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Disease of the Optic Nerve in Myxedema

Its Relationship to the Thyroid Gland and to the Hypophysis

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DISEASE OF THE OPTIC NERVE IN MYXEDEMA

ITS RELATIONSHIP TO THE THYROID GLAND AND TO THE HYPOPHYSIS

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The title of this paper suggests a very limited field in ophthalmology, and probably one that is of immediate interest to only a few in our Section. Unless some particular clinical experience, or one of the infrequent references in the literature has directed our attention to an undoubted connection between the thyroid gland and the hypophysis cerebri, their relationship may never have come to our notice. On this ground, and also in the hope of making some small contribution to the knowledge of the subject, the following two rare cases are reported:

CASE 1.—Myxedema with optic atrophy and bitemporal hemianopsia dependent on a probable enlargement of the hypophysis.

Patient.—Mrs. A. B., 56 years old, was referred to me Oct. 13, 1910, by Dr. W. L. Richardson and Dr. W. H. Smith. Dr. Smith, from whom I obtained her history, saw her first Aug. 29, 1910. Family history and previous history were negative, except that some years before she had suffered from arsenical poisoning. She complained of nothing except stiffness in her right knee and trifling swelling of her feet. She sought medical advice because her family had noticed a considerable degree of stillness in her mental actions and in her general condition. The members of her family said that she forgot easily, had a tendency to marked drowsiness, and had changed much in her general appearance.

General Examination.—Pulse was 72; temperature slightly subnormal. Hemoglobin 90 per cent.; differential count, polymorphonuclears 54 per cent., lymphocytes 44 per cent., eosinophils 2 per cent. Pupils equal; reacted. Teeth normal. Blood-pressure was 135. No glandular enlargement. Patient's appearance and actions myxedematous. Lungs negative. Heart-sounds faint; soft systolic murmur at apex; no cardiac

enlargement. Very slight amount of hair in the axilla; the hair on the scalp thin. Very little perspiration. Abdomen negative. Knee-jerks not obtained; some stiffness of the right knee with limitation of motion. Trifling edema of the feet.

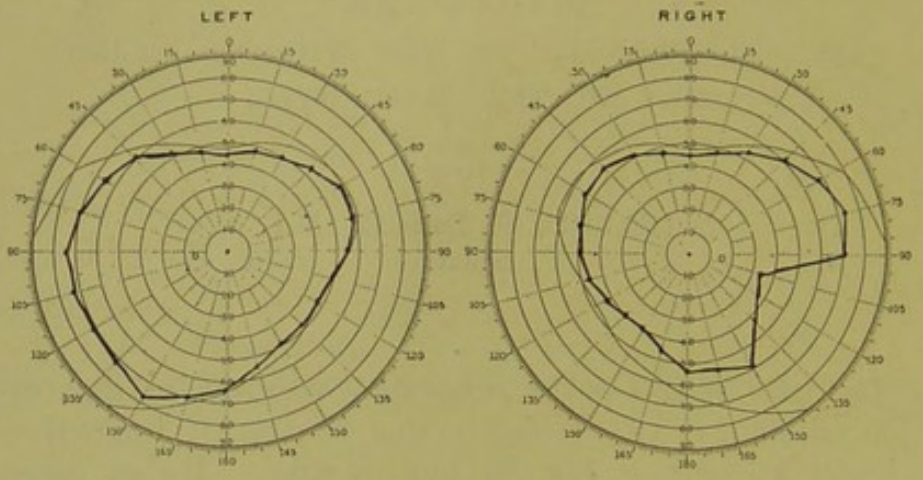

Fig. 1.—Author's Case 1, Oct. 20, 1910.

Moderate psoriasis. Nails brittle. Urine: twenty-four-hour amount 54 ounces; normal acid; specific gravity 1,012; slightest possible trace of albumin; urea 13.7 gm., no bile and no sugar; sediment negative.

Ophthalmic Examination.—Mrs. B. complained of difficulty especially in reading. Her sight had always been good until recently, when she had noticed a general haziness. Through the kindness of Dr. O. F. Wadsworth and Dr. C. H. Williams, I am enabled to record her ocular condition on two previous occasions.

In 1902, Dr. Wadsworth found:

V. R. — .75 sph. = 6/4.
V. L. — 1.0 sph. = 6/4.

Muscles were normal; fundi normal.

In August, 1909, Dr. C. H. Williams made the following notes:

V. R. — 1.0 sph. ⌣ — .50 cyl. axis 180 = 6/10.
V. L. — 1.0 sph. = 6/12.

The ophthalmoscopic examination showed "retinal arteries rather small, especially in the right eye; disks slightly grayer than normal." "Pupils reacted feebly to light."

At the time of her visit to me, vision was as follows:

V. R. = 6/60 not improved.
V. L. — 1.0 sph. = 6/15.

The pupils were equal and reacted sluggishly to light. The tension was normal to the finger. The ophthalmoscope showed marked atrophy of the right nerve-head, moderate pallor of the left nerve-head, with possible slight diminution in the size of the vessels.

The lower temporal quadrant of the right field was markedly contracted, while the left field showed a slight contraction on the temporal side. A satisfactory color field could not be taken on account of the mental condition of the patient. In fact, it was difficult to take the field for form, as she tired so easily.

Jan. 17, 1912, she presented herself again for examination.

V. R. = 2/60, not improved.
V. L. — 2.0 sph. = 6/15 —.

The field showed a well-defined bitemporal hemianopsia extending beyond the fixation point in the right eye, and reaching that point in the left.

The ophthalmoscopic examination showed a marked atrophy of the right nerve-head with vessels apparently of normal size, and little, if any, sign of a previous inflammation. The left nerve-head was somewhat atrophic, but of much better color than the right. It was somewhat pale on the temporal

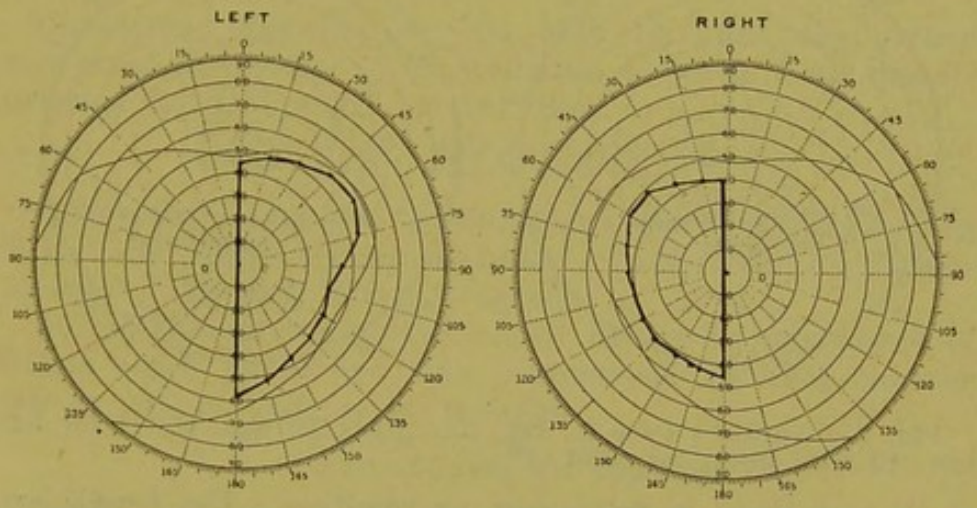

Fig. 2.—Author's Case 1, Jan. 17, 1912; 10 mm. object.

side. The outlines were clear, and the vessels seemed to be nearly of normal size. A few small rounded flecks of hemorrhage were seen in the surrounding retina.

Mrs. B. was put on thyroid extract with very marked improvement. She grew a complete set of perfect nails, and her mental condition improved considerably.

Case 2.—Myxedema with concentric contraction of the fields, low-grade optic neuritis, chorioretinitis.

Patient.—F. M. S., a man, aged 49, married, hotel-keeper, living in Maine, was referred by Dr. F. T. Lord, to whom I am indebted for the history and general examination. Family history is negative; no consanguineous marriages. Father and mother, nine brothers and sisters are living and well. Patient had children's diseases; was twice injured by being kicked in the face by a horse, fifteen and thirteen years ago. He had lumbago twelve years ago; no rheumatism. He

denies venereal disease and any opportunity for infection. He has one daughter, aged 24, healthy. His wife had one still-born child, but no miscarriages. He uses no alcohol or tobacco; has been a hard worker.

Present Illness.—Ten years ago he began gradually to lose his hair, that of the scalp, beard and mustache becoming very thin, while the axillary and pubic hair, the eyebrows and eyelashes entirely disappeared. For three or four years the ankles and hands had been slightly swollen. For the last three years, the patient has suffered a progressive loss of sight which affected both eyes, the left, however, more than the right. At times, he has a feeling of pressure in his eyes, occasional slight headache and dizziness. He has no cough, but some dyspnea and palpitation. The appetite is

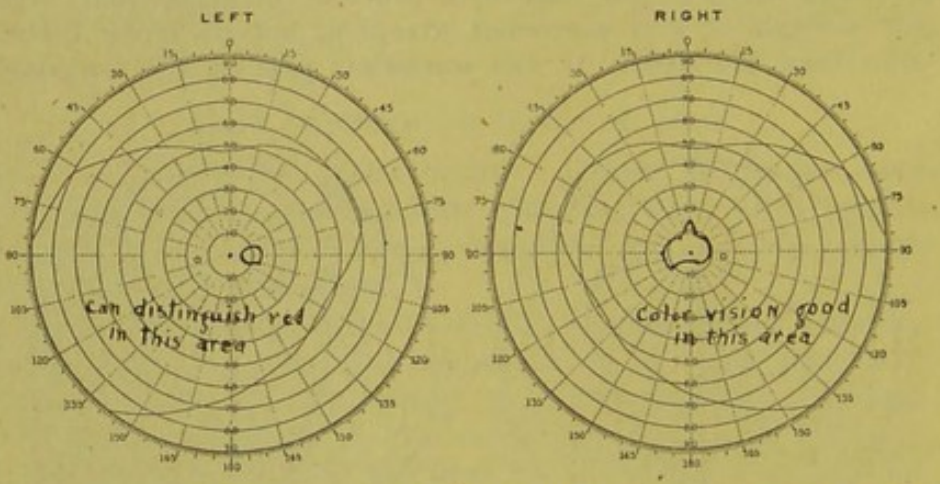

Fig. 3.—Author's Case 2, Jan. 22, 1912; 20 mm. object for left eye; 10 mm. object for right eye.

good, and there is no nausea or vomiting. The bowels are regular. Patient is never uncomfortable from the heat in summer, but feels the winter cold severely. He is mentally active; memory is unimpaired. There is no change in his disposition, which is exceptionally even. He is vigorous physically, but much troubled by his impaired sight. There is no loss of sexual power. Weight was about 180 three years ago; 160 now.

General Examination.—Patient well developed and nourished; good color, glands not enlarged. Cheeks red. Nose, lips and tongue negative. Teeth carious and neglected. Neck, lungs and mediastinum negative. Heart impulse palpable in fifth space, nipple line. No enlargement to right or above. Sounds regular and of good quality. On one occasion heart sounds 120, and very irregular with a nondescript, disorderly rhythm; no murmurs. Aortic second slightly plus. Abdomen negative; liver, spleen and kidneys not felt. Knee-jerks present and equal. Genital organs normal. Skin rough and dry; small

patch of eczema on helix of right ear. The hair of scalp, beard and mustache very thin and soft, fine rather than coarse. Axillæ, pubes, eyebrows and eyelids devoid of hair. Upper lids abnormally thick with obliteration of normal folds and depressions, but no obvious edema. Hands large, and the skin over the dorsal surface slightly thickened, rough and dry, but without edema. Tips of the fingers slightly clubbed. Anteroposterior and lateral convexity of the nails. Nails somewhat ridged and brittle. Feet of normal size. Marked edema of the legs, pitting regularly on pressure. No varicose veins. (It may be remarked that the patient has always had rather large hands.) Blood-pressure 150. Urine normal color; specific gravity 1.012; albumin and sugar present; sediment negative. Blood: hemoglobin 100 per cent.; no leukocytosis, differential count negative.

Stereoscopic radiographs of skull show nothing abnormal. Mr. S.'s vision began to fail three years ago, beginning in the right eye.

Ophthalmic Examination.—On May 10, 1910, the patient was examined by Dr. C. H. Williams, to whom I am greatly indebted for his record at that time.

V. R. — .50 cyl. axis 90 = 6/30.
V. L. — .50 cyl. axis 90 = 6/12.

"The ophthalmoscopic examination showed smoky-looking disks, and small retinal arteries. There were no fundus lesions." The field was not taken.

At the time of the patient's visit to me, he complained of failing sight, which had been continuous. He said that he saw as well at dusk as in daylight.

V. R. — 1.0 sph. = 6/60.
V. L. = 2/60 excentric not improved.

Pupils equal, but react sluggishly to light.

Ophthalmoscopic examination showed: Right: Optic disk is pale, and of a grayish color on the borders. Slightly hyperemic in the center. Outlines are blurred; the vessels decidedly small. The arteries are slightly small, and show white lines along them. The veins apparently slightly narrow also. In the macula region is a moderate-sized whitish area of atrophy liberally sprinkled with dark pigment. In the periphery of the fundus are numerous small masses of pigment of bone-corpuscle shape. The retina throughout is of a granular appearance.

Left: The optic nerve-head is paler than in the right eye. Its outlines are slightly indistinct; no swelling; the vessels are decidedly smaller than normal. The arteries show white lines. A short distance downward and out from the disk are three small rounded areas of chorioidal atrophy sprinkled with pigment. Below these is a similar area, but of larger size. In the periphery of the retina are many small masses of pigment of bone-corpuscle shape. In this eye, also, tne

retina is sprinkled with minute dark spots, and presents a decidedly granular appearance.

The field of vision in the right eye, taken with a 10 mm. object, shows a concentric contraction, so that only an irregular area of about 12 degrees in its greatest diameter remains centrally. This area approaches the fixation point below. In this area, the patient distinguishes colors.

In the left eye, the field shows a small remaining area, not much over 5 degrees in diameter, of uncertain outline and situated, as far as can be determined, slightly to the nasal side of the center. In this area, white and red can be distinguished.

Before discussing these two cases, it may be well to consider others of a similar nature which have been reported. There are few of them, and unfortunately several are incompletely described.

A search through the literature has disclosed cases of a somewhat similar nature reported by Schmidt-Rimpler, Sanesi, Wagner, Burchard, Bolte, Pollack, Meyer, Gourfein-Welt, Moore, Berliner, Souroff and Hennicke. For convenience they are abstracted at the end of this article.

If the condition of the optic nerve, as evidenced by the ophthalmoscopic examination, be analyzed in these fourteen cases, the most marked change is found to be a low-grade optic neuritis.

In Bolte's case, for instance, the outlines of the nerve-head were irregular and blurred; the veins were rather swollen and tortuous; the vessels projected forward on the disk. Wagner, in his case, reported an outspoken neuroretinitis with a slightly swollen and indistinctly outlined disk. In several cases, blurring or pallor of the temporal half of the nerve-head was observed. Post-neuritic atrophy was seen in some. Optic atrophy without further details was reported by Pollack and by Meyer. In my own first case, the right eye showed only very indefinite signs of a previous inflammation. In no case was there a papillitis of great intensity. The changes, therefore, may be said to range from a low-grade optic neuritis to an atrophy without definite signs of a previous inflammation. All these appearances can be explained by a low-grade inflammation taking place in some part of the nerve-trunk between the chiasm and the disk, and varying in clinical signs according to the location of the process.

The fields of vision present points of striking interest. Unfortunately, in Pollack's case there is no mention of

a perimetric examination. In Moore's, the field of vision could not be mapped out on account of the mental condition of the patient; while in Bolte's case it was normal.

In seven cases, those of Sanesi, Wagner, Meyer, Gourfein-Welt, Berliner, Hennicke and in my own first case, one or both eyes presented evidence of a temporal hemianopsia.

In two cases, Souroff's and my own (Case 2), the changes show a striking similarity. There was a concentric narrowing of the fields, so that in one eye of each patient a paracentral area remained with vision of 2/60 or lower and perception of white and red. In the other eye, there was apparently a central area of vision preserved of 6/21 in Souroff's and 6/60 in my own case, and good perception of colors.

Two cases, those of Schmidt-Rimpler and Burchard, presenting a central scotoma will not be included here, but will be spoken of later.

The condition of the fields in the first seven cases points almost inevitably to pressure on the optic chiasm by an hypertrophy or new growth of the hypophysis — and this finding is in accord with numerous observations made on the relationship between the thyroid gland and the pituitary body.[1]

For a number of years, evidence has been accumulating which points to a close relationship between those glands of the body which possess an internal secretion, and especially between the hypophysis and the thyroid. A study of this evidence shows the following facts: The thyroid gland and the anterior lobe of the hypophysis develop from the same embryonic structures, and show a close histological similarity. Furthermore, in all but exceptional cases of acromegaly the colloid degeneration, with or without cyst formation, which is found in the hypophysis, is also present in the thyroid.

Conversely, Boyce and Beadles, de Coulon, Bourneville and Brisson, Langhans, Ponfick and others have found in myxedema, cretinism and similar conditions, enlargement of the sella turcica and disease of the hypophysis.

Rogowitsch, Stieda, Gley and Hofmeister observed enlargement of the hypophysis after extirpation of the thyroid gland.

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1. Pineles, in an excellent article (Die Beziehungen der Akromegalie zum Myxoedem . . . Samml. klin. Vortr., No. 242; Inn. Med., No. 73) gives a very full consideration of this subject.

Schönemann examined a number of cadavers from a region where goiter was common, and although there was no hypertrophy of the pituitary body, he found similar degenerative changes in both organs. Certain chemical studies also support the view of a close relationship between the two.

Clinically, the signs of acromegaly may be combined so closely with those of myxedema that it is hard to decide which set of symptoms is preponderant.

Cases are occasionally found which present a combined picture of exophthalmic goiter and acromegaly (I have had the opportunity of following one of these during the past four years), and signs of exophthalmic goiter, myxedema and hypophyseal enlargement may be present in the same patient at different times, as is evidenced by Bolte's case.

Other glands possessing an internal secretion show a similar relationship. Polyuria, glycosuria and diabetes with changes in the pancreas, have been reported in acromegaly; while one of the commonest accompaniments of pituitary enlargement is the change in the generative organs, as shown by amenorrhea in the female and impotence in the male.

Other recorded facts which are also of interest tend to show that the amount of pathologic change found in these various conditions bears apparently no true relationship to the clinical condition. Hence, we may have greatly enlarged thyroids without the symptoms of exophthalmic goiter; marked atrophy of the thyroid without signs of myxedema; while enlargement of the hypophysis may produce several pictures clinically. It is Uhthoff's[2] view that in youth it produces general disturbances of growth (giantism and dwarfism) not infrequently accompanied by a general adiposity, but without true acromegaly. Brissaud and Meige hold the view that increase in the function of the hypophysis leads, in childhood particularly, to giantism, in adults to acromegaly, and in later life to thickening of the soft parts.

The question as to how often an enlargement of the hypophysis is sufficient to produce disease of the optic nerve has been investigated, notably by Ottolenghi and by Hitschmann. Ottolenghi[3] examined the fields of vision of thirty cretins, and found no definite change

2. Uhthoff: Beitrag z. d. Wachstums-Anomalien b. d. temporalen Hemianopsie, etc., Berl. d. ophth. Gesellsch., 1907, p. 140.
3. Ottolenghi: Cited by Hitschmann (Note 4).

which could be laid to an enlargement of the hypophysis. In no case could he demonstrate a temporal hemianopsia. In three cases, however, he found changes in the fundus; in Case 17, a beginning optic atrophy in each eye; in Case 25 papillitis in each eye; in Case 27 optic neuritis in each eye.

Hitschmann,[4] in an exhaustive research, examined fifty-eight cretins, and came to similar conclusions. He found, however, one case of optic atrophy, which possibly was due to an intercurrent tabes. Hitschmann's fundus observations will be referred to later.

We see, therefore, only in the rarest cases of myxedema, cretinism and similar diseases, an enlargement of the hypophysis sufficient to cause involvement of the optic nerve. It has occurred, undoubtedly, in only seven of the cases, and in some of these, striking symptoms of acromegaly were present.

In Sanesi's case, there were characteristic symptoms of both diseases. Preference was given to myxedema on account of the order in which the symptoms developed and from the success of the treatment with a thyroid preparation.

Wagner's case presented as many signs of acromegaly as myxedema. In it, also, a thyroid preparation was of benefit.

Burchard made the diagnosis of acromegaly combined with partial myxedema, and the case presented by Gourfein-Welt also showed many characteristic features of acromegaly, but was much helped by a thyroid preparation.

It should be noted in this connection that Parsons, Caton, Byron-Bramwell, Bruns and others have used a thyroid preparation in acromegaly, and have observed a noticeable improvement where the symptoms of the disease were like those of myxedema (Pineles).

Formerly, the enlargement of the hypophysis, which is found in myxedema and allied conditions, was thought to be a compensatory hypertrophy. The enlargement found in these cases, however, is not parallel with that found experimentally in animals after the operative removal of the thyroid gland. It seems more likely here that we have some primary condition which affects both glands, and according to how each gland reacts to the

4. Hitschmann: Augenuntersuchungen bei Kretinismus, Zwergwuchs u. verwandten Zustünden, Wien. klin. Wchnschr., 1908, No. 27, p. 655.

primary disease we get a varying clinical picture ranging from myxedema with pathologic changes in the pituitary body but no clinical symptoms, to acromegaly with degeneration of the thyroid gland, but without symptoms of myxedema. The cases cited here would seem to be representative of this symptom-complex. What makes them so unusual is the fact that the myxedematous symptoms are in the foreground.

There is no reason to doubt, then, that disease of the optic nerve presenting a picture of a temporal hemianopsia occurring in the course of a myxedema is due to an enlargement of the pituitary body.

It should be noted, however, in this connection, that Hennicke ascribes the condition in his case to the effect of thyroid extract, basing his views on an article by Coppez,[5] which describes a case of blindness occurring in a dog to which thyroid extract had been administered, complete recovery occurring when it was withdrawn. Coppez also reports five cases of retrobulbar neuritis due to a thyroid preparation. These all occurred in obese people who had been taking the drug for a long time, and in excessive doses. The affection always takes the form of a chronic retrobulbar neuritis with central scotoma, and improves when thyroid treatment is omitted. That the bitemporal hemianopsia described in Hennicke's case could be due to such a cause seems highly improbable. We must consider it as due to pituitary involvement, in spite of the negative evidence of the *x*-ray.

A further question remains: Will pressure on the chiasm always account for the diseased optic nerve in myxedema?

Berliner ends his study of the subject with the following conclusion: "In pure myxedema, naturally if we exclude accidental complications, an optic atrophy does not occur. It is always the result of a concurrent tumor of the hypophysis. . . . ."

If this is so, how can I explain the two cases of concentric narrowing of the field? In one eye of each patient the field was reduced to a small central area around the fixation point, which did not suggest an hemianopic defect. The second eye of my case showed a small rounded paracentral area remaining, also not suggesting hemianopsia. Nor did the field of the second

5. Coppez: Névrite Optique par Absorption de Thyroïdine, Arch. d'Ophthal., 1900, xx, 656.

eye in Souroff's case suggest it from the description given. Such fields could hardly be produced by hypophyseal enlargement. And furthermore, if we except the amenorrhea in Souroff's case, neither patient presented signs in accordance with such a process.

The radiographic examination made in my case by a roentgenologist of great experience and skill was negative. In this connection, however, it must be said, that the *x*-ray examination was negative in Hennicke's case also, in spite of the clinical evidence of pituitary enlargement.

In theory, the disease of the optic nerve in these cases might be caused by some toxic or infectious substances, possibly some toxic product of metabolism allowed to work through the diminished antitoxic power of the thyroid secretion. In support of this view, we have the very striking nervous symptoms of myxedema, the loss of memory, slow mental process, listlessness, hallucinations of speech and hearing, even insanity; also weak reflexes, cramps, spasms, frequent headache and reduced temperature.[6]

On the other hand, as Berliner well remarks, why, if this is so, do we not see optic neuritis more frequently in myxedema and in its allied diseases? Also why has there never been found in myxedema a pathologic condition of the central nervous system which can be considered as parallel with an atrophy of the optic nerve?

Another possibility should be mentioned. A general increase of intracranial pressure could cause an optic neuritis and a concentric contraction of the field. If it existed, one would expect, however, a choked disk and other clinical signs which were not present in these cases. It is likewise hard to see how a hypophyseal growth could expand sufficiently to cause increased intracranial pressure without first producing a direct pressure on the chiasm.

The chorioretinitis seen in my second case presents another element of a most unusual character. In appearance, it strongly suggested a syphilitic process from the marked vascular involvement and the striking migration of pigment from the periphery. Syphilis would also

6. It may be noted in regard to optic-nerve disease occurring in other diseases of the blood glands that in tetany Marshner has observed a case of neuroretinitis, while Cássel has seen atrophy of the optic nerves (Possek: Schilddruse und Auge, Klin. Monatsbl. f. Augenh., 1907, Bellageheft, p. 1), as has Hanke (Cataract, Neuritis Optica, Degeneration des Pigmentepithels des Irishhinterfläche bei Tetanie, Ber. d. ophth. Gesellsh., 1907, p. 329), also.

explain the disease of the optic nerve. No other evidence could be obtained, however, except that the patient's wife had had one still-born child. There was no scar on the genital organs, no history of miscarriage by his wife, and their only child is 24 years of age and perfectly healthy. One carefully questioning the patient, he denied gonorrhea or syphilis, as well as any opportunity for infection. Two separate Wassermann tests carried out by different observers were negative. In spite of this negative evidence, syphilis could not be ruled out, and the patient was put on large doses of mercury and iodid, in the hope of influencing the ocular condition. It cannot be denied, however, that these pathologic changes could be produced by the same hypothetical toxic or infectious agent which may have been responsible for the change in the optic nerve.

Turning to similar changes in other cases of myxedema or allied conditions with optic-nerve disease, Hitschmann in his studies on cretinism noted in Case 4 of his series slight pigment changes in the macula of the right eye; chorioiditis in the macula of the left eye; in Case 6, circumpapillary chorioidal atrophy with pigment deposit. Bolte noted on the edge of the disk of his case, irregular gatherings of pigment. These lesions probably bear little relationship to the changes in my case. Hitschmann, however, presents an observation of greater similarity.

CASE 56.—Patient 19 years old. Right eye floating vitreous opacities, diffuse chorioiditis. Left eye, posterior cortical cataract, floating vitreous opacities, and separation of almost the whole lower half of the retina. About one disk diameter up and out from the nerve-head, there is a large area of chorioiditis with marked pigment deposits; several smaller areas in the neighborhood.

V. R. = 2/60, not improved.
V. L. = distinguishes light at 1.5 meters.

Projection faulty. Field of vision in right eye, concentric contraction. White is seen nasally 45 degrees, on the temporal side over 50 degrees, upward and downward 30 degrees.

Hanke,[6] in a case of parathyroid disease (chronic tetany), examined pathologically, found, besides lenticular changes, the extraordinarily rare complication of a postneuritic optic atrophy, and also a very marked degeneration of the pigment layer of the iris which suggested the changes found in diabetes. He attributed

these changes to toxic substances circulating in the blood.

Taking it all in all, I can come to no definite conclusion in regard to the changes in my case. I cannot rule out an intercurrent disease; I cannot prove a toxic cause allied or similar to that of myxedema. One thing seems probable, however, and that is that the process in all probability was not due to hypophyseal enlargement, and I do not believe that the present evidence is sufficient to allow me to agree with Berliner's conclusion in the affirmative.

One final point remains to be considered. How can we explain the two cases reported by Schmidt-Rimpler and Burchard in which central scotomata were observed? There seem to be two possible methods of accounting for them. They may have represented the early stage of a temporal hemianopsia.

Uhthoff[7] has discussed this subject very fully in his "Eye Changes in Disease of the Nervous System," and refers first to the observation of Nettleship[8] on the occasional occurrence in tumors of the chiasm of amblyopia combined with central scotoma as a precursory of a bitemporal hemianopsia. Uhthoff believes these cases to be exceedingly rare, and says that the scotoma shows certain characteristics if carefully measured. In the few cases with which he is familiar, a paracentral scotoma developed which came exactly to the middle line and stretched from here outward. The temporal half of the visual field also showed some peripheral contraction. He pictures such a field (from a case of his own) which developed from a paracentral scotoma to a bitemporal hemianopsia during the course of five years.

A second possibility may be mentioned. The disease in these cases might be due to the same theoretical toxic substances to which reference has been made before, and which, for some reason, on this occasion selected the papillomacula fibers of the nerves.

ABSTRACT OF CASES

Case 1. Schmidt-Rimpler[9] reports a case referred to him by Dr. Betke in which later myxedema developed. In each eye there existed a central scotoma for colors, without any discoverable change in the optic nerves, suggesting a retro-

7. Uhthoff: Graefe-Saemisch Handbuch, Ed. 2, Part 2, p. 1168.
8. Nettleship: Cited by Uhthoff.[7]
9. Schmidt-Rimpler: Die Erkrankungen des Auges im Zusammenhang mit anderen Krankheiten, Wien, 1898, p. 382.

bulbar neuritis in its early stages. Improvement took place under treatment with a thyroid preparation.[10]

CASE 2.—Sanesi[11] reports the case of a man in whom a myxedematous state developed. There was a characteristic infiltration of the skin and lowering of the intellectual faculties, with atrophy of the thyroid gland. Later bitemporal hemianopsia was found, and persistent headaches developed. Sanesi hesitated between a diagnosis of myxedema and acromegaly. Basing the diagnosis on the group of symptoms that appeared first, he declared in favor of myxedema. Some improvement took place, also, on the use of a thyroid preparation.

CASE 3.—Wagner[12] reports the case of a woman, 26 years old, unmarried, who came to him complaining of seeing badly with the left eye for some months, and with the right eye for two weeks. The general condition had been getting poor for more than a year.

She had a bloated face, with large, broad nose, thickened lips and ears, an idiotic expression, and large neck. The backs of her hands were swollen and thickened, and her fingers were thick and stumpy. Everywhere, there was a swelling of the skin; it was dry and could be drawn into folds with difficulty. Intelligence was reduced. Speech was difficult, and on account of the thickened skin, the thyroid gland could not be felt. Urine was negative. There had been amenorrhea for several months previously.

In the right eye, there was an outspoken neuroretinitis with a slight swelling of the disk. Its borders were indistinct, and the vessels somewhat obscured. A small zone around the disk was blurred. Vision equaled 1/10. Field of vision was apparently free.

In the left eye, the nerve-head was white; arteries thin. Vision equaled 1/10, not improved. There was marked temporal hemianopsia.

Wagner made a diagnosis of myxedema, without, however, being able entirely to rule out an acromegaly, as it seemed to him that the border-line between the two diseases could not be definitely fixed. He ordered a thyroid preparation. During the treatment severe headaches set in. Considerable improvement took place. Vision in the right eye improved up to 7/10 and then to normal. In the left eye there was no change.

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10. As this thyroid preparation used is a proprietary which has not been passed on by the Council on Pharmacy and Chemistry, the name by which it is known commercially is here omitted.—ED.

11. Sanesi: Missoedema spontaneo degli adulti, Clin. med. ital., 1899. Cited by Gourfein-Welt.[17]

12. Wagner: Augenerkrankungen bei Myxoedem, Klin. Monatsbl. f. Augenh., 1900, p. 473.

CASE 4.—Burchard[13] reports the case of a woman, aged 23, with no hereditary disease. Menstruation began at 15 years. Five years before, the nose and lips began to swell, and the hands and feet were numb and began to enlarge. Memory was weak; intelligence, as well as hearing and sight, became reduced. There was intense headache; frequent sweating; for two years amenorrhea. The skull was relatively large; the nose enlarged; the lips were voluminous; the mucous membrane of the mouth was thickened and the tongue was large. There was a paresis of the inferior rectus muscle of the right eye. Pupillary reaction on each side was reduced. In the right eye, there was a temporal pallor of the optic nerve-head and a central color scotoma. The patient had almost constant headache. Her temperament was changed; she would sit quietly and was apathetic. Speech was slow; the voice deep and rough. The thyroid gland was palpable. The patient's hands were enlarged, and the skin of the hands thickened, but not dry. The nails were not deformed. The feet were enlarged; the left foot was much larger than the right. Skin seemed edematous, but showed no pitting. The left foot presented the picture of a myxedematous disease. Under thyroidin treatment, this condition of the foot almost disappeared in a month. The other diseased conditions were wholly uninfluenced. Burchard made a diagnosis of acromegaly combined with partial myxedema.

CASE 5.—Bolte[14] reports a case of myxedema with special reference to the nervous symptoms. Anna P., seamstress, born in 1860, came to the hospital Jan. 7, 1909. Patient was scrofulous. First menstruation occurred at 17 years. Some years previously patient had had some sort of cerebral attack from which she got a paralysis and a difficulty of speech which lasted eighteen weeks. Since that time, on different occasions, similar trouble developed. Present attack began with dizziness, twitching of the left and then of right eye, right leg and finally of the left arm. Weakness of the extremities. Since September, 1900, she noticed that her neck was increasing in size. The eyes were protruding. There was frequent insomnia and palpitation of the heart, and she developed forgetfulness and frequent vomiting. She came to hospital on account of severe pain in right temple and eyes.

Skin was pale and dry; mucous membrane anemic. Face had peculiar porcelain-like color; somewhat swollen. Arms and legs had slight elastic swellings. Eyes were somewhat prominent; Graefe's sign present. Pupils were moderate-sized; reacted to light and convergence. There was no regular tremor of the hands, slight tremor of the tongue.

13. Burchard: Ein Fall van Akromegalie kombiniert mit Myxoedem, Petersb. med. Wchnschr., 1901, p. 481. Cited by Berliner.[19]
14. Bolte: Beitrag zur Kausistik des Myxoedems, Char. Ann., 1903, xxviii.

Reflexes were lively. Thyroid gland was somewhat enlarged, especially on the right. The heart was enlarged toward the left. Urine was normal.

January 10, she had a protracted attack of slight twitchings in her left arm. Marked weakness in left half of the face. On the right side, the outlines of the optic disk were blurred and the vessels tortuous.

January 19, she had general epileptiform convulsions.

During the following weeks, very considerable improvement took place from a thyroid preparation.

In July she came in again. Left palpebral fissure was wider than the right. Border of the disk somewhat blurred. Vision was 4/5 in each eye. Field of vision was unchanged.

In September of the following year, she complained of irregular menstruation. In December she had further attacks of twitchings of the extremities. Skin of the extremities became thickened. Palpebral fissures were equal. Optic neuritis was present. Later her hair began to fall out. She had several epileptiform attacks.

On October 20, eye examination showed optic disks on both sides hazy and irregularly outlined. On the edge of the disk irregular gatherings of pigment. Vessels projected forward on disk. Three months later, no sign of optic neuritis could be made out. Vision was 5/7 to 5/5.

The first symptoms suggested exophthalmic goiter, but these soon disappeared and gave way to signs suggesting myxedema. Bolte is inclined to account for all the later symptoms, including the cerebral signs and the amenorrhea, by a diagnosis of myxedema. He cites the improvement under a thyroid preparation as additional evidence. Tumor of the brain (hypophysis?) cannot be ruled out.

Case 6.—Pollack[15] demonstrated at a meeting of the Berlin Ophthalmological Society a girl, aged 9, who had been sick since her sixth year, and in whom he had made a diagnosis of myxedema. Three years previously she had begun to see poorly, and had been treated for optic atrophy during that time. Right vision = hand movements; left = 0. Administration of a thyroid preparation showed extraordinary success. After three weeks right vision was 1/25. Colors were promptly recognized. Weight became reduced. The thickened tongue became normal. Headache and vomiting disappeared. The child felt entirely well.

Case 7.—W. Meyer[16] reported in discussion a case observed by him in Breslau. In a small boy with optic atrophy and a bitemporal hemianopsia myxedema developed. Von Mikulicz found a complete absence of the thyroid gland. Vicarious

15. Pollack: Fall von Myxodem mit Sehnerven-atrophie, Verhandl. d. Berl. Ophth. Gesellsch., Centralbl. f. prakt. Augenheilk, 1905, p. 359.

16. Meyer, W.: Verhandl. d. Gesellsch. deutsch. Naturforscher u. Aerzte zu Stuttgart, 1906, ii, 234. Cited by Berliner (Note 19).

enlargement of the hypophysis was believed to have taken place. A considerable improvement followed the use of a thyroid preparation.

CASE 8.—Gourfein-Welt[17] reported the case of a woman, aged 47, who came for treatment Nov. 9, 1906. She complained of loss of sight for one and one-half to two years. Family history was negative. Patient was married at 20, had three children. Four years previously she began to feel fatigued. There was a noticeable psychic change with loss of memory. She lost her teeth, and her hair began to fall out and became hard and friable. There was growth of hands and feet. Speech was difficult, and the tone of her voice was changed. The face was puffed and enlarged. The eyelids were enlarged; skin dry; tongue of large size. There was no prognathism. Skin of neck thickened. The thyroid gland was not palpable. There were pads of tissue on the clavicle. This was due to thickening of the skin, but not to myxedema. The hands were short; the nails large and breakable. There was slight hypertrophy of heart. Menstruation was regular; reflexes normal. There was polyurics with traces of sugar in the urine.

Left eye was slightly divergent; vision = 0. Slight pupillary reaction to light and consensual reaction were present. The optic disk was discolored. Caliber of vessels diminished.

In the right eye, vision was 1/3, improved to 5/10; good pupillary reaction. Accommodation was normal. The nasal half of the papilla was of same color as the temporal. The vessels were normal. The nasal half of the field was slightly contracted; temporal half, abolished.

Thyroid preparations produced rapid improvement. The state of eyes improved. The vision of the right eye increased from 5/10 to 5/5. The temporal half of the field in the right eye began to return, leaving a large paracentral scotoma. In the left eye, vision in the lower periphery began to improve. There was enlargement of the sella turcica.

CASE 9.—Moore[18] reported the case of a waiter, aged 44. One and one-half years previously he thought that there was a diminution in the sight of the left eye. Nine months later the right began to fail. Patient was sleepy; eyes held half closed. Thyroid present. The face was pale. The skin was dry and thick everywhere, looking edematous, but not pitting on pressure; the mucous membrane of the mouth was thickened. The fingers were thick. There was a tremor of the hands, with increased reflexes. Optic atrophy was present on both sides, much more marked on left than right.

Field of vision could not be mapped out on account of poor vision. Patient could perceive light with left eye, and tell

17. Gourfein-Welt: Lésions ocularies dans le myxoedème spontané des adulters, Arch. d'Ophth., 1907, p. 561.
18. Moore: Myxedema with Optic Atrophy, Proc. Roy. Soc. Med., May, 1908, p. 194.

objects with right. There was improvement under the use of a thyroid preparation.

Case 10.—Berliner[19] reported the case of a woman, M. B., aged 26, who came to the Freiburg Clinic in September, 1908, complaining of loss of vision. Patient was abnormally small and rather stout, with broad face, thickened nose and fat under the lower jaw. The skin of the face was pasty and thickly infiltrated, but did not pit on pressure; it felt dry. The skin of the rest of the body of similar character. The mucous membrane of the mouth considerably thickened. The thyroid gland was small. The heart was enlarged to the right. The urine normal. Knee-jerks weak. Patient gave the impression of being weak-minded; intellectually about 6 years old. She came from a consanguineous marriage. She was always stupid as a child. Diphtheria at 9 years of age. Much smaller than her two younger sisters. Menstruation began at 18 years, irregular. She had had amenorrhea for the last year.

Eye examination showed sluggish pupillary reaction. Ophthalmoscopic examination of the right eye showed the temporal half of the disk porcelain-white; the nasal half still reddish; the vessels small, especially the arteries. The rest of the fundus was normal. In the left eye the whole optic papilla was white and atrophic; the vessels narrow; the fundus otherwise normal.

Refraction 2 diopters myopia. Vision was hard to obtain on account of the mental condition of patient; apparently about fingers at 3 meters in the right; fingers at 1.5 in the left eye.

Under a thyroid preparation general condition improved markedly. At the end of six weeks vision in the right eye equaled 2.5/60; left equaled hand movements close to the eye.

November 12, the vision had risen to: right 2/30, Nieden No. 10 in 15 cm.; left almost amaurosis.

March, 1909, there was a very marked myxedematous appearance. At this time the right disk showed a very distinct temporal pallor. The left showed a complete pallor. Borders of the disk were sharp; caliber of the vessels normal.

V. R. = fingers at 2 meters.
V. L. = fingers close to the eye.

The field showed a slight concentric contraction, probably due to the lowered intelligence of the patient. No hemianopic defect. A thyroid preparation was again ordered.

May, 1909, there was marked mental improvement. Patient was then working in a factory. On this occasion, it was possible to obtain a more satisfactory field. The patient could recognize colors toward the nasal side upward and outward, and not on the temporal side.

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19. Berliner: Opticusatrophie bei Myxoedem, Inaug. Dissert., Freiburg i. Br., 1909.

In June it was possible to learn that she saw better on the nasal side than on the temporal side.

CASE 11.—Souroff[20] reports the case of a woman, A. E., a dressmaker, aged 43, who came for examination Sept. 3, 1908, complaining of weakness of sight in the right eye. Family history was negative. Patient has had typhoid and malaria. The menopause occurred at 29 years of age. Eleven to twelve years before examination patient began to feel weak; she became irritable, suffered from headaches, and the weakness increased. During the last three years the patient's external appearance had changed; there was swelling of the tissues and edema. She tired very quickly; was apathetic, irritable, and always cold. Her speech was slow and stammering; her tongue seemed to be getting thicker. Vision of the right eye had been almost absent for some time, and lately the left had become poor.

Patient was of middle-size. The expression of the face was apathetic and mask-like; the skin of the face and extremities swollen and edematous. The upper and lower lips were edematous. The hands were wide; the nostrils thick. The skin over the wrist and fingers was especially white and thick, but there was no pitting on pressure. The skin over and under the clavicle was swollen and forming pads. The skin was dry and rough. The thyroid gland was not palpable. The hair of the head was dry; easily removed. The teeth were decayed. There was no prognathism. The tongue was thick. The reflexes were slightly exaggerated. The pupils were irregular, the right somewhat wider than left. The right pupil reacted slightly to light. Accommodation was entirely absent.

V. R. = 1/∞
V. L. = 20/70.

Field of vision of the right eye was narrow, only red and white being recognized. The field was contracted in the left eye, from 10 to 15 degrees in all meridians. Perception of colors was normal; refraction emmetropic.

Ophthalmoscopic examination of right eye showed outspoken pallor of the optic disk and narrowing of the arteries and veins. In the left eye there was pallor of the external half of the disk and narrowing of the arteries.

Urine was negative.

The only symptoms which suggested acromegaly in this case were the lengthened face, the somewhat enlarged bones of the lower jaw and the amenorrhea. Under a thyroid preparation she improved. Right vision came up to 1/200; left to 20/40. July, 1909, patient was able to work quite freely, and her general condition was much better.

20. Souroff: A Case of Simple Myxedema Complicated by Atrophy of the Optic Nerve, Westnik. Ophthal., xxvi, 637. I am indebted to Dr. M. J. Konikow of Boston for a literal translation of this article.

Case 12.—Hennicke[21] reports the case of C. V., a man aged 53, school teacher, who came in October, 1907, complaining that he had lost the outer half of the field of vision in his right eye. His face was swollen; the eyelids were thickened; and gait was unsteady. The speech was slow and stumbling. Eye examination showed vision 6/9 in each eye. Ophthalmoscopic examination normal in the left eye. In the right eye, the disk was somewhat reddened and the outlines blurred; arteries narrow; veins normal.

His physician reported that he treated the patient for myxedema for five and one-half years, and during that time there had been marked progress in the disease.

On July 23, 1910, he appeared again, complaining of flashes of light in front of both eyes. Right vision was 6/36; the outer half of the field of vision was completely lacking; left vision equaled 6/12; field of vision about normal. The ophthalmoscopic finding was the same as in 1907. Since 1903, he had been treated with a thyroid preparation which improved his condition. If he did not take it, he was unable to work.

He returned two months later. During this time, the condition of the eyes had become very much worse. Right vision equaled hand movements; left vision, 6/24. In the left side now, the outer half of the field of vision was contracted. The right optic disk was pale; the edges blurred. The arteries could hardly be seen. In the left eye, the disk was swollen and reddened; the edges blurred; and the surroundings of the disk were opaque; the arteries were small and the veins full.

Hennicke advised that the thyroid preparation should be omitted, as he believed that it caused the ocular disease. Patient was placed on Fowler's solution. Under this treatment some improvement took place.

Jan. 27, 1911, right vision was 6/30; left, 6/12. The field of vision in both eyes showed an absence of the outer half of the field. Patient was again taking thyroid preparation. *X*-ray examination was totally negative.

Hennicke is of the opinion that, in this case, it was not the myxedema that was responsible for the disease, but the thyroid preparation. Improvement in the vision took place when this preparation was left off, but the patient's general condition became so poor that it had to be taken up again.

Hennicke based his views on the work of Coppez.

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21. Hennicke: Augenerkrankung bei Myxoedem, Klin. Monatsbl. f. Augenheilk., November, 1911, p. 589.