THE TREATMENT OF LEPROSY WITH CHLORAMPHENICOL

AN EXPERIMENTAL TRIAL WITH NEGATIVE RESULTS [1]

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Chloramphenicol (chloromycetin) is a crystalline antibiotic originally obtained from a soil organism isolated in Venezuela and at present synthesized at the laboratories of Parke, Davis and Company. Chemically it is a nitrobenzene compound, d-threo-2-dichloracetaminido-1-p-nitrophenyl-1,3-propanediol. It has been found to be effective in the treatment of typhoid fever, salmonellosis, pertussis, typhus fever and other rickettsioses, and it has shown promising results in atypical virus pneumonia, psittacosis, lymphogranuloma venereum, brucellosis, urinary infections, and other bacterial diseases.

Chloramphenicol is well tolerated by man, and no toxic or allergic reactions of importance have been observed even with doses above the therapeutic level. It is rapidly excreted in the intestinal contents and in the urine. It is administered orally in capsules of 250 milligrams, and the usual dose is 50 milligrams per kilogram of body weight per day. In some infections, such as typhoid fever and typhus fever, an initial dose of 60 mgm./kgm. is advised, followed by the usual 50 mgm./kgm. dosage for the following 8 to 15 days. Rectal administration has been used in unconscious patients with excellent results. In the average case the total dose should be so distributed that no more than 8 hours elapse without renewed medication. As a rule 250 mgm. every 3 to 4 hours satisfies the needs of the average patient.

Although *in vitro* chloramphenicol seems to exert a bacteriostatic action on *M. tuberculosis*, clinically there does not seem to be a worthwhile therapeutic activity as compared to that of streptomycin.

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The mycobacterium of leprosy not being cultivable, it cannot be used for *in vitro* tests, so that the only method is the clinical trial on a number of cases. Sufficient chloramphenicol for use on six cases of leprosy was obtained.[2] The dose administered was 50 mgm./kgm. for 6 consecutive days, repeating the same course after 6 or 7 days of rest.

REPORT OF CASES

CASE 1.—Patient J. E. H. L., a white male 23 years of age, suffering from lepromatous leprosy of 12 years duration, had not been treated with any sulfone. The patient was well nourished, with no intercurrent disease. The hemogram was: red cells, 4,300,000; hemoglobin, 80 per cent; white cells, 8,250; polymorphonuclears, 66; lymphocytes, 20; eosinophiles, 6; mononuclears, 8. The erythrosedimentation rate was 25 mm. in one hour. Urinalysis was negative. Bacteriological examination showed abundant acid-fast rods in globi as well as scattered.

Between August 25 and 31, 1949, the patient received 72 capsules of chloramphenicol at the rate of 12 daily, 2 every 4 hours. At the end of these 6 days the blood count, urinalysis and bacteriological examination showed no significant change; the erythrosedimentation rate was 18 mm. in one hour. On September 9 the treatment was resumed with the same dosage for another 6 days. The total amount of chloramphenicol received in the two periods of treatment, totalling 12 days, was 36 gm. The patient tolerated the drug well. There was no change in the bacteriological findings or the general or local conditions; the only significant change was the reduction of the erythrosedimentation rate to 12 mm. On October 7 and October 24, clinical and laboratory findings remained essentially the same except that the sedimentation rate increased to 23 and then to 29 mm. The patient was observed clinically for 7 months but showed no noticeable clinical improvement.

CASE 2.—Patient M. H. S., a well-nourished white male, 75 years of age, with lepromatous leprosy of 5 years duration, previously untreated. No evidence of intercurrent disease was elicited. Hemogram and urinalysis were normal; the sedimentation rate was 25 mm. Bacteriological examination showed numerous acid-fast bacilli.

Treatment with chloramphenicol was started on September 8, 1949, and continued for 6 consecutive days, with 5 capsules of 250 mgm. each every 8 hours, making a total of 3.75 gm. After a rest of 7 days the course was repeated for 6 more days. The erythrosedimentation rate, determined every 6 days, was 25 mm., 30 mm. and 20 mm. during and after the treatment. There were no significant changes in the blood or urine or in the bacteriological findings. On November 11 the patient was still clinically and bacteriologically unchanged. The total dose of chloramphenicol administered was 45 gm. Seven months after cessation of treatment the condition still remained unchanged.

CASE 3.—Patient H. F. V., white, 34 years of age, suffering from lepromatous leprosy of 15 years duration. Previously treated with promin,

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[2] Kindly supplied by Dr. Eugene H. Payne, of the Department of Clinical Investigation of Parke, Davis & Co.

that drug had had to be stopped because of gastric and general intolerance. Hemogram normal; sedimentation rate 28 mm.; bacteriological examination showed acid-fast bacilli in the lesions of the skin and mucous membrane.

Chloramphenicol was administered every 8 hours in doses of 6 capsules of 250 mgm. each for 6 consecutive days; after 6 days of rest the same dosage was repeated for another 6 days. Six days after this second period the medication was resumed for another 3 days, when it was stopped for lack of further supply. The total amount administered was 56.25 gm. There was no appreciable improvement, clinically or otherwise. Acid-fast bacilli were still present 10 weeks after the end of the treatment. The patient complained of nausea, increased diuresis and diarrhea during the treatment.

CASE 4.—Patient J. D. R., a Negro 41 years old, suffering from lepromatous leprosy of several years duration, with numerous partially involuted lepromata on face, ears and extremities. Treated with promin from February to December, 1949, a total of 704 gm. being given. In January 1950 diamidin was used for two weeks (18 tablets).

Chloramphenicol was started on January 24, at which time the erythrosedimentation rate was 105 mm.; there were abundant acid-fast bacilli in the cutaneous lesions. The total amount of chloramphenicol administered was 56.25 gm. Gastralgia and vomiting were experienced at the beginning, but later the drug was well tolerated. Diuresis was notably increased during the treatment, day and night. There was no noticeable improvement either clinical or bacteriological, two months after the treatment.

CASE 5.—Patient M. A. R. G., a Negro 27 years old, a case of lepromatous leprosy of several years duration, with numerous lepromata on the face, chest and extremities. Treatment with diasone, beginning in September 1947, at the rate of 3 capsules a day, was followed by slight improvement, but it was irregular—lasting only 3 or 4 weeks at a time over several months—because of gastric intolerance; and there had been no such treatment for a year or more prior to the present experimental one.

Treatment with chloramphenicol was started on January 30, 1950. At that time the hemogram was normal, the sedimentation rate was 24 mm., and the bacteriological examination showed numerous acid-fast bacilli in all specimens taken. Chloramphenicol was administered every 8 hours for 6 days, followed by a rest of 6 days and then another course of treatment for 6 days, the total amount of drug administered being 45 gm. No significant symptoms of intolerance were experienced by this patient. At the end of April no change, clinical or bacteriological, had been observed.

CASE 6.—Patient A. P. R., white, 27 years old, entered the San Lazaro Hospital suffering from lepromatous leprosy in September 1942. Since 1947 this patient had been in an almost continuous state of lepra reaction with fever, high sedimentation rate, anorexia, and tendency to loss of weight. Treated irregularly with diasone, there were continuous interruptions because of gastric intolerance and diarrhea.

On March 2, 1950, a course of chloramphenicol was started, 4 capsules being administered every 8 hours for 6 days. At that time the hemoglobin determination was 70 per cent, red blood cells 4,300,000, sedimentation rate 120 mm., bacteriological findings positive for Hansen bacilli. The total amount of chloramphenicol administered was 32 gm. in two courses of 6 days each, with the usual 6-day interval. A cutaneous reaction of the

erythema nodosum type remained unimproved, as did the other cutaneous lesions. At the time of administration of the drug the patient was afebrile and remained so. The sedimentation rate and bacteriological examinations were unchanged.

SUMMARY AND CONCLUSIONS

Six cases of lepromatous leprosy have been treated with chloramphenicol in doses according to the weights of the patients, the amount averaging 50 milligrams per kilogram of body weight. The drug was administered at intervals of 4, 6 or 8 hours for 6 consecutive days, followed by a rest period of 6 or 7 days and by a second course of treatment which also lasted 6 days. In two of the cases a short third course was also administered. Tolerance was good except for temporary nausea, vomiting and diarrhea in the first two or three days. The highest total amount of the drug taken by a patient was 56.25 gm., and the lowest dose used was 32.0 gm., the latter in a patient weighing only 120 pounds.

No improvement was noticed with this treatment either clinically or bacteriologically.

Chloramphenicol, in the doses employed by us, does not seem to be useful in the treatment of leprosy.