CHLORAMPHENICOL IN TREATMENT OF CUTANEOUS ANTHRAX

BY

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Chloramphenicol in concentrations of 5 µg./ml. has been shown to inhibit *in vitro* several strains of *Bacillus anthracis*, one strain being rather more susceptible (McLean, Schwab, Hillegas, Schlingman, 1949). Its clinical effect was therefore tried on four cases of cutaneous anthrax in Indian labourers.

Case 1

An Indian labourer was admitted to hospital on June 7, 1950, in a restless comatose condition. His temperature was 96° F. (35.6° C.), pulse 74, and respirations 30. The spleen was palpable. On examination the pulmonary condition was normal. A blood slide showed the presence of malaria parasites. Kernig's sign was positive and neck rigidity was present. There was a vesicular pustular eruption with an oedematous base over the proximal end of the left fibula. A smear from this sore showed *B. anthracis* ++. He was treated with "acetylsan," 3 ml. intramuscularly, and procaine penicillin in oil, 300,000 units. Sustaining measures and lumbar punctures were impossible owing to his restlessness, and he died seven hours after admission. Post-mortem examination was refused. A provisional diagnosis of anthrax meningitis, with possibly intestinal anthrax, was made.

Immediate inquiries elicited that a cow had died under suspicious circumstances seven days previously, and that he, with about 50 others, had cut it up and eaten it. All these contacts were immediately examined, and four further cases of anthrax were discovered. All belonged to the scavenger class.

Case 2

A man aged 35 was admitted at 7 p.m. on June 7. There was a history of carving and eating the same cow. His temperature was 100° F. (37.8° C.), pulse 100, and respirations 28. He was anaemic, and his heart was slightly enlarged (a usual condition in these people). There was a sore on the left thumb $\frac{1}{2}$ in. (1.25 cm.) in diameter which had been present for a week. It had started, after some itching, as a circular red papule; it had then become vesiculated and a dark scab had formed in the centre. By this time the base was very oedematous and the whole sore steadily grew bigger, the scab softening and becoming a dirty colour rather than black; a number of surrounding vesicles became confluent and exuded serum. The regional lymph nodes were not enlarged or tender. There was a second oval sore $2\frac{1}{2}$ in. (6.3 cm.) long on his back, and a third on the lateral aspect of the left knee. Slides from all three sores showed a heavy infection of anthrax.

He was treated on traditional lines with procaine penicillin in oil, 300,000 units daily for seven days. Sulphadiazine was given as follows: 3 g. immediately, 1 g. four-hourly for three days, and 1 g. thrice daily on the fourth day. Acetylsan, 3 ml., was given on the first day and neoarsphenamine, 0.3 g., on the second day. Neoarsphenamine, 0.15 g., was given on the fourth and eighth days. The temperature and pulse settled to normal by the fourth day, and all sores had diminished in size; oedema was much less. The cultures remained positive until the ninth day and were thereafter negative. All sores were healed on the twenty-fifth day.

Case 3

A girl aged 12 was admitted on June 7 with a sore over the insertion of the left deltoid. She had eaten some of

the same cow, and her brother (Case 4) was also affected. The sore had started with an itching place, and a circular red papule soon appeared. On June 4 this had grown and become vesicular. On her admission there was a depressed black scab at the centre surrounded by a confluent unbroken vesicle $\frac{1}{2}$ in. (1.25 cm.) in diameter, the whole lying on an oedematous base. One secondary papule was present immediately outside the ring of vesicles. Her temperature was 100° F. (37.8° C.), pulse 104, and respirations 39. The regional lymph nodes were enlarged and tender. A slide showed *B. anthracis* +.

Chloramphenicol, 1.75 g. (60 mg. per kg. of body weight) orally, divided into four doses given every hour, was administered that night, and 750 mg. (26 mg./kg.) thrice daily was started next day and continued for three days. The doses were then reduced to half this amount for a further three days. Pulse and temperature were normal by the fourth day, and the sore had dried up; oedema had disappeared and the slide was negative for anthrax. On the thirteenth day the lymph nodes had entirely subsided and the scab separated, and slide and culture were negative for *B. anthracis*. All sores were completely healed on the twenty-third day.

Case 4

A boy aged 10 was admitted on June 7 with a history identical to that of his sister (Case 3). On admission he had a sore measuring $1\frac{1}{2}$ by $1\frac{1}{2}$ in. (3.2 by 4.4 cm.) on the back of his knee. In the centre there was a dark tough scab which was surrounded by a vesicle that had burst. The base was grossly oedematous. The regional glands were enlarged and tender. His temperature was 100° F. (37.8° C.), pulse 108, and respirations 32. A slide showed *B. anthracis* +.

Chloramphenicol, 1.25 g. (52 mg./kg.) divided into four doses, was given at hourly intervals, and from next morning 620 mg. (26 mg./kg.) thrice daily was given for three days, and then the dose was halved for two days and finally reduced to 60 mg. thrice daily for three days. The temperature had settled by the second day, and on the third day the slide was negative. By the fourth day there was much less oedema, and the sore was cleaner. On the eighth day a culture gave a positive result, but thereafter eight daily cultures were negative. He made an uneventful recovery, and all sores were completely healed on the twenty-ninth day.

Case 5

An infant aged 10 months was admitted on June 7. There was no history of eating or handling affected meat. Case 2 stated that after he had cut off his portion from the cow and taken it home he had taken the infant on his knee and played with it. The mother, who had cooked and eaten the meat and had nursed the child at the breast throughout the whole illness, was not affected. Four sores were present—two on the abdomen each 1 in. (2.5 cm.) in diameter, one on the right forearm $\frac{1}{2}$ in. (1.25 cm.) in diameter (see illustration), and a small sore starting on the

Case 5. Showing two sores on abdomen and one on right forearm.

leg. The temperature was 100° F. (37.8° C.), pulse 150, and respirations 50. A slide showed *B. anthracis* +.

Chloramphenicol, 0.375 g. (64 mg./kg.), was given in powder form followed immediately by breast-feeding. No further dose was given that night. From next morning 188 mg. (32 mg./kg.) thrice daily was given for 60 hours; then the dose was reduced by half for a further 60 hours and again halved for a further 48 hours. On the second day the temperature was 102° F. (38.9° C.), pulse 160, and respirations 50. The sores and the general condition were the same. A slide showed *B. anthracis* ++. Next day the general condition was the same except for mild diarrhoea. The sore on the leg had not increased in size, but a vesicle had formed and burst. A slide showed *B. anthracis* +. On the fourth day the general condition was good, the diarrhoea less, all sores were slightly smaller, and the leg sore was drier. The dark scabs were more pronounced. On the fifth day the general condition was good, stools were normal, and the sores dry. A negative slide but positive culture were found on the eighth day by lifting the scab and culturing the underlying pus. Thereafter the sores gradually healed. All further slides were negative, but a further positive culture was obtained on the thirteenth day. Cultures on the ninth, tenth, fourteenth, and fifteenth days were negative. A peculiarity of this case was the persistently oedematous base, which only gradually subsided, whereas in the other cases oedema disappeared rapidly. After some secondary infection the sores were completely healed on the thirty-ninth day.

Case 6

A man aged 55 was admitted to hospital on July 8 with a sore on his back and with fever. This was an isolated case occurring in a different district in a member of a different caste. On July 3 he had felt an itching on his back and rubbed it. He then noticed a lump and a vesicular sore on his back. This gradually enlarged, and on July 5 he felt feverish. There was no history of how the infection could have occurred. On admission a malignant pustule was seen on his back about 3 in. (7.5 cm.) above the right iliac crest, in the same position as one of the sores in Case 2, and presumably caused by carrying infected meat on the back. The sore measured 1½ by 1½ in. (4.4 by 3.8 cm.) and had a black centre surrounded by ruptured vesicles exuding serum. The skin surrounding the sore was oedematous for about 12 in. (30 cm.) and for a rather greater distance downwards and over the abdominal wall. The right axillary glands were enlarged and tender. The spleen was not palpable. His temperature was 101.4° F. (38.6° C.), pulse 90, and respirations 28. His weight was 112 lb. (50.9 kg.). A slide was negative for *B. anthracis*, but culture was positive.

Treatment was not given on July 9 owing to administrative difficulties. On July 10 chloramphenicol, 3.25 g. (64 mg./kg.) divided into four doses was given every hour. Nothing further was given that night. On July 11, 12, and 13, 1.5 g. (29.6 mg./kg.) was given thrice daily. The dose was halved on July 14 and 15. On July 10 his temperature was 101.4° F. (38.6° C.), pulse 80, and respirations 20. The sore looked slightly bigger and had an angry-looking edge with increased serous discharge. The pain and irritation were more marked. The oedema had spread round to the nipple and was more pronounced. Regional lymphadenitis was increased. A slide was negative for *B. anthracis*, but culture was positive. Next day, 12 hours after starting treatment, there was a dramatic improvement: the sore was the same size, but there was no pain or itching, the serous discharge was less, the central slough rather bigger, and oedema had definitely diminished in area and severity. Regional lymph nodes were smaller and not tender. On July 12 further rapid improvement occurred. A slide and culture were negative. All further slides and cultures were negative. On July 13 there was no oedema. The whole sore was dry and covered by a black scab.

The patient was discharged on July 19 to the out-patient department. On discharge he still had a slightly enlarged axillary gland and the sore was covered with a firmly adherent tough black scab measuring 1½ by 1 in. (3.8 by 2.5 cm.). The wound healed in the usual fashion.

Discussion

The opportunity given by a small outbreak of anthrax was used to test the clinical efficiency of chloramphenicol in cutaneous anthrax. Except for Case 1, in which the patient was *in extremis* on admission and died, all cases recovered. Only Case 1 had an enlarged spleen, and the disease appeared to be limited to the skin; but, owing to a lack of blood culture facilities, septicaemia cannot be entirely excluded. The small proportion of those affected compared with those at risk and the continued exposure of the mother of Case 4 raise a suspicion that these Indian labourers have a certain amount of resistance against acquiring this infection. Experience at other times has shown that the untreated disease is uniformly fatal. Case 1 shows that the strain was a virulent one.

Clinical appearances were typical of anthrax. All smears showed the typical morphological characters, and cultures on nutrient gelatin gave the typical spore-forming organism. Capsules were demonstrated by polychrome staining, and the suspensions of the cultures were positive to the malachite green test.

Summary

Cutaneous anthrax in four patients aged from 10 months to 55 years was treated with chloramphenicol with an initial dose of 60 mg. per kg. of body weight and a maintenance dose of 30 mg./kg. eight-hourly for 60 hours, then 15 mg./kg. eight-hourly for 48 hours, and finally 7.5 mg./kg. eight-hourly for a further 48 hours. All four cases showed rapid improvement leading to cure.

One case was treated on the usual lines with penicillin, sulphadiazine, and arsenic as a control. The series is too small to demonstrate the superiority of either method, each appearing equally effective.

It is a pleasure to acknowledge the help given by Messrs. Parke, Davis and Co., who supplied the chloramphenicol ("chloromycetin") and obtained permission from the Government of India to use it in these cases.

REFERENCE

McLean, I. W., jun., Schwab, J. L., Hillegas, A. B., Schlingman, A. S. (1949). *J. clin. Invest.*, **28**, 953.

The medical section of the Library Association will hold its first week-end conference at University Hall, Liverpool, from Friday evening, March 28, to Monday midday, March 31. The programme will include an address by Sir Henry Cohen on the romance of words; a symposium on three types of medical libraries by Miss I. B. Jones, Mr. W. A. Lee, and Mr. G. Wilson; visits to the libraries of the Liverpool Medical Institution, Liverpool University, and the School of Tropical Medicine, and to the Speke Works of Evans' Medical Supplies. There will be a reception at the Liverpool Medical Institution, a visit to Speke Hall, and a coach excursion to Llangollen. Attendance at the conference is open to medical men as well as to librarians, and those who are interested are invited to write to the hon. secretary of the Medical Section of the Library Association, c/o the British Dental Association Library, 13, Hill Street, London, W.1.