Concerning a possible etiological factor in tobacco-alcohol amblyopia revealed by an analysis of the urine of cases of this character / by G. E. de Schweinitz and David L. Edsall.

CONCERNING A POSSIBLE ETIOLOGICAL FACTOR IN TOBACCO-ALCOHOL AMBLYOPIA REVEALED BY AN ANALYSIS OF THE URINE OF CASES OF THIS CHARACTER.

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In recent times the pathogenesis of the toxic amblyopias in general and particularly the alterations which are produced in the ganglion cells of the retina and optic nerve by the action of quinine, methyl alcohol, and filix mas have attracted much attention. For a full consideration of the literature of this subject and the various views of experimenters and observers, the reader is referred to the papers of Ward Holden[1], Drualt[2], Nuel[3], Uhthoff[4], Siegrist[5], Uhthoff and Groenouw[6], Nohl[7], Birch-Hirschfeld[8], de Schweinitz[9], and Schieck[10]. It is not, however,

[1] Transactions of the American Ophthalmological Society, 1898.

[2] Recherches sur la Pathogenie de l'amaurose quinine, Paris, 1900, and Archives d'Ophth., January, 1902, p. 19.

[3] The XIII Congrès International de Médecine, Section d'Ophthalmologie, Paris, 1900.

[4] Ibid.

[5] Archiv. f. Augenheilk., March, 1900.

[6] Graefe-Saemisch, Handbuch der Gesamten Augenheilkunde, Zweite Auflage, 32. Lieferung, 1901.

[7] Beiträge zur Augenheilkunde, Heft 48, 1901, p. 51.

[8] Archiv. f. Ophthalmologie, Bd. 52, 1900, p. 358; ibid, 53, 1901-1902, p. 79; ibid, 54, 1902, p. 68; ibid, 55, 1903, p. 380.

[9] Ophthalmic Record, April, 1902.

[10] Archiv. f. Ophth., 54, 1902, p. 458.

the purpose of the present paper to discuss whether the alcohol or the tobacco produces primarily a lesion in the optic nerve fibers or the ganglion cells of the retina; what significance should be ascribed to the vessel changes which have been demonstrated in the opticus, or whether the inflammation of the interstitial connective tissue of the optic nerve should be regarded as an essential cause of the disease, or only as an accidental condition, that is to say, whether the nerve degeneration in the optic apparatus is a primary one, or whether it is secondary to a proliferation of the interstitial connective tissue; but to attempt to throw some light on what the possible poison is which produces one or other or all of these changes, which in their turn interpret themselves by the clinical symptoms of this well-known form of amblyopia.

Writing on this subject in 1900, one of us (Dr. de Schweinitz)[1] said: "It is quite possible that nicotin, or one or more of the many principles freely present in tobacco smoke, liberates some toxic influence in the system which must be held accountable for the disease, which, in other words, depends upon a species of *auto-intoxication.* Horner long ago contended that neither alcohol nor tobacco, as such, was the direct toxic agent in cases of central amblyopia, but that together these drugs produced chronic gastric catarrh, which in its turn established a chronic anemia of the optic nerve, terminating in the pathological changes which are found in this disease. Sachs maintained that even in the pure tobacco cases certain complex chemical combinations occur in the stomach, and there was a resulting transformation of the normal gastric juices into acids of the fatty type, which combined with nicotin into substances which were more injurious than the simple tobacco bases themselves. This observation is important in connection with certain experimental work under the direction of Dr. Casey Wood, not yet published, which indicates that certain stomachic toxins are capable of causing in animals blindness probably of the type now under consideration."

[1] System of Diseases of the Eye, edited by Norris and Oliver, Vol. IV, p. 183.

It therefore seemed to us that one method to approach this study was to submit the urine of patients suffering from tobacco amblyopia to a thorough analysis, according to the methods of modern physiological chemistry, to regulate the patient's diet according to the findings until the normal standard in the excretions of the body was reached, and to note the effect of such treatment upon the amblyopia from which he suffered. Necessarily, such a research in order to be satisfactory would require the examination of a great number of patients and the observation of the effect of treatment over long periods of time, but even though the present communication is based upon an investigation of few patients of this class, and though the observations cover a comparatively short time, they are reported with the hope that they may stimulate still further research along this line, on the one hand, and on the other, because they at least give an indication that Horner's views expressed years ago were not without foundation.

Case 1. A. F., male, aged 46, American by birth, a negative retoucher by occupation, applied for treatment on account of failing vision September 2, 1902. There is nothing of importance in the family history, and in general terms he has been a fairly healthy man except for some gastric disturbance, and he is free from syphilis. He has smoked for many years, but, according to his statement, never immoderately. He has been accustomed to drink beer, and occasionally whisky, but has not been dissipated in the sense in which that term is ordinarily used. In the spring of 1902 he noted blurring of vision which seriously interfered with his occupation and which was attributed to refractive error, the correction of which failed to bring about improvement.

Ocular Examination. — V. of O. D. 6/30, D.= 1.50 was read with difficulty with $+2^{s}$. The pupil reaction was normal, the media were clear, and the optic disc was a vertical oval with distinct pallor on the temporal side, especially in the region of the papillo-macular bundle.

V. of O. S. 6/30, D.= 1.50 read at 25 cm. with +2D with difficulty. The pupil reaction was normal, the media were clear,

the disc was a vertical oval and was distinctly more pallid on the temporal side than elsewhere and more pallid than upon the opposite side. The form fields were normal, there was slight contraction of the red fields, and a faint negative scotoma in the center of each field. The patient was directed to discontinue smoking and drinking and was ordered strychnia. At the end of a month there was absolutely no improvement in vision and also no depreciation, and he was submitted to a thorough *general examination*, as follows:

There was slight dyspnœa, attributable to a moderate grade of emphysema, but otherwise the physical examination by ordinary methods was negative. The blood count showed hæmoglobin 75 per cent., red cells 5,910,000, leucocytes 11,700. The high counts were probably due to a slight cyanosis caused by his emphysema. Stained specimens of the blood were negative. Examination of the gastric contents after the test meal showed no free hydrochloric acid and a considerable amount of tough mucus, indicating the presence of chronic gastritis.

The urine examination was as follows:

	Oct. 6, 1902.	Nov. 8, 1903.
Amount,	2280 cc.	2176 cc.
Indican,	Extremely marked; unchanged by heat.	Negative.
Phenol,	Negative.	"
Acetone,	"	"
Vol. fatty acids,	191.4.	114.8.
NH_3 nitrogen,	0.7404 gm.	0.5115 gm.
Total "	14.946 gm.	13.267 gm.
Preformed sulphates,	2.311 gm.	2.095 gm.
Conjugate sulphates,	0.4249 gm.	0.2897 gm.
Urobilin,	Present upon extracting 15 cc. of urine.	A trace upon extracting 30 cc. of urine.

The patient was placed upon suitable diet, all medication discontinued, and at the end of six weeks, when the last examination was made and when there was practical disappearance of the abnormal conditions revealed by urinalysis, the vision with suitable correction had risen to 6/12 in each eye, and the central scotoma could not be demonstrated.

Case 2. C. H., male, aged 36, American by birth, a merchant by occupation, applied for treatment June 6, 1902, on account of dull vision, which, however, was nearly normal with test types. The optic discs were congested, and there was a small capillary hemorrhage on the edge of the right disc. He was not seen again until the 19th of September of the same year, when there was marked increase in the blurred vision. The family history is unimportant. The patient denies syphilis. He has been an inveterate smoker for years and consumes great quantities of cigarettes. He also drinks freely, especially whisky, and is not above the suspicion of having taken other drugs. In general terms, he has always been dyspeptic, exceedingly nervous, subject to vertigo and violent headaches, and was told that all of his symptoms depended upon uric acid.

Ocular Examination. — V. of each eye 6/12, D.= 0.75 was read with difficulty. The pupil reactions were normal, the media clear, each optic disc was slightly congested, the retinal veins were rather full and the fiber layer of the retinas markedly streaked. A suggestion of pallor in the deeper portions of the optic nerves, especially on the temporal sides, was evident. The visual fields for form and red were normal in extent, and in the center of each there was a small, almost circular, negative scotoma.

General physical examination, which was made by Dr. Alfred Stengel, revealed the following state of affairs: There was slight accentuation of his second heart sound, with some suggestion of beginning arterial change. There was no discoverable kidney change, either in the form of albumin or casts. There was a moderate degree of psoriasis, which was attributed to his general systemic condition. The blood examination was negative.

The urine examination was as follows:

	Oct. 7, 1902.	Oct. 8, 1902.
Amount,	375 cc.	520 cc.
Indican,	Marked; lessened by heat.	Slight.
Phenol,	Negative.	Negative.
Acetone,	"	"

	Oct. 7, 1902.	Oct. 8, 1902.
Vol. fatty acids,	60.	62.4
NH_3 nitrogen,	0.2184 gm.	0.1512 gm.
Total "	4.977 gm.	5.4739 gm.
Pref. sulphates,	1.246 gm.	0.5724 gm.
Conj. "	0.092 gm.	0.0718 gm.
Urobilin,	An intense band on the first washing and first extraction, which persisted to the third dilution.	An intense band on the first extraction, which persisted to the fourth dilution.

Commenting on this examination and others which he made, Dr. Stengel writes as follows: "There is a profound disturbance of food assimilation with reduction of its utilization. There is probably a marked disorder of the liver, which plays an important part in this metabolic inactivity. There is no evidence of any acid intoxication or uric acid diathesis, whatever that term may mean."

The treatment consisted in the regulation of diet and abstinence from tobacco and alcohol. At the end of a week vision had risen in the right eye to 6/6, in the left eye to 6/7.5, and D.= 0.50 could be read at 22 cm. The slight color scotoma was no longer demonstrable. Since this date the patient has not been seen.

Case 3. R. J., male, aged 52, American by birth, a cook by occupation, applied for treatment in the Eye Dispensary of the University Hospital, November 11, 1902, on account of failing vision, which had been particularly marked for ten weeks. In general terms, the patient had been a fairly healthy man; specific taint is denied. On the 8th of July, 1902, his back was injured, although apparently not severely, by a fall, and he maintains that since that time he has had attacks of urticaria which came on in the evening and lasted until early morning. He has smoked excessively since he was fifteen, as much as two ounces *per diem* in a pipe, and has drunk whisky to excess.

Ocular Examination. — V. of O. D. 6/150, V. of O. S. 6/60. Ophthalmoscopically, the media were clear, the optic discs vertical ovals, with marked pallor of their temporal sides; no

changes in the retinal circulation or in the general expanse of the eyegrounds were present. The visual fields for form and red were normal, and in the center of each there was a typical oval scotoma for colors.

The urine examination was as follows:

	Nov. 17, 1902.
Amount,	1675 cc.
Indican,	Moderate.
Phenol,	Negative.
Acetone,	"
Vol. fatty acids,	200.7
NH_3 nitrogen,	0.2998 gm.
Total "	10.5867 gm. $\frac{a}{3}$
Pref. sulphates,	1.6757 gm.
Conj. "	0.2892 gm.
Urobilin,	Slight band on first extraction.

The patient was exceedingly irregular in attendance; indeed, he returned but once after the urinary examination was made. At that time, namely, on the 15th of November, 1902, vision was slightly better; O. D. 6/45, O. S. 6/22; the scotomas were smaller but present. The patient had not smoked; it is doubtful whether he stopped drinking. He had taken 1/30 of a grain of strychnia three times a day. The effects of diet in this case could not be tried.

Case 4. O. M., aged 51, American by birth, a night watchman by occupation, applied for treatment in the Eye Dispensary of the University Hospital November 17, 1902, for failing vision which he had tried to remedy unavailingly by purchasing various kinds of glasses. In general terms, the family and personal history are negative; specific infection is denied. There was a large scar on the cheek, extending from the margin of the orbit to below the malar bone, which had been produced by the kick of a horse many years ago, and which had caused an ectropion of the right lower lid. The patient had been an incessant smoker for many years. He drank some beer, but, as he expressed it, "spirits mainly."

Ocular Examination.—V. of O. D. 4/60, V. of O. S. 6/30, unimproved by glasses. The media were clear and the pupil

reactions normal. The ophthalmoscope revealed vertically oval optic discs, with marked pallor of their temporal halves. The peripheral fields for white and red were normal, and in the center of each field there was a large typically oval scotoma.

The urine examination was as follows:

	Nov. 24, 1902.	Nov. 28, 1902.
Amount,	720 cc.	1120 cc.
Indican,	Intense; less marked after boiling.	Slight.
Phenol,	Marked.	Negative.
Acetone,	Negative.	"
Vol. fatty acids,	59.	44.9
NH_3 nitrogen,	0.4435 gm.	0.5644 gm.
Total "	6.773 gm.	11.101 gm.
Pref. sulphates,	1.773 gm.	1.401 gm.
Conj. sulphates,	0.2432 gm.	0.2919 gm.
Urobilin,	Slight band on first extraction.	Negative.

NOTE.— Examinations of this man's urine were made every day that he was in the hospital, for another purpose. The volatile fatty acids ran, for the first three days, between 60 and 95. After this they decreased to about 40. There was a constant decrease in the intensity of the reactions for phenol and indican. The total conjugate sulphates did not vary greatly.

The patient was placed upon the proper diet. At the last examination in the Eye Dispensary, namely on December 11, 1902, the vision of the right eye had risen to 6/30 and of the left eye to 6/22; central color perception improved, but not restored. Since this date he has not reported.

Case 5. T. T., aged 55, American by birth, a laborer, applied for treatment in the Eye Dispensary of the University Hospital January 15, 1903, for relief from failing eyesight, which had been particularly marked in the last week. He denied recent illness of any kind and there is no history of specific taint. He has been an incessant smoker for years. He denied the abuse of intoxicating drinks, but not their use.

Ocular Examination.—V. of O. D. 6/45, V. of O. S. 6/30, unimproved by glasses. The pupillary reactions were normal, the media clear, the optic disc of each eye slightly blurred and discolored, especially upon the outer side. The veins were dilated, irregular in caliber, and pressed upon by arteries which

showed the stiffening of beginning endarterial changes. In the right eye below the temporal vein there was a small linear hemorrhage. The conditions of the left eye were similar but no hemorrhages were discovered. The visual fields for form and red were practically normal, and occupied in their centers by negative scotomas, the one on the right side being the larger.

The urine examination was as follows:

	January 22, 1903.
Amount,	900 cc.
Indican,	Extremely intense.
Phenol,	Negative.
Acetone,	"
Vol. fatty acids,	54.
NH_3 nitrogen,	0.5036 gm.
Total "	10.1462 gm.
Pref. sulphates,	Not estimated.
Conj. "	0.3254 gm.
Urobilin,	A distinct band on direct examination of urine.

The patient was advised to stop tobacco and alcohol and was given a regulated diet. At the last examination, namely on January 22, vision in the right eye was 6/45 and in the left eye 6/22; therefore only a very slight improvement.

Case 6. H. F., aged 41, American by birth, a railroad employee by occupation, applied to the Eye Dispensary of the University Hospital on November 15, 1902, on account of failing vision, especially marked for the last week. There is nothing important in the patient's family history. Seventeen years ago he had malaria, but since then no other acute illness. He had hemorrhoids, which were successfully operated upon three months before he applied for examination. He had gonorrhoea many years ago, but there is no syphilitic history. He has used tobacco to excess and also whisky, drinking sometimes as much as a quart a day.

Ocular Examination.—V. of each eye 6/150, unimproved by glasses. Pupil reactions present but light reactions slightly sluggish. Ophthalmoscopically there was evident a low-grade interstitial neuritis with perivasculitis on each side; the veins

were full, uneven, and tortuous, and the arteries streaked with white lines. The visual fields were moderately contracted and there was entire lack of all color perception, so that the presence of scotomas as such could not be demonstrated.

General physical examination failed to reveal any well-marked disease except in so far as the liver was concerned, which was distinctly enlarged. There was also a history of liver trouble for the last three or four years. The blood examination was as follows: Hæmoglobin, 83 per cent.; red blood corpuscles, 5,540,000, white blood corpuscles, 9,600.

The urine examination was as follows:

Amount,	900 cc.
Indican,	Extremely intense.
Phenol,	Most intense ever noted.
Acetone,	Negative.
Vol. fatty acids,	37.2
NH_3 nitrogen,	0.434 gm.
Total "	9.763 gm.
Pref. sulphates,	Record lost.
Conj. "	" "
Urobilin,	A marked band on direct examination of the urine.

NOTE.— Repeated examinations were made during his stay in the hospital, and there was a constant decrease in the intensity of the urobilinuria and of the reactions for indican and phenol. Urobilin nearly disappeared by January 10th, and was quite gone by the 15th. The phenol and indican reactions were still positive when the man left, but less markedly so. The volatile fatty acids varied little, and were always low.

The patient was admitted to the University Hospital on December 18, and remained there until the 4th of February. The treatment consisted in suitable regulation of the diet, and, as required, saline purges and calomel. Visual improvement was manifest at the end of two weeks. By the 10th of January vision had risen to 1/2 of normal, and on the 25th of January, or a few days prior to his discharge from the hospital, it was 6/5 in each eye. The visual fields were practically normal for form and color; no scotomas.

Case 7. T. J. W., aged 54, American by birth, a bookkeeper by occupation, reported for treatment in the Eye Dispensary of the University Hospital July 9, 1901, on account of failing vision,

which was marked for three weeks. His general clinical and family history is unimportant. Specific taint is denied, but the patient had used tobacco and alcohol to very great excess for years.

Ocular Examination. — V. of O. D. 3/150, V. of O. S. 3/150. Media clear, pupils normal, and on each side the optic discs round, the nasal edges hazy, the temporal halves gray, especially at the papillo-macular bundles. There was almost entire lack of color perception, the note on the book being that it was impossible to obtain fields for colors at all.

This patient continued to attend the Dispensary of the University Hospital, and took from time to time bichloride of mercury, iodide of potassium and strychnia, and stopped at once his tobacco and alcohol. There was a slow improvement, and when he first came under our observation, that is, on December 6, 1902, the field of vision of each eye was slightly contracted for form and red, and there was a small central scotoma for all colors. The ophthalmoscope revealed marked pallor of the temporal half of each optic disc, indeed, there was distinct atrophy of the papillo-macular bundle. Otherwise there were no changes. The visual acuity was O. D. 6/30, O. S. 6/15. The patient had not used tobacco or alcohol in any form for seventeen months.

The urine examination was as follows:

	December 10, 1902.
Amount,	940 cc.
Indican,	Moderate.
Phenol,	Marked.
Acetone,	Negative.
Vol. fatty acids,	152.2.
NH_3 nitrogen,	0.4421 gm.
Total "	9.6594 gm.
Pref. sulphates,	2.2458 gm.
Conj. "	0.1748 gm.
Urobilin,	A band on extracting 30 cc. of urine.

NOTE.— A second examination, made December 24, 1902, showed no indican; no phenol; conj. sulphates, 0.1253; volatile fatty acids, 60.4; urobilin, absent.

A third examination, made February 27, 1903, showed normal conditions.

All medication was stopped, the patient placed upon strict diet, and on the 14th of February, 1903, or two months after treatment, the vision of the right eye was 6/12 and that of the left eye 6/15, a slight improvement in the right eye and stationary vision in the left. The patient, however, was quite sure that his vision was better, that is to say, as he walked the streets and in his ordinary occupation, and this improvement in vision corresponded with the restoration of the normal conditions in the urinalysis.

The methods adopted in order to determine whether recognizable signs of any intoxication were present in the first case examined (Case I) were as follows: The blood corpuscles were counted, the hemoglobin was estimated, and stained blood-smears were examined. The blood-pressure was determined with Stanton's modification of the Riva-Rocci instrument. The stomach was inflated and the stomach contents were examined. The feces were examined, and the urine was examined for albumin and sugar. The degree of intestinal composition was investigated by determining quantitatively the preformed sulphates and the conjugate sulphates (Baumann-Salkowski method), the volatile fatty acids (Blumenthal's method), and by determining the intensity of the qualitative reaction for indican (Obermayer's reagent) and for phenol (bromine test of the distillate). Urobilinuria was also looked for, and its intensity was approximately determined by Riva's method. Tests were made for acetone in the distillate and the ammonia nitrogen and the total nitrogen of the urine determined, in order to see whether there was any evidence of acid intoxication. The same methods were subsequently used, as far as possible, in examining all the other cases.[1]

The examinations of the blood and of the blood pressure were wholly negative and need no further comment. The examination of the feces also yielded nothing of consequence. The stomach contents could be examined in only five cases.[2]

[1] All of the chemical examinations and general medical examinations were made by Dr. Edsall, except the general examination of case 2, which was made by Dr. Stengel.

[2] Case 2 was not under Dr. Edsall's personal observation, and case 3 did not return for examination.

All these five cases, however, showed marked evidence of chronic gastritis. Cases 1, 4, 5, and 6 all showed an acidity, with much mucus and very poor digestion of the test meal. Case 7 showed similar conditions, and differed only in that there was a slight acidity (15) and a faint reaction for free HCl. There was no noteworthy disturbance of motility in any of these patients. None had glycosuria. Albumin was absent in all instances, except that Case 6 showed a trace for a time. This disappeared, however, while he was under observation. There was also no evidence of acid intoxication in any instance, so far as exhibited in the results for acetone and ammonia. The determinations of the intestinal decomposition-products and of the urobilin showed much more marked abnormalities. The results are given in the urinalysis appended to each case history, acetone, ammonia, and total nitrogen being included in the tables.

These conditions as compared with the normal, are, in brief, as follows:

In Case 1 there were at first very high figures for conjugate sulphates, but at the second examination nearly normal conditions; intense indicanuria at first, which disappeared; slight urobilinuria at first, which disappeared; the figures for the volatile fatty acids, at first very high, approached the normal at the second examination.

In Case 2 there was an intense urobilinuria. The results for the sulphates and volatile fatty acids were negative, but the figures for the quantitative determinations are unreliable, as they are so low that it is probable that the urine was not carefully saved.

In Case 3 there was moderate urobilinuria and the volatile fatty acids were extremely high.

In Case 4 there was a moderate urobilinuria, a marked indicanuria, and a decided reaction for phenol, all of which disappeared quickly under treatment. The volatile fatty acids tended towards the high limit of normal figures. The conjugate sulphates were constantly somewhat high.

Case 5 showed an intense indicanuria, a moderate increase of the conjugate sulphates, and a marked urobilinuria. He gave no opportunity for a second examination.

Case 6 was not specially examined until he had been in the ward a week, when his vision had somewhat improved. At first he showed intense urobilinuria and indicanuria, and a most intense reaction for phenol. The records for the sulphates have been lost. Under treatment, there was a gradual decrease in the intensity of all these reactions, and some time before he left the hospital the urobilinuria had disappeared entirely. The reactions for indican and phenol, though still present, were much less marked.

Case 7 showed at first a marked reaction for phenol and notably high values for volatile fatty acids, with a slight urobilinuria. Subsequently these abnormalities entirely disappeared.

In three of the cases examined (Cases 1, 3, and 7) the volatile fatty acids were very high. In Case 2 they were relatively high, and if the urine had been carefully saved they would probably have been absolutely high. This made it seem possible that the absorption of excessive amounts of volatile fatty acids had had something to do with the amblyopia, — a suspicion that perhaps might be increased by Kraus's report of retro-bulbar optic neuritis in his two cases of cryptogenic acid intoxication. It is possible that there is something in this view, as the figures in Case 4 are also somewhat high, and the urine of Case 6 was examined only when he had already improved, and it is possible that he would have shown an increase earlier. Case 5, however, definitely showed a normal condition of the volatile fatty acids. The actual results, therefore, are, at best, doubtful as to this point. An experimental study of the effect of the prolonged administration of acids, particularly of some of the fatty acids, might be of value.

The results in general show that there was in all cases (except, perhaps, in Case 2, in which the results are unreliable) an excessive excretion of enterogenous decomposition-products in the urine; and in all there was a more or less marked urobili-

nuria. In all the patients repeatedly examined these abnormalities nearly or quite disappeared under treatment, coincidently with improvement in the eye conditions, as follows:

In Case 1 there was absolutely no improvement in vision under the ordinary strychnia and potassium treatment. At the expiration of six weeks of special dietetic regimen, or when the results of urinalysis approached the normal standard, vision had risen to 6/12, or double that which it was at the first examination, and the scotomas had disappeared.

In Case 2, vision, which had fallen to 1/2 of normal, regained the normal standard at the end of one week of treatment, the patient being confined to a room in the hospital where he was under strict surveillance, and when there had been improvement in the abnormalities revealed by urine analysis. The doubt in regard to this case has been recorded.

Case 3 showed slight improvement in vision at the end of five days, which, however, cannot be attributed to any influence of diet and alteration in the habits, inasmuch as the patient had been exceedingly irregular in attendance and probably did not stop drinking, although he did stop smoking for at least a week.

Case 4 exhibited a moderate improvement in the vision of the right eye and a slight improvement in the vision of the left at the expiration of two weeks under the influence of dietetic management. Since this date he has not reported.

Case 5, who was under somewhat irregular observation for only seven days, showed a very slight improvement in vision.

Case 6, the most noteworthy of the series, regained, with the restoration of a normal urinary analysis, complete visual acuity. It is moreover noteworthy, that although there had been a slight improvement in vision before the urine analyses were made, that is, after one month of dispensary treatment and one week of hospital treatment, during which time the patient probably entirely abstained from alcohol and tobacco, the marked restoration of central acuity of sight exactly corresponds with the restoration to the normal or nearly normal standard of urinary analysis.

Case 7, who had not used tobacco or alcohol for seventeen months before he was submitted to the analyses which have been described, is noteworthy because, although the test-types failed to reveal much improvement in sight, that is, only from 6/15 to 6/12, the patient was so certain that his general vision had improved that he was willing to continue the strict diet on which he had been placed. That he could not expect much improvement was evident from the ophthalmoscopic change of permanent atrophy in the papillo-macular bundle.

In this connection it is proper to refer to a patient with moderate, well nigh stationary optic nerve atrophy who has been coming to the dispensary for years, his original examinations having been made ten years prior to the present time. The etiology of the optic nerve disease could not positively be determined, but apparently it was not due to the abuse of alcohol and tobacco, as the man has been for many years a total abstainer. He therefore was used as a control and showed entirely negative conditions. There was very slight reaction for indican and none for phenol. The volatile fatty acids were 50.4, the NH_3 nitrogen 0.1412 gm. The sulphates were not estimated.

In these cases there were evidences of a marked disturbance of digestion or of metabolism, or of both; furthermore, this disturbance may persist for a long time after the use of alcohol or tobacco has been stopped, as in Case 7, and the study of Case 1 apparently indicates that treatment of this secondary nutritive disturbance will cause improvement in a persistent amblyopia. These facts, we think, give just ground for the belief that toxic substances produced in the digestive tract, or in the course of metabolic processes, have, at least, a certain part in the production of the amblyopia in most of these cases; and that at times they are probably the direct cause of the continuance of the symptoms when the latter do not disappear after alcohol and tobacco have been stopped. We do not think that more should be claimed from these results.

This view is entirely in consonance with the results of investigations concerning the manner in which other toxic effects of

alcoholism are produced, and it also accords with our knowledge of the effects of some other chronic poisonings. There are, for instance, excellent reasons for the belief that many of the cerebral and other nervous symptoms in lead poisoning are not due directly to lead itself, but to nutritive disturbances set in motion by the lead. In the cases herein described it is quite evident that there was a marked disturbance of the alimentary tract; the disturbance was not, however, confined to that tract. Cases 4, 5, and 6 all showed easily recognizable enlargement and some tenderness of the liver; and all had marked urobilinuria. All the others examined likewise had some urobilinuria. In the three cases just mentioned, therefore, and perhaps in others, there was disorder of the liver as well as alimentary tract disturbance.