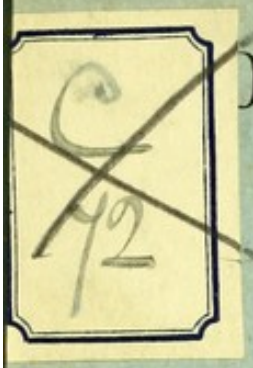
Optic nerve atrophy from toxic agents / by G. E. de Schweinitz.



OPTIC NERVE ATROPHY FROM TOXIC AGENTS.

Read in Discussion on Optic Nerve Atrophy in the Section on Ophthalmology, at the Forty-seventh Annual Meeting of the American Medical Association, held at Atlanta, Ga., May 5–8, 1896.

BY G. E. DE SCHWEINITZ, A.M., M.D.
PHILADELPHIA.

REPRINTED FROM THE
JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION,
OCTOBER 31, 1896.

CHICAGO:
AMERICAN MEDICAL ASSOCIATION PRESS.
1896.

OPTIC NERVE ATROPHY FROM TOXIC AGENTS.

BY G. E. DE SCHWEINITZ, A.M., M.D.

Toxic optic nerve atrophy naturally includes, 1, those cases of atrophy which result from a direct action of the poisonous substance, or its systemic results, upon the nerve cells, the nerve fibers or their vascular supply, and, 2, those cases of atrophy which are secondary to retino-choroidal or constitutional changes, which in their turn have been called into existence by toxic agents.

The first class is separable into three subdivisions, namely, *a*, partial atrophy of the optic nerve with special reference to degeneration of its papillo-macular bundle, *b*, scotomatous atrophy of the optic nerve, which is progressive and may become total, and *c*, general atrophy of the optic nerve.

1. Toxic atrophy of the papillo-macular bundle of the optic nerve preceded by inflammation or degenerative changes in this tract and associated with scotoma.—Cases of this class manifest themselves either in the form of a chronic retro-bulbar neuritis, or else as an intoxication-amblyopia, because we may with propriety draw a clinical distinction between these two manifestions, although anatomico-pathologically they are in close accord, the intoxication-amblyopia, as Groenouw puts it, being a special form of retro-bulbar neuritis.

Axial neuritis, a term sometimes employed, according to the same author, should be reserved for those cases characterized by a lesion, confined to the papillo-macular bundle where it is axial in its course.

Following Groenouw[1], the papillo-macular bundle may be described as consisting of those fibers in the optic nerve which supply the retina between the macula lutea and the papilla, and which lie in the temporal portion of the nerve tip, in a wedge-shaped segment. The apex of this triangular portion is directed toward the vessels and occupies about one-third of the surface of the papilla. As it pursues its way through the orbital portion, it gradually approaches the axis of the nerve, which it reaches in the optic canal. At the foot of the chiasm it occupies its upper and inner portion, but in the tractus it sinks to the central portion and remains there until it arrives at the brain.

According to Sachs[2], the papillo-macular bundle in the papilla is a triangle with its apex at the vessels, and the base toward the supero-temporal quadrant. Going backward, the bundle becomes elongated and assumes a crescentic form as it nears the optic canal.

It would not be profitable at present to discuss the differences of opinion as to the disposition of these fibers in the optic nerve trunk, in the region of the vessel-entrance, and their division in the chiasm. For their full consideration the reader is referred to the examinations of Samelsohn,[3] Vossius,[4] Nettleship and Edmunds,[5] Uhthoff,[6] Bunge,[7] Sachs[8] and Stöltzing.[9]

Upon this papillo-macular tract the baleful influence of certain toxic agents falls, and there result an augmentation of nuclei, a hypertrophy of the connective tissue and a wasting of the nerve fibers, the process being most intense, according to Sachs, in one small

---

1 Graefe's Archiv, 1892, xxxviii, Abth. I, pp. 1-70.
2 Archives of Ophthalmology, 1889, xviii, No. 2. pp. 133-162.
3 Graefe's Archiv, 1882, xxviii, Abth. I, pp. 1-110
4 Graefe's Archiv, 1882, xxviii, Abth. III, p. 201.
5 Trans. of Ophth. Soc. of the U. K. 1881, I, p. 124.
6 Graefe's Archiv, 1886, xxxii, Abth. IV, 95-108, and Ibid, xxxiii, Abth. 1, pp. 257-318.
7 Ueber die Gesichtsfeld und Faserverlauf im optischen Leistung's Apparat, Halle, 1884.
8 Archives of Ophthalmology, 1889, xviii, No. 2, pp. 133-162, and Ibid, 1894, xxiii, No. 4, pp. 426-444.
9 Klinische und Anatomische Beiträge zur Intoxikations Amblyopie. Inaug. Dissert., Marburg, 1893.

area, which he calls the "nuclear group." There is, in fact, an interstitial sclerosing inflammation comparable, according to Samelsohn, to the same pathologic process visible in interstitial hepatitis.[10]

Some difference of opinion exists as to the exact nature of the nerve changes. By certain observers the inflammatory nature of the process has been emphasized; by others (Sachs) its degenerative character. To quote from Sachs, the diseased process starts in the interstitial connective tissue and the nerve fibers suffer secondarily from pressure, in the same manner as the hepatic cells are destroyed in cirrhosis of the liver. The vascular changes of the two affections are also analogous, and, according to Sachs, there may be found "not only a proliferating endophlebitis, leading to connective tissue obstruction of the vascular lumen, but a peri-phlebitis, resulting first in a choking of the peripheral capillaries and afterward in small extravasations from them."

The pathologic lesions thus briefly described are based upon the results of about sixteen autopsies. The most important of these are as follows:

1. Samelsohn:[11] The patient suffered from double retro-bulbar neuritis, which began with the clinical picture of an intoxication-amblyopia, the central scotoma being at first relative and later absolute; death resulted from chronic heart disease. The abuse of tobacco and alcohol was not substantiated.

2. Nettleship and Edmunds:[11] The patient was a diabetic and an excessive smoker. The fields of vision were normal and in each there was a nearly cen-

[10] Recently Nuel (British Medical Journal, Sept. 12, 1896, p. 629) insists that central toxic scotoma is not primarily a neuritis of the macular bundle, but a disease of the macula lutea, causing degeneration of its cells, and that the optic nerve changes are secondary to the destruction of the nerve cells of the macula. Some experimental confirmation of this view may be found in the research of Usher and Dean (Ophthalmic Review, July, 1896), who have observed macular-fiber degeneration follow experimentally produced retinal lesions. Clinically, we know that atrophy of the tissue of the macula lutea, e.g. in atrophic central retinochoroiditis, will cause ophthalmoscopic quadrant atrophy of the disc. As long ago as 1874, Schoen, and later Baer and Treitel, advocated the retinal origin of central scotoma, believing that it indicated a functional weakness of the center of the retina, due to toxic agents.

[11] Loc. cit.

tral scotoma for red. Death resulted from carbuncle.

3. Vossius:[11] The patient suffered from alcohol-amblyopia, had at one time a central scotoma, and died hemiplegic and aphasic.

4. Bunge:[11] The patient was a tabetic and also probably under the influence of tobacco and alcohol.

5. Uhthoff:[11] (Six cases.) The first patient was a chronic alcoholic, with marked blanching of the temporal halves of the papilla, but without record of scotoma, who died from the effects of alcoholism. The second was a patient with atrophic discoloration of the temporal halves of the papillæ, absolute central scotoma, who died in an attack of delirium tremens from intercurrent pneumonia. The third was a patient with atrophy of the temporal halves of the papillæ, who suffered from delirium tremens succeeded by dementia paranoica and died a lunatic. It was not possible to test the visual fields. The fourth was a chronic alcoholic who died of meningitis during an attack of delirium tremens. No visual fields were obtained, but the temporal halves of the papillæ were atrophic. The fifth was a confirmed drunkard, with atrophic papillæ but without demonstrable color scotoma, who died phthisical, and who suffered also from interstitial hepatitis. The sixth was a drunkard with atrophic temporal halves of the papillæ without defect in the color fields, who died of pulmonary edema supervening on general paralysis of the insane.

6. Wildbrand:[12] The patient suffered from polyarthritis and central scotoma which developed suddenly; death resulted from cardiac failure.

7. Theodore Sachs:[13] The patient was an alcohol-tobacco amblyopic, who had typical central scotomata and who died from intercurrent pneumonia during nephritis.

8. Stöltzing:[14] The patient was a tobacco-alcohol amblyopic, who died from pleurisy, fatty heart and atheroma of the aorta; scotomata are not mentioned or described.

---

[12] Bericht über die Versammlung der Ophthalmolog. Gesellschaft, xxii, Heidelberg, 1892, p. 84.

9. Theodore Sachs:[13] The patient was believed to suffer from intoxication-amblyopia, although the abuse of alcohol and tobacco was denied. He had typical scotomata for all colors on both sides; death from pulmonary tuberculosis.

Eight of these fourteen patients had demonstrable central amblyopia and central scotomas. Of the remaining six, in one, although the case is described as an intoxication-amblyopia, the scotoma is not mentioned, and in others either it was not present or the patient's general condition was such that it was not possible to demonstrate it. In all of these, however, the ophthalmoscopic appearances were those usually found with central scotoma.

Alcohol was probably the cause of the optic nerve lesion in seven, alcohol and tobacco combined in two, diabetes and tobacco combined in one, tabes dorsalis associated with the abuse of tobacco and alcohol in one; tobacco was the probable cause in one, although its abuse was denied and the patient died of tuberculosis; in another, although the influence of tobacco and alcohol could not be proved, the clinical symptoms indicated intoxication-amblyopia, and in one the central scotoma existed without such influence. Even in those cases in which alcohol seemed to be the most potent agent, the effect of tobacco could not be entirely excluded. Finally, it will be noted that all of the patients suffered from various types of widespread disease. Therefore we are not actually in possession of the results of an autopsy on a perfectly pure case of intoxication-amblyopia. My endeavors to establish toxic amaurosis in monkeys and dogs were failures, probably because the drug was not continued for a sufficiently long time.

When, however, a definite set of clinical symptoms are taken into consideration, with the results of autopsies thus far recorded, we have reason to believe that the pathologic process which determines an intoxica-

---

[13] Loc. cit.
[14] Loc. cit.

tion-amblyopia is situated in the optic nerve, and especially in that portion which is known as the papillo-macular bundle.

These *clinical symptoms* are as follows: Diminution of sight, associated with fogginess in center of field of vision, unimproved by glasses; reduced acuity of vision, which varies from counting fingers to 20–30 (according to Groenouw from 5–200 to 20–30); pallor of the temporal half of the disc, or of a quadrant-shaped portion of the papilla; normal peripheral boundaries of the field of vision; symmetrical central color scotomas, especially for red and green, usually oval in shape, stretching from the fixing point to the blind spot, and rarely passing much to the nasal side of the former; defective light-sense (Berry, Abney), but according to R. Wallace Henry, normal light-perceptive power.

Of these symptoms the most important is the *central scotoma*,[15] and did time permit, it would be profitable to study in detail its development, enlargement and retrogression, which, as Groenouw remarks, represent a characteristic picture—a picture, moreover, according to Wildbrand, which is analogous to that produced by retro-bulbar axial neuritis, except that in the latter the defect is absolute.

The average size of this scotoma, according to Sachs's measurements of fifty-three fields is out 18 degrees, in 5 degrees, up 7 degrees, down 6 degrees. My own average measurements are out 18 degrees, in 3 degrees, up 7 degrees, down 6 degrees. It is thus, as we see, an oval with its pointed end toward the blind spot and its blunt end toward the fixing spot, to the nasal side of which it passes only slightly.

This scotoma represents a red-green-blind area, and commonly the extent of green blindness is greater than that of red, which in its turn may be surrounded by an area of imperfect color-sense. The "culmination spot," or "nuclear spot," to use the phraseology

[15] Sachs objects to the designation "paracentral," or "central," as conveying a false impression and contends, with justice, for the term "papillo-macular scotoma."

of Sachs, of the scotoma "lies horizontally from 1 degree to 8 degrees in a lateral direction from the fixation point, its breadth, vertically, being mostly below the horizontal line." Sometimes, however, as we know from Groenouw's observations, the beginning is a small, easily overlooked scotoma exactly over the fixing point.

When the typical egg-shaped scotoma is developed which, according to Groenouw, results from the union of the scotoma from the fixing spot with a supplemental scotoma around the blind spot, the process may cease, or there may be a stage of progression, characterized by an increase in the size of the color defect, usually above, until it meets the limit of the red field, *i. e.*, the scotoma has "broken through." If this goes on the patient may eventually resemble a congenitally color-blind person. In severe cases scotomas for blue and yellow form in similar manner to the red-green scotomas, especially, according to Baas,[16] in the period of "breaking through." Finally, small absolute defects may be found, particularly at the "nuclear spot," but also elsewhere, and in neglected cases, or in those not typically toxic, the scotoma becomes absolute.

Instead of the typical egg-shaped or oval scotoma, the visual defect may pass up and out or down and out. Occasionally a circular scotoma surrounding the fixing point has been described, for example, by Nettleship, Nelson and by myself.

In cases supposed to be more purely alcoholic in origin, either in addition to the relative scotoma for red and green, or instead of it there may be, according to Uhthoff, complete or partial peripheral defects for these colors. In rare instances a small central scotoma for blue appears, and exceptionally there are absolute scotomata surrounded by a blue-blind zone and more peripherally by a red-green-blind region, the periphery for white being normal. According to R. Wallace Henry,[17] if the visual field is full, nicotin

[16] Das Gesichtfeld; Stuttgart, 1896, p 164.
[17] Ophthalmic Review, xv, No. 172, 1896.

is the determining cause of the amblyopia; if spirally contracted (a "retinal exhaustion" field), alcohol is the determining factor. A differential diagnosis between alcohol and tobacco cases, based upon the "pericentral" or "paracentral" position of the scotoma, as originally suggested by Hirschberg, has been shown to be inaccurate.

The various drugs and toxic substances which may be responsible for the clinical symptoms which have just been detailed are tobacco, alcohol, either singly or combined, stramonium, cannabis indica, chloroform, opium, cocain (?), bisulphid of carbon, nitrobenzol, arsenic, lead, iodoform, the toxin of diabetes and probably, according to Baas, ioduret and thiuret, two modern antiseptic preparations.

Clinically, at least, tobacco is *facile princeps* of these deleterious agents, although its effect on the system is usually combined with that of alcohol, the relation of alcohol being not only that of an additional poison, but also that of a substance which predisposes the system to the influence of tobacco by depressing nutrition and creating chronic gastritis, because there seems little doubt that the influence of the tobacco is much more potent if the patient is the subject of chronic gastric catarrh. Indeed, Horner at one time believed that this was the sole influence of tobacco. It did not, according to this author, produce the amblyopia, but it created the nutritive disturbances which in their turn were responsible for the visual defects.

Sachs seeks to explain the action of tobacco in relation to toxic amblyopia in the presence of stomachic catarrh by assuming "that certain complex chemic combinations occur chiefly in the stomach and probably result from the transformation of the normal gastric juices into acids of the fatty type, whose compounds with nicotin are either more readily absorbed, or are with greater difficulty eliminated from the system than the simple tobacco bases." There is no doubt that nicotin is neither alone nor chiefly

responsible for the deleterious effects of tobacco upon the visual apparatus, or, indeed, upon the nervous centers generally. It is not unlikely that the nicotin of tobacco smoke is almost completely, if not entirely, decomposed during the combustion of the tobacco, and we must probably look to other compounds, pyridin, collodin, carbonic acid, etc., for influences which have usually been solely attributed to nicotin.

The action of alcohol on the optic nerve is no doubt analogous to its influence on nervous tissue generally and on individual organs, for example, the liver and the kidneys; indeed, we have seen that the pathologic processes are similar.

In the absence of microscopic investigations we assume by clinical symptoms that the other drugs in this list produce a papillo-macular scotoma in like manner. Four of them, lead, arsenic, nitro-benzol and bisulphid of carbon, find their chief subjects among workmen who are engaged in handling these substances. Three of them, cannabis indica, chloroform and opium, to which list perhaps stramonium, arsenic and probably cocain should be added, are potent among drug-drunkards. Three of them manifest their deleterious influences chiefly after absorption through the skin, namely, iodoform, ioduret and thiuret, although iodoform may enter the system by stomachic absorption.

With the exception of cannabis indica, stramonium, opium, cocain (?), iodoform and perhaps some of the cases of bisulphid of carbon and nitro-benzol poisoning, the clinical symptoms of the visual defects of this list of substances are more analogous to those of an axial neuritis than of pure intoxication-amblyopia. This is notably the case with lead.

The prognosis of toxic amblyopia is favorable when only a color scotoma exists and recovery is probable as Groenouw points out, even when small absolute defects are present. In the earlier stages, especially of the tobacco cases, the indications are rather of

vascular disturbance than of true neuritis, or perhaps, as Sachs points out, the alterations do not at first affect the nerve fibers, but merely the areolar septa. The nervous tissue is temporarily injured, and cure is therefore possible. When optic nerve atrophy ensues, we may assume a real retro-bulbar neuritis. Nevertheless there appears to be a type of optic nerve atrophy in which, as Lawford[18] has said, although tobacco may not be the sole cause, it has some share in originating or aggravating the changes in the optic nerve; or again, as Browne[19] has suggested, "there are cases of retro-bulbar neuritis which begin with the ordinary clinical symptoms of intoxication-amblyopia, but which do not tend to recovery, the progression of the central defect indicating that atrophy of the papillo-macular bundle takes place." What is the rôle played by tobacco and the other agents thus far mentioned in these cases has not been positively determined. No doubt recovery or progression of the visual defect is largely determined by the length of time during which the poisonous substance has maintained its influence, as well as by the type of the lesion which it produces, as we shall see in the subsequent sections.

2. Progressive and scotomatous atrophy of the optic nerve the result of toxic agents.—The class of cases included under this heading, and it is not a large one, comprises those in which the symptoms are an absolute central scotoma of the type seen in retro-bulbar neuritis, that is one not typically oval and lying between the fixing spot and the blind spot; a scotoma, moreover, which increases and tends to "break through," joining the outer limits of the form field, which, at first normal, progressively contracts *pari passu* with the enlargement of the central visual defect.

It will be remembered that cases of this character have been dominated "scotomatous optic nerve

---

[18] Trans. Ophth. Soc. of the U. K., 1890, x, p. 166.
[19] Trans. Ophth. Soc. of the U. K., 1888, viii, p. 235.

atrophy," and are said to occur in young men between the 20th and 25th years, often without discoverable cause and with some hereditary tendency. They are similar to the cases which Edgar A. Browne[20] thus describes: "The affection begins in the central tract, but gradually spreads until the whole nerve is more or less involved and atrophy results. Here a distinct personal proclivity is shown in young persons, members of the same family. Whether there is any ascertainable difference between those cases in which tobacco is the exciting cause and those which occur spontaneously requires investigation." They are probably analogous to the progressive scotomatous atrophy which Jensen[21] has described and which has been regarded by him and by others as a particular form of the development of tabetic atrophy. As has been said before, the relation of toxic substances to this form of optic nerve atrophy is uncertain, but a few cases seem to indicate that they may be at least exciting causes. Of those agents already mentioned, tobacco and alcohol are probably preëminent, lead less certainly. Of the others I am unprepared to speak.

3. General atrophy of the optic nerve the result of toxic agents.—General atrophy of the optic nerve as the result of toxic agents may be divided thus:

1. Those cases in which there is a preceding retrobulbar neuritis or neuritis papillo-macularis, with central scotoma, and in which the diseased process has spread from the papillo-macular bundle and the axis of the optic nerve until it has involved the peripheral and intermediary fibers. To these cases I have already referred in the two preceding sections, and have pointed out that they probably may be due to tobacco and more certainly to alcohol and lead. To this class I may add bisulphid of carbon and probably arsenic.

2. Those cases in which there is a preëxisting intraocular optic neuritis, usually of moderate degree,

[20] Loc. cit.
[21] Abstract in Ophthalmic Review, x, No. 3, p. 13.

which is succeeded by an ordinary atrophy, that is, a post-papillitic atrophy. Scotomata are not present in these cases.

The most prominent drugs responsible for this state of affairs are bisulphid of carbon (probably), mercury, iodoform (one case only), and especially lead. Exceptionally subjects of chronic alcoholism exhibit optic neuritis. The same is true of patients who are subjects of the chloral habit. Of all the drugs mentioned the most potent in this relation is lead. For example, in sixty-four cases which I have analyzed there were thirteen with optic neuritis, four with neuroretinitis and seventeen with optic nerve atrophy, while in seventeen cases the patients were stated to be blind without description of the ophthalmoscopic appearance, and no doubt in many of these atrophy or neuritis was present.[22]

3. Those cases in which there is primary atrophy of the optic nerve, that is, an atrophy due to a primary effect of the poison on the visual apparatus without history or signs of preëxisting intra-ocular or retro-ocular neuritis. It is confessedly difficult to maintain this class with exactness, because while the patient may present himself for treatment with complete optic nerve atrophy, there may have been at an earlier stage of his disease an axial neuritis with scotoma or even a general neuritis, neither of which has left signs of its presence.

Of the various drugs which have been named no doubt it would be proper to include in this list those already recited in connection with the previous classification, and we may with reasonable accuracy state that this visual defect is possible under the influence of chronic mercury, chronic arsenic and especially chronic lead poisoning. Referring to the latter I may say that there is certainly an optic nerve atrophy due to the primary effect to lead on the visual apparatus, an atrophy which has been believed by some

---

[22] De Schweinitz: The Toxic Amblyopias; Their Classification, Symptoms, Pathology and Treatment. Philadelphia, 1896, p. 157.

observers, for example, Parisotti,[23] to be due to changes which lead causes in the nutrient arteries of the optic nerve, changes which we know it may cause in the general retinal circulation.

It is probable also that atrophy may occur under the influence of nitrate of silver, in a manner analogous to lead and bromid of potassium. It certainly results from the toxic influence of filix mas, although thus far reports of this condition are largely confined to Japanese literature. A few cases, however, have appeared in French and German reports, and recently filix mas atrophy has been attributed to filicic acid, Van Aubel[24] believing that this agent acts upon the central nervous system, the spinal cord and the sympathetic, causing dilatation of the pupil and through the vaso-motor nerves contraction of the retinal arteries. It is interesting to observe that the blindness comes on acutely, generally after the ingestion of the drug for the purpose of driving out intestinal parasites, and that within a few weeks or even shorter time, the arteries shrink and the discs become pallid and atrophic.

In this particular the drug may be classed with two others that are able to produce what I may call an acute *optic-nerve atrophy*, namely, quinin and salicylic acid, or to speak more accurately, various preparations of the cinchona bark, and the salicylates. The last named drugs, namely, quinin and salicylic acid, produce symptoms so exactly alike that they may be classed together, although the effect of quinin is much more potent than that of salicylic acid.

The symptoms are as follows: Blindness, complete or incomplete, usually developed with great suddenness and more absolute than in any other recoverable condition (Mellinger and Browne); dilatation of the pupils, absence of the light reflex, imperfect response to accommodative effort, nystagmus, proptosis, occa-

---

[23] Rec. d'Ophth., 1885, 3 s., vii, p. 350.
[24] Annales d'Oculistique, T. 114, 1895, p. 400.

sionally divergent strabismus and increased intraocular tension (Tiffany); anesthesia of the conjunctiva and cornea (Voorhies); extreme pallor of the optic discs and diminution of the retinal vessels simulating the appearances of progressive atrophy; occasionally retinal haze and the cherry-colored spot in the macula, resembling embolism of the central artery of the retina; gradually partial or complete restoration of the central vision, associated at first with complete or partial color blindness; later slow renewal of the color-sense, which may ultimately return; more often permanent diminution of the light-sense and color-sense and contraction of the field of vision, the contraction usually assuming an elliptical shape; very exceptionally permanent blindness (Claiborne).

As we know from the experiments of H. Brunner[25] and myself,[26] as well as from those of a recent Italian observer, De Bono,[27] the exact picture of quinin blindness may be repeated in animals, so that there is do doubt as to a selective influence of this drug upon the visual apparatus—an influence, as I have shown in dogs, which extends from the intraocular end of the optic nerve throughout the visual tract as far as this can be traced in the brain. But, even now, the mechanism of the blindness is somewhat uncertain. Probably it depends upon an influence of the drug on the peripheral circulation of the visual apparatus, which produces at first a pure ischemia, later an endo-vasculitis, and still later, as I have further shown, thrombosis in the vessels and extensive secondary degenerative changes in the optic nerve fibers.

Parisotti's idea of the mechanism of primary lead atrophy, to which I have already referred, is similar, namely, that it depends upon changes in the nutrient arteries of the optic nerve. Indeed, the analogy does not cease here, because referring to Sachs's observations on intoxication-amblyopia pure and simple, we remember that he suggests, and in fact demon-

[25] Ueber Chininamaurose. Inaug. Dissert., Zürich., 1882.
[26] Trans. Amer. Ophthalmological Soc., 1891.
[27] Archiv. di Ottal., 1894, ii, pp. 171, 227.

strates, that vascular changes in the diseased tissues of tobacco-alcohol atrophy, producing proliferating endo-phlebitis and leading to connective tissue obstruction of their vascular lumen, are important factors in the anatomico-pathologic basis of this affection.

4. Atrophy of the optic nerve secondary to retinal and other lesions, in their turn the result of toxic agents.—Thus far we have discussed the visual defects caused by an action of toxic substances falling primarily upon the papillo-macular bundle and ceasing at this point, or spreading and involving other tracts in the nerve, or by an action on the entire optic nerve, preceded or not by an intraocular optic neuritis. In a certain number of instances atrophy of the optic nerve is secondary to lesions either in the retina itself, or elsewhere in the body. The cases may be divided into:

1. Those in which the action of the drug has fallen upon the retinal circulation.

Preëminent among substances of this character quinin and salicylic acid should be placed, that is, they should be thus placed if we accept the theories of certain observers in regard to their action, namely, that it is upon the retinal vessels, causing endo-vasculitis and secondary changes. My own observations indicate that they affect the vessels of the optic nerve apparatus especially—perhaps, however, an extension of the original retinal lesion.

2. Those cases in which the toxic agent has produced tissue change, either in the retina or in the retinal vessels.

Preëminent among drugs of this class is phosporus, which early in its toxemia causes retinal hemorrhages and later a fatty degeneration of the retinal tissue itself, which, should the patient live long, would no doubt produce secondary changes in the optic nerve. Probably other poisons, chiefly irritant in their effects, have an analogous action, notably the bichlorid and other soluble preparations of mercury. The influence

of acute poisons upon the retina and the secondary changes in the optic nerve require further investigations. If subsequent investigation substantiate the view that toxic scotoma is caused primarily by degeneration in the macula, tobacco and alcohol would find place in this class.

3. Those cases in which the primary action of the poison falls upon some organ or tissue of the body, causing a disease which in its turn is responsible for a retinal and secondary optic nerve change.

The most notable drug of this class is lead, which, as we know, may produce a nephritis, a neuro-retinitis as the result of this nephritis, and finally optic nerve atrophy. Lead, in like manner, may produce an encephalitis, or a meningo-encephalitis and secondary optic nerve changes. The effect of alcohol upon the meninges of the brain, causing optic neuritis and secondary atrophy, has already been described. Whether the optic neuritis of chloral, mercury, arsenic and nitrate of silver may have a similar origin, I do not know. It seems probable that iodoform may cause meningo-encephalitis and optic atrophy.