Clinical and Other Notes

I—BRUCELLOSIS

AN ACCOUNT OF THREE CASES TREATED WITH CHLOROMYCETIN AND AUREOMYCIN

BY

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BruCELLOSIS is a specific infection of man and animals produced by Brucella abortus, Br. melitensis and Br. suis. It occurs in acute and chronic forms. The acute form is characterized by remittent fever which may exhibit a series of relapses with brief apyrexial intervals. The disease occurs in most parts of the world. Here in Malta it is still common among the indigenous population, but it is now rare for British service personnel to contract the disease.

The clinical characteristics vary with the type of infection, but that caused by Br. melitensis tends more often to produce the prolonged relapsing type of fever which has caused the disease to be called undulant fever. The clinical characteristics even in the Br. melitensis group vary enormously, as the three following case reports demonstrate.

Case 1.—C. V., aged 16, son of Gunner V., of the Royal Malta Artillery. This Maltese boy was admitted to hospital on 21st February, 1950, with a history of having had undulant fever in July and August, 1949. He had apparently made a slow recovery from this illness, but had been able thereafter to return to a normal mode of life. Two weeks before admission he began to have severe pain in the right knee and hip joints. The pain had become less since its onset and the knee joint was less troublesome than the hip. He had no other symptoms. On examination he was found to have a temperature of 100° F. He was noted to be thin, pale and undernourished. No tenderness was elicited in the abdomen, but the spleen was palpable two finger-breadths below the costal margin. There were no abnormal physical signs in the respiratory, cardiovascular, central nervous or genito-urinary systems. Examination of the legs showed marked tilting of the pelvis to the right with limitation of movement of the right hip joint on flexion, extension, and both internal and external rotation. Pain was elicited on movement of the joint. The right knee was apparently normal.

Clinically the case was one of brucellosis with involvement of the right hip joint.
The diagnosis was confirmed by the agglutination reaction of the patient's serum which with *Br. melitensis* went to a titre of 1 in 1,250.

The Mantoux reaction was negative. X-ray of the hip joints showed that there was a slight increase in the width of the joint spaces with a definite circumscribed osteoporosis in the region of the acetabula; the appearance was strongly suggestive of a bilateral infective arthritis.

The patient continued to run an irregular fever and on the advice of the Surgical Specialist the right hip was encased in a plaster-of-Paris spica. In this he was more comfortable and his general condition improved a little, although he continued to run an irregular fever.

In May, 1950, some chloromycetin was received and the patient was given an initial dose of 2 grammes, followed by 0.5 grammes every six hours. After he had had 15 grammes his temperature fell for the first time in weeks, but the period of apyrexia was short-lived. It was clear, after 31 grammes of chloromycetin had been given, that no appreciable benefit had accrued from its use. The spleen was still palpable and the patient's temperature was still above normal. At the end of the course of treatment the plaster-of-Paris hip spica was removed and it was apparent that there was a collection of fluid in the right hip joint. Furthermore, X-ray of the joint showed that there was osteosclerosis of the head of the femur due to avascular necrosis. From now on it was necessary to aspirate the right hip joint at weekly intervals whilst maintaining skin traction on the leg. Approximately 100 c.c. of turbid, and later blood-stained, glairy fluid was aspirated each week. The fluid gave an agglutination reaction with *Br. melitensis* to a titre of 1 in 1,250. This continued throughout the summer months; the patient's general condition improved but little and he continued to have an irregular fever. In September, 1950, a supply of aureomycin was received. In spite of a large dose of this drug (41 grammes in all) little improvement ensued. Fluid was still collecting in the right hip joint, the patient was pyrexial, and his spleen was still palpable. Six weeks after cessation of treatment with aureomycin, fluid stopped collecting in the right hip joint; simultaneously the patient became apyrexial, and his general condition began to improve. More active treatment for the joint was begun, and in February, 1951, there had been a considerable general improvement, although much more care and orthopaedic treatment will be required before the condition of the hip joint can be called satisfactory.

Chloromycetin and aureomycin had no appreciable effect on this chronic case of brucellosis in contrast to the results reported below in acute cases.

**Case 2.**—Sapper B., aged 29, a Maltese soldier, who habitually drank raw goats' milk, was admitted to hospital on 24th May, 1950, complaining of fever, headache, and occasional rigors for fourteen days.

On examination he was noted to be febrile, but apart from this no abnormal signs were elicited. The liver and spleen were not palpable. Investigations carried out showed no notable changes in the R.B.C. or W.B.C., but the E.S.R. was 20 mms. fall in one hour. Blood culture on 28th May, 1950, was sterile, but when repeated on 16th June, 1950, *Br. melitensis* was grown. This confirmed the diagnosis which had been obvious when it was shown on 28th May, 1950, that the patient's serum agglutinated a suspension of *Br. melitensis* to a titre of 1 in 500.

The patient was given a course of chloromycetin thus: 3 grammes initially followed by 0.5 grammes every six hours. He received a total of 31 grammes. He became apyrexial and symptom free forty-eight hours after beginning treatment. He has remained well ever since and now, after fifteen months, has not had a relapse.
**Case 3.**—T. C., aged 13, son of Gunner C., R.M.A. This Maltese boy was admitted to hospital on 19th June, 1951, with a history of abdominal colic and fever of one month's duration. On admission he was febrile and the spleen was palpable two finger-breadths below the costal margin.

**Blood:**

- Hb—90 per cent. (Sahli)
- R.B.C.—4,840,000/cu.mm.
- W.B.C.—6,000/cu.mm.

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Agglutinations with *Brucella* were positive to a titre of 1 in 250. Blood culture was sterile.

Treatment with aureomycin was begun on 22nd June, 1951. He was given 250 mgm. every six hours. The temperature fell by lysis and was normal forty-eight hours after treatment was begun. He had 11 grammes of aureomycin in all. The spleen diminished in size and was impalpable at the end of treatment. He was discharged from hospital on 5th July, 1951. He was readmitted on 31st July, 1951, with four days' history of fever. The spleen was again palpable two finger-breadths below the costal margin. Agglutinations with *Brucella* were positive up to a titre of 1 in 200.

This time the temperature settled spontaneously and the spleen became appreciably smaller, but after five days he again developed a high temperature and the spleen was again enlarged to two finger-breadths.

A second course of aureomycin was begun on 5th August, 1951, and the temperature became normal thirty-six hours after treatment was begun. The spleen became impalpable six days later.

In this case the response to aureomycin in two occasions was dramatic, but relapse occurred within a month of the first course.

**DISCUSSION ON TREATMENT**

Until chloromycetin and aureomycin were discovered the treatment of brucellosis can only be described as unsatisfactory. The sulphonamides (alone or in combination with streptomycin) had proved helpful in certain cases, but they could not be relied upon. Treatment was therefore almost entirely supportive and symptomatic.

**Chloromycetin**

In 1947 chloromycetin, a new antibiotic, was obtained from cultures of the species *Streptomyces venezuelae* (Ehrlich *et al.*., 1947), and is now also prepared synthetically. It was demonstrated to possess antimicrobial effects against certain Gram negative organisms, including the *Brucella* group.

Woodward *et al.* (1948) treated nine cases of brucellosis with chloromycetin. Six of the cases were experiencing an attack, whereas the other three showed a relapse of fever two, three and five months respectively after the primary illness had been treated with streptomycin and sulphasalazine. The results were
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striking. The mean duration of fever prior to treatment in the nine treated patients was thirty days. Within thirty-six hours after the start of the specific treatment, two who were more seriously ill were resting more comfortably, and the other seven patients experienced an immediate improvement of the body and joint pains. The mean duration of the fever after beginning chloromycetin treatment was 2.7 days and the temperature remained normal thereafter. Splenomegaly, which had been noted in seven of the cases, disappeared either during treatment or very shortly afterwards. There was one relapse thirty-one days following discontinuation of chloromycetin, but prompt clinical response was obtained when chloromycetin was readministered. There were no complications.

Knight et al. (1949) had a similar experience when treating twelve cases of brucellosis. They found that relapses were not uncommon following short periods of therapy with chloromycetin, and that relapse occurred within six weeks of the cessation of therapy in five of the twelve cases.

Later, Ralston and Payne (1950) reported on 41 cases treated with chloromycetin. Of these, 28 (70 per cent.) were completely relieved or much improved, 7 (17 per cent.) were partially relieved, but no improvement was apparent in 5 (12.5 per cent.).

In Woodward's (1948) series the régime adopted was empirical and based upon prior experience in scrub typhus and typhoid fever. The initial dose, based on 50 mgm. kilo body-weight, was adhered to, and the subsequent dosage was 0.25 gramme given every three hours until at least five days of normal temperature ensued. The antibiotic was tolerated well orally and no clinical evidence of toxicity was noted.

In Ralston and Payne's series the dosage varied between 18 and 27 grammes by mouth in seven to twelve days, using a dosage schedule very much like that used in Woodward's series.

Aureomycin

Aureomycin was first isolated by Duggar (1948) from the mould Streptomyces aureofaciens. Its in vitro and in vivo range of activity approximates very closely to that of chloromycetin. Bryer et al. (1948) demonstrated its in vitro activity against Brucella. Woodward (1949), reporting on the therapeutic results of aureomycin on brucellosis, found that the response to treatment closely followed that observed with chloromycetin. The drug was given orally. The dosage schedule used was 1 gramme initially, followed by 0.5 gramme every four hours for three days, and then 0.5 grammé every six hours for an additional five to eleven days. The average total dose per patient was 21.99 grammes given over a period of 11.6 days. No clinical evidence of toxicity was observed apart from nausea and occasional vomiting and diarrhœa. There were no complications and no relapses in five treated cases after a minimum period of two months. Spink et al. (1948) report on a larger series of cases treated in Mexico. Of 24 patients with Br. melitensis infection there was a rapid response to aureomycin in all, but three later relapsed.

The results of treatment of brucellosis with chloromycetin and aureomycin, while not always entirely satisfactory, are, by far, better than with any previously
tried form of therapy. Chronic brucellosis is less likely to respond than the acute form. Much remains to be done in the field of prevention before the disease is eradicated.

**SUMMARY**

Three cases of brucellosis are described. One, a chronic case, did not respond either to chloromycetin or to aureomycin. The second, acutely ill, made a good recovery on chloromycetin, while the third responded to aureomycin, although relapse occurred after the initial course of treatment.

The treatment of brucellosis with chloromycetin and aureomycin is briefly reviewed.

I wish to thank Lieut.-Colonel H. C. Benson, R.A.M.C., O.C. David Bruce Military Hospital, Malta, for his helpful suggestions and Colonel T. B. H. Tabuteau, O.B.E., D.D.M.S., Malta Garrison, for permission to publish.

**REFERENCES**


**II—DIVERTICULUM OF THE STOMACH**

BY


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It has been estimated that the stomach accounts for about 3 per cent. of all diverticula from the gut, and that of these a large proportion are symptomless and have only been incidental findings during a barium meal or a laparotomy. Occasionally a diverticulum may result from ulceration or degeneration in myomata or other tumours, but the great majority are autonomous and are of three types—congenital, traction and pulsion.

Walters considers that all true diverticula, in which all layers of the gastric wall are intact, are caused by malformations or by arrested development during foetal life, and he maintains that there is no evidence of organic disease as a causative factor.

Keith is of the opinion that a localized congenital weakness of the muscular