The toxic amblyopias : their classification, history, symptoms, pathology, and treatment / by G.E. De Schweinitz.

TOXIC AMBLYOPIAS

BY

G. E. DE SCHWEINITZ M.D.

THE

TOXIC AMBLYOPIAS:

THEIR CLASSIFICATION, HISTORY, SYMPTOMS, PATHOLOGY, AND TREATMENT.

BEING AN ESSAY TO WHICH WAS AWARDED THE ALVARENGA PRIZE OF THE COLLEGE OF PHYSICIANS OF PHILADELPHIA, OCTOBER, 1894.

BY

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

PROFESSOR OF OPHTHALMOLOGY IN THE PHILADELPHIA POLYCLINIC; CLINICAL PROFESSOR OF OPHTHALMOLOGY IN THE JEFFERSON MEDICAL COLLEGE; OPHTHALMIC SURGEON TO PHILADELPHIA HOSPITAL, CHILDREN'S HOSPITAL AND METHODIST HOSPITAL; OPHTHALMOLOGIST TO THE ORTHOPEDIC HOSPITAL AND INFIRMARY FOR NERVOUS DISEASES.

With Forty-six Illustrations and Nine Plates.

PHILADELPHIA:
LEA BROTHERS & CO.
1896.

PHILADELPHIA:
DORNAN, PRINTER.

DEDICATED TO

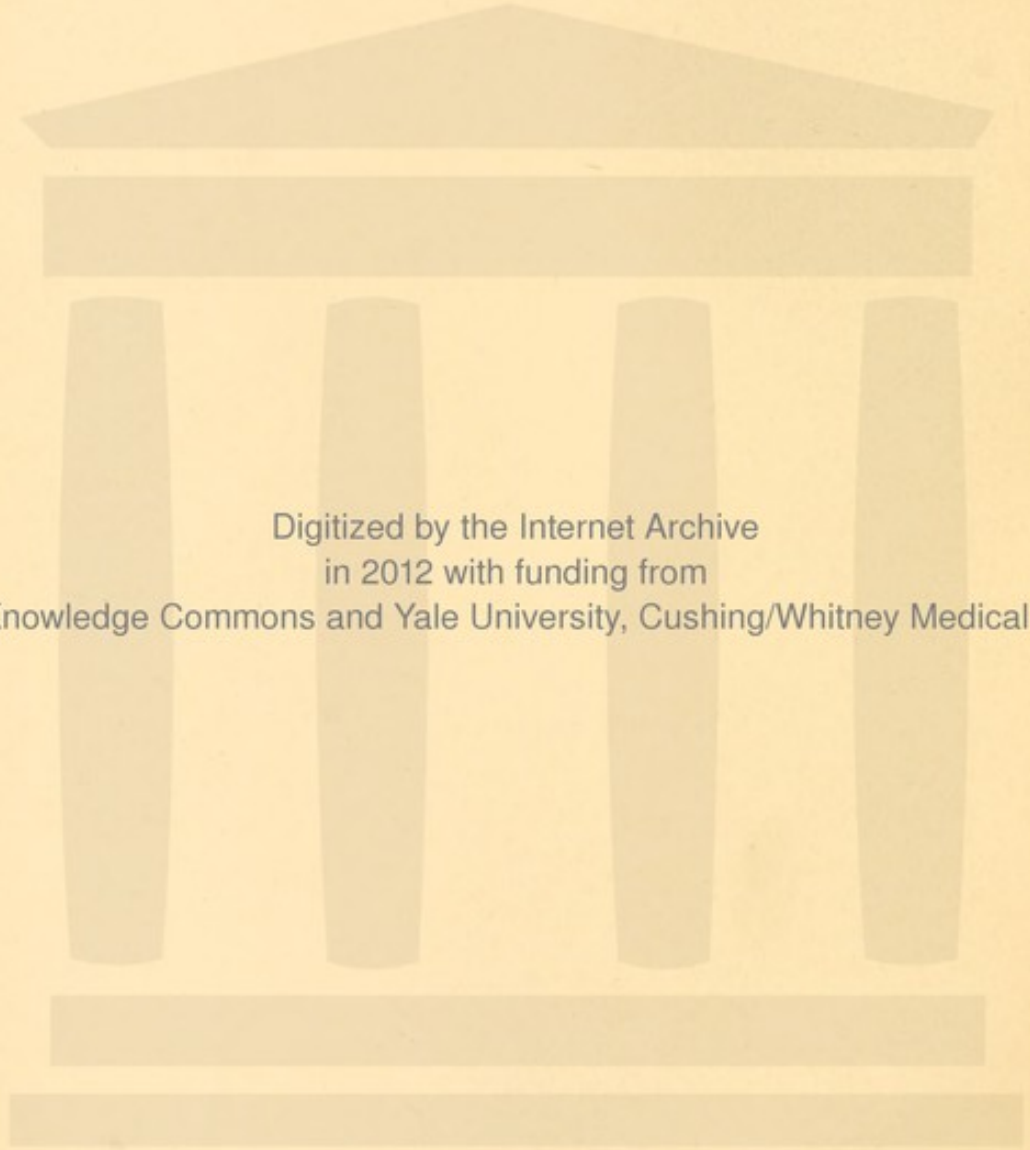
MY

FRIENDS AND COLLEAGUES,

HOBART AMORY HARE

AND

EDWARD MARTIN.



PREFACE.

ALTHOUGH the demonstration of axial neuritis has done much to clear away the fog which prevented the penetration of knowledge into the exact nature of the most important visual disturbances which arise under the influence of certain toxic substances, there are still many facts to be learned in regard to the etiology and pathology of a number of drug-amblyopias, and they furnish an inviting field for study and research. Therefore, a collection of our information with reference to them is desirable. To this end the present essay has been written.

The literature, which has assumed large proportions, has been carefully studied, and as far as possible the references contained in the following pages have been verified and original sources have been consulted. From this study have resulted the paragraphs devoted to the history, etiology, symptoms, diagnosis, prognosis, pathology, and treatment of the various types of visual disturbance which may be caused by drugs and toxic agents.

A considerable amount of experimental work has been introduced, chiefly with reference to alcohol-amblyopia, quinine-, cinchonine-, and salicylic-acid amaurosis, and the so-called filix-mas amblyopia. One of these researches has been published; the others are new.

Some space has been devoted to abstracts of important cases of amblyopia due to alcohol, nitrobenzol, iodoform, and filix mas, because they bear somewhat the same relation to the general

description which the details of physiological experiments do to the conclusions which are reached.

While this essay was in process of preparation three publications bearing upon the same topic appeared: *Les Maladies des Yeux dans leurs Rapports avec la Pathologie Générale.* By Emil Berger, Paris, 1892; *Die Beziehungen des Sehorgans und seiner Erkrankungen zu den übrigen Krankheiten des Körpers und seiner Organe.* By Max Knies, Wiesbaden, 1893; and *The Toxic Amblyopias.* By Casey A. Wood, *Annals of Ophthalmology and Otology,* 1892–94. To each of these sources I am indebted for several facts and references not previously contained in my collection. In the work of verifying references I have received material aid from Mr. Charles Perry Fisher, the accomplished Librarian of the College of Physicians of Philadelphia, and from Miss M. C. Rutherford, the Assistant Librarian.

PHILADELPHIA, 1401 LOCUST STREET, 1896.

CONTENTS.

SECTION IX.

SECTION X.

ADDENDUM.

TOXIC AMBLYOPIAS:
THEIR SYMPTOMS, PATHOLOGY AND TREATMENT.

SECTION I.

INTRODUCTION AND CLASSIFICATION.

In pre-ophthalmoscopic days numerous cases of blindness, of diverse and unknown nature, were grouped under the general term, Black Cataract—the "Schwarzer Staar" of the Germans.

This term practically disappeared after the discovery of the ophthalmoscope, and another name, which, as Groenouw remarks, is equally vague, took its place, viz., "Amblyopia without Ophthalmoscopic Change"—the "Amblyopia ohne Befund" of the Germans.

As skill in using the ophthalmoscope increased, and particularly as the introduction of other instruments of precision, chiefly the perimeter, aided in the study of these cases, fewer examples of ocular disorders were grouped under the "amblyopias without fundus-alterations." Soon a large number, forming the important class denominated, on account of etiological considerations, the "Toxic Amblyopias," received special attention, and their study has resulted in solving many important problems, and has added much to our knowledge of the pathology of the visual tract.

The opening sentence of Leber's[1] article on the toxic amblyopias (Intoxicationsamblyopien) reads: "We include under this name all amblyopias which are caused by the influence of toxic substances." The same definition applies to the present essay, and the words "amblyopia" and "amaurosis," inasmuch as they are etymologically synonymous, both signifying "dimness of vision," are used to describe the various defects of vision called into existence by the poisonous actions of certain drugs and chemical substances, with the understanding that amblyopia denotes obscurity, and amaurosis more or less complete loss of vision. Thus, we usually speak of "tobacco-amblyopia;" but of "quinine-amaurosis."

Classification. Amblyopia and amaurosis are symptoms, and indicate the most evident phenomena of the affections to which these terms are applied. It is the custom to particularize each toxic amblyopia or amaurosis by prefixing the name of the drug which has caused the visual defect; *e. g.*, alcoholic amblyopia. If we were in possession of sufficient pathological data a more scientific nomenclature would be possible, but even then it would be undesirable to dispense with the name of the toxic agent, which bears the same descriptive relation to the disease of the optic nerve it causes, that, for example, "albuminuric" does to the retinitis which is common in chronic Bright's disease.

Several attempts at classification have been made by systematic writers, for example, the separation of these amblyopias into (1) retrobulbar neuritis, and (2) toxic amblyopias—an attempt which would be praiseworthy if our knowledge were sufficient to maintain the distinction with exactness.

[1] Graefe und Saemisch: Handbuch der Augenheilkunde, Bd. v, p. 880.

Others, disregarding all symptomatic or pathological classifications, cut the knot by arranging the drugs in alphabetical order, giving with each a description of its effects on vision. A similar arrangement has been adopted by some authors in works on materia medica and therapeutics; for example, H. A. Hare's *Practical Therapeutics.*

Casey A. Wood[1] suggests, and with good reason, the following classification:

Class I. Poisons that directly affect the optic nerve.

Division 1. Poisons that produce a chronic retro-bulbar neuritis.

Division 2. Poisons producing other forms of optic nerve and retinal disease.

Class II. Poisons whose amblyopic symptoms are unaccompanied by retinal or optic nerve lesions.

Division 1. Agents that produce chiefly mydriasis.

Division 2. Agents that bring about a toxic stage whose chief ocular sign is a contracted pupil.

Division 3. Poisons producing various or irregular eye symptoms.

Max Knies[2] considers it impossible to establish a satisfactory chemical or clinical classification of the poisons in relation to their effects on vision, because substances chemically different may produce singularly analogous clinical pictures, and he therefore adopts the alphabetical arrangement.

Emile Berger[3] has made an effort to classify and

[1] The Toxic Amblyopias: Their Symptoms, Varieties, Pathology and Treatment. Annals of Ophthalmology and Otology, 1892, I, p. 123. Dr. Wood's papers have been collected and published in a separate monograph.

[2] Die Beziehungen des Sehorgans und Seiner Erkrankungen zu den übrigen Krankheiten des Körpers und seiner Organe. Wiesbaden, 1893.

[3] Les Maladies des Yeux dans leurs Rapports avec la Pathologie Générale. Paris, 1892.

gather together those substances which produce somewhat similar effects upon the organism, but has not followed this rule as strictly as the circumstances and present knowledge would permit.

Fully aware of the impossibility of presenting any classification that is free from objections, I have nevertheless, for convenience sake, adopted an arrangement based upon prominent physiological and toxic actions.

I. Drugs chemically diverse and, when given in physiological dose, producing greatly different effects, but when acting as chronic and sometimes as acute poisons, capable of originating definite tissue changes and degenerations, including alterations in the blood:

Alcohol.
Amyl-alcohol.
Methyl-alcohol.

Tobacco.
Carbon Bisulphide.
Iodoform.
Iodine and Iodide of Potassium.
Chlorate of Potassium.
Nitro- and Dinitro-benzol.
Benzine (Petrol-ether).
Hydrocyanic Acid and Cyanide of Potassium.
Nitrite of Amyl and Nitrite of Ethyl.
Coal Tar Products, including Aniline, Naphthaline, Safranine, Fuchsine, etc., Carbolic Acid, Hydracetin, Picric Acid.
Arsenic.
Lead.
Mercury.
Nitrate of Silver.
Oxalic Acid.
Phosphorus.
Osmic Acid.
Chromic Acid.

Sulphuric Acid.
Ergot.

II. Drugs and chemical compounds which in full or toxic doses depress the cerebro-spinal axis or the peripheral nerves:

Chloroform.
Ether.
Ethyl-Chloride.
Methyl-Chloride.
Opium (Morphine).
Chloral.
Sulphonal.
Bromide of Potassium.
Cannabis Indica.
Curare.
Carbonic Acid.
Carbonic Oxide.

III. Drugs which are cerebral stimulants in physiological and nervous depressants in toxic dose:

Caffein.
Thein.
Chocolate.

IV. Drugs which in full dose reduce bodily temperature and in poisonous doses are nervous sedatives, and which may have selective influence upon the organs of special sense (ear and eye):

Acetanilid (Antifebrine).
Phenozone (Antipyrine).
Quinine.
Salicylic Acid.

V. Drugs whose prominent action is concerned with the central organ of the circulation, acting either as stimulants or depressants:

Aconite.
Alcohol (included also in Class I).
Digitalis.

VI. Drugs whose chief effect on the eye is mydriasis:

Atropine.
Cocaine.
Conium.
Daturine.
Duboisine.
Ephedrine.
Gelsemine.
Homatropine.
Hyoscyamine.
Hyoscine.
Scopolamine.

VII. Drugs whose chief effect on the eye is myosis:

Eserine.
Muscarine.
Pilocarpine.

VIII. Drugs whose medicinal use is concerned with the expulsion of intestinal parasites, but when acting as poisons capable of originating diverse visual disturbances:

Filix Mas.
Pomegranate.
Santonin.
Pink-root.

IX. Drugs and poisons not included in the former lists as possessing no definite actions worthy of special grouping:

Aesculin.
Apomorphine.
Chrysarobin.
Cystisin.
Menthol.
Sulphur.
Piscidia.
Podophyllin.
Saponin (From Quellaga Saponaria. Also Saponaria Officinalis.)
Sulphuretted Hydrogen.

X. Ptomaïnes. Meat, fish and sausage poison. Snake poison:

Ethyl-Diamin.
Fungus Poison.
Meat and Fish Poison.
Ptomaines.
Snake Poison.

SECTION II.

DRUGS INCLUDED IN CLASS I, WITH ESPECIAL REFERENCE TO ALCOHOL AND TOBACCO.

AMBLYOPIA FROM ALCOHOL AND THE ABUSE OF DISTILLED AND MALT LIQUORS. (*Amblyopia alcoholica, Amblyopia potatorum, Amblyopia crapulosa, Amblyopia ex abusu.*)

History. Amblyopia as the result of chronic alcoholic intoxication, or from the abuse of alcoholic stimulants, has probably been known for a long time, although in the early days of medical writing it receives very little distinct mention. In 1751 Boerhaave[1] refers to the matter, and in the articles devoted to amaurosis in the writings of Joseph Beer,[2] alcoholic drinks, for example, bitter beer, are placed in the list of those poisons which cause disturbance of sight. In 1837 J. Sichel[3] described the affection with more minuteness, referring to delirium tremens from the abuse of alcohol as a cause of "amblyopia-amaurotica," as well as "irritative amaurosis." The question of alcoholic amaurosis is discussed by Klaunig in 1850, and also in a thesis by Edward Doebbelin, written in the same year. The latter author gives an extensive bibliography, including the earlier writings on amaurosis related to toxic agencies. The most important references in this thesis are here appended for the

[1] Augenkrankheiten. German Translation. Neurenberg. Paragraph 110, S. 12. Cited by Leber.

[2] Lehre von den Augenkrankheiten. Wien., 1813–1817. Bd. 2, p. 499.

[3] Traité de l'ophth. la Cataracte et l'Amaurose. Paris, 1837.

benefit of those who may wish to pursue the history of this subject.[1]

Deval, in his well-known treatise,[2] devotes a chapter to amaurosis from the abuse of alcohol, quoting Giacomini and his observations on the effect of liquor upon the nervous system, including delirium tremens and amaurosis.

In the decade which follows we may refer particularly to the article of Pagenstecher, who cited a number of cases of amblyopia from the abuse of alcohol, but even in the earlier consideration of this matter we are met with the difficulty, which has never entirely disappeared,

[1] *Richter, G. G. C.* Diss. inaug. med. Chir. de Amaurosi, 46 pp., 4to., Gottingae, 1793.

Crampton, John. De Amaurosi, 3 p. l., 31 pp., 8vo., Edinburgi, 1793.

Beer, Georg Joseph. Lehre von den Augenkrankheiten, 2 vols., 8vo., Wien., 1813–1817 (Schwarzer Staar), vol. ii. pp. 419–586.

Juengken, J. C. Die Lehre von den Augenoperationen, xx. 960 pp., 4 tab., 8vo., Berlin, 1832.

Ruete, C. G. T. Lehrbuch der Ophthalmologie für Aerzte uud Studerinde, xvi. 820 pp., 8vo, Braunschweig., 1845 (Abschnitte ueber den Schwarzen Staar); 2 Aufl., 2 vols., 8vo., Braunschweig, 1853–55 (Amblyopie und Amaurosis), vol. ii. pp. 456–479.

Trnka de Krzowitz. Historia amauroseos omnis ævi observata medica continens, 3 p. I., 705 pp. 15 l., 8 vo., Vindobonæ, 1781. (Part 2.)

Ware, James. Observations on the Cataract and Gutta Serena, 3d edition, xvi. 460 pp., 1 pl., 8vo., London, 1812.

Himly, K. Bemerkungen über die Hauptarten der Amblyopie und Amaurose. Ophth. Biblioth., Jena, 1804, ii. 351, 124–141.

Von Ammon, F. A. Klinische Darstellungen der Krankheiten und Bildungsfehler des menschlichen Auges, 3 Theile, in 1 v. fol., Berlin, 1838–41. Th. iii.

Himly, K. Die Krankheiten und Missbildungen des menschlichen Auges und deren Heilung, 2 vols., 8vo., Berlin, 1843 (Der Schwarze Staar), vol. ii. pp. 399–448.

Kieser, D. G. Ueber die Natur, Ursachen, Kennzeichen und Heilung des Schwarzen Staars, 175 pp., 8vo., Göttingen, 1811.

Stevenson, John. On the Nature, Symptoms, and Treatment of the Different Species of Amaurosis, ix., 277, 8vo., London, 1821.

[2] Traité de l'Amaurose. Paris, 1851.

of separating the amblyopia which occurs under the influence of alcohol from that which results from tobacco. The well-known admixture of these two poisons in the system, inasmuch as most drinkers are also smokers, or at least users of tobacco in some form or other, has rendered many writers skeptical on the subject of pure alcohol-amblyopia. For example, Nettleship, Eales of Birmingham, Marcus Gunn, and others, have never seen cases of amblyopia in drinkers who did not smoke, although they are willing to ascribe a certain influence to the alcoholic habit, even if it is not in direct causal relation.

On the other hand, extensive investigations and the reports of cases[1] render it certain that a definite form of amblyopia is caused by alcohol, and is one of the conditions present in chronic alcoholic poisoning, even when this occurs in people who are not addicted to the use of tobacco. The chief research bearing upon this matter is contained in Uhthoff's papers,[2] to which reference will be made more fully in the following pages.

Etiology: Pathway of Entrance of the Poison. Naturally the subjects of alcoholic poisoning are divided into two classes, the *acute* and the *chronic* cases.

In so far as the visual effects are concerned, the acute cases may be dismissed with comparatively short notice, inasmuch as, except in rare instances, the visual phenomena are of temporary character, and amblyopia, if it occurs at all, is exceedingly uncommon. The ocular symptoms consist chiefly in paresis of one or other of the external ocular muscles, occasionally permanent in its results owing to lesions in the nuclear centres, and an

[1] Consult Connor. Journ. Amer. Med. Assoc., 1890, vol. xiv. p. 217.

[2] Graefe's Archiv., 1886, xxxii. Abth. 4, 95–108, and Ibid. 1887, xxxiii. Abth. 1, pp. 257–318.

inhibition of the iris-movements secondary to the deep narcosis caused by the direct action of the drug upon the brain cortex.

Now and then acute alcoholism seems to have been responsible for almost complete blindness without ophthalmoscopic change, rapidly disappearing under antiphlogistic treatment and total abstinence. This was the condition in Deneffe's[1] patient, who indulged in excessive use of whisky for several weeks. Still more remarkable are the cases of ocular lesion which seem to have resulted from the medicinal use of alcohol in the form of whisky. Perhaps the best observed of these cases is the one reported by Knapp,[2] whose patient, aged sixty-four years, took a glass of strong whisky to relieve a diarrhœa from which he suffered, and was immediately troubled with flashes of light and detachment of the lower half of the retina. It should be stated that he was myopic, and therefore predisposed to retinal detachment. According to Mengin, quoted by Knies, *methyl alcohol* taken in a toxic dose has produced blindness within twenty-four hours.

My experimental work on acute alcoholism in rabbits and dogs, undertaken for the purpose of observing whether or not optic nerve lesions could be produced, will be described later, but it may be stated now that the results were negative.

The visual phenomena of chronic alcoholism, or the chronic abuse of alcoholic stimulants, are matters of more moment. It is probably correct, as Fuchs maintains in his prize essay,[3] that two factors are required to

[1] Described by Leber, loc. cit., p. 882.

[2] Archives of Ophthalmology and Otology, 1876, v. p. 32.

[3] The Causes and Prevention of Blindness. Translated by Dr. R. E. Dudgeon. London, 1885, p. 99.

produce chronic alcoholic poisoning, namely, the consumption of a sufficient quantity of alcohol for a long time, and the presence of fusel oil in the drink; that is to say, it is probable that amblyopia, as well as other symptoms of chronic alcoholism, are more likely to occur, as Hutchinson has suggested, when there are impurities in the spirituous liquors consumed, than when they are free from such admixtures. There is not, however, as Casey Wood points out, evidence to prove that adulterations, for example, amylic alcohol, empyreumatic oils, wormwood, oil of juniper, and the like, are of themselves capable of producing alcoholic amblyopia, or, rather, a clinical picture resembling this disease. While the abuse of any liquor containing alcohol is capable of originating visual disturbance, over-indulgence in spirits, in the broadest acceptation of that term (whisky, brandy, etc.), is more likely to be followed by this complication than milder beverages.

The *relative frequency* of alcohol-amblyopia, if it be admitted, and I think it must, as a distinct affection, has been diversely stated.

Galezowski makes alcohol responsible for 1 per cent. of all the cases of toxic amblyopia.

Uhthoff[1] records 204 cases of retrobulbar neuritis, including the toxic-amblyopia-cases examined at Schoeler's Clinic in Berlin, among 30,000 patients. This affection, that is, retrobulbar neuritis, was present in 0.68 per cent. of the cases, while diseases of the retina and nerve in general occurred in about 2.5 per cent. of the cases. The following table, which includes only toxic cases, the disease always being bilateral and the

[1] Loc. cit.

patients males, gives some idea as to the comparative frequency of the causes of the affection there recorded:

Alcohol	64
Alcohol and tobacco	45
Tobacco	23
Diabetes	3
Lead	1
Bisulphide of carbon	2
Total	138

If this table is accepted, it will be noted that alcohol is the most frequent cause of toxic amblyopia, at least as far as Berlin patients are concerned, its frequency being to that of tobacco as 64 is to 23.

But as a reviewer of this paper,[1] commenting upon this table, points out, Uhthoff has classed the cases as alcoholic when there was an evidence that alcohol was taken in excess, while tobacco was used only in moderation. If drink was taken in moderation, and tobacco in excess he classed the case as tobacco amblyopia. In 45 cases he could not decide which agent predominated.

Uhthoff rejects the theory that the combination of alcohol with tobacco tends to act as an antidote to the effect of the latter poison, although, as is well known, some English observers have held a different view. This will be referred to again in the section in tobacco.

For obvious reasons men are more frequently affected than women. The amblyopia is exceedingly uncommon before the thirty-fifth year.

Symptoms. Acute drunkenness, or acute alcoholic poisoning, may be omitted from the present consideration. The rare instances in which this has produced amblyopic symptoms have already been described.

[1] The Ophthalmic Review, 1888, vii., p. 105.

Naturally, the other symptoms are divided into those which are *general* and those which are *special*, *i. e.*, those which concern the visual function. The former include the well-known phenomena of chronic alcoholism, and comprise the various morbid states of the system induced by alcoholic excesses. The most common symptoms are tremor, insomnia, irritability, restlessness, and gastro-intestinal disturbances, or there may be peripheral neuritis, chronic and subacute myelitis, and finally mental deterioration and insanity.

Independently of the ocular symptoms which are more or less characteristic of toxic amblyopia, optic neuritis may develop in the subjects of chronic alcoholism, perhaps as the result of a slight meningitis, which is not an uncommon lesion.

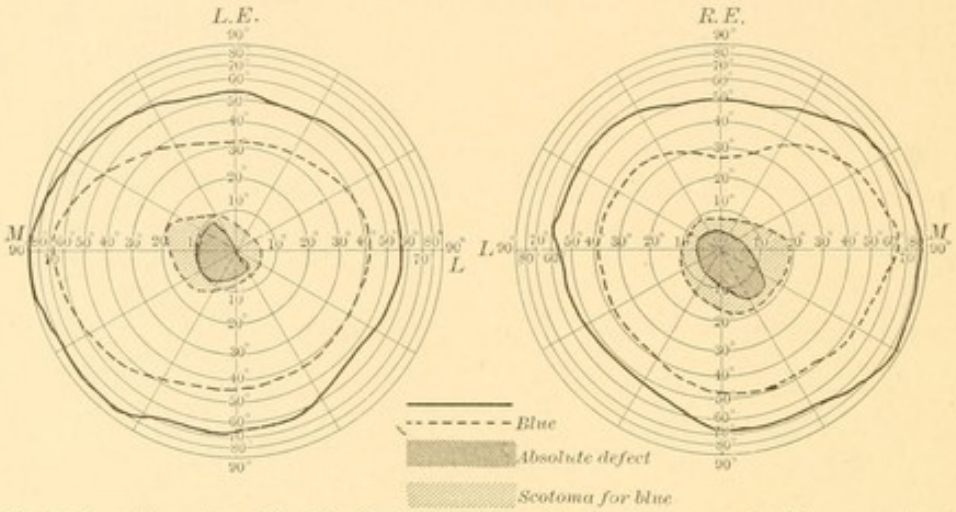
The latter, or ocular symptoms, if we may judge from the investigations of Uhthoff among 1000 patients, may thus be summarized: Pathological whiteness of the temporal half of the optic papilla; occasional haziness of the nerve-head or hyperæmia of its surface; rarely, retinal hemorrhages, and then only in connection with other symptoms, for example, convulsive seizures.

The pathological whiteness of the temporal half of the papilla, or sometimes only of a quadrant in the lower and outer portion, is the most frequent sign, and occurred in 13.9 per cent. of the cases examined by Uhthoff; sixty of these patients had amblyopia. Comparative examinations among lunatics and healthy people, the influence of alcohol being excluded, showed this phenomenon to be present only in very rare instances.

In the earlier stages *a relative scotoma* for red and green is present in the field of vision. Sometimes complete or partial peripheral defects for the same colors are present. In rare cases there may be a small central scotoma for

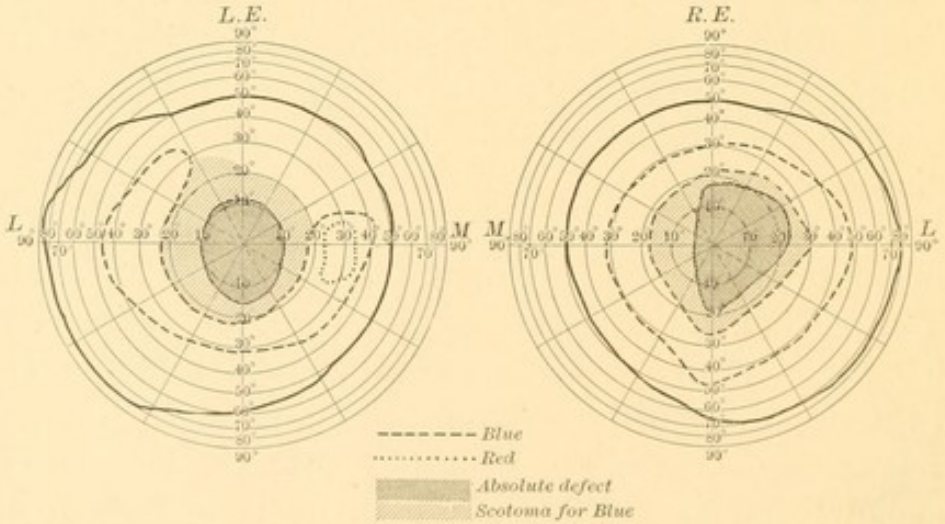
blue, and exceptionally there are small absolute central scotomata surrounded by a blue-blind zone, and more

FIG. 1.



Alcohol-amblyopia. Small absolute central defect, surrounded by a scotoma for blue. (UHTHOFF.)

FIG. 2.

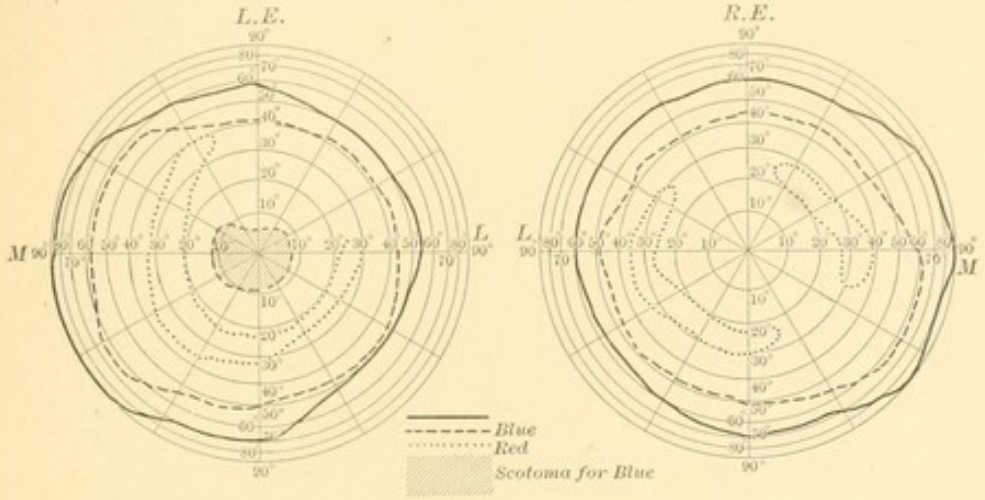


Alcohol-amblyopia. Unusual type, illustrating large absolute central scotoma, surrounded by a scotoma for blue. (UHTHOFF.)

peripherally by a red-green-blind region, the periphery for white being normal. These are the defects of the visual fields, according to Uhthoff, in toxic amblyopias.

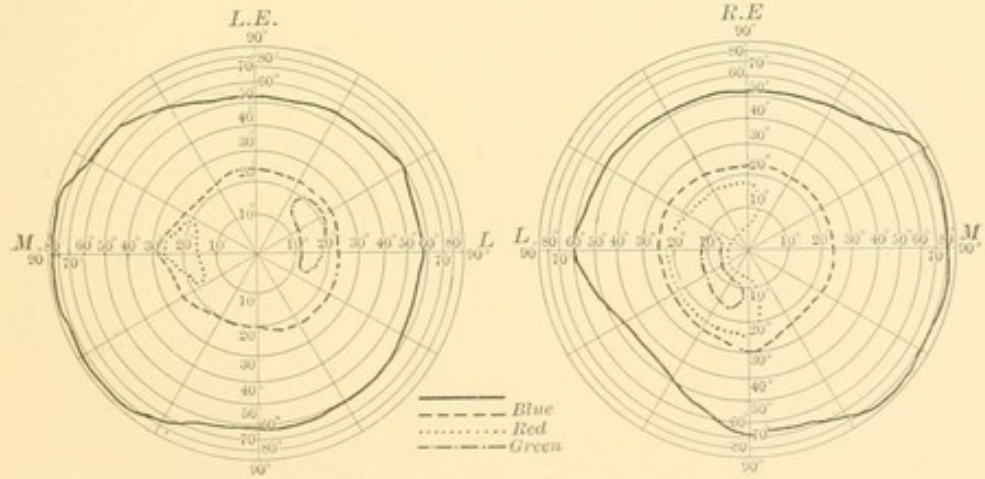
Consult Figs. 1, 2, 3, 4. Other peculiarities are illustrated in the diagrams which follow.

FIG. 3.



Alcohol-amblyopia, illustrating partial red-green blindness and small central scotoma for blue. Green is nowhere appreciated, and red only in the small zones marked with a dotted line. (UHTHOFF.)

FIG. 4.

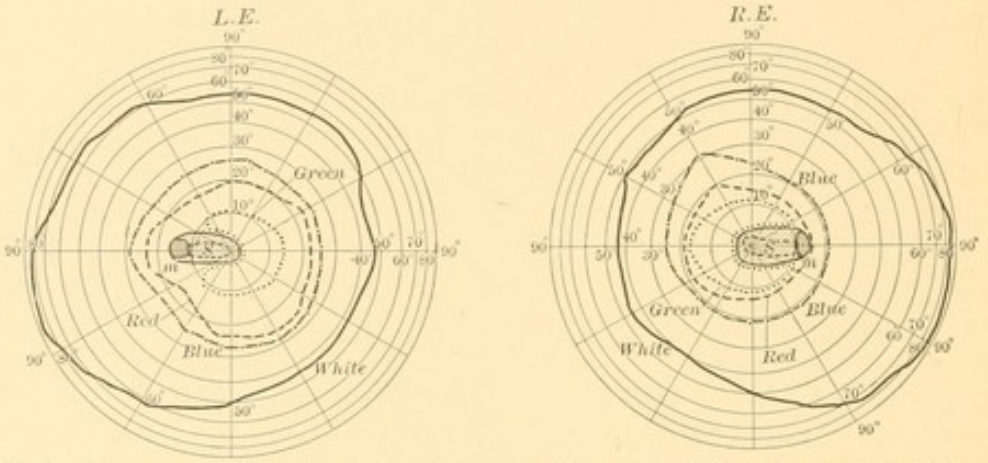


Alcohol-amblyopia. Unusual type, illustrating peripheral contraction of the color fields, without central scotoma. (UHTHOFF.)

Occasionally attempts have been made, especially by Hirschberg, to establish a differential diagnosis between tobacco-amblyopia, alcohol-amblyopia, and the mixed types of the affection by the form of the scotoma. For

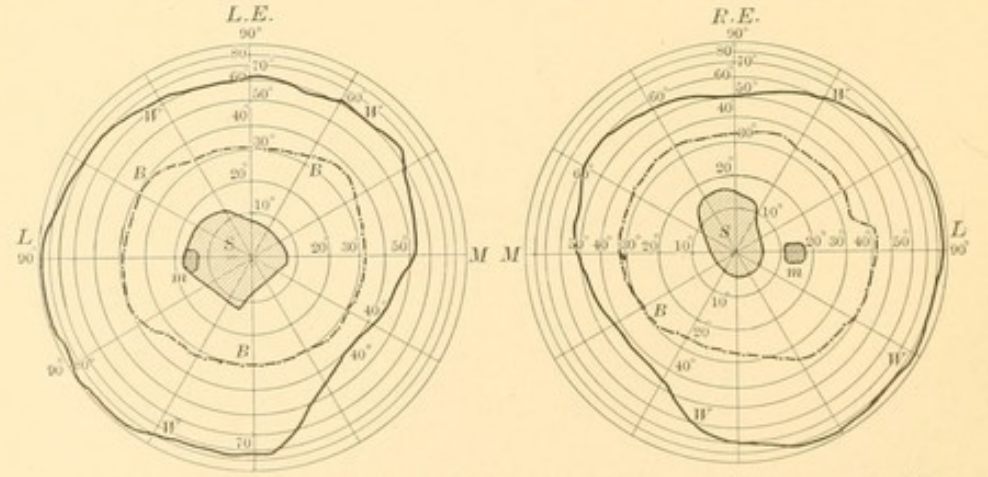
example, in alcohol-amblyopia of a true type the scotoma is *pericentral* in situation, and while the fixation point may not form the mathematical centre of the defect, the

FIG. 5.



Typical paracentral scotoma in tobacco-amblyopia. (HIRSCHBERG.) Compare with Figs. 6 and 7.

FIG. 6.

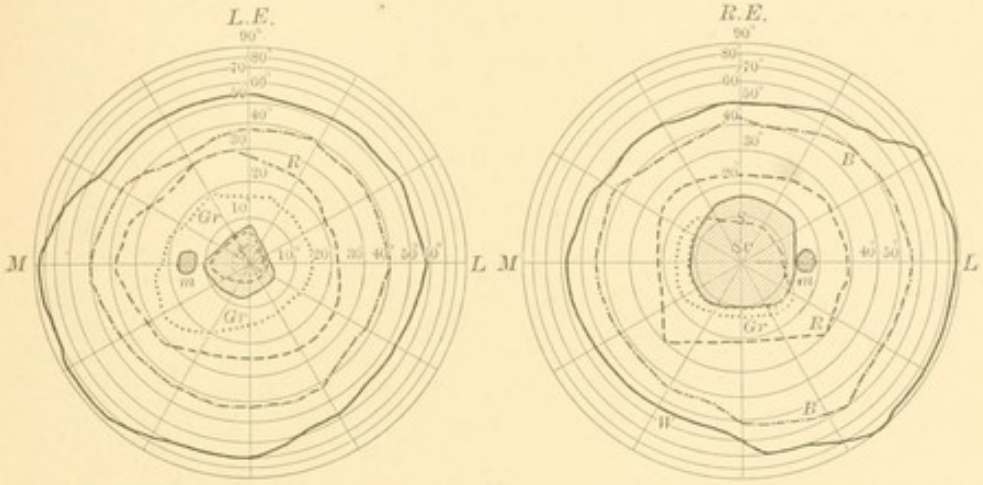


Typical pericentral scotoma in alcohol-amblyopia. (HIRSCHBERG.)

scotoma is not an oval passing from the fixing point toward the blind spot, as it usually is in the tobacco cases. (See Figs. 5, 6, 7.) I shall have occasion to refer to this again when discussing tobacco, but may say at

present that other observers, Uhthoff amongst the rest, have never been able to substantiate this point.

FIG. 7.



Pericentral scotomas in alcoholic-amblyopia. (HIRSCHBERG.)

Visual acuity in alcohol-amblyopia varies with the intensity of the affection, from one-third of normal vision to one-fortieth.

The pupillary phenomena are unimportant, and unless cerebral disease is present, are of no symptomatic value.

Prognosis. The prognosis depends upon three points: the extent of the damage to the optic nerve, the faithfulness with which the patient abstains from the use of alcohol, and the amount of damage either to the general nervous system, or to the organs of the body, for example, the liver and the kidneys. Under favorable circumstances there is no reason why an alcoholic amblyopia should not be cured or improved in the same manner as cure or improvement occurs in other toxic cases.[1] There is more danger, however, that permanent blanching of the optic nerve may remain than in the pure tobacco cases

[1] For anatomical reasons for this consult p. 47.

(in which this is exceptional), or even in the mixed varieties, and atrophy of the nerve may be the final result, even when treatment has been actively carried on.

As an illustration of progressive scotomatous atrophy of the optic nerve, in which the abuse of alcohol and tobacco, but more decidedly the former agent, was the only etiological factor discoverable, the following case, together with the charts of vision, is appended:

Albert F., American by birth, came for treatment, August 8, 1891. In January of that year his vision began to fail, and in three weeks he was unable to read or write. He began vigorous treatment, January 26, under the best advice, and continued it without serious interruption (except one lapse as to smoking) until March, 1892 He had always enjoyed good health. He had smoked and chewed tobacco for a number of years, and used whisky inordinately for six years previous to his attack of amblyopia.

His physical examination revealed the following conditions: A spare, but well-formed man; digestive apparatus in good condition; abdominal viscera normal; pulmonary organs sound; pulse 112; first sound of the heart murmurish, but no hypertrophy; the urine contains neither albumin, casts, nor sugar; the knee-jerk is even and normal in impulse; the reinforcement is prompt.

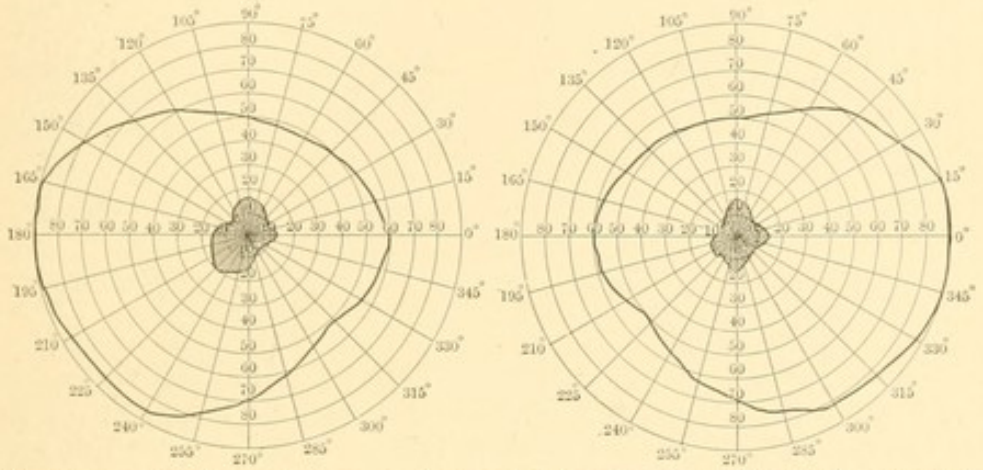
The vision of the right eye equals counting fingers in the upper field; with the left eye he sees movements of the hand.

Right eye. An irregular disk, quite atrophic; small arteries; central lymph sheaths full and veins larger than normal; a faint haze covers the papilla, the nasal half of which is less pronouncedly discolored than the infero-temporal quadrant.

Left eye. The disk is oval; a black line encircles it below; the same atrophic appearances which have been described upon the opposite side are visible.

In the centre of each field of vision there was an absolute scotoma, irregular in outline; the peripheral boundaries of the fields were not far from normal. (Fig. 8.)

FIG. 8.



Absolute central scotomas; peripheral boundaries of the field normal in extent.

The patient was put upon ascending doses of iodide of potassium and strychnine. Later on he took nitroglycerin and also a number of Turkish baths. In September the gloniin was stopped and bichloride of mercury was administered.

On the 21st of this month D = 20 could be picked out when held close to the eye. October 2d vision continued about the same, but a more careful map of the field of vision presented the characters exhibited in Fig. 9 of the series, namely, in the right field an absolute scotoma, surrounded by a broad ring-shaped area in which the loss of the perception of the object was not absolute, and beginning contraction in the supero-nasal quadrant. In the left field there was a central scotoma

as before, which, in the infero-temporal quadrant, joined a wedge-shaped absolute scotoma, in its turn extending into a peripheral contraction of the field of vision.

FIG. 9.

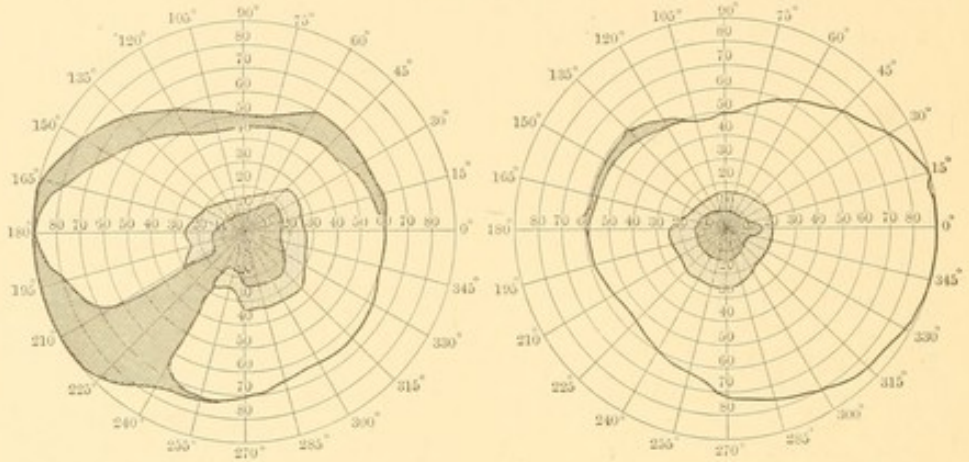


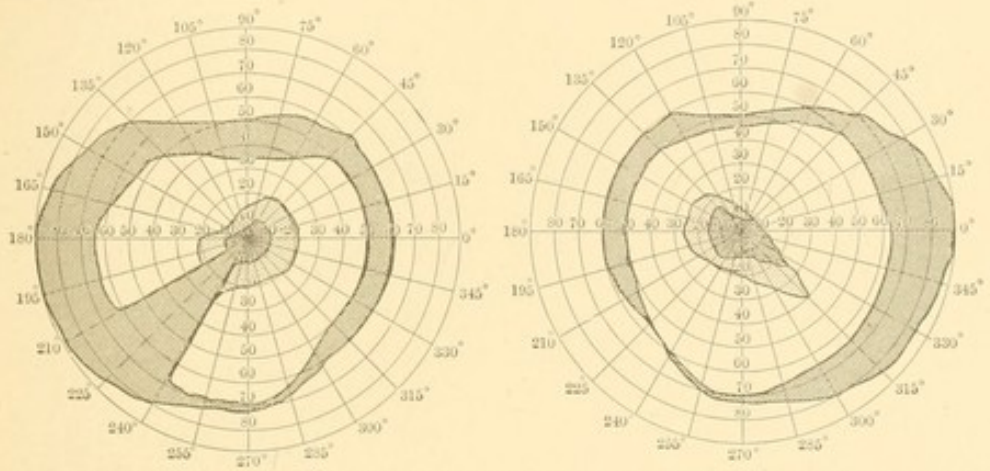
Diagram of the field of vision of the right eye representing an absolute central scotoma surrounded by a broad ring-shaped area of relative scotoma and just beginning contraction of the supero-nasal quadrant. In the left field there is a central scotoma which in the infero-temporal quadrant joins a wedge-shaped absolute scotoma, which in its turn unites with the peripheral obliteration of the field of vision.

The vision from this time altered very slightly; sometimes, according to the light, the patient could decipher D = 20, and sometimes D = 30, by holding the letters very close to his eyes.

On the 24th of November galvanism was advised, and a current varying from one-half to two milliampères was applied three times a week. On the 8th of December he had attended five seances of this character, and the vision equalled D = 18, when the letters were held close to the eyes. On the 19th vision equalled D = 12. On the 31st of December twelve seances had been given, and then the field of vision presented the characters which are seen in Fig. 10, namely, very marked peripheral contraction in the right field where vision had previ-

ously been unaffected, and an irregular, tongue-shaped area of partial scotoma and a somewhat similarly shaped area of absolute scotoma. In the left field there was very decided contraction and the same general character

FIG. 10.



Marked peripheral contraction of the right field of vision previously unaffected; irregular tongue-shaped area of relative scotoma and a somewhat similarly shaped area of absolute scotoma. Considerable contraction of the left field of vision and the same general character of relative and absolute scotoma, the latter being joined with the peripheral contraction of the field of vision. Fields taken after twelve applications of galvanism.

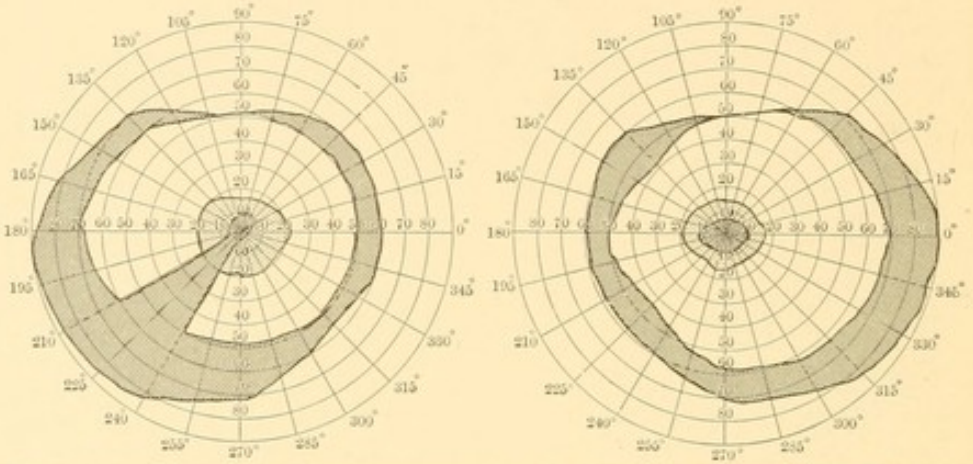
of partial and complete scotoma and the joining of the latter with the peripheral contraction, save only that the central dark area was distinctly smaller than it had been.

The seances of electricity were continued, nitrate of silver was also given, and on the 23d of January the field of vision presented the condition found in Fig. 11.

It will be noted that the peripheral contraction is about the same; that on the right side the central scotoma is distinctly smaller, the area of partial scotoma being about the same size. The vision, however, now equalled D = 10, and the patient declared that the cloud was not so thick.

The field of vision (the electricity still being continued) shows about the same characteristics as those exhibited in the last diagram. See Fig. 12.

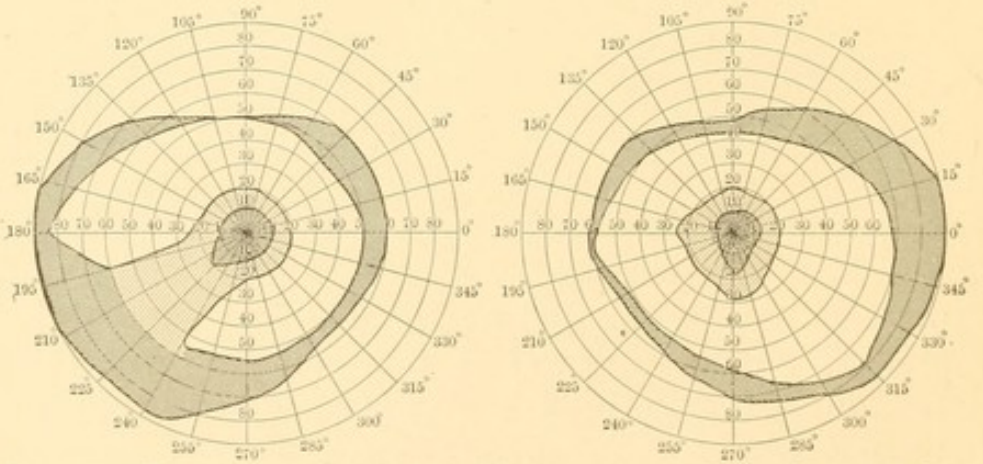
FIG. 11.



Fields of vision taken about one month after those represented in Fig. 10.

One point of interest in this case evidently is whether or not it should be regarded as a case of toxic amblyopia.

FIG. 12.



Diagrams illustrating a later stage of the progress of the disease. Compare with Fig. 11.

There was absolutely nothing in the young man's history to account for optic nerve atrophy except the abuse of

liquor and tobacco, although the condition was practically non-responsive to treatment. Another point of interest is that the remedies employed to improve the state of the optic nerve were ineffectual, namely, iodide of potassium, mercury, very large doses of strychnine sweats, etc., but that galvanism, although there was a progressive contraction of the visual field, appears to have limited the extension of the central defect, and still more interesting is the fact that the eye which in the beginning seemed to be the more affected at the close of treatment appeared to be the one which was regaining some sight.

It is possible that this case should be relegated to those which have been denominated *scotomatous optic-nerve atrophy*, a disease which occurs in young men between the twentieth and twenty-fifth years, often without demonstrable cause and with some hereditary tendency. (An uncle of this young man is said to have been blind from optic nerve atrophy.)

Such cases and others recorded in literature[1] indicate that occasionally blindness occurs in toxic amblyopia even when treatment is instituted early and vigorously prosecuted. Among 2528 cases of blindness[2] of both eyes observed by Schmidt-Rimpler, Stolte, Uhthoff, Hirschberg, Landesberg, Bremer, Seidelmann, Katz, and Magnus, 463 cases were attributed to constitutional diseases, and of these only one case, or 0.039 per cent. is credited to toxic amaurosis.

Pathology and Pathological Anatomy. The lesion which causes the symptoms of a central amblyopia of toxic origin of the type just considered is an interstitial

[1] Compare Lawford: Trans. Ophth. Soc. United Kingdom, 1890, vol. x. p. 166.

[2] Quoted by Noyes: Diseases of the Eye. Second Edition, p. 773.

inflammation, followed by atrophy, of the axial fibres of the optic nerve, and its demonstration, as Noyes observes, forms one of the most interesting discoveries in recent ophthalmology. (*Vide* Plates I, II, and III.)

Von Graefe, Leber, and Förster foretold, or, more properly, surmised, that central scotoma was a symptom of lesion of the optic nerve, but absolute proof of this conclusion was not reached until 1882, when Samelsohn[1] published his now famous paper on the anatomy of retrobulbar neuritis (central amblyopia).

Some earlier but imperfect observations are on record. For example, Erisman[2] examined post-mortem the optic nerves from a case of chronic alcoholism, and found extensive gelatinous and fatty degeneration, and Leber[3] demonstrated degeneration of the optic nerve fibres beneath the sheath of the nerve in a case of chronic alcoholism; but, as Uhthoff observes, neither of these cases is a pure example of intoxication-amblyopia. Therefore Samelsohn's case[4] of a double retrobulbar neuritis, which came to autopsy, is of the utmost interest. The visual disturbance began with the clinical picture of an intoxication-amblyopia, although the abuse of tobacco and alcohol was not substantiated. The relative scotoma for red and green afterward became a larger visual defect, and the final diagnosis was retrobulbar neuritis. Investigation of the optic nerves revealed atrophy of their macular bundles.

Following this case came the observation of Nettleship and Edmunds,[5] who examined the optic nerves of a

[1] Graefe's Archiv., 1882, xxviii. Abth. i. pp. 1–110.
[2] Ueber Intoxicationsamblyopie. Inaug. Dissert. Zurich, 1867.
[3] Loc. cit., and Archiv. f. Ophthalmologie, 1869. Bd. xv., S. 60.
[4] Loc. cit.
[5] Trans. of the Ophth. Soc. of the United Kingdom, 1881, i. p. 124.

patient who had diabetes and who also used tobacco, and found lesions closely analogous to those just described. (*Vide* Plate I.) Next in order is the case of Vossius,[1] probably an example of alcoholic-amblyopia in which the degeneration of the nerve-fibres was similar to that in Samelsohn's patient. In 1884 Bunge[2] described the microscopic lesions of the optic nerves of a case of amblyopia, with relative central color scotomata and perfect discoloration of the temporal halves of the papillæ. The patient was a tabetic, and Bunge regarded the double-sided symmetrical degeneration-processes in both optic nerves as lesions connected with tabes, and consequently as a true gray degeneration. Uhthoff, commenting upon this case and comparing it with one of his own, thinks it likely that there was really a partial interstitial neuritis, and not a partial tabetic optic nerve atrophy. In other words, he believes that the optic nerve lesion was the result of an intoxication influence—tobacco or alcohol—which happened to exist in a tabetic patient.

The observations of Uhthoff are six in number, and include one on a tabetic patient. This author, after referring to the previous literature, insists that his own cases are the only ones in which with positiveness alcohol may be considered as the cause of the pathological change in the optic nerves, although, as we have already pointed out, they were not free from the influence of tobacco. The moderation, however, with which tobacco was used as compared with the immoderate indulgence in alcohol, seems to substantiate his claims.

The following abstracts of his cases submitted to

[1] Graefe's Archiv., 1882, xxviii. Abth. ii. p. 201.

[2] Ueber die Gesichtsfeld und Faserverlauf im optischen Leistungs-Apparat. Halle, 1884.

autopsy are here recorded, together with the illustrations, because they form an important chapter in pathological histology.[1]

Case I. "A male, aged thirty-four years, after several attacks of delirium tremens and severe general symptoms of chronic alcoholism, eventually died of the effects of the poison. During life a marked blanching of the temporal halves of the papillæ was observed, and the patient complained of typical visual troubles (fog, haze, etc.). The visual acuity had improved somewhat during the last months of life. There was no history of any considerable use or abuse of tobacco.

"The microscope revealed degeneration of the whole outer half of the optic nerve, of a conical form, the apex of the cone pointing toward the central vessels; 6 or 7 mm. behind the globe this atrophic area became half-moon shaped; 7 or 8 mm. further back it was an oval, with its long axis vertical, and it gradually shifted more toward the axis of the nerve, till in the canalis opticus it lay nearly centrally. It could be traced up the intracranial portion of the nerve and through the chiasma to the optic tract. The lesion was a symmetrical one in the two nerves. Pathologically the disease was an interstitial neuritis, quite distinct from the appearances seen in simple gray atrophy. The inflammatory changes were found in the whole orbital portion of the nerve, somewhat less intense as they were traced backward, but becoming more marked again in the canalis opticus; from this point backward they assumed more and more the characteristics of simple degeneration. (*Vide* Plate II, 6 and 6 *a*.)

[1] The abstracts of these cases have been taken from Mr. Story's excellent review of Uhthoff's paper, Ophthalmic Review, 1888, vii. p. 100.

Case II. "A male, aged sixty-one years, died of pneumonia during an attack of delirium tremens. He had been for many years an immoderate drinker, but was not known to have been a smoker. Some fourteen years previously his sight had failed, and, though it improved somewhat, it never quite recovered. There was a large central absolute color-scotoma in each visual field, and, ophthalmoscopically, atrophic discoloration of the temporal halves of the papillæ. The microscope showed almost precisely similar changes to those in Case I. (*Vide* Plate III, 7.)

Case III. "A male, aged forty-four years, a heavy drinker, suffered from delirium tremens, succeeded by dementia paranoica, and died a lunatic. It was not possible to test the visual fields, but the papillæ exhibited the typical atrophy of their temporal halves. The changes observed microscopically were similar to those seen in the other cases, but less intense.

Case IV. "A man, aged twenty-nine years, a heavy drinker, died of meningitis during an attack of delirium tremens. No visual tests possible. Temporal halves of papillæ atrophic-looking on ophthalmoscopic examination. Microscopic changes similar to those in Case III, but somewhat more intense.

Case V. "A man, aged thirty-five years, a confirmed drinker, admitted for delirium tremens, had, some fourteen years previously, suffered from "blindness" of five or six weeks' duration. Visual acuity diminished, temporal halves of papillæ atrophic-looking, and in the right eye the nasal side as well. No demonstrable color-scotoma, Pupillary light reflex absent, but contraction with convergence. Died phthisical, with chronic arachnitis, pleuritis, and interstitial hepatitis. Microscopically the optic tracts, the chiasma, and the nerves were normal, except

immediately behind the globes, where an interstitial neuritis was found, as in the other four cases.

Case VI. "A man, aged forty-eight years, after repeated attacks of delirium tremens, died of œdema of the lungs, supervening on general paralysis of the insane. Opthalmoscopically the temporal halves of the papillæ were atrophic, the nasal halves dull and slightly hazy. Six months after this note the left papilla appeared almost normal. No defect in visual fields. Microscopical changes analogous to those in the former cases were found in the optic nerves, but on the right side they disappeared entirely before the nerve left the orbit, and on the left side they did not extend even as far back as the entrance of the central artery.

Case VII. "A man, aged forty-three years, a tabetic case, which was reported at the Heidelberg Congress."[1] (See Plate III, 8.)

The pathological changes in the alcoholic optic nerves were quite distinct from those found in simple gray atrophy as this occurs in tabes and in progressive paralysis. In gray atrophy the connective tissue of the nerve is not thickened, at least in the earlier stages, and its network, except its finest twigs, which are atrophic, appears to be unaltered. In alcoholic neuritis there are thickening and proliferation of these fine twigs. In the later stages of gray atrophy the larger connective-tissue bundles are often thickened, but the original structure of the opticus is always visible; it never suffers complete obliteration of the network and absolute disappearance of the nerve substance, as it does in alcoholic neuritis. In simple gray atrophy again, when it affects only a

[1] Consult Bericht über die Versammlung der Ophthalmologischen Gesellschaft, xvi. Heidelberg, 1884, p. 14.

portion of the nerve, Uhthoff has observed that normal nerve fibres are never found in the diseased area, while they are frequently seen in the midst of the atrophic region in alcoholic neuritis.

There was no evidence of syphilis or renal disease in any of the cases examined by Uhthoff.

An obvious criticism upon these observations is the failure to exclude the action of tobacco, but the great extent of the lesions (general paralysis, etc.) produced by alcoholism renders it probable that the changes in the optic nerves were due to the same poison which had attacked so many other portions of the nervous system.

Wilbrand[1] describes the microscopic examination of the optic nerves of a case of retrobulbar neuritis (male, aged thirty-six years, with polyarthritis; central scotoma developed suddenly; death from heart failure). There was atrophy of the papillo-macular bundle similar to that found in cases of intoxication-amblyopia. The intensity of the diseased process was more developed in some portions of the affected bundle than in others.

Wilhelm Stöltzing[2] has examined microscopically the papilla and optic nerve of a case of tobacco-alcohol-amblyopia, with the result of finding a distinct disappearance of the nerve-fibres in the temporal half of the papilla and also a sector-shaped and later a crescentic

[1] Bericht über die Versammlung der Ophthalmologischen Gesellschaft, xxii. Heidelberg, 1892, p. 84.

[2] Klinische und Anatomische Beiträge zur Intoxikationsamblyopie und Idiopathischen retrobulbären Neuritis, Inaug. Dissert. Marburg, 1893.

In this thesis may be found a brief review of previous microscopic examinations and a clinical report, from the Marburg Clinic, of 9 cases of retrobulbar neuritis, caused respectively by diabetes, exposure to cold, multiple sclerosis, and influenza, and 29 cases of intoxication-amblyopia. Of the latter 4 were due to alcohol, 18 to tobacco and alcohol combined, and 4 to tobacco, although in the last series alcohol could not be positively excluded.

area of degeneration in the outer half of the optic nerve. The microscopic details resemble those described by Samelsohn, Vossius, and Uhthoff.

These various examinations of cases of central amblyopia yield definite information in regard to the fibres which are diseased. The pathway is described thus: "The papillo-macular bundle, according to Bunge's nomenclature, which consists of those fibres in the optic nerve which supply the retina between the macula lutea and the papilla, and are more or less diseased in all of these cases, lie in the temporal portion of the nerve-tip in a wedge-shaped segment. The triangular portion is directed with its apex 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 optical canal. At the front 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. With the entrance of the vessels into the optic nerve-trunk the cross-section of the diseased fibres, according to Samelsohn, quickly, or according to other observers, gradually, presents the form of an oval, reaching from the temporal side of the optic nerve more toward the centre. In the intracranial portion of the optic nerve the bundle first reaches a central position, while in the chiasm and the tractus it occupies the positions just noted. Bunge believes that the papillo-macular bundle divides into two portions in the posterior portion of the chiasm, an upper and a lower part, while Vossius finds this division in the tractus." (See Fig. 14.)

Sachs[1] also has had the opportunity of examining the

[1] Archives of Ophthalmology, 1889, xviii., p. 133.

nerves of a patient who suffered from alcohol- and tobacco-amblyopia, with central scotoma, and gives a somewhat different description of the affected fibres. He represents the diseased bundle in the papilla as a triangle with the 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 optical canal. It lies between the centre and the periphery in the outer and lower quadrant, and just inside the optical canal is situated upon the lower side of the nerve between the centre and the periphery, equalling in length about three-fifths of the nerve diameter.

Some of Uhthoff's specimens, demonstrated by Knapp[1] before the New York Academy of Medicine, and which, by the courtesy of Dr. Knapp, I have had the opportunity of studying, show clearly the central interstitial neuritis in a period of nuclear infiltration and also the stage of connective-tissue hypertrophy. As Knapp has pointed out, the process is characterized by limitation of its area of inflammation, and the circumscribed and triangular portion is visible with the ophthalmoscope as an atrophic patch on the disk. Sometimes the diseased area passes straight across the disk when the tendency of the atrophy is to become general. (Plate III.) The preservation of healthy fibres within the atrophic areas explains, as Knapp has pointed out, why the alcoholic subjects rarely become totally blind, and, on the other hand, why in the visual fields of people blind from retro-ocular neuritis islets of useful sight may be preserved. These Knapp has somewhat poetically called "oases in the desert."

Sachs differs from Samelsohn, Vossius, and Uhthoff

[1] Archives of Ophthalmology, 1891, xx. p. 129.

in regard to the nature of the *nerve-changes.* The last three observers emphasize the inflammatory character of the process, at least so far as its operation in the optic canal is concerned, but Sachs found nothing to justify this supposition in his case, although it was apparent that the atrophy of the nerve elements had reached its highest degree in the optic canal. The preponderance of connective tissue which he found he believed to be the result, not of an interstitial inflammatory hyperplasia, but of a secondary formation due to the collapse and falling together of the connective tissue septa after the loss of the nerve tissue between them.

The *pathological process* found in these diseased optic nerves may start at different points. Samelsohn found in his case that the origin was in the optic canal. In two of Uhthoff's cases the changes in the nerve reached the optic foramen and entered the cranial cavity. In four others they were present only in the distal end of the orbital portion of the nerve at its entrance into the eye, and from six to twelve millimetres posterior to this point.

Sachs has convinced himself that the initial lesion, or beginning of the process, is to be found in the optic canal, from which the intensity of the atrophic changes shades off both toward the brain and the globe.

To sum up: Most of the investigations show that the anatomical basis of this affection consists of an augmentation of nuclei, hypertrophy of the connective tissue, and wasting of the nerve fibres of a limited portion of the optic nerve known as the papillo-macular bundle; in fact, that there is an interstitial, sclerosing inflammation comparable, according to Samelsohn, to the same pathological process which alcohol produces in the liver, for example, an interstitial hepatitis.

PLATE I.

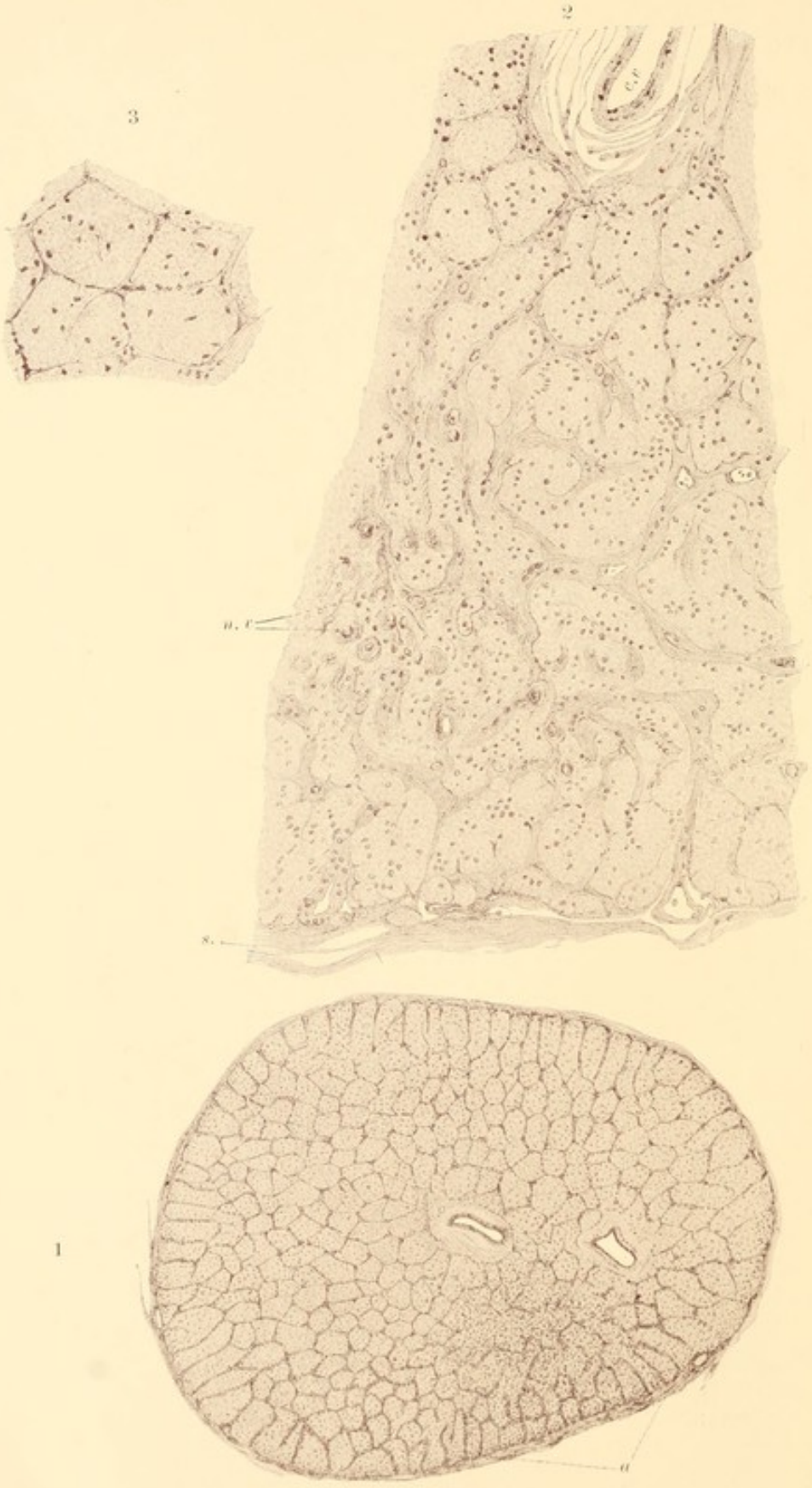
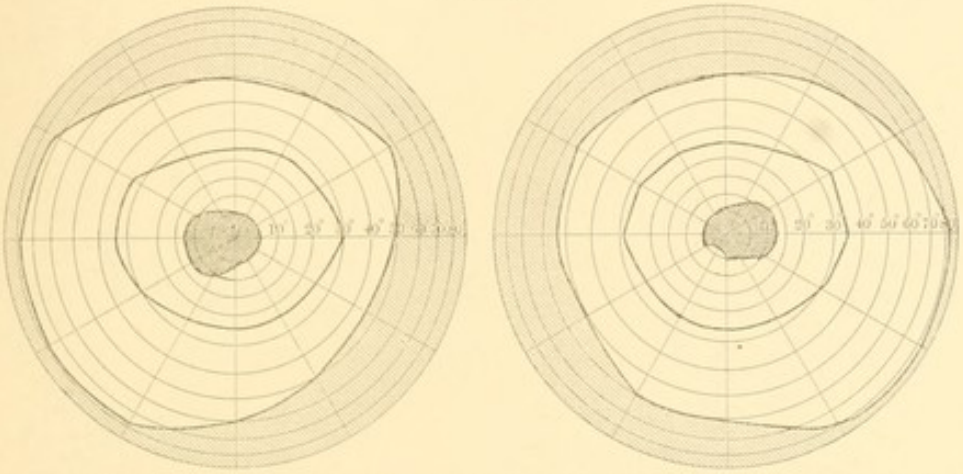


Plate illustrating the microscopical lesions in Nettleship's and Edmunds's case of central scotoma. For explanation see page 49. The numbers and letters on the diagram correspond with those in the text.

The following diagrams illustrate the pathological processes in toxic amblyopia, and should be studied in connection with the text under Pathology and Pathological Histology :

FIG. 13

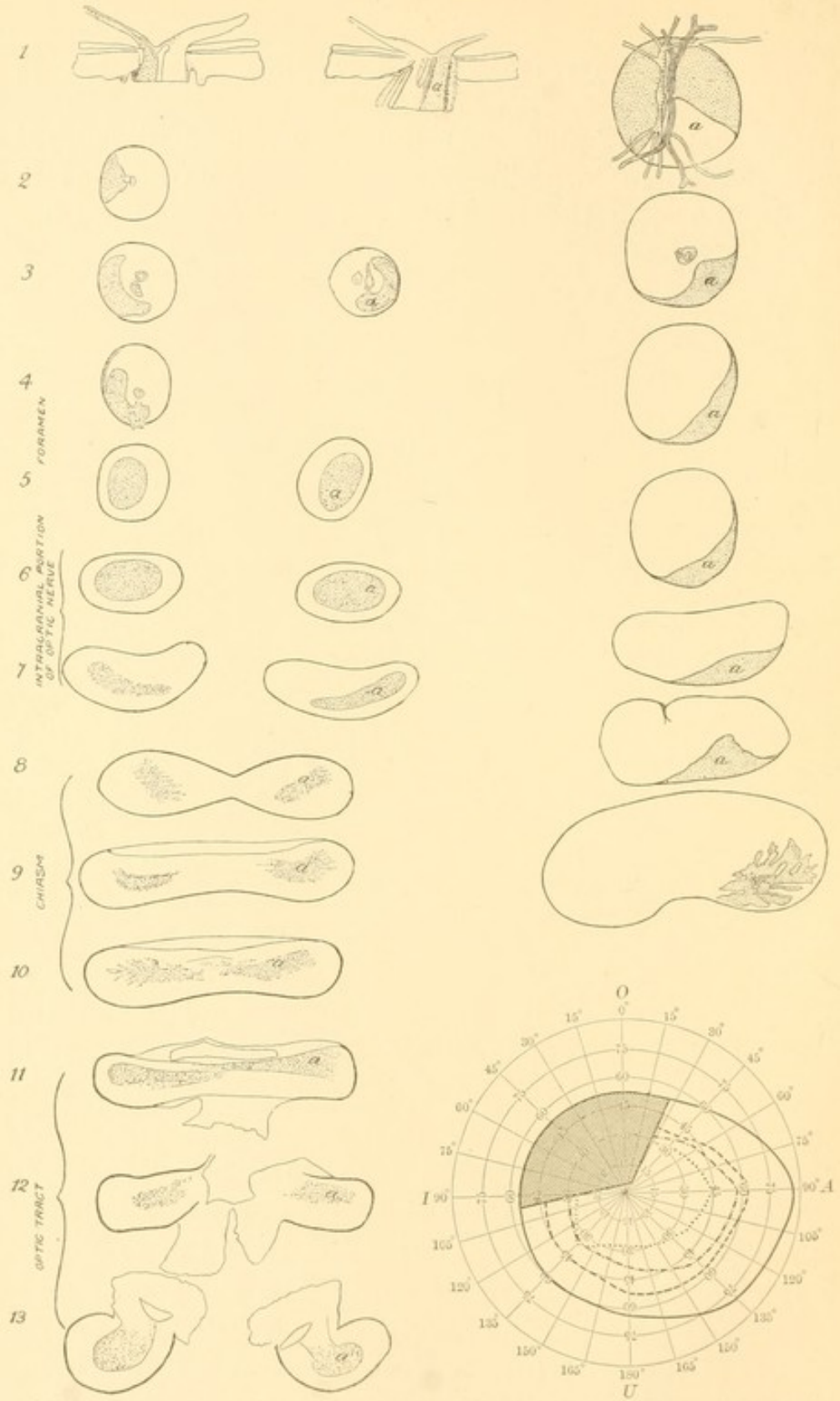


Visual fields of a diabetic, with central amblyopia; patient also smoked. Compare with Plate I. The central shaded area is the scotoma for red. (NETTLESHIP and EDMUNDS.)

Plate I illustrates the lesions found in the case of central amblyopia by Mr. Nettleship and Dr. Walter Edmunds.

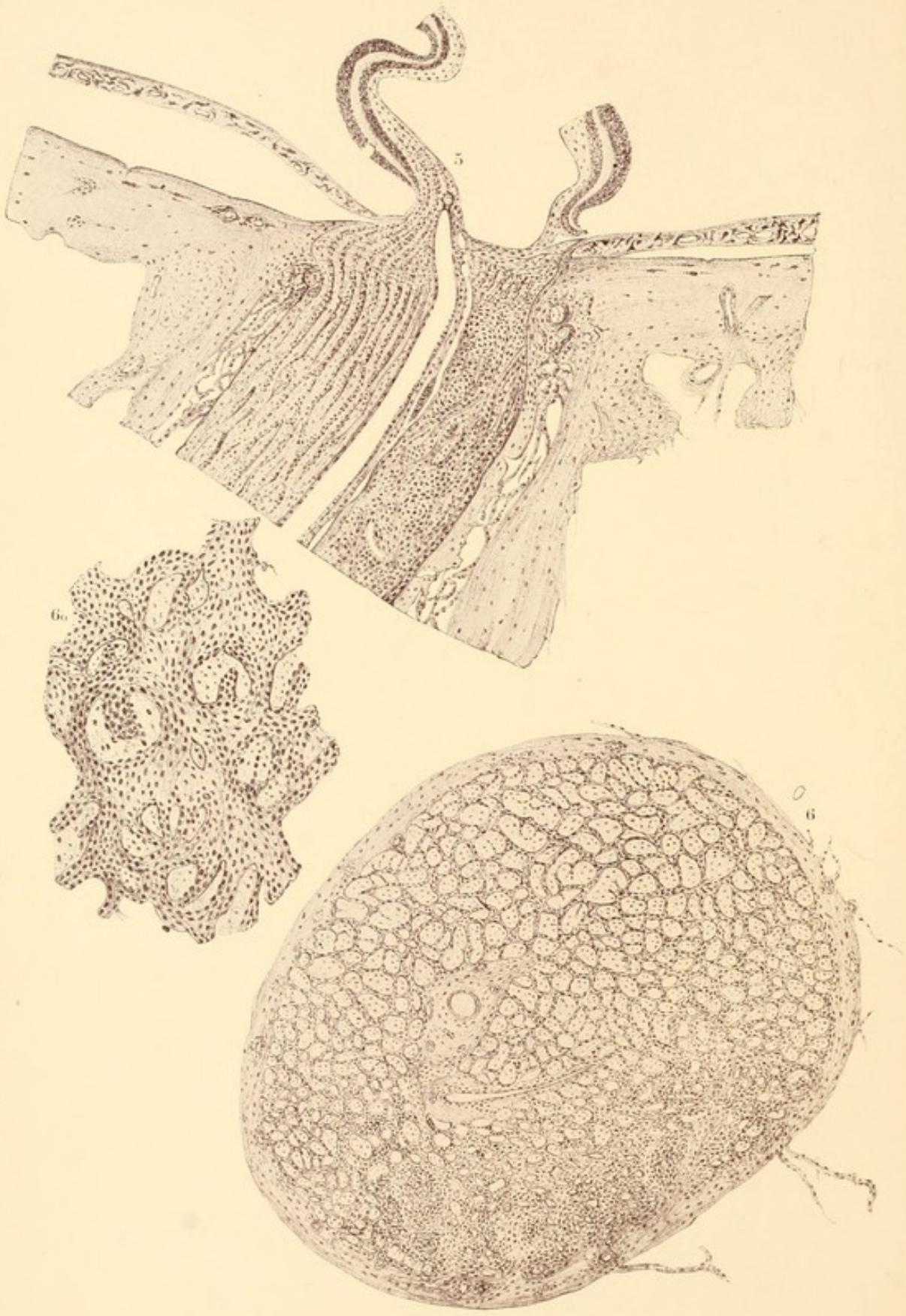
Plate I., fig. 1. Transverse section of the optic nerve a little in front of the point of entrance of the central artery and vein. The outer sheath is wanting. A patch, somewhat sector-shaped (*a*), extending from the inner sheath of the nerve almost to the central vessels, shows a general increase of nuclei both in the fibrous septa which separate the bundles of nerve fibres and in those bundles themselves. The inner sheath at the same part is thicker than at any other part. There is considerable increase of nuclei in the fibrous septa to the left (in the figure) of the patch (*a*), showing probably a commencing invasion of that part of the nerve by the morbid process. × 20.

I. FIG. 14. II.



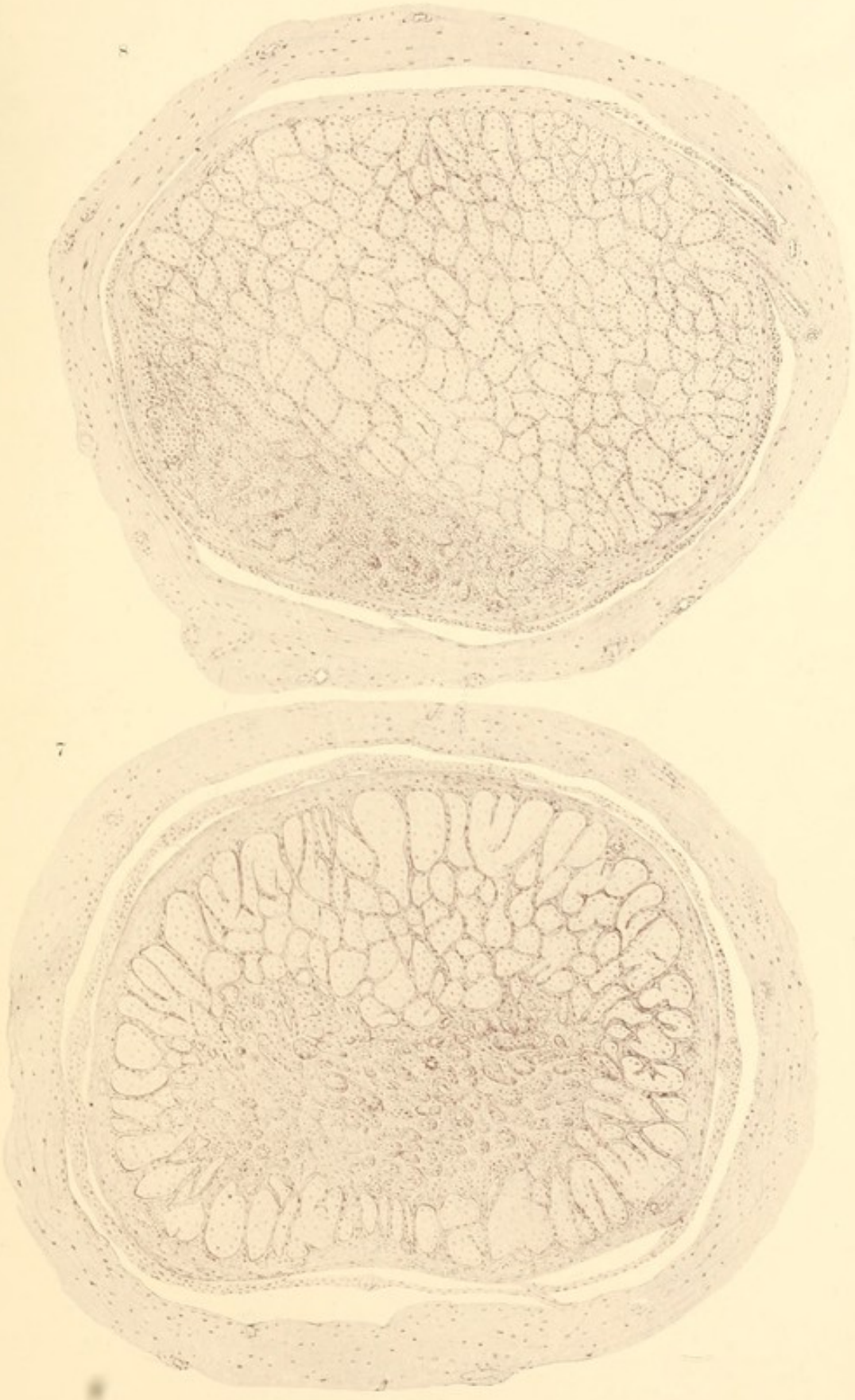
Schema I. Schematic representation of the degenerated papillo-macular bundle in the optic nerve, chiasm, and optic tracts (dark areas represent degenerated portions), according to Case I. of Uhthoff's series. (Compare with Plate III.) Schema II. Schematic representation of the course of the nerve fibres in the optic stem, which comprise its lower and outer portion, and which when degenerated produce a quadrant defect in the visual field, upward and inward—tabes dorsalis, Case 7 of the series. (UHTHOFF.)

PLATE II.



Case 2 of Uhthoff's series. (5) Interstitial degeneration of the outer half of the optic nerve entrance. (6) Case 1 of the series. Alcohol-amblyopia—showing half-moon-shaped neuritic degeneration; ophthalmoscopically the temporal half of the papilla was discolored. (6a) Small portion of degenerated area more highly magnified.

PLATE III.



(7) Case 2 of Uhthoff's series. Oval patch of optic nerve degeneration somewhat eccentrically placed. (8) Case 7 of the series. Partial simple degeneration of the optic nerve in tabes dorsalis. There was a quadrant defect in the visual field, and partial discoloration of the papilla.

Plate I., fig. 2. Part of the diseased sector of nerve rather nearer to the eyeball than Fig. 1, Plate I. × 84. *s.* Inner sheath of the optic nerve. *c, v.* One of the central vessels. *n, v.* Small nutrient vessels of the optic nerve. The fibrous septa are several times thicker than in health (*c, f*, Fig. 3, Plate I.), and many secondary bands, which in health are hardly visible, are so thick as to be very apparent. There is also great increase of fibrous tissue around the minute vessels (*n, v*). There is a decided excess of nuclei, especially in and along the finer fibrous septa, but this is less marked than in sections further from the eye.

Plate I., fig. 3. Small part from the same section near the opposite side of the nerve. The appearances are exactly those of a healthy optic nerve. × 84. (*Trans. Ophth. Soc. United Kingdom*, vol. i.)

In order to determine the exact relation of alcohol to this sclerosing inflammation, or, according to Sachs, degeneration, experimental evidence is desirable. Thus, in Uhthoff's cases, care was taken to exclude syphilis and renal disease, but it was not possible entirely to eliminate the effect of tobacco. The influence of alcohol could be demonstrated if the optic nerves of an animal, otherwise sound, which had been poisoned for long periods of time with alcohol, exhibited disease of the papillo-macular bundle, in other words, adopting Leber's name, *neuritis papillo-macularis.*

With this end in view, I performed the following experiment:

In November, 1892, a small, ring-tailed monkey, weighing eight pounds, was secured, and the daily administration of a definite quantity of alcohol mixed

with a little milk was begun. The animal was sound and each fundus oculi normal.

On November 26, 1 fluidrachm of 95 per cent. alcohol, mixed with milk, was administered, producing marked drowsiness. This dose was repeated on the 28th, with the same effect. On the 29th, 30th, and the 1st, 2d, 3d, 5th, 6th, and 7th of December, 2 drachms daily were administered, on each occasion causing a period of liveliness, followed by drowsiness. This administration of alcohol was continued with as much regularity as possible until June, 1893.

On numerous occasions the typical symptoms of acute drunkenness were produced—a period of exaltation, followed by staggering, incoördination, and finally deep sleep, and on two occasions a coma so pronounced that it was feared that death would ensue. After each of these excesses several days elapsed before it was possible to induce the animal to touch the drug again, and success was achieved only by starving him into subjection.

It is impossible accurately to estimate the exact amount of alcohol administered, owing to the fact that some of the milk-punch was spilled It may be stated, however, that, from the 26th of November, 1892, to the 1st of June, 1893, there was an average administration of 1 drachm daily of alcohol, or, in other words, about 187 drachms of 95 per cent. alcohol, or nearly 24 ounces. During this period there was no evidence of failure of sight, either by the ordinary tests or by ophthalmoscopic examination. Toward the close of the experiment, in the latter part of May, ulcerations appeared around the roots of the nails, which gradually became misshapen and dropped off. It was, however, impossible to tell whether this was induced by the action of the drug, or whether the monkey had in some way injured these structures.

In the early part of June the animal was killed, and the following organs were removed for microscopic examination: The eyes, optic nerves, chiasms, optic tracts, entire brain, and the radial and ulnar nerves.

These were placed in Müller's fluid and sections prepared. They were stained with carmine and Weigert's stain, but evidences of inflammation or degeneration were entirely lacking in the optic pathway from the nerve entrance to the cortical centres. The radial and ulnar nerves showed no special changes, and it may be broadly stated that the results, except in some minor details not relevant here, were negative.

I have performed many experiments on animals with alcohol, but have never been able to discover the least ophthalmoscopic or microscopic change in the optic nerves. If success is to be achieved in this line of research the effect of the alcohol must be greatly prolonged.

The *differential diagnosis* between alcohol-amblyopia and tobacco-amblyopia, and the relation of these conditions to non-toxic retro-bulbar neuritis, are deferred until the conclusion of the consideration of tobacco in its relation to visual defects.

The treatment of intoxication-amblyopia (alcohol and tobacco) will be recorded at the end of the section on tobacco.

AMBLYOPIA FROM THE ABUSE OF TOBACCO (*Tobacco-Amblyopia; Nicotine-Amblyopia*).

History. As early as 1792 Beer appears to have been acquainted with some form of tobacco-amblyopia (see p. 58), but the first scientific statement in regard to the deleterious influence of tobacco upon visual acuity probably originated with Mackenzie in 1832, and in the third

edition of his text-book[1] he writes as follows: "I have already had occasion repeatedly to hint my suspicion that one of the narcotico-acrids, which custom has foolishly introduced into common use, namely, tobacco, is a frequent cause of amaurosis. A majority of the amaurotic patients by whom I have been consulted have been in the habit of chewing, and still oftener of smoking tobacco, in large quantities. It is difficult, of course, to prove that blindness is owing to any one particular cause, when perhaps several causes favorable to its production have for a length of time been acting on the individual; and it is especially difficult to trace the operation of a poison, daily applied to the body for years, in such quantities as to produce at a time only a very small amount of deleterious influence, the accumulative effect being at last merely the insensibility of a certain set of nervous organs. At the same time we are familiar with the consequence of minute portions of other poisons, which are permitted to operate for a length of time on the constitution, such as alcohol, opium, lead, arsenic, mercury, etc., and we can scarcely doubt that a poison so deleterious as tobacco must also produce its own peculiar injurious effects."

J. Sichel,[2] who after Mackenzie first studied tobacco-amblyopia, maintained that few men could consume more than 20 grammes of tobacco per day, *i. e.*, in a year $14\frac{1}{2}$ pounds, without deleterious effects upon vision.

In 1863 Jonathan Hutchinson,[3] in England, investigated the matter most carefully, and collected statistics[4]

[1] A Practical Treatise on the Diseases of the Eye, 3d Ed. London, 1840.

[2] Soc. méd., Chir. de Paris, seánce du 23 Février, 1863. Annales d'Oculistique, 1863, l., p. 83.

[3] Lancet, London, 1863, ii., 536–538.

[4] Med.-Chir. Journ. London, 1867, i., 411–429.

showing the relation of tobacco to amblyopia; indeed, his contributions should be regarded as among the most important which have been published on the subject.[1]

Graefe,[2] in 1865, referred to cases of central scotoma, the periphery of the field being relatively normal, and quoted as causes of this condition the irrational use of alcohol and frequent smoking of strong cigars, regarding the latter, in the majority of cases, as of only collateral importance.

Two years later Friedrich Erismann[3] gave a very good description of the intoxication-amblyopias, and, as we know from the previous section on alcohol, he had the opportunity of making one of the earlier examinations of the optic nerves under these conditions. He ascribed the cause of this degeneration of the optic nerves to tobacco, alcohol, and sometimes to both drugs.

In the next year Förster[4] published an account of the affection, and in his article in Graefe and Saemisch's *Handbuch der Augenheilkunde*, vol. vii., pp. 201–205, we find a clear account of the visual disturbance occurring under the influence of chronic nicotine-intoxication and chronic alcoholism, and especially a description of the characteristic scotoma for red, of more or less constant form, which is found in the centre of the visual field, the periphery of which is unaffected. He regarded tobacco as an important cause of amblyopia in persons suffering also from the effects of depressed nutrition.

Leber,[5] discussing the anomalies of color-sense, refers to intoxication-amblyopia and central scotoma, and

[1] For additional papers by Hutchinson, see Bibliography.

[2] Vorträge aus der v. Gräfe'schen Klinik zusammengestellt und mitgetheilt von Dr. Engelhardt. Klin. Monatsbl. f. Augenheilk., 1865, iii., p. 151.

[3] Ueber Intoxicationsamblyopie. Inaug. Diss. Zurich, 1867.

[4] Ueber den schädlichen Einfluss des Tabakrauchens auf das Sehvermögen. Jahresbericht der schles. Gesellsch. f. Vaterland. Kultur pro. 1868, p. 183.

[5] Graefe's Archiv, 1869, xv. 3 Abth., pp. 1–25.

regards the blanching of the temporal half of the optic nerve as indicative of the condition. He sought to explain the scotomas by assuming a perineuritis of the optic nerve, because he believed the fibres which supplied the centre of the retina were situated in the periphery of the optic nerve, an idea which later investigations have shown to be inaccurate. Leber also discusses the matter in his well-known chapter: "Die Krankheiten der Netzhaut und der Sehnerven."[1]

In 1874 Schoen[2] strongly advocated the retinal origin of the central scotoma of the amblyopia of intoxication. The almost constant form of the visual defect and its tendency to retrogression led him to believe that the scotoma was the functional expression of a physiological weakness of the centre of the retina, heightened by chronic intoxication. Somewhat similar views were also advocated by Treitel and O. Baer.[3]

In 1878 Hirschberg[4] undertook to establish a differential diagnosis between tobacco- and alcohol-amblyopia by the shape of the central scotoma, believing that in the tobacco cases the scotoma was paracentral and in the alcohol cases pericentral. (Compare with pp. 32 and 33, and with Figs. 5, 6, and 7.)

Nettleship[5] was the first observer in England to draw accurate attention to color-scotomas in central amblyopia.

After this time the literature rapidly increased, and numerous papers appeared with reference to intoxication-amblyopia, which was ascribed sometimes to alcohol, sometimes to tobacco, and sometimes to both drugs.

[1] Graefe und Saemisch, Handbuch der Augenheilkunde, Bd. v., pp. 880–886.

[2] De Lehre von Gesichtsfeld. Berlin, 1874, p. 116.

[3] Ueber Gesichtsfeld-messung und deren Allgem. diag. Bedeutung. Volkmannsche Vorträge, No. 246, S. 29.

[4] Deutsch. Zeit. f. prakt. Med., 1878, pp. 193, 205.

[5] St. Thomas's Hospital Reports, 1879.

Thus far clinical observation had demonstrated that intoxication-amblyopia might occur under the influence of tobacco as well as of alcohol; that tobacco was a very important agent in many of the cases, and probably the only factor in numerous others; that the amblyopia was practically always bilateral; and that the chief clinical characters of the affection consisted in blanching of the temporal portion of the optic nerve, preservation of the periphery of the visual field, and the formation of a color-scotoma between the blind spot and the fixation point. Most of the authors referred the lesion to some defect in the fibres of the optic nerve.

We now come to that period in which the interesting investigations of Samelsohn, Nettleship and Edmunds, Vossius, Bunge, and Sachs demonstrated in cases of intoxication-amblyopia the lesions in the *papillo-macular bundle*, which have been fully and thoroughly described in the paragraphs relating to alcohol-amblyopia.

The whole subject has recently been reviewed in a masterly manner by Groenouw,[1] who argues strongly in favor of the potent influence of tobacco. He analyzes the literature of the subject to the end of 1889. I desire to acknowledge indebtedness to this paper, from which I have frequently quoted in the preceding section.

ETIOLOGY: PATHWAY OF ENTRANCE OF THE POISON. *Acute Tobacco Poisoning.* If the drug has been consumed in any considerable dose, the results are usually so quickly fatal that visual phenomena are not likely to arise. Sometimes, however, sudden blindness may take place in acute tobacco-intoxication, as, for example, in Kosminsky's[2] patient, who suffered from blindness after

[1] Graefe's Archiv, 1892, xxxviii. Abth. 1, pp. 1–70.

[2] Quoted by Leber, loc. cit.

the application of tobacco to a hollow tooth, and in a case of tobacco-poisoning recorded by J. B. Wilkinson,[1] which followed an enema of this drug. I have experimentally proven that acute poisoning, either from nicotine or fluid extract of the Virginia leaves, does not produce demonstrable lesions in the optic nerves of dogs and rabbits.

Chronic Tobacco Poisoning. Amblyopia, of the type at present under discussion, occurs only after tobacco has been used for long periods of time, and may ensue no matter how the tobacco is introduced into the system. Most frequently it is caused by smoking strong tobacco, either in pipes or in cigars. Perhaps with nearly equal frequency, although it is difficult to obtain statistical information on this point, it may arise from excessive chewing of tobacco.[2]

It least commonly occurs from taking snuff.[3] Casey A. Wood[4] has been unable to find the report of a case of amblyopia from this cause. He attributes the comparative immunity, under these circumstances, to the fact that snuff is much poorer in nicotine than natural leaf tobacco.[5]

"Dipping," or the habit of rubbing snuff upon the

[1] Medical Chronicle, 1888–89, p. 472.

[2] A. M. Ramsay, Lancet, London, May 11, 1895, has never seen a case of tobacco-amblyopia in a patient who chewed but did not smoke.

[3] Consult Berry: Trans. of the Ophth. Soc. of the United Kingdom, 1887, vii., p. 92. See Nettleship on the Influence of Snuff. Ophthalmic Hospital Reports, 1886–87, xi., p. 70.

[4] Loc. cit.

[5] The following interesting statement is recorded by Beer in his "Lehre der Augenkrankheiten," Wien., 1792, Zweiter Theil, p. 66: "Gradual withdrawal of the humors of the body, as, for example, the spittle in tobacco-smoking, and the nasal mucous through the abuse of snuff, can slowly cause black cataract (Schwarzer-Staar)." He then quotes the case of a fifty-year old woman who "got a complete black cataract solely from the abuse of snuff."

gums with a brush or chewed stick, and which is said to be a practice confined to certain women of the poorer class in the south of the United States, has been supposed by Minor and others not to cause tobacco-amblyopia. Wood, however, has found some cases on record, and in one instance described by Blitz,[1] a woman, aged thirty-five years, became nearly blind from "dipping" a large quantity of snuff. G. P. Hall[2] contributes a typical example of the affection in a woman, aged forty years. In one eye the atrophy of the disk was complete; in the other recovery of vision took place after the patient ceased using snuff.

Finally, amblyopia may occur in those who do not use tobacco in any form, but who work in tobacco manufactories. I have seen a very remarkable case of this character in a young woman. There was pallor of the optic disk, some contraction in the size of the arteries and a scotoma for red and green. All of these symptoms disappeared when she was removed from the tobacco factory. Dowling[3] has made some interesting investigations in the tobacco manufactories of Cincinnati. He examined 150 employés, forty-five of whom showed more or less evidence of tobacco-amblyopia. Of the women examined none were affected except one, aged forty years, who presented well-marked tobacco-amblyopia, and who had been working in the factory for five or six years, but had never used tobacco. Dowling at first believed that inhalation of the dust and the odor of tobacco might cause the amblyopia, but doubts this later, because those who did not smoke or chew were almost uniformly free from visual disturbances.

[1] Journ. of the Amer. Med. Assoc., 1890, xiv.

[2] Internat. Med. Mag., 1894–95, iii., 178–181.

[3] The Cincinnati Lancet-Clinic, 1892, xxix., pp. 585–590.

The quantity of tobacco which is likely to be followed by deleterious effects varies. J. Sichel, who, it will be remembered, after Mackenzie, first studied tobacco-amblyopia, maintained that few men could stand more than 20 grammes of tobacco a day; that is, in the year about 14½ pounds. Now, as, Hirschberg points out, a half dozen cigars in a day are not usually considered an excessive quantity. This would make 2190 cigars in a year, and as 100 cigars generally weigh from 500 to 750 grammes, this would amount to at least 21 pounds a year, or 50 per cent. over Sichel's maximum dose. Hirschberg, therefore, regards 30 grammes a day as the maximum dose, but Groenouw[1] believes that 15 grammes daily, or about three cigars during the waking hours, is the maximum quantity which is absolutely safe. In Hutchinson's cases, so carefully examined and recorded, shag tobacco, that is, tobacco cut in fine shreds and probably very strong and often of inferior quality, was usually consumed and generally in quantities of more than 15 grammes a day. Berry[2] states that the amount of tobacco which causes amblyopia varies from 1 ounce to ½ pound or more weekly.

Hirschberg makes some interesting calculations based upon the amount of tobacco which is imported and used in Germany, showing that about 2.4 to 3 pounds are consumed per head, while in Great Britain 1.2 pounds, and in France and Austria 1.7 to 1.8 pounds per head are consumed. Calculating the amount according to the people who smoke, 10 or 12 pounds of tobacco come yearly to each smoking German.

A good deal depends upon the *quality*, as well as the

[1] Loc. cit.

[2] Trans. Opthalmological Soc. United Kingdom, vol. vii., p. 91.

quantity, of the tobacco which is smoked. Thus, as has been pointed out by Fuchs, the cheaper sorts of tobacco contain more nicotine, and consequently are more deleterious. Therefore we see more tobacco-amblyopia among poor people. However, it has also been noted that very excellent tobaccos may produce the same effect. The percentage of nicotine in tobaccos varies considerably. According to the analysis of Orfila, Havana tobacco contains 2 per cent., Maryland tobacco $2\frac{1}{3}$ per cent., Virginia tobacco $6\frac{9}{10}$ per cent., and Alsatian tobacco $3\frac{3}{10}$ per cent. of nicotine.

A. H. Allen[1] writes concerning this point as follows: "According to Schloesing dried French tobacco contains 5 to 8 per cent. of the alkaloid, Virginia and Kentucky tobacco 6 to 7 per cent, while Maryland and Havana tobacco contain only about 2 per cent." One analysis (authority not stated) declares that Turkish tobacco contains only 0.75 to 1.25 per cent. of nicotine. (Compare with p. 66.)

In addition to the quality and quantity of the tobacco, a very important factor, as pointed out by Cohn,[2] is the *weight of the cigars* which are smoked. Thus, a patient smoked twelve or fifteen Havana cigars daily without trouble, but the same number of Holland cigars produced visual disturbances. Cohn analyzed the two brands, and found that the strong Havana cigars, which the patient smoked without harm, contained 2.02 per cent. of nicotine, while the light Holland cigars, which caused his amblyopia, contained only 1.8 per cent. of nicotine. The reason, however, became evident when the cigars were weighed, the Havanas weighing 4.7

[1] Commercial Organic Analysis, vol. iii., Part II., 1892, p. 192.

[2] Lehrbuch der Hygiene des Auges. Wien., 1892.

grammes and the Hollands 9 grammes, so that, in spite of the consumption of the same number of cigars of each variety during a day, the patient nearly doubled the quantity of nicotine, consuming with the Holland cigars 1.944 grammes, and with the Havana cigars 1.142 grammes.

It is important to ascertain *the method of smoking or using tobacco* and the *time of the day* at which the habit is practised. Many patients confess that the tobacco has been smoked while the stomach was empty; others that the smoke has been inhaled, and thus has come in contact with a large surface for absorption. The danger of inhalation is well illustrated by a case of tobacco-amblyopia, caused by cigarettes, described by Groenouw.[1] The patient did not drink, but smoked at the time he presented himself for examination about eight cigarettes a day. Before this time he had for several years smoked from fifty to sixty cigarettes daily, and always had inhaled the smoke.

In all cases it is necessary to take into consideration the *idiosyncrasy* of persons toward tobacco. As Berry remarks,[2] "Any one with any experience of smokers must have been struck by the different degrees in which different men are affected by tobacco; how some never smoke any but mild tobacco and seldom, except after meals, whereas others smoke the strongest tobacco atany time of the day. The fact of such idiosyncrasy being a matter of daily experience, is strongly suggestive of most cases of tobacco-amblyopia being found amongst the former class."

The relation of nicotine to the production of this amblyopia is a question of much interest. According to clin-

[1] Loc. cit.

[2] Royal London Ophthalmic Hospital Reports, 1880–82, x., p. 47.

ical observation, when the percentage of nicotine is high, for example, in tobacco of inferior quality; or, when more nicotine is consumed, because of the greater weight of the cigars, amblyopia is more frequent. But the great volatility of nicotine, and the numerous other substances present in tobacco-smoke, many of which are distinct poisons, indicate that nicotine is not alone responsible for the deleterious effects on vision.

In cases of general tobacco poisoning there is very little doubt that the constitutional disturbances are not due only to nicotine. For example, Le Bon has found prussic acid, and Vohl, Eulenberg, and Zulinsky have separated from tobacco-smoke pyridine, picoline, lutidine, parvoline, collodine, rubidine, viridine, in addition to carbolic acid and marsh gas. Krause states that cyanogen is also present. The individual compounds, except pyridine, have not been very thoroughly studied. Even when deprived of nicotine this group may cause contraction of the pupil, dyspnœa, general convulsions and death. Pyridine has been carefully investigated, and in large doses has been shown to be a respiratory paralyzant and depressor of the spinal cord.[1] A. Maitland Ramsay,[2] after referring to Brunton's observations that the poisonous effects may be produced by the volatile alkaloids formed during the combustion of tobacco, as much stronger tobacco can be smoked in the form of a cigar than in a pipe, writes: "Cigar and cigarette smokers are probably more exposed to the risk of nicotine poisoning than others, and possibly their comparative immunity arises from the fact that 'according to Vohl and Eulenberg, the tobacco which is smoked in a pipe yields a very much larger pro-

[1] Consult editorial in the Therapeutic Gazette, 1892, xvi., p. 36, by H. A. Hare, on the "Toxic Properties of Tobacco."

[2] Loc. cit.

portion of volatile bases, and especially a larger quantity of the very volatile and stupefying pyridine, while in a cigar little pyridine and much collidine is formed, the latter being less volatile and active than pyridine.'"[1]

In the face of these facts it is idle to maintain that nicotine is either alone or chiefly responsible for the deleterious effects of tobacco upon the visual apparatus or the nervous centres generally, and I venture to predict that future investigations will show that some of the principles mentioned are concerned in the development of so-called tobacco-amblyopia.

The relation of alcohol to central (toxic) amblyopia has been discussed and reference has been made to the vexed question whether there is a pure alcohol-amblyopia and a pure tobacco-amblyopia, or whether the so-called intoxication-amblyopia always indicates a mixed influence. At one time alcohol was given the first place in etiological relationship to central amblyopia, and in France the inclination to hold to this view of the case still obtains among many writers. At the present time, even in Germany, tobacco is regarded as the more potent agent, and most observers are in accord with the statement that cases of central (toxic) amblyopia from which the influence of tobacco can be excluded are rare.[2] Indeed, Berry, Nettleship, Marcus Gunn, Adams,

[1] According to A. H. Allen (Commercial Organic Analysis, vol. iii., Part II., 1892, p. 193), Vohl and Eulenberg conclude that the nicotine of tobacco-smoke is completely decomposed during the process of smoking, and that the intense action of tobacco-smoke on the nervous system is due to the presence of bases of the pyridine series. Melsen's experiments, however, appear to be conclusive as to the presence of nicotine, which he isolated in the proportion of about one-seventh of the quantity originally present.

[2] Occasionally reports appear which endeavor to throw doubt upon the existence of a true tobacco-amblyopia. For example, Minor (American Journal of Ophthalmology, 1886, iii., p. 26), on the strength of eight cases of supposed tobacco-amblyopia, whose subjects were cured without stopping

Frost, and others,[1] maintain that they never see cases of central amblyopia due to alcohol alone.

A true alcohol-amblyopia, however, as already pointed out, has been demonstrated with sufficient frequency to quell all reasonable doubt. Connor, for example,[2] who has taken the trouble to collect twenty-seven cases of pure tobacco-amblyopia, to which list many others might be added, reports a couple of instances of equally pure alcohol-amblyopia.

Mr. Jonathan Hutchinson was of the opinion that the effect of alcohol was antagonistic to tobacco (an influence denied by Groenouw), and Dr. Berry,[3] on the whole, is inclined to agree with him, but insists that there must be a distinction made between alcoholic stimulation and alcoholism, when the vital powers are actually lowered and notoriously unable to withstand unusual strain. He thinks that the toxic effect of tobacco may not assert itself until the antagonistic effect of alcohol from over-stimulation has given place to a certain amount of depression and the equilibrium is destroyed. This would appear to explain why a man who has smoked all his life with impunity may suddenly be affected by tobacco.

In most of the cases, however (and this is my own experience, and has been admitted by Nettleship and other English surgeons), alcohol, freely used, predisposes the patient to central amblyopia.[4]

the tobacco, but who ceased the use of liquor, doubts the relation of tobacco to the disease. He thinks it resembles hereditary amblyopia and retinitis nyctalopia, and shows no alliance with or dependence upon tobacco. Fumagalli (quoted by Knies) denies the occurrence of tobacco-amblyopia.

[1] Trans. of the Ophthal. Soc. of the United Kingdom, 1887, vii., pp. 36–100.

[2] Journ. of the Amer. Med. Assoc., 1890, xiv., p. 217.

[3] Royal London Ophthalmic Hospital Reports, vol. x., p. 46.

[4] It has been aptly stated by Dr. B. A. Randall, that a man who drinks and smokes excessively makes "a tincture of his tobacco" and thus enhances his chances of an evil result.

Other circumstances which favor a deleterious effect of tobacco on vision are malnutrition from any source, chronic gastritis, dyspepsia, mental worry, and particularly insomnia.

Racial peculiarities and methods of smoking or using tobacco (consult also p. 62) have much to do with its toxic or non-toxic effect. It is well known that the Turkish race, although the consumption of tobacco in the Levant is enormous, is practically free from amblyopia. Van Millingen[1] states that he has never seen a case of central scotoma in a Turkish woman or man, and hence naturally believes that the absence of the disease can only be due to the quality of the tobacco or to the manner in which it is smoked. Now, although shag contains 6.87 per cent. of nicotine, Turkish contains from 3 to 4 per cent., and, as we have already pointed out, if the quantity smoked is excessive, the quality of the tobacco and percentage of the nicotine are of secondary importance. That the quality of the tobacco does not cause the immunity of the Turk is indicated by the following calculation, made by Van Millingen: "Taking it that the smallest amount of shag which is known to have produced amblyopia is ½ ounce a week, giving off 2.3 parts of nicotine, it will at once be evident that a Turk, smoking at the lowest estimate ½ ounce of tobacco per day, amounting to 3 or 4 grammes of nicotine per week, will stand twice as much risk of getting poisoned as would a shag smoker." Turks while smoking cigarettes are particular that no tobacco shall come in contact with the buccal mucous membrane, and, although they inhale the smoke vigorously, they are not poisoned because, according to Van Millingen, tobacco poisoning (and

[1] Trans. of the Ophth. Soc. of the United Kingdom, 1888, viii., p. 242.

hence amblyopia) is possible only when nicotine in solution is brought in contact with the mucous membrane of the mouth and swallowed.

Other races, whose consumption of tobacco is excessive, for example, the South Americans and the inhabitants of the Island of Cuba, are practically immune, as we know from the writings of Fernandez.[1] The liability of the pure negro and the full-blood Indian I am unable to state from personal observation. In this connection I quote the following letter from Dr. Chas. W. Kollock, of Charleston, S. C.:

"I have seen a number (probably a dozen) of cases of tobacco- and alcohol-amblyopia in the full-blooded negro. Among these were two cases of tobacco-amblyopia in negro women, who smoked 'plug tobacco' in pipes. My experience shows that the pipe-smokers are most often affected, next, those who smoke cigars, but I have never seen a case when the tobacco was used only for chewing. Of course, most men who chew smoke also; but there are a good number who simply chew. I have also had a number of cases of tobacco-amblyopia among mulattoes."

The *male sex* is much more frequently affected than the female, but there is no reason for this except the more general use of tobacco among men than among women. The statement that tobacco-amblyopia is never seen in women has often been disproved. For example, Hill-Griffith[2] thinks that more cases would be found if the investigations of central visual defects in women were carefully made, especially by searching for color-scoto-

[1] Clinica de Enfermedades de los Ojos. Habana, 1887, p. 345.
[2] British Medical Journal, 1886, ii., p. 1102.

mata. He records fourteen cases of toxic amblyopia in women.[1] Berry has seen about eight cases in women, and numerous others have been reported, some of the most interesting character, for example, one by Chisolm,[2] of a refined woman, living in an isolated district, who learned to smoke a pipe to keep her husband company, and became typically affected.

The *age* at which tobacco-amblyopia develops varies considerably. It is stated by Förster to occur between the 26th and 74th years. Groenouw has observed cases between the 25th and 68th years, and among 178 patients he records the following results:

25 to 29 years	6 cases.
30 to 39 "	53 "
40 to 49 "	71 "
50 to 59 "	33 "
60 to 69 "	15 "

Berry has observed the disease between the nineteenth and seventieth years, nineteen years being, so far as I know, the youngest case on record. In my own experience, a girl aged twenty-five years, was the youngest patient.

Usually *the length of time required to produce toxic amblyopia* consumes a number of years, as is evident from the fact that it is exceedingly uncommon before the thirty-fifth year of life. Generally fifteen or more years elapse before amblyopia appears. A few exceptional instances of rapid development are on record, for example, those reported by Nettleship.[3] One of these was a man who had smoked for a year, and during half that time had been a total abstainer from

[1] Trans. of the Ophth. Soc. of the United Kingdom, 1887, vii., p. 84.
[2] Amer. Journ. of Ophthalmology, 1886, iii., p. 68.
[3] Trans. of the Ophth. Soc. of the United Kingdom, 1887, vii., p. 43.

alcohol. In another man, aged forty-nine years, the amblyopia appeared at the end of three years.

The *relative frequency* of tobacco-amblyopia is difficult to determine, because in many statistical reports no attempt is made to separate tobacco from alcohol cases; indeed, most of the cases belong to the mixed varieties. During sixteen years of a rich clinical service, Groenouw found recorded 185 cases of intoxication-amblyopia. In Hirschberg's statistics tobacco-amblyopia comprises 0.6 per cent. of the whole number of cases. The following table, published by Priestly Smith,[1] gives the statistics of tobacco-amblyopia in Queen's Hospital, Birmingham, and also those of his private practice:

EYE DEPARTMENT. QUEEN'S HOSPITAL.

Statistics of Tobacco Amblyopia.

Year.	Out Patients.	Tobacco Amblyopia.		Percentage.
1879	293	4		1.70
1880	357	4		1.12
1881	439	5		1.14
1882	574	2		0.35
1883	670	6		0.88
1884	1,037	13		1.25
1885	1,581	14		0.88
1886	1,722	29		1.68
1887	1,770	17		0.96
1888	2,004	29		1.44
1889	2,197	29		1.36
	12,644	152	=	1.20
Last 1,500 private patients.	1,500	13	=	0.85

In the Eye Department of the Jefferson Medical College Hospital during 1893 there were 1751 cases,

[1] Report of the Committee on Color Vision. Presented to both Houses of Parliament, June, 1892. London: Harrison & Sons.

and only two of tobacco-amblyopia, or 0.11 per cent.; in other years the percentage has been higher. In the Report of the Dispensary for Diseases of the Eye, 1893, in the Hospital of the University of Pennsylvania, among 1467 cases there were 2 of tobacco-amblyopia, or 0.14 per cent. The total number of patients treated in the Wills Eye Hospital of Philadelphia in 1891 amounted to 12,280, and among these 13 cases of amblyopia from tobacco toxæmia are recorded, or 0.10 per cent. In the Dispensary of the New York Ophthalmic and Aural Institute 7355 cases were treated during 1891, among which are included 20 cases of toxic amblyopia, or 0.25 per cent. Among the last 1500 of my own private patients, there were 7 with tobacco-amblyopia, or 0.47 per cent. It is probable that the disease is more common in Great Britain than in this country or in Germany.

To summarize: A form of central amblyopia is undoubtedly due to tobacco, no matter how it is introduced into the system. Most frequently amblyopia is caused by smoking and chewing tobacco, less frequently by the inhalation of its vapors or the contact of the skin with its decoction or its moistened leaves, occasionally by the process of "dipping," and rarely, if ever, by taking snuff.

The susceptibility to the toxic influence of tobacco increases with age, and about the fortieth year the daily quantity of tobacco must be lessened, or disturbances of vision are likely to arise.

The maximum dose permissible varies from 15 to 30 grammes a day, but it should be remembered that $\frac{1}{2}$ ounce (about 16 grammes) of strong tobacco per week has produced amblyopia.

The toxic effect of the tobacco depends more upon the quantity consumed than upon the quality. Other

things being equal, however, the stronger the tobacco the more likely the development of amblyopia.

The method of smoking tobacco appears to exercise a decided influence, the patient being more susceptible if much tobacco comes in contact with the mucous membrane of the mouth, or if the saliva becomes impregnated with it and is swallowed. Inhalation of the smoke increases the potency of the poison, which probably depends for its activities, not alone upon nicotine, but upon a variety of other toxic agents.

Distinctly predisposing causes are chronic alcoholism, and all circumstances which depress the nervous system, particularly lack of sleep, worry, and chronic indigestion.

The disease is much more frequent in males than in females, not because the former are more predisposed, but because they are more exposed to the influence of tobacco.

Certain races, for example, the Turks and Spaniards (Island of Cuba), appear to enjoy a comparative immunity from this affection and to withstand the evil influence of excessive inhalation of smoke.

Symptoms. Excluding for the moment acute nicotinism, the symptoms of tobacco-poisoning of the chronic type may be divided into those which are *constitutional* and those which are purely *ocular*.

The constitutional symptoms are poor appetite, irregular alimentary action, restlessness, sleeplessness, lack of concentration, failure of memory, impaired sexual functions, and disturbances of the circulation, particularly that type of irritable heart which is known as "tobacco-heart." Either with or without these symptoms, the *ocular signs* of chronic tobacco-poisoning may be present, for it is a curious fact that in many of the cases of marked amblyopia there are practically no other signs of the

toxic influence of tobacco upon the nervous or vascular system. The patients complain of a diminution of sight, which cannot be improved by glasses. The mistiness of vision varies at different times, and sight is usually better in a dull light than in a bright glare. There is an indescribable fogginess in the centre of the field of vision. The improvement of vision in a dull light is probably due to a slight hyperæsthesia of the retina, although Berry thinks that this is only relative; that is, the difference between the indistinctness of direct vision and the clearness of indirect vision is not so marked.

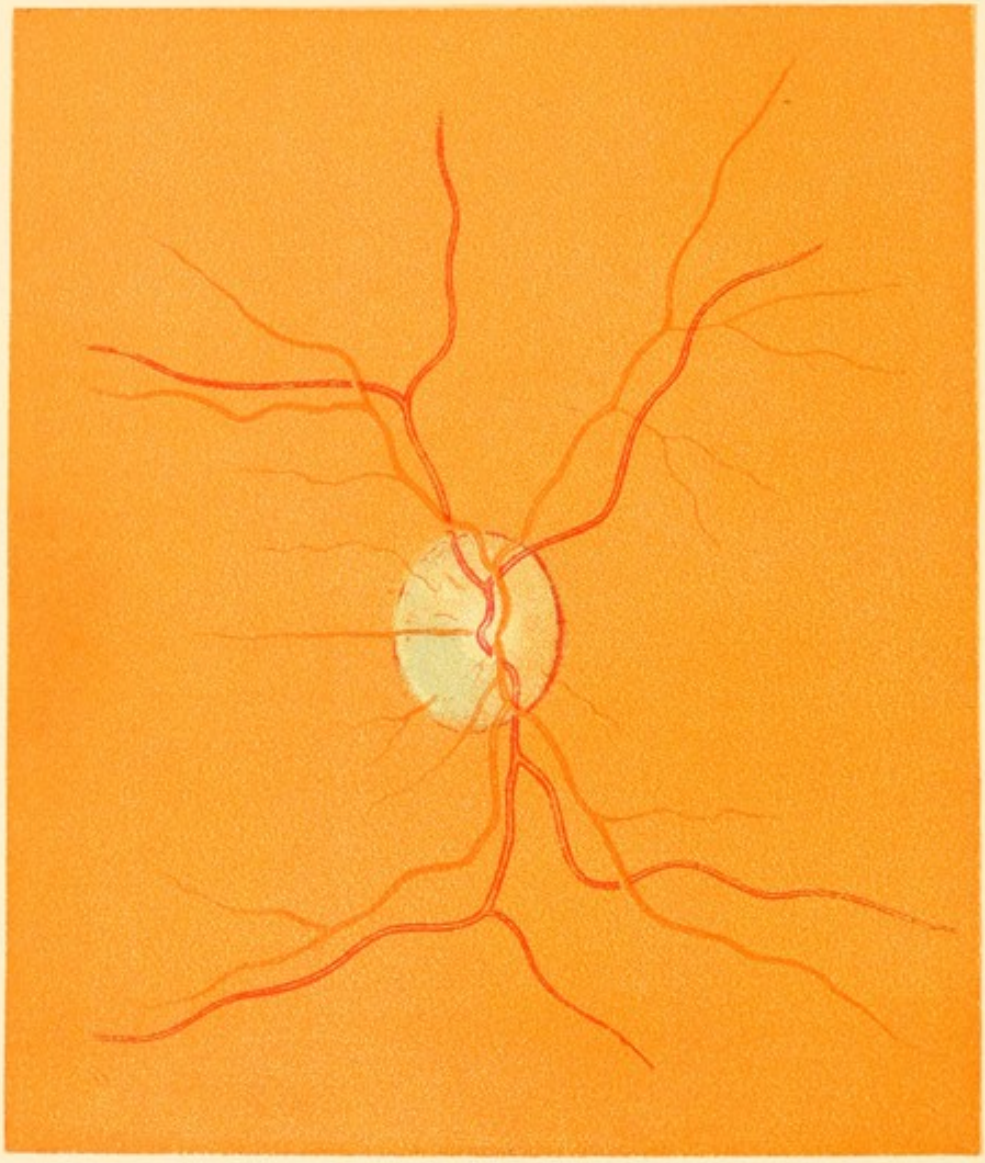
The visual acuity often is diminished decidedly before patients apply for treatment. Groenouw[1] finds that it varies from 5/200 and the ability to read with the help of convex glasses only very large test-types (Snellen xvi or x), to 20/30, with which vision, Snellen $1\frac{1}{2}$, can readily be deciphered. I have recorded vision from counting fingers to 20/30, and in one instance, just in the first stage of tobacco-amblyopia, 20/20 was read, as if through a fog. Sometimes, as Groenouw points out, there is a surprising difference between the near and the far vision. For example, a patient may read 20/50 and yet be unable to decipher Snellen $1\frac{1}{2}$ at close ranges, while another patient, having a vision of 20/200 can read the smaller type at closer range.

The pupils vary, and there is nothing characteristic in the iris-movements. In acute tobacco-poisoning the myotic action of the drug is manifest, but in the cases of amblyopia there is often a tendency to dilatation of the pupil.

There are no phenomena of importance connected with

[1] Loc. cit.

PLATE IV.



Tobacco Amblyopia—Atrophy of the Papillo-macular Area of the Disc.

the external ocular muscles in ordinary tobacco-amblyopia. True, Fontan[1] has described the case of an immoderate smoker who suffered from sudden double oculomotor palsy and narrow pupils, which disappeared after he ceased smoking. This case and others reported by Jan and Strümpell[2] belong to the nuclear ophthalmoplegias caused by chronic nicotine toxæmia. Mauthner himself states that with these exceptions, it may be doubted whether the misuse of tobacco ever produces external ocular palsies.

The ophthalmoscope does not reveal a characteristic appearance of the nerve-head, which may be called the "tobacco-disk"—a careless phrase sometimes employed; *i. e.*, there is no pathognomonic fundus-lesion, although, as we shall presently see, the optic nerve-tip may, in connection with other signs, afford diagnostic information.

There may be no abnormality in the papilla, or at most only a slight veiling of its edges and discoloration of its surface ("dirty disk"), or there may be a quadrant-shaped atrophy in the lower and outer part. Under rare circumstances complete atrophy ensues. The peculiar discoloraton of the disk, commonly wedge-shaped in form, when taken into consideration with other symptoms, is suggestive of intoxication-amblyopia, and assumes diagnostic import if the visual-field phenomena, presently to be described, are demonstrable. (See Plate IV.)

Exceptionally unusual lesions are revealed by the ophthalmoscope. Thus, Ponti[3] describes actual neuritis,

[1] Recueil d'Ophtalmologie, 1883, 3d ser., v., p. 309.

[2] Quoted by Mauthner, Diagnostik und Therapie der Augenmuskellanmungen, Wiesbaden, 1889, p. 662.

[3] Annali di Ottalm., 1873, fasc. iii., p. 107.

and Nettleship[1] two cases of retinal hemorrhage, one associated with neuritis. One or two additional instances of small retinal hemorrhages are on record,[2] for example, a case reported by A. Stanford Morton. The patient, aged thirty years, smoked 1½ pounds of shag weekly, had central scotomas for red, green, and blue, temporary pallor of the disks, and a small linear hemorrhage near each optic papilla. Albumin and sugar were absent.

Occasionally slight changes are found in the macular region, but there is nothing significant in them, and nothing to indicate that they have aught to do with the formation of the scotoma. Thus, in a series of cases analyzed by Hill Griffith,[3] some of these lesions are referred to and described as "fine white ticks at the central region," or "fine yellowish dots at the central region." There is no statement as to the condition of the urine. I have found this lesion in several cases, the most marked one being a patient between fifty and sixty years of age, who smoked inordinately and also abused alcohol. He had typical scotomata and quadrant-shaped discoloration of the optic nerves. Albumin and tube-casts were present in the urine. Nettleship also describes the presence of "fine guttate choroidal, or choroido-retinal changes" at the central region in a certain proportion of his tobacco cases, but regards them only as coincidences.

The *visual field* in tobacco-amblyopia, as, indeed, in all forms of intoxication-amblyopia, presents interesting features. Briefly, they are as follows:

The peripheral boundaries of the visual field are normal, and there is a color-scotoma, especially for red

[1] Ophthalmic Hospital Reports, 1886–87, xi., p. 360.

[2] See discussion on toxic amblyopia, Trans. Ophth. Soc. of the United Kingdom, 1887, vii.

[3] Trans. Ophth. Soc. of the United Kingdom, 1887, vii., pp. 81–90.

and green, which is usually oval in shape, and is situated between the point of fixation and the blind spot. These colors are not recognized in their true character in this area; green appears dirty white; red, brownish.

FIG. 15.

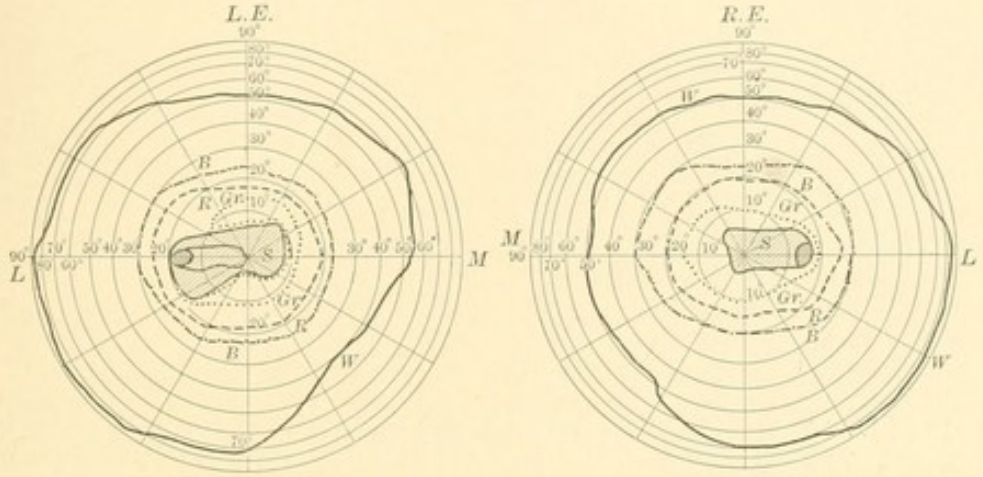
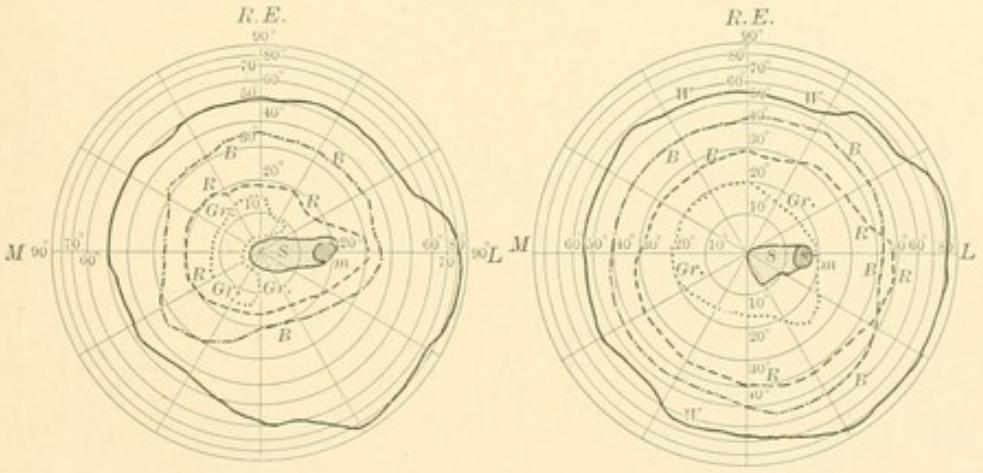


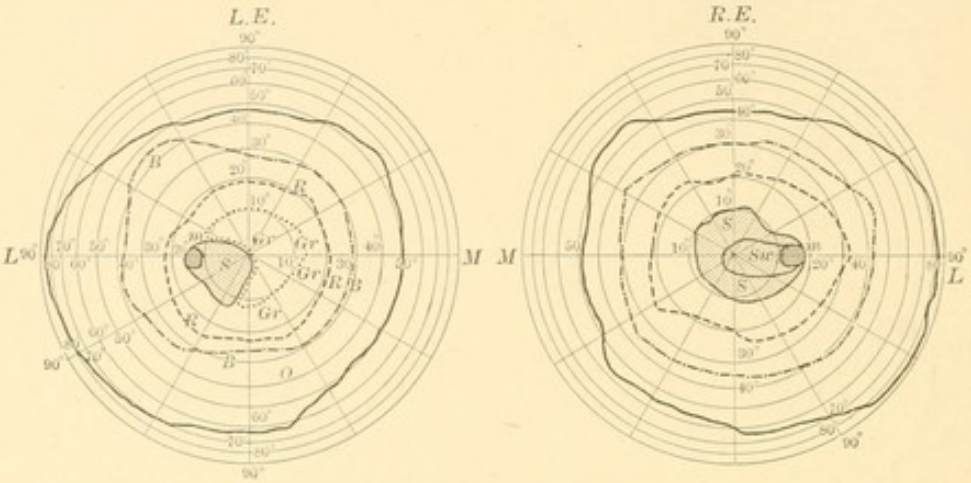
FIG. 16.



Before deciding that there is a scotoma for red and green, the examiner should be sure that there is no non-toxic red-green blindness. Under these circumstances he would be obliged to make use of blue and yellow tests, and under any conditions it is well to employ these colors.

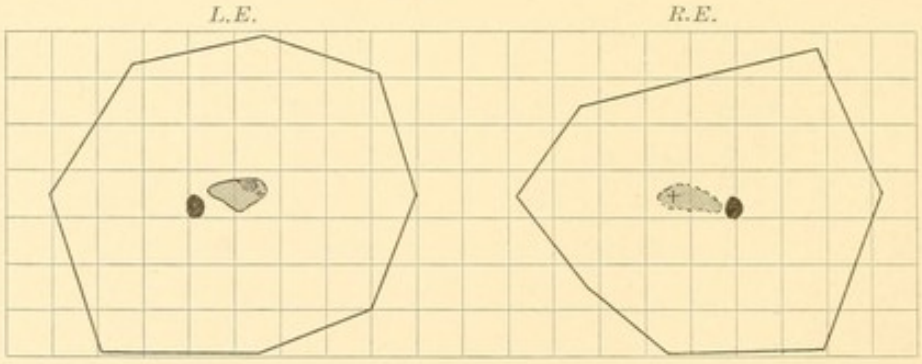
In the beginning of the tobacco-amblyopia the scotoma is *relative*. It is a *color-scotoma*, and the patient

FIG. 17.



Figs. 15, 16, and 17. Variously shaped scotomas for red and green in tobacco-amblyopia. The shaded area represents the scotoma, the continuous line the field for white, and the broken lines the limits of the field for colors. (After HIRSCHBERG.)

FIG. 18.

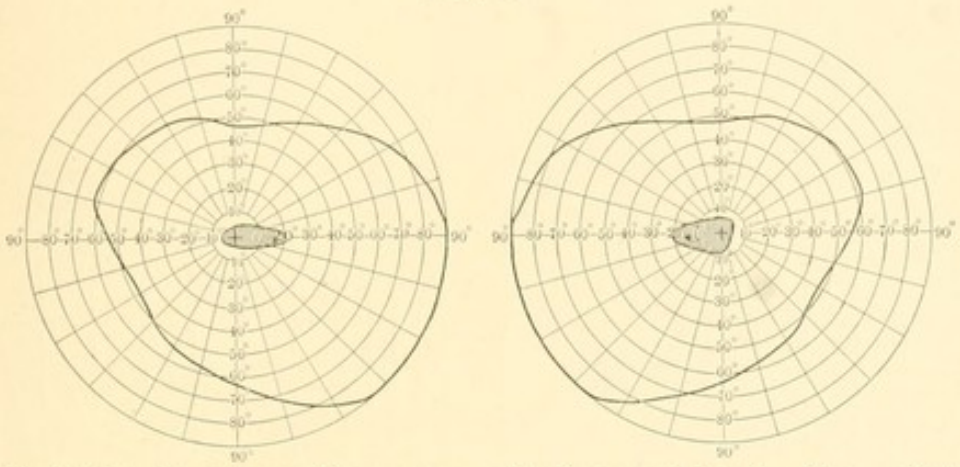


Scotomas drawn upon a blackboard from a case of tobacco-amblyopia. The patient, aged fifty, smoked ten cigars a day for many years. In the left scotoma there is a small absolute defect.

is usually unconscious of its existence. (See Figs. 15, 16, 17, 18, 19, and 20.) Later there may be a scotoma for white; indeed, white usually appears somewhat gray-

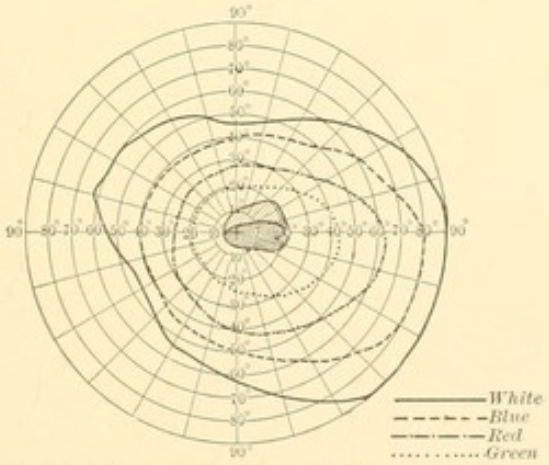
ish within the area of the central defect. In severe and neglected cases the scotoma becomes *absolute;* that

FIG. 19.



Typical oval scotomas from a case of tobacco-amblyopia. The patient, aged sixty, had smoked four pipes of tobacco daily and an occasional cigar since he was nineteen; a moderate beer drinker.

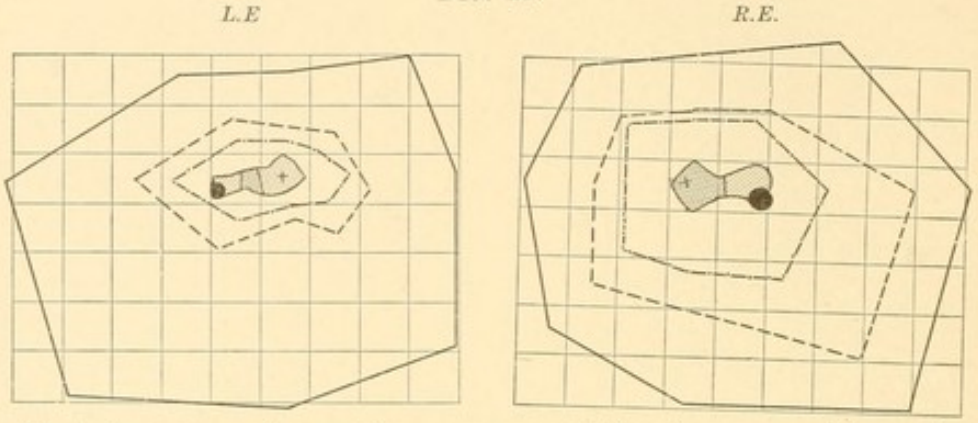
FIG. 20.



Typical oval central scotoma (red-green-blind area) represented by double cross hatching, capped by an area in which there was diminished color perception, represented by shading with single lines. The patient was a man aged thirty-four, who for ten years smoked twelve to fifteen cigars a day, for two years drank an ounce a day of compound tincture of cinchona, occasionally used beer, but did not drink whisky; much business worry and many sleepless nights. The visual field of the left eye was almost exactly similar. V. of O. D., 6/60; V. of O. S., 6/20. The patient recovered. The ophthalmoscopic appearances of the right fundus are illustrated in Plate IV., namely, typical quadrant atrophy of the disk.

is, within its limits all perception of light is wanting. The characteristic form of the scotoma, as already noted, is oval, stretching from the fixing point to the blind spot, and rarely passing much to the nasal side of the former.

FIG. 21.



Central scotomas from a tobacco-case, aged fifty-four years. The patient also had locomotor ataxia. The double cross-hatching indicates spots of absolute defect within the relative area.

FIG. 22.

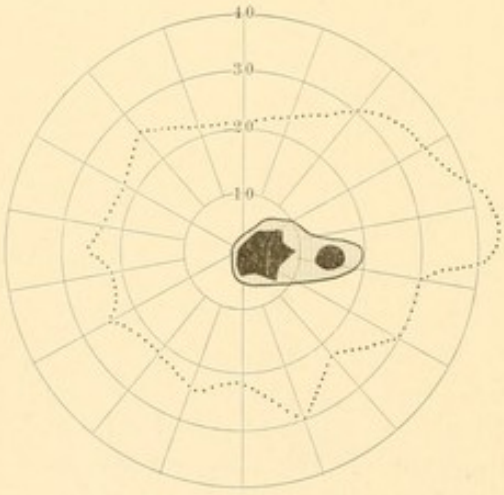
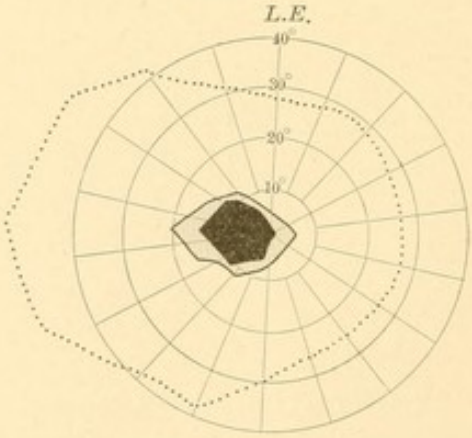


FIG. 23.



Sometimes there are islands of absolute defect within the relative scotoma. I have described several typical cases of this character. (Fig. 21; also Figs. 22, 23, 24, and 25 from Groenouw.) Occasionally a circular scotoma, sur-

rounding the fixing point, has been noted in tobacco-amblyopia, for example, by Nelson, Nettleship, and myself. (Fig. 26.)

FIG. 24.

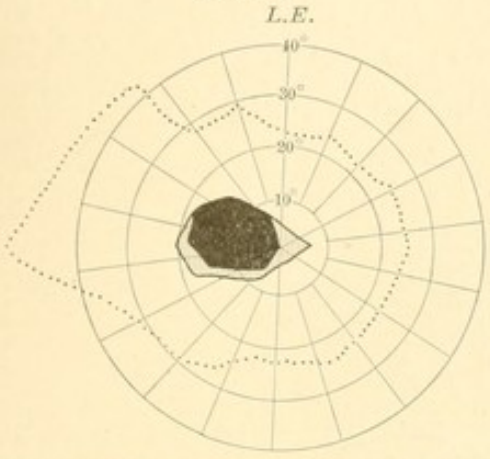
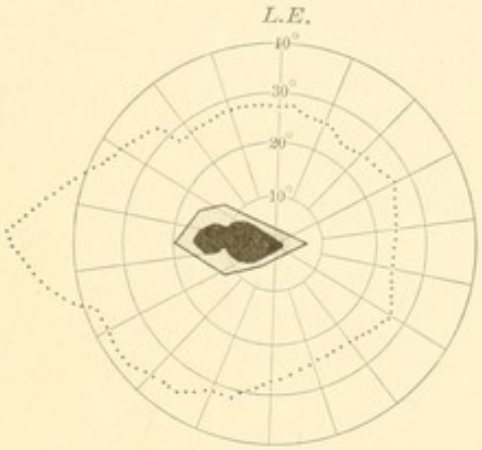
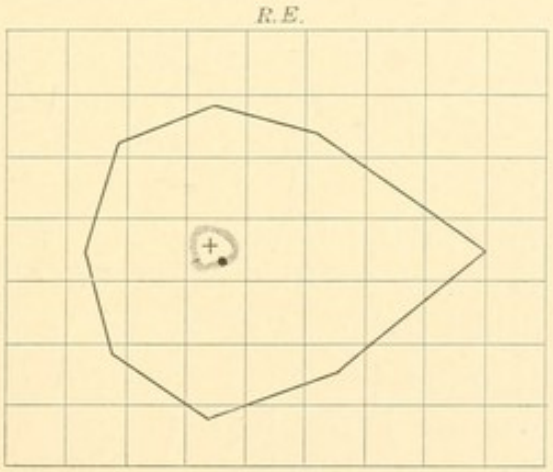


FIG. 25.



Figs. 22, 23, 24, and 25 from Groenouw, illustrating islands of absolute defect within the relative scomatous areas.

FIG. 26.



Perimacular scotoma in a girl who worked in a tobacco factory, but did not use tobacco. From a case studied in the service of Dr. William F. Norris in the University Hospital.

Groenouw,[1] who studied 185 cases of toxic amblyopia, and about 400 charts of the visual field, has made some

[1] Loc. cit.

interesting observations on the scotoma for color. According to him, it never reaches more than a degree or two beyond the nasal side of the fixation point, an observation which accords with my own experience. (Well shown in Figs. 18, 19, and 20.) In the early stages of the affection it is often confined to the fixation point and its immediate neighborhood (Fig. 27); later it stretches

FIG. 27.

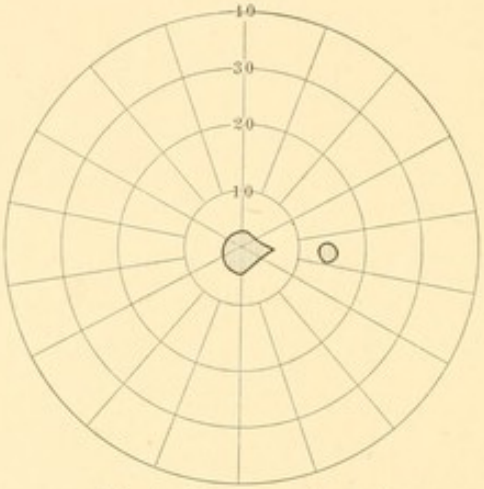


Diagram from Groenouw illustrating small scotoma confined to fixation point, often overlooked.

directly outward to the blind spot, or more often outward and upward. At the same time it is usually demonstrable that there is a second or supplemental color-scotoma around the blind spot, and that these two color-blind areas are joined by a process which extends from the fixing point, thus forming the fully developed egg-shaped scotoma. Sometimes the defective color-sense begins first in the neighborhood of the blind spot. The scotoma occasionally reaches to the limits of the field for red, as a rule "breaking through" above, and thus dividing the red field into a nasal and temporal half. (See Figs. 28, 29, 30, 31, and 32.) Finally, the entire

field for red and for green may be abolished by extension of the scotoma, the patient's condition being very much like that of a congenitally color-blind person.

FIG. 28.

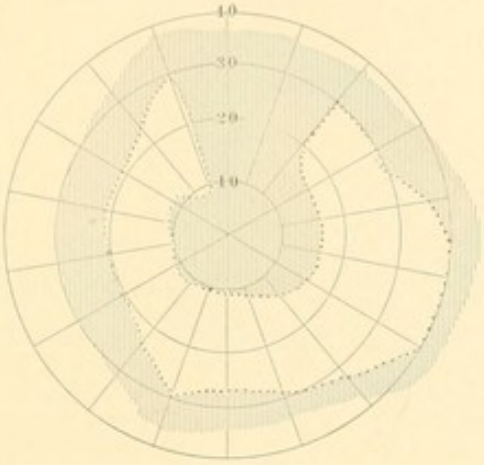


FIG. 29.

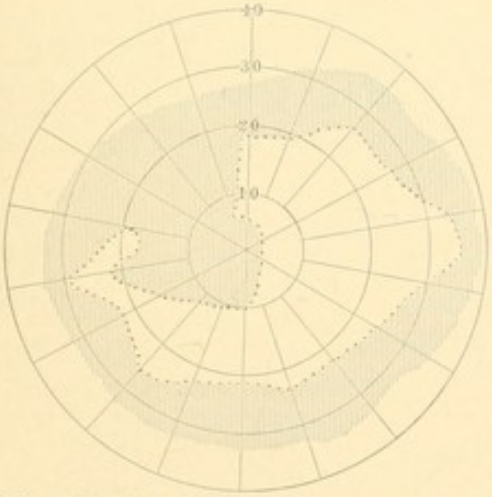
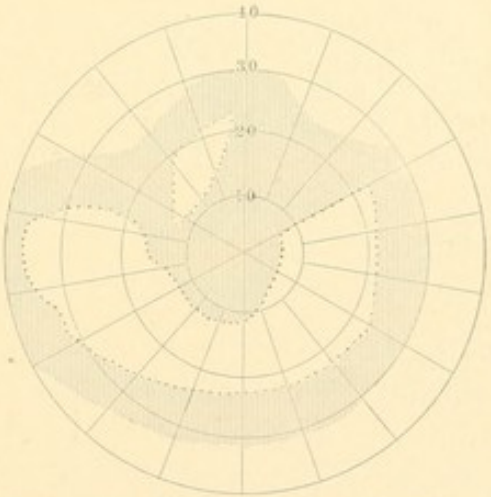


FIG. 30.



Figs. 28, 29, and 30. Diagrams from Groenouw illustrating the "breaking through" the red limit of the scotoma.

This "breaking through" is well illustrated by a case in my practice. (See Fig. 31.)

Symmetry of the visual defect was for a long time considered characteristic of the affection, and certainly is

the rule; but cases of tobacco-poisoning with unilateral scotoma have been described. Rampoldi,[1] Netettleship, Jonathan Hutchinson, Sr., and Webster, of New York, have published cases in which, while the

Fig. 31.

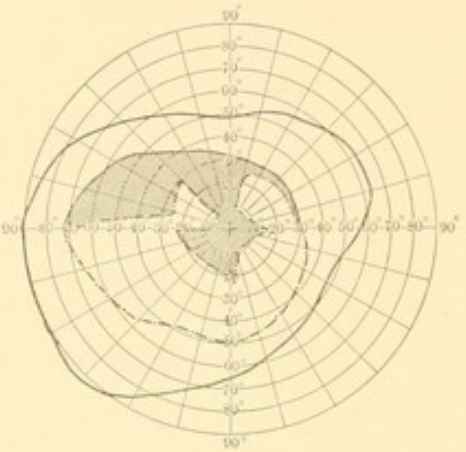
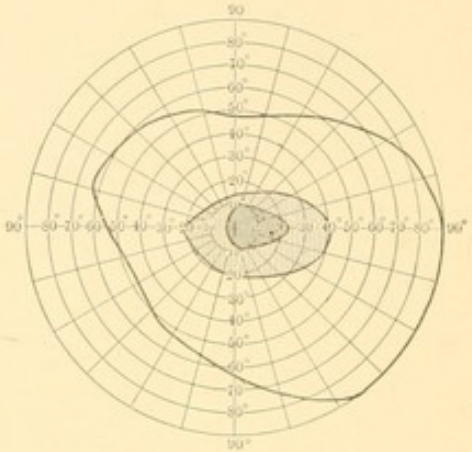


Fig. 32.



Figs. 31 and 32. Diagrams from a patient, aged sixty, who had smoked for fifty years, and for many years consumed six cigars daily and about five pipes of tobacco. He drank five or six ounces of whisky a day. In the right field there is a typical scotoma for red and green, represented by double cross-hatching, surrounded by an area of imperfect color-perception. In the left field typical "breaking through" of the scotoma above.

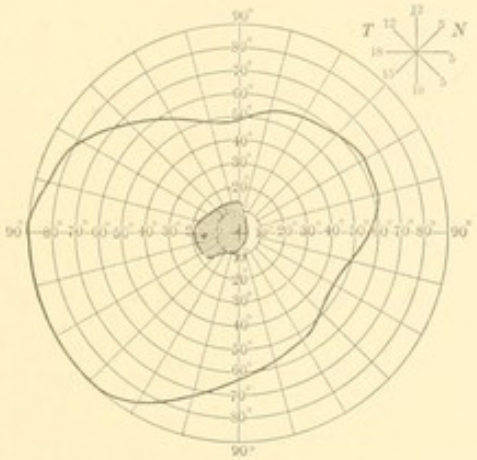
vision of both eyes failed at the same time, there was yet some degree of asymmetry. Jonathan Hutchinson, Jr.,[2] records a case in which one eye retained its normal vision until no less than six months had elapsed from the first failure of the other eye. He considers this a unique observation, but in addition to the asymmetrical cases of Rampoldi, Galezowski and others, the observations of Groenouw and Uhthoff are on record. I have seen one unilateral tobacco-scotoma. (See Fig. 33.)

[1] Annali di Ottalmologia, Anno xiv., fasc. 23.

[2] Trans. of the Ophth. Soc. of the United Kingdom, 1887, vii., p. 62, and Royal London Ophthalmic Hospital Reports, 1886–87, xi., p. 188.

Hutchinson, Jr., has noted a central scotoma for yellow, with or without limitation of the color-field. More rarely there is scotoma for blue; that is, red, green, yellow, and blue are all confused or mistaken in the central part of the field. This condition has been

FIG. 33.



Unilateral scotoma in tobacco-amblyopia. A man, aged fifty-eight, smoked six cigars daily and drank whisky moderately (two drinks a day), V. O. D. 6/6 and no scotoma, but diminished green-sense over-fixing spot. V. O. S. 6/15 and scotoma for red and green represented in diagram.

observed by Simi,[1] who has likewise seen xanthopsia. Finally, the color-scotoma may be absent for a time. Indeed, Vossius has described a case of high grade intoxication-amblyopia without central scotoma, ending in complete recovery.[2]

Berry has found decided defects of the light-sense in abnormal states of the macular fibres of the optic nerve, and therefore, in those cases in which the central scotoma has not yet developed, he suggests this method of examination as a diagnostic test of intoxication-amblyopia.

[1] Boll. di Ocul., vol. xiii., 12. Abst. Archives of Ophthalmology, 1892, xxi., p. 408.

[2] Klinische Monatsbl. f. Augenheilk, 1883, p. 291.

W. de W. Abney[1] has made some interesting examinations of the color- and light-sense in cases of tobacco-blindness. One case was deprived of the sensation of any color except blue. Tested for the illuminating value of white light, it was found that the patient's appreciation of light to the standard was about one-half to two-thirds. In another case the final sensitiveness to light of the central part of the eye was nearly twelve times less than that of a person possessing normal light-sense.

Diagnosis. The diagnosis of intoxication-amblyopia as the result of tobacco depends upon the history of the abuse of the drug, failure of vision unimproved by optical therapeutics, and the presence of a scotoma stretching between the fixing point and the blind spot, usually oval in shape and negative in character, particularly for red and green, while the periphery of the field of vision remains unaltered. If, in addition, there is a quadrant-shaped patch of atrophic pallor in the nerve-head, the diagnosis becomes still more certain.

In order to prove the influence of tobacco alone, however, it is necessary to exclude the effect of alcohol, bisulphide of carbon, nitro-benzol, iodoform, stramonium, cannabis indica, and certain diseases, particularly diabetes, multiple sclerosis, and locomotor ataxia. As we know, tobacco alone causes central amblyopia in numbers of cases; in others there is a mixed influence, namely, alcohol and tobacco; and in still others we have a similar scotoma as the result of a non-toxic retrobulbar neuritis. A differential diagnosis based upon the shape of the scotoma, pericentral in alcohol-amblyopia, paracentral in tobacco-amblyopia, and a mixture of the type

[1] Proceedings of the Royal Society of London, 1891, xlix., p. 49.

in cases when both poisons had been consumed (Hirschberg[1]) has been shown by a number of observers, particularly Uhthoff and Groenouw, to be untrustworthy. Injections of pilocarpine have been suggested as a therapeutic test. They are stated to produce rapid amelioration of the symptoms in toxic amblyopia, but only indifferent effects in retrobulbar neuritis. This procedure is of doubtful value.

The following tables give some of the main points in the differential diagnosis between various types of central amblyopia:

TOXIC AMBLYOPIA. (*Intoxication-amblyopia.*)	NON-TOXIC RETROBULBAR AXIAL NEURITIS.
History of abuse of alcohol or tobacco; much more frequent in males than females; uncommon before thirty-fifth year.	History of chilling of the body, excessive exertion, suppression of menses; or of infectious diseases, rheumatism, etc. No special relation to sex or age.
Visual acuity varies from 5/200 to 20/30.	Visual acuity usually greatly disturbed; often complete blindness.
Scotoma of oval shape stretching from fixation outward, usually not passing to nasal side; generally for colors only (relative), and, if for white, having the general shape described.	Absolute and often positive scotoma, except in beginning, tending to pass to nasal side of fixation, and not specially horizontally oval in shape.
Peripheral visual field intact.	Peripheral contraction of field for colors and form.
Ophthalmoscopic appearances negative, or a quadrant-shaped atrophy of lower and outer (temporal) portion of disk.	Generally some woolliness of disk, distention of veins; rarely ischæmia of vessels.
General symptoms not characteristic, if present at all; no other eye symptoms.	General symptoms absent, except such as are likely to be present from probable cause.
Slow in onset; usually promptly amenable to treatment.	Often rapid in onset; frequently slow in responding to treatment.

[1] Loc. cit.

DISSEMINATED SCLEROSIS.	LOCOMOTOR ATAXIA.	SCOTOMATOUS ATROPHY OF OPTIC DISK.
History of exposure to cold, mental distress, overwork, acute diseases, injury to central nervous system, or specific febrile disease; no special relation to sexes; usually appears between twenty and thirty-five years; sometimes in childhood.	History of syphilis common; occasional history of injury; also exhaustion; uncommon in women. Half the cases between thirty and forty years.	Hereditary tendency; history of exhaustion and lack of sleep; usually appears in males before thirty-fourth year.
Visual acuity varies with stage of disorder.	Varies with condition of optic nerve.	Marked depreciation of central acuity.
Central scotoma analogous to toxic variety.	Scotoma at first similar to toxic variety, but progressive.	Scotoma like toxic variety in form, but absolute.
Concentric contraction of visual field; sometimes retention of peripheral borders.	Contraction of the field for colors and form, especially peripheral reëntering angles; often restriction of the temporal half of field.	Often marked contraction of field, especially in hereditary optic-nerve atrophy.
A. General atrophic pallor of disk; B. incomplete discoloration; C. temporal atrophy; D. slight neuritis. (UHTHOFF.)	General atrophic pallor (gray degeneration); in the early stages grayness of the deeper layers of the disk and undue broadening of scleral ring.	Appearance of optic-nerve atrophy; sometimes slight neuritis.
Characteristic tremor; staccato speech, etc.; nystagmus exceedingly common.	K. J. absent; ataxia; lightning pains, etc.; often reflex pupillary immobility and diplopia.	No special general symptoms.
Very imperfect results from treatment.	Optic-nerve change usually progressive.	Scotoma stationary, but unaffected by treatment.

Prognosis. The prognosis of pure tobacco-amblyopia is always good, provided the patient will abstain from

tobacco. The observations of Minor, already referred to, that in many cases of central amblyopia attributed to the abuse of tobacco, recovery takes place even though tobacco is continued, are so contrary to the accepted opinion that it is difficult to believe in their accuracy. My own experience agrees with Nettleship's, that perfect recovery does not ensue without at least a diminution of the ordinary allowance of tobacco, and this experience coincides with that of most observers.

Relapses of amblyopia due to tobacco are not common, according to Mr. Nettleship, who gives only one well-marked case; and Eales, of Birmingham, states that he has never met with the recurrence of this condition. This has not been my own experience, as I have notes of several decided relapses on the resumption of tobacco-smoking. In one instance, a man of forty-five years, after the disappearance of a well-marked color-scotoma, the vision, which had been scant 20/200, rose practically to normal, but speedily sank to 20/200 again, with reappearance of the scotoma after a week's smoking.

There is no doubt that permanent changes in the disk may occur in cases of long-standing tobacco-amblyopia, and probably complete atrophy may result if the use of tobacco is continued; but, as in alcohol-amblyopia, it is uncommon to find permanent blindness. Indeed, there may be persistent pallor of the entire optic disk, and yet the vision may return to normal, precisely as this occurs in quinine-blindness. Berry considers that relapses are rare, and in those cases in which he has observed them they have always occurred after long intervals of time. It is the experience of this observer, that cases in which the vision is reduced much below 20/200, and in which the scotoma stretches to the inner side, or in which there

is peripheral limitation of the field of vision, do not completely recover.

Hutchinson[1] analyzed 64 cases of tobacco-amblyopia with reference to the prognosis, and found: Recovery in 48 cases, stationary sight in 4, and 7 became worse while under treatment. Five were blind when first seen, and remained so. There were no relapses; 26 stopped smoking; 13 continued the practice, but more moderately. Age does not influence the prognosis. Persistent amaurosis in a smoker exposed to much heat may occur, as reported by Hutchinson.[2]

Edgar A. Browne,[3] after describing optic atrophy in three brothers (smokers), suggests "that groups of cases like the following may be provisionally admitted:

"1. The ordinary tobacco-amblyopia, involving only the central fibres, transient, and passing on to resolution on removal of the cause.

"2. A class of retrobulbar neuritis, beginning with negative central scotomata, but which do not tend toward recovery, the central defect progressing to such a degree that axial atrophy may be assumed, peripheral vision remaining unaffected. The *rôle* played by tobacco or other causes in these cases requires investigation.

"3. Cases where the affection begins in the central tract, but gradually spreads peripherally till 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."

[1] Ophthalmic Hospital Reports, 1874–1876, viii., pp. 356–487.

[2] Archives of Surgery, ii., 1890–91, p. ii., 151.

[3] Trans. Ophthalmological Soc. United Kingdom, 1888, viii., p. 235.

J. B. Lawford[1] is inclined to believe in a type of optic-nerve atrophy in which tobacco, although not the sole cause, has some share in originating or aggravating the changes in the optic nerve. My own experience leads me to a similar conclusion.

Pathology and Pathological Anatomy. We have already discussed at some length the seat of the pathological lesion, or at least its probable seat, in cases of so-called intoxication-amblyopia. As Groenouw[2] points out, three situations are possible. Either the toxic process directly or indirectly affects the light-perceiving elements, that is, the retina; or it attacks the fibres endowed with the transmission of light, that is, the optic nerve, chiasm, or optic tracts; or, finally, it vitiates the central organ, that is, the cortex of the brain.

Baer[3] (compare p. 56) endeavored to remove the amblyopia of intoxication from the list of diseases of the optic nerve and to classify it with retinal affections, and Schoen has advocated similar views. The evidence, however, is contrary to their acceptance. As Sachs points out, if the scotoma was the result of a disturbance of the function of the macula, its relation to the vertical partition-line would be symmetrical, while we know it shows a marked tendency to extend from the macula toward the blind spot, very little of it lying in the middle near the vertical meridian. Baer's theory that the cause of amblyopia in chronic nicotine-intoxication depends upon spasm of the vessels is disproved by ophthalmoscopic examination and by the anatomical observations already detailed.

The central situation of the affection has been advo-

[1] Trans. Ophth. Soc. United Kingdom, 1890, x., p. 166.

[2] Loc. cit.

[3] Loc. cit.

cated by Filehne,[1] himself the subject of tobacco-amblyopia, but without good grounds on which to base his beliefs. Therefore we are forced to the conclusion, based upon clinical as well as anatomical investigation, that *the situation of the pathological process is in the optic nerve, and especially in that portion which is known as the papillo-macular bundle.*

The *clinical* evidence depends upon ophthalmoscopic examination—the discoloration of the temporal half of the optic papilla—the phenomena of the visual field, and the improvement of visual acuity by diminished illumination and its depreciation in bright light—a symptom which we know from Förster's investigations belongs to diseases of the light-conducting fibres of the optic nerve.

The *anatomical* proof rests upon the examinations of the optic nerve which have been made, and which I have fully described in the section devoted to alcohol-amblyopia. Even now, however, we are by no means in a position to speak with certainty, and it is desirable that no opportunity to make microscopical examination should be lost, and that positive experimental evidence should be adduced.

Although the difference between retrobulbar neuritis and intoxication-amblyopia has been pointed out from the clinical standpoint, from the anatomical side it is difficult to make a distinction.

According to Berry,[2] there is no proof that cases of toxic amblyopia are really cases of retrobulbar neuritis. The cases examined have exhibited other evidence of disease, *e. g.*, diabetes; hence it does not follow that the typical central scotoma, found in the centre of each visual

[1] Graefe's Archiv, 1895, xxxi., 2, p. 1.
[2] British Medical Journal, 1893, ii., p. 784.

field, which is met with in toxic amblyopia has the same origin as that which occurs in retro-ocular neuritis. A. Maitland Ramsay,[1] discussing this point, refers to the fact that the papillo-macular bundle in certain toxic conditions passes into a state of interstitial neuritis, the inflammatory process leading to proliferation of the connective tissue and ultimate cicatricial contraction—a pathological condition analogous to that which is seen in the liver and kidneys. He doubts, however, whether typical cases of tobacco-amblyopia, which often improve after a single good night's rest, and which, on the other hand, grow worse after fatigue, are consistent with the theory that the papillo-macular bundle is inflamed. They point rather to the existence of some lesion of a vascular kind. He thinks it is probable that in the simpler forms of tobacco-amblyopia the directly hurtful action of the nicotine, or of the products of its combustion, produces such a functional derangement of the macular fibres that in severe cases, especially in those complicated by alcoholism, anatomical changes in the nerve probably become superadded, and a true retro-bulbar neuritis results. Under these circumstances there is peripheral contraction of the visual field, indicating organic disease of the optic nerve.

Treatment of Intoxication-amblyopia. The treatment of this affection consists, in the first place, in abstinence from tobacco and alcohol. In the majority of cases it is useless for the patients to temporize or merely to lessen their accustomed consumption of these drugs. Absolute cessation from smoking and drinking will, if the disease has not progressed far, be sufficient to effect a cure.

In other cases it is important to administer those

[1] Loc. cit.

drugs which are known to stimulate the optic nerve, or which have the power of favorably altering vascular, inflammatory, or degenerative processes. Of these, the most important are bichloride of mercury, iodide of potassium, and strychnine, the first two acting as alteratives, the last as a vasomotor and nervous stimulant. The strychnine may be administered by the mouth, in pill or solution, but it produces its results more promptly by the hypodermic method.[1]

As has been pointed out by a number of observers, temporary improvement will take place in cases of tobacco-amblyopia during the inhalation of nitrite of amyl, because the capillaries are dilated, and for the moment the nutrition of the optic nerve is improved. A more permanent but similar vasomotor influence may be obtained by giving glonoin, or tablets of nitroglycerin, beginning with $\frac{1}{100}$ of a grain and gradually increasing the dose. Digitalis serves a useful purpose on account of its action on the circulation.

As was recorded in a previous section, pilocarpine has been employed in this disease, and with the happiest results. A free sweat may be induced every second or third day, either by administering the hydrochlorate of pilocarpine (gr. $\frac{1}{10}$ to gr. $\frac{1}{4}$) hypodermically, or using rectal injections of the fluid extract of jaborandi, 40 to 60 minims in each injection. Pilocarpine is especially indicated when the influence of alcohol predominates or when we encounter a pure alcohol-amblyopia. In the absence of pilocarpine, Turkish-baths are useful, or pro-

[1] It is an interesting fact that the administration of strychnine during the inflammatory stage of a lesion of nervous tissue, *e. g.*, an ordinary peripheral neuritis, usually aggravates the disorder, except in axial optic neuritis of tobacco-poisoning, in which this drug is beneficial. Perhaps this may be a therapeutic test that vascular change and not inflammation is the early underlying pathological process in the optic nerve in a simple tobacco-amblyopia.

fuse diaphoresis may be secured by more homely means —hot drinks, hot foot-baths, etc.

If the cessation from accustomed stimulants or the absence of tobacco causes much restlessness at night, bromide of potassium may be ordered, which of itself has some reputation in the cure of drug-amblyopia. The craving for liquor and tobacco is somewhat allayed by the use of strychnine or tincture nux vomica (the latter given in large doses, 25–60 drops *t. i. d.*). Indeed, it has been stated, but upon insufficient evidence, that nitrate of strychnine has some antidotal power in so far as the alcohol-habit is concerned.

The effect of the remedies, or of the total abstinence from tobacco and alcohol, may be measured by frequent investigation of the scotoma. This gradually disappears; breaking up begins in the centre, then the darkness clears near the blind spot, and finally only a trace is left at fixation, which finally also disappears. The length of time required for a cure varies, according to the extent of the poisoning and the faithfulness of the patient to instructions, from a few weeks to a number of months.

If atrophy of the nerve results, the treatment described on pages 35 to 39 is applicable, and particularly full doses of strychnine. Electricity may be tried, and according to Riggs, L. Webster Fox, and Granville Faught, voltaic alternatives furnish the best results. My own experience has not taught me to place much reliance on electricity in the treatment of optic-nerve atrophy. Finally, reference may be made to subconjunctival injections of corrosive sublimate, which have been much used in France, particularly by Darier, Lagrange, and Abadie, in the treatment of syphilitic diseases of the uveal tract. Some surgeons have employed them in toxic amblyopia, but without material benefit.

Alcohol-tobacco Amblyopia. To the toxic amblyopias, *i. e.*, those caused by alcohol and tobacco, a third class is usually added, namely, the *alcohol-tobacco type*, or the *mixed variety;* indeed, this is the form usually encountered, pure alcohol-amblyopia, as we know, being exceedingly rare, and pure tobacco-amblyopia not common.

The symptoms, treatment, and pathological changes just recited apply to the mixed as well as to the pure types of this affection. Usually, in these cases, the influence of one or the other drug predominates, and, as we have already seen, the consensus of opinion is that tobacco is the more potent of the two in its deleterious effects on vision.

The Relation of Tobacco and Alcohol to Acquired Color-blindness is an important matter. We know from Groenouw's observations, and from such a case as the one whose visual fields are figured on page 81, that the patient's condition may become like that of a congenitally color-blind person by extension of the scotoma Even in the earlier stages, when the scotoma is much less marked, it might interfere with the perfect recognition of distant color.

The great consumption of tobacco by sailors and railway employés renders it desirable that examinations for central scotoma should be made among those who are obliged to watch colored signal lamps. Priestley Smith[1] has testified that tobacco-amblyopia would prevent a man from recognizing the color of a distant lamp, although he might recognize the colors of skeins of wool such as are used in testing the color-sense. Nettleship[2] believes that the defect of form-sense in tobacco-amblyopia is sufficient to guard the man against false

[1] Report of the Committee on Color-vision, loc. cit. [2] Ibid.

security; he soon seeks advice. Nevertheless, as affected persons might continue their occupations for a time, the examinations for color-scotoma should be included with the tests for color-sense of railroad employés and of sailors.

Tobacco-amblyopia among the Lower Animals. It is well known that the Virginia deer eat the leaves of the tobacco-plant (*Nicotiana Tabacum*) without detriment. They have probably become, by reason of many years of residence in the tobacco district, entirely immune to the influence of the drug, precisely as the monkeys of certain districts of the East Indies are said to eat the seeds of the *Strychnos Nux-vomica* without harm, while to other tribes they are a deadly poison.

My experiments with acute nicotine-poisoning in animals, as before stated, yielded negative results so far as the optic nerves were concerned. I did not succeed in producing chronic tobacco-toxæmia.

Recently several notices of tobacco-amblyopia in horses have appeared in the journals, and the following account by Th. Husemann is reproduced:

Husemann[1] refers to the observations on epizootic blindness in horses, described by W. T. Kendall and S. S. Cameron in the *Australasian* of July 4, 1894—a mysterious form of amaurosis which is prevalent in New South Wales. This has become a very serious affection, with inflammatory symptoms of the external tunics of the eye. Two cases were examined in Melbourne by J. J. Barrett and J. J. Miller, who found no structural changes. There was reduction of the iris-movement to light. At first there is dimness of vision, but gradually the blindness becomes total.

[1] Deutsch med. Wochenschr., 1894, xx., 819.

Many theories have been advanced to explain the disease, but it is generally conceded to be due to a chronic alkaloid-toxæmia, the active principle being contained in the Australian tobacco (*Nicotiana Suaveolens*), the leaves of which are eaten by the horses. The acute action of this drug does not differ from that of ordinary tobacco, and the toxic symptoms are analogous. The essential cause of the blindness is degeneration and atrophy of the optic nerve. This could be discovered by a naked-eye examination, and was further proven by microscopic investigation. Epizootic blindness has also been ascribed by F. von Müller to a grass lily in Western Australia, but this plant does not grow in New South Wales, where the blind horses are found.

Should future investigations confirm the accuracy of these observations, the reality of tobacco-blindness would be proven beyond cavil, as the cases practically assume the importance of a physiological experiment.

BIBLIOGRAPHY.

Doebbelin, E. De amblyopia et amaurosi alcoholica, 8vo., Berolini, 1840. Earlier references are found on p. 24, foot-note.

Klaunig. Amblyopia potatorum. Deutsche Klinik, Berlin, 1850, ii., 505.

Hutchinson, J. Clinical Data Respecting Amaurosis, More Especially that Form of it Supposed to be Induced by Tobacco. Lancet, Lond., 1863, ii., 536–538. The earliest complete account of tobacco-amblyopia is by Mackenzie (1832); not included here, as it is in a text-book. Tobacco-amblyopia is also described by Beer: Lehre der Augenkrankheiten, Wien., 1792, Zweiter Theil, p. 66.

Sichel. De l'influence du tabac à priser sur la production de l'amaurose. Ann. d'ocul., Brux., 1863, l., 83.

Wordsworth, J. C. Three Cases of Amaurosis Produced by Tobacco. Lancet, Lond., 1863, ii., 95.

Hutchinson, J. Clinical Data Respecting Cerebral Amaurosis, More Especially with that Form Supposed to be Connected with the Use of Tobacco. Clin. Lec. and Rep. of Lond. Hosp., 1864, i., 33–82.

Frey, M. Tabak und Alkohol in ihrer Beziehung zu Amblyopie und Amaurose. Allg. Wien. med. Ztg., 1865, x., 359, 389.

Sichel. Nouvelles recherches pratiques sur l'amblyopie et l'amaurose causée par l'abus du tabac à fumer, avec des remarques sur l'amblyopie et l'amaurose des buveurs. Ann. d'ocul., Brux., 1865, liii., 122–136.

Erismann, F. Ueber Intoxications-Amblyopieen, 8vo., Zurich, 1867, 76 pp.

Hutchinson, J. Statistical Details of Three Years' Experience in Respect to the Form of Amaurosis Supposed to be Due to Tobacco. Med.-Chir. Trans., Lond., 1867, l., 411–429.

Thilesen, P. Amaurose efter Misbrug af Tobak. Norsk Mag. f. Laegevidensk., Christiania, 1867, xxi., 139–145. Also transl. Med. Press and Circ., Dubl., 1867, iv., 229–231.

Viardin. Amblyopie causée par abus du tabac á fumer, Bull. Gen. de Thérap., Paris, 1867, lxxii., 141.

Velut, P. J. De l'amblyopie par l'alcool et le tabac, 4to, Paris, 1868.

Hutchinson. Case of Tobacco Amaurosis Ending in Absolute Blindness. Med. Times and Gaz., Lond., 1869, ii., 279.

Leber, Th. Einfache Amblyopie ohne Gesichtsfeldbeschränkung. Arch. f. Ophth., Berl., 1869, Abth. iii., 60–65; 236–247.

Daguenet. Quelques considérations sur l'amblyopie alcoolique. Ann. d'ocul., Brux., 1869, lxii., 136–142. Also Rec. de mém. de méd. . . . mil., Paris, 1870, 3 s., xxiv., 23–29.

Curtis, E. M. Amblyopia Potatorum. Trans. Med. Soc., California, 1871–72, 101–113.

Hirschler, I. Ueber den Missbrauch von Spirituosen und Taback als Ursache von Amblyopie. Arch. f. Ophth., Berl., 1871, xvii., 1 St., 221–236.

Hutchinson, J. Statistical Details of Four Years' Experience in Respect to the Form of Amaurosis Supposed to be Due to Tobacco. Ophth. Hosp. Rep., Lond., 1871–73, vii., 169–185.

Apostoli, G. Étude sur l'amblyopie alcoolique. Journ. d'Ophth., Paris, 1872, i., 462–477.

Masselon, J. De l'amblyopie nicotique. 4to., Paris, 1872.

Fumagalli, A. Sulla cura dell'ambliopia per abuso di bevande spiritose col bromuro di potassio. Ann. di ottal., Milano, 1873–74, iii., 201–208.

Ponti, F. Amaurosi nicotinica e solfato di chinino. Lettera in risposta a quella del G. Rava. 8vo., Parma, 1873.

Ponti, F. Il sofato di chinina contro l'amblyopia da neuro-retinite per abuso di tobacco. Ann. univ. di med., Milano, 1873, ccxxiii., 176–187. Also reprint.

Quaglino, A. Sui vantaggiosi effetti del bromuro di potassio nella cura delle ambliopie dipendenti dall'abuso delle bevande spiritose. Annotazioni cliniche. Ann. di ottal., Milano, 1873, iii., 24–40.

Rava, G. Sull'amaurosi nicotinica. Lettera al Floriano Ponti. 8vo., Sassari, 1873.

Diagnostic interessant d'un cas d'amaurose par le tabac. Ann. d'ocul., Brux., 1874, lxxi., 99.

Drysdale, C. R. Case of Tobacco Amaurosis. Med. Press and Circ., Lond., 1874, n. s., xvii., 377.

Bull, C. S. Observations on Toxic Amblyopia. N. Y. Med. Journ., 1875, ii., 247–258.

Burnett, S. M. Tobacco Amaurosis. Med. and Surg. Rep., Phila., 1875, xxxiii., 382.

Dickinson, W. The Effects of Nicotine in the Production of Tobacco-amaurosis or Optic-nerve Atrophy. St. Louis Med. and Surg. Journ., 1875, n. s., xii., 25–57.

Hutchinson, J. Report on the Prognosis in Tobacco-amaurosis. Ophth. Hosp. Rep., Lond., 1876, viii., 456–487.

Santos Fernandez, J. De la amblyopia alcoholica en la isla de Cuba, y de un sintoma coadyuvante no descrito, para diagnosticaria. 8vo., Habana, 1876.

Santos Fernandez, J. De la ambliopia alcoholica en la isla de Cuba, y de un sintoma coadyuvante, no descrito, para diagnosticaria. Memoria. Crón. méd. quir. de la Habana, 1876, i., 531–639.

Simi, A. Sull'uso del bromuro di potassio nella ambliopia alcoolica. Imparziale, Firenze, 1876, xvi., 65–67.

Galezowski. De l'amblyopie nicotinique binoculaire scotome. Rec. d'ophth., Paris, 1887, 2 s., iv., 360. Also Le Mouvement Med., Paris, 1877, xv., 283.

Galezowski. Troubles visuels occasionés par le tabac et la nicotine. Rec. d'ophth., Paris, 1877, 2 s., iv., 1–17.

Guélliott, C. Amaurose nicotinique. Progrès méd., Paris, 1877, v., 426. Also transl., Med. Press and Circ., Lond., 1877, n. s., xxii., 466–468.

Nettleship. Cases of Tobacco-amblyopia. Med. Times and Gaz., Lond., 1877, ii., 434–436.

Stoltenhoff, E. A. Ueber Amblyopia nicotiana. 26 pp., iv., 8vo. Bonn. 1877.

Chisolm, J. J. Blindness Induced by the Use of Tobacco, and How to Prevent It. North Carolina Med. Journ., Wilmington, 1878, ii., 369–380.

Claren, L. Ueber Tabaks-Amblyopie. 8vo., Bonn, [1878].

Hirschberg, J. Die acute Schnaps-Amaurose. Arch. f. Augenh., Weisb., 1878–79, viii., 180. Also transl. by I. Furst: Arch. Ophth., N. Y., 1879–80, viii., 363.

Hirschberg, J. Ueber Tabaksamblyopie und verwandte Zustände. Deutsche. Ztschr. f. prakt. Med., Leipz., 1878, v., 193, 205.

Mahiels. Amblyopie par l'abus du tabac. Arch. méd. belges, Brux., 1878, xiv., 3 s., 368–373.

Martin, C. De l'amblyopie nicotique. 4to., Paris, 1878.

Nuel. L'amblyopie alcoolique et le daltonisme. Ann. d'ocul., Brux., 1878, 11 s., x. 105–117. Also Bull. Acad., roy de méd. de Belg., Brux., 1878, xii., 3 s., 686–701, 1 pl.

Ruvioli, F. Dell'effiaccia del bromuro di potassio nelle ambliopie e amaurosi dei bevitori. Ann. di ottal., Milano, 1878, vii., 522-534.

Alexander, L. G. Narcotine (Nicotine) Amaurosis, with Four Cases. Med. and Surg. Reporter, Phila., 1879, xli., 469–471.

Calhoun, A. W. Tobacco Poisoning and its Effects Upon the Eyesight. South. Med. Record, Atlanta, 1879, ix., 321–324.

Cohn, H. Notiz zur Tabakamblyopie. Centralbl. f. prakt. Augenh., Leipz., 1879, iii., 300.

Coursserant, H. De l'amblyopie alcoolo-nicotienne et de son traitement pars les injections sous-cutanées de chlorhydrate de pilocarpine. Journ. d. conn. méd. prat., Paris, 1879, 3 s., i., 239–241.

Hirschberg, J. Tobacco- and Alcohol-amblyopia. Brit. Med. Journ., Lond., 1879, ii., 810.

Hutchinson, J. Clinical Groups of Cases of Amaurosis. Ophth. Hosp. Rep., Lond., 1879, pt. 3, 310–312.

Lasègue, Ch. Les troubles visuels de l'alcoolisme. Arch. gen. de méd., Paris, 1879, 7 s., iv., 342–357.

Mengin. Note relative à un cas d'intoxication par l'alcool méthylique ayant amené en 24 heures une cecité complète. Rec. d'ophth., Paris, 1879, 3 s., i., 663–667.

Nettleship, E. Notes on the Diagnosis of Tobacco-amblyopia. St. Thomas's Hosp. Rep., Lond., 1879, n. s., ix., 51–74.

Santos Fernandez, J. De la ambliopia alchólica. In his Clín. de enfermed. de l. ojos. 8vo., Paris, 1879, 72–97.

Berry, G. W. On Central Amblyopia. Ophth. Hosp. Rep., Lond., 1880–82, x., 44–55.

Ely, E. T. Observations Upon the Effects of Tobacco. N. Y. Med. Journ., 1880, xxxi., 367–383.

Fano. Abus d'alcooliques pendant des années; amaurose bilatérale très avancee, etc. Journ. d'ocul. et chir., Paris, 1880, viii., 232.

Nelson, J. On Tobacco-amblyopia. Brit. Med. Journ., Lond., 1880, ii., 774.

Santos Fernandez, J. Trastomos visuales observados en los tabaqueros y modo de evitarlos. Rev. de Med. y cirug. pract., Madrid, 1880, vi., 569–572.

Secondi, R. Sul l'ambliopia dei bevitori e fumatori. Gior. internaz. d. sc. med., Napoli, 1880, ii., 1128–1134.

Webster, D. Amblyopia from the Abuse of Tobacco and Alcohol. Med. Rec., N. Y., 1880, xviii., 649, 665.

Dehenne, A. et P. Bonnefé. De l'amblyopie toxique. Rev. de therap. Med. chir., Paris, 1881, xlviii., 203, 230.

Quelques remarques sur l'amblyopie nicotinique et sur l'amblyopie alcoolique. Journ. d'ocul. et chir., Paris, 1881, ix., 86.

Romiée, H. De l'amblyopie alcoolique. Rec. d'ophth., Paris, 1881, 3 s., iii., 33–53; 79–92.

Sahn, M. Tobacco and Alcohol, and Their Effect Upon the Eyesight. Texas Med. and Surg. Rec., Galveston, 1881, i., 305–309.

Sewny, K. H. Amblyopia from Tobacco. Med. Rec., N. Y., 1881, xix., 329.

Ayres, S. C. Tobacco-amblyopia. Cincin. Lancet and Clinic, 1882, n. s., viii., 126.

Borthen, L. Amblyopia centralis nicotianica. Norsk Mag. f. Laegevidensk, Christiania, 1882, xii., 837–843.

Lang, W. A Case of Central Amblyopia in a Smoker with Diabetes. Trans. Ophth. Soc. United Kingdom, Lond., 1882–83, iii., 162.

Lawford, J. B. A Case of Stationary Tobacco-amblyopia in a Man Subsequently Affected by Diabetes. Trans. Ophth. Soc. United Kingdom, Lond., 1882–83, iii., 163–165.

Morton, A. S. Case of Central Amblyopia in a Smoker Suffering from Diabetes. Trans. Ophth. Soc. United Kingdom, Lond., 1882–83, iii., 159.

Nettleship, E. and W. Edmunds. On Central Amblyopia in Diabetes, especially as to its Dependence on, or Independence of, Tobacco-smoking. Trans. Ophth. Soc. United Kingdom, Lond., 1882–83, iii., 165–178.

Segura, M. Amblyopia nicotinica. Clinica de Málaga, 1882, iii., 119–126.

Shorthen Krondhjem. Amblyopie centrale nicotinique. Rec. d'ophth., Paris, 1882, 3 s., iv., 210–216.

Borthen de Throndhjem. Amblyopie centrale nicotinique. Rec. d'ophth., Paris, 1882, 3 s., iv., 210–216.

Weinberg, A. Cate-va cuvinte asurpa ambliopici prin intoxicatiune. [Tobacco-amblyopia.] Progresul med roman. Bucuresci, 1882, iv., 50, 59.

Buzzard, T. On Two Cases of Tobacco-amblyopia. Lancet, Lond., 1883, ii., 52.

David H. Essai sur les altérations fonctionnelles et organiques de l'appareil de la vision survenant sous l'influence combinée de l'alcool et du tabac. Paris, 1883, 43 pp., 4to., No. 116.

Fontan, J. Paralysie simultanée des deux moteurs oculaires communs par nicotinisme. Rec. d'ophth., Paris, 1883, 3 s., v., 309–314.

Galezowski. Des troubles visuels consécutifs a l'abus du tabac. Rec. d'ophth., Paris, 1883, 3 s., v. 677–683.

Guilliot, C. De l'amaurose nicotinique; moyens de la distinguer de l'amaurose alcoolique. Gaz. méd. de l'Algérie, Alger, 1883, xxviii., 27–30.

Masselon, J. Diagnostic de l'amblyopic nicotinique. Rev. clin. d'ocul., Bordeaux, 1883, iii., 196–202.

Vossius, A. Ein Fall von hockgradiger Intoxications-amblyopie ohne centrales Scotom mit Ausgang in vollständige Heilung. Klin. Monatsbl. f. Augenh., Stuttg., 1883, xxi., 291.

Berry, G. A. Note on Tobacco-amblyopia in Women, with Remarks. Ophth. Rev., London, 1884, iii., 101–104.

Coleman, W. T. Does Tobacco Produce Amblyopia? Maryland Med. Journ., Balt., 1884–85, xii., 371–374. Also Chicago Med. Journ. and Ex., 1885, li., 216–227.

Galezowski. Discussion de la communication de M. le Dr. Vallin sur quelques accidents causés par le tabac. Ann. d'Hygiene, Paris, 1884, 3 s., xi., 47–51.

Hutchinson, J. Extract from a Clinical Lecture on Tobacco Poisoning. Med. Times and Gaz., Lond., 1884, i., 40, 41.

Masselon, J. Diagnostic de l'amblyopie nicotinique. Uniao Med., Rio de Jan., 1884, iv., 280–288.

Panas. De l'amblyopie toxique. Union Méd., Paris, 1884, 3 s., xxxvii., 657–660.

Shears, C. Tobacco-amblyopia. Brit. Med. Journ., Lond., 1884, i., 1199–1202.

Uhthoff, W. Ueber die Veränderungen des Augenhuntergrundes in Folge von Alkoholismes, souie über die pathologisch-anatomischen Veränderungen bei der Alcohol-amblyopie. Berl. klin. Wochnschr., 1884, xxi., 385, 397.

Ayres, S. C. Amblyopia alcoholica. Amer. Journ. Ophth., St. Louis, 1885, ii., 91–97.

Cheatham, W. Eye Clinic. Amer. Journ. Ophth., St. Louis, 1885, ii., 102.

Coursserant, H. Du traitement et du diagnostic des amblyopies toxiques alcoolo-nicotiennes par les injections sous-cutanées de chlorhydrate de pilocarpine. Gaz. d hôp., Paris, 1885, lviii., 154–156.

Rampoldi, R. Della amblyopia nicotinica. Pavia, 1885, 8vo.

Rampoldi, R. Della ambliopia nicotinica. Ann. di ottal, Pavia, 1885, xiv., 113–125.

Bergmeister, O. Die Intoxications-amblyopien. Wien. Klinik, 1886, xii., 53–74.

Bruns, H. D. Amblyopia Following Sudden Discontinuance of Accustomed Alcoholic Stimulant. New Orleans Med. and Surg. Journ., 1886–87, n. s., xiv., 759.

de Schweinitz, G. E. Eight Cases of Tobacco-amblyopia, One Complicated with Disease of the Spinal Cord. Med. News, Phila., 1886, xlix., 550–553. Also Journ. Nerv. and Ment. Dis., N. Y., 1886, n. s., xi., 766–773; also Med. and Surg. Reporter, Phila., 1886, lv., 713–717; also Polyclinic, Phila., 1886–87, iv., 184–186.

Griffith, A. H. Tobacco-amblyopia in Women. Brit. Med. Journ., Lond., 1886, ii., 1212.

Hartridge, G. Tobacco-amblyopia. Brit. Med. Journ., Lond., 1886, i., 200.

Hutchinson, J., Jr. On a Case of Unsymmetrical Tobacco-amaurosis. Ophth. Hosp. Rep., Lond., 1886, xi., 188–190.

Minor, J. L. The Present Standing of Tobacco-amblyopia. Amer. Journ. Ophth., St. Louis, 1886, iii., 26–45.

Nettleship, E. Central Amblyopia in a Smoker Suffering from Diabetes. Ophth. Hosp. Rep., Lond., 1886, xi., 72.

Pötschke, O. Die Verwerthung der Gesichtsfeldprüfung fur die Diagnostik und Prognostik der Amblyopien. 99 pp., 8 pl., 8vo. Dorpat, 1886.

Standish, M. Case of Alcoholic Paralysis Preceded and Accompanied by Amblyopia ex Abusu, with Remarks Thereon. Bost. Med. and Surg. Journ., 1886, cxiv., 361–364.

Trousseau, A. Amblyopia dans le psuedo-tabes alcoolique. Gaz. hebd. de méd., Paris, 1886, 2 s., xxiii., 4–6.

Uhthoff, W. Untersuchungen über der Einfluss des Chronischen Alkoholismus auf das menschliche Sehorgan. Arch. f. Ophth., Berl., 1886, xxxii., Abth. 2, 95–188; xxxiii., Abth. 1, 257–316.

Alt, A. Ueber Intoxikationsamblyopieen. N. Yorker med. Presse, 1887, iv., 13–17.

Armaignac, H. Amblyopie nicotinique rapidement guérie par la suppression du tabac et les injections hypodermiques de strychnine. Rev. chir. d'ocul., Paris, 1887, viii., 55.

Bendell, H. Tobacco-amblyopia. Albany Med. Ann., 1887, viii., 169–174.

Chisolm, J. J. An Interesting Case of Tobacco amblyopia in a Lady. Amer. Journ. Ophth., St. Louis, 1887, iv., 68–71.

Howe, G. Tobacco-amblyopia. Trans. South Carolina Med. Assoc., Charleston, 1887, 103–105.

Nettleship. Discussion on Toxic Amblyopia. Ophth. Review, 1887, vi., 227–232.

Nettleship. Toxic Amblyopia. Brit. Med. Journ., Lond., 1887, ii., 21.

Ray, J. M. Three Cases of Tobacco-amblyopia, Showing the Results Gained by Hypodermic Injections of Strychnine. Southwest Med. Gaz., Louisville, 1887, i., 262–265.

Skinner, D. N. A Contribution to the Subject of Tobacco-amblyopia. Trans. Maine Med. Assoc., Portland, 1887, 247–252.

Special Meeting for the Collection of Facts as to Toxic Amblyopia. Trans. Ophth. Soc. United Kingdom, 1886–87, Lond., 1887, vii., 36–100.

Baker, A. R. Tobacco-amblyopia, with a Report of Six Cases Treated. Cincin. Lancet-Clinic, 1888, n. s., xx., 711–716.

Browne, E. A. Notes on Tobacco-amblyopia. Liverpool Med.-Chir. Journ., 1888, viii., 107–126.

Bruns. A Case of Rapid Recovery from Tobacco-amblyopia. New Orleans Med. and Surg. Journ., 1888–89, n. s., xvi., 110.

Buxton, A. St. C. Tobacco-amblyopia. Lancet, Lond., 1888, i., 367.

Doyne, R. W. Observations on Tobacco-amblyopia. Ophth. Hosp. Rep., Lond., 1888, xii., 51–58.

Hene, I. G. Sluch. amblyopiæ nicotinicæ. Vestnik oftalmol., Kieff, 1888, v., 356–361.

Madan, D. Consideraciones acerca de la ambliopia alcoholica. Cron. méd.-quir. de la Habana, 1888, xiv., 375, 440.

Van Millingen. Toxic Amblyopia. Trans. Ophth. Soc. United Kingdom, Lond., 1888, viii., 240–248.

Webster, D. A Case of Tobacco-amblyopia. N. Y. Med. Journ., 1888, xlviii., 256.

D'Oench, F. E. Die toxischen Amblyopien. Med. Monatschr,, N. Y., 1889, i., 169–176.

Murray, J. K. Toxic Amblyopia. South African Med. Journ., East Lond., 1889–90, v. 6.

Wheelock, K. K. A Case of Alcohol and Tobacco-amblyopia. Journ. Amer. Med. Assoc., Chicago, 1889, xii., 292–295.

Whisky- and Tobacco-amblyopia. St. Louis Med. and Surg. Journ., 1889, lvi., 374, 375.

Gould, G. M. A Query as to the Relation of Leucocythæmic Retinitis and Tobacco-Poisoning. University Med. Mag., 1889–90, ii. 148.

Brauchli, U. Ueber die durch Tabak und Alcohol verursachte Intoxications amblyopie. Zürich, 1890, Hofer and Burger, 57 pp., 6 tab., 8vo.

Chaltin. Amblyopies toxiques. Arch. méd. belges, Brux., 1890, 3 s., xxxviii., 361–376. Also Loire méd., St. Étienne, 1891, x., 286–289.

Connor, L. Tobacco-amblyopia. Journ. Amer. Med. Ass., Chicago, 1890, xiv., 217–225.

Fortunati, A. Lo stiramento del nervo ottico nell' ambliopia tabica. Sperimentale, Firenze, 1890, lxv., 498–506.

Hutchinson, J. Symmetrical Amaurosis Occurring Quite Suddenly in a Smoker Exposed to Much Heat, and Persistent for Seven Years, Without Alteration. Arch. Surg. Lond., 1890-91, ii., 151.

Martin, A. Tobacco-amblyopia. New Zealand Med. Journ., Dunedin, 1890–91, iv., 172–174.

Pestour, Hippolyte, F. H. De l'amblyopie toxique (alcoolo-nicotinique). Lille, 1890, pp. 52, 4to., No. 86.

Black, G. M. Strychnine Nitrate in Toxic Amblyopia from Alcohol and Tobacco. N. Y. Med. Journ., 1891, liv., 287.

Despagnet. Note clinique sur l'amblyopie alcoolique pendant la guerre de Cuba (1868–78). Rec. d'ophth. Paris, 1891, 3 s., xiii., 663–665.

Kirkpatrick, E. A. Tobacco-amblyopia. Maritime Med. News, Halifax, 1891, iii., 120.

Rydel. Contribution à l'amaurose par intoxication alcoolique et nicotinique. Ann. d'ocul., Paris, 1891, cvi., 277.

Santos Fernández, J. Diagnostic diferencial entre les amblyopias producidas por el alcohol ye el tabaco. Gac. méd., México, 1891, xxvi., 201–204,

Barraquer, J. Amblyopia alcohólica-nicótica. Gac. méd. catal., Barcel. 1892, xv., 161–165.

Groenouw. Ueber die Intoxicationsamblyopie. Archiv. f. Ophth., Leipz., 1892, xxxviii., i. Abth., 1–70, 3 pl.

Hinde, A. A Case of Toxic Central Amblyopia Terminating in Progressive Atrophy. Med. Record, N. Y., 1892, xlii., 70–72.

Wood, C. A. The Toxic Amblyopias; their Symptoms, Varieties, Pathology, and Treatment. Ann. Ophth. and Otol., Kansas City, 1892, i., 123, 171, 253, 1893, ii., 237.

Report of the Committee on Color-vision. 118 pp. Lond., 1892, Harrison & Sons.

Löwegren, M. K. On tobaksamblyopi. Hygiea, Stockholm, 1893, lv., 433–444.

Pope, B. A. Notes on Treatment of Tobacco-amblyopia. Trans. Texas Med. Assoc., Galveston, 1893, xxv., 385–387.

Frohner. Ein Fall von Amaurose mit beginnen der Atrophie der Papille

gebessert durch Strychnin, Monatsh. f. prakt. Thierh., Stuttg , 1893–94, v., 206–210.

Stöltzing, W. Klinische und anatomische Beiträge zur Intoxications—amblyopie und idiopathischen retrobulbären neuritis. Inaug. Diss., 1893, Marburg.

Hall, G. P. Some of the Toxic Effects of Tobacco on the General Organism, with Especial Reference to Its Effect on the Eye. Internat. Med, Mag., Phila., 1894–95, iii., 178–181.

D'Oench, F. E. An Unusual Case of Toxic Amblyopia. Med. Rec., N. Y., 1894, xlvi., 45.

Lydston, J. A. Toxic Amblyopia. Journ. Amer. Med. Assoc., Chicago, 1894, xxiii., 603–605.

Snell, S. On the Relation of Some Occupations to Eyesight. Med. Press and Circ., Lond., 1894, vii., 185; Quart. Med. Journ., Sheffield, 1894–95, iii., 1–16, 1 pl.; Ophthal. Rec., Nashville, 1894–95, iv., 161–177.

Wood, C. A. The Toxic Amblyopias; their Symptoms, Varieties, Pathology, and Treatment. Ann. Ophth. and Otol., St. Louis, 1894, iii., 77, 276, 381.

Kissling, R. Beiträge zur Kenntniss des Tabakaurches. Arch. f. Hyg., München u. Leipzig, 1894, xx., 211–213.

Husemann, T. Zur Tabaksamaurose. Deutsche med. Wochenschr., Leipz. u. Berl., 1894 xx., 819.

Ramsay, A. M. Paper on Tobacco-amblyopia. Glasgow Med. Journ., 1894, xlii., 461–464; Lancet, Lond., 1895, i., 1174–1177.

Gomez, V. Report of a Case of Amblyopia ex Abusu. New York Med. Journ., 1895, lxi., 692-93.

Hilbert, R. Die durch Einwirkung gewisser toxischer Kôrper hervorgerufenen subjectiven Farbenempfindungen. Arch. f. Augenh., Wiesb., 1894, xxix., 28–31.

Kuhnigk, Franz. Zur Ætiolgie der Amaurose. Inaug. Dissert., 8vo., Grufswald, 1894.

Capp, W. M. A Case of Tobacco- and Alcohol-amblyopia. The Philadelphia Polyclinic, 1895, iv., 480.

Abney. Color-vision. New York, 1895, William Wood & Co., chap. xii., 148.

SECTION III.

CONTINUATION OF DRUGS IN CLASS I., WITH SPECIAL REFERENCE TO BISULPHIDE OF CARBON, IODOFORM, NITROBENZOL, THE COAL-TAR PRODUCTS, ARSENIC AND LEAD.

AMBLYOPIA FROM BISULPHIDE OF CARBON AND CHLORIDE OF SULPHUR.

History. The poisonous effects of bisulphide of carbon on the workers in that branch of the india-rubber manufacture in which the rubber is vulcanized by immersion in a solution of chloride of sulphur in bisulphide of carbon has long been known, and was first systematically described by Delpech, in Paris, in 1856[1] and 1863.[2] This observer reports thirty-three cases, fifteen of which suffered from amblyopia. Delpech's observations were followed by several Paris theses on the same subject, notably those by Tavera, Gourdon, Huguin, and Marche. Galezowski[3] devotes a chapter to this affection, and reports two cases.

In England the first cases appear to be those recorded by Dr. Alexander Bruce[4] and Nettleship.[5]

[1] Mémoire sur les accidents que développe daz les ouvriers en Caoutchouc l'inhalation du Sulfure de Carbone en Vapeur. Paris, 1856.

[2] Nouvelles recherches sur l'intoxication spéciale que détermine le Sulfure de Carbone l'industrie du caoutchouc souffle. Paris, 1863.

[3] Des Amblyopies et des Amauroses Toxiques. Paris, 1878, pp. 86 and 143. See also Recueil d'Ophtalmologie, 1877, II., p. 121.

[4] Chronic Poisoning by Bisulphide of Carbon. Edinburgh Medical Journal, May, 1884, xxix., p. 1009.

[5] Trans. Ophth. Soc. of the United Kingdom, session 1884–85, vol. v., p. 149.

In 1885, Fuchs,[1] in Belgium, observed a case at the Ophthalmic Department of the Liége Hospital.

After the publication of Nettleship and Fuchs a committee was appointed by the Ophthalmological Society of the United Kingdom,[2] which thoroughly investigated the subject and tabulated twenty-four cases gathered from the literature.

In 1886, Hirschberg,[3] in Germany, described an example of this affection, and since this date additional cases have been recorded in France, Belgium, Germany, and England, but none, so far as I am aware, in the United States of America.

Etiology: Pathway of Entrance of the Poison. Toxic symptoms are no doubt always the result of the workman's exposure to the fumes of the fluid used in the caoutchouc manufacture, although the skin of the hands and arms also comes in contact with the liquid, which consists of 2 parts of chloride of sulphur to 98 of bisulphide of carbon.[4] That the lungs are the pathway of entrance is proven by the facts, as the Committee of the Ophthalmological Society has shown, that the rapidity and severity of the poisoning are in direct relation to the amount of vapor that men who never touch the fluid, but breathe the vapor, are affected, and that when inhalation is prevented by suitably adjusted apparatus, although immersion of hands and arms in the liquid is long continued, toxic symptoms do not arise.

Although workmen attribute their symptoms to the chloride of sulphur on account of its pungent odor, Del-

[1] Reported by Nettleship in Trans. Ophth. Soc. of the United Kingdom, 1885, v., p. 152.

[2] Trans. of this Society, vol. v., p. 157.

[3] Centralblatt f. prakt. Augenheilkunde, 1886, x., p. 49.

[4] See Committee's Report, loc. cit.

pech has experimentally shown that bisulphide of carbon is the more noxious of the two agents, and that the mixture of the two is not more toxic than the bisulphide alone.

Among twenty-four cases analyzed by the Committee before referred to, and twenty-four additional cases which I have collected, the ages varied from fifteen to sixty-six years; in six the age was not stated. Only five cases occurred in women, probably because males are more frequently exposed to the vapors.

Amblyopia occurs in about 40 per cent. of the cases of chronic bisulphide of carbon poisoning.

Symptoms. These may be divided into the *general* and *ocular* symptoms.

(*a*) *General Symptoms.* According to Delpech, these appear in two stages, viz., (1) exaltation and (2) collapse. At first there is severe headache, perhaps due to the offensive smell of the compound. The exalted stage is characterized by vertigo, hilarity, alternating with depression and irritability of temper, increased appetite, cutaneous hyperæsthesia, and sexual excitement. In the later stages Delpech observed insomnia, dejected spirits, loss of memory, cutaneous anæsthesia of limbs, muscular weakness, and cramps and impairment of sexual power. Finally, there may be emaciation and wasting of muscles, just as in progressive atrophy. (Fuchs.) Some of the cases, as pointed out by Ross and others, resemble pseudo-tabes.

(*b*) *Ocular Symptoms.* These may arise in the first stage, objects seeming "veiled in a mist," especially at the end of the day, but they are more common at a later period, when a fog appears before the eyes, the phenomenon being most marked in bright daylight.

The pupils are usually dilated, but the movements of

the iris are unimpaired; loss of the power of accommodation has been noted.

Ophthalmoscopically, various appearances have been described, viz., pallor of the disks, perineuritis, slight neuritis, and partial or complete atrophy. Usually on careful examination distinct lesions are discovered in the nerve-head, although completely normal fundi are reported. (Gallemaerts.)

Hirschberg[1] describes and figures stippling in the macular region, analogous to that seen in the eyes of animals poisoned with naphthalin, which is dependent upon the separation of crystals in the centre of the retina. The remainder of the fundus was unaffected.

Field of Vision. In the earlier cases the visual field is stated to have been normal, but exact examinations for scotoma were probably wanting. In the more recent and more accurately studied examples of this affection the usual phenomena consist of decided lowering of central visual acuity (counting fingers at 3 metres, or seeing only large type, J. 16–20), normal or nearly normal boundaries of the peripheral visual field, and a central scotoma, which is most marked for red and green, but may also be present for white, blue, and yellow. (See Figs. 34–37.)

Occasionally the scotoma is absent, but there is complete red-green blindness (Little,[2] Gunn[3]); in others, there is no scotoma, but contraction of the color-fields (Little,[4] Lavigerie[5]). In one case only is color perception said to have been entirely normal (Du-

[1] Centralbl. f. prakt. Augenheilk., 1889, xiii., p. 269.

[2] Trans. Ophth. Soc. of the United Kingdom, 1887, vii., p. 73. See also Med. Chronicle, January, 1887, v., pp. 261, 296.

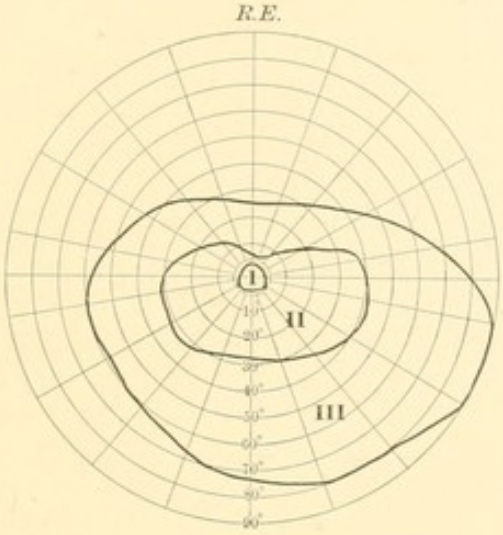
[3] Ibid., 1886, vi., p. 372.

[4] Loc. cit.

[5] Recueil d'Ophtalmologie, 1887, 3 ser., ix.

mont[1]), an observation difficult to credit, in view of all other carefully examined cases. The scotoma may be minute, central, and only detected with small test-objects (Fuchs[2]), ring-shaped or paracentral, or massive, and, if centrally situated, extending more to the temporal side than to the median side. (F. Becker.[3]) See Figs. 34, 35, 36, and 37.

FIG. 34.



Visual field of Fuchs's case of bisulphide of carbon-amblyopia.
I. Minute central scotoma for red.
II. Zone in which the red square ($\frac{1}{2}$ cm. side) is recognized as red.
III. Zone in which the red square ($\frac{1}{2}$ cm. side) is not recognized as red.

Diagnosis. The visual field-phenomena of chronic bisulphide of carbon poisoning are in most instances analogous to those of tobacco-amblyopia, or, at least of toxic amblyopia associated with central scotoma. In many instances the workers in the caoutchouc manufacture have been addicted to the use of tobacco and

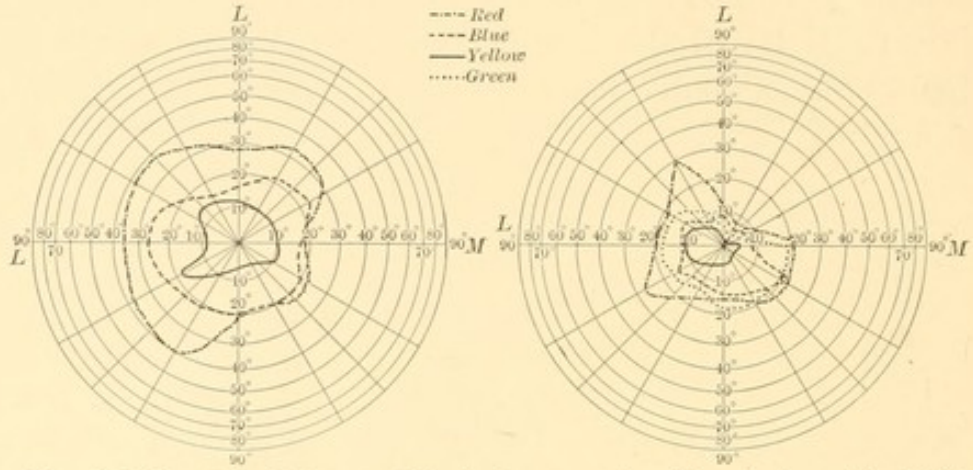
[1] Bulletin de la Clinique nationale Ophthalmologiques des Quinz-Vingts, 1887, v.

[2] Loc. cit.

[3] Centralbl. f. prakt. Augenheilk., 1889, xiii., p. 138.

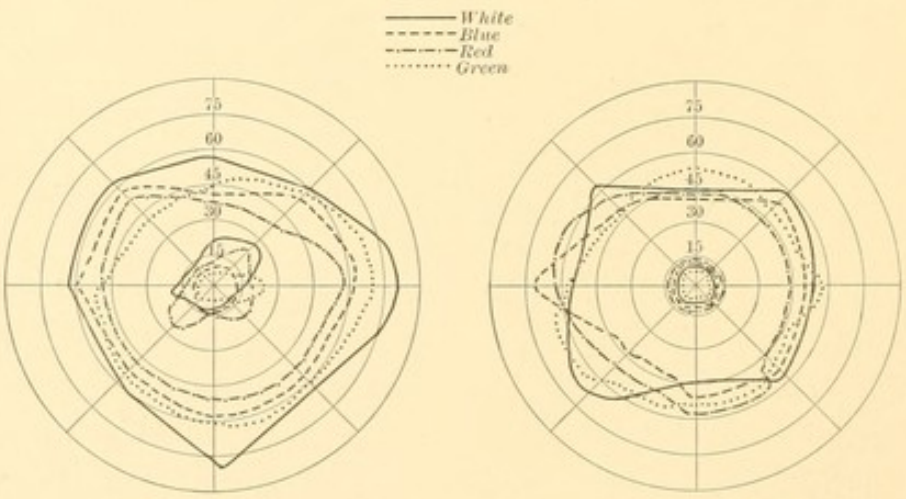
liquor, and Becker has suggested that these agents may predispose the optic nerve to the influence of this poison.

FIG. 35.



Visual fields of the left eye of Becker's case of amblyopia from bisulphide of carbon poisoning. Large central scotoma for red, blue, yellow, and green. The boundaries of the scotoma are indicated by continuous and broken lines in the centre of the maps. Two months between records.

FIG. 36.

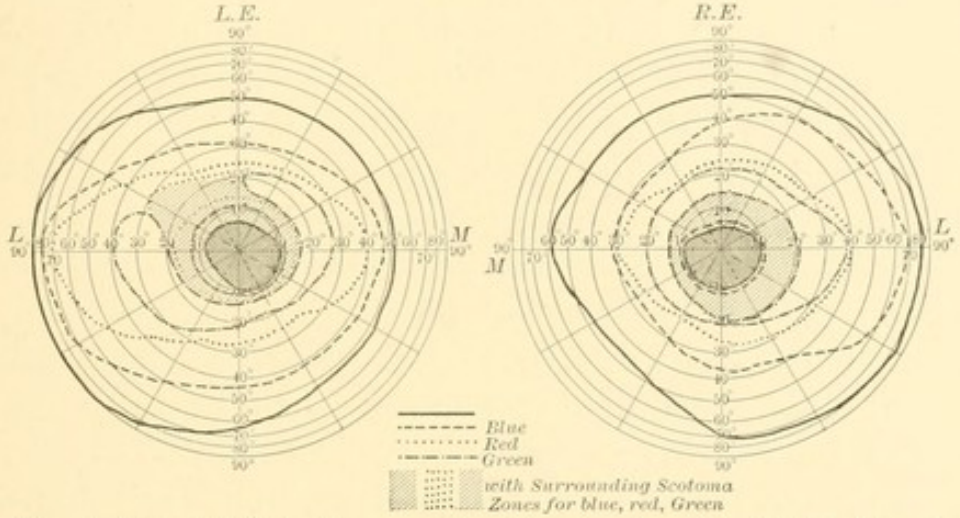


Visual field of Gallemaerts's case of amblyopia from bisulphide of carbon poisoning. Large central color-scotoma, and the limits of the peripheral field for form and colors.

In several instances, especially in those recorded by Nuel, Leplat, and Gallemaerts, the patients were young (six-

teen to twenty-three years), and used neither alcohol nor tobacco. Therefore, in them, at least, the bisulphide of carbon was responsible for the visual defect. In the list of cases analyzed by the Committee of the Ophthalmological Society of the United Kingdom, although several of the patients are noted as smokers, none are said to have

FIG. 37.



Visual field of Uhthoff's case of amblyopia from bisulphide of carbon poisoning. Absolute central defect, surrounded by a scotoma-zone for blue, red, and green.

been drinkers, one was a total abstainer, and several are described particularly as being temperate. I have reached a similar result in my collection.

The form of the scotoma differs somewhat from that of tobacco-amblyopia, although like the tobacco-scotoma it is usually more produced on the temporal than on the nasal side of the fixation spot.

Given the case of a worker exposed to the fumes in the curing-room of a caoutchouc manufactory, with defective vision, which appeared with other symptoms of chronic poisoning (for the visual defect seems never to be the only sign of the toxæmia), with central scotoma, espe-

cially for red and green, but also, at times, for white, blue, and yellow, there is little doubt that the case is one of bisulphide of carbon amblyopia.

Prognosis. This depends entirely upon the removal of the patient from his noxious surroundings. If this is possible, it is good. In the list of the Committee of the Ophthalmological Society of the United Kingdom among 24 cases, 33 per cent. recovered, 25 per cent. improved, 20 per cent. showed little or no improvement. This includes one doubtful case and one of relapse; of the remainder the notes are incomplete. In my collection 15 recovered or were greatly improved, 5 were unimproved, and the result is not stated in 3.

Pathology and Pathological Anatomy. Bisulphide of carbon amblyopia belongs to the intoxication-amblyopias, and is, as we have seen, for the most part characterized by a central defect in the visual field. Autopsies are lacking and the microscopic examination therefore wanting, but the clinical signs indicate that a retrobulbar or axial neuritis is likely to be discovered.

Hirschberg's observation of macular changes, perhaps of a crystalline nature, is not to be disregarded. These lesions may help to explain the central defect of vision in this amblyopia, as perhaps in some other forms of toxic amblyopia.

Treatment. This may be divided into the *prophylactic* and *curative* measures.

It is worth noting that cold weather predisposes toward the affection, as has been pointed out by Becker, because then there is more imperfect ventilation in the curing-rooms than in warm seasons.

It has been proven that the pathway of entrance is by the lungs. Therefore specially devised apparatus to prevent the inhalation of the fumes is strenuously indicated.

The Committee of the Ophthalmological Society of the United Kingdom concluded that the ordinary respirators provided were useless unless charged with some substance capable of chemically separating the deleterious vapor from the inspired air. They suggested a face-piece and an inspiration-tube communicating directly with the outer air.

An apparatus designed by one of Delpech's patients, for avoiding the inhalation of the fumes, is described in the *Transactions of the Ophthalmological Society of the United Kingdom*, as follows: In a chamber, which can be freely ventilated through its two extremities, a horizontal board is fixed to the sides by its two ends; from its anterior edge a board descends to the floor of the chamber; from its posterior rises a vertical plank, fourteen inches high; this is pierced by three pairs of apertures, so arranged as conveniently to give passage to the hands and forearms of three workmen. From the upper border of this vertical plank a sheet of glass passes upward and forward, and allows the workers to see their hands. The closure of the chamber is completed anteriorly, so that the only communication between it and the remainder of the room is through the six circular apertures. These are protected by impermeable and supple india-rubber, which fits closely to the wrists of the workers by means of bracelets. The workmen sit with their legs beneath the horizontal table. All the operations are carried on within the chamber. It is stated that no odor was perceptible, and that although the operations were slightly retarded, they were not so to any inconvenient extent.

Workmen should be advised against the use of tobacco or alcohol, as these substances may predispose to the affection.

The *medicinal* treatment, after the removal of the patient from his noxious surroundings, consists, so far as relief from the visual disturbance is concerned, of phosphorus, iodide of potassium, nux vomica, strychnine, and all measures which tend to build up the general health, particularly iron, in the form of the syrup of the iodide. For cases which have progressed to wasting of the muscles and a condition resembling multiple neuritis and the so-called pseudo-tabes, special therapeutic indications exist. Probably benefit would ensue from electricity at the proper stage, massage and forced feeding.

This interesting amblyopia should receive more attention in the United States. So far as I know, workmen exposed to sulphur-fumes alone, *e. g.*, in the smelting-room of zinc works, do not suffer from amblyopia. An inquiry, instituted at my request, among zinc smelters, failed to discover cases of defective vision attributable to their occupation.

Bibliography—Bisulphide of Carbon.

Pereira, J. Physiological Action of Vapor of Bisulphide of Carbon. Elements of Materia Medica. 3d Amer. ed., vol. i., p. 377, Phila., 1852.

Delpech, A. L. D. Mémoire sur les accidents que développe chez les ouvriers en caoutchouc l'inhalation du Sulfure de Charbone en Vapeur. Paris, 1856.

Delpech, A. L. D. Nouvelles recherches sur l'intoxication spéciale que détermine le Sulfure de Carbone l'industrie du caoutchouc soufflé. Paris, 1863.

Tavera, J. B. De l'intoxication par le Sulfure de Carbone. (Thesis.) Paris, 1865.

Gallard, T. Intoxication par le Sulfure le Carbone, chez les ouvriers employés a la vulcanisation du caoutchouc. Union Médical, Paris, 1866, 2d ser., xxix., pp. 339, 356, 374.

Gourdon, P. De l'intoxication par le Sulfure de Carbone. (Thesis.) Paris, 1867.

Pharmaceutical Journal, 2d series, vol. xi., pp. 640, 641, 1869–70.

Huguin, L. Contribution à l'étude de l'intoxication par le Sulfure de Carbon chez les ouvriers en caoutchouc soufflé. (Thesis.) Paris, 1874.

Marche, A. De l'intoxication par le Sulfure de Carbone. (Thesis.) Paris, 1876.

Galezowski. Recueil d'Ophthalmologie. 1877, 2d ser., ii., pp. 121, 130–32.

Galezowski. Des Amblyopies et des Amauroses Toxiques. Paris, 1878, pp. 86, 143.

Payen, A. Industrial Chemistry. Paul's translation, 1878.

Poincaré, L. Recherches expérimentales sur les effets des vapeurs du Sulfure de Carbone. Archives de Physiologie normale et pathologique, 2d ser., vol. vi., 1879, p. 19.

Lewin, L. Ueber das Verhalten der Xanthogensäure und der Xanthogensauren alkalien im thierischen Organismus und die Giftwirkung des Schwefelkohlenstoffs. Virchow's Archiv., 1879, vol. lxxviii., p. 113.

Gallard, T. De l'intoxication par le Sulfure de Carbone. Progrès Médical. Paris, 1879, vii., p. 217.

Cooley. Cyclopædia, 1880, p. 404.

Spon. Encyclopædia of Industrial Arts, 1882; Articles on "Sugar Refining," "Chloride of Sulphur," "Carbon Bisulphide," "Oils."

Bruce, A. Chronic Poisoning by Bisulphide of Carbon. Edinburgh Medical Journal, May, 1884, vol. xxix., p. 1009.

Nettleship. A Case of Amblyopia, with Partial Optic Atrophy and General Nervous Depression and Emaciation Caused by the Vapor of Bisulphide of Carbon and Chloride of Sulphur. Trans. Ophth. Soc. United Kingdom, 1884–85, vol. v., p. 149.

Fuchs. Amblyopia with Slight Neuritis, Followed by Pallor of the Disks, Caused by the Vapor of Bisulphide of Carbon and Chloride of Sulphur; Severe Nervous Depression. Trans. Ophth. Soc. United Kingdom, 1884–85, vol. v., p. 152.

Report of Committee Appointed to Investigate the Action of the Vapors of Bisulphide of Carbon and Chloride of Sulphur on the Sight and Health Trans. Ophth. Soc. United Kingdom, 1884–85, vol v., p. 157 [24 cases].

Berbés, Paul. Observation de Pseudo-tabes dû à l'intoxication par le Sulfure de Carbone. La France Médicale, Paris, 1885, i. p. 3.

Gunn, R Marcus. Toxic Amblyopia from Bisulphide of Carbon. Trans. Ophth. Soc. United Kingdom, vol. vi., 1885–86, Lond., 1886, p. 372.

Changarnier. Amblyopie par le Sulfure de Carbone. Recueil d'ophthalmologie, Paris, 1886, viii., 3d ser., p. 280.

Gand. Amblyopie toxique. Bull. de la Clinique nationale Ophthalmologique de l'Hospice des Quinze-Vingts. Paris, 1886, iv., No. 41, 576; xl., *Ibid.*, No. 33, 555.

Gunn, R. Marcus. Amblyopia from Bisulphide of Carbon. Ophthalmic Review, Lond., 1886, v. p. 56; Trans. Ophth. Soc. United Kingdom, 1887, vii.

Hirschberg, J. Brief Abstract of a Case in a Foot-note. Centralbl. für prakt. Augenheilk, August, 1886, p. 49.

Ross, James. Two Cases of Chronic Poisoning by Bisulphide of Carbon. Medical Chronicle, Manchester and London, 1886–87, vol. v., p. 257.

Little, D. Toxic Amblyopia—Bisulphide of Carbon. Trans. Ophth. Soc. United Kingdom, 1886–87, vol. vii., p. 73, Lond., 1887; Medical Chronicle, January, 1887, vol. v., p. 257.

Smith, Watson. Poisoning with Bisulphide of Carbon and Other Factory Gases. Part I. Medical Chronicle, Manchester and London, 1886–87, vol. v., pp. 353–359.

Duboys de Lavigerie. Accidents oculaires produits par l'inhalation du Sulfure de Carbone. Recueil d'Ophthalmologie, 3d ser., vol. ix. p. 535.

Dumont. Atrophie papillaire toxique (Sulfure de Carbone). Bull. de la clinique Nat. Ophthalmoligue de l'Hospice des Quinze-Vingts. Paris, 1887–88, v. vi. No. 39, 960.

Becker, F. Schwefelkohlenstoff-amblyopie. Centralbl. für prakt. Augenheilk., Leipz., 1889, xiii., p. 138.

Hirschberg, J. Schwefelkohlenstoffvergiftung. Centralbl. für prakt. Augenheilk., Leipz., 1889, xiii., pp. 268–269.

Nuel and *Leplat.* Amblyopia due a l'intoxication par le Sulfure de Carbon. Ann. d'oculistique, Brux., 1889, 101–102, 14 sér., iii.–iv., f. 145.

Gallemaerts, E. Amblyopie par le Sulfure de Carbone. Ann. d'Oculistique, Bruxelles, 1890, 103–104, 15 sér., iv., pp. 154–158.

AMBLYOPIA FROM IODOFORM.

History. General iodoform poisoning has been divided into six varieties, characterized by various symptoms—fever, gastro-intestinal irritation, and peculiarities in the circulation, especially a rapid and soft pulse. In some cases the phenomena resemble meningitis, namely, contracted pupils, restlessness, headache, active delirium, stupor, and death; in others, cerebral congestion. Fatty degeneration is a prominent pathological lesion.

Although iodoform was discovered in 1822, it was not until 1882 that a case of toxic amblyopia attributed to this drug was recorded by Hirschberg.[1] Four years later Dr. E. Hutchinson,[2] of Utica, N. Y., described a

[1] Centralbl. f. prakt. Augenheilk, 1882, vi., p. 92.

[2] N. Y. Med. Journ., 1886, xliii., p. 16.

second case, and recently Priestley Smith,[1] in England, and Valude,[2] in France, have added two additional cases to the literature.

Etiology: Pathway of Entrance of the Poison. As is well known, many of the cases of general iodoform poisoning have resulted from its absorption after it was sprinkled over wounds of large area, hence in the toxic amblyopias arising under its influence a similar source of entrance into the economy might be expected. This is true in Hirschberg's and Valude's cases, but in Hutchinson's and Priestley Smith's patients the toxæmia followed the absorption of iodoform pills, in the former instance associated for a time with the administration of creosote. The latter drug, however, was proven to have been without effect upon vision.

Two of the four patients were young, Valude's case being a child of twelve years. The other two were adult males, Priestley Smith's patient being thirty-one years. The age in Hutchinson's case is not given.

The influence of tobacco or alcohol was practically excluded in Hutchinson's case; his patient did not smoke, and drank only a little wine at dinner, while Smith's patient was not an excessive smoker. Moreover, the rapid onset of the amblyopia occurred seven weeks after he had discontinued smoking. The other two patients, namely, those of Hirschberg and Valude, both girls, one sixteen years and the other twelve years, are not likely to have come under the influence of either tobacco or alcohol. Hence it may be fairly assumed that the disturbance of vision in these cases was the result of the toxic influence of iodoform. Michel,[3]

[1] The Ophthalmic Review, 1893, xii., p. 101.

[2] Annales d'Oculistique, 1893, cix., p. 378.

[3] Jahresbericht f. Ophthalmologie, 1893, xxiv., p. 470.

commenting on Smith's case (see Case III.), regards it as one of tubercular disease of the nerve-head. How he reconciles this diagnosis with the comparatively rapid improvement of the patient is difficult to understand.

The *quantity* necessary to produce amblyopia appears to be considerable; thus, Smith's patient consumed 1000 grains in forty-one days, and then toxic symptoms appeared. The daily dose of iodoform in Hutchinson's case was 9 grains, begun in June, 1884, and continued until the following February. During this time 6 grains of creosote were also daily consumed. In the other two cases it would be difficult to estimate the amount of iodoform, as the absorption was through an abraded surface.

Symptoms. These vary in the several cases which have been reported, but all appear to have one symptom in common, namely, marked reduction of central acuity of vision. The vision of Hirschberg's patient was 1/20 and 1/30, of Hutchinson's 1/100, and of Priestley Smith's 6/30 and 6/24. In Valude's case the vision was extremely bad, owing to atrophy of the disks.

The pupils may be widely dilated and sluggish in their reactions. Exact observations of the effect of this drug on accommodation have not been recorded.

In one case the *ophthalmoscopic appearances* were normal; in another the disk appeared grayish white, somewhat resembling that seen in tobacco-amblyopia; in a third there was haziness of the nerve-tip's margin, but no pronounced papillitis, while in one instance there was atrophy of the papilla.

The *field of vision* has been reported normal and the color-perception good, but in each of the two best studied cases (those of Hirschberg and Priestley Smith), there was a *bilateral central scotoma*, in the former from four to

eight degrees radius, and in the latter well-marked and absolute for white paper at or near the fixation point. Otherwise the visual field appeared to be intact.

Hence we may expect in typical iodoform-amblyopia marked reduction of the central acuity of vision, unimproved by glasses; preservation of the peripheral visual field, but a central scotoma at or near the fixing point; and negative ophthalmoscopic appearances, or, at most, some grayness of the disk with blurring of its margins. True, complete atrophy is reported in one instance, but, as will be seen from the abstract of the case, it is by no means certain that iodoform was responsible for the visual conditions. The close analogy between this disease and a similar affection arising under the influence of tobacco and alcohol will be readily recognized.

Diagnosis and Prognosis. The *diagnosis* must of course be based upon the history of the case, *i. e.*, long-continued internal administration of iodoform, or the use of the powder over an extensively abraded surface, in connection with the visual disturbance. There are no distinguishing features in the visual phenomena upon which to rest an absolute diagnosis.

The *prognosis*, if Valude's case is excluded, is good, provided the patient is freed from the influence of the drug which has created the defect in vision.

The duration of the amblyopia depends somewhat upon the quantity which has been taken and absorbed. In one case restoration occurred in eight days, while in another nearly three months elapsed before the central scotoma disappeared.

Pathology and Pathological Anatomy. Judging from clinical symptoms this form of amblyopia should be relegated to those of peripheral origin, and probably depends upon some influence of the drug on the fibres

of the papillo-macular bundle, analogous to the effect of tobacco, lead, alcohol, and other poisons.

It is not without interest to recall in this connection that iodoform is broken up in the system into iodic acid and iodine, and that Binz believes that it is the latter ingredient which influences the general nutrition. Furthermore, it is one of the drugs which, in a pronounced degree, has the power, in toxic doses, of producing fatty change in the various tissues of the body.

Treatment. This consists, first, in the separation of the patient from all possible influence of the drug. Internally, strychnine appears to have been of the greatest service, and should be administered, as in other toxic amblyopias, by the hypodermic method. General anæmia, which is not unlikely to be present, may be combated with iron. Should actual atrophy of the disk supervene, the usual measures, alterative and stimulating, may be tried. Two of the cases were promptly relieved by the strychnine treatment.

The following are extracts of the four cases thus far recorded:

Case I. Hirschberg reports the case of a sixteen-year-old girl operated upon for disease of the hip, the wound being dressed with iodoform. During this time visual disturbances set in; vision in O. D. equalled 1/20 and in O. S. 1/30, and there was a central scotoma. The peripheral visual field was intact, the fundus normal, and the pupils widely dilated. Recovery took place in eight days.

Case II. E. Hutchinson reports a case of toxic amblyopia from the prolonged internal use of iodoform and creosote, as follows: The patient took creosote with benzoic acid for cough; afterward iodoform, which he began in January, 1884, and continued until the following Feb-

ruary, when vision failed. From June, 1884, the daily dose of creosote was 6 grains and of iodoform 9 grains. He did not smoke, and drank wine only at meals. The vision was 1/100, unimproved by glasses. Normal visual field, good color perception, and grayish-looking disks were present when the patient was examined in February, 1885. The pills were stopped, and under the influence of strychnine the vision improved, and by April was 20/40 and 20/70; then the cough returned, and the pills without the iodoform were again administered without harm, thus practically proving that it was the iodoform which had exercised the pernicious influence on the optic nerve.

Case III. Priestley Smith reports the following case, which is reproduced in his own words: "Harry B., aged thirty-one, was admitted November 18, 1891. He had been treated three months earlier for pleuritic effusion. He was now suffering from diarrhœa, vomiting, emaciation, and rapid loss of strength. He was found to have, among other changes, dry pleurisy at both bases, and a solid substance in the abdomen, which was regarded as being probably due to tuberculosis of the omentum. The diagnosis was chronic tubercular pleurisy and peritonitis.

"From December 5th to January 15th, a period of forty-one days, he was treated with iodoform in pills, and during this time took no other drug excepting five-grain doses of bicarbonate of soda in infusion of calumba. He took at first two grains of iodoform three times a day, and the quantity was steadily increased until during the last ten days he took four grains eight times a day, *i. e.*, *thirty-two grains per diem.* He took altogether about 1000 grains in forty-one days. The iodoform was then stopped on account of toxic symptoms, especially amblyopia.

"The onset of the amblyopia was associated with headache, giddiness, and faintness, the latter being due probably to a weak heart; also with diarrhœa, a constant taste and smell of iodoform, twitching of the hands, and emotional depression; also with a marked change in the urine, viz., from high acidity with uric acid and urates to alkalinity with triple phosphates. On the third day after the iodoform was stopped there were great drowsiness and slight left ptosis; the next day the drowsiness had given place to irritability, and the ptosis was gone. There were numbness and tingling in the legs, and the knee-jerks were increased.

"Four days after the iodoform had been discontinued I examined the patient with regard to his eyes. The refraction was normal, the media were clear in both eyes. In both there was slight haziness of the disk margin, but no pronounced papillitis. Vision was greatly impaired, a well-marked central scotoma, absolute for white paper at or near the fixation point, being present in each eye. Tested with red the scotoma appeared to be larger than those commonly found in tobacco amblyopia. The loss of vision appeared to have begun a day or two before the iodoform was stopped, and whilst the patient was taking the maximum quantity of thirty-two grains a day, and to have rapidly increased from day to day. Up to this time he had certainly seen well, for he had observed the pictures on the far side of the ward and had read the newspaper as he lay in bed. Re-examined seven days after the iodoform was stopped, the haziness of the disk margins was rather more pronounced. The patient thought his vision had already begun to improve.

"Four weeks later he came again under my notice, and had still a central color scotoma just below the fixation point. Vision: R. 6/36, L. 6/24. He then received sub-

cutaneous injections of strychnine for a week, and later iron and strychnine by the mouth. Vision improved steadily, and on April 8th, *i. e.*, about three months after the onset of the amblyopia it had risen to 6/8 in each eye, and no scotoma could be found. The patient's general condition was much better than at the time of his admission into the hospital.

"The following facts as to the patient's use of tobacco appear to exclude that agent as a possible cause of the amblyopia. Before admission he had habitually smoked about two ounces a week; during his stay he did not smoke at all, excepting about a quarter of an ounce on Christmas day. It was, therefore, about seven weeks after the discontinuance of regular smoking, and three weeks after the one indulgence at Christmas, that the rapid onset of the amblyopia occurred. Moreover, during the period of recovery from the amblyopia, when he was no longer an in-patient, he resumed his smoking, though probably in smaller amount than before."

Case IV. Valude reports a case of optic neuritis and optic nerve atrophy caused by iodoform intoxication in a case of burn, as follows: A child, twelve years of age, received a large burn, covering the right side of his body, on August 25, 1891. The burn, mainly of the third degree, covered the right side of the thorax, the external surface of the right thigh, and the posterior external surface of the right upper arm; in addition were two burns on the left thigh. From the beginning the child was dressed with iodoform constantly. Eight months after the accident general toxic symptoms developed—anæmia, diarrhœa, cephalalgia, vomiting, and fever. At the same time vision declined rapidly, and in a few days there was amaurosis. Previous to this time normal visual acute-

ness had been present. When these symptoms were pronounced the iodoform was stopped and replaced by salol. All of the general symptoms disappeared, but the amblyopia persisted.

Valude examined the patient sixteen months after the injury and eleven months after the beginning of the amblyopia and observed the following symptoms: light reflex of the pupils normal; vision in the right eye, fingers at 10 centimetres—in the left, fingers at 20 centimetres; total color blindness. The visual field for light did not seem to be diminished. There was complete double optic-nerve atrophy without positive indication of previous neuritis; the vessels were slightly contracted.

Valude thinks the appearance of the amblyopia during the iodoform intoxication indicates a relation of cause and effect, although he recognizes the fact that there may have been a meningo-encephalitis, causing a neuritis of the optic nerve. Another possibility is a retrobulbar neuritis from the direct action of the iodoform. Finally the atrophy may be ascribed to the extensive burn, or at least may be regarded as an anomalous symptom of such a condition, since we are well aware that widespread destruction of the integument by burns is capable of producing astonishing alterations of nutrition in the deeper structures—witness the so-called duodenal ulcers. Under similar circumstances retinal hemorrhages may occur (Knies, Mooren, Wangenman).

Iodine and Iodide of Potassium. It is improbable that true cases of amblyopia or amaurosis, in the sense in which these words are used in this essay, attributable to the toxic influence of iodine and iodide of potassium, have been described.

Hyperæmia of the conjunctiva, watering of the eyes, etc., are well-known symptoms of various types of iodism,

and the conjunctivitis ("calomel conjunctivitis") which follows dusting calomel into the conjunctival cul-de-sac of a patient who at the same time is taking iodine or iodide of potassium, is well known; but visual disturbances referable either to affections of the optic nerve or the retina, caused by these drugs, do not seem to occur.[1]

Chlorate of Potassium, in poisonous doses, in addition to producing extensive alteration of the composition of the blood, may cause an active nephritis. Hence Knies and other writers have suggested that a uræmic amaurosis might be the result of its toxæmia, precisely as this occurs in saturnine poisoning. Cases, however, in which this actually has been observed are not quoted, and, so far as I am aware, are not on record.

Hydrocyanic Acid and Cyanide of Potassium, both quickly fatal in toxic doses, cause a peculiar staring of the eyeballs and wide dilatation of the pupils, due, no doubt, to rapid asphyxia and cardiac failure.

Temporary amaurosis has also been reported, for example, by H. De Tatham.[2] The patient was a woman who was exposed to the vapor of dilute hydrocyanic acid, which she used in cleaning lace. About one-half ounce of the drug was employed in rubbing the fabric. Unfortunately, ophthalmoscopic examination was not made. The external appearance of the eyes was normal; there was well-marked hemiopia; all of the symptoms disappeared in a few hours.

A case of this character is to be explained by some decided disturbance, either of the retinal circulation, or, more likely, of that supplying the cortical centres.

[1] Some vague references are found in early writings. Consult Deval (loc. cit.).

[2] British Medical Journal, 1884, i., p. 409.

Nitrite of Amyl, Nitrite of Ethyl, and Nitro-Glycerin, in addition to their actions as vasomotor paralyzants and depressors of the motor centres of the spinal cord, in toxic doses have the power of changing the blood to a chocolate color, owing to the development of methæmoglobin. Visual disturbances during poisoning are due to these circulatory effects. There are, however, so far as I know, no cases on record, either experimental or clinical, in which any of these drugs has produced a true toxic amblyopia, or, indeed, symptoms analogous to such a condition.

Like santonin and one or two other drugs, nitrite of amyl in toxic doses causes *xanthopsia*. This has been noted by Peck, Landendorf, and other observers.[1]

Some reporters, for example, Aldridge,[2] believe that they have seen dilatation of the retinal vessels and flushing of the optic papilla during the inhalation of nitrite of amyl; but these observations have not been confirmed. In the later stages of the poisoning the pupil is widely dilated.

An interesting therapeutic point, in connection with nitrite of amyl, is its power of temporarily improving the vision of those who suffer from tobacco-amblyopia. I have confirmed this observation in a few instances, but I have never been able to see any ophthalmoscopic change in the retinal circulation during its inhalation.

AMBLYOPIA FROM NITROBENZOL AND DINITROBENZOL.

History. *Nitrobenzol* (oil of mirbane) is produced by the action of strong nitric acid on benzol, and forms an

[1] See Therapeutics, Materia Medica, and Toxicology, by H. C. Wood, 5th ed., p. 358.

[2] West Riding Lunatic Reports, vol. i., p. 187.

oily liquid with an odor like that of oil of bitter almonds, and hence it is sometimes called "artificial oil of bitter almonds." It is used in the manufacture of aniline, and also for scenting soaps, etc.

Dinitrobenzol results from the action of nitric acid on benzol at a high temperature, and is used in making explosives, such as "roburite" and "sicherheit."

Attention was first called to the effect of these substances on the visual functions by Nieden,[1] who found defective vision in one person among twenty-five, who suffered from the toxic influence of the chemical. Ross[2] mentions the case of a miner who used roburite, and who "felt blind" when fixing his eyes in a certain position, *i. e.*, on a mirror placed above their level. The imperfect vision was probably due to the nystagmus from which he suffered and not to the nitrobenzol.

Professor White[3] has made a thorough study of nitrobenzol poisoning, and refers to the eye affections as comparatively rare, six cases only having come under his observation in a wide experience.

Litten[4] reports a typical case of amblyopia from this cause, and Simeon Snell[5] contributes a thorough paper on the ocular lesions in dinitrobenzol-amblyopia, and describes five cases, in addition to many examinations among the workers. Recently F. A. Pockley has recorded a case in Australia.[6]

Etiology: Pathway of Entrance of the Poison. Nitrobenzol or dinitrobenzol may enter the system through

[1] Centralbl. f. prakt. Augenheilk., 1888, xii., p. 194.

[2] Medical Chronicle, 1889, x., p. 89.

[3] The Practitioner, 1889, xliii., p. 14, and Provincial Med. Journal, 1892, ii., p. 462.

[4] Centralbl. f. prakt. Augenheilk., 1891, xv., p. 118.

[5] British Medical Journal, 1894, ii., p. 449.

[6] Australas. Med. Gaz., Sydney, 1894, xiii., p. 340.

the mouth, or through the lungs by the inhalation of the fumes or the fine dust, or through the skin. Workers in manufactories are the ones most exposed, especially to absorption through the integument, or through the respiratory tract.

Snell makes the following interesting observations: "The presence of impure products increases the danger of working with dinitrobenzol. The dinitrobenzol arrives at an explosive factory in slabs, say, of 15 inches square and about 4 inches thick. These are first ground in an apparatus with steam rollers not at all unlike a small mortar machine. In this process a good deal of dust is given off, and the men remark on the smell of bitter almonds. The next step is to take the yellowish powder thus obtained to the mixing-shed, where it is put into a large pan and mixed with oxidizing salts and other materials and heated with steam. It may be put into one of these pans, say, at 7.30 A.M., and be heated until noon. Then it is cooled by cold water being pumped on the outside of the shell. When cool the material is turned out of the 'mixer.' It is during the taking out of the material from the mixer that workmen are especially exposed to the vapor. The dangers are lessened by the adoption of a 'cowl' to the mixer, and also by the use of fans. Thus prepared, the explosive is put away in cylinders and kept until required. The next step is to take it to the filling-room, where it is put into cartridges, wedged and stamped, and finally it goes to the dipping-shed, where the cartridges are waterproofed by dipping them in liquid paraffin wax.

"The most injurious work is that of 'grinding' and 'mixing,' especially the latter. Men are employed in these processes. For the 'filling' of the cartridges, and for the dipping also, women and girls are employed. In

the first named the powder is shovelled into the cartridges and directly handled; a good deal of dust is also given off. Respirators and gloves are used, as they are also by the men mixing and grinding. The 'dippers' are the least exposed to the effects, it would appear, but they do suffer. The greasiness about the hands from the paraffin may also aid absorption. Here also gloves and respirators are worn. There is not much dust, the powder being confined inside the cases."

Age, sex, and previous general condition appear to exercise no special influence on the liability to the noxious effect of these substances.

No definite rule can be formulated as to how long "workers" may continue at their employment with impunity. Symptoms of poisoning may come on rapidly, or gradually appear after many months of occupation, during which the sufferer may often feel the poisonous influence.

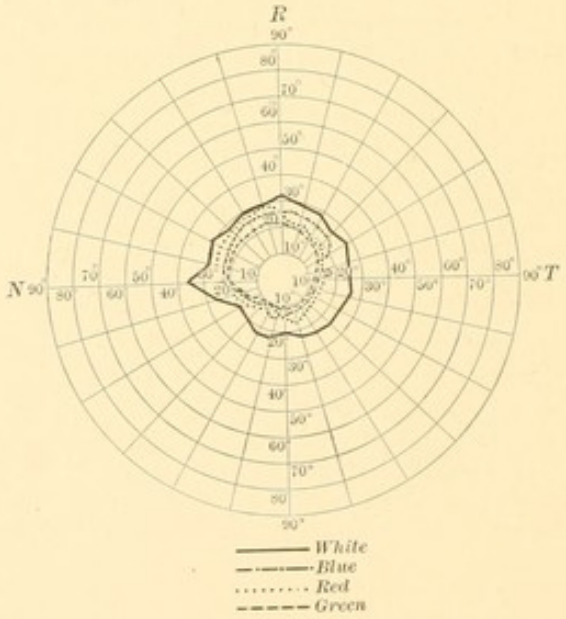
As some of the workers have used tobacco, the relation of this drug to the production of amblyopia must be considered. Touching this point, Snell writes: "My men were smokers, but before coming under observation they had reduced the quantity consumed. Further than this, in one case, well observed for a long time, complete recovery took place, whilst tobacco was persevered in without restriction." We may conclude that the carefully reported cases of amblyopia were due to the direct effect of the poison and not to any intercurrent disease or evil habit.

Symptoms. The general symptoms of nitrobenzol poisoning may be thus summarized: headache, muscular weakness and bluish color of the face; later, general cyanosis, disturbed consciousness, dilated pupils, general muscular relaxation, rapid, shallow respiration and thready, failing pulse.

The *ocular symptoms* are: Diminished central acuity, varying from 6/24 to 4/60, normal pupillary reactions, although somewhat sluggishly performed (Nieden), contraction of the visual field, sometimes a color scotoma, and definite ophthalmoscopic changes.

The latter are: A darker color of the fundus than normal, "as if stained with ink" (Litten); naturally, or only moderately overfilled arteries, and decided venous hyperæmia, the veins being dark, full, and tortuous; pale optic disks, with occasional slight blurring of their margins. Decided extravasations appear not to have been observed, except in Nieden's case, in which there was an exudate near the papilla; small retinal hemorrhages were noted by Litten.

FIG. 38.



Field of vision of Nieden's patient suffering from nitrobenzol amblyopia. There are concentric contraction and partial reversal of the color lines.

The *field of vision* for white is concentrically contracted, and also that for color, the blue field being in general smaller than the red field (Nieden); in other

words, a partial reversal of the color lines. (See Fig. 38.[1]) In some cases there is a central scotoma for red and green (Snell). The visual field-phenomena appear to be similar in each eye; in other words, they indicate symmetrical defects.

The venous hyperæmia and discolored fundus oculi are present in those who work in the manufactories, even though they have no visual disturbances. This has been demonstrated by a number of examinations made by Snell.

Diagnosis. This amblyopia resembles that caused by iodoform and bisulphide of carbon in so far as an occasional central scotoma and disturbances in the field of vision are concerned. It also, but less nearly, is related to tobacco-amblyopia, except that there is contraction of the peripheral visual field. The most distinguishing feature is the ophthalmoscopic appearance; the dark tint of the eye-ground, and the unusually swollen, tortuous, and dark veins are not present in other toxic amblyopias.

Prognosis. If the patient leaves the work in which he is engaged the prognosis is good. Restoration to perfect vision eventually takes place, although some months may elapse before this is accomplished. The serious general conditions which arise in this toxæmia may ultimately place the patient in a condition of chronic invalidism.

Pathology and Pathological Anatomy. The pathology of these cases of poisoning is by no means settled. The effects of these chemicals upon the system, according to Buzzard, Ross, and other writers, suggest multiple or peripheral neuritis, a condition which we know is caused

[1] This field is analogous to many seen in hysterical subjects. Compare paragraph on toxic hysteria.

by arsenic, alcohol, lead, and probably bisulphide of carbon. There is also evidence to show that the drug has a centric action and causes death from paralysis of the motor centres.

So far as the eye is concerned it is evident, as Nieden has pointed out, that there is vasomotor paralysis, which would account for the over-filling of the veins, and perhaps indirectly for the retinal exudations which have been observed in a few cases. Finally, it is to be remembered that nitrobenzol belongs to the group of substances which have the power of changing the blood to a deep chocolate brown and causing it to lose its power of absorbing oxygen.

The scotoma for colors suggests axial disturbance in the optic nerve, although the exact lesion, if such there be, cannot be determined without microscopic examination, opportunity for which has not yet occurred.

Treatment. The treatment consists in removing the patient from the noxious influences of the poison and the management of his case on general principles. The usual remedies are indicated, namely, strychnine to stimulate the optic nerve and alteratives to help absorb the exudations in the retina and possibly in the nerve fibres. Of these no doubt the bichloride of mercury and the iodide of potassium would fulfil the most important indications.

The *preventive treatment* of this condition, as well as of the general poisoning, is a matter of importance, and Simeon Snell suggests a number of rules: First, that the different processes should be conducted as much as possible in the open air; second, that in mixing, closed vessels should be employed; third, that fans might be of service; fourth, that in the mixing process some form of respirator should be employed; fifth, that handling of the

substances with the bare hand, or direct exposure to the vapor, should be avoided. As in lead manufactories, great stress should be laid upon proper washing of the hands, etc., after the day's work is done.

The following are abstracts of the most important cases of amblyopia caused by nitrobenzol or dinitrobenzol which have thus far been reported:

CASE I. Nieden,[1] in one case out of twenty-five which he examined, found that the poison had affected the eyes. Vision was reduced to 10/200; there was concentric restriction of the field of vision; ophthalmoscopically there was marked hyperæmia of the retina and a distinct exudation surrounding the principal veins. Vision remained much the same for four weeks, and then slowly became normal.

CASE II. Litten[2] gives the following description of a case of poisoning: The patient was comatose. The skin and as much of the mucous membrane as could be seen were colored from blue to gray-blue. The breath smelled of bitter almonds. The fundus oculi was of an intense violet color; not only the retina, but the papilla, arteries, and veins were colored and appeared as if stained with ink. The veins were fuller than normal. There were some small hemorrhages in their neighborhood. Later it was found that vision was normal; there was no color disturbance.

CASES III. and IV. Professor White[3] has seen six cases of amblyopia, four of which were referred to Mr. Richard Williams for ocular examination. Two of these are reported, as follows: James C., aged twenty-

[1] Loc. cit.

[2] Berlin. klin. Wochenschr., 1881, xviii. pp. 6, 23.

[3] Loc. cit.

four, could not see objects distinctly; vision 20/200; fundus darker in color than normal, veins very tortuous and hidden by effusion here and there; no hemorrhages. William C., aged thirty-nine, had worked in nitrobenzol for two years, and had found nothing wrong with his sight until two months before coming for treatment. Ophthalmoscopic examination in the right eye showed the fundus darker than normal; in the left eye abnormal tortuosity of the veins; vision, O. D. 4/60, O. S. 6/60.

The following five cases are reported by Simeon Snell, the report being accompanied by charts of the field of vision, showing concentric contraction. They are reproduced, somewhat condensed, in Mr. Snell's own words:

CASE V. "J. H., aged thirty-five years, presented himself on February 11, 1892. He stated that just before the previous Christmas his sight commenced to fail. On reaching home at night he could not recognize his wife across the table. During the next few days it became much worse, and then deterioration was more gradual. Recently his vision has remained about stationary, and this, as will be explained, has been associated with an alteration of work. Vision in each eye is 3/60, and he reads J. 16. Both optic disks are decidedly pale, the edges are quite defined, and there is no appreciable diminution in calibre of vessels. The field of vision is somewhat contracted concentrically, and there is small, fairly defined central scotoma for red and green. The pupils are normal in all ways. The patient has been a smoker for twenty years, consuming generally about one and one-half ounces a week; he has not been smoking more nor less than usual lately; the kind of tobacco he smokes is cut cavendish. He takes very little alcohol, being almost a teetotaler. His face is pallid, lips bluish, and conjunc-

tivæ yellowish. The man's occupation properly is that of a blacksmith, but being out of employment, and failing to get anything to do at his own trade, he went to work in July, 1891, for a company where explosives, in which nitrobenzol was used, were made. Previously to undertaking this work he asserts that his health was perfectly good and sight excellent. On the first day he asserts he felt the poisonous effects of the benzol. A marked effect had been wrought on his sexual functions. The only other point to mention is that he suffered from an attack of influenza before going to the explosive works.

"He was advised to avoid all contact from the benzol compounds, and the firm provided an occupation away from these for him. He was prescribed liq. strych. in a mixture. He was advised to continue his smoking precisely as he had been accustomed to do. Progress toward recovery was steady.

"On March 12 vision = 6/12 in each eye. A few days later he said that his functions were restored to normal. On April 24 V = 6/6, and shortly after this he discontinued the strychnine. On May 20 vision still the same, taking no medicine. A final note may be recorded. On November 19, no red scotoma, and field of vision good. Vision is excellent, and he reads J. I. easily and V = 6/6. There is still some pallor of optic papillæ. He looks well, has a good color, does not suffer from fatigue, and can work as hard as ever he could. He is still a little shorter in breath than formerly, and there is some remaining numbness in hands and toes.

Case VI. "C. W. F., aged thirty-eight years, came to see me on April 9, 1892, complaining of defective sight. He had been employed at the same factory as the last patient. He had worked there as a 'mixer' off and on

for twelve months. His skin is jaundiced and the conjunctiva is distinctly yellow, and the lips markedly blue. He suffers from shortness of breath. After a day's work he experiences aching of forearms and of legs, and also tingling of fingers. Occasionally he has had vomiting and nausea. Sometimes at work, or after leaving it, he has felt as if he were drunk; weak, giddy, and staggering. He cannot drink anything now, because of the greater effect it has on him. His urine is black; specific gravity 1024. He had a pulmonary systolic murmur. His sight had been failing since the previous Christmas, about four months. Vision in the right eye was 6/24, left 6/36; both optic papillæ were somewhat pale. In each eye there was a central scotoma for red, and concentric contraction of field. He has been a smoker since the age of seventeen years; for the last three years the quantity he has smoked per week has been one and one-half ounces; before that time it was about three and one-half ounces a week. His sight had been much better since he discontinued working at the factory. More recently I heard that he had re-enlisted in the army.

Case VII. "F. E. was seen on April 19, 1892. He had been a 'mixer' at the same explosive works as the cases already mentioned, but had left the place twelve months previously. Since then he had been employed as a laborer at some mills. When working with the nitrobenzol, after a day's labor, he often had attacks of giddiness, but no nausea nor vomiting. Before going to this work his health and eyesight were both good. After being employed there, however, for about seven months, he noticed that his sight was affected. It was when he had been occupied with 'mixing' for about two weeks that his sight became impaired. He relinquished the work altogether, for he feared that he

would become perfectly blind, and since discontinuing it he states that his vision has become better. He has been a smoker for fourteen years, and is as much addicted to it now as he ever was. Two ounces of 'twist' a week is his usual quantity. When his sight commenced to fail he was smoking less, because the breathlessness compelled him to do so; he was only at that time smoking about one-half ounce a week. In each eye V = 6/36; the disks are pale, but there is no diminution in calibre of vessels, and the edges of papillæ are well defined. The visual field is contracted concentrically, but there is no scotoma for red.

CASE VIII. "S. E. C., aged seventeeen, was first seen by me on the occasion of my visiting the works in February, 1892. The following note was entered: Has been 'filling' for six months; marked shortness of breath; very anæmic; lips bluish; pulmonary systolic murmur; loud venous hum; tips of the fingers feel cold to the touch, although she is not apparently conscious of it herself.

"She was seen again on March 10 and examined with the ophthalmoscope; it is stated that the retinal veins were full.

"On April 12 she came over to see me for more complete examination. She had, it appeared, been employed at the works since August 12, 1891. She now made no complaint of any impairment in sight, and V = 6/6 in each eye. The retinal arteries and veins were both rather full, but especially the veins; the optic papillæ did not indicate any alteration. There was less difference in color between the arteries and veins than usual; the veins were readily traced to the periphery. There was no scotoma for red.

"July 12, 1892. Her sight began to fail shortly after

her visit to me in April. She could not read nor keep any account of the work which was done, which was a part of her occupation. She does not think she is worse now than she has been for the last two or three weeks. There is increased pallor of face, mingled with a bluish tinge; the lips are blue. The color of the hair has curiously altered from a golden to a sort of red. Urine has been very black lately. There is a hæmic murmur over the pulmonary artery, and a very marked *bruit de diable;* pulse is very soft and compressible—about 80, and regular; vision R = 6/36, L = 6/24; she reads J. 2 with each eye. Field of vision appears a good deal contracted concentrically; there is no scotoma for red or green, but there is a good deal of retinal hyperæsthesia, which interferes with trustworthy use of the perimeter. The retinal veins are full; the disks are pale, but the edges are sharp. Her sight, when she was last heard of, remained about the same as at my examination.

Case IX. "C. S., aged fifty-six, was first seen by me on a visit to the explosive works on February 10, 1892. He was then working as a 'mixer,' and he had been doing so for twelve months. With the ophthalmoscope the retinal veins are seen to be much larger than arteries. He made no complaint of his eyesight at this time, but from what he told us later it would appear to have then attracted his attention. From other sources I heard of this man from time to time, and that he was suffering, as it was said, a good deal from the 'powder.' On December 28, 1892, he came to me on account of his eyesight, which he said was failing.

"He had now been a 'mixer' for two years, 'the worst job about the place.' He says his sight had been failing for twelve months, but it had been during the past few months that it had become so much worse. He

could not read the newspaper. V. L = 6/60, R = 6/60, and he reads J. 18. The optic disks were less rosy looking than normal, indeed somewhat grayish; the edges were also a little less defined; the veins were rather full, but there was no diminution in calibre of arteries. The field of vision was contracted concentrically, there was no definite color scotoma, but the central perception of red and green was somewhat dulled. He had been a smoker for forty years; the kind of tobacco had been cut cavendish, and, while formerly he consumed two ounces a week, for the last year it had only been one ounce a week. He had smoked less, he told me, because he had not had the inclination for it, and when he had been working in the mixing-room he had scarcely had the 'wind' for it."

Case X. F. A. Pockley[1] records the case of a man, aged thirty-one years, a mixer in a roburite factory, who presented the following symptoms: He was very pale; otherwise seemed in good health. His vision was very defective; he could only count fingers at a distance of three yards; both eyes were equally affected. There was no central scotoma for red or green, but there appeared to be slight concentric contraction of both fields. The pupils were slightly enlarged and sluggish. Both disks were uniformly pale and flat. Nothing abnormal about arteries or veins or rest of fundus. The patient was placed upon liquor strychninæ and the vision gradually improved, and in six months had returned to normal.

[1] Loc. cit.

AMBLYOPIA AND VISUAL DISTURBANCES CAUSED BY VARIOUS COAL-TAR PRODUCTS.

Visual troubles in men who work in dye factories and in manufactories requiring the handling and preparation of the various coal-tar products have been reported from time to time. Galezowski,[1] for example, describes the workers as suffering from headache, dizziness, malaise, *deficiency in visual acuity*, photophobia, and ciliary injection;[2] but, as Knies remarks, the exact relation of the aniline to these ocular complaints is uncertain.

Galezowski further quotes Manouvrier's[3] observation of a worker, who for ten years had been employed in the manufacture of coal-tar products, suffering from amblyopia, with reduction of the amplitude of accommodation, hemeralopia, and photophobia. In another case the optic papilla was gray and the vessels were reduced in size. Vision improved after stopping the work. He also quotes from Dr. Kohn a case of iritis with amblyopia, the result of intoxication with fuchsin and aniline, and believes that in the coal-tar products the two substances just named are the ones which probably constitute the active poisons.

Of the many products from this source, ANILINE (phenyl-amine), which, as we know, is also more immediately derived from nitrobenzol, was first believed to be an innoxious product, but numerous experiments, as well as cases of poisoning, demonstrate that it is a powerful toxic agent, producing cyanosis, dilatation of the pupil,

[1] Des Amblyopies et des Amauroses toxique. Paris, 1878.

[2] See also Recueil d'Ophthalmologie, 1876, p. 210.

[3] Maladies et hygiéne des ouvriers travaillant à la fabrication des agglomérés de honille et de brai. Annales d'Hygiene Publique et de Méd. légale, 1876, 2d ser., xlv., 3d part, p. 459.

weak pulse, irregular respiration, hæmoglobinuria, and methæmoglobin in the blood. Sometimes its violent local effects have been due to contamination with arsenic, a point that should not be forgotten in connection with the cases of visual disturbances attributed to its influence.

Intense pigmentation of the cornea and conjunctiva has been observed among the workers in aniline dyes, a good example of which is recorded by Mackinlay.[1] The vision was also reduced in this case, but the discoloration of the cornea was so great that ophthalmoscopic examination of the transparent media and fundus was impossible.

As we have seen in the section devoted to nitrobenzol, when aniline exists in this compound as an impurity, it is capable of producing poisoning, in which, with only moderate disturbance of vision, there is developed a form of retinitis characterized by distended veins, discoloration of the eyeground, and a few hemorrhages.[2]

Galezowski was inclined to attribute especial toxic influence to *fuchsin* as well as to aniline. This is not an accurate observation, because we know from the experiments of Cazeneuv and Lépine that *fuchsin* is free from toxic properties, while *safranin*, which is much used as a coloring agent, especially in the red wines, is capable of producing very decided poisonous symptoms.

Creolin, which is a product of the dry distillation of coal and much used as an antiseptic, especially by gynecologists, according to Bitter,[3] is capable, in conjunction with other poisonous symptoms, of causing dull vision in the patients.

[1] Trans. of the Ophth. Soc. of the United Kingdom, 1886, vi., p. 144.

[2] Compare Litten's case on p. 133.

[3] Quoted by Berger. Les Maladies des Yeux, Paris, 1892, p. 48.

Naphthalin, officinal in the U. S. Pharmacopœia under the name of *naphthalinum*, a hydrocarbon obtained from coal-tar, is interesting, from the ocular standpoint, because Bouchard discovered that if rabbits were daily given one gramme of the drug to each kilogramme of weight, in from three to twenty days double cataract developed. In addition to this, sometimes before the development of cataract, there were decided disturbances in the transparent media—opacities in the vitreous, spots of fatty degeneration, and œdema of the retina, followed by atrophy of this membrane and the underlying choroid. So, also, hemorrhages have been described, especially in the ciliary body.

So far as I am aware, no similar lesions have been observed in human beings. An interesting research, with entirely negative results, has been carried on, according to Casey Wood,[1] at the Alexian Hospital, in Chicago, where Dr. Burton has carefully examined a large number of typhoid-fever patients treated with maximum daily doses of naphthalin for several weeks. Not the least trace of cataract was discovered.

VISUAL DISTURBANCES IN CARBOLIC ACID POISONING.

In carbolic acid poisoning, especially when this occurs from the medicinal use of the drug, for example, with the old-fashioned spray, or its application to suppurating surfaces, the pupils are usually contracted. Sometimes, however, dilatation has been observed, and sometimes sluggish reaction to the changes of light and shade.

The only definite case of amaurosis from carbolic acid poisoning has been reported by Nieden.[2] The patient

[1] Loc. cit.

[2] Berlin klin. Wochenschr., 1882, xix., p. 748.

was a man suffering from empyema, who had the pleural sac washed out with 100 grammes of a 3 per cent. solution of carbolic acid. This was followed by complete blindness, lasting for twenty hours. There was slight veiling of the margins of the disk, otherwise normal ophthalmoscopic appearance. The convergence reaction of the pupils was natural. There was complete recovery in two days. Nieden ascribes the amaurosis to a species of trophic change caused by an action of the carbolic acid on the retina; but to the other complications in the case an equal responsibility may be attributed.

Resorcin, a diatomic phenol, usually manufactured from benzine and much used locally in the treatment of certain diseases of the skin, as well as for its antiseptic properties both intestinal and external, has the power, as have one or two other similar substances, particularly *chrysarobin*, of producing a violent conjunctival irritation. In poisonous doses it causes disturbance of sight, no doubt, however, due to its general depressing effect, rather than to any action upon the eye itself. Thus, Andeer[1] took 160 grains of resorcin dissolved in a quart of water in the course of two hours, and later repeated the dose dissolved in a pint of water. This was followed by flashes before the eyes, amblyopia, and abolition of hearing and smell, and, finally, by serious disturbances of the nervous system, for example, convulsions. Murrell has also reported a case of poisoning in a woman, but without special visual phenomena. It is not unlikely had Andeer's eyes been examined with the ophthalmoscope during the stage of dim vision, or amblyopia, that an ischæmic condition of the retina would have been found, such, for instance, as is produced by large

[1] Quoted by Stillé in the National Dispensatory, 1893, p. 1731.

doses of salicylic acid or quinine, as these drugs have certain analogous properties in so far as their physiological action is concerned.

Benzine (petrol-ether) is stated by Knies, on the authority of a case recorded in Schmidt's *Jahrbucher*, 1891, i. p. 34, to cause in poisonous doses an immobile pupil and nystagmus.

Picric Acid, prepared by acting with carbolic acid on nitric acid, has been used in medicine with indifferent success, being chiefly valuable as a chemical test. It produces very curious symptoms when given in toxic doses, namely, yellowness of the conjunctiva and disintegration of the red-blood disks.

No positive ocular symptoms—*i. e.*, amblyopia or amaurosis—have been detected in these cases of poisoning; at least if they have, they have not been reported. The drug is mentioned merely because it is one of those which may cause *xanthopsia*, or yellow vision, and, as there is no discoloration of the media of the eye, this phenomenon has been ascribed to a centric action.

Hydracetin. Gruenthal[1] has reported the case of a man who suffered from psoriasis, and during four days rubbed about 30 grammes of hydracetin in a 20 per cent. lanoline salve over the surface of his body. In a few days he became violently ill, cyanotic, feverish, and albumin appeared in the urine. This was followed by violent bleeding of the nose. Gradually the symptoms disappeared, with the exception of considerable anæmia.

Examination with the ophthalmoscope revealed in the left eye two small retinal hemorrhages; the periphery of the visual field was normal, but the two hemorrhages created near the fixation point a small absolute scotoma.

[1] Centralbl. f. prakt. Augenheilk., 1890, xiv., p. 73.

The author thinks it not unlikely that disorganization of the blood, as the result of the hydracetin intoxication, was the cause of the hemorrhage, especially as Guttmann has proved that this drug can destroy the red-blood corpuscles.

VISUAL DISTURBANCES FROM ARSENIC-POISONING.

Arsenical poisoning may be either *acute* or *chronic*, and the symptoms—gastro-intestinal or nervous—depend largely upon the manner in which the drug is taken into the system. Its action may be mainly local on the skin, or it may be absorbed through the stomach, or reach the blood and tissues by inhalation through the lungs. The extensive use of arsenic in the arts has led to many cases of poisoning; for example, from wall paper or articles of clothing.[1]

The widespread pathological lesions which occur in arsenical poisoning, namely, fatty degeneration and peripheral neuritis, would seem to indicate that visual disturbances from its prolonged use ought to be frequent, and that arsenic should produce optic neuritis, optic-nerve atrophy, and other changes which are common enough from lead and allied poisons. H. Derby[2] has reported optic neuritis and amblyopia possibly caused by arsenic. Casey Wood refers to the fact that makers of Paris-green, painters, and paper-hangers, as well as those who take the drug for medicinal or cosmetic purposes, are liable to suffer visual disturbance apart from conjunctival hyperæmia and eczema of the lid.

[1] Those interested in this relation of arsenical poisoning should consult Transactions of the Pathological Society of Philadelphia, vol. xvi., p. 285, which contains an admirable paper upon this subject by Dr. Frederick C. Shattuck, of Boston.

[2] Boston Med. and Surg. Journ., 1891, i., 124, p. 603.

At least one case of supposed arsenical retrobulbar neuritis in all particulars resembling a toxic amblyopia has been reported by Liebrecht.[1] The patient, a male, aged thirty, consulted the reporter for defective vision. With the right eye fingers were counted, and with the left V = 15/200. The pupil-reaction was good. The ophthalmoscope revealed sector-shaped decoloration in the temporal half of the optic papilla, the periphery of the visual field was intact, and there was a paracentral negative scotoma for red and green. The patient denied the use of spirits, drank beer in moderation, had formerly smoked from four to five cigars a day, but had ceased the use of tobacco for four weeks previous to his application for treatment. He had taken arsenic pills regularly for three and one-half years to relieve a psoriasis. The quantity of the arsenic consumed was not calculated.

In spite of the former use of tobacco and a history of syphilis this retrobulbar neuritis is attributed by the author to the consumption of arsenic. This seems to be a far-fetched diagnosis, especially as among the arsenic-eaters of Styria, so far as I know, cases of amblyopia are not reported.

It is to be regretted that in numerous cases of arsenical poisoning which are on record the ocular examinations are imperfect. The fact that they have not been made, or that attention has not been directed to the eye, indicates the probable absence of marked amblyopia.

It has been stated that the prolonged use of arsenic may cause vitreous opacities (Hutchinson).

[1] Klin. Monatsbl. f. Augenheilk., 1891, xxix., p. 181.

VISUAL DISTURBANCES FROM NITRATE OF SILVER.

The long-continued internal use of nitrate of silver causes, as is well known, a peculiar pigmentation of the skin, which has received the name *argyria*. When a solution of the drug is painted on the conjunctiva for any great length of time it may stain this membrane a bluish-black color.

A few ill-defined cases of amblyopia from absorption of the drug through the skin have been recorded. The one usually quoted is the case of Bresgen.[1] This author describes a man suffering from chronic nitrate of silver poisoning as the result of using it in the form of a dye to color his beard black. He had tinnitus aurium and disturbances of vision (amblyopia). The latter was attributed to spasm of various eye muscles; but as there was no ophthalmic examination, the evidence is exceedingly untrustworthy, and we may conclude that it was scarcely a case of toxic amblyopia; indeed, this is the criticism of Uhthoff on this case.

Gowers[2] states that silver poisoning is said to be accompanied by amblyopia in addition to the other symptoms of argyria. He refers to the fact, however, that ophthalmoscopic changes are not recorded, but that silver has been found in the sclerotic sheath of the optic nerve by Reimer. His own observation is that its effect is closely analogous to that of lead, and therefore it is highly probable that the same ocular changes may result in some cases.

[1] Berlin klin. Wochenschr., 1872, ix., p. 72.
[2] Medical Ophthalmoscopy, 3d Edition, p. 279.

VISUAL DISTURBANCES FROM MERCURY-POISONING.

Considering the alterative power of mercury, the fact that in cases of chronic poisoning remarkable symptoms appear, referable to the nervous system, and that in the so-called *mercurial cachexia*, which arises from exposure to the vapor of mercury or its persistent medicinal use, a depraved state of nutrition develops closely resembling scurvy, it is not unreasonable that visual disturbances should also have been reported. Indeed, these are referred to by the older writers, and mercury always finds place among their lists of the drugs capable of producing amaurosis. Thus Deval[1] describes amaurosis under the influence of long-continued action of mercury, and quotes Ramazzini, who regards the amaurosis as largely depending upon the asthenic condition of the patient's system, while Haffner[2] believes that mercurial amaurosis is called into existence by an inflammation of the retina, in its turn the result of absorption of the drug. Himly,[3] in his description of amaurosis occurring from paralysis of the nervous force of the retina, includes among the toxic agents the vapor of mercury.

In more modern times we have a case of optic neuritis reported by Square,[4] and optic atrophy by Galezowski.[5] Dyes[6] observed temporary blindness after a fourteen days' inunction with gray salve, which, aided by profuse diaphoresis, passed away in a few days. Leber, however,

[1] Traite de l'Amaurose, Paris, 1851, p. 268.

[2] Kleinert's Repertorium, X Anno, Leipsic, 1836.

[3] Die Krankheiten und Missbildungen des menschlichen Auges und deren Heilung. Zweiter Theil, Berlin, 1843, p. 428.

[4] Ophthalmic Hospital Reports, 1869, vi., p. 54.

[5] Des Amblyopies et Amauroses toxique, p. 141.

[6] Zeitschrift. f. prakt. Heilkunde, ii., 1865, p. 260.

in his discussion of quicksilver amaurosis, regards these cases as entirely too indefinite to prove that the drug was actually responsible for the symptoms which have been ascribed to its toxic effects. Knies suggests that in the acute mercurial poisoning, for example, when caused by sublimate, hemorrhages and fatty degeneration of the retina are likely to occur.

In connection with mercury it is worth mentioning that Dr. MacAdam,[1] in an address on advances in chemistry, refers to the fact that mercuric methyde, which contains about 80 per cent. of the vapor of mercury, has been known to produce, together with many nervous symptoms marked amaurosis.

Treatment. It is evident that the most appropriate treatment is iodide of potassium, according to the well-known law that after courses of mercury a salt of potassium, particularly the iodide, should be administered in order to liberate the metal stored up in the system. The ordinary treatment of optic nerve atrophy, should this supervene, would be indicated, particularly the administration of hypodermics of strychnine.

The same treatment applies to arsenic-amblyopia.

VISUAL DISTURBANCES IN CHRONIC LEAD-POISONING.

(*Lead-amaurosis; Amblyopia saturnina.*)

History. Saturnine amblyopia has probably been known for more than two hundred years, one of the earliest accounts being a description by Henricus Smetius,[2] of total amaurosis in a woman, who also suffered from saturnine colic and palsy of the legs and arms.

[1] Edinburgh Medical Journal, 1866, xi., Part II., p. 718.

[2] Miscellania medica cun Theodoro Erasto Bruneo. Frankforto, 1611, p. 440.

Several other cases are referred to in the same communication.

The "mysterious colic of the ancients," associated with trouble of innervation and amaurosis, Tanquerel attributes to lead, and Grisolle, in a thesis on lead-colic, printed in 1835, observed three cases of double lead amaurosis. He also refers to the mysterious colic of the ancients, associated with amaurosis, and gives the following interesting references.[1]

Tanquerel[2] recorded twelve cases of amaurosis, nine of which recovered, mostly in about eight days, while the other three died in from two to six days. The autopsies gave negative results, and he concluded that the disease depended upon a stupefying action of the lead upon the retina. Dana, in his translation of Tanquerel's book, refers to nineteen cases of amaurosis, in five of which the amaurosis preceded and in fourteen followed other forms of lead affection. The disease was always bilateral and the pupils immobile.

In discussing the diagnosis, Tanquerel says: "In case of paralysis of the retina produced by lead, the base of the eye is black, and there is perfect transparency of the middle, which the luminous rays must traverse to reach the retina, while often in amaurosis not produced by poison, the color of the bottom of the eye is greenish, grayish, yellowish, nebulous, reddish, brilliant, whitish,

[1] Felix Plater (Felicis Plateri observat., Basle, 1680, in 8vo.); H. F. Hildesius (Observationum medicarum rararum, Frankfort, 1 vol. in folio); Lucas Schroeick (Ephémérides des curieux de la Nature) quotes an observation from 1683. An observation is also given from D. D. Traw in the Commercium literarium ad rei Medicæ incrementum, etc. Nuremberg, 1737, t. 7.

[2] Traité des Maladies de plomb on Saturnines. Tome ii., Paris, 1839. See also Lead Diseases, a Treatise from the French of L. Tanquerel des Planches, with Notes and Additions on the Use of Lead-pipe and its Substitutes. By Samuel L. Dana, M.D., LL.D., 1848.

etc. These changes appear to be the result of an alteration of the retina. (Marjolin, Langenbeck, Kieser, Beer.)" [1]

With the introduction of the ophthalmoscope much of the uncertainty of these cases of amaurosis disappeared, and it was found that the blindness was due, in many instances, to a distinct lesion in the optic nerve or retina, although in a certain number of the cases the diagnosis of "amaurosis without ophthalmoscopic findings" was recorded.

In 1866 Hirschler[2] described alteration in the nerve-head, and Hutchinson[3] recorded cases of neuritis and subsequent atrophy, and a description of defects in the field of vision especially central scotoma are found in the paper of Schneller.[4]

Based on these cases and on others in the literature which justify it, Leber[5] gives the following classification: (1) Cases of sudden bilateral blindness, with bare light perception, but with slight ophthalmoscopic changes. These cases generally recover completely. They resemble uræmic amaurosis, and probably depend upon a specific action on the nervous system of the lead accumu-

[1] Many of the older writers devote considerable space to lead amaurosis, for example, Beer (Lehre von Augenkrankhelten, ii., p. 499) and Duplay, who gives an accurate description of the amaurosis with lead colic. (Archiv. gén. de méd., second series, 1834, Tome v., pp. 5–32); Himly (Die Krankheiten und Missbildungen des menslichen Auges und deren Heilung. Zweiter Theil., Berlin, 1843, p. 428), gives the following interesting references, which may be of interest to those desiring to investigate the older literature: Hufeland's Journal, Bd. 7, 1799, s. 73; Montanceix (Archiv. gén. de Méd., Tome xviii., p. 373); Andral (Journal gen. des Hôpitaux de Paris, 1828, Sept. 5, No. 20); Deshais-Gendron. Lettre sur plusieurs maladies des yeux, causees par l'usage du rouge et du blanc. Paris, 1760.

[2] Wien. med. Wochenschr., 1866, xvi., pp. 105–121.

[3] Ophthalmic Hospital Reports, vol. vi. and vii.

[4] Klinische Monatsbl. f. Augenheilk., 1871, p. 240.

[5] Graefe und Saemische, Handbuch der Augenheilkunde, Bd. v., p. 886.

lated in the body by temporary renal failure. (2) Cases of gradually increasing amblyopia, with central scotoma, contraction, or sometimes normal condition of the visual field, and hyperæmia of the papilla and retina. (3) Cases of sudden or gradual neuritis, which end in amaurosis; and, (4), Cases resembling albuminuric retinitis.

Galezowski[1] thus classifies the different disturbances of vision which may occur under the influence of lead: Plumbic incrustations of the cornea and conjunctiva; saturnine amblyopia and general tremors; optic neuritis; atrophy of the papilla; albuminuric saturnine retinitis, paralysis of the eye muscles, and atrophy of the papilla, with locomotor ataxia.

In 1876 Breuer[2] reviewed the subject of lead-amaurosis and gathered together all of the cases thus far reported. The next important communication upon this subject was made some years later by Hirschberg,[3] who, following in general Leber's classification, collected numerous cases from the literature and added some of his own.

In 1884 Stood[4] presented a communication on the pathology of saturnine amblyopia, including six cases of his own, three being peripheral retrobulbar neuritis and two optic neuritis. The paper contains an ample discussion on the pathology of the various types of lead-amaurosis. In the following year Theodor von Schroeder[5] published a case of lead neuroretinitis and very thoroughly reviewed the literature, quoting most of the cases in the years preceding the date of his publication. Since this time additional cases of lead-neuritis and other types

[1] Des Amblyopies et des Amauroses toxiques. Paris, 1878.
[2] Ueber Amblyopia saturnina. Bonn, 1876.
[3] Berlin. klin. Wochenschr., 1883, xx., p. 529.
[4] Graefe's Archiv, 1884, xxx., Part III., p. 215.
[5] Graefe's Archiv, 1885, xxxi., Part I., pp. 229–248.

of visual disturbances have been published without adding new facts to our knowledge of the pathology of this affection.

Occasionally doubt has been cast upon the specific power of lead to cause optic neuritis, particularly by C. F. Jeaffreson,[1] who has examined many lead workers without finding ocular affections. He believes that when neuritis does occur it may be due to renal trouble and other disorders. The fact, however, that lead is specifically the cause of optic neuritis seems definitely proven, especially by Thomas Oliver.[2]

Finally, the so-called *hysterical lead paralysis* seen in the workers should be remembered. They have hemianæsthesia and amblyopia on the same side, and anosmia on the opposite side. There are reduced vision, dyschromatopsia and reversal of the normal sequence of color-perception, exactly as these symptoms occur in hysteric cases.[3]

Etiology: Pathway of Entrance of the Poison. The lead enters the system either with articles of food or drink, contaminated by being stored in leaden vessels, or through the skin by handling paints or other substances composed largely of white lead, or by using hair-dyes and cosmetics. Occasionally the source of the lead is most obscure, and great care must be exercised in investigating all possible media of contamination. For example, not a few cases of lead poisoning occur in tailors and seamstresses, who bite, instead of break, the threads they use in sewing. These threads are

[1] Brit. Med. Journ., 1886, i., p. 390.

[2] Brit. Med. Journ., 1885, ii., pp. 731–735; also "Lead Poisoning with Acute and Chronic Forms."

[3] Consult Pontain, Recueil d'Ophthalmologie, third series, 1887, ix., p. 620. Compare with visual field in nitrobenzol poisoning, Fig. 38.

"weighted" with sugar of lead, which is thus gradually introduced into the system. I have seen one such case in which, in addition to general lead-toxæmia, there was optic neuritis.

Stood,[1] in his collection of cases of lead-amblyopia, records twelve white-lead workers, ten artists, and nine house-painters; of the other crafts not more than two examples are contributed by each. I find the following occupations represented: lead miner, white-lead worker, pottery hand, type-foundry hand, color-grinder, manufacturer of leaden shrines, painter, colorist, artist, cooper, costermonger, and locksmith. The remaining cases include those who used lead as a hair dye, but not those who were accidentally poisoned with food or drink. By far the greatest contingent of the sufferers comes from painters and workers in white-lead manufactories; others are found among those who work in chromate of lead.

Of fifty-eight cases collected by Stood forty-six were males and twelve females, the predominance of males being due, no doubt, partly to the fact that far more males than females are employed in lead works. Of eighty-seven cases which I have gathered sixty-three were males and twenty-one females; in the remainder the sex was not stated.

The *length of time* which may elapse before lead causes poisonous symptoms varies considerably; toxic symptoms may appear after twelve days' exposure, and there may be immunity at the end of many years. It is always difficult to gather accurate information on this point, as men and women differ so much in their susceptibilities to toxic influences. Exhaustion and depraved general health no doubt predispose to visual disturbances, but the chief cause resides in carelessness on the part of the

[1] Loc. cit.

workers and failure to cleanse their hands, clothes, hair, etc., from the lead.

Age. Of the eighty-seven cases in my list, the age is not stated in eighteen, and ranges from twelve to fifty-seven years in the remaining sixty-nine, thus:

12 to 19 years	10 patients.
20 to 29 "	20 "
30 to 39 "	25 "
40 to 49 "	10 "
50 to 57 "	4 "

There is no evidence to show that race influences the toxic action of lead.

It is not a little remarkable that so few cases of visual disturbance from this source are reported in this country, where general plumbic symptoms among the workers are common enough. I have seen one case among two thousand patients examined in the Jefferson Medical College Hospital from December, 1892, to January, 1894. This patient had slight optic neuritis. He was a house painter and had suffered from ordinary lead colic on several occasions. I have also observed one case of neuro-retinitis, probably due to lead, in the Philadelphia Hospital.[1]

Symptoms. The symptoms of lead poisoning may be divided into the *acute* and the *chronic*; but as there is no special significance attached to the acute phenomena, except when these result in changes in the nervous system, which secondarily cause ocular lesions, they require no description here.

Chronic plumbism nearly always precedes the visual disturbances, and in almost all the histories of the cases colic, headache, wrist-drop and other palsies, as well as

[1] For a full account of this case and other types of lead-poisoning, see a paper by Dr. F. A. Packard, Phila. Hosp. Reports, 1896, vol. iii.

less evident signs of lead poisoning are recorded. In this respect there is a resemblance between lead amblyopia and that produced by bisulphide of carbon.

The various types which the symptoms of lead poisoning may assume, according to Leber and Galezowski have already been described. I may modify these classifications and suggest the following syllabus of symptoms from the ophthalmoscopic appearances:

1. Transient amblyopia, without ophthalmoscopic change, due to an anæsthetic effect of the lead on the retina and optic nerve (Thomas Oliver), and not unlike amaurosis from uræmia without fundus-lesions.

2. Permanent amblyopia, without distinct fundus-changes, or, at most, some hyperæmia of the nerve-tip and undue filling of the retinal circulation, due to a retro-bulbar neuritis, analogous to that occurring under the influence of other toxic agents. This type may terminate in blindness from optic-nerve atrophy.

3. Optic neuritis, or neuroretinitis, either specifically due to the lead, or secondary to changes in the brain or kidneys.

4. Optic-nerve atrophy, either consecutive to a plumbic papillitis or due to the primary effect of the lead on the visual apparatus.

5. Various types of retinitis, often due to lead-nephritis, but also primary and appearing in the form of vasculitis and perivasculitis.[1]

A specific action of lead upon the optic nerve, resulting in neuritis, has often been denied, for example, by Jeaffreson;[2] but many investigations, particularly those

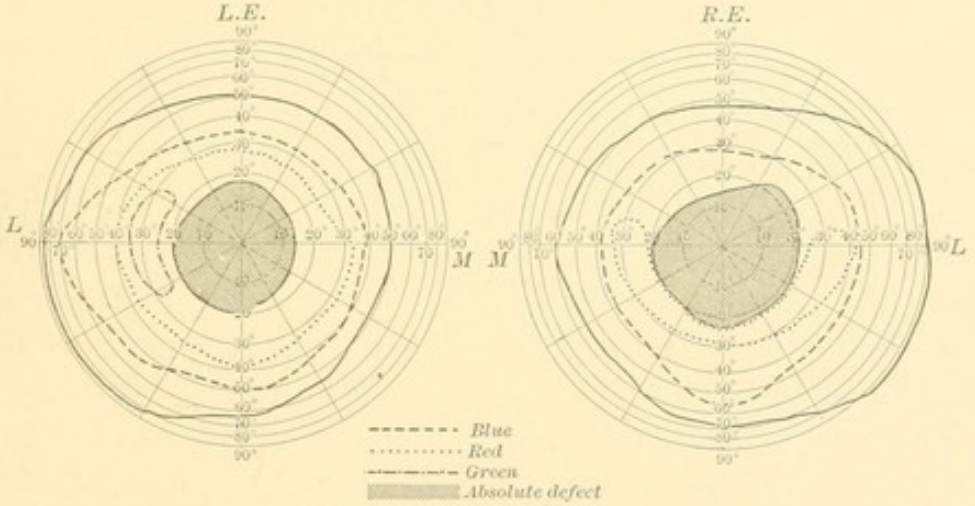
[1] For chromo-lithographs illustrating these conditions consult Thomas Oliver: Lead Poisoning in its Acute and Chronic Forms. Edinburgh and London, 1891.

[2] Brit. Med. Journ., 1886, i. p. 390.

of Thomas Oliver,[1] prove the validity of the claim that lead produces optic neuritis independently of nephritis or cerebritis.

The same is true of optic-nerve atrophy, both primary and secondary. Of thirty-four cases collected by Stood one-half suffered from optic-nerve atrophy or neuritis. Sixty-four cases which I have analyzed to determine this point yielded the following result: optic neuritis, 13; neuroretinitis, 4; and optic-nerve atrophy, 17. Seventeen cases were stated to be "blind," without description of the ophthalmoscopic appearance, and no doubt in many of these instances atrophy or neuritis was present. Hence Stood's result of 50 per cent. of organic nerve change is not too high.

FIG. 39.



Field of vision from Uhthoff's case of lead-amblyopia with ophthalmoscopic appearances resembling intoxication-amblyopia (temporal half of papilla discolored). Normal form field and absolute central scotoma.

In my list nineteen cases are described as having negative ophthalmic appearances, or, at most, hyperæmia of the disk and slight over-filling of the vessels, and belong to classes 1 and 2 in the syllabus.

[1] Loc. cit.

The iris-movements vary with the condition of the optic nerve and retina from absolute immobility to normal reaction. Chronic lead poisoning is a well-recognized cause of paralysis of the external ocular muscles, particularly the external rectus. Nystagmus is common.

The *field of vision* may present the following changes: (1) Concentric contraction for form and colors; (2) contraction and peripheral relative scotomata (Stood); and, finally, typical central scotomata, such as are found in intoxication-amblyopia. (See Fig. 39.)

The color perception may be normal, or, as, for example, in Bramwell's case, there may be partial color-blindness, vision being especially defective for yellow and blue, blue and green being confused. Hirschberg's[1] patient called red green and green yellow; blue was correctly recognized, but only over 10 degrees.

Visual acuity varies from complete absence of light perception to 6/6. Accommodative power is frequently markedly weakened.

Diagnosis. There are no ocular symptoms characteristic of chronic plumbism, and amblyopia, papillitis, neuroretinitis, or retinitis, can be ascribed to lead only when this is proven to be present in the system by chemical tests and when other causes have been eliminated.

Prognosis. This depends upon an early recognition of the cause of the visual defect and the prompt institution of measures of relief. Hutchinson's cases indicate that retention of such vision as remains is the best that may be expected in neuritic cases, but in one of Stood's patients the result was much better than this, and my patient recovered perfectly. I have seen one case—post-papillitic atrophy attributed to lead—which was practi-

[1] Loc. cit.

cally blind. In a case of so-called lead-neuroretinitis, the patient also suffering from nephritis, the vision was poor, one-fifth of normal, and remained unchanged when he was last seen.[1]

Of 67 cases which I examined with reference to the ultimate result, this was not stated in 9, recovery occurred in 33, and there was no improvement in 25. In some of these 25 cases the general symptoms improved, but eyesight was not restored. These cases include all varieties of ocular disturbances.

Pathology and Pathological Anatomy. This varies with the lesion. Much difference of opinion has been expressed as to the relation of influences other than the lead itself, to the so-called lead-neuritis. Thus, Jeaffreson[2] ascribes the neuritis to renal disorders, in women to menstrual derangements (which are exceedingly common among operatives), and in both sexes to sudden effusion into the brain and subarachnoid spaces.

To ascertain the frequency of albumin in these cases I have examined 87 reports, and find that the condition of the urine is not stated in 56; is recorded as normal, or, at least, free from albumin in 20, and is reported to contain albumin in 11. Granting at once that there may be cases of saturnine albuminuric retinitis and optic neuritis, we may agree with Thomas Oliver that optic neuritis also occurs in lead workers who are free from renal and other disorders, and that lead may be the direct cause of this neuritis; *i. e.*, the lead acts immediately on the optic nerve.

Stood argues from his cases of peripheral scotoma that they represent a peripheral retrobulbar lead-neuritis analogous to the condition which lead causes in the musculospiral nerve (wrist-drop).

[1] See paper by Dr. F. A. Packard, loc. cit.

[2] Loc. cit.

Parisotti[1] believes that the atrophy of the papilla which takes place without preceding neuritis is due to the changes which lead causes in the nutrient arteries of the optic nerve, changes which we know it may cause in the general retinal circulation.

The temporary amblyopia, without fundus-changes, may be due, as Thomas Oliver suggests,[2] to an anæsthetic effect of the absorbed metal on the retina and optic nerve.

Finally, such cases as Uhthoff's indicate that lead may especially affect the papillo-macular bundle of the optic nerve.

Treatment. It is most important that this should be begun early, and should be vigorously prosecuted if good results are to be obtained.

The medicinal indications are fulfilled by the administration of iodide of potassium and the use of baths of sulphuret of potassium, two to six ounces of the salt to thirty gallons of water. The iodide should be freely administered, beginning with fifteen grains three times a day. Should optic-nerve atrophy supervene, the usual treatment is indicated. Sweats with pilocarpine in the manner already described are important adjuvants.

The renal complications and associated retinitis may require additional measures suggested by the symptoms.

The *preventive treatment* consists of ventilation of the workshops; allaying dust with water-sprinkling; the use of respirators and gloves; frequent washings of the hands and mouth, the former with dilute sulphuric acid; and the employment of a general sulphur-bath. Other measures naturally suggest themselves, according to the character of special lines of work.

[1] Rec. d'Ophth., 1885, 3 s., vii., p. 350.

[2] Loc. cit.

Bibliography of Lead-Amblyopia.

Smetius, H. Miscellanea medica cun Theodoro Erasto Bruceo. Frankforto, 1611, p. 440.

Plater, Felix. Felicis Plateris Observationum. Basle, 8vo., 1680.

Hildesius, J. F. Observationum medicarum rararum. Frankfort, 1 vol. fol.

Schroecik, Lucas. (Éphémérides des curieux de la Nature) quotes an observation from 1683.

An observation is also given from D. D. Traw in the "Commercium literarium ad rei medicæ et scientiæ naturalis incrementum institutum," etc. Vol. vii. Nuremberg, 1737, 4to.

Deshais-Gendron. Lettre sur plusieurs maladies des yeux, causées par l'usage du rouge et du blanc. Paris, 1760.

Zinken, genannt Sommer. Geschichte einer mit dem Schwarzen-Staare verbundenen Bleykolik. Journal der practischen Arzneykunde und Wundarzneykunst. [Hufeland's.] Bd. 7, Jena, 1799, p. 73.

Montanceix, D. De traitement de la colique métalique par l'alum. Archives générales de médecine, 1828, xviii., p. 370.

Andral. Journal gen. des Hôpitaux de Paris, 1828, Sept. 5, No. 20.

Tanquerel des Planches L. Essai sur la Paralysie de Plomb ou Saturnine [Thèse]. Paris, 1834, pp. 91–95. This essay contains numerous references to the old literature.

Duplay, A. De l'amaurose suite de la colique de plomb. Arch. gén. de méd. Paris, 1834, 2 s. v., pp. 5–32.

Tanquerel des Planches, L. Traité des maladies de Plomb. ou Saturnines, vol. ii. Paris, 1839, pp. 208–221.

Weiss, F. Amaurose Saturnine bornée a l'œil droit. Annales d'Oculistique, Bruxelles, 1839, ii., pp. 232–34.

Himly, K. Die Krankheiten und Missbildungen des menschlichen Auges und deren Heilung. 2 Thiel., Berlin, 1843, p. 428.

Romberg, M. H. Klinische Ergebnisse. Berlin, 1846, p. 17.

Tanquerel des Planches. Lead Diseases, with Notes and Additions on the Use of Lead-pipe and its Substitutes. By Samuel L. Dana, M.D., LL.D., Lowell, 1848, 8vo.

Deval, C. Traité de l'Amaurose. Paris, 1851, pp. 263–68.

Rau, W. Graefe's Archiv für Ophthalmologie. Berlin, 1854, I Abth. 2, pp. 205–208.

Orr, R. Scott. On Lead-Amaurosis. Glasgow Medical Journal, 1860–61, vol. viii., pp. 249–268.

Ibid. Cites a doubtful case of Dr. William White's. [In Medical and Philosophical Commentaries, by a Society in Edinburgh, vol. iii., Part I., p 74, Lond., 1784.]

Ibid. Cites also the following two cases from Dr. Pemberton: Case I., 1833; Case II., 1835.

Lancereaux, E. Un cas de paralysie Saturnine avec altération des cordons nerveux et des muscles paralysés. Gazette Médical de Paris, 3d ser., xvii., Paris, 1862, p. 709.

Bouchut, M. Colique de plomb suirie d'encephalopathie et de paralysie de las sixième paire. L'Union Médicale, 2d ser., 31–32, Paris, 1866, No. 78.

Hirschler, J. Amaurosis Saturnina. Wiener med. Wochenschrift, Vienna, 1866, xvi., pp. 105, 121.

Haase, G. Amaurosis Saturnina. Klinische Monatsblätter für Augenheilkunde, Erlangen, 1867, v., pp. 225–28.

Hutchinson, J. Symmetrical Optic Neuritis in Connection with Lead-Poisoning. Royal Ophth. Hospital Reports, 1867–69, Lond., vol. vi., p. 55.

Meyer, E. Deux cas d'amaurose saturnine. Union Médicale, Paris, 1868, 3 s., v. pp. 982–84.

Réau, Gustave. Des Amauroses en général et de quelques Amblyopies toxiques en particulier. [Thèse] Paris, 1868.

Noyes, J. F. Temporary Amaurosis from Lead Poisoning. Detroit Review of Medicine and Pharmacy, 1869, iv., 81–83.

Hutchinson, J. On Lead Poisoning as a Cause of Optic Neuritis. Ophthalmic Hospital Reports, vol. vi., 1869, p. 55, London, 1869; *Ibid.*, vol. vii., 1871–73, p. 6, London, 1873.

Soelberg-Wells, J. A Treatise on the Diseases of the Eye. Lond, 1869, p. 412.

Hutchinson, J. On Lead Poisoning as a Cause of Optic Neuritis. Royal Ophthal. Hospital Reports, Lond., 1871, vii., Part I., p. 6.

Schneller. Neuriris optica Bleinergiftung. Klinische Monatsblätter für Augenheilkunde, 1871, p. 240.

Despres. Nature de l'Amaurose dans l'intoxication saturnine. Bull. de la Soc. de chir. de Paris, 1872, 3 ser., T., p. 555.

Elliott. Medical Times and Gazette. Lond., 1872, i., p. 685.

Lunn. Medical Times and Gazette. Lond., 1872, i., p. 685.

Samelsohn, J. Zur casuistik der Amblyopia Saturnina. Klinische Monatsblätter für Augenheilkunde, Erlangen, 1873, xi., 246.

Breuer. Ueber Amblyopia Saturnina. Bonn, 1876.

Stricker. Bleiintoxication mit doppelseitiger neuroretinitis. Charité Annalen, Berlin, 1874, i., p. 322.

Leber, Th. Die Amaurose durch Bleivergiftung Graefe und Saemisch, Handbuch der Augenheilkunde, Bd. v., p. 886, Leipzig, 1877, 8vo.

Galezowski. Recueil d'Ophthalmologie. Paris, 1877, pp. 245, 302.

Galezowski. Des Amblyopies et des Amauroses toxiques. Paris, 1878.

Lediard. Transitory Amblyopia from Lead. Medical Times and Gazette, Lond., 1878, ii., p. 217.

Debove. Note sur l'hemiplégie saturnine et sur sou traitement par l'application d'un aimant. Progrès Médical, Paris, 1879, vol. vii., pp. 99, 117.

Hirschler, J. Lead-Amaurosis. Archives of Ophthalmology, New York, 1879, viii., p. 363.

Landesberg, M. Affections of the Eye Consequent Upon Lead-Poisoning. Medical Bulletin, Phila., 1880, vol. ii., p. 108.

Landolt. Troubles de la Vision observés dans un cas d hémiplégie Saturnine. Annales d'Oculistique, ser. 12, iii.–iv. (83–84), 1880, p. 165.

Schubert, P. Amaurose bei Bleivergiftung. Arztliches Intelligenzblatt, München, 1880, xxvii., pp. 123, 138.

Oller, J. N. Ueber hyaline gefässdegeneration als ursache einer Amblyopia Saturnina. Virchow's Archiv, Berlin, 1881, lxxxvi., pp. 329–359.

Frank, J. Ein fall von encephalopathia cum Amaurosi Saturnina. Weiner Medizinische Presse, 1882, xxiii., p. 698.

Hirschberg, J. Ueber Blei-amblyopie. Berliner klinische Wochenschrift, 1883, xx., p. 529.

Formiggini, D. Rivista clinica di Bologna, 1884, 3 ser., iv., pp. 494 et seq.

Lubrecht, R. Ein beitrag zur encephalopathia Saturnina cum Amaurosi. Berliner klinische Wochenschrift, 1884, xxi., No. 24, p. 370.

Stood. Zur pathologie der Amblyopia Saturnina. Graefe's Archiv für Ophthalmologie, 1884, Berlin, xxx., Part II., p. 215.

Weber, G. De l'Amaurose Saturnine [Thèse]. Paris, 1884.

Oliver, T. Clinical Lectures on Lead-Poisoning. British Medical Journal, 1885. ii., pp. 731–735.

Parisotti, O., et Malatti, J. Un cas d'atrophie des deux papilles par intoxication saturnine. Recueil d'Ophthalmologie, 1885, 3 ser., vii., p. 520.

Schroeder, T. von. Beiträg zur casuistik und literatur der Amblyopia Saturnina. Graefe's Archiv für Ophthalmologie, 1885, xxxi., Part I., pp. 229–248.

Jeaffreson, C. S. A Note on So-called Lead Neuritis. British Medical Journal, 1886, i., p. 390.

Mader. Ber. d. K. K. Krankenstaldt. Rudolph Stiftung in Wien., 1887 (1886), p. 301.

Pontain. Troubels visuels dans la paralysie hystero-saturnine. Recueil d'Ophthalmologie, 3 ser., ix. 1887, p. 620.

Rampoldi, R. Annali di ottalmologia. Pavia, 1887, xvi., pp. 54–58.

Bramwell, B. A Peculiar Case of Lead Poisoning in Which There Was Marked Loss of Vision, both for White and for Colors. . . . Brain: A Journal of Neurology, London, 1887–88, x., pp. 507–511.

Mackenzie, S. Ophthalmic Cases. Illust. Med. News, London, 1888, vol. i., p. 49.

Günsburg, Fr. Zur Kenntniss der transitorchen Amaurose bei Bleiintoxication. Archiv für Augenheilkunde, Wiesbaden, 1889, xx., p. 255.

Lehmann, P. Bleiintoxikation. [Thesis.] Halle, 1890.

OXALIC ACID, an active irritant poison having the property of altering the composition of the blood, has

sometimes been mentioned in the list of those substances which produce visual disturbances, but probably only in the sense that the failure of sight is secondary to exhaustion.

It should be remembered, however, as Kobert and Kürsner have shown, that glycosuria may occur in oxalic acid poisoning; possibly this complication may explain some of the visual disturbances which have been recorded.

Phosphorus. Retinal hemorrhages have been described even early in phosphorus-toxæmia, before, in fact, there are any changes in the bloodvessels. Later there is fatty degeneration of the retinal tissue and an ophthalmoscopic picture not unlike retinitis albuminurica. These lesions have been particularly described by Niederhauser.[1] It is possible that some of the ocular symptoms may be secondary to intracranial changes, although there is no inherent reason why the singular power of phosphorus to produce fatty degeneration should not affect the retinal elements as well as other tissues of the body.[2]

Osmic Acid has been credited by Dr. Henry D. Noyes,[3] of New York, with the power of producing a temporary amaurosis. His patient was a chemist who was heating in a crucible a mixture containing osmium and iridium and exposed his eye to the action of the vapor. Very quickly there was marked depreciation of vision, as well as accommodative power, negative ophthalmoscopic appearances, and intense watering of the conjunctiva. The depreciation of vision, however, was proven not to be due to the local irritation, and hence was ascribed by Dr. Noyes, as well as by the patient, to

[1] Inaug. Diss. Zurich, 1875. Quoted by Knies, loc. cit.
[2] Consult, also, Berger: Les Maladies des Yeux, p. 412.
[3] Trans. of the Amer. Ophthalmol. Soc., 1866.

an action of the vapor of osmic acid upon the retina. The patient had experienced this accident once before under similar circumstances, and was aware of a like case reported by a Russian chemist, the details of which are not given.

Dr. Noyes informs me that since he reported his case of osmic acid-amblyopia another example of this affection has found its way into medical literature; but I have not been able to find the reference. In confirmation of Dr. Noyes's observation I am told by Dr. Robert Formad, of the University of Pennsylvania, that he is very sensitive to osmic acid, and that after handling the drug or being exposed to its vapor his vision becomes as dim as if he had instilled a mydriatic into his conjunctival sac. This disturbance of sight does not appear until several hours after exposure. He is equally sensitive to the action of *formalin*.

Chromic Acid, much used as a cauterant, has occasionally produced remarkable toxic symptoms when applied locally, especially to extensive venereal sores,[1] but the reports fail to describe ocular symptoms or lesions in the optic nerve or retina. Other organs, particularly the kidneys, may suffer from secondary degenerations.

Curiously enough, like santonin, digitalis, nitrite of amyl, and one or two other drugs, chromic acid has the power of producing yellow vision. In one case bathing the feet with a 5 per cent. solution of chromic acid was followed by a temporary xanthopsia.

Sulphuric Acid, another violent cauterant, produces no symptoms during its toxic action specially referable to

[1] Those interested in the toxic action of chromic acid used as a cauterant should consult an article on this topic by J. William White (University Med. Mag., 1889–90, ii., p. 54), which, in addition to the report of a case, gives full reference to the literature.

the eye, although, as Knies points out, it is important to remember that it is one of the substances which can cause acute ophthalmoplegia externa, probably owing to a polio-encephalitis (Wernicke).

Ergot is interesting chiefly because opacity of the crystalline lens has been observed in connection with *ergotism;* or, in other words, chronic poisoning with this drug is sometimes followed by the formation of what is technically termed "*raphanic cataract.*" The chief reports of this condition are by Russian observers.

There is no real evidence to show that the ergot itself produces the cataract; it is much more likely that the lenticular opacity is secondary to the convulsive disorders which the chronic toxæmia of the drug induces.[1]

Dr. H. V. Würdemann, of Milwaukee, has kindly sent me the notes of a case of amblyopia, with relative central scotomata, in which ergot was suspected as an etiological factor. Lithæmia, alcohol, and tobacco, however, could not be excluded.

[1] I have analyzed the most important papers upon raphanic cataract in a paper entitled "The Relation of Disease and of Morbid Conditions Other Than Those Located in the Eye to the Formation of Cataract." Transactions of the Philadelphia County Medical Society, 1893.

SECTION IV.

DRUGS INCLUDED IN CLASS II., WITH SPECIAL REFERENCE TO THE ANÆSTHETICS, OPIUM, CHLORAL, BROMIDE OF POTASSIUM, AND CANNABIS INDICA.

THE ANÆSTHETICS, PARTICULARLY CHLOROFORM AND ETHER.

During chloroform narcosis the pupil is usually small, as it is in sleep; but unless the effect of the drug is exceedingly pronounced, it will dilate when the skin of the neck is irritated. On the other hand, in the earlier stages of chloroformization, and especially that of etherization, the pupil may be dilated. Sudden dilatation of the pupil during the deeper stages of anæsthesia indicates asphyxia. Impurities in the chloroform may give rise to anomalous pupillary phenomena, and probably to other visual disturbances.

R. Schirmer[1] reports a case of retinal detachment occurring during chloroform narcosis. To be sure, the patient was highly myopic, and there was extensive posterior staphyloma; therefore there was a strong predisposition to such an accident. The similarity of this case to the one reported by Knapp[2] in connection with a draught of whiskey is striking.

Amblyopia from an affection of the papillo-macular bundle, or torpor of the retina, is very exceptionally caused by the anæsthetics; indeed, C. L. Lemprier[3]

[1] Klinische Monatsbl. f. Augenheilk., 1871, ix., p. 246. [2] Loc. cit.

[3] Internat. Journ. of Surgery, 1893, vi., No. 1, p. 2. See, however, Reymond's case, described on page 169.

declares that the optic nerves and motor nerves of the eyeball are not affected.

Chloride of Ethyl, as was originally pointed out by Dubois and Roux, causes loss of vision in animals, owing to a decided opacity of the cornea. This, as Panas and other observers have shown, depends upon a serous infiltration of the parenchyma of this membrane. It is probable that the chloride of ethyl destroys the endothelium of the cornea and permits infiltration of aqueous humor, and consequently the œdema, which in in its turn disturbs vision.[1]

VISUAL DISTURBANCE FROM OPIUM OR ITS ALKALOIDS.

For a long time the abuse of opium has been mentioned as one of the causes of amblyopia. For example, the older writers, Beer and Himly, in the long list of substances to the misuse of which they attributed amaurosis, invariably give opium a place without, however, any definite information as to the character of the loss of vision.

In more modern times W. Wagner[2] reports the case of a man aged thirty-two years, who for a long time had been accustomed to subcutaneous injections of morphine, and who during five days injected 32 grains of acetate of morphine. The last dose had been taken about twenty-four hours before the reporter examined him. The pupils were narrow and motionless, the optic nerves on each side slightly opaque and their edges veiled. The retinal veins were normal in appearance; the arteries, on the other hand, were markedly narrowed. The blindness was com-

[1] Consult Compt. rend. de l'Acad. des Sciences, 1889, cviii., Jan. 28.

[2] Klin. Monatsbl. f. Augenheilk., 1872, x. p. 335.

plete, light perception being absent. For two days these symptoms remained unchanged; then the patient was removed without permission, and the further history of the case is unknown.

Galezowski[1] records cases of opium-amblyopia without ophthalmoscopic lesions and with intact visual fields, perhaps due to an irregular and spasmodic contraction of the muscle of accommodation. Many of the patients took enormous quantities of opium, in one or two instances two or three grammes per day.

A case more to the point is the one reported by Reymond, in his work on the *Torpor of the Retina*[2] which presented the aspect of atrophy of the optic papilla, restriction of the visual field, and a *central scotoma* attributed to chronic poisoning by opium and chloroform.

Hammerle[3] has described a case, in some respects analogous to Wagner's, of temporary loss of sight from the internal use of tincture of opium. The patient, to relieve colic, took within twelve hours a sufficient quantity of the tincture to equal 1.5 grammes of opium. The pupils became the size of pins' points, and there was complete loss of sight, which returned in four days after vigorous purging. The reporter attributes the blindness to cramp of the retinal vessels.

Knies[4] quotes a case observed by Schiess-Gemuseus, namely, a sixty-five-year-old man, who, after a sleeping powder, was somnolent for thirty hours, and then had considerable disturbance of vision and hearing. After three weeks there was right-sided half-blindness, and on the left side concentric contraction of the visual field.

[1] Des Amblyopies et des Amauroses toxique.

[2] Annali di Ottalm., 2 Année, 1872, 1 fasc. analyzed by Haltenhoff in Annales d'Oculistique, 1873, lxix., p. 165.

[3] Deutsch. med. Wochenschr., 1888, xiv., p. 838.

[4] Loc. cit., p. 360.

The papilla was analogous in appearance to that seen in intoxication-amblyopia, namely, red on the inner side and white on the outer half.

I have examined a number of opium-eaters, one being a woman in middle life who daily consumed an enormous quantity of the drug, and have not found the slightest indication of toxic amblyopia.

Experimenting on rabbits with morphine, Laborde[1] noticed congestion of the eye-ground, followed, after some days, by a persistent pallor of the nerve-head. Loring could find no change in the fundus during the physiological action of opium, an observation which corresponds with my own experience.

Opium and morphine poisoning, as Leber points out, have not been proven to produce toxic amblyopia in the true sense of the word; but the cases of Reymond and of Schiess-Gemuseus indicate that careful ophthalmoscopic examination, as well as color tests, should be made in all cases of opium habit. It is possible we may find that under certain circumstances this drug should be relegated to those substances which have the power of producing some change in the fibres of the optic nerve which are specially gathered in the papillo-macular bundle.

VISUAL DISTURBANCES FROM HYDRATE OF CHLORAL.

Soon after the discovery of chloral various abnormal visual phenomena were ascribed to its influence. Thus Fischer-Dietschy[2] and Kirkpatrick Murphy,[3] both quoted by Förster, have observed, in addition to other symptoms

[1] Gaz. des Hôp., 1877, p. 45.
[2] Correspondenz-blatt f. Schweitzer Aërzte, 1873, iii., No. 1.
[3] Lancet, 1873, ii., p. 150.

temporary amaurosis. A number of reporters have described swelling of the lids, irritation, hyperæmia, and even positive inflammation of the conjunctiva after the use of choral; for example, C. H. Felton[1] and other physicians.[2]

Levingstein[3] describes visual disturbances as the result of the chronic use of chloral, as well as of morphine and nicotine, and Mittendorf[4] has recorded a case of chloral-amblyopia after six months' use of the drug, 40 to 60 grains being consumed daily, which disappeared after the habit was stopped. There is no ophthalmoscopic record.

It would seem that a drug having such decided action on the brain, spinal cord, and circulation should also exert its toxic influence on the visual apparatus; but the cases thus far reported are exceedingly indefinite, and, as Nuel[5] very properly remarks, many of the visual disturbances attributed to the drug have been merely coincidences.

Ulrich,[6] experimenting with hydrate of chloral, observed dilatation of the pupil and a congestion of the optic papilla. There was stasis of the blood in the retinal veins, and after a time myosis, which is considered to be one of the symptoms of the poisoning. Simple pressure with the finger upon the eyeball caused the blood of the vessels of the papilla and its surroundings to disappear. The tension of the eye was diminished.

Finally, it should not be forgotten that in chronic

[1] New York Med. Record, 1877, xii., p. 2.

[2] Ibid.: a number of letters.

[3] Inaug. Diss. Berlin, 1883. Access to the original communication has not been possible. It is referred to in Nagel's Jahresb., 1883, xiv., 302.

[4] New York. Medical Record, 1889, xxxvi., p. 134.

[5] Wecker and Landolt. Traité Complet d'Ophtalmologie, Tome iii., 663.

[6] Graefe's Archiv., 1887, xxxiii., Abth. 2.

chloral intoxication Förster[1] has described visual troubles analogous to those which are seen in hysteria, due probably to a paretic condition of the muscle of accommodation.

SULPHONAL, much used as a hypnotic, produces some very remarkable nervous phenomena, and it is possible that future observations will show that it has direct influence upon the optic nerve. Ptosis has been reported by Dillingham.[2]

Sulphonal poisoning is not common, and in the cases thus far reported the ocular symptoms have not been well studied.[3]

VISUAL DISTURBANCES FROM BROMIDE OF POTASSIUM.

The depressing influence of bromide of potassium upon the nervous system, and its extraordinary effects when allowed to accumulate in the system (bromism), indicate that its power might just as well fall upon the visual organs as elsewhere. Indeed, trophic changes following its administration have been described, for example, by Gifford,[4] who records a central keratitis apparently the result of the daily administration of large doses of bromide to a boy who suffered from convulsions. Conjunctivitis, even of the phlyctenular type (Knies), has resulted from bromide intoxication, especially if the bromide eruptions were also present.

The only example of disturbances of vision properly belonging to the toxic amblyopias is the one reported by Ruebel.[5] The patient, twenty-three years old, suffered

[1] Graefe und Saemisch's Handbuch, loc. cit.
[2] New York Medical Record, 1890, xxxviii., p. 664.
[3] Consult Wiener med. Blätter, 1892, xv.
[4] American Journal of Ophthalmology, 1890, vii., p. 245.
[5] Centralbl. f. prakt. Augenheilk., 1884, viii.

from epileptic attacks and received daily 10 to 15 grammes of bromide of potassium. One day it was noted that the patient was blind. The optic papilla was white, and there was marked contraction of the retinal arteries. The administration of the bromide of potassium was stopped, and in five weeks there was a return of normal visual acuity. Renewed doses of bromide of potassium again caused blindness. Amblyopia under its influence must be extremely rare, and even in Ruebel's case other conditions may have contributed to the blindness.

VISUAL DISTURBANCES FROM CANNABIS INDICA.

In acute cannabis indica, or hashish poisoning, visual hallucinations have been noted; but the only report indicating that the abuse of this drug, which is common in Eastern countries, may cause a true toxic amblyopia, is by Ali.[1] This observer describes cases precisely similar to tobacco-amblyopia, with central scotoma and intact peripheral visual field. They differ, however, from the tobacco cases, because the scotoma is frequently monolateral.

Mydriasis has been reported after the poisoning, and James Oliver,[2] in addition to dimness of vision, has observed contracted pupil and disturbances of the accommodative power. Werner[3] has described violet vision and a foggy appearance before the eyes after the internal administration of two-thirds of a grain of the extract of cannabis indica taken in nine single doses.

There have been a number of cases of acute poisoning

[1] Recueil d'Ophtalmologie, 1876, p. 258.
[2] British Medical Journal, 1883, i.
[3] Nagel's Jahresbericht f. Ophtalmologie, 1886, xvii., p. 255.

by cannabis indica in this country. Some of these have been intentional, but most of them the result of foolish experimentation, particularly on the part of medical students. I have knowledge of several of them, but in none has there been the slightest permanent effect upon vision, although they were watched with great care by competent observers. There may have been temporary depreciation of accommodative power, visual hallucinations, or darkenings before the eyes, but no symptoms indicating disturbances of the retina or optic nerve. Chronic cannabis indica poisoning, on the other hand, is rare, and smoking or using hashish quite uncommon. Therefore observations such as those of Ali have not been made except in the Orient.

Carbonic Oxide and Carbonic Acid may produce peculiar ocular symptoms, but chiefly on account of their toxic influences on the general system. Carbonic oxide may cause paralysis of the external ocular muscles. Raffegeau [1] observed in a case of carbonic oxide poisoning inferior hemianopsia and a certain degree of interstitial neuritis of the optic nerves. He suspected a diffuse lesion of the occipital lobes. Curiously enough retinal hemorrhages seem to be rare, perhaps, however, because they have not been searched for with sufficient care. Schmitz [2] describes two cases of carbonic oxide-poisoning. In one there was 1/6 vision, concentric contraction of the visual field, with loss of color sense. Ophthalmoscopically the veins were enlarged and the arteries diminished in size. Recovery took place in five months.

Carbonic acid, according to Knies, who quotes Schiff, on account of its action on the sympathetic, produces a

[1] Annales Médico-psychologique, Paris, 1889, ix., 7 s., p. 455.

[2] Abstract in Annales d'Oculistique, 1893, T. 109–110, p. 393.

dark coloration of the blood columns in the retinal vessels, and, if it causes much respiratory or circulatory disturbance, hemorrhages into the eye-ground.

The toxic influence of ordinary illuminating gas is not different from that just described, and consequently the ocular symptoms are analogous.

Fire-damp (light carburetted hydrogen-gas, or marsh-gas) does not cause visual disturbances, although some authors have attributed to it an influence in the production of the nystagmus from which the miners so commonly suffer.

Nitrous Oxide, enormously used as an anæsthetic, especially in dental practice, has, so far as I am aware, never originated permanent visual disturbances. According to Aldridge, it causes dilatation of the retinal arteries and increased redness of the optic papilla.

SECTION V.

DRUGS INCLUDED IN CLASS III. CAFFEIN AND THEIN.

The older writers—for example, Beer and Himly—refer to the misuse of coffee as a probable cause of amaurosis, the latter author describing it with the list of substances which he believes produce loss of vision by paralysis of the nervous force of the retina. These references in the earlier and pre-ophthalmoscopic days are always exceedingly indefinite, but there is some evidence, vaguely hinted at here and there by more modern authors, that the abuse of coffee may cause disturbances of sight. It has a slight mydriatic effect.

Hutchinson is quoted by Knies as having seen "a coffee-amblyopia" analogous in its phenomena to quinine-amaurosis, and this case is several times referred to in literature. What Hutchinson appears to have said[1] is that he had seen deafness produced by the abuse of coffee.

Tea-tasters may suffer from visual disturbances, and a discussion of this subject will be found in the London *Lancet* for 1887. Wolfe[2] described fluidity of the vitreous and numerous floating opacities as the result of excessive tea drinking; but the etiological relation of tea to these lesions seems highly improbable. So good an observer as Dr. Berry, in relating the causes which he believes potent in the production of toxic amblyopia in

[1] British Medical Journal, 1887, ii., p. 127.
[2] British Medical Journal, 1879, ii., p. 328.

general, mentions tea.[1] He does not, however, give more definite information than is contained in the words, "I have suspected tea."

Some of the earlier writers include chocolate among the substances capable of producing amaurosis. Recently Casey A. Wood[2] records a case of temporary amblyopia from chocolate. The patient, a man aged fifty-four, of gouty habit, was subject to attacks of migraine associated with central scotoma (scotoma scintillans). Eating chocolate in any form invariably precipitated an attack of this kind. Wood thinks this case indicates that chocolate occasionally affects the visual centres.

[1] Trans. of the Ophth. Soc. of the United Kingdom, 1887, vii., p. 91.
[2] Medical Record, New York, 1895, vol. xlviii., p. 843.

SECTION VI.

DRUGS INCLUDED IN CLASS IV., WITH SPECIAL REFERENCE TO QUININE AND SALICYLIC ACID.

QUININE-AMAUROSIS, INCLUDING DISTURBANCES OF VISION UNDER THE INFLUENCE OF OTHER SALTS AND PREPARATIONS OF THE CINCHONA BARK.

History. The alkaloid quinine was first separated from other ingredients of the bark by Pelletier and Caventou, in 1820, and soon visual disturbances were observed after repeated ingestions or single large doses of the drug.

Thus, Berandi[1] experimented on healthy individuals with 15 to 20-grain doses of quinine and noted headache, tinnitus aurium, and obscuration of vision; Rombach[2] observed vertigo, tinnitus, and foggy vision; and Beydler,[3] after a single dose of forty grains of sulphate of quinine, temporary amaurosis.

In spite of these and similar examples it is usually stated that the first case of quinine-amaurosis is the one recorded by Giacomini in 1841,[4] whose patient took by mistake about three drachms (180 to 225 grains) of the sulphate, and became unconscious, deaf, and blind. The visual and aural difficulties lasted a long time.

Interesting instances in pre-ophthalmoscopic days are

[1] Annali univers. de medicina, Milano, 1829, vol. 52, p. 312.

[2] Schmidt's Jahrbuch, 1838, xx., p. 18.

[3] Ibid., 1838, xviii., p. 292.

[4] Annali univ. di med., Milano, 1841, xcvii., p. 325, quoted by Guersant in Dictionnaire de Médicine, 2d ed., vol. xxvi., p, 567.

recorded in American literature by Henry C. Lewis[1] (one case), John McLean[2] (four cases), and William O. Baldwin[3] (two cases); and in French literature by Trousseau and Pidoux,[4] Guersant,[5] and Briquet,[6] who quotes Monneret and Hatin as having observed both temporary and long-continued amaurosis from excessive doses of quinine.

The first cases examined with the ophthalmoscope appear to be the incompletely developed ones reported by Von Graefe,[7] in which, although there was amblyopia, the fundus oculi was normal and the visual field intact.

The well observed, more fully developed and complete cases of quinine-amaurosis begin in 1879 with Voorhies's[8] and Roosa's[9] descriptions, and are soon followed by a number of other carefully recorded examples, notably those by Roosa and Ely,[10] De Wecker,[11] Gruening,[12] Knapp,[13] and Michel.[14] Since this time the literature has been enriched by numerous additional cases published in England, Germany, France, Italy, Spain, the West Indies, and the United States of America.

Visual disturbances have been observed during experimental work on man and animals, and long ago Baldwin,[15] in this country, particularly investigated, in his experi-

[1] Western Med. and Surg. Journ., 1845, n. s., p. 396.
[2] Illinois and Indiana Med. and Surg. Journ., 1846, n. s., vol. i., p. 385.
[3] Amer. Journ. of the Med. Sciences, 1847, n. s., vol. xiii., pp. 292–294.
[4] Traité de Materière medicale, 1841, p. 323. [5] Loc. cit.
[6] Traité Therapeutique de Quinquina, Paris, 1855.
[7] Graefe's Archiv, 1857, iii., pp. 2, 396.
[8] Trans. of the Amer. Med. Assoc., 1879, p. 411.
[9] Archives of Ophthalmology, 1879, viii., p. 392.
[10] Ibid., 1880, ix., p. 41.
[11] Ocular Therapeutics. Translation by Forbes. London, 1879, p. 448.
[12] Archives of Ophthalmology, 1881, x., p. 81.
[13] Ibid., 1881, x. p. 220. [14] Ibid., 1881, x. p. 214.
[15] Loc. cit.

ments on dogs, the effect of the drug on vision, when given in large doses by the stomach, the cavity of the abdomen, and the jugular vein, noting in all instances maximum dilatation of the pupil and complete blindness. In recent times quinine-amaurosis in cats, rabbits, and dogs, has been carefully studied by H. Brunner,[1] and by myself[2] in dogs, the latter research including full microscopic examination of the optic nerves, chiasms, and cortical visual centres. Finally, Paul Barabaschew[3] experimented with large doses of quinine upon healthy men and studied the visual and general phenomena—a line of research which was more than once pursued in pre-ophthalmoscopic days.

Etiology: Pathway and Entrance of the Poison. The drug has made its entrance into the economy through the stomach in most of the cases of poisoning which have occurred.

Any of the alkaloids derived from the cinchona bark, when given in sufficient dose, is capable of causing amblyopia, and not only have the alkaloids this power, but, as in Roosa's case, the tincture of the bark. The sulphate and bisulphate of quinine are more active than other salts in this respect. In my experiments on dogs, quininæ bimuriatica carbamas appeared to possess the greatest potency.

It has sometimes been doubted whether the quinine alone is responsible for the toxic effects on vision, because most of the cases have occurred during diseases

[1] Ueber Chininamaurose. Inaug. Diss., Zürich, 1882.

[2] Some Experiments to Determine the Lesion in Quinine-Blindness, Trans. of the College of Physicians of Philadelphia, November, 1890; and Additional Experiments to Determine the Lesion in Quinine-Blindness, Trans. of the American Ophthalmological Society, 1891.

[3] Archiv. f. Augenheilkunde, 1877, xxiii., Heft 2.

calling for the exhibition of large doses of the drug; diseases, moreover, capable of seriously damaging the nervous system and possibly the optic nerves. For example, in my collection of cases the following diseases are recorded: Asthma, gastro-enteritis, remittent fever, alcohol habit, intermittent fever, malaria,[1] chills, cerebro-spinal meningitis, ague, miscarriage, supra-orbital neuralgia, pneumonia, cholera-morbus, Congo fever, syphilis septicæmia, pernicious fever, typhoid fever, *la grippe*, and marsh fever. The fact, however, that perfectly healthy persons who have taken quinine by mistake have been blinded, as, for example, Giacomini's patient, and that the exact clinical picture of quinine-amaurosis can be experimentally produced in dogs, proves that the drug itself is responsible for the visual defect, and also that it has a distinct selective influence upon the optic nerve, and probably the retinal circulation.

Usually the dose which causes blindness is a large one, but it has varied from fifteen grains to an ounce in twenty-four hours. Many of the records are indefinite; the quantity is stated to have been "large," "immense," "a handful of 2-grain quinine-pills at once," etc. Occasionally temporary amaurosis occurs from very small quantities of the drug. Thus, H. C. Wood has seen this effect in a woman produced by twelve grains of quinine. I have had practically the same experience after the ad-

[1] The malarial poison probably neutralizes to some extent the effect of quinine on the visual apparatus, otherwise more cases of amaurosis would occur in those regions, for example, the southwestern portion of the United States, where malarial fevers are prevalent and where huge quantities of the alkaloid are often administered. When I was house-surgeon in the University Hospital I gave, partly hypodermically, by direction of Dr. H. C. Wood, eighty grains of quinine to an adult patient suffering from a congestive malarial chill, in less than twenty-four hours, without causing the slightest visual or aural disturbance.

ministration of fifteen grains, in divided doses, during twenty-four hours.[1] Enormous doses of quinine, *e. g.*, one ounce, have been taken without disastrous results, perhaps, as Wood suggests, because the drug passed through the intestines without absorption.

Of sixty-nine cases which I have gathered from the literature forty-two were males and twenty females, while in seven the sex is not stated.

The ages of the patients ranged from five to sixty-five years. Thus:

3 to 9 years	8 patients.
10 to 19 "	5 "
20 to 29 "	11 "
30 to 39 "	10 "
40 to 49 "	5 "
50 to 59 "	4 "
60 to 65 "	2 "

Twelve patients are described as "adults," one as a "boy," and four as "young." In the remainder (six cases) the age is not given. Although more cases occurred in men than in women, there is no proof that this is more than an accident, and apparently age and sex have little to do with preventing or encouraging the poisonous effect of the drug. A highly neurotic temperament probably renders the patient more susceptible to all the influences of quinine. The amaurosis may occur in the colored races, *e. g.*, Baldwin's patient was a negro woman.

Symptoms. These may be divided into the *general* and the *ocular* symptoms. The earlier symptoms of cinchonism are ringing in the ears, fulness in the head, and

[1] Dr. Joseph Leidy, Jr., and Dr. W. S. Carter inform me they have observed amblyopia under the influence of doses even smaller than those just mentioned.

slight deafness. Under the influence of large doses the deafness becomes marked, the vision, at first disturbed (there may be visual hallucinations), is entirely obliterated, the face is flushed, and, finally, there is giddiness, staggering, headache, delirium, stupor, embarrassed respiration, convulsions, and paralysis. If the dose has been a lethal one, these phenomena are followed by collapse, and the patient dies comatose or delirious.

The *ocular* symptoms of the milder type consist of temporary amblyopia, diminution of accommodative power, and moderate dilatation of the pupil; or this may be of normal size and reaction. Under the influence of larger doses the blindness becomes complete and may develop with great suddenness. It has been compared to the extinguishment of the light of a lamp. Sometimes it takes a day for its full development, sometimes several days. During the time of total blindness there is absence of light perception (although there may be subjective sensations of colored light) lasting from a few hours (Webster) to several weeks; thus, Gruening's patient was blind for three, Michel's for five, and Voorhies's for ten weeks. In Dewey's case the blindness lasted for three months (*i. e.* day could hardly be distinguished from night), and at the end of eighteen months vision had somewhat returned, but by no means perfectly.

In experimental quinine-blindness, for example, in my dogs, the loss of vision in some instances was still total at the expiration of two months.

During the stage of complete amaurosis the pupils are widely dilated and irresponsive to light impulse; but, according to Gruening, they react sluggishly on strong convergence. In Voorhies's case the cornea and conjunctiva were anæsthetic, while nystagmus, both vertical and lateral, has been noted in human beings—for

example, by Knapp, E. Williams, and Roosa—and in animals by myself. Divergent strabismus appeared in Knapp's, Browne's, Peña's, and Claiborne's cases, and I have observed prominence of the eyeballs amounting to exophthalmos in some of my dogs. Tiffany records increased intra-ocular tension.

The *ophthalmoscopic* phenomena in well studied and complete cases are singularly uniform and consist of pallor of the optic disk, simulating the appearance of advanced atrophy, extreme diminution in the size of the retinal vessels, both veins and arteries,[1] and occasionally a grayish haze of the retina and a cherry-colored spot in the macula, almost exactly repeating the picture of embolism of the central artery. (Gruening, Buller, Browne.) The choroids are pale; hemorrhages and extravasations have not been noted. Geschwind has described vitreous opacities. They probably antedated the quinine influence. Dickinson[2] has recorded congestion of the retinal and choroidal vessels, tumefaction of the optic nerve, or, in other words, appearances similar to papillitis. It can scarcely be doubted that factors other than quinine (the patient suffered from ague) were responsible for these phenomena.[3]

[1] In the early stage of Buller's case the veins were large, the arteries normal, or actually or relatively diminished in calibre; later the usual contraction supervened. The patient had sepsis.

[2] St. Louis Medical and Surgical Journal, 1881, xli., p. 352.

[3] In a few cases, for example Jodko's, Von Graefe's, in the earlier stages of Garofolo's, and in L. W. Fox's, the ophthalmoscopic appearances were negative. The only explanation of this is that the effect of the drug was incomplete, or possibly, in two of them at least, that the observations were not made at a time when the usual phenomena are present. This is the more likely, because occasionally in dogs, although the blindness is complete, the shrinking of the vessels does not occur until some days afterward.

The bilateral character of the blindness is almost universal. Graefe's case, however, was unilateral, and in Hobby's case one eye was more affected and earlier than the other.

In Mellinger's case[1] there was a curious and somewhat unusual order in which the ischæmia developed, namely, the larger retinal bloodvesels were first emptied of blood and contracted to threads; but the capillaries, even those in the disk, remained filled. This condition, however, was soon succeeded by their collapse, and the appearances of progressive atrophy supervened.

As soon as vision becomes sufficiently restored, in order to map the *visual field*, this is found to be contracted. According to Knapp, the contraction is concentrical or elliptical, with the longest axis in the horizontal direction, although reference to the accompanying diagrams will show that this type of field is not constantly present. (See Figs. 40, 41, 42, 43, 44, 45, 46.) Uncontracted visual field has also been reported (Galezowski).

A rare phenomenon, of which at least one example has been recorded, is a double central scotoma. This occurred in a patient of Jodko,[2] who took 110 grammes of quinine-muriate in seven days. Ophthalmoscopically there were no changes. Galezowski's patient during convalescence had for a time central scotomata, and De Wecker's case islands of blindness in the visual field.

At first there is partial or complete color-blindness and light-sense is diminished. Gradually there is a return of central vision, which may become normal after some days, or only after the lapse of weeks and months; but some permanent injury to the optical apparatus is likely to occur. This will be more fully considered in the paragraph devoted to prognosis.

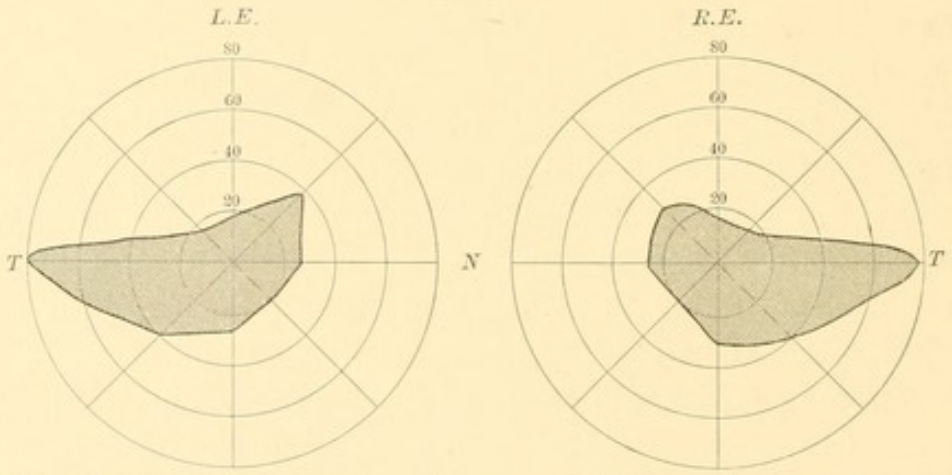
Several authors, on the strength of reported cases, have compiled a well defined symptom-complex of quinine-

[1] Klinische Monatsblätter f. Augenheilkunde, 1887, xxv., p. 57.

[2] Abstract in Nagel's Jahresbericht, 1877, viii., p. 217.

amaurosis, particularly I. E. Atkinson,[1] in his capital paper on the graver and rarer forms of cinchonism, and Knapp, in his report of three cases of this affection. I have somewhat modified this 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, occasionally divergent strabismus, and increased intraocular tension (Tiffany); anæsthesia of the conjunctiva

FIG. 40.



Visual field from one of Knapp's cases, exhibitiong symmetrical figures (the shaded areas represent the limits of the fields). The patient, a boy aged eight and one-half years, was made blind when three years old by enormous doses of quinine. V. when fields were taken = 20/L.

and cornea (Voorhies); extreme pallor of the optic disks and diminution of the retinal vessels, simulating the appearances of progressive atrophy; occasionally retinal haze and a cherry-colored spot in the macula, resembling embolism of the central artery of the retina; gradually,

[1] Journ. Amer. Med. Assoc., Chicago, 1889, xiii., pp. 431–441.

partial or complete restoration of central vision, associated at first with complete or partial color-blindness; later, slow renewal of the color-sense, which may ultimately return; often permanent diminution of the light-sense

FIG. 41.

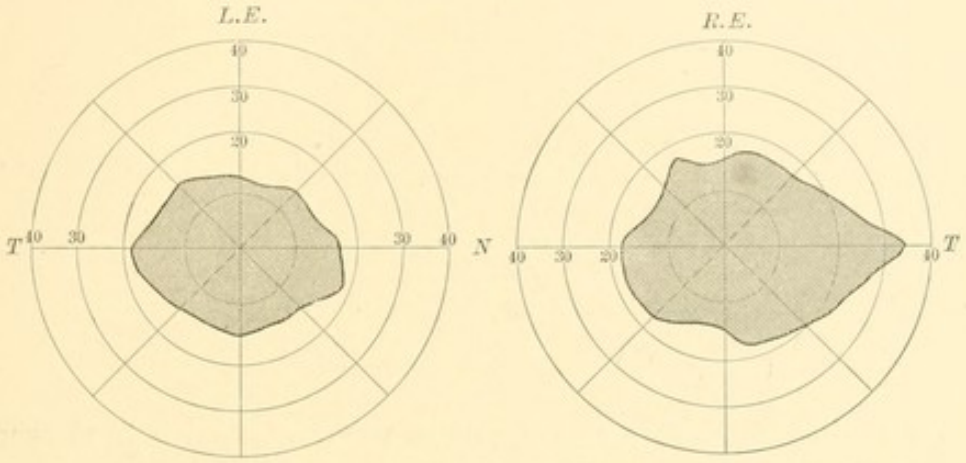
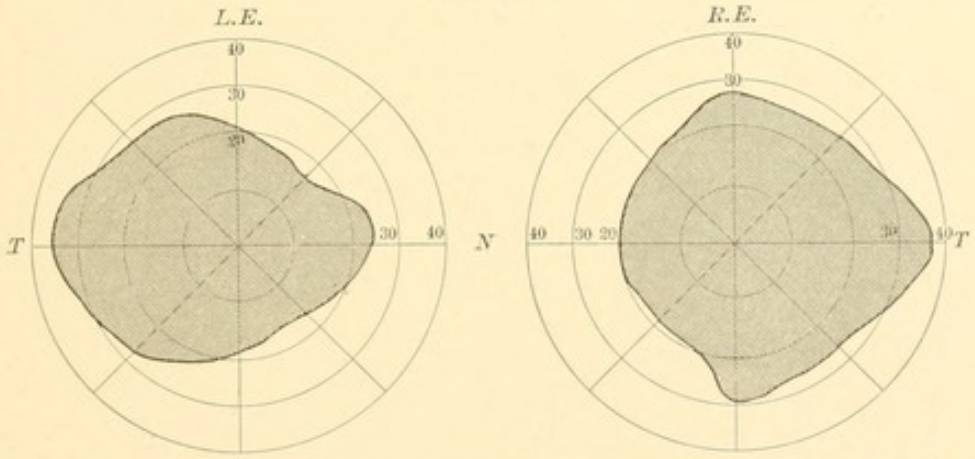


FIG. 42.



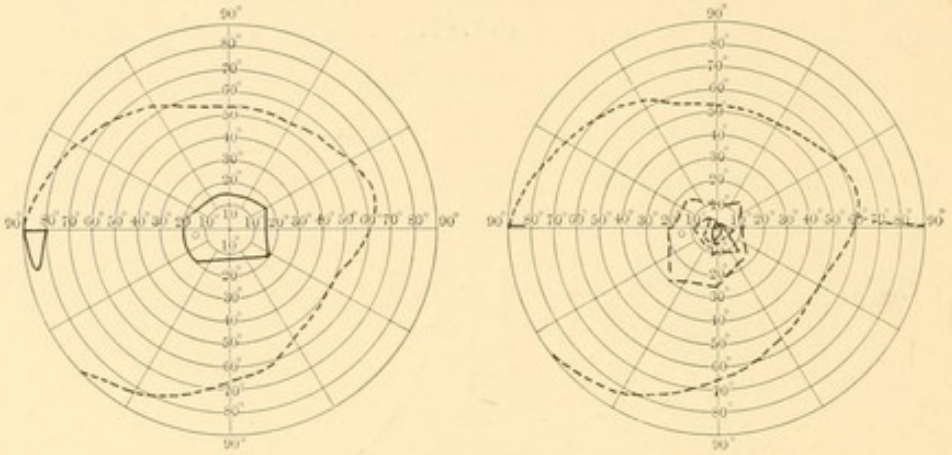
Visual fields from Gruening's case; shading as before; the upper map three and the lower six months afer recovery from complete blindness.

and color-sense and contraction of the field of vision, the contraction usually assuming an elliptical shape; very exceptionally permanent blindness.

Diagnosis. This presents little difficulty. With the history of excessive doses of quinine, accidentally or de-

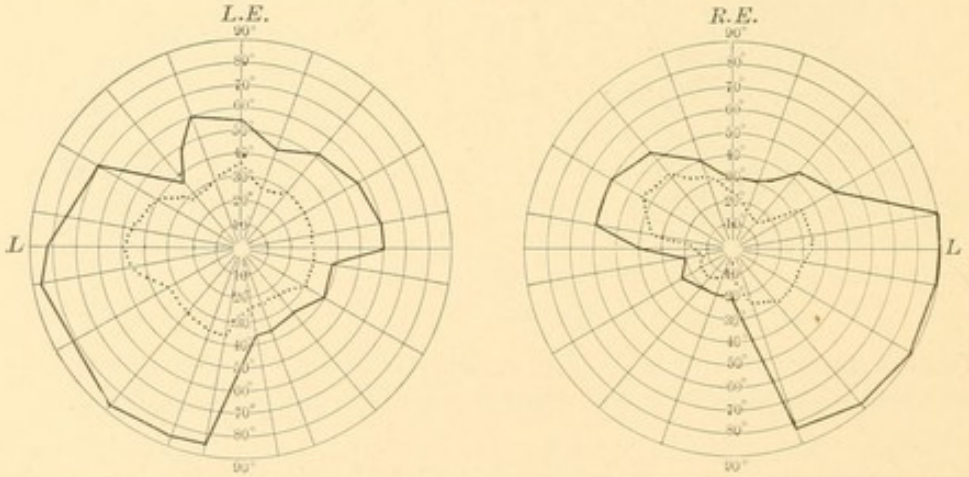
signedly ingested, and the symptom-complex just detailed, there is scarcely room for doubt as to the etiology of the blindness.

FIG. 43. FIG. 44.



Visual fields of Browne's case of quinine-amaurosis, the left hand figure representing the greatly contracted field four months, and the right-hand figure eleven months, after complete blindness had ceased. The broken lines in right-hand figure represent the color lines.

FIG. 45.

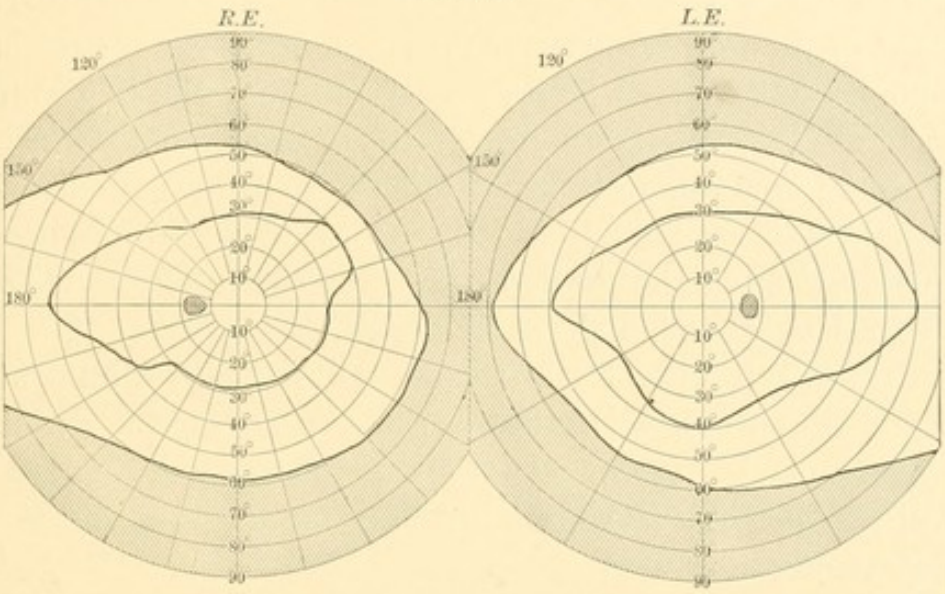


Visual fields of Mellinger's case of quinine-amaurosis, showing symmetrical contraction of the visual fields eight months after blindness.

Prognosis. In spite of the complete absence of light perception, which ushers in severe types of the affection,

permanent blindness from this cause in human beings is almost unknown; indeed, until the report of Claiborne's case it had not been recorded, although several examples of visual disabilities of long duration had been described. Nearly two years after the primary poisoning of Claiborne's patient the vision of the right eye was: move-

FIG. 46.



Visual fields of Tiffany's case of quinine-amaurosis five weeks after complete blindness. V. at this time O. D. 20/40; O. S. 20/30.

ments of the hand at six feet, candle-field elliptical; left eye, perception of light, vessels almost obliterated; pupils irresponsive.

In nearly all of the cases, however, which have been examined with care some impairment of vision remained when the patient was last observed, and complete restoration of the visual field when once contracted (in Galezwoski's case the visual field was not restricted) does not occur in grave forms of quinine-amaurosis.

Atkinson calls attention to these points, as follows: Six months after the beginning of blindness one of Gruening's cases was still partially color-blind and the

fields of vision remained contracted. In one of Roosa's cases the visual fields continued contracted, the optic disks pale, and the arteries small; in another, at the expiration of two years, the patient felt as if there was a veil over her eyes. Perfectly white optic disks were present in Voorheis's patient at the expiration of a year, and the central artery looked like a twig. Buller's case had perfect central vision, but color-perception only at the point of fixation after twenty-two months. Webster has reported a case in which seven years after the beginning of blindness, which was total only a few hours, sight remained impaired, and Browne states that in one case the visual field remained greatly contracted after fifteen years, so that the patient had only telescopic vision. Roosa has observed the same result.

Clinically, then, with these limitations (Claiborne's case being excepted), the prognosis, so far as the improvement in central vision is concerned, is good. Experimentally, the prolongation of quinine-blindness may result in true atrophy.

An interesting feature in the prognosis of the case is the liability to relapse after the administration of small doses. This has been pointed out by Knapp and Nettleship, and I have noted the same effect in animals.

The occasional idiosyncrasy of patients toward the influence of quinine, as evidenced by temporary amaurosis after perfectly physiological or unusually small doses, is a matter worthy of consideration. As Atkinson says, "Immense doses of quinine are frequently taken without disastrous consequences, and while blindness may always be expected in cases of lethal poisoning, it is impossible to fix within definite limits the non-lethal doses that are likely to induce it. It unquestionably largely depends upon idiosyncrasy, and although it hardly

ever develops except after the ingestion of large quantities of the drug, and even then with comparative rarity, the results are so terrible that even the remote possibility of its occurrence should have influence in placing some check upon the lavishness with which quinine is but too often used in the treatment of disease."

Pathology and Pathological Anatomy. The toxic effects of quinine on the visual apparatus were ascribed by the earlier writers to an influence of the drug upon the cerebrum, and in my experiments on dogs[1] I found peculiar vacuolation of the cells in the cortical centres of vision. This observation has not been confirmed, and I attribute the lesion to imperfect technique.

Buller[2] assumes that the blindness is caused by a rapid effusion into the lymph spaces around the optic nerves, too transient to produce papillitis, but sufficient to induce œdema, blanching of the retina and impediment of the blood-carrying capacity of the arteries.

Edgar A. Browne[3] points out the resemblance of the subjective symptoms to embolism of the central artery of the retina, but believes the theory of such a lesion is untenable.[4] He refers the probable local nature of the retinal anæmia, the influence of the vasomotor system, and the absence of perineuritis, and suggests the possible influence of highly cinchonized blood upon a peripheral circulation, causing sufficient contraction to prevent the ingress of the blood.

From the experiments of Brunner and myself on dogs, and Barbaschew on healthy human beings, we know that the clinical phenomena usually described under the name

[1] Loc. cit. [2] Trans. of the American Ophth. Assoc., 1881, p, 262.

[3] Trans. of the Ophth. Soc. of the United Kingdom, 1887, vii., p. 193.

[4] Some of my specimens show the formation of a thrombus in the central vessel.

of quinine-amaurosis may actually be due to the drug and not to the disease for which it may have been given. The ophthalmoscopic picture in animals is like that in human beings, and Barbaschew has secured similar results in healthy individuals, although the duration of the amaurosis was very brief.

Brunner, discussing the mechanism of quinine-blindness, suggests the following possibilities: (1) That the alkaloid circulating in the blood creates in the peripheral end-organs of the retina a functional disturbance, and makes the rods and cones insensitive to light perception. (2) That this effect results indirectly from a circulation-disturbance, that is, ischæmia caused by the quinine. (3) That quinine-blindness should be referred to a diminished sensitiveness to impressions on the part of the optic nerve, and should be regarded as a functional disturbance. (4) That the blindness depends upon circulatory disturbances followed by gross lesions, for example, inflammation and blood extravasation, which cause the amaurosis. (5) That the blindness has a cerebral origin, the central ganglia of the cortex of the cerebri being affected. (6) That the later loss of function depends upon circulatory disturbances, or inflammatory processes in the cerebral cortex of the visual centres.

He reaches the conclusion that all of these possibilities should be rejected except such as indicate that the seat of the lesion is a peripheral one, and he holds that quinine-amaurosis depends upon a pure ischæmia of the retinal vessels, following which there may be an endovasculitis, the final result being secondary changes which cause obliteration of the vessels and thickening of their walls.

I experimented on exactly the same line nearly ten years later (at that time without knowledge of Brunner's

work), and carried my researches somewhat further by first producing quinine-blindness in dogs, noting the exact reproduction of the clinical picture in human beings, and finally submitting, at different stages of the blindness, the optic nerves, chiasms, tracts, and visual centres to microscopic examination. The chief points in this research are here reproduced.[1]

"In the first research, the effect of the quin. bimur. carbamidat. was found to be more pronounced than the ordinary bisulphate of quinine, although it was shown that the latter was active. Since then in a number of instances I have produced blindness by using quinine dissolved with the aid of tartaric acid or dilute hydrochloric acid, and have used quinine from several different sources. It is needless to detail these experiments. The results were the same as those already published.[2] The following experiment bears upon the question of permanent blindness as the result of quinine-intoxication.

"*Experiment.* Black dog, weight 15 pounds, was given 30 grains of bisulphate of quinine at 4.15 P.M., October 28, 1890, previous examination having shown normal fundus oculi, pupil-reactions, and cornea.

"*October* 29. Partially blind. Runs with nose stretched out and apparently finding his way by the sense of smell; frequently butts his head against objects, as one whose field of vision in deficient. *Ophthalmoscope.* Pupils widely dilated. Cornea not anæsthetic. No evident change in the color of the disk or calibre of the veins; arteries smaller than on previous day. Thirty additional grains of quinine injected.

[1] Trans. of the American Ophth. Soc., 1891.

[2] Trans. of the College of Physicians of Philadelphia, 1890; also Ophthalmic Review, February, 1891.

"*October* 30. Dog entirely blind, but not deaf. Slight vertical nystagmus. Pupil dilated. No anæsthesia of cornea. *Ophthalmoscope.* No change in veins; arteries small.

"*November* 17. Daily record of animal's ocular conditions omitted, which may be summarized as gradual shrinking of the arteries, loss in color of disk, and contraction of veins. No general symptoms occurred, and on this date (November 17, 1890) disk entirely white; arteries not distinguishable. Only faint traces of the lower veins in each eye.

"*December* 25. There has been practically no change in the animal. During the last day or two, however, there appears to be some return of sight, as he now avoids certain objects in the room and fails to respond promptly to the ordinary tests. The *ophthalmoscope* shows no new changes in the fundus.

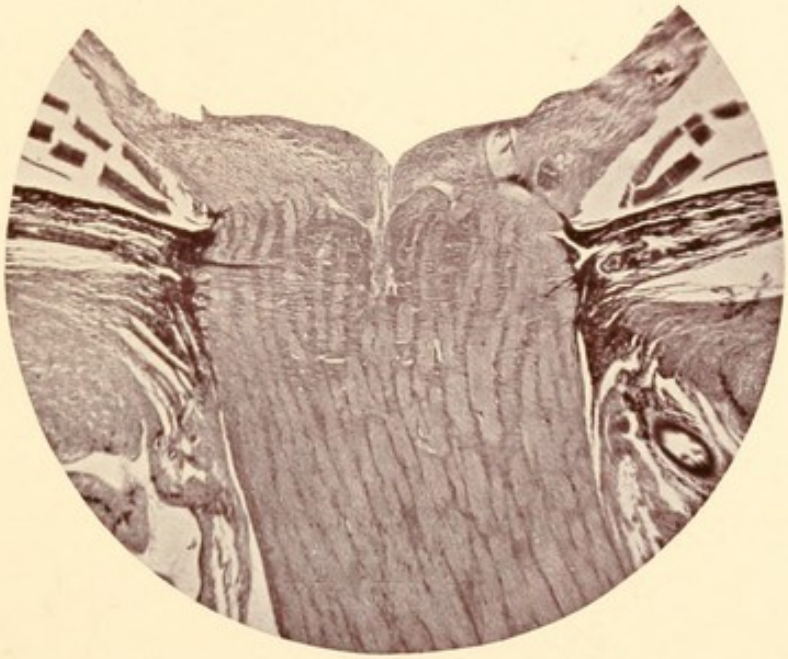
"*December* 26. Fifteen additional grains of quinine administered.

"*December* 29. Dog apparently completely blind. *Ophthalmoscope.* In each eye the disks entirely white, only the lower temporal veins being visible. The position of the arteries is marked by faint white threads. The animal was killed, and the eyeballs, optic nerves, chiasms, and entire brain were placed in Müller's fluid and prepared with the utmost care for section. Some days later a normal dog was similarly killed and the same organs removed and placed in Müller's fluid for comparison.

The following are the results of the microscopic examination of sections kindly prepared by Dr. William M. Gray (Plate V.):

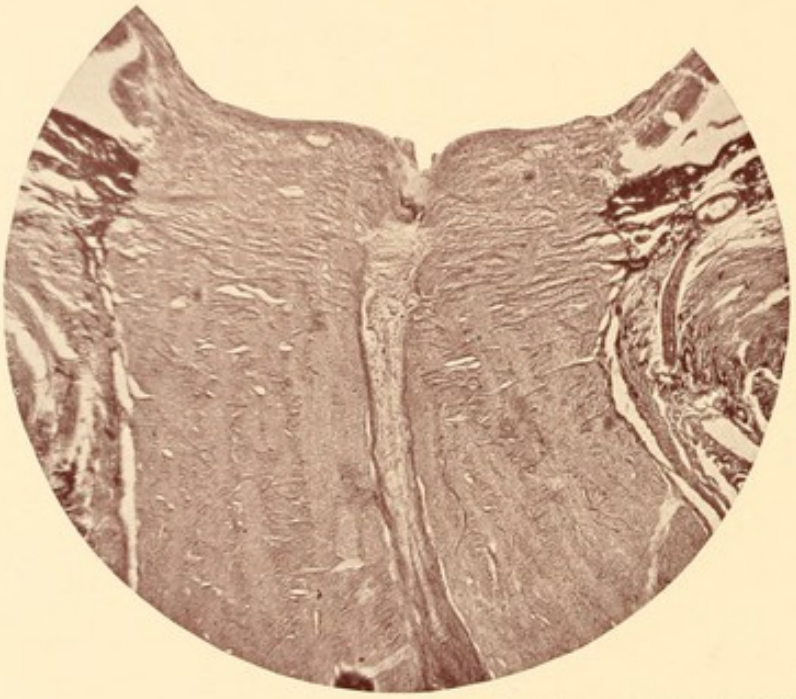
"At the point of entrance of the central vessels—the vessel infundibulum—a cup has been formed somewhat similar to the excavation seen in glaucoma. This cup is

PLATE V.



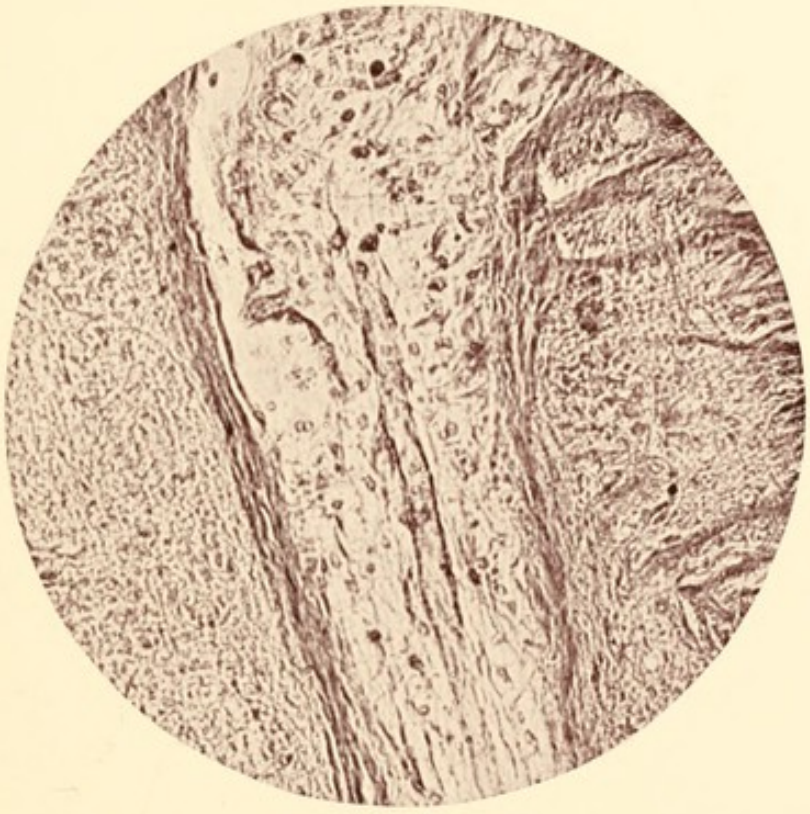
Optic nerve entrance of the normal dog. (x75).

PLATE VI.



Optic nerve entrance from a case of quinine-amaurosis in a dog. Thrombus in central vessel. (x100).

PLATE VII.



Same section as Plate VI, showing tissue filling the vessel, with capillary running through the centre of the thrombus, and a large cavity formed in it. (x250).

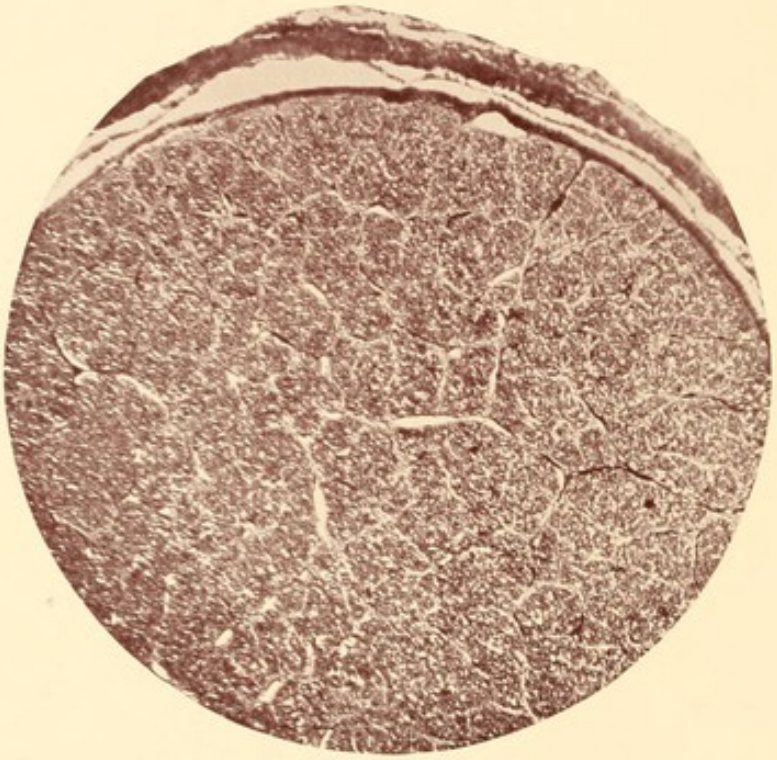
partly filled by a fine granular substance, a portion of which is arranged in threads holding, in its meshes a few blood corpuscles. A little below the cupped entrance is a dense plug of this granular substance. Below this plug the central vessel is seen, the walls of which are somewhat thickened, and its lumen almost entirely filled by a connective tissue growth composed of fine reticular fibrous connective tissue, small spindle cells with long processes, and small round cells. (Plate VI.) Scattered through this structure and in relation to the cells is a small quantity of pigment. Running through the centre of this mass of tissue which fills the vessel there is a small capillary arteriole, narrow at its upper extremity, but at its lower fourth suddenly expanding to at least double the size of the upper portion. (Plate VII.) At one side of the upper extremity of this capillary vessel is an irregularly-shaped space, formed in the connective tissue filling the large vessels. This space contains a few blood corpuscles and seemingly is lined by endothelium, a few nuclei being seen around the edge. (Plate VII.) At its upper extremity this space leads off into a series of branching capillary vessels, which run into and are lost in the surrounding nerve tissue. At the lower portion of the large occluded central vessel there is a blood sinus which also leads off into the surrounding nerve tissue. There are other, but smaller, sinuses or vessels passing from the main vessel along its entire course. In a number of the sections, both in the first series of quinine dogs and from the one which is under consideration in the present paper, the cup at the central vessel-entrance is seen, and, protruding from the cup, masses of material, partly homogeneous and partly granular, containing a few nuclei. In one section the lower portion of this cupped entrance is constricted, and below

the point of constriction the vessel rapidly expands, its lumen being filled by a finely-reticular fibrous connective tissue, holding in its meshes a mass of small round cells. Here and there in this mass of tissue there are blood sinuses which contain a few blood cells. At one side of the central cup, where Müller's fibres enter the nerve from the retina, there is an expanded bloodvessel filled with a blood clot. In one dog, of the original series of quinine-experiments, the cupping is well marked, and protruding from the cupped entrance is a mass of the granular and homogeneous material such as has been described. The entrance to the vessel is greatly constricted immediately after passing into the upper opening, and it is partly filled by the granular material. In one section is shown a small vessel formed in this granular homogeneous material which extends through the constricted entrance to the central vessel. Below the entrance and constriction the central vessel is lost in a mass of dense fibrous tissue. This tissue contains numerous small bloodvessels or channels, some of which lead off into the surrounding nerve tissue.

"Transverse sections of the optic nerve and chiasm of the dog blind for two months, stained by Weigert's process, show marked degenerative changes. Plate VIII. represents a transverse cut of a normal dog's optic nerve stained by this process, while Plate IX. has been prepared from a similar cut taken from the dog blind from the effects of quinine for two months. The contrast in these two sections is well shown. In the quinine-dog there is complete destruction of the nerve fibres, some increase of connective tissue, and a small amount of fatty infiltration.

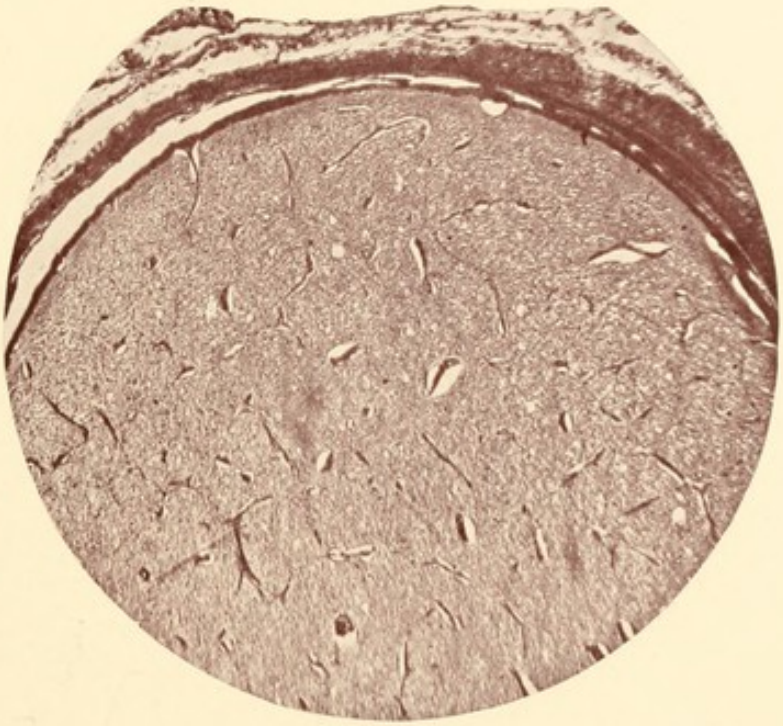
"In one specimen the section has passed through the lenticular ganglion, showing the development of the

PLATE VIII.



Normal optic nerve of a dog. Transverse section (x125 Weigert's stain).

PLATE IX.



Optic nerve of a dog, blind from the effects of quinine for two months, showing atrophy and degeneration. (x125 Weigert's stain).

ciliary nerves and slight degenerative changes in the ganglion itself. A section of a normal ganglion stained by Weigert's process compared with the ganglion from the quinine specimen, prepared by exactly the same process, illustrates the degeneration in the fibres.

"Transverse sections of the chiasm compared with similar sections taken from the normal dog make it evident that the degenerative process and complete atrophy exist in all of the fibres up to the chiasm, in the chiasm itself, as far backward as it has been possible to trace the optic tracts.

"The dilatation of the pericellular lymph-spaces through the brain in the first series, especially in the cuneus, has been shown by a number of experiments to be unconnected with any action of quinine, being easily produced by any slight fault in the technique.

"In *résumé* I may say in regard to the microscopical appearances, that there are thickening and changes in the walls of the optic-nerve vessels (endovasculitis); organization of a clot, the result of thrombosis, an organization which has been carried on even to the extent of its being channelled by new vessels; widening of the infundibulum of the vessels as the result of the constriction of the surrounding nerve fibres, causing appearances not unlike a glaucomatous excavation; and, finally, practically complete atrophy of the visual path, including the optic nerves, optic chiasm, and optic tracts, as far as they could be traced.

"It seems, then, very likely that the original effect of quinine is upon the vasomotor centres, producing constriction of the vessels; that finally changes in the vessels themselves are set up, owing to an endovasculitis; that thrombosis may occur, and that the result of all of these is an extensive atrophy of the visual tract.

"Not the least remarkable is the selective influence of quinine on the optic nerves and the optic tract. In the sections it may be seen that the ciliary and oculomotor nerves, side by side with the atrophic optic nerve, are perfectly normal, and that even in the lenticular ganglion most of the fibres are perfectly intact, although a few appear to have undergone a slight degeneration. The selective action of drugs is, of course, well known, the characteristic influence of digitalis upon the heart being, perhaps, the most typical example. This, however, in addition to the well-known physiological action of drugs, appears to be a histological demonstration of such affinities. Why quinine should produce these lesions upon the nerves of special sense which supply the eye and the ear it is difficult to understand; that it has such action is unquestioned, and here meets with a positive microscopic demonstration. While, no doubt, the original effect is in some sense due to the influence of this drug upon the vasomotor centres, this cannot be the entire explanation, or we should have similar actions under the action of well-known vasomotor stimulants like ergot."

Barabaschew,[1] from his experiments on human beings, comes to the following conclusions: In quinine-poisoning the vascular system plays an important *rôle*, essentially through the medium of the vasomotor centres, which, by reason of its condition of irritability, causes strong contraction of the peripheral vessels. Whether the changes in the peripheral vessels are entirely dependent on this condition of irritability of the centre cannot be decided at the present time.

[1] He also produced quinine-blindness in dogs and found the same ophthalmoscopic picture which Brunner and I have described.

Recently De Bono[1] has observed three cases of quinine-blindness in human beings and has made experiments on dogs and frogs. He returns to an old theory, and believes that quinine paralyzes the movements produced in the retinitic elements under the action of light by an intoxication of the protoplasm, and further believes that the action of the drug is upon the rods and cones. The following table is a brief *résumé* of his experiments on dogs.

No. Dog.	Weight in Kilos.	Quantity of Salt of Quinine.	Result.
1	4.5	2.5 gr.	Amaurosis.
2	4.4	4.0 "	Dead after one hour.
3	4.0	1.0 "	Amaurosis.
4	6.0	6.0 "	Amaurosis.
5	5.0	2.0 "	Amaurosis.
6	3.5	2.0 "	Amaurosis.
7	3.2	1.5 "	Dead after one hour.
8	5.7	2.0 "	Amaurosis.
9	2.3	1.0 "	Amaurosis.
10	5.0	2.0 "	Amaurosis.
11	10.0	2.5 "	Amaurosis.

EXPERIMENTS WITH SULPHATE OF CINCHONINE. I have also experimented with the less powerful alkaloids of the cinchona bark, notably with the sulphate of cinchonine. With this drug the effects were the same as with the sulphate of quinine, save only that the dose required was much larger. In my original experiments the sulphate of quinine was given hypodermically to dogs in quantities varying from one to four grains to the pound, and blindness resulted in from three to fourteen hours, the earliest appearance of the amaurosis after injection being three hours.

A dose of five grains of sulphate of cinchonine to the pound given to a twenty-four-pound white dog produced no ophthalmoscopic lesions, and no evident

[1] Archiv. di ottal., Palermo, 1894, ii., pp. 171, 227.

disturbance of vision at the end of forty-eight hours. An additional dose of seventy-two grains produced a moderate temporary amaurosis with blanching of the retinal vessels, from which recovery occurred, however, without permanent atrophy.

In a *second experiment* a sixteeen-pound black dog received sixty grains of cinchonine sulphate, or about four grains to the pound, and seventeen hours later died in convulsions. The dog, however, for some hours before death, and when non-convulsed, was completely blind.

In a *third* experiment a white and black bitch, twenty-four pounds in weight, received two grains of sulphate of cinchonine to the pound. Five days later the animal was partially blind, but light-perception was present. The vascular circle on the disk was much shrunken. Recovery, however, took place without permanent atrophy. This is interesting as possibly showing the greater susceptibility on the part of the female animal to the action of the drug. (See also page 182.)

Therefore Casey Wood's[1] belief that cinchonine and cinchonidine will produce visual effects similar to those of quinine itself meets with experimental confirmation, in so far, at least, as the sulphate of cinchonine is concerned.

Treatment. The earlier cases of quinine amblyopia, especially those reported by Von Graefe, were treated by depleting the patient, which, as Knapp points out, is a method not based upon scientific principles. Necessarily great care should be taken that no additional preparation of the cinchona barks is administered, owing to the extreme susceptibility of the patient to the smallest quantities of the drug under these circum-

[1] Loc. cit.

stances. The inhalation of nitrite of amyl, as practised by Buller, De Gouvea and Tiffany, and the administration of digitalis, as in Gruening's case, represent rational modes of treatment. Probably recovery within the limits already explained will take place without the administration of any drug, but the well-known effect of strychnine as a direct stimulant to the optic nerve fibres indicates the necessity for its employment, especially by the hypodermic method. Indeed, this drug, in one or two of the reported cases, has been of the utmost service, notably in Jodko's case of central scotoma. Galvanism was employed by Buller and may be tried in suitable cases. Tiffany used eserine locally, partly to contract the dilated pupil and partly because there was increased intraocular tension. On the recommendation of L. Webster Fox the administration of hydrobromic acid in full doses may be tried, as this was effectual in relieving his patient. This is especially interesting in connection with the observations of Fumagalli, who was successful in treating alcoholic amblyopia by the administration of bromide of potassium. Calderai[1] recommends iodide of potassium on the strength of a case of quinine-amaurosis observed during an attack of malaria in which the potash salt produced a favorable influence.

Bibliography—Quinine.

Beraudi, L. Sperienze intorno agli effeti dei sali di chinina e di cinconina nell' uoneo sans. Annali Universali de Medicina. Milano, 1829, vol. lii., p. 312.

Beydler. Chinin amaurose. Schmidt's Jahrbuch, xviii., 1838, p. 292.

Rombach, K. A. Chinins gegen Tertianfieber. Schmidt's Jahrbuch, xx., 1838, p. 18.

Giacomini, G. Effeti del solfato di chinina sugli animali, ed avvelena-

[1] Bollet, d'ocul., 1893, No. 24, xv.

mento del solfato di chinina nell' uoneo sans. Annali Universali di Med., Milano, 1841, xcvii., p. 325.

Trousseau and *Pidoux*. Traité de Thérapeutique et de Matière Médicale, vol. ii., 1841, p. 323.

Trousseau. Dictionnaire de Médecine. Paris, 1842, xxxi., 2d ed., pp. 544 et seq.

Guersant. Dictionnaire de Médecine. Paris, 1842, xxvi., 2d ed., pp. 544 et seq.

Giacomini, Prof. Dictionnaire de Médecine. Paris, 1842, xxvi., 2d ed., pp. 544 et seq.

Mélier. Expériences et observations sur les proprietés toxiques du sulfate, de quinine à haute doses. Bull. de l'Acad. Roy. de Méd., Paris, 1842–43 viii., pp. 898–918.

Briquet. Réflexions sur l'emploi du sulfate de quinine à hautes doses. Bull. de l'Acad. Roy. de Méd., Paris, 1842–43, viii., pp. 898–918.

Lewis, Henry C. Case of Total Blindness Occurring During the Administration of Large Doses of the Sulphate of Quinine. Western Journ. of Med. and Surg., Louisville, Ky., 1845, new series; Chicago, 1889, xiii., pp. 433–441.

McLean, John. Illniois and Indiana Med. and Surg. Journ., new series, 1846, p. 385.

Baldwin, W. O. Observations on the Poisonous Qualities of the Sulphate of Quinine. Amer. Journ. of Med. Sciences, Phila., 1847, xiii., pp. 292–294.

Briquet, P. Traité thérapeutique du quinquina et des preparations. Paris, 1855.

Von Graefe. Fälle von Amaurose nach Chiningebrauch. Archiv für Ophthalmologie, Berlin, 1857, iii., p. 396.

Solomon, J. V. Anæsthesia of the Retina Produced by an Overdose of Quinine. Ranking's Abstract, Lond., 1872, lv., p. 219.

Jodko, Dr. Pamietnik Towarzystva. Lekarskiegs Warszawkisgo (Records of the Med. Assoc. of Warsaw), Warsaw, 1877, lxxiii., pp. 514–515 [Polish].

Jodko. Abstract in Nagel's Jahresbericht., vol. viii., 1877, p. 217.

Galezowski. Les Amblyopies toxiques. Paris, 1878, 8vo., p. 148.

Roosa, D. B. St. J. A Case of Poisoning from the Use of the Compound Tincture of Cinchona. Archives of Ophthalmology, N. Y., 1879, vol. viii., p. 392.

Voorhies, A. H. Temporary Blindness from Quinine. Trans. of the Amer. Med. Assoc., 1879, p. 411.

De Wecker. Ocular Therapeutics. Trans. by Forbes, London, 1879, p. 448.

Horner. Quoted by Brunner, loc. cit., p. 11.

Baumgarten. Effect of Quinine on Sight and Hearing. St. Louis Courier Med., Nov., 1880, iv., p. 466.

Roosa and *Ely*. Amblyopia from Quinine. Archives of Ophthalmology, N. Y., 1880, vol. ix., p. 41.

Buller, F. A Case of Sudden and Complete Loss of Vision after Large Doses of Quinine. Trans. of the Amer. Ophthal. Assoc., 1881, p. 262.

Dickinson, Wm. Quinine Amaurosis. St. Louis Med. and Surg. Journ., St. Louis, 1881, xli., p. 352.

Knapp, H. On Quinine Amaurosis, with Three Cases. Archives of Ophthalmology, N. Y., 1881, x., pp. 220–231.

Gruening, E. On Quinine Amaurosis. Archives of Ophthalmology, N. Y., 1881, vol. x., p. 81.

Ibid. Ein fall von chinin-blindheit. Archiv für Augenheilkunde, Wiesbaden, 1881–82, xi., p. 145.

Michel, C. E. Ein fall von chininamaurose. Archiv für Augenheilkunde, Wiesbaden, 1881–82, p. 151.

Ibid. A Case of Quinine Amaurosis. Archives of Ophthalmology, N. Y., 1881, x., p. 214.

Brunner, H. Ueber chinamaurose. Inaug. Diss., Zürich, 1882.

Dewey, G. M. Sulphate of Quinine, Its Use and Abuse. Trans. Med. Assoc. of Missouri, 1882, p. 161.

Hobby, C. M. A Case of Quinine Amaurosis Manifesting Itself Principally in One Eye Only. Archives of Ophthalmology, N. Y., 1882, xi., p. 34.

Rogers, J. G. Some Peculiar Effects of Cinchonia. (No cases given.) Alienist and Neurologist, St. Louis, 1882, iii., p. 445.

Roosa, D. B. St. J. A Case of Amaurosis after the Administration of Large Doses of Quinine—Recovery. Trans. Amer. Ophthal. Soc., Boston, 1885–87, iv., pp. 431, 602.

Saunders, D. D. Quinine Amaurosis. Mississippi Valley Med. Monthly, Meridian, Miss., 1882, No. 11, p. 433.

Diez. La Ophthalmologie practica. Madrid, 1883, 2, p. 13.

Peña. Centralblatt für Praktische Augenheilkunde, Leipzig, 1883, vii., p. 171.

Webster, David. Two Cases of Quinine Amaurosis. Archives of Medicine, N. Y., 1883, x., p. 338.

Fox, L. Webster. Quinine Amblyopia Cured by the Internal Administration of Hydrobromic Acid. Amer. Journ. of Ophthalmology, St. Louis, 1884, i., p. 115.

Williams, E. Quinine Amaurosis—Report of Two Cases. Trans. Amer. Ophth. Soc., Boston, 1885–87, iv., p. 66.

Nettleship. Severe Quinine Amblyopia. Trans. Ophthal. Soc. of United Kingdom (1886–87), vii., pp. 218, 219, London.

O'Bryen, J. J. Case of Quinine Blindness. British Med. Journ., Lond., 1886, i., p. 823.

Prewitt, R. C. Amaurosis. Mississippi Valley Med. Monthly, Memphis, 1886, vi., pp. 116–118.

Browne, E. A. A Case of Quinine Amaurosis. Trans. Ophthal. Soc. of United Kingdom, Lond., 1887, vii., p. 193.

Bruns, H. D. On a Case of Quinine Amaurosis reported by Dr. Thos.

Herbert, of New Iberia, La. New Orleans Med. and Surg. Journ., June, 1888; 1887–88, n. s., xv., p. 961.

Championnière. Quoted by Galezowski, loc. cit.

Doyne. Severe Quinine Amblyopia. Trans. Ophthal. Soc. of United Kingdom, Lond., 1887, vii., p. 221.

Gruening, E. Trans. Amer. Ophthal. Soc., Boston, 1887.

Mellinger, Carl. Ein fall von Amblyopie nach Chinin-intoxication. Klinische Monatsblätter für Augenheilkunde, Stuttgart, 1887, xxv., p. 57.

Peschel. Chinin-amaurosis. Centralblatt für Praktische Augenheilkunde, 1887, p. 338.

Peschel. Annali di Ottamologia. Pavia, 1887–88, xvi., p. 421.

Shulz, Hugo. Studien über die wirkung des chinins beim gesunden menschen. Virchow's Archiv, Berlin, 1887, cix., pp. 21–86.

Lopez. Amblyopie Quinique. Recueil d'Ophthalmologie, Paris, 1888, 3 s., x., p. 79.

Atkinson, I. E. Some of the Graver and Rarer Forms of Cinchonism. Journ. Amer. Med. Assoc., Chicago, 1889, xiii., pp. 433–441.

Herbert, Dr. Ueber Chininamaurose. Wiener Medicinische Blätter, Wien., 1889, xii., p. 602.

Garofolo, Isidoro. Ein Fall von Chininamaurose. Wiener Medicinische Blätter, Wien, 1890, xiii., p. 227.

De Schweinitz, G. E. Some Experiments to Determine the Lesion in Quinine Blindness. Trans. Coll. of Physicians, Phila., Nov. 1890; and Additional Experiments to Determine the Lesion in Quinine Blindness. Trans. of the Amer. Ophthal. Soc., 1891.

Tiffany, F. B. Cécité Amenée par la Quinine ou Amaurose Quinique. Recueil d'Ophthalmologie, Paris, 1890, 3 ser., xii., pp. 321–325.

Barabaschew, Paul. Zur frage von der Chinin-amaurose. Archiv für Augenheilkunde, Wiesbaden, 1891, Bd. xxiii., p. 91.

Berger, Émile. Intoxication par le Quinine. Les Maladies des Yeux. Paris, 1892, p. 410.

Geschwind, H. Opacités du corps vitré dans un cas d'Amblyopie Quinique, Arch. de méd et pharm. militaires, Paris, 1892, xix., pp. 43–46.

Wakefield Alice. New York Polyclinic, N. Y., 1893, ii., p. 46.

Pischl, Kaspar. Quinine Blindness. Medical News, Phila., 1893, July 29.

Calderai. Due casi di amaurosi chinica quariti con l'ioduro disodio, Bollet d'ocul, 1893, 15. No. 4.

Claiborne, J. H. Case of Quinine Amaurosis. N. Y. Med. Journ., 1894, lix., Part I., p. 819.

De Bono, T. P. L'amaurosi e l'ambliopia da chinina. Arch. di ottal., Palermo, 1894, ii., 171, 227.

De Gouvea. Amaurose quinique. Ann. d'Oculistique, Paris, 1894, cxi. 363.

Hamlisch, H. Ein Fall von Amaurose nach Chinin. Wiener klin. Rundschau, 1895, No. 31.

VISUAL DISTURBANCES FROM SALICYLIC ACID AND FROM SALICYLATE OF SODIUM. (*Salicylic-acid amblyopia.*)

It is not unnatural, in view of the physiological action of salicylic acid and the salicylates, and the well-known symptoms which they produce in full doses—symptoms which closely resemble in many particulars those known under the general name of cinchonism, that visual disturbances analogous to quinine-amaurosis should arise under the toxic influence of these drugs.

The first case of importance is the one reported by E. Gatti.[1] A sixteen-year-old, robust peasant girl was given, on account of articular rheumatism, eight grammes of salicylate of sodium divided into ten doses, a dose to be taken hourly. After receiving the last dose she fell asleep and awoke entirely blind. The sensibility of the cornea and sclera was normal; there was well-marked mydriasis; the media were clear. There was a light gray reflex from the retina depending upon the decided choroidal pigment. The optic papilla was normal, its borders sharply marked, and the retinal veins well filled—conditions which continued after the restoration of vision. Other symptoms were dulness of hearing, weak heart-sounds, small pulse, and slight perspiration. The urine was free from albumin and sugar. Ten hours later the patient could count fingers, and twenty-four hours after the blindness began vision was restored. Mydriasis persisted for several days. The amaurosis was explained by a direct action of the salicylate of sodium upon the retina and optic nerve.

Somewhat earlier than this observation by Gatti is one

[1] Gaz. degli Ospital, 1880, i., 4. Abstract in Nagel's Jahresbericht f. Ophtalmologie, 1885, vol. xi., p. 243.

by Riess,[1] who, in his researches on the effect of salicylate of sodium on healthy people, noted tinnitus aurium and disturbance of vision after 5-gramme doses.

Knapp,[2] describing quinine-blindness, states that he has seen three cases presenting precisely analogous symptoms due to large doses of salicylic acid and salicylate of sodium.

H. Brunner[3] refers to salicylic-acid amblyopia, and declares that it has been described by several authors, but gives no particulars.

Evidently an amblyopia in all particulars resembling that produced by quinine may result from large doses of salicylic acid or one of its salts.

EXPERIMENTS WITH SALICYLATE OF SODIUM.

In order to test the effect of large doses of salicylic acid on the optic nerve apparatus of dogs, I performed a number of experiments analogous to those of Brunner and myself with quinine.

Experiment I.—March 21, 1892. Yellow, short-haired dog; weight 22½ pounds. Sixty grains of salicylate of sodium injected. The eye-grounds and vision previously determined to be normal.

23*d*. No change in vision. Sixty grains of salicylic acid dissolved in ammonia, so that one-half grain of the salicylic acid was contained in each minim of the solution, were injected.

24*th*. Dog partially blind; hangs his head and fails to

[1] Berlin. klin. Wochenschr., 1875, xii., pp. 673, 690.

[2] Bericht ueber die Versammlung der Ophtalmologischen Gesellschaft. Heidelberg, 1881, xiii., p. 103.

[3] Ueber chininamaurose, loc. cit.

avoid objects in moving around the room. No positive change in the eye-grounds, unless perhaps a slight diminution in the size of the arteries. Pupils react normally.

28*th*. Dog partially blind, but there is slight conjunctivitis, and it is difficult, on account of the haziness of the cornea, to examine the eye-ground. Abscess at the point of injection opened and carefully sterilized.

April 1*st*. No new symptoms, but there is distinct return of vision, as the dog no longer avoids objects.

4*th*. Optic nerves decidedly pale, and arteries smaller than before, although the dog sees in the centre of the visual field; it is probable that the periphery is somewhat contracted.

Experiment II. Long-haired black-dog; weight 13 pounds. Sixty grains of salicylate of sodium injected at 4 P. M., March 28, 1892.

29*th*. Dog very weak, drags the hind legs, and apparently blind, but there is haziness of the cornea and some conjunctivitis. Abscess at point of injection.

April 1*st*. Pyæmic symptoms. There is a large hypopyon-keratitis. Dog killed; eyes, optic nerves, and chiasms removed.

Experiment III. Original salicylic-acid dog; was given sixty more grains of salicylate of sodium, April 4, 1892.

8*th*. Corneas have become hazy, and a small spot of suppuration developed in the upper and outer part of each one. Cornea is not anæsthetic.

In several similar experiments partial blindness or conjunctivitis resulted without constitutional symptoms.

Evidently, it is possible to produce partial blindness with large doses of salicylic acid or salicylate of sodium,

the ophthalmoscopic appearances resembling in minor degree those seen in quinine-amaurosis. Injections of this drug may be followed by marked irritation of the eyes resulting in corneal abscess, provided we exclude the possibility of this having been a pyæmic symptom. The dogs may suffer from a mild conjunctivitis without systemic disturbance, which is analogous to a similar condition sometimes observed in human beings after the administration of salicylic acid.[1]

Pathology and Pathological Anatomy. The vessels of the eyes, which were removed, presented no evidence of endovasculitis, such as I have described in dogs poisoned with quinine. The salicylic-acid dogs, however, were not allowed to remain alive for any great length of time after the blindness began, which may account for the absence of vascular lesions. I have no doubt future experimentation will prove that the lesions in quinine-amaurosis and salicylic-acid blindness are analogous if not identical.

ANTIFEBRIN, or, more properly, ACETANILID, and ANTIPYRIN, or PHENOZONE, have not been studied with accuracy in their relation to the visual apparatus.

According to Knies, who quotes Müller, acetanilid may cause widening of the retinal veins. Simpson, after large doses, observed narrow and immobile pupils. (Quoted by Knies.)

Guttmann[2] records a case of amaurosis lasting one minute in a twenty-five-year old woman who took a gramme of antipyrin to relieve headache. Following this there was some reddening and swelling of the face, especially of the eyelids. Ophthalmoscopic details are not given.

[1] Consult Rosenberg: Deutsche med. Wochenschr., 1886, xii., p. 569.

[2] Therapeutische Monatshefte, 1887, i., p. 274.

I have experimented somewhat on myself with large doses of antipyrin, and noted a curious visual disturbance, characterized by undulations in the atmosphere, something like those caused by the ascent of heated air, followed by an apparent shower of sparkling points of light—phenomena, in other words, which are the frequent prodromes of migraine. No pain succeeded, but for a time accommodation-power was diminished. No doubt these and other abnormal ocular manifestations should be attributed to the influence of this drug upon the circulation.

Neither of these drugs produces amblyopia in the manner of quinine and salicylic acid, at least there is no record of such a condition.

SECTION VII.

DRUGS INCLUDED IN CLASSES V., VI., AND VII., WITH SPECIAL REFERENCE TO THE MYDRIATICS AND MYOTICS.

Drugs whose prominent action is concerned with the central organ of the circulation, either as stimulants or depressants, do not cause toxic amblyopia by an action on the optic nerve, provided we exclude alcohol, which has already been considered in another class.

Two of them, aconite and digitalis, have been credited with the power of producing visual disturbances. The symptoms, however, are chiefly concerned with mydriasis, as, for example, in the case of poisoning from aconite reported by F. H. O'Brien,[1] so frequently quoted. Other cases have been recorded by Steward, Hooper, and Duigenam. It is most likely that the circulatory disturbances have had as much to do with the visual phenomena as any direct action of the drug on the eye.

Knies quotes Jeanton's case[2] of *digitalis-poisoning*, in which a fifty-seven-year-old man took ninety grammes of the tincture of digitalis, and, amongst other things, had mydriasis and nebulous vision, followed later by xanthopsia; recovery in eight days. In this, as well as in other cases of poisoning by digitalis, there has been mydriasis. Occasionally the very opposite condition of myosis has been noted. No amblyopia from an action on the optic nerve, however, has been observed.

[1] New York Med. Record, 1887, xxxii., p. 138.

[2] Gaz. des Hôp., 1885, lviii., p. 441.

Drugs whose prominent action on the eye is the production of mydriasis constitute a large number of substances, all of which, having the property of dilating the pupil, and some of them the power of markedly paralyzing the function of the ciliary muscle, necessarily cause visual disturbances. The most prominent of these are

BELLADONNA AND ITS ACTIVE PRINCIPLE, ATROPINE. The early writers so often referred to, Himly, Beer, and others, include belladonna in the list of substances capable of producing amaurosis, especially if used for any great length of time. Kneschke,[1] for example, describes "amblyopia amaurotica" as the result of a long-continued local application of belladonna; but this and many other instances are uncertain examples, because it is impossible to determine whether the imperfect vision was due to an effect of the drug on the accommodative power or to an actual impairment in the optic-nerve apparatus.

Galezowski[2] devotes a section to "atropine-amblyopia" and refers to the fact that Mackenzie, as well as other older writers, believed that the long-continued instillation of atropine could produce amblyopia. Galezowski regards most of the instances as due to paralysis of accommodation, and not to any effect upon the optic nerve.

Excluding those cases in which the instillation of atropine has been followed by glaucomatous manifestations, so far as I am aware, there is no proof that blindness has ever been caused by this drug.

HYOSCINE and HYOSCYAMINE, both alkaloids of *hyoscyamus* or *henbane*, are mydriatics of great activity, fully

[1] Serm. d. Neuest. ad. gen. Med. Leipzig, 1835, xii., 177.

[2] Des Amblyopies et des Amauroses, loc. cit.

paralyzing the ciliary muscle and consequently producing visual disturbances from this effect; but in ordinary medical doses, or even when long continued in the form of eye-drops, they do not cause amblyopia in eyes suited to their application.

DATURINE, the alkaloid of the *Datura Stramonium*, or the common Jamestown weed, is an active mydriatic and cycloplegic agent. Its visual disturbances are the same as those produced by other mydriatics.

STRAMONIUM itself, however, appears, at least in one very well-observed instance, to have affected the papillo-macular bundle of the optic-nerve fibres. This is the case recorded by Fuchs.[1] The patient from his youth up had smoked stramonium leaves in great quantities on account of asthmatic attacks, and from this cause had acquired an amblyopia with central *color scotoma*. The man neither used tobacco nor drank liquors of any kind.

DUBOISINE, the alkaloid of the leaves of the *Duboisia myoporoides*, a plant of Australia, is a mydriatic much employed by some ophthalmic surgeons for the purpose of paralyzing the ciliary muscle. It is also an efficient hypnotic, especially in insanity. Marked constitutional disturbances often follow an instillation of a solution of the drug into the conjunctival sac.

Amblyopia and great narrowing of the visual field have been recorded by J. P. Worrell[2] as the result of using the alkaloid for the purpose of correcting the refractive error of a woman, aged thirty-six. The fundus oculi was normal; recovery gradually took place in about three weeks.

HOMATROPINE, a much more feeble alkaloid than the others thus far mentioned, has never been made respon-

[1] Text-Book of Ophthalmology, Amer. ed., N. Y., 1892, p. 441.

[2] Trans. Amer. Ophthalmological Soc., 1881, vol. iii., Part II., p. 273.

sible for amblyopia other than that occasioned by its action on the ciliary muscle. Occasionally the mydriasis from this drug is very long continued. Such cases have been reported by Cheney, Wadsworth, and myself.[1] With Dr. H. A. Hare I have experimented with this drug and studied its action on the eye and on the general circulation in men, rabbits, and frogs. We never observed the slightest indication of amblyopia.[2]

COCAINE. When a solution of this alkaloid is dropped into the eye it produces local anæsthesia, mydriasis, widening of the palpebral fissure, and, if used carelessly or for too long a period, drying the epithelium of the cornea. Disturbances of vision which have been credited to it are generally due to this wrinkling of the epithelial layer.

In acute cocaine-poisoning maximum mydriasis is a prominent symptom. The blindness which has been described is due to the accompanying syncope. According to Saury,[3] visual hallucinations, diplopia, amblyopia, chromatopsia, and micropsia have been observed in chronic cocaine-poisoning and with those who have acquired the cocaine-habit. I am not familiar with ophthalmoscopic or perimetric observations under these circumstances. Schubert[4] reports temporary amblyopia and contracted retinal arteries after an injection of cocaine into the gum.

ERYTHROPHLOEINE, an alkaloid studied in the hope that it might find rank among those drugs that have the power of anæsthetizing the cornea and conjunctiva, but which has been set aside, owing to the irritative qualities which it possesses, does not seem, in so far as experiments have gone, to cause amblyopia.

[1] Consult Ophthalmic Review, December, 1890, ix., p. 353.
[2] Medical News, Phila., December, 1887, li., p. 731.
[3] Annales Méd. Psych., 1889, ix., 7 s., p. 439.
[4] Centralblatt f. prakt. Augenheilk., 1886, 10, p. 17.

Gelsemium and Conium, the former at one time used as a mydriatic, are drugs which, either in the form of their active principles or as tinctures or fluid extracts, have very decided actions upon the human system, paralyzing peripheral motor nerves, and therefore affecting the iris and ciliary body. They do not, however, produce disturbance of vision in other respects.

Scopolamine, generally used in the form of the hydrochlorate, an atropoid alkaloid derived from the roots of the *Scopolia Atropoides*, and especially brought into prominence by Raehlmann,[1] is an active mydriatic and paralyzant of the ciliary muscle. Several cases of poisoning have occurred under its influence, but perhaps only when it was injudiciously employed. A very remarkable result recorded by Thomas R. Pooley[2] is a notable diminution of visual acuteness after the full effect of the drug on accommodation. Pooley does not consider this temporary amblyopia of much moment; but the fact that it occurs at all is a matter of considerable importance and deserves investigation.

If we except the excessive smoking of stramonium leaves, the visual disturbances caused by mydriatics are for the most part, then, due to their action on the ciliary muscle, and have no connection with the optic nerve or retina, unless future experience should show that scopolamine is more active in this respect than it is known to be at present

Drugs whose prominent action on the eye is the production of myosis include four substances, the most important of which is eserine, the other three being pilocarpine, muscarine, and curare.

Eserine, one of the alkaloids of the *Physostigma*

[1] Klin. Monatsbl. f. Augenheilk., February, 1893, xxxi.

[2] Therapeutic Gazette, 1894, n. s., x., p. 162.

Venenosum, or Calabar bean, much used in ophthalmology as a myotic and to reduce increased intraocular tension, produces disturbance of vision chiefly by contracting the pupil and approximating the near and the far points. Temporary blindness in cases of general poisoning has been observed, one instance noted by Knies being an example of temporary total blindness.[1]

PILOCARPINE, one of the active principles of the *Pilocarpus Jaborandi*, is much used as a myotic. Having the same effect upon the pupil and ciliary muscle as eserine, the visual phenomena are analogous. It is stated by Fuhrmann[2] that after injections of pilocarpine, owing, no doubt, to its effect upon the general organism, there may be temporary amblyopia.

MUSCARINE, the alkaloid of the *Agaricus Muscarius*, and also existing as a ptomaine in putrid fish, produces marked cramp of the accommodation and afterward myosis. In this sense it has the power of disturbing vision.

CURARE, the drug much used in physiological experiments to paralyze motor nerves, is said to cause myosis when given internally. Galezowski and Mangin have shown that a collyrium of the drug instilled into rabbits' eyes causes anæmia of the papilla by diminishing the calibre of the capillaries.

It has been suggested by Schubert[3] that nitrite of amyl should be administered during cocaine-amblyopia.

[1] The case is recorded by Carreras Arago, and may be found in abstract in the Jahresbericht f. Ophtalmologie, 1874, p. 265. I have been unable to find the original reference.

[2] Wiener med. Wochenschr., xl., s. 1445–1446. Quoted by Knies.

[3] Loc. cit.

SECTION VIII.

DRUGS INCLUDED IN CLASS VIII., WITH SPECIAL REFERENCE TO THE VISUAL EFFECTS OF FILIX MAS.

Class VIII. has been made to include those drugs whose medicinal use is concerned with the expulsion of intestinal parasites. When acting as poisons they are capable of originating diverse visual disturbances and, under certain circumstances, symptoms which indicate that they should be included among the drugs which cause a true toxic amblyopia.

AMBLYOPIA FROM ASPIDIUM (U. S.) OR FILIX MAS (B. P.).

History. Filix mas is the rhizome of the *Aspidium filix mas*, or male fern of Europe, and is employed in medicine as a tæniacide, in this country usually in the form of the oleoresin, but also, as is the custom abroad, as a liquid extract. It is a distinctly toxic agent in overdose, acting as a violent gastro-intestinal poison, and has in many instances caused death, even in the adult. It contains filicic acid, an active crystalline principle. In conjunction with other toxic effects it may produce marked amblyopia, and even permanent atrophy of the optic nerve.

According to Drs. K. Katayama and I. OKamoto,[1] Reinlein, in a monograph published in Vienna in 1812, refers to its toxic properties. After this date literature appears to be quiet on the subject until about 1881, when

[1] The Sei-I-Kwai Medical Journal, 1892, xi., pp. 101, 121; also Vittjschr. f. gerichet. Med., Berlin, 1894, 3 F. viii.

May reported two cases of disturbed vision from its use, one patient ultimately becoming blind in one eye and the other in both.

Katayama and OKamoto have collected twenty-three cases of poisoning, ten with temporary or permanent amblyopia of one or both eyes, five of them having occurred in Japan. They attribute the apparent increase of the toxicity of this agent chiefly to the fact that in recent years the doses have been greater than those heretofore employed. In order to test the effect of this drug upon visual acuity, the Japanese observers experimented on dogs and rabbits, and succeeded in producing amblyopia. I have repeated their experiments, with the results detailed in a future paragraph.

Etiology: Pathway of Entrance of the Poison. Practically all of the cases have been the result of the absorption of undue doses of this medicament when it has been administered as an anthelmintic. Inasmuch as the preparation of the patient has often consisted in active purgation and other depressing measures, it is not unlikely that the system was in a condition to be rapidly and seriously affected; in other words, the medicine acts deleteriously only, or chiefly, on those whose nutrition is depraved. Other than the fact that it is a violent gastro-intestinal irritant, there is no particular reason from its physiological action to anticipate a selective influence upon the optic nerve.

The *size of the dose* which produces poisoning varies considerably; thus, three grammes of the extract daily for twelve consecutive days have caused blindness, and very large doses have been given, even lethal in their effects, without the development of visual disturbances.

Symptoms. The general symptoms are those of a violent gastro-enteritis and circulatory depression. The

blindness has usually come on, according to the size of the dose, from twenty-four hours to twelve days after its administration.

The ocular phenomena of most of the cases have been very inaccurately observed. In a few, however, ophthalmoscopic examinations have been made; thus, Baer and Schleier, during the stages of blindness, noted negative ophthalmoscopic appearances. A Japanese observer, Mikiji Yoda, observed first contracted arteries, and three weeks after the blindness, which remained practically complete, pallid disks and small arteries. Grosz found optic-nerve atrophy. No study of the field of vision, of the color-perception, or light-sense appears to have been made.

Diagnosis. There are no symptoms characteristic of this form of amblyopia, and the diagnosis would have to be based upon the history of the case, and the exclusion of other causes or toxic agencies.

Prognosis. The prognosis, judging from the cases reported, is grave, inasmuch as in several instances permanent atrophy of the nerve has resulted.

Pathology and Pathological Anatomy. The Japanese observers failed to utilize their material in order to throw light upon the character of the optic nerve lesions, if such there be, which this drug produces. Judging from clinical experience filix mas belongs to those drugs which produce amblyopia by an action on the optic-nerve fibres, resulting in their atrophy. The double amaurosis, without ophthalmoscopic lesions, and the immobile pupil indicate peripheral visual disturbance. In Schleier's case the patient had albuminuria, and therefore uræmic blindness cannot be excluded. Van Aubel[1] ascribes the

[1] Le Scalpel, October 6, 1895, abstract, Annales d'oculistique, T. 114, 1895, p. 400.

amaurotic effect of male fern to filicic acid. He believes this agent acts upon the central nervous system, the spinal cord and the sympathetic, causing dilatation of the pupil, and, through the vasomotor nerves, contraction of the retinal arteries.

CASES. The following cases are briefly detailed, and represent the best examples which have been reported of the effects of filix mas, or its extract, upon vision :

CASE I. Patient, age not stated, took for twelve consecutive days 3 grammes of the extract of filix mas to relieve anchylostomum duodenale. Sight failed on the tenth day and was lost on the twelfth.[1]

CASES II. and III. Among 100 cases of anchylostomum disease treated with male fern extract, two became blind.[2]

CASE IV. Baer[3] records the case of a woman, aged twenty-six years, who took within a few minutes 15 grammes each of pulverized male fern and the extract, producing violent general poisoning, and twenty hours later blindness of the left eye, together with immobile pupil. Ophthalmoscopic examination negative. Recovery in two weeks.

CASE V. Schleier[4] records the case of a girl, aged twenty-two years, who took $7\frac{3}{10}$ grammes each of the pulverized male fern and the fresh extract, producing violent general poisoning, and three days later total blindness, with normal ophthalmoscopic appearances.

[1] Zeitschrift der Tokio Med. Gesellsch., Bd. v., Heft 10. Quoted by Katayama and OKamoto. Original paper not accessible.

[2] Gezotta Medica Italian, No. 27. Quoted by Katayama and OKamoto. Original reference not accessible.

[3] Prag. med. Wochenschr., 1888, p. 41.

[4] Muench. med. Wochenschrift, No. 32, 1890.

Case VI. Mikiji Yoda gave a farmer, aged twenty-three years, with anchylostomum duodenale, 20 grammes of castor oil, followed by a prescription containing 10 grammes of the extract of male fern, 0.2 gramme of santonin, divided into three parts. The same prescription was repeated on the three following days, and produced slight poisoning. The next day the vision was blurred, the pupils dilated, and the retinal arteries contracted. Three weeks later the left eye was blind, and the right eye had vision equal to counting fingers. Both optic disks were pallid and the retinal arteries contracted.[1]

Case VII. Kono gave the extract of male fern, dose not stated, for some days to a girl, aged twenty years, producing headache and blindness. Vision returned in three months to one eye, but only partly to the other.[2]

Case VIII. Korach[3] had a patient, aged thirty years, who took 15 grammes of the extract; he suffered from general poisoning and had widely dilated pupils which failed to react to light, probably from non-conductivity in the optic nerve.

Case IX. Y. Tanaka gave a soldier with anchylostomum duodenale 5 grammes of the extract of male fern daily for two days; then the pupils dilated and the vision failed. There was gradual recovery of vision, especially slow in the left eye.[4]

Case X. Dr. Y. Kumagaye describes a case of total blindness with immobile pupils occurring under the influence of male-fern poisoning.[5]

Case XI. Grosz[6] reports the case of a man, aged

[1] This case is quoted by Katayama and OKamoto.
[2] Ibid.
[3] Deutsch. med. Wochenschr., 1891, Nr. 32.
[4] This case is quoted by Katayama and OKamoto.
[5] Ibid.
[6] Annales d'ocul., 1895, cxiii., p. 207.

twenty-nine years, who took, after purgation by castor oil, thirty-two capsules, each of which contained 0.25 gramme of a mixture of ethereal oil of male fern and extract of pomegranate. Poisoning ensued and the next day he was blind. Examination revealed complete mydriasis, absence of light-reaction, at first normal fundus, but later atrophy of both optic disks. The blindness was attributed to the extract of male fern.

Experimental Filix-Mas Amblyopia. As before stated, Katayama and OKamoto experimented on dogs and rabbits with the extract of male fern and succeeded in producing dilatation of the pupils in puppies, and in two of them blindness. The proportion of the drug administered may be judged from the fact that one dog, two months old, weighing 36.40 grammes, received in three days one and one-tenth grammes of the extract.

Unfortunately these observers do not even mention the ophthalmoscopic appearances, neither do they seem to have removed the optic nerves, chiasms, and visual centres for microscopic examination. Their research is interesting, however, as it demonstrates the possibility of repeating in animals the clinical symptoms which have been observed in human beings. All of their animals were sufficiently ill, in the general sense of the term, to render somewhat doubtful the exact relationship of the drug to the blindness. They came to the following conclusions:

"1. The extract of male fern has a toxic property, and it acts particularly upon the digestive system and the nerve centres, producing such symptoms as vomiting, diarrhœa, colic, cephalalgia, difficulty of locomotion, dilatation of the pupil, impaired vision, hurried respiration, motor paralysis, and depression.

"2. After use of the extract of male fern loss of

vision sometimes appears, but it is not constant, making its appearance only under certain conditions.

"3. Loss of vision is one of the symptoms of poisoning by the extract of male fern, and it is a matter of course that it may appear along with other symptoms. However, it does not seem to be necessarily contingent upon the size of the dose and the mode of administration.

"4. Patients who had failure of vision consequent upon the use of the extract of male fern were all persons of poor health; the dogs which became blind were also young and weak."

I have performed a number of experiments on dogs with the oleoresin of male fern. The following may be quoted:

Experiment 1. Skye terrier; weight, eleven and one-half pounds.

October 28*th*. Two drachms of the oleoresin administered by the mouth.

29*th*. Dose repeated.

November 3*d*. Three drachms administered.

4*th*. Three drachms administered. First signs of poisonous effect, namely, bloody discharges from the bowels.

5*th*. Dose repeated on this day, the seventh, eighth, and ninth. After the last dose the dog was very ill, depressed, dragging his legs, with frequent bloody alvine discharges. No ophthalmoscopic changes and no evidence of blindness. Dose repeated on the tenth.

11*th*. Dog died this morning. Eyes immediately removed for microscopic examination.

Carefully prepared sections of the eyes and optic nerves failed to give evidence of any lesion. These were stained in the usual manner with carmine and also by Weigert's method.

Experiment 2. Black and white bitch; fifteen pounds in weight.

November 11*th*. On this day and the twelfth, fourteenth, fifteenth, sixteenth, seventeenth, eighteenth, twenty-first, twenty-second, twenty-third, and twenty-fifth the dog received a fluidrachm of the oleoresin by the mouth, or in all 11 drachms of the drug, producing practically no general result except disturbance of the gastro-intestinal tract; no sign of blindness or ophthalmoscopic change.

26*th*. On this day and on the twenty-eighth, twenty-ninth, and thirtieth the dog received 2 drachms daily of the oleoresin. On the twenty-eighth the general toxic symptoms supervened; she was slightly better on the twenty-ninth, very ill on the thirtieth, with the symptoms previously detailed, and died on the first of December. The eyes and optic nerves were immediately removed and placed in Müller's fluid. This dog received in all 19 drachms of the oleoresin.

Sections of the tissue removed yielded negative results. The stains were the same as those used in the former specimens.

Similar experiments produced similar results and need not be detailed. In no instance was ophthalmoscopic change demonstrable, and in none positive signs of blindness, although the depression during the stage of the full toxic influence of the drug is so great as to make this difficult to determine. The results with rabbits were extremely unsatisfactory. The animals died without evidence of any other action of the drug than that of a depressant poison.

Treatment. The treatment of this form of amblyopia, after suitable remedies for the general condition have been applied, need not differ from that which we are

wont to apply to all cases of amblyopia of peripheral origin and should consist in the administration of remedies which stimulate the optic nerve directly, as strychnine, or improve its circulation, namely, cardiac stimulants and nitroglycerin, and probably of small doses of bichloride and biniodide of mercury. Van Aubel particularly recommends nitrite of amyl and strychnia.

VISUAL DISTURBANCES FROM SANTONIN.

SANTONIN, or SANTONINIC ACID, a crystalline principle found in the flowers of the *Artemisia Contra*, is much used in medicine on account of its poisonous action upon the entozoa.

It is interesting in connection with the drugs which produce visual disturbances, not because the symptoms of its poisonous action, which are very violent, include blindness, but because of the xanthopsia, or "yellow seeing," which is present, and which may also appear after the ingestion of non-toxic doses. A deep yellow tint is imparted to everything in the range of vision, and has been compared to the appearances produced by looking through a piece of yellow glass. Sometimes the yellow is replaced by green, and it is stated that the tint may be red and even blue. Most elaborate investigations of this chromatopsia have been made, particularly by F. Rose.[1] Knies[2] has also investigated the matter. The latter observer describes the phenomena somewhat as follows: "Yellow seeing" occurs in from ten to fifteen minutes after the toxic or full physiological action of the drug sets in, and is preceded by a temporary

[1] Virchow's Archives, xvi., 233; xviii., 15; xix., 522; xx., 255; xxviii., 30.
[2] Loc. cit. See also Archives f. Augenheilk., 1887–88, xviii., p. 64.

period of "violet-seeing." Knies, experimenting on himself, observed that the color was a citron-yellow. Very interesting spectroscopic examinations have been made, but as they are not germane to the present subject the reader is referred to the references already given.

The central vision, the fundus oculi, the pupil, and the visual field are unaffected in uncomplicated cases, although there is some diminution of the adaptability of the retina to diminished illumination; in other words, "the light-difference" is deficient.

Occasionally santonin-poisoning is very serious in its nature, producing most violent disturbances of the nervous system, and under these circumstances there may be mydriasis and unequal pupils. Direct influence upon the optic nerve is unknown, and the peculiar actions of the drug must be attributed to a centric influence.

PINK-ROOT, the root of the *Spigelia Marilandica*, is a very decided poison. The symptoms of its toxic action are not unlike those of the mydriatics, and therefore they may include disturbance of sight. The preparation which has generally been used is the fluid extract.

POMEGRANATE. The bark of the pomegranate-root is used particularly in the treatment of tapeworm, and contains an active principle known as *pelletierine*, which, like curare, has the power of paralyzing motor nerves. Dujardin-Beaumetz[1] states that hypodermic injections, in addition to causing vertigo and muscular weakness, produce retinal congestion. Other than this, so far as I am aware, no special visual disturbances occur under its influence.

[1] Quoted by H. C. Wood, loc. cit.

SECTION IX.

UNCLASSIFIED DRUGS.

The drugs included in Class 9 have such indefinite actions, as far as the visual apparatus is concerned, that they have not been deemed worthy of special grouping; in fact, it is doubtful whether any of them have more than the most remote connection with the present topic. They are, however, usually referred to in treatises upon this subject, and for this reason are included. It may be stated at once, however, that none of them produces a true toxic amblyopia.

Apomorphine, a drug used as a centric emetic, has occasionally created visual disturbances; for example, Bergmeister and Ludwig[1] found that the drug in 2 per cent. solution produced after ten minutes anæsthesia of the cornea and conjunctiva, and at the same time distinct clouding of the corneal epithelium. This solution was instilled into the conjunctival cul-de-sac, and therefore the action was probably due to its irritant qualities.

Experiments were made with a number of drugs, after the introduction of cocaine, in the hope of finding another local anæsthetic; for example, M. Gley[2] pointed out that *strophanthin* and *ouabœine* produced corneo-conjunctival anæsthesia, and Steinbach attributed a similar action to Arnaud's strophanthin. Dr. H. A. Hare and myself[3] repeated the work of these observers. We

[1] Centralblatt f. d. ges. Therapie, 1885, iii. pp. 193–196.

[2] Comp. Rendus hebdom. des Séances de la Societé de Biologie, Février, 1890.

[3] Theraupeutic Gazette, 1889, 3 s., v. p. 821.

found that anæsthesia could be produced in dogs, but that it was effected at the expense of clouding of the corneal tissue, which lasted several days.

CHRYSAROBIN may cause violent conjunctivitis when used as a local application to the skin. Ulcers are said to have been associated with this conjunctivitis. Other than this its action is unimportant from the ocular standpoint.

CYTISIN, the active principle of the *Cystisis Laburnum*, according to Allbutt,[1] has caused in one case, together with general symptoms of poisoning, dilated pupils, blanched optic papillæ, and contracted retinal vessels; in other words, symptoms analogous to those seen in acute ergot-poisoning.

MENTHOL, like naphthalin, is said to produce lenticular opacities, provided it is given in doses sufficiently toxic to produce death and the lens is examined soon afterward. Similar lesions in the living animal, as far as I know, have not been observed.

SULPHUR, used in the form of a 10 per cent. ointment for many years, is said to have produced, according to Eichbaum, who is quoted by Knies, symptoms of general poisoning, associated with which there was a wide and immobile pupil. It can scarcely be doubted that some agent other than the sulphur was responsible for this phenomenon, and Knies, commenting on the case in a single word, suggests atropine.

PISCIDIUM, or Jamaica dog-wood, which is a narcotic in its action, is also said to produce mydriasis when its extract is freely administered, and consequently disturbance of vision from this cause.

PODOPHYLLIN has often been included in lists of drugs

[1] Quoted by Knies, loc. cit.

which produce intoxication-symptoms, so far as the eye is concerned. The only ocular relationship, however, is connected with the fact that those who gather the podophyllin roots, dry them, etc., are often affected with a conjunctivitis, owing to the irritating properties of the plant.

Saponin, which may come from the *Quillaia saponaria*, or from the *Saponaria officinalis*, is reported by Keppler[1] as capable of producing strabismus and exophthalmos. There seems, however, to have been no accurate investigation of the other visual phenomena and no reason to believe that there was amblyopia.

Sulphuretted Hydrogen. Casey Wood mentions this as a very rare cause of amblyopia, without giving other particulars than the case of Brouardel and Loye,[2] in which poisoning from this substance produced mydriasis, exophthalmos, loss of the pupillary reflex, and anæsthesia of the cornea. The same case is quoted by Knies. I have not been able to find records of amblyopia due to this substance.

[1] Berlin. klin. Wochenschr., 1872, ix., Nr. xxxii.

[2] Abstract in Nagel's Jahresbericht f. Ophthalmologie, 1885, xvi. p. 266.

SECTION X.

SUBSTANCES WHICH HAVE BEEN PLACED IN CLASS X., NAMELY, THE PTOMAINES, TOXALBUMINS, CASES OF MEAT-, FISH-, AND SAUSAGE-POISONING, AND, FINALLY, SERPENT-VIRUS.

The final section includes those visual disturbances which have been noted in cases of poisoning the result of putrefactive changes in animal tissue; in other words, ptomaine-poisoning in the widest acceptance of the word.

As is well known, many of the ptomaines are basic compounds closely simulating the vegetable alkaloids. Thus, there are those which resemble conicine, nicotine, atropine, veratrine, curare, and strychnine, and consequently the ocular symptoms which may arise under their influence are similar to those which the alkaloids themselves produce, and need not be recapitulated. Muscarine and its action upon accommodation have been described. Although visual acuity, in the ordinary use of the term, is usually not much affected, Knies points out that there may be temporary amblyopia without ophthalmoscopic changes.

Cases of poisoning in human beings dependent upon ptomaines and toxalbumins have generally occurred from the ingestion of spoiled meat, fish, sausage, cream, pastry, etc., and the usual ocular symptom is *accommodative paralysis* with or without *mydriasis*. This symptom, for example, has been noted by Cohn[1] in patients poisoned from eating wild-rabbit pie and pike, by Eichen-

[1] Centralbl. f. Augenheilk., 1879–80, ix. p. 148.

berg[1] in sausage-poisoning, and by Ulrich[2] in five members of one family suffering from meat-poisoning. The failure of accommodation may last for many weeks.

The most interesting ocular lesions are palsies of the external ocular muscles, symptoms which do not pertain to the present topic.[3] The amblyopia in these cases, if it occurs at all, is poorly understood, and in most instances is probably attributable to accommodative palsy.

Serpent-virus. The violent general disturbances which follow the bite of a venomous serpent may account for visual phenomena which have been reported, especially if hemorrhages have occurred. Indeed, Laurençao,[4] who examined one case of snake-bite, finding congestion of the optic papilla and amaurosis lasting for four months, explained the symptoms by a hemorrhage into the visual centres. Galezowski[5] cites Dr. Armaral, of Brazil, as an authority for the statement that blindness after the bite of serpents is common. Careful reports of the symptoms of rattlesnake-bite in our country do not mention amaurosis,[6] and Mr. Arthur Brown, the accomplished superintendent of the Philadelphia Zoological Gardens, an authority on all matters pertaining to the ophidia, informs me that he is unacquainted with blindness as the result of a serpent's bite.

RELATION OF HYSTERIA TO CERTAIN VARIETIES OF TOXIC AMBLYOPIA.

In the section devoted to lead reference was made to *hysterical saturnism*. It has also been pointed out that

[1] Nagel's Jahresbericht, 1880, xi. p. 243.
[2] Klin. Monatsbl. f. Augenheilk., 1882, xx. p. 235.
[3] Those interested may consult Knies, loc. cit., p. 371.
[4] Recueil d'Ophtalmologie, 1875, p. 10.
[5] Des Amblyopies et des Amauroses toxiques, loc. cit.
[6] Consult Barber, Therapeutic Gazette, 1891, 3d s., viii. p. 9.

the visual field of Nieden's case of nitrobenzol-poisoning, in the reversal of the color-lines, exactly simulated the typical hysterical visual chart.

For a long time, particularly in France, certain toxic agents have been regarded as capable of originating hysteria, and in the long list of agents provocative of this state of the nervous system enumerated by G. Goinon,[1] lead, alcohol, mercury, and bisulphide of carbon find a conspicuous place. The subjects of saturnism may suffer from hemianæsthesia, hemiplegia, restriction of the visual field, etc., and may be cured by suggestion, or by remedies of indifferent potency. In like manner, although perhaps with less striking effect, the subjects of chronic alcoholism, and of the other poisons just named, may present any or all of the well-marked hysterical stigmata. The entire literature of this most interesting topic is reviewed by Goinon,[2] who quotes numerous typical instances.

The important deduction from this brief reference to *toxic hysteria* is the necessity of carefully examining cases of toxic amblyopia for signs of this disorder, and particularly of investigating the surface of the body for anæsthesia, which is sometimes found only in spots, or "islands," as they have aptly been called by J. K. Mitchell.

[1] Les Agents provocateurs d l'Hystérie. Thèse, Paris, 1889.

[2] Loc. cit., chapter v., pp. 135–205.

INDEX.

Date Due

Demco 293-5