1. Langston, W. C., Day, P. L., and Cosgrove, K. W.: Cataract in the Albino Mouse Resulting From a Deficiency of Vitamin G (B₂). *Arch. Ophthalm.*, **10**, 508, 1933.
2. Yudkin, A. M.: Ocular Disturbances Produced in Experimental Animals by Dietary Changes, *J. Am. Med. Assn.*, **101**, 921, 1933.
3. O'Brien, C. S.: Experimental Cataract in Vitamin G Deficiency, *Ibid.*, **8**, 880, 1932.
4. Yudkin, A. M., and Arnold, C. H.: Cataracts Produced in Albino Rats on a Ration Containing a High Proportion of Lactose or Galactose, *Ibid.*, **14**, 960, 1935.
5. Cosgrove, K. W.: Discussion of Yudkin's Paper on Ocular Disturbances Produced in Experimental Animals by Dietary Changes, *Ibid.*, **101**, 925, 1933.
6. Levine, J.: Pellagra as a Cause of Optic Neuritis, *Arch. Ophthalm.*, **12**, 902, 1934.
7. Bristow, W. J.: Pellagra as a Cause of Optic Neuritis, *Ibid.*, **13**, 99, 1935.
8. Fernando, A. S.: The Eye in Beri-beri, *Am. J. Ophthalm.*, **6**, 385, 1923.
9. Kutajama, J.: B-Avitaminose (enthülster-Reis-Krankheit) und ihr Einfluss auf das Sehorgan, besonders den Sehnerven, *Acta Soc. Ophthalm. Japan*, **38**, 63, 1934; Abstract, *Zentrabl. f. d. ges. Ophthalm. u. Grenzgeb.*, **31**, 701, 1934.
10. Moore, D. G. F.: Retrobulbar Neuritis and Partial Optic Atrophy as Sequela of Avitaminosis, *Ann. Trop. Med. and Parasitol.*, **28**, 295, 1934.

11. Kepler, E. J.: Beriberi From a Diet of Raw Starch, *J. Am. Med. Assn.*, **85**, 409, 1925.
12. Christopher, F., Paskind, H., and Snorf, L. D.: Multiple Neuritis Following Biliary Tract Operations, *Am. J. Surg.*, **22**, 280, 1933.
13. Wechsler, I. S.: Unrecognized Cases of Deficiency Polyneuritis (Avitaminosis?), *Med. J. and Rec.*, **131**, 441, 1930.
14. Jolliffe, N., Colbert, C. N., and Joffe, P. M.: Observations on the Etiologic Relationship of Vitamin B (B₁) to Polyneuritis in the Alcohol Addict, *AM. J. MED. SCR.*, **191**, 515, 1936.
15. Shastid, T. H.: Optic Neuritis and Vitamin B₁, *Am. J. Ophth.*, **12**, 903, 1929.
16. Keefer, C. S.: Some Clinical Aspects of Deficiency Diseases, *New England J. Med.*, **205**, 1086, 1931.
17. Winans, H. M., and Perry, E. M.: Deficiency Polyneuritis, *South. Med. J.*, **29**, 309, 1936.
18. Berkwitz, N. J., and Lufkin, N. H.: Toxic Neuronitis of Pregnancy: A Clinicopathological Report, *Surg., Gynec. and Obst.*, **54**, 743, 1932.
19. Stander, H. J.: Haemorrhagic Retinitis in Vomiting of Pregnancy, *Ibid.*, **54**, 129, 1932.

ERRATUM.

In the page advertisement in the July issue of THE NATIONAL DRUG COMPANY of Philadelphia the word grand appeared instead of the word GIANT. The paragraph should have read: "We offer a special Rag Weed Antigen Outfit complete for diagnosis and treatment of Fall Hay Féver for \$10. Contains two diagnostic tests for mixed grasses and giant and dwarf rag weeds; 1 ampul-vial each Series 'AA', 'A' and 'B' Rag Weed Antigen; 25 cc. ampul-vial Sterile Salt Solution for dilution of antigen if needed; 25 cc. ampul-vial Epinephrin 1-1000 to control local or systemic reactions."

Notice to Contributors.—Manuscripts intended for publication in the AMERICAN JOURNAL OF THE MEDICAL SCIENCES, and correspondence, should be sent to the Editor, DR. EDWARD B. KRUMBHAAAR, School of Medicine, University of Pennsylvania, Philadelphia, Pa.

Articles are accepted for publication in the AMERICAN JOURNAL OF THE MEDICAL SCIENCES exclusively.

All manuscripts should be typewritten on one side of the paper only, and should be double spaced with liberal margins. The author's chief position and, when possible, the Department from which the work is produced should be indicated in the subtitle. Illustrations accompanying articles should be numbered and have captions bearing corresponding numbers. For identification they should also have the author's name written on the margin. The recommendations of the American Medical Association Style Book should be followed. It is important that references should be at the end of the articles and should be complete, that is, author's name, journal, volume, page and year (in Arabic numbers). Titles can be included for less than 25 references.

Return postage should accompany all manuscripts but will be returned to the author if the manuscript is accepted.

Two hundred and fifty reprints, with covers, are furnished gratis; additional reprints may be had in multiples of 250 at the expense of the author. They should be asked for when the galley proofs are returned.

Contributions in a foreign language, if found desirable for the JOURNAL, will be translated at its expense.