GRANULOMA INGUINALE IN SOUTHERN RHODESIA AND ITS TREATMENT WITH ANTIBIOTICS

BY

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Recently the writer has had the good fortune to make a prolonged survey of venereal diseases in Southern Rhodesia. During this undertaking some 17 cases of granuloma inguinale were observed during six months in widely scattered parts of the country from Concession, north of Salisbury, to Belingwe, south east of Bulawayo. 10 were males and 6 were females. It was estimated that to find these, some 1,500 venereal diseases patients were examined in over 50 institutions and, as many had already been in-patients for long periods far in excess of those of patients with the more ordinary venereal conditions, that the incidence was probably of the order of 0·25 per cent or less of venereal diseases patients seen. In the Report (Willcox, 1949) reference was made to 16 cases: 1 additional case was seen after the Report had been written.

Some of these patients it was found possible personally to treat. Others were prescribed for and the results of treatment obtained from the medical officers concerned by post; others again were merely seen en passant. Those cared for personally, and some of those seen only periodically, were given streptomycin, aureomycin or chloromycetin. Although one is well aware of the deficiencies of this paper, both as regards pathological control and follow-up, it is felt, all the same, that the experience is worth recording.

Case 1: Salisbury.—A middle-aged man, exact age unknown but who remembered World War One, and who was then living in the Reserve in the north-east of Southern Rhodesia, was admitted to hospital on May 19, 1949. He had a lesion in the groin of one week's duration. On examination there was a velvety granulomatous area in the right groin about 4 cm. by 1·5 cm. in size with smaller granulomatous areas on the prepuce and near the peno-scrotal junction. There was also some generalized oedema of both penis and scrotum, a rubbery non-tender enlargement of the left inguinal glands, a papulo-squamous rash of the forearms and neck, and the left supraclavicular and both epitrochlear glands were palpable.

The next three days were spent in investigation. Three daily dark-fields proved negative for *T. pallidum* the Dmelcos and Lygranum skin tests were negative for soft sore and lymphogranuloma venereum but the Wassermann and Ide tests for syphilis, however, were both strongly positive. During this time he was given 1 gramme of sulphathiazole orally four times daily without effect. On May 22 a diagnosis of secondary syphilis was made and he was treated with a course of eight daily intra-
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muscular injections of 600,000 units of penicillin in oil-beeswax again without visible improvement of either the granulomatous areas or the genital oedema. A biopsy was made and he was photographed.

He was then given 0.5 gramme of streptomycin three times daily for eight days until 11.5 grammes had been administered without toxic effects. The lesions had quite healed on June 13 two weeks after the onset of treatment and he was discharged on the following day.

Case 2: Concession.—A young female native with chronic granulomatous lesions of the vulva was seen here but unfortunately discharged herself before anything could be done.

Case 3: Concession.—A middle-aged male native of Southern Rhodesia, who stated that he was a small boy at the time of the first Great War, had had a penile sore in 1939 but more recently had an ulceration of the groin of one year’s standing. He now had a large dry somewhat serpiginous ulceration, heaped along the edges, extending along the left groin fold backwards through the crutch and fusing with a moist ulcerated area on both sides, but predominantly on the left side, of the anus.

Dark-field examination of the lesions was negative for T. pallidum and the Lygranum skin test was also negative. The Dmelcos skin test for soft sore, however, was positive, possibly as a result of his penile lesions of ten years previously. The Wassermann test was negative. A few organisms only, resembling Donovania granulolasis were seen in the biopsy smear.

During the previous three weeks he had already received six injections of neoarsphenamine and ten daily injections of penicillin in oil-beeswax (total 3,750,000 units) without effect. He was then given 1 gramme of streptomycin three times daily for one week (total 21 grammes and when seen again at the conclusion of treatment the condition was static and apparently quiescent. Five days later the condition had improved still further but was not healed. No further treatment was advised. Twelve days after treatment epithelialization was taking place and he was ready for discharge on the sixteenth day.

Case 4: Marandellas.—A prematurely-aged native of Nyasaland, who had been five years in Southern Rhodesia and who was a young boy during World War One, had an ulcerated groin of four months’ duration. There was no history of penile sore. When seen he had been in hospital for three months during which time he had received eight injections of neoarsphenamine and bismuth, 25,000 units of penicillin four times a day for six days, 2 c.c. of antimonial daily for twenty days and later 1 gramme S.A.T. daily for twelve days, all without improvement.

The groin lesion, a projection of which extended medially, was about 10 cm. by 4½ cm. in size and had hard raised crusted edges while a yellow crust grossly heaped in the centre covered the whole and when he moved revealed a pink fleshy area. A biopsy was done but no Donovan bodies were seen—possibly as a result of antimony treatment.

On June 13 he was given one 250 mg. capsule of aureomycin three times daily and this was continued for five days until 4,000 mg. had been administered. When seen six days after the onset of treatment the lesion looked a little cleaner but otherwise there was no change. A letter from the medical officer under whose care the patient then was, written twenty-two days after the onset of treatment, announced that the granulations had closed and that the edges were epithelializing. A further letter forty-two days after the onset of treatment stated that the skin was growing well over the wound and that he was being discharged.

Case 5: Umvuma.—A young Karanga lady of child-bearing age from the Fort Victoria district was admitted to hospital with genital ulceration of six months’ duration. There was a previous history of miscarriage at two months, and her Wassermann reaction was strongly positive. Commencing three months previously she had already had two courses of neoarsphenamine and bismuth the first being of ten weekly injections of both drugs and the second being of six. She had also had
ten daily injections of 125,000 units of penicillin in oil-beeswax without effect. One injection only of sodium antimony tartrate had been given on the day of examination.

The woman had an extensive moist ulceration of the entire external genitalia and the condition remained unaltered by previous therapy. A biopsy specimen personally taken unfortunately was mislaid before the mobile laboratory had again been established. A supply of streptomycin, however, was arranged for her to be given 1 gramme three times daily for one week (total 21 gramme) and it was intended to call back and see her again after about six weeks. The result, however, was dramatic for the lesions had completely healed in two weeks and she was discharged.

Case 6: Chitando.—A man of about 25, whose father was a Shangaan and his mother a Karanga, was admitted with an hour-glass-shaped area of red granulations in the left groin, with a small velvety area on the prepuce and glans penis in addition, of two and a half weeks’ duration. There was no previous history of venereal syphilis although he admitted to the “njovera” which, in the opinion of the writer, is a form of endemic syphilis found in the southern part of the country. It was not found possible to make a dark-field examination in this isolated rural clinic although a specimen of blood gave a negative Kahn reaction. A biopsy was also taken from the groin but there was not agreement on the findings.

He was given 250 mg. aureomycin orally three times a day for five days (total 4,000 mg.) and, when seen again one week later, the penile lesions were apparently healing although the groin still appeared exuberant. Unfortunately no further contact was made.

Case 7: Belingwe.—An old lady with clinical granuloma inguinale was seen at Belingwe on August 3. She had had diffuse genital ulceration since March. A second case was in a male (Case 8) whose lesions were present since January while yet another, a male, was seen at Shabani (Case 9).

Case 10: Fort Usher.—This young man had been an in-patient for fifteen months with bilateral ulcerated granulomatous groins with additional smaller lesions on the glans and shaft of the penis and on the scrotum. Repeated Wassermann tests had been negative. In the present year he had received ten weekly injections of arsenic and bismuth and, a month previously, three million units of penicillin all with no result. It was decided to treat him with aureomycin, and he was given one 250 mg. capsule three times daily for five days (total 4,000 mg.). He was seen again nine days later by which time he was delighted with his progress, the penile lesions healing well and the groin lesions being smaller. A letter on August 30, however, ten days later, stated that although the condition had improved considerably it had again deteriorated. He was prescribed streptomycin 3 grammes daily for one week and on October 14 his condition was stated to be much improved. Shortly afterwards he healed completely and a letter dated January 17, 1950, stated that he was working locally and that there had been no recurrence.

Case 11: Bulawayo.—An indigenous native of Southern Rhodesia, aged about 30, had a small patch of chronic granulo-ulceration in the left groin of one month’s duration. He had already received 20 antimony and six neo-arsphenamine and bismuth injections without healing. His Wassermann was positive. Biopsy failed to show D. granulomatis. He received 0·5 gramme streptomycin twice daily for three days after which time the groin healed and he was discharged seven days after the onset of treatment.

Case 12: Bulawayo.—A young female Southern Rhodesia native had extensive ulcerogranulomatous lesions of the whole vulvar area and around the anus. The inguinal glands were not involved and the blood Wassermann reaction was negative. There was a three months’ history but she was so far untreated. A scanty number of organisms resembling D. granulomatis was found by biopsy.

On August 13 she was given one 250 mg. capsule of aureomycin orally three times daily for five days. Seven days later the lesions were cleaner but not reduced in size and no further treatment was given at this stage. Seventeen days after treatment about
half of the area affected had healed or was obviously healing. Further treatment, however, was asked for and before further supplies of the antibiotic could be obtained the patient was given antimonial. After receiving 14 c.c. in nineteen days the lesions had healed and she was discharged. The consort of this case was unaffected.

Case 13: Gwelo.—A middle-aged female native, who had been in hospital for four months, had had extensive vulvar and peri-anal ulceration for one year. She was also cachectic.

She had received numerous courses of sulphapyridine, two full courses of neoarsphenamine and bismuth, one course of sodium antimony tartrate and four weeks of treatment with penicillin in oil-beeswax all without effect. It was recommended that she be given streptomycin. I was later informed that she received 20 grammes over ten days without any immediate effect although a sudden improvement took place three-and-a-half weeks after cessation of treatment only to relapse subsequently with phases of local healing and breakdown.

Case 14: Que Que.—A young native admitted three weeks previously on account of granulomatous lesions of the groin and prepuce stated that they had been present a week before admission. He had already received three neoarsphenamine and three bismuth injections. Streptomycin was recommended.

Case 15: Gatooma.—A married male native of Nyasaland, ten years in Southern Rhodesia, had granulomatous lesions in both groins and on the penis of two months' duration. He had been an in-patient for three weeks and had received three weekly injections of neoarsphenamine and bismuth without effect. He was given streptomycin 3 grammes daily for seven days and the lesions healed in twelve days.

Case 16: Gatooma.—A male native with lesions in the left groin had been an in-patient for eight and half months and had had his lesions for two months before that. He had received two full courses of neoarsphenamine and bismuth and also 300,000 units of penicillin in oil-beeswax once daily for one week all without effect. He was given streptomycin 3 grammes daily for seven days and the groin had healed by the thirteenth day.

Case 17: Salisbury.—A male native of Southern Rhodesia had a velvety granulomatous lesion of the coronal sulcus about the size of an olive of two and a half months' duration. Three dark-field examinations were negative for T. pallidum and the serum
Wassermann reaction was also negative. He was treated with one capsule of chloromycetin given orally three times a day for two days followed by one capsule twice daily to a total of 13 tablets (3.25 gramme). Healing was noticeable by the fifth day and he had completely healed in eight days when he was discharged from hospital. No other treatment was given.

Information was forthcoming later that the patient was again in hospital some nine weeks later with a sore on the site of the original lesion. He was given one injection of 2.4 mega units of procaine penicillin with aluminium monostearate, improved but was admitted a few days later with a further recurrence. This was also treated with a similar dose of penicillin and the sore apparently healed in a week, the serum Wassermann remaining negative. A few days later the sore broke down again. This case must be regarded as one of relapse.

**DISCUSSION**

Granuloma venereum, described by Greenblatt (1949) as “the enfant terrible of the diseases which plague the South” is considered in the U.S.A. as being on its way to extinction as a result of modern treatment with antibiotics.

The disease is certainly present in tropical and sub-tropical Africa and is met in Nigeria and Sierra Leone (Willcox, 1946). In these places rectal strictures are encountered in the females. Possibly because the disease is less prevalent in Southern Rhodesia, no indisputable case of rectal stricture in females was personally seen during the venereal diseases survey. Its large-scale eradication by antibiotics has not yet been attempted in Africa.

The responsible organism, *Donovania granulomatis*, has been shown to be sensitive to streptomycin both in the chick embryo (Rake and Dunham, 1947) and in the clinical infection (Greenblatt *et al.*, 1947 *a* and *b*), and several series of considerable size (Kupperman *et al.*, 1948; Chen *et al.*, 1948; Zimmerman and Smith, 1948) proved beyond a doubt that streptomycin was the best curative agent yet discovered for this disease.

Aureomycin was also shown to be effective in granuloma inguinale. Wright *et al.*, 1948, and Greenblatt *et al.*, 1948c reported success with 5 patients who had proved resistant to streptomycin and prefer the newer drug. The latter workers also state that the drug is only really effective if given by the oral route and consider that 20 grammes given over ten days is an average effective dose. Chloromycetin was used in one case mentioned in this report.

**SUMMARY**

(1) 17 cases of granuloma inguinale were observed during a six months’ survey of venereal diseases in Southern Rhodesia. All were Bantu negroes and 11 were males and 6 females.

(2) 10 of the cases had had lesions for longer than three months and the average duration of symptoms was four-and-a-half months.

(3) 8 patients were treated with streptomycin (1 an aureomycin failure), 4 with aureomycin and 1 with chloromycetin.
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(4) Most of those treated with streptomycin were given 21 grammes over one week and this proved effective. Those that received aureomycin had only 4,000 mg. over five days and this was insufficient. The one patient treated with only 3.25 grammes of chloromycetin (chloramphenicol) likewise relapsed.

(5) The response to modern treatments, which allowed patients to be discharged from hospital within a few days or weeks, having previously sometimes having spent many months receiving other ineffective drugs, was most dramatic.

(6) It is concluded that granuloma inguinale is present in Southern Rhodesia and that in the Bantu the reaction of the disease to antibiotics is similar to that in the American Negro.

REFERENCES