

CHLOROMYCETIN IN TYPHOID AND PARATYPHOID FEVER

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THE first reports on the action of chloromycetin on typhoid were published about two years ago (Woodward *et al.*, 1948), but it is only since last year that this new antibiotic has become available in India. A fair number of reports have appeared since in the literature in India and abroad which show that chloromycetin has a specific action in typhoid fever.

Typhoid fevers, apart from occasional outbreaks, have become a rarity in Western countries. In India, typhoid is still a very common disease, and, though its treatment underwent a profound change during the years before the war, when it was believed that typhoid cases had to be starved, even with improved nursing and a diet containing liberal amounts of calories and vitamins, it still carried a high mortality. Every typhoid case presented a serious problem and there was never any certainty as to what the next day might bring until the temperature had remained normal for a fairly long period.

Since the middle of 1949, when chloromycetin first became available here, seven cases have come under my observation, who were successfully treated. Three of them were cases of paratyphoid. Two of those paratyphoid cases were severe, and are particularly worth recording as they came under treatment within the first few days of the disease. All cases, except one, were treated within the first week of the disease.

The first opportunity to use chloromycetin came on 8th July, 1949, when I saw a European male, aged 29 years, who had become ill with fever and headache on 3rd July, but had still attended office on 4th July. On 8th July his highest temperature was 103.6°F., on 10th July it rose to 104°F. and he showed a few typical rose-spots. There also was some enlargement of the spleen. There were no severe constitutional symptoms. The agglutination test was confusing, the Widal being positive: 1/50 for para A and 1/25 *Sal. typhi* and negative for para B and C.

Blood culture was negative. Chloromycetin treatment was started on 11th July. Only three bottles were available at the time. One bottle was taken as the first dose, followed by one capsule 2-hourly. Within two days the temperature had become normal, but the chloromycetin was exhausted. On 17th July, the temperature rose again above 99. Only one bottle of chloromycetin was obtainable which was given 4-hourly. Within two days the temperature had settled down to normal again and remained normal.

Stool examination on 16th August, one month after defervescence, still showed typical colonies

of *Sal. typhi*. Two weeks later stool examination had become negative. Urine culture was twice negative for *Sal. typhi*.

A typical example of abortive treatment of typhoid is the following one: A European girl, aged 18 years, seen first on 1st January, 1950. For the last three or four days she had not felt quite well, but had not taken any notice of it. On 31st December, 1949, she had gone to a party from which she was forced to return home as her temperature rose to over 103°F. On 1st January at 1 p.m., her temperature was 103°F. but there were no severe constitutional symptoms. The Widal test taken on 2nd January was positive for *Sal. typhi* 1/125. Chloromycetin was started on the evening of 2nd January: on 5th January the temperature was normal and remained normal. Culture of blood and stool and urine remained negative (chart 1).

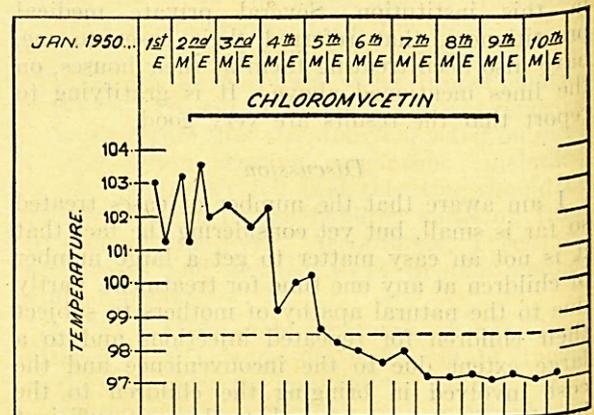


Chart 1.

The following case must be considered a severe infection complicated by malaria:

The patient, European male, aged 30 years, fell ill with slight fever, 99.4°F. on the evening of 29th December, 1949, outside Calcutta. During the following days his temperature was always high, around 103°F., not below 100°F. On 30th and 31st December he was repeatedly sick, vomiting bile with fair amounts of blood. A tentative diagnosis of malaria was made, but given up when no plasmodia were seen, and no specific treatment was given until 8th January when the patient whose condition was deteriorating very fast was brought by plane to Calcutta. When I saw him first, on 8th January, 1950, rather late in the evening, he was extremely toxæmic. It was very difficult to obtain a history from him because of his drowsiness. His pulse was rather weak and dicrotic, his abdomen was tympanitic and his spleen was very large, 4 inches below the costal margin and very tender. There were no rose-spots. The patient appeared to be so critically ill and the diagnosis of typhoid so obvious that chloromycetin was started at once, without waiting for the result of blood examinations which could not have been performed until the following day. However,

I took a blood slide in order to see whether the blood count was in accordance with the diagnosis of typhoid. To my great surprise I saw a fairly heavy infection with B.T. On 10th January, the Widal test was positive 1/125 for *Sal. typhi*. The clinical course is shown in chart 2. Treatment for malaria was instituted on 9th January with quinine orally. The rise of temperature on 10th January is more likely to have been caused by malaria than by typhoid. Plasmodia were not seen any more on 12th January. Chloromycetin dosage : first dose 3 g., followed 2-hourly by one capsule 0.25 g., in all 6 g. It is of interest to note that chloromycetin was tolerated extremely well even in the combination with quinine and there was not any accentuation of toxic symptoms as described in the literature.

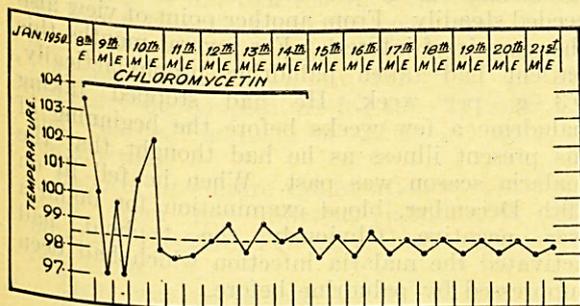


Chart 2.

Of the three paratyphoid cases treated with chloromycetin, one, a European male, aged 38 years, was of very mild nature. His temperature was only 100.4°F., highest at the beginning of the treatment, and chloromycetin brought the temperature to normal after 48 hours. Blood culture was negative, the Widal test for paratyphoid B was positive 1/250, negative for *Sal. typhi* and para A.

In the following case, however, the effect of chloromycetin was dramatic. This patient, a European male, aged 36 years, consulted me on 19th November, 1949, with the history of slight rise of temperature for four days, up to 100°F. in the evening and stated that the disease had started with some diarrhoea. He had been working until the day before and his temperature had been normal every morning. On examination nothing of importance was found. His blood was taken for Widal tests and for malaria and he was advised to stay in bed. That same afternoon his temperature rose to 102.2°F., he looked and felt now quite ill and was transferred to a nursing home. Late in the evening the blood examination was reported : positive 1/125 for paratyphoid B, negative for paratyphoid A and *Sal. typhi*. During the night the patient became extremely ill. He was shivering and perspiring alternatively and next morning he was very toxæmic, unable to speak coherently, unable to empty his bladder and the clinical picture of this sudden, severe prostration

resembled much more that of a cerebral malaria than of typhoid. Chloromycetin treatment was instituted, 3 g. first dose, followed by 0.25 g. 2-hourly. Repeated examinations for malaria plasmodia remained negative, though again on the following day the clinical impression was far more that of cerebral malaria than of paratyphoid. The patient remained confused and almost unable to speak. During the following night, however, there was a sudden improvement, the temperature fell to normal and remained there (chart 3).

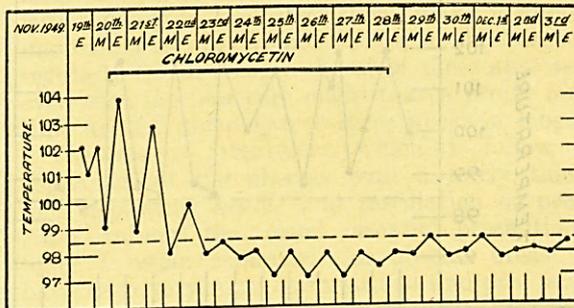


Chart 3.

Although there had been only two and a half days of fever, this short attack had been accompanied by such severe toxæmia that the patient was not able to stand when he was allowed to get up for the first time after his temperature had remained normal for ten days. If chloromycetin had not been available in this case, the prognosis would have been very grave. The severity of the condition had become manifest before chloromycetin treatment was started. Within 48 hours this severe paratyphoid infection had been brought under control without producing any unpleasant by-effects. Culture examination of stool, blood and urine remained negative.

Total dose of chloromycetin was 21 g.

The next case, European male, aged 20½ years, probably derived his infection from the same source as the previous case. Though he acquired his infection in another house, both patients obtained their food from the same kitchen.

When seen first on 19th December, 1949, he reported that his disease had begun five days before with diarrhoea, lasting for two days. Since then he had had slight fever in the evening and normal temperature in the morning. On 19th December his temperature rose to 102°F. (*vide* chart 4, axillary temperature). Next day the fever remained unchanged but blood examination for malaria was negative. On 21st December Widal was found positive 1/125 for *Sal. typhi* and para B. Chloromycetin was started, 3 g. first dose, followed by one capsule 2-hourly. On the day chloromycetin was started, the patient looked severely ill for the first time, he was slightly drowsy and also showed a definite enlargement of the spleen. No rose-spots were

seen. On the 4th day after beginning of chloromycetin treatment, the temperature became normal and remained so. Blood culture showed *Sal. typhi* as well as *Sal. paratyphi B*. On 3rd January, 1950, eight days after defervescence, the stool culture still showed presence of *Sal. paratyphi B*. A fortnight later stool examination was negative for *Sal. paratyphi B*.

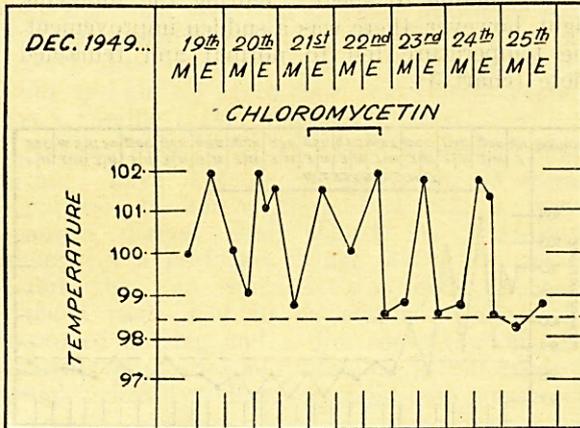


Chart 4.

In all 18 g. were given which were well tolerated and from the beginning of the chloromycetin treatment it was obvious that there was a steady subjective improvement though the temperature remained high for over three days.

One more case, comparatively mild of typhoid infection, was successfully treated with fall of temperature within 48 hours. The treatment was started on the 5th day of the disease. The Widal reaction was positive 1/125. The cultural examination of the blood was negative.

Discussion

In the present series of typhoid and paratyphoid cases, with the exception of one, treatment was begun at a very early stage of the disease. In all cases the Widal test was positive, though somewhat confusing in the first case, who, however, was exhibiting rose-spots, an enlarged spleen and who had a positive stool culture several weeks after defervescence. This case is of interest in another respect as chloromycetin could be given for three days only after which his temperature started to rise again. With one more phial of chloromycetin spread over two days the temperature was brought down.

There has been no relapse in the whole series. Patel, Banker and Modi's (1949) series of six typhoid cases, all with positive blood culture, came under treatment rather late, and they agree with Bradley (1949) that the full advantages of chloromycetin should be exploited best in cases whose treatment is begun within the first week. This desideratum is fulfilled in most cases of the present series and the dramatic effect of chloromycetin has been particularly striking in case 5 in whom treatment was begun on the 5th day of the disease, the second day of manifest illness.

This patient had been ambulant on the day before he became so severely ill that there was reason for the gravest anxiety if chloromycetin had not been available. The temptation to administer quinine as well was very strong, in spite of the negative findings for malaria because such sudden deterioration was thought to be not quite in keeping with the diagnosis of paratyphoid.

As far as I am aware, case 3 is the first described in whom malaria and typhoid have been treated simultaneously with quinine and chloromycetin. This combination did not appear in its effect to be more unpleasant than is expected from 30 g. of quinine per day. After three days of quinine treatment, while chloromycetin was continued, the patient was given paludrine, 0.6 g. per day, and recovery proceeded steadily. From another point of view also this case is of interest. For several months this patient had taken paludrine prophylactically, 0.3 g. per week. He had stopped taking paludrine a few weeks before the beginning of his present illness as he had thought that the malaria season was past. When he fell ill on 29th December, blood examination for malaria was negative. Obviously the typhoid had activated the malaria infection which had been suppressed by paludrine before.

Summary

Seven cases of typhoid and paratyphoid have been treated with chloromycetin, all, with the exception of one, having come under treatment within the first week.

In six cases the temperature returned to normal within 48 hours. In one case, in which paratyphoid B and *Sal. typhi* could be cultured from the blood, it took 72 hours for the temperature to become normal.

There has been no relapse in this series.

Chloromycetin had no unpleasant by-effects in any of these cases, not even when it was combined with full doses of quinine.

The effect of chloromycetin on *Salmonella* appears to be rather bacteriostatic than bactericidal as in two cases several weeks after conclusion of treatment *Salmonella* was still found in the stool.

My thanks are due to Dr. S. M. Ghosh of Central Calcutta Laboratories for his assistance in carrying out the serological and culture examinations.

REFERENCES

- BRADLEY, W. H. (1949). *Lancet*, i, 869.
 PATEL, J. C., BANKER, D. D., and MODI, C. J. (1949). *Brit. Med. J.*, ii, 908.
 WOODWARD, T. E., SMADEL, J. E., LEY, H. L., GREEN, R., and MAN-
 KIKAR, D. S. (1948). *Ann. Intern. Med.*, 29, 131.

After conclusion of this paper the following remarkable case was observed:

The patient, a European woman, aged 40 years, had been inoculated against typhoid and paratyphoid in September 1949. On 19th February,

1950, she was feeling perfectly well and attended work in the morning as usual and a party in the afternoon. On 19th February morning she still felt well, but towards afternoon she was seized with a headache which became so unbearable that I was called to see her at 11 p.m. when her temperature was 102°F. Examination of the C.N.S. gave no clue to this extreme headache which had remained unchanged even after large doses of aspirin, and there was no rigidity of the neck.

Next morning at 7 a.m. the temperature had risen to 105°F. The patient was feeling very ill and drowsy. The examination of the C.N.S. as well as of chest and abdomen revealed nothing pathological. She was transferred to a nursing home. Blood examination on the morning of 20th February showed an essentially normal blood count, absence of malaria parasites, but a positive Widal reaction for *Sal. typhi* 1/125. At about 12 o'clock chloromycetin was started, 3 g. first dose; the evening temperature on 20th February came down to 102.4°F.; on 21st February the temperature fell steadily to 99.4°F. and reached normal on 22nd February, to remain there.

Reports of culture examination of blood and stool from two different laboratories were obtained on 23rd February, both positive for *Sal. typhi*.

There was no relapse.

Total dose of chloromycetin : 18 g.

In this case the very unusual features are the rise of temperature to 105°F. within the first 24 hours and beginning of chloromycetin treatment also within the first 24 hours. Proof of the diagnosis beyond doubt was obtained at a time when the temperature had already returned to normal.

The patient was so gravely ill that the impression was general that chloromycetin was life-saving in this case in which the disease began with extremely toxic manifestations.

A Mirror of Hospital Practice

ABSCESS BREAST

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I AM not sure whether I am writing anything new, but being encouraged with the excellent results obtained, I thought I would share my experience with others.

Abscess breast is a very common complaint down here in South India. The children are nursed not every three or four hours, but often every half an hour or oftener if necessary to stop the children from crying. The antenatal care of the nipples is unknown and no wonder the disease is so prevalent even among the educated. Added to this is the reluctance of the women-folk to reveal the nature of their complaint even to their own close relatives. The patients

come to us when they cannot bear the pain of the abscess any longer after spending many sleepless nights. The abscess by then is well formed and almost at the point of bursting.

The usual treatment with the majority of surgeons is incision, drainage and daily dressing, giving in conjunction with sulphadiazine or any of their favourite sulphanilamide preparations, or penicillin.

The difficulties of the rural medical practitioners are manifold. The patients have to come from a distance of even three to four miles. The transport difficulties and high fares, and the presence of other children at home with nobody to look after them, make it almost impossible for the women to attend the hospital regularly for dressings. Most of these abscesses even with the best care might take a pretty long time to heal, about two to three weeks or longer.

The routine treatment which I follow is aspiration of the abscess with a fairly thick, long aspirating needle and instillation of penicillin taking the usual aseptic precautions. Since I began aspiration for abscess breast, I have been very much surprised to find pus, more often than my previous estimate suggested. These abscesses are very thick-walled and it is very difficult to elicit fluctuation or other usual signs of an abscess. The amount of penicillin depends upon the size of the abscess cavity. About 2 or 3 lakh units of penicillin in aqueous solution can be injected in an abscess cavity of moderate size through the same needle which has been used for aspiration. The opening is sealed off with collodion or with tincture benzoin co. Sulphathiazole in the usual doses by mouth or penicillin intramuscularly can be given if the patient can be hospitalized. These are not absolutely necessary. For patients living far off, I do nothing but aspiration and instillation of penicillin, to be repeated after two or three days.

Generally after two or three aspirations and instillations of penicillin, the abscesses heal up completely. Even at the time of the second aspiration, the aspirated material is much less viscous. As everybody knows, the response to treatment depends on the sensitivity of the bacterial organisms to penicillin and I am referring in this article only to those abscesses infected with the common pyogenic organisms.

Two case records may be interesting :—

Mrs. A., aged 25, pain and swelling of the right breast, 5 days' duration, temperature 101°F. Aspirated from the breast 2 ounces of thick pus and injected 2 lakh units of penicillin. Sulphathiazole 4 gm. a day also given. Patient came again on the 3rd day—no fever, pain much relieved. She does not want any more aspiration as she says she is cured. Aspirated again and a little clear fluid obtained—injected another 2 lakh units of penicillin into the abscess cavity. Patient completely cured.

Mrs. P., extremely poor and living about 4 miles away, came with all signs of abscess left