J. C. CRAWHALL *ET AL.*: DISSOLUTION OF CYSTINE STONES DURING D-PENICILLAMINE TREATMENT

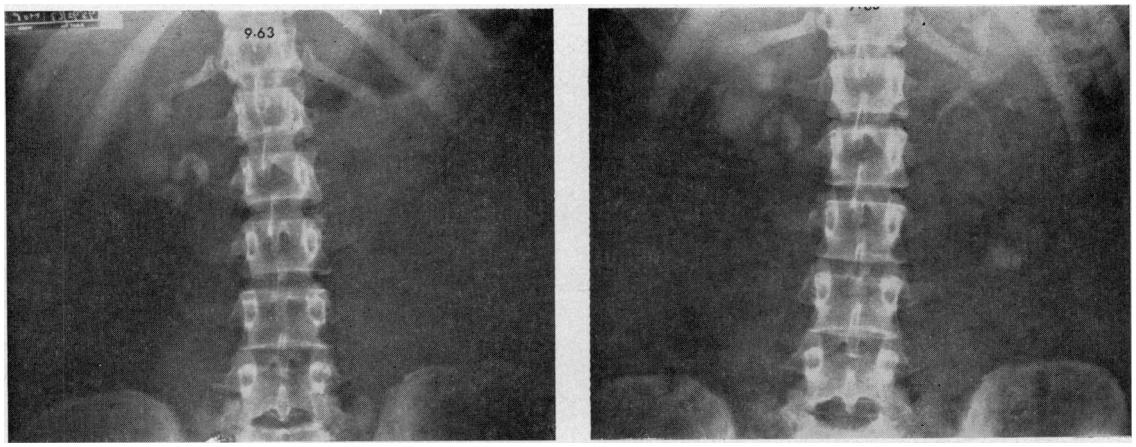

FIG. 1.—Plain abdominal radiograph and intravenous pyelogram before treatment with D-penicillamine.

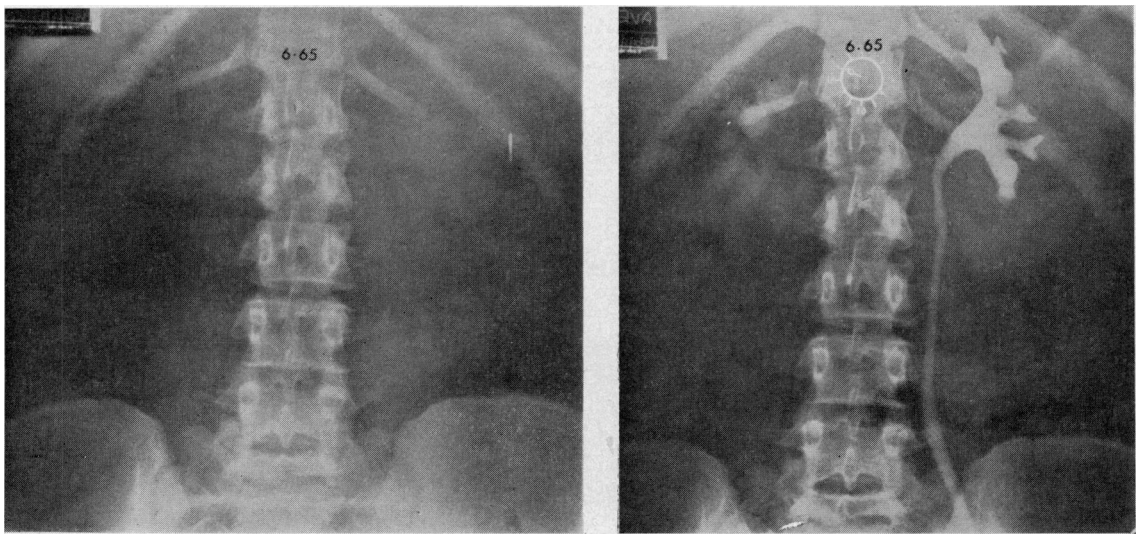

FIG. 2.—Plain abdominal radiograph and intravenous pyelogram after 18 months' treatment with D-penicillamine.

A. EBRINGER AND P. COLVILLE: CHLOROQUINE NEUROMYOPATHY

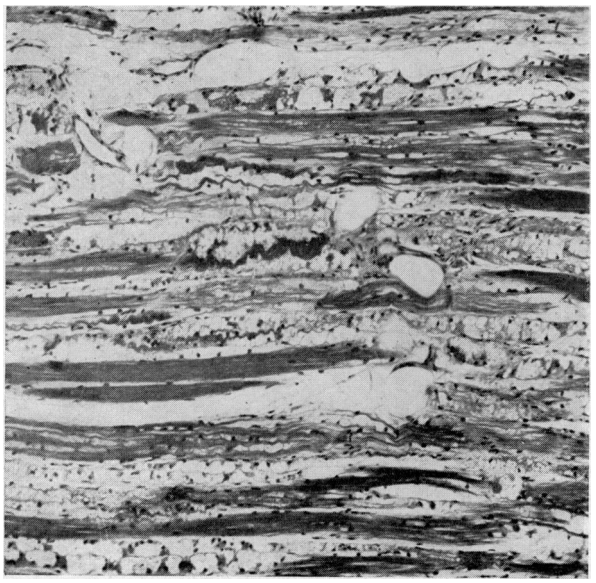

FIG. 2.—Biopsy from the weak left tibialis anterior muscle: there is replacement of a large proportion of the sarcoplasm by vacuoles and only occasional myofibrils are intact. (H. and E ×75.)

FIG. 3.—Biopsy from the left tibialis anterior muscle three months after stopping chloroquine, when strength had returned: there is almost complete disappearance of vacuoles and there are more intact muscle fibres than in the previous biopsy. (H. and E. ×75.)

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gap between the onset of the condition and facing the patient up to the diagnosis. The reason in Case 2 was to gain sympathy, and on one occasion admission to hospital.

The handling of artifact patients is not easy, but the fundamental approach of making them understand themselves is all-important. This should be done as early as possible. They must realize that one knows the origin of the lesions, and firmness, but not ruthlessness, is essential. "How do you produce them?" is a good opening gambit, which tends to elicit dissociated replies of great use in ascertaining the reason for the lesions. Gentian violet 0.5% with 25% water in emulsifying ointment is sometimes a useful application which helps healing and provides evidence of its use. It is messy enough to discourage the production of further lesions. The colour of the treatment gives the patient an excuse for getting better, and only if relapse takes place is it necessary to discuss the problem openly with the relatives. Between 1954 and 1959 one of us (R. H. S.) treated seven recently developed miscellaneous artifact cases, and all cleared within a few weeks of being seen, without subsequent relapse. It is not understood why, with the exception of Case 1, there have been no further artifacts from 1960 to 1966. In the total of nine patients there were three males.

Summary

Two cases of artifact ulcers and considerable nipping of bone, caused by rubber bands, are described. In one case the band was removed at operation; in the other case three bands were removed during dressings. The satisfactory treatment of eight other artifact cases from different causes is briefly mentioned, as well as some observations on general case management.

Medical Memoranda

Chloroquine Neuromyopathy Associated with Keratopathy and Retinopathy*

[WITH SPECIAL PLATE]

Brit. med. J., 1967, 2, 219–220

Chloroquine has been used to treat rheumatoid arthritis and discoid lupus erythematosus since 1951. Toxic effects include keratopathy and perifoveal retinopathy (Hobbs *et al.*, 1959), acute psychosis (Dornhorst and Robinson, 1963), and neuromyopathy (Whisnant *et al.*, 1963). We present a further example of severe chloroquine neuromyopathy associated with ocular lesions.

CASE HISTORY

A woman aged 49 of nervous disposition presented with extreme myopathy and poor vision. She had received three courses of electric convulsion therapy, and since 1960 had taken tranylcypromine, 20 mg. daily.

In July 1962 she had numbness and pain in the right shoulder and received chloroquine, 250 mg. daily, until June 1965. She also received phenylbutazone, which was not thought to be related to the ensuing disabilities. After 12 months she saw haloes and rainbow-like effects around street lights. After 18 months her legs became weak and "like lead," giving way beneath her, and she had difficulty in rising from a squatting position and in walking upstairs. After two years she complained of blurred vision and a white glare around objects. After three years her muscles had become so weak that she could hardly get out of bed, and when walking she had to hold on to furniture; she could read only one word of newsprint at a time and could see the rim of her dinner-plate but not the food. She had a persistent metallic taste in her mouth.

The only abnormal physical findings related to the ocular and muscular systems. There was profound generalized muscular weakness, no wasting or fasciculation, and all tendon reflexes were absent. She could not flex her head when lying, rise from a supine or squatting position, or stand on her heels. Her grip-strength in both hands, measured with an ergometer, was 8 kg. The vital capacity was 1,500 ml. There was no sensory loss. Ocular examination showed a visual acuity of 6/9 for both eyes, macular stippling, a ring-scotoma in both visual fields extending from 2 to 10 degrees with normal central and peripheral vision (Fig. 1), and, by slit-lamp, microscopic corneal deposits arranged in radial lines.

Relevant Laboratory Investigations.—Serum aldolase 34 units (normal 4–10 Bucher units), creatine phosphokinase 231 units (normal 0–40 units), glutamic oxaloacetic transaminase 56 units (normal 0–35 Sigma-Frankel units); total serum protein 7.2 g. and gamma-globulin 0.8 g./100 ml.; daily urinary creatine excretion 361 mg.; E.S.R. 5 mm./hour; lupus erythematosus cell test negative; test for rheumatoid factor negative. A muscle biopsy from the weak left tibialis anterior showed loss of muscle fibres with most of the sarcoplasm replaced by vacuoles, while cell walls, nuclei, and interstitial tissues were intact; there was scanty cellular infiltration (Special Plate, Fig. 2).

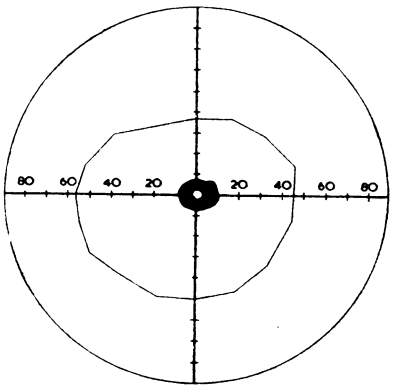

FIG. 1.—Right visual field showing macular ring-scotoma in black. Peripheral and central vision were normal. The left visual field was similar to the right one.

Progress.—Chloroquine was stopped. After three months muscle strength had improved, her strength of grip had increased from 8 to 28–30 kg. in both hands, the vital capacity had increased from 1,500 to 2,530 ml., and a second muscle biopsy showed considerable improvement (Special Plate, Fig. 3).

DISCUSSION

A middle-aged woman with arthritis developed severe weakness of muscles and defective vision due to treatment with chloroquine. Chloroquine neuromyopathy was described by Whisnant *et al.* (1963) in four patients, of whom three had

* This paper is Publication No. 1056 from the Walter and Eliza Hall Institute.

keratopathy and two retinopathy, and also by Loftus (1963) and Covo *et al.* (1963). Symptoms appear only after prolonged treatment, the duration being 18 months in the present case, and the muscles of the legs and feet are particularly affected. Recovery of muscular power occurs shortly after stopping chloroquine. Whisnant *et al.* (1963) called the syndrome neuromyopathy because nerves and muscles were affected on electromyography, there being decreased nerve-conduction velocities and increased numbers of myofibrillar spike potentials. Electromyography was not performed in our case.

Histologically there is vacuolar degeneration of muscle fibres with sparing of sarcolemmal sheaths. Rewcastle and Humphrey (1965) described the electron-microscopical appearances of muscles in "vacuolar myopathy" due to chloroquine. There was extensive dilatation of the longitudinally oriented endoplasmic reticulum, resulting in formation of irregular large vacuoles surrounded by a single electron-dense membrane.

Myopathies described previously in patients with systemic lupus erythematosus and related diseases could be due to chloroquine toxicity. Dubois (1956) described a "myasthenic-like syndrome" in 6 out of 12 patients with systemic lupus erythematosus treated with chloroquine, and some also complained of a "metallic taste," as did our patient. Lang *et al.* (1965) reported "vacuolar myopathy" in a patient with systemic lupus erythematosus treated with chloroquine for four years. She had muscle weakness and retinopathy, and muscle strength improved after stopping chloroquine: the relation of the myopathy to chloroquine was not emphasized. Rees and Maibach (1963) stated that chloroquine aggravated the symptoms of porphyria, myasthenia gravis, and multiple sclerosis, perhaps as a result of an associated myopathy due to chloroquine.

We thank Dr. Ian R. Mackay and Dr. W. H. Marshall for their help, Dr. G. Goldstein for describing the muscle biopsies, Dr. P. Hardy-Smith for describing the ocular lesions, and the Department of Audio-Visual Aids of the University of Melbourne for the photomicrographs.

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Behçet's Disease with Retinal Vascular Lesions

[WITH SPECIAL PLATE]

Brit. med. J., 1967, 2, 220–221

Behçet (1937) reported three cases with a triad of recurrent oral and genital ulceration and ocular lesions. Many features have since been added to the original triad, the most serious being involvement of the brain stem, meningomyelitis, and confusional syndromes. Thrombophlebitis involving superficial and deep veins, dural sinuses, and retinal veins has also been described. Arthritis and various skin manifestations have been reported. Ocular lesions that have been described include conjunctivitis, episcleritis, iritis, choroiditis, and retinal vascular lesions. Though the dominant clinical picture is that of an anterior uveitis, the presence of retinal lesions can often be obscured by the severity of the anterior uveal reaction (Perkins, 1961). Retinal lesions have been reported in 50% of cases (Mavioğlu, 1958). Sezer (1953) thought that ocular disease actually began in the retina and optic nerve. The initial retinal lesions usually take the form of a periarteritis or periphlebitis, sometimes with thrombosis of either arteries or veins, and occasionally retinal and vitreous haemorrhages may occur (Perkins, 1961).

Principal Findings in Five Patients with Behçet's Disease

Case No.	Sex	Age at Onset	Duration (years)	Mouth	Genitalia	Eyes	Other Conditions
1	M	28	4	Ulcers	Ulcers	Uveitis; retinal and vitreous haemorrhages; micro-aneurysms; new vessel formation	Alcohol excess
2	F	33	13	,,	Normal	Uveitis; periphlebitis of retina; vitreous haemorrhages; marked visual impairment	Psoriasis; arthritis knee
3	M	21	7	,,	Ulcers	Conjunctivitis	*Trichophyton rubrum* skin lesions on legs
4	F	63	1	,,	,	Conjunctivitis; cataracts obscure fundus	Pneumonia; ulcers in trachea and bronchi; total alopecia
5	F	24	1	,,	,,	Normal	Arthritis knee

Five patients, all Caucasians, with Behçet's disease have been seen by us at Wellington Hospital during the past year (see Table). Retinal involvement was present in two. One patient had previously shown changes of retinal periphlebitis and vitreous haemorrhages, but was nearly blind, and examination of the retina was obscured by uveal changes. One patient showing extensive retinal and vitreous haemorrhages and microaneurysms is of particular interest; this case is reported in detail.

CASE REPORT

A 29-year-old brewery-vat-cleaner presented in April 1963 with painful ulcers on his scrotum which had arisen 10 days previously as red swellings. He had had recurrent ulcers of the mouth for five months. There had been a transient episode of pain in both eyes, with visual blurring, one month before we saw him. He had had infectious hepatitis in September 1961. There was no significant family history. He was a heavy beer-drinker.

When first seen he was mildly obese and edentulous, but had no mouth ulcers. There were several punched-out ulcers with extensive erythema over his scrotum and penis. His left optic fundus showed a large haemorrhage in the upper nasal quadrant, with very congested veins, and there were smaller haemorrhages on the temporal side, with marked new vessel formation around the temporal edge of the disc. The right side showed similar new vessel formation superotemporally, venous congestion, and occasional haemorrhages. Visual acuity was 6/12 in the left eye and 6/9 in the right. Slit-lamp examination showed cells in the vitreous of both eyes, with