OPTIC NEURITIS CAUSED BY ARSENICALS* TREATMENT WITH B.A.L.

BY

C. OEHNINGER, R. RODRIGUEZ BARRIOS, AND C. A. GOMEZ HAEDO

*From the Medical Clinic "A" of the Faculty of Medicine (Professor J. C. Garcia Otero),
Montevideo, Uruguay*

THE use of pentavalent arsenicals in the treatment of syphilis in its different phases has recently diminished, and in consequence accidents due to arsenic toxicity have become fewer.

Two cases with optic neuritis produced by "Stovarsol" were greatly improved by the administration of B.A.L.†, which offers a useful remedy in accidents that may still occur when the syphilologist considers that arsenical treatment must be applied.

Case Reports

Case 1, a man aged 24 had had a genital lesion 5 years previously. When examined he showed a positive Kahn test with a negative Wassermann reaction and a weak positive globulin reaction in the spinal fluid with 0.43 g. albumin per litre. A series of "Stovarsol" injections was started (1 g. daily). These were suspended on the 18th day because the patient presented with subjective visual disorders (cloudy vision) and in this condition was admitted to hospital. After the first injections he had had transitory fever and exanthema. A week later his general condition was good, and the skin and mucosae were well coloured. He was afebrile, with normal pulse and blood pressure. Neurological signs in the trunk and extremities were normal.

Optic Nerve.—The visual fields on admission (4 July, 1952) are shown in Fig. 1. Colour

FIG. 1.—Case 1, visual fields on admission, July 4, 1952.

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† British Anti-Lewisite, provided by Boots Pure Drug Co., Ltd., Nottingham.

vision was normal. Fundus examination showed a slight pallor of both papillae. Visual acuity in the right eye was 0.5, and in the left 0.7. The ocular movements were normal.

Cerebrospinal Fluid.—Three examinations were made (Table).

TABLE
CEREBROSPINAL FLUID EXAMINATIONS

Tests	On admission	After One Week	After One Month
Albumin (g. %)	0.95	1.50	0.75
R. of Pandy	++	++	+
Cytology	48	12	5
Glucose	0.5	—	—
Chloride	6.5	—	—
Wassermann	Negative	Negative	Negative
Colloidal Gold	Negative	Negative	Negative

Blood Tests.—Wassermann negative and urea normal.

Red cells 4,090,000—Hb 78 per cent.—globulin 0.97; white cells 8,800 (granulocytes neutrophilic 77 per cent., eosinophilic 3 per cent., basophilic 0 per cent.; monocytes 3 per cent.; lymphocytes 17 per cent.).

Progress.—Treatment with antihistaminic drugs and vitamins was given, and the cerebrospinal fluid improved in successive examinations, but the visual fields remained unchanged and the patient complained of orbital headaches.

As the ocular symptomatology did not improve, B.A.L. was administered at the rate of 300 mg. for 4 days and 200 mg. for 3 days (in all eighteen injections during one week). Immediate subjective and objective improvement was observed. Fig. 2 shows the increase in the visual field which was noted on August 22, 1952, at the expense of an eccentric extension of the peripheral temporal "isoptre". Fig. 3 (overleaf) shows the visual field a year later, when only a small improvement is seen in relation to Fig. 2; at this date apart from the ocular damage the patient was normal.

FIG. 2.—Case 1, visual fields on August 22, 1952.

FIG. 3.—Case 1, visual fields on July 29, 1953.

Case 2, a man aged 43 years, had relapsing syphilis with persistent cerebrospinal fluid changes in spite of intense treatment with penicillin and bismuth; the syphilologist decided to administer "Stovarsol" at the rate of 1 g. daily; and twenty injections were given. On the 14th day the patient complained of cloudy vision. He had a past history of eye disease; an attack of chorioretinitis juxtapapillaris which had affected his vision 10 years before had been attributed to focal infection of the throat.

Clinical Examination.—His general condition and nervous system were normal.

Optic Nerve.—Fig. 4 (20 April, 1953) shows a contraction of the visual fields similar to that in Case 1. The visual acuity was normal in both eyes.

FIG. 4.—Case 2, visual fields on admission, April 20, 1953.

Fundus Examination.—The right eye showed a deeply excavated disc with incomplete atrophy. The left eye showed a gross scar of an old superior nasal chorioretinitis, and an excavated and atrophic disc principally in the nasal sector.

Blood and Cerebrospinal Fluid.—Normal.

Progress.—Six weeks after the Stovarsol series was finished, treatment with B.A.L. was begun with one daily injection of 100 mg. for 20 days. As in the first case an evident subjective and objective improvement was obtained, and enlargement of the visual fields, at the expense of the peripheral temporal "isoptre", was observed (Figs 5 and 6).

FIG. 5.—Case 2, visual fields on April 24, 1953.

FIG. 6.—Case 2, visual fields on July 6, 1953.

Discussion

Both patients presented an ocular syndrome:

- (1) Subjective manifestations described by the patient (cloudy vision).
- (2) Characteristic field changes, showing extreme contraction to a narrow oval shape with depression of the superior and inferior nasal sectors and a wedge in the temporal sector.
- (3) Preservation of visual acuity.
- (4) Ophthalmoscopic alterations:

Case 1 showed pallor of both papillae.

Case 2 showed excavated and atrophic papillae with a scar from old chorio-retinitis.

This clear disagreement between the marked narrowing of the visual fields and the preservation of a reasonable degree of visual acuity (indicating normality of the macular region), with absence of optic atrophy at least at the beginning of the process, is characteristic of the optic neuritis produced by pentavalent arsenicals.

The peripheral field, except the papillo-macular region, is altered simultaneously and symmetrically in both eyes. This feature of the ocular syndrome excludes the possibility of optic atrophy of syphilitic origin in these two cases, since syphilitic involvement of the optic tract entails diminished visual acuity as well as narrowing of the visual fields and optic atrophy.

Other reasons in favour of the hypothesis of arsenical poisoning in our patients are:

(a) The rapid development of the ocular manifestations after several injections of Stovarsol; in both patients they appeared towards the end of the series of injections.

(b) The close relation of the beginning of the ocular symptoms to arsenical treatment. The changes began with this treatment and remained stable when it was discontinued until B.A.L. was administered.

(c) The possibility of a Herxheimer reaction is excluded as that should appear after the initial arsenical injections. Case 1 presented early symptoms and cerebrospinal fluid alterations that might have been attributed to a Herxheimer reaction, but these symptoms gradually receded, and the toxic reactions due to arsenical treatment came later.

After treatment both patients were enabled to carry on their usual occupations, whereas before the advent of B.A.L. arsenical optic neuropathy offered a poor prognosis (Walsh, 1947; Merritt and others, 1946; Dattner and others, 1944).

Friedenberg (1947) published the first observation of visual recovery after treatment with B.A.L. in a patient with optic neuritis provoked by Tryparsamide, and we have found no other reference to this form of therapy in the literature.

Sloan and Woods (1936) distinguish two clinical evolutive forms in arsenical optic neuritis:

(a) Subjective symptoms corresponding to the early stage which may be reversible (cloudy vision or shimmering).

(b) Objective symptoms, which may be acute (involving blindness) or chronic.

The second and more common form was presented by our two patients with characteristic field changes.

The mechanism by which the optic nerve is attacked by the pentavalent arsenicals is unknown. Lees (1932) thought it to be a form of Herxheimer reaction, Lillie (1924), arguing from an autopsied case, thought that it was due to a process of syphilitic perineuritis. Walsh (1947) thought it could not be a form of retrobulbar neuritis because of the characteristic field changes, and suggested that the lesion might be located in the peripheral fibres of the geniculate bodies; Merritt and others (1946) localized the lesion in the ganglionic cells of the retina rather than in the optic nerve.

It seems that previous damage to the optic nerve disposes it to attack by arsenicals. Sézary and Font-Réaulx (1932), Sutherland-Campbell (1940), Merritt and others (1946), and Walsh (1947) say that arsenotherapy is contraindicated whenever there is a previous lesion of the optic nerve. Di Bello and Rodriguez Barrios (1945) extend this contraindication to lesions of the "infundibulo tuberiana" region; Lillie (1924), on the other hand, had suggested that a previous lesion of the optic nerve might be improved by pentavalent arsenotherapy since the latter was beneficial in neurosyphilis.

It should be noted that our two patients did not improve until about 2 months after receiving B.A.L. which seems to indicate the persistence of the metal at the point affected. We cannot be sure whether the beneficial effect of B.A.L. is due to its known mechanism of forming atoxic bodies with the metal, which are then eliminated by the organism, or to its action on cellular respiration and on the non-specific enzymatic mechanism, as recently observed in non-metallic neuritis by Furmanski (1946), Nielsen (1950), and Kane (1952).

Summary

In two patients with optic neuritis caused by "Stovarsol" used in anti-syphilitic treatment, marked improvement was obtained with B.A.L. The characteristic ocular picture of arsenical neuritis, the predisposing causes of the lesion, and the manner of action of B.A.L. are discussed.

The favourable results in these two patients show that we now possess a therapeutic element of great efficacy, but a periodical check by an eye specialist during arsenotherapy should not be omitted.

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