BLINDNESS DURING STREPTOMYCIN AND CHLORAMPHENICOL THERAPY*

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ALTHOUGH the toxic effects of streptomycin on the eighth nerve are well known, it is perhaps not so widely appreciated that loss of vision may complicate the administration both of streptomycin and of chloramphenicol.

A patient is described who became partially blind during combined streptomycin and chloramphenicol therapy and in whom streptomycin was at first considered to be the toxic agent. However, from a review of the world literature, it is evident that either drug may be incriminated.

Case Report

An Englishman developed leprosy of the face, hands, and feet in 1950, while living in India. He was then aged 24.

In 1955 he returned to the United Kingdom and in the following years underwent various surgical procedures at the Royal National Orthopaedic Hospital.

In June, 1959, when aged 34, he was admitted with a discharging ulcer on his left heel, and examination revealed an anaesthetic foot with an underlying osteomyelitis of the os calcis.

At this time the leprosy was controlled by 100 mg. daily of Dapsone, a drug which he had received steadily since 1954.

At operation on August 4, 1959, sequestrectomy was performed and for the first time in his life the patient started to receive antibiotics; chloramphenicol 0·5 g. 6-hourly and streptomycin 0·5 g. twice daily.

On December 21, 20 weeks later, he complained of failing vision, and said that this had arisen during the previous fortnight, worsening rapidly in the preceding week. He was having considerable difficulty in reading newsprint.

One week later examination revealed gross impairment of vision with bilateral central scotomata. All chemotherapy was immediately stopped and treatment with massive doses of the vitamin B complex was instituted. This included Parentervite (Forte) intramuscularly twice a day for a week, and then daily for a fortnight, together with 1,000 μg. vitamin B12 three times weekly for a month. He was also advised to reduce his cigarette consumption from a customary fifteen per day, although the findings were not suggestive of a tobacco amblyopia.

By January 8, 1960, the vision was improving a little and he could watch television; 3 days later (January 11) he was looking at pictures in books, and improvement continued until by January 22 he was able to read small print.

Ophthalmological examination on January 26, 1960, one month after withdrawal of the drugs, revealed a visual acuity of 6/12 in the right eye and 6/9 – 1 in the left, and as

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the foot had healed he was discharged from hospital. He continued to take Orovit, vitamin C, and Vitamin B_{12}.

When he was seen as an out-patient on March 2, 1960, the visual acuity had returned to 6/9 in each eye, and he felt he could see as well as ever.

**Discussion**

**Streptomycin.**—Visual complications during administration of streptomycin reported in the literature may be divided loosely into three categories:

1. Patients receiving streptomycin may suffer general side-effects, including slowness of accommodation, trembling of distant objects, and the continuance of image movement on turning the head (Jullien, Behague, Garderes, and Doncet, 1948). These symptoms are not permanent and there are no physical signs. Eiselt and Kloubeck (1948) reported disturbances of colour vision and perception in a patient receiving 2 g. daily, which cleared when the dose was halved; they felt this might have been due to a mild allergic encephalitis. Sannella (1953) reported two further cases in which the movement of objects persisted after passive movement of the head, but as this was followed by vertigo and nystagmus, involvement of the eighth nerve seems likely. Altenberger and Segal (1951) described a patient who developed papilloedema of both discs while receiving streptomycin for pulmonary tuberculosis; this cleared with anti-histamine therapy (Antistin), and they considered that an allergic reaction in the optic nerve to impurities in the streptomycin was likely to be the cause.

2. There are several reports of optic neuritis developing during streptomycin therapy for tuberculous meningitis. In many cases the drug was being given intrathecally, and there is some difference of opinion whether the neuritis was due to direct involvement of the nerve by the infection, or to the streptomycin. In some cases exhibition of the drug was stopped, while in others it was continued.

Beissel (1949), Benhamou and Foissin (1951), Matos Sousa (1949), Jacob, Favory, and Maillard (1949), Lebas and Hubert (1949), Licht and Paprocka (1952), von Mejer (1949), and Tokavera (1956) all reported cases of tuberculous meningitis treated with streptomycin, in which either the eye symptoms were considered not to be due to intramuscular or intrathecal streptomycin, or improvement followed the use of the drug. Da Pozzo (1956), in a review of the literature up to 1956, also concluded that streptomycin was unlikely to produce important ocular lesions when used in tuberculous meningitis, but he stressed that the situation should be watched. Monbrun and Lavat (1949) also quoted several authors, and again stated that streptomycin was not toxic to the optic nerve.

On the other hand, Béthoux, Isnel, Cau, and Valois (1949), Pierre-Bourgeois, Vic-Dupont, Dubois-Verrière, and Delmas (1954), Janssen and Böke (1955), Böke (1955), and Janssen, Böke, and von Eicken (1956) all felt that streptomycin, especially intrathecally, might directly affect the optic nerve.
Montenegro Feijóo (1949), Gouryanova (1954), and Schindel (1957) described cases of optic neuritis and atrophy in patients receiving streptomycin for tuberculous meningitis, but did not directly incriminate either streptomycin or the disease process.  

(3) There are reports of optic neuritis developing during streptomycin therapy for conditions other than tuberculous meningitis. Sykowski (1951) described a patient who was given the drug for severe pyelitis, who on the ninth day of receiving 0.37 g. 3-hourly developed a retrobulbar optic neuritis with bilateral central scotomata. This luckily cleared on withdrawal of the drug, and in 4 months vision had returned to normal. Majumdar (1953) reported a patient with pulmonary tuberculosis whose vision deteriorated to 6/60 after twenty daily doses of one g. There were no scotomata, and the condition was considered to be probably a toxic neuritis due to streptomycin. Thomas (1950), who was looking for scotomata in patients receiving streptomycin, found ten in cases of pulmonary tuberculosis and one in a case of B. coli urinary infection. Only six, however, had noticed vague blurring of vision, and the scotomata, which in some instances were found several months after the cessation of treatment, were of small size in all but one patient. 

Lozinskii and Bogdanova (1958) reported a case of toxic allergic optic neuritis during streptomycin therapy for disseminated pulmonary tuberculosis, with a rapid fall in visual acuity to zero. Almost full recovery occurred in 46 days after autohaemotherapy, detoxication, and desensitization. In an answer to “Any Questions” (Brit. med. J., 1957), it was admitted that blurring could occur from a toxic effect on the nerve, but the expert knew of no case in which a permanent optic atrophy had resulted from streptomycin therapy. Meyler (1952) also mentioned blindness as a possible complication of streptomycin treatment, but gave no details. 

Chloramphenicol.—Wallenstein and Snyder (1952) described a 24-year-old woman who received 2.5 g. daily for ulcerative colitis during a period of 5 months. At this stage she developed bilateral loss of vision due to an optic neuritis, with severe peripheral neuritis of the lower limbs and leucopenia. Discontinuance of the chloramphenicol and supportive treatment allowed a return of her sight in 2 months, although her legs were affected for at least another 3 months. Cole, Cole, and Janoff (1957) reported a similar case in which a 44-year-old patient with endocarditis received 2 g. daily for 7 weeks and then 1.5 g. daily for 5 months. He then complained of blurred vision and was found to have optic neuritis with pericentral scotomata. The condition cleared in
one month after withdrawal of the drug and treatment with vitamin B and Diamox.

Lasky, Pincus, and Katlan (1953) described a 14-year-old boy who was given 6 g. chloramphenicol daily for staphylococcal endocarditis. At the completion of a 6-week course he complained of cloudy vision and the next day was totally blind. It appears from their report that unfortunately there was little recovery of the boy's sight.

Gewin and Frion (1951) reported another patient with endocarditis who received both aureomycin 3 g. daily for 22 days and chloramphenicol 3 g. daily for 33 days. This patient then complained of blurring of vision and was found to have enlarged bilateral blind spots. In just under a month from the withdrawal of treatment, vision had returned to normal.

Harris (1950) mentioned a brief visual disturbance during the treatment of brucellosis with 25 g. chloramphenicol in a 10-day course.

Dapsone.—No report of blindness following Dapsone therapy has been found, indeed Cochrane (1959) stated that, as a result of the discovery of the sulphone and cortisone groups, ... “It can therefore be stated that blindness from leprosy should be a thing of the past, if the signs are recognized in time and if appropriate measures are undertaken.”

Bucalossi (1951) emphasized the significant absence of new ocular manifestations in patients with leprosy who presented none at the beginning of the treatment, and also the therapeutic value of sulphone in cases in which the lesions were still reversible.

It now seems clear that the most disturbing, although transient, blindness which occurred in our patient could have been due to streptomycin or chloramphenicol, or even to the drugs acting together.

Summary

A case of transient blindness occurring during long-term therapy with streptomycin and chloramphenicol is described.

The literature is reviewed.

It is not possible to decide whether streptomycin or chloramphenicol acting alone or in conjunction was responsible for this unfortunate complication.

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