

## RESULTS OF PENICILLIN THERAPY IN SYPHILITIC PRIMARY OPTIC ATROPHY\*

BY

PAWEŁ SEGĄŁ, B. JANISZEWSKA-GELDNER, AND  
J. LEONOWICZ-MICHNIEWSKA

*From the Ophthalmological Clinic W.A.M., Łódź, Poland*

Syphilitic primary optic atrophy is one of the most serious eye diseases. Untreated, it usually leads to blindness; bilateral blindness occurred within one year in 35 per cent., within 3 years in 81 per cent., and within 6 years in 94 per cent. of eighty-one untreated patients (Klauder and Gross, 1954). Worster-Drought (1947) reported that blindness supervened in 100 per cent. of patients within 5 years.

Treatment of syphilitic primary optic atrophy has been highly unrewarding in the past. Preparations of arsenic and bismuth and fever therapy gave no satisfactory results. Blatt (1949) treated 119 patients with malaria and found that they all became blind within 2 years, even sooner than untreated patients.

All authors agree that penicillin therapy of optic atrophy is not detrimental, except that Moore (1947) reported one case of sudden deterioration after commencement of treatment which resulted in bilateral blindness within 7 weeks; this was considered to be due to a Herxheimer reaction.

However, the reported results of penicillin therapy differ and some authors are sceptical of its value; Moore (1947) felt that penicillin therapy had contributed no advantages, and Zlámal (1955), Suster (1955), and Tron (1955) observed further progress of the disease in most of their patients. Other authors, however, have reported very good results; Stokes, Beerman, and Ingraham (1944) noted that the disease was arrested in six patients, and improved in one; from the results in thirty-one patients, Thomas (1949) considered that penicillin was valuable and at any rate more effective than fever therapy; Dattner, Thomas, and de Mello (1951) thought that penicillin alone was better than penicillin combined with malaria.

Some authors have noted considerable individual differences between the responses of different patients. Klauder and Gross (1954) obtained better

results in 104 patients treated with penicillin than in a group treated with arsenic and bismuth, and emphasized that in some cases one course prevented further changes, whereas in others repeated courses failed to arrest deterioration of sight. Benton and Harris (1952) found that deterioration of sight was arrested in thirteen of twenty-three treated cases, and Kenney and Curtis (1953) noted this in twenty-five of thirty-seven cases.

### Present Study

**Material.**—Thirty-seven patients with primary optic atrophy were under direct ophthalmological supervision in 1950 to 1957. They all had tabes dorsalis or taboparesis confirmed by serological fluid tests, and were all observed for from 3 to 6 years. The optic fundus, visual acuity, and visual fields for white and red were examined in all of them. Thirty-two patients reported when the disease was in its active stage, complaining of progressive deterioration of sight; the other five were at the stationary phase, and it was several years since the vision had deteriorated. A further twenty-one patients with syphilitic primary optic atrophy have been excluded from the present study because of inadequate follow-up. Altogether, therefore, primary optic atrophy was diagnosed in fifty-eight of 584 patients with tabes dorsalis or taboparesis (9.9 per cent.).

The age and sex of the patients is shown in Table I.

TABLE I  
AGE AND SEX OF PATIENTS

Age	40 or less	41-50	51-59	Total
Men	5	9	12	26
Women	4	4	3	11
Total	9	13	15	37

\* Received for publication March 1, 1960.

**Treatment.**—All the patients received from 6 to 32 million units of penicillin as basic treatment in daily doses of 300,000 to 600,000 units. Treatment consisted of one to four courses of 6 to 12 million units each, at intervals of a few months.

In thirteen cases, fever therapy was given in addition to penicillin (eleven patients received typhoid vaccine intravenously, and two were treated with malaria). In twelve patients, the treatment was supplemented by tissue therapy as advocated by Filatov. Neither fever nor tissue therapy seemed to affect the course of the disease and these patients are not grouped separately. This supplementary therapy was usually given during the second or third course of penicillin in severe cases in which visual acuity deteriorated in spite of penicillin. In particularly serious cases, ACTH, vitamin B<sub>12</sub>, nitrogen mustard, and Bogomolets serum, were also given in addition, but did not arrest the progress of the disease.

In addition to the basic treatment, all patients received large doses of vitamin B<sub>1</sub>, B<sub>2</sub>, or B complex, vitamins C and PP, and small doses of strychnine.

**Stage of Disease.**—In sixteen of 32 patients in whom treatment was started when the disease was acute and the vision was steadily deteriorating, the disease process and the impairment of the visual acuity and visual fields were arrested during the entire period of observation. (This group is referred to below as "stationary".)

In the sixteen other patients, however, the visual acuity continued to deteriorate in spite of treatment. This group (referred to below as "deteriorating") includes patients in whom the visual fields became progressively narrower although the visual acuity was unchanged.

In the other five patients (classed as "inactive") there was neither improvement nor deterioration. This group included some patients in whom the visual acuity was already reduced to perception of light or hand movements before treatment was started.

**Interval between Infection and Visual Symptoms.**—No correlation was found between the results of treatment and the interval which had elapsed between the infection and the first appearance of symptoms of deteriorating vision (Table II).

Fourteen patients could not say how much time had elapsed between infection and the first symptoms of optic atrophy because the infection had been asymptomatic or the symptoms had not been noticed.

TABLE II  
INTERVAL BETWEEN INFECTION AND FIRST SYMPTOMS OF OPTIC ATROPHY

Time Since Syphilitic Infection (years) .. ..		5-10	11-20	20-35	Not known	Total
Stage of Disease before Treatment	Stationary ..	3	3	5	5	16
	Deteriorating	4	1	5	6	16
	Inactive ..	2	—	—	3	5
Total ..		9	4	10	14	37

**Previous Treatment.**—Table III shows the numbers of patients who had previously received courses of treatment with arsenicals and bismuth.

TABLE III  
PREVIOUS TREATMENT WITH ARSENICALS AND BISMUTH

Previous Courses of Treatment ..		0	1-2	3-8	Total
Stage of Disease before Treatment	Stationary ..	5	6	5	16
	Deteriorating	10	5	1	16
	Inactive ..	4	1	—	5
Total ..		19	12	6	37

Nineteen patients had had no treatment at all; fourteen were unaware that they were infected, and the others had ignored the infection and had either had no treatment at all or had neglected it very soon. Treatment in the early stages was considered adequate in only six cases, and in five of these the disease was successfully arrested.

### Results

The visual acuity before penicillin treatment and after several years of observation is given for the thirty-two eyes of the sixteen patients in the "stationary" group in Table IV. It remained unchanged in fourteen patients, and two showed improvement: one from 0.2 to 0.6 and the other from 0.015 to 0.04.

TABLE IV  
VISUAL ACUITY IN "STATIONARY" GROUP (32 EYES)

Visual Acuity .. ..		1.0-0.5	0.35-0.1	0.08-0.001	$\frac{1}{\infty}$ -0	Total
Time of Assessment	Initial ..	19	2	6	5	32
	Final ..	20	1	6	5	32

In nine of the sixteen patients the visual acuity in both eyes was 1.0 to 0.5, in three the better eye saw 1.0 to 0.3 and the worse eye 0.08 to 0, and the other four were technically blind (better eye less than 0.1).

In the thirty-two eyes of the sixteen cases in the "deteriorating" group, the visual acuity deteriorated in twenty-two, and in the ten remaining eyes which showed no deterioration, the visual acuity before treatment was only perception of light; furthermore, in two eyes, although the visual acuity remained unchanged, the visual fields were reduced. Thus only three out of thirty-two eyes in this group suffered no change in vision. In one of the sixteen patients both eyes were better than 0.5; in seven, the better eye was 1.0 to 0.15 and the worse eye 0.08 to 0; eight patients were technically "blind" (Table V).

TABLE V  
VISUAL ACUITY IN "DETERIORATING" GROUP  
(32 EYES)

Visual Acuity		1.0-0.5	0.35-0.1	0.08-0.001	1 ~0	Total
Time of Assessment	Initial Final	5 2	7 3	13 10	7 17	32 32

At the end of the observation period, not one patient had binocular visual acuity better than 0.5, in two the better eye was above 0.15, nine were technically blind, and five were completely blind.

The results of treatment are related to the stage of disease before starting penicillin therapy as based on the visual acuity of the worse eye (Table VI).

TABLE VI  
VISUAL ACUITY IN WORSE EYE RELATED TO  
STAGE OF DISEASE

Visual Acuity		1.0-0.5	0.35-0.1	0.08-0.001	1 ~0
Stage of Disease before Treatment	Stationary Deteriorating	7 3	3 1	4 4	2 8

A comparison of Tables IV, V, and VI clearly shows that the best results were obtained when penicillin therapy was started in the early stages of the disease, when the visual acuity was only slightly impaired.

**Progress of Disease**

The course of the optic atrophy differed in individual patients. In some cases, the process was rapid, lasting for only 2 to 4 months, while in others it went on slowly for many years.

The patients are classified in Table VII according to the rate of visual deterioration and the final result as judged from the visual acuity of the worse eye.

TABLE VII  
RATE OF DETERIORATION RELATED TO SEVERITY  
OF VISUAL SYMPTOMS

Visual Acuity in the Worse Eye	Rate of Deterioration before Treatment			
	0-6 mths	7-12 mths	Several Years	Not Known
0-0.01	12	4	3	2
0.02-0.1	—	1	3	—
Above 0.1	—	1	10	1

In twelve patients the disease progressed rapidly in spite of treatment, and caused considerable visual impairment. In ten patients the disease ran a slow course and treatment with penicillin successfully arrested further deterioration.

**Discussion**

It appears that the duration of infection before the onset of symptoms of optic atrophy (Table II) has little or no effect on the course of the disease and the results of treatment. However, a large proportion of our patients (fourteen out of thirty-seven) did not know that they were infected, and could not say what the interval was. This emphasizes the importance of routine serological examinations which may enable late syphilis to be detected in the asymptomatic period. Nineteen of the thirty-seven patients had had no treatment at all in the early stage, and only six had a more or less adequate treatment with arsenicals and bismuth (Table III).

Treatment of a disease which runs so slow and variable a course as syphilitic primary atrophy is difficult to evaluate, and the follow-up period must be very long, at least 3 years' observation being required to assess its efficacy. In the present study this minimum applied only to patients in whom considerable deterioration or blindness had occurred in spite of treatment, so that further observation could contribute little. Most of the patients in whom the progress of the disease was arrested (stationary group) were observed for from 4 to 6 years.

It must also be remembered that, in a disease involving atrophy of the optic nerve, treatment can hardly be expected to cause any fundamental improvement. The result may be considered good if the progress of the disease is controlled, and even then the visual acuity may continue to deteriorate for some time after starting the treatment, although the disease process has actually been arrested.

When the reported results are considered with the above points in mind, penicillin therapy undoubtedly appears to be valuable. In half of the thirty-two patients treated when the disease was in

the active stage, deterioration of the visual acuity and visual fields was arrested. The results largely depended on the stage at which treatment was started. The better the visual acuity at the beginning, that is, the sooner penicillin therapy was started after the infection was recognized the better were the results.

Syphilitic primary optic atrophy used to be regarded as a primary degenerative process without distinct signs of preceding inflammation. Our results seem to support the theory of its pathogenesis put forward by Bruetsch (1953). The fact that a specific anti-syphilitic drug such as penicillin is more effective in the early stages of the disease, suggests that its efficacy is associated with inhibition of the syphilitic inflammatory process involving the lower optic tract at the base of the skull. It is then easy to understand the lack of evident improvement when penicillin is given at a later stage, when atrophy of the optic nerve is already established and the damaging inflammatory process has already become inactive.

Table VII shows that two clinical forms of syphilitic primary optic atrophy may be distinguished: one is chronic and may cause blindness only after many years, and here penicillin may be useful, in the other, vision deteriorates rapidly, and penicillin is unable to arrest the process because irreversible changes occur before the antisymphilitic treatment is started.

#### Summary

The results obtained in thirty-seven patients with syphilitic primary optic atrophy, treated with penicillin in doses of 6,000,000 to 32,000,000 units and observed for from 3 to 6 years, are discussed.

In five patients treated while the disease was in the inactive stage no effects were noted. In sixteen of the remaining thirty-two patients who received treatment while the visual acuity was deteriorating, the progress of the disease was permanently arrested.

Better results were obtained in patients in whom the treatment was started at an early stage in the development of the ocular changes.

Two clinical varieties of syphilitic primary optic atrophy can be distinguished. One runs a chronic

course and offers a better prognosis. In the other, the disease progresses rapidly and blindness ensues within a few months in spite of penicillin or any other treatment.

It appears that penicillin controls the progress of the disease in a high percentage of patients, especially if treatment is started when symptoms are first noticed.

#### REFERENCES

- Benton, C. D. Jr., and Harris, J. F., (1952). *A.M.A. Arch. Ophthalm.*, **48**, (449).  
 Blatt, N., (1949). *Ann. Oculist. (Paris)*, **182**, 513.  
 Bruetsch, W. L., (1953). "Syphilitic Optic Atrophy." Thomas, Springfield, Ill.  
 Dattner, B., Thomas, E. W., and de Mello, L., (1951). *J. vener. Dis. Inform.*, **32**, 33.  
 Kenney, J. A. Jr., and Curtis, A. C., (1953). *Amer. J. Syph.*, **37**, 449.  
 Klauder, J. V., and Gross, B. A., (1954). *Ibid.*, **38**, 270.  
 Moore, J. E., (1947). "Penicillin in Syphilis." Thomas, Springfield, Ill.  
 Stokes, J. H., Beerman, H., and Ingraham, N. R., (1944). "Modern Clinical Syphilology," 3rd ed., Saunders, Philadelphia.  
 Šuster, J., (1955). *Čsl. Ophthalm.*, **11**, 29.  
 Thomas, E. W., (1949). "Syphilis: Its Course and Management." Macmillan, New York.  
 Tron, E. Z., (1955). "Diseases of the Optic Pathway" (in Russian). Medgiz, Leningrad.  
 Worster-Drought, C., (1947). *Brit. med. J.*, **2**, 559.  
 Zlámal, J., (1955). *Čsl. Ophthalm.*, **11**, 26.

#### Résultats de la thérapie à la pénicilline de l'atrophie optique primaire syphilitique

##### Résumé

Les résultats obtenus dans l'atrophie optique primaire syphilitique chez 37 malades traités à la pénicilline aux doses de 6.000.000 à 32.000.000 unités et observés pendant une période allant de 3 à 6 ans, sont discutés.

On n'observa aucun effet sur 5 malades traités quand la maladie était au stade inactif. Sur 16 des 32 malades restants, traités alors que leur acuité visuelle diminuait, le progrès de la maladie fut définitivement arrêté.

On obtint les meilleurs résultats sur les malades que l'on commença à traiter à un stade peu avancé des altérations oculaires.

On peut distinguer deux variétés cliniques d'atrophie optique primaire syphilitique. L'une suit un cours chronique et offre un meilleur pronostic. Dans l'autre le mal progresse rapidement et la cécité s'ensuit en quelques mois en dépit de la pénicilline ou de tout autre traitement.

Il semble que la pénicilline reprime le progrès de la maladie sur un pourcentage élevé de malades, surtout si l'on commence le traitement dès que l'on observe les symptômes.