STREPTOMYCIN IN THE TREATMENT OF TYPHOID
AND PARA-TYPHOID FEVER

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(Introduced by Prof. M. Heki, Director)

Prior to the appearance of chloromycetin as a specific agent for the
treatment of typhoid fever, one had centred hope on streptomycine to con-
quered the disease, because of its wide bacillary spectrum and, especially
of the powerful activity on the growth of Eberthella typhosa in vitro. The
results of the most reliable record by Keefer and others on 51 cases of
typhoid fever were however disappointing, in which cases were treated
with a large does of streptomycin. Since then, workers in this field seem
to have abandoned to repeat similar experiment. But could streptomycin
be really ineffective for the treatment of typhoid fever? Cases, dealt with
by the above and other authors\(^1\),\(^2\),\(^3\) were relatively advanced in the course
of disease, therefore, we believe that the question still remains open to dis-
cussions. Argument naturally may exist that streptomycin is no more
useful since the appearance of chloromycetin, while even the latter is not
omnipotent in every case of typhoid fever as an established fact. It is our
duty, we believe, to evaluate the effect of an agent precisely as it is to
provide the knowledge in time of need.

The author has had the opportunity from the beginning of 1950, in the
year which chloromycetin was not yet available for the general use in our
hospital, to treat the patients of typhoid and paratyphoid fever chiefly
with streptomycin and has obtained a different results from that by Keefer
and others, the record of which is reported in the present paper.

CLINICAL MATERIALS

Eleven cases of typhoid fever (3 of which were suspected cases) and
6 of paratyphoid fever (3 of which were clinically diagnosed) have been
experienced between April 1950 and May 1951. They were treated chiefly
with streptomycin. The age of patients ranged from 1 to 38 years. The
commencement of the treatment ranged from the 2nd to 30th day of dise-
ase.
CASE REPORTS

Case 1. Y. A., a 4 years old female. Diagnosis: typhoid fever. Her father died recently of a feverous disease. She felt shick on October 12, 1950 and had a high fever. On the following morning, she had diarrhea several times without abdominal pain, and had fever and was admitted to the hospital on the 17th.

Present status and course: Temperature, 39.5°C with pluse rate of 88. She was a little apathetic. The tongue was furred. Pharynx, chest and abdomen revealed no special change. Culture of the blood, urine and feces negative. Widal’s reaction: TO 1: 800, TH 1: 400 (+), PA(—), PB(—). Beginning at noon on the same day, 0.25g of streptomycin was injected intramuscularly every 12 hours for a total of 3.5g. A slight decline of fever was observed during the treatment but the conditions become worse again after the termination of injection. Since October 29, 9.25g of chloromycetin was administered, every 4 hours in the beginning and every 8 hours afterwards for 7 days. She was free from fever on the very day the drug was given.

Case 2. H. K., a 1 year and 5 months old male. Diagnosis: typhoid fever. Since the morning on August 8, 1950 he had fever and admitted to the hospital on the following day.

Present status and course: Temperature, 38.9°C. The facial expression was slightly apathetic but no remarkable symptoms otherwise. Mucous stool was obtained by clisis in abundance. August 10. Culture of urine and feces for Eb. typhosa or paratyphosa negative. Culture of feces for Sh. dysenteriae negative. An amount of 0.5g streptomycin was injected intramuscularly in 2 doses but without effect. Erythrocyte count was 4.80 million per cu. mm.; leukocyte count, 5,800 per cu. mm. and hemoglobin, 93%. Albumen positive in the urine. Diazo reaction (—). August 18. Culture of feces for Eb. typhosa positive. August 19. An amount of 0.25g streptomycin injected intramuscularly twice a day. August 20. Treated in the similar way. August 21. Fever begun to decline. Only a slight fever in the afternoon. No recidivation observed thereafter. (Fig. 1)

Case 3. H. I., a 3 years old male. Diagnosis: typhoid fever. He became ill since July 7, 1950 with severe cough, constipation and fever. Fever of 39°—40°C had continued since July 15 and he was admitted to the hospital on July 29.
Present status and course: On admission, he was mal-nourished and stuporous. On auscultation, the breath sounds were generally sharp and especially rough in both hili. Roentgenographic examination of the chest revealed dense bronchial branches but nothing else. The abdomen was flat. Erythrocyte count was 3.95 million per cu. mm.; leukocyte count, 4,600 per cu. mm. and hemoglobin content, 80%. Examination of the urine revealed albuminuria and positive diazo reaction. Culture of the urine and feces for Eb. typhosa or paratyphosa negative. August 2. He was free from fever temporarily but no recovery of strength. August 5. Beginning from the evening, 0.25g streptomycin was injected intramuscularly every 12 hours, 4 injections in total, as moderate fever appeared since August 3. August 9. Beginning from the morning, 0.25g streptomycin was injected every 12 hours again, 4 injections in total. Further decline in fever was noticed after the termination of this treatment. August 12. Eb. typhosa still found in the feces. August 26. No Eb. typhosa found in the feces thereafter.
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Had good appetite. Eb. typhosa disappeared entirely from this day and he was discharged from the hospital on September 11.

It seems that, in this case, streptomycin was not without effect but it is also probable that the patient recovered naturally in this late stage of the disease. (Fig 2)

Case 4. Y. A., a 30 years old female. Diagnosis: typhoid fever. Admitted to the hospital on September 11, 1950 with fever (38°C) accompanied by chills and severe headache.

Present status and course: On admission, consciousness was clear. Temperature, 39.2°C with a pulse rate of 94. The tongue was furred. On percussion and auscultation the chest revealed no marked change. A slight pressure pain was recognized in the ileo-cecal region. Neither liver nor spleen was palpable. Erythrocyte count was 4.25 million per cu. mm.; leukocyte count, 4,100 per cu. mm. and hemoglobin content was 95%. Blood culture was positive for Eb. typhosa. Widal's reaction: TH 1:200 (+), TO 1:50, PA 1:25, PB 1:25. Examination of urine revealed no abnormalities. Culture of urine and feces negative for Eb. typhosa.

September 13. Beginning from this day, 0.5g dihydrostreptomycin was injected intramuscularly every 12 hours for 4 days. Simultaneously 100 mg vitamin K bisulfite was intravenously injected once a day for 4 days.

September 15. The patient became afebrile. No more Eb. typhosa found in the blood. Widal's reaction: TH 1:400, TO 1:50, PA 1:50, PB 1:25.
September 21. The patient suffered from mastitis with slight fever during the following 2 days which was treated with sulfathiazol with success. Thence no Eb. typhosa was cultivated from the discharge and soon she left the hospital. (Fig 3)

Fig. 3

Case 5. T. Y., a 33 years old male. Diagnosis: typhoid fever. On August 18, 1950 he had slight headache and weakness in the evening. The temperature rose to 38°C with severer headache and lumbago. Admitted to the hospital on the following day.

Present status and course: The patient complained of severe headache but had clear consciousness. Temperature, 39.3°C with a pulse rate of 90. The tongue was thickly furred. No marked change in the chest. Abdomen was slightly distended and slight resistance in the ileo-cecal region. Spleen palpated. Erythrocyte count was 4.20 million per cu. mm.; leukocyte count, 4,500 per cu. mm. and hemoglobin content, 87%.

Blood culture was positive for Eb. typhosa. Widal's reaction: TH 1:200, TO 1:100, PA 1:50, PB(−). Urine: free from albumen. Culture for Eb. typhosa negative. August 21. Commencing on this day 100 mg vitamin K bisulfite injected intravenously once a day for a total of 500 mg. August 22. Leukocyte count was 2,800 per cu. mm. Diazo reaction in the urine
positive. From this day, 0.5g streptomycin was injected intramuscularly every 12 hours, 6 injections in total. Headache was considerably subsided and fever became moderate. August 24. He was restored quite well subjectively. Splenomegalis disappeared. August 25. Fever declined to normal. Widal's reaction: TH 1:800, TO 1:200, PA 1:25, PB 1:50. Culture from urine and feces negative. Since then no more Eb. typhosa detected. (Fig. 4)

Case 6. K. M., a 28 years old male. Diagnosis: typhoid fever. Since the beginning of May 1950 he felt weakness and in the early morning of May 5, temperature rose suddenly to 40°C with chills. He had severe headache and lumbago. Fever continued since then, and he was suffering from constipation. Admitted to the hospital on May 10.

Present status and course: Temperature 39.1°C with a pulse rate of 90 on admission. He complained of oppression of the chest and perspiration. The skin was red but with no eruption. Conjunctival hyperemia was observed. Lips were dry with rhagades; the tongue was furred; tonsils were swollen and the mucous membrane of pharynx was hyperemic. On auscultation of the chest no special abnormalities were observed. The abdomen was generally distended and the edge of liver 1.5 finger width below
the costal margin palpable with pain. The spleen was also palpable.
Gurgling and pressure pain in the ileo-cecal region. Erythrocyte count
was 3.80 million per cu. mm., leukocyte count, 5,000 per cu. mm. and he-
moglobin, 70%. Widal’s reaction: TH 1:100, TO 1:25, PA 1:50 (±),
PB 1:25. Blood culture for Eb. typhosa positive. Albumen and diazo
reaction in urine positive. Culture of urine for Eb. typhosa also positive.
Intramuscular injection of 0.5g streptomycin every 12 hours was commenced,
although the results of cultures were unknown on this day. The injection
was given 6 times in total (the total amount of streptomycin given was
6g). Simultaneously, 100 mg of vitamin K bisulfite was injected intraven-
ously once a day, and the injection was continued during the following 5
days. May 12. Afebrile in the morning. The patient recovered remark-
ably. Still the tongue was furred, swelling of the liver and the spleen
were noticeable. May 15. The patient was entirely free from fever. May
17. Culture from urine and feces was negative. May 20. Widal’s reac-
tion: TH 1:400 (±), TO(—), PA(—), PB(—). Culture of urine and feces
negative. (Fig. 5)

Fig. 5

Case No 6. Typhoid Fever

Case 7. T. D., a 35 years old male. Diagnosis: typhoid fever. The
patient had abdominal pain and diarrhea with tenesmus since April 9, 1950,
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became worse day by day on April 15 had diarrhea 10 time a day. Fever appeared since April 20 and he was constipated on the same day. He suffered from weakness, severe headache and lumbago since then. Admitted to the hospital on April 22.

Present status and course: Moderately ill with anemic appearance, Temperature, 38.3°C with a pulse rate of 66 per minute. The tongue was thickly furred and the mucous membrane of pharynx hyperemic. Auscultation of the chest revealed marked acceleration of the 2nd pulmonary sound and the diminution of breathing sounds on the right upper lobe. The abdomen was slightly distended. Splenomegaly was observed. The erythrocyte count was 3.80 million per cu. mm.; leukocyte count, 7,500 and hemoglobin, 85%. Blood culture for Eb. typhosa or paratyphosa negative. Widal's reaktion: TH 1:400, TO 1:200, PA 1:200, PB 1:200 (+). Urine: albumen positive but diazo reaction negative. Leukocytes and erythrocytes present in the sediment. Culture of urine for Eb. typhosa or paratyphosa negative. April 26. Intramuscular injection every 12 hours of 0.5g streptomycin was commenced from this day. The injection was given 11 times and the total amount of the drug reached 5.5g. April 28. During the whole day he was afebrile. May 26. Discharged. (Fig. 6)
Case 8. M. S., a 19 years old male. Diagnosis: typhoid fever. Admitted to the hospital on July 13 with a complaint of fever and slight diarrhea since July 7.

Present status and course: Temperature 39.2°C, with a pulse rate of 74 per minute. The tongue was moderately furred. Gurling in the whole abdomen. Blood, urine and faces cultures negative. July 14. The patient perspired cosiderably. At 3 p.m., he had shaking chills and severe headache and lumbago in the evening. July 15. He complained of pain in the ileocecal region in the morning. Culture of blood, urine and feces for Eb. typhosa or paratyphosa negative. Widal’s reaction: TH 1:400, TO 1:400, PA 1:100, PB(−). Beginning from the evening of the very day, 0.5g streptomycin was injected intramuscularly every 12 hours. The injection was given 4 times in total. July 17. Fever declined to normal and his appetite was restored. July 19. Widal’s reaction: TH 1:1,600(±), TO 1:1,600(±), PA 1:50, PB 1:50. Slight fever recognized from time to time during further course, may not have been related to typhoid fever directly. The patient left the hospital on August 10. (Fig. 7)

Fig. 7

The temperature ranged from 37.5°C to 38°C continuously. On August 6 the temperature rose to 40°C and she had dry cough. Leukocyte count was 8,400 per cu. mm. on that day. Admitted to the hospital on August 7.

Present status and course: Temperature, 39.8°C with a pulse rate of 110 per minute. The facial expression was a little apathetic. Breathing was accelerated and superficial. The tongue was thickly furred. No remarkable abnormalities in the chest and abdomen. Leukocyte count was 6,400 per cu. mm. Widal's reaction: TH 1:200. Blood culture was negative but feces and urine were positive for Eb. typhosa. The patient had incontinency of urine and feces. August 9. Beginning from the evening, 0.5g streptomycin was injected intramuscularly every 12 hours for a total of 3g. August 11. Fever declined to the level of 37°C. No more incontinency of feces and urine. General condition was much improved. August 17. Fever dropped to normal. (Fig. 8)

Case 10. T. T., a 30 years old female. Diagnosis: typhoid fever. Admitted to the hospital on September 19 with complaints of high fever, headache and lumbago since September 4.

Present status and course: Temperature, 39.6°C with a pulse rate of 120
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per minute. The patient had apathetic appearance. Cardiac sounds were not clear. Rales were heard on lower lobes on the back. The abdomen was slightly meteoric and gurgling present in the ileo-cecal region. Neither liver nor spleen was palpable. Widal’s reaction: TH 1:100, TO (−), PA 1:100, PB 1:25. Culture of blood, faces and urine negative. September 26. Beginning from the evening, 0.5g streptomycin was injected intramuscularly every 12 hours. A total of 4g of the drug was injected; but no response of the medical effect was noticed. September 26. Beginning from this day, 300 thousand units of procain penicillin were injected intramuscularly every day and a total of 1,200 thousand units were given during 4 days, but also without effect. October 1. The patient vomitted once. Widal’s reaction: TH 1:800. October 2. The patient became delirious. Nasal breathing was observed and the face appeared pale. The rigidity of neck (±), Kernig’s sign (±), Babinski’s reflex (±). Culture of blood showed the presence of Eb. typhosa. Examination of urine gave positive albumen, positive diazo reaktion. Culture of Eb. typhosa in urine was positive. October 3. An amount of 2 g chloromycetin was given to the patient at 10 a.m., then 0.25 g of the drug every 4 hours, 8 g in total, and 0.25 g every 6 hours, 2 g in total. October 4. Culture of blood, feces and urine negative. October 9. Temperature restored to the normal. Still no appetite. Culture of blood, feces and urine negative. October 8. Vomitted once. October 10. Culture of feces showed the presence of Eb. typhosa. October 13. Culture of feces still positive for Eb. typhosa. Ever since the pathogenic organismus disappeared from excrete. This was a case, where streptomycin was ineffective.

Case 11. T. S., a 36 years old female. Diagnosis: typhoid fever. High fever continued since the evening of July 8, 1950 with headache and cough. Pneumonia was suspected by the family doctor and penicillin was injected, 2,100 thousand units in total. There was no improvement of the condition became delirious and admitted to the hospital on July 29.

Present status and course: The patient have severe perspiration. The face was red and the conjunctiva hyperemic. The rigidity of the neck (±), Kernig’s sign (±). The tongue was thickly furred. Roseola was observed on the chest and the upper abdomen. Gurgling and pressure pain in the ileo-cecal region. The edge of liver 1.5 finger width below the costal margin palpated with pain. Muscle pain was noticeable on the whole body. Erythrocyte count was 3.50 million per cu. mm.; leukocyte count, 3,800
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and hemoglobin, 71%. Widal's reaction: TH 1:200, TO 1:400, PA 1:25, PB(−). Blood culture negative. Examination of urine revealed positive diazo reaction and albuminuria. The patient had incontinency of feces and urine. August 3. The patient sometimes lost consciousness. Widal's reaction: TH 1:400(±), TO 1:800, PA(−), PB(−). August 4. Beginning on this day, 0.5 g streptomycin was intramuscularly injected every 12 hours, 6 injections in total. August 5. Fever declined slightly. The patient recovered subjectively since the afternoon and incontinency disappeared. August 7. No more headache of lumbago. Eb. typhosa detected in feces. August 9. Eb. typhosa still found in feces. August 14. Temperature declined to normal. Eb. typhosa still found in feces. August 19, 22, 25. Culture from feces for Eb. typhosa all negative. August 25. Left the hospital. In this case, streptomycin was administered in the later stage of disease and the effect was not eclatant and yet it must have been helpful in accelerating the cure of disease. (Fig. 9)

![Fig. 9](Image)

Case No. 11. Typhus abdominalis.

Case 12. N. M., a 26 years old male. Diagnosis: paratyphoid fever. Since August 20, 1950 he felt weakness and loss of appetite. In the morning of August 22 high fever appeared suddenly with chills, headache and lumbago. Admitted to the hospital on the same day. Present status and course: Temperature, 39.4°C with a pulse rate of 86 per minute. The conjunctiva was slightly hyperemic. The tongue was
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furred and the mucous membrane of pharynx hyperemic. Physical as well as roentgenographic examination of the chest revealed no abnormalities. A slight resistance with pressure pain was palpated in the ileo-cecal region. No enlargement of spleen. Erythrocyte count was 4.95 million per cu. mm.; leukocyte count, 5,000 per cu. mm. and hemoglobin content, 98%. Widal's reaction; TH 1:25, TO 1:25, PA 1:50, PB 1:50(±). Examination of urine revealed albuminuria, but negative diazo reaction. Culture was negative for Eb. typhosa or paratyphosa. August 23. Headache and lumbago became severe. Beginning in the afternoon of this day, he was given 0.5 g dihydrostreptomycin every 12 hours for the total of 2 g. An amount of 100 mg of vitamin K bisulfite was intravenously injected simultaneously once a day. August 24. Fever dropped suddenly to the level of 37°C. August 25. He was entirely afebrile. August 26. Widal's reaction: TH 1:25, TO 1:50, PA 1:200(±), PB 1:50. No more recidivation of the disease was observed. (Fig. 10)

Fig. 10

Case No. 12. Paratyphoid Fever

Case 13. H. Y., a 22 years old male. Diagnosis: Paratyphoid fever. Admitted to the hospital on July 22, 1950 with complaints of high fever, headache and lumbago since the day before. Present status and course: Temperature, 40°C with a pulse rate of 84 per minute. Conjunctiva was hyperemic. The tongue was furred and the
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mucous membrane of pharynx strongly hyperemic. Physical examination of the chest revealed no abnormalities except the acceleration of the 2nd pulmonary sound. The abdomen was distended with slight resistance and gurgling in the ileo-cecal region. Erythrocyte count was 4.80 million per cu. mm.; leukocyte count, 3,200 per cu. mm. and hemoglobin content, 98%.

Widal's reaction: TH 1: 25, TO 1 : 25, PA 1 : 400(±), PB 1 : 100(±). Blood culture revealed the presence of Eb. paratyphosa A. Examination of urine: albumen positive, diazo reaction negative. Culture of feces and urine for Eb. paratyphosa negative. July 22. Beginning from the evening, 0.5 g dihydrostreptomycin was injected intramuscularly every 12 hours for a total of 4g. Simultaneously, 100 mg vitamin K bisulfite was injected intravenously once a day. The injection was continued for the following 4 days.

July 24. Temperature showed a moderate decrease. General condition was restored and the patient complained of hunger. July 26. He became afebrile in the afternoon. July 27. Widal's reaction: TH 1: 25, TO 1 : 25, PA 1 : 800(±), PB 1 : 200(±). No more Eb. paratyphosa was found in feces and urine thence. The patient left the hospital on August 4. (Fig. 11)

Case 14. N. S., a 19 years old female. Diagnosis: paratyphoid fever. Admitted to the hospital on February 26, 1951 with complaints of high
fever, severe headache and lumbago since the evening of February 24. During that time, 300 thousand units of penicillin was injected in vain. Present status and course: Temperature, 40.2°C with a pulse rate of 84 per minute. Her face was red with perspiration. The tongue was thickly furred. Physical examination of the chest revealed no abnormalities. A moderate enlargement of spleen with pressure pain was recognized. Slight pain and gurgling in the ileo-cecal region was present. Erythrocyte count was 4.20 million per cu. mm.; leukocyte count, 4,200 per cu. mm. and hemoglobin content, 80%. Widal's reaction: TH 1:25, TO 1:25, PA 1:100(±), PB 1:50(±). Blood culture, negative. February 27. Beginning from the evening, 0.5 g streptomycin was given intramuscularly every 12 hours for a total of 4 g. Further, 100 mg vitamin K bisulfite was intravenously injected once a day. March 1. The patient was entirely free from fever and feeling hungry. March 3. Widal's reaction: TH 1:25, TO 1:50, PA 1:800(±), PB 1:50. Culture of feces and urine negative for Eb. typhosa or paratyphosa. No recurrence of the disease was observed and the patient permitted to leave the hospital on March 15. (Fig. 12)

Fig. 12

Case 15. N. O., a 35 years old female. Diagnosis: paratyphoid fever. On August 18, 1950 she had fever with chills, headache and lumbago.
She lost appetite entirely. The fever continued. Since August 20, she vomitted very often and was exhausted. On August 22 admitted to the hospital.

Present status and course: Temperature 38.2°C with a pulse rate of 90 per minute on admission. She was delirious, in a slight perspiration and tossing about in bed. The conjunctiva was hyperemic and the iris was a little enlarged. The tongue was furred and the mucous membrane of pharynx inflammatory. She complained of cough but physical examination of the chest revealed on particular symptoms, except rough breathing sounds corresponding to the lung hili on both sides. Some roseola were observed on the chest. The abdomen was slightly distended, gurgling and pressure pain in the ileo-cecal region recognized. A moderate splenomegalia was present. Erythrocyte count was 4.00 million per cu. mm.; leukocyte caunt, 3,300 per cu. mm. and hemoglobin content 82%. Widal's reaction: TH 1:25, TO 1:25, PA 1:100, PB 1:100. Blood culture was positive for Eb. paratyphosa A. Examination of urine revealed nothing except positive diazo reaction. Culture of feces and urine, negative for Eb. paratyphosa. August 22. Beginning in the evening, 0.5 g streptomycin was intramuscularly injected every 12 hours for a total of 3.0 g. Simultaneously, 100 mg vitamin K bisulfite was also injected intravenously once a day. August 24.
Blood culture was negative. August 25. Fever declined to the level of 37.0°C. Spleen was no more palpable. August 26. Widal’s reaction: TH 1:25, TO 1:25, PA 1:800(±), PB 1:400(±). Culture of feces and urine negative for Eb. paratyphosa. August 27. Normal temperature. No more recurrence of the disease was observed.

Case 16. T. T., a 32 years old female. Diagnosis: paratyphoid fever. Admitted to the hospital on May 6, 1951 with complaints of fever, headache and lumbago since the day before.

Present status and course: Temperature 38.9°C with a pulse rate of 116 per minute on admission. The tongue was thickly furred. A slight resistance and pressure pain was noticed in the ileo-cecal region but nothing else in the chest and in the abdomen. Splenomegalia was recognized. Erythrocyte count was 5.20 million per cu. mm.; leukocyte count, 8,400 per cu. mm. and hemoglobin content, 77%. Blood culture was negative for Eb. typhosa or paratyphosa. Widal’s reaction: TH 1:60, TO 1:50, PA1: 200, PB1: 500.

Examination of urine revealed positive urobilinogen reaction but nothing otherwise. Culture of feces and urine was negative for Eb. typhosa or paratyphosa. May 7. Beginning at noon, 0.25 g chloromycetin was given to the patient every 4 hours for a total of 2 g and
the treatment had to be discontinued because of shortage of the drug. The injection of 100 mg vitamin K bisulfite was given daily for 4 days simultaneously. May 8. Widal's reaction: TH 1:25, TO 1:25, PH 1:200 (±), PB 1:800 (±). May 9. The temperature showed the tendency to decline but rose again in the afternoon. Beginning at 8 p.m., 0.5 g streptomycin was injected every 12 hours for a total of 2 g. Simultaneously, 100 mg vitamin K bisulfite was intravenously injected daily for 4 days. May 10. She had only slight fever through the whole day. Yet, splenomegaly was manifestly present. She felt hunger. The temperature became normal since May 12 and thence no recurrence of the disease. Culture of feces urine was negative consistently in spite of several repeat examinations.

Case 17. H. O., a 14 years old male. Diagnosis: paratyphoid fever. Admitted to the hospital on May 14, 1950 with a complaint of continued high fever since May 10. Present status and course: Temperature, 38°C with a pulse rate of 90 per minute on admission. The tongue was furred and the mucous mem-

Fig. 15

brance of pharynx hyperemic. Physical examination of the chest revealed no abnormalities. The abdomen was slightly distended. Resistance and pressure pain was recognized in the ileo-cecal region. Moderate spleno-
megalia was present. Erythrocyte count was 4.80 million per cu. mm.;
leukocyte count, 4,800 and hemoglobin content, 83%. Widal's reaction:
TH 1:25, TO (−), PA 1:200, PB 1:100. Blood culture was positive for Eb.
paratyphosa A. Examination of urine revealed no albuminuria but posi-
tive diazo reaction. Culture of feces and urine was negative for Eb.
 typhosa or paratyphosa. May 15. Fever at the level of 38°C continued.
In the evening, roseola appeared on the chest and abdomen. May 16.
From the evening, injection of dihydrostreptomycin every 12 hours was
commenced. Doses of 0.3 g of the drug was administered for the first
3 times, then 0.5 g 4 times. Simultaneously, 100 mg vitamin K bisulfite
was injected once a day for 5 days. May 19. Fever declined to the level
of 37°C. General condition was much improved. May 20. Widal's reac-
tion: TH 1:50, TO (−), PA 1:400(±), PB 1:100. May 22. Afebrile. Cul-
ture of feces and urine negative for Eb. typhosa or paratyphosa. No re-
currence of the disease thence.

DISCUSSION

The data of the above cases are summarized in the following table.

**TABLE 1.**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Day of disease before stm. administration</th>
<th>Amount of stm. used (g)</th>
<th>Culture of blood, urine or feces</th>
<th>Days until defervescence</th>
<th>Effect of streptomycin and other comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. 1</td>
<td>4 y.</td>
<td>6</td>
<td>3.5</td>
<td>−</td>
<td>−</td>
<td>No effect of stm. Healed with chloromycetin.</td>
</tr>
<tr>
<td>No. 2</td>
<td>1 y. 5 m.</td>
<td>12</td>
<td>1.0</td>
<td>+</td>
<td>5</td>
<td>++</td>
</tr>
<tr>
<td>No. 3</td>
<td>3 y. 5 m.</td>
<td>30</td>
<td>3.0</td>
<td>+</td>
<td>−</td>
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</tr>
</tbody>
</table>

**TYPHOID AND PARATYPHOID FEVER IN ADULTS**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (years)</th>
<th>Day of disease before stm. administration</th>
<th>Amount of stm. used (g)</th>
<th>Culture of blood, urine or feces</th>
<th>Days until defervescence</th>
<th>Effect of streptomycin and other comment</th>
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<td>No. 4</td>
<td>30</td>
<td>3</td>
<td>2.0</td>
<td>+</td>
<td>1</td>
<td>++ Vitamin K given simultaneously.</td>
</tr>
<tr>
<td>No. 5</td>
<td>33</td>
<td>5</td>
<td>3.0</td>
<td>+</td>
<td>2</td>
<td>++ do</td>
</tr>
<tr>
<td>No. 6</td>
<td>28</td>
<td>6</td>
<td>3.0</td>
<td>+</td>
<td>4</td>
<td>++ do</td>
</tr>
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<td>No. 7</td>
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<td>7</td>
<td>5.5</td>
<td>−</td>
<td>4</td>
<td>++</td>
</tr>
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<td>No. 8</td>
<td>19</td>
<td>9</td>
<td>2.0</td>
<td>−</td>
<td>2</td>
<td>++</td>
</tr>
</tbody>
</table>
Remarkable effect of streptomycin was recognized in 13 out of 17 cases. In three cases, on which the effect of streptomycin was not recognized, streptomycin treatment was commenced in the later stage of disease. In one case, in which the administration of the drug was begun on the 28th day of disease, there was certainly decline of fever following the treatment, but the effect was not prompt, therefore, it might also be reasonable to consider that the improvement of condition has happened in the stage of natural healing.

It seems that streptomycin should be administered in the early stage of disease, at the latest within 10 days, to expect its marked effect. An exceptional case, however, was observed in an infant suffering from typhoid fever, which was treated with streptomycin without effect, in spite of the administration on the 6th day of disease and was cured with chloromycetin. On the other hand, it was peculiar in Case 16 that chloromycetin demonstrated little effect while streptomycin induced a sudden decline of fever.

Further, it must be taken into consideration that in some instances vitamin K₃ preparation was given simultaneously. We have experienced that the activity of streptomycin to inhibit the growth of Eb. typhosa or paratyphosa is enhanced twice as much or more by combining with vitamin K₃ bisulfite in the concentration of above 1:3,000. But the intravenous injection of the above vitamin in a dose of 100 mg per day is obviously insufficient to maintain such concentration in the recipient individual, therefore, the direct influence of the vitamin on our favorable
results may be uncertain. Actually, the difference of results between those cases, which were treated with and without the vitamin, is negligible. The defeverescence in the former cases was observed 0.6 day earlier than in the latter cases in average.

In all of our cases, the pathogenic agents disappeared from urine or feces shortly after streptomycin was administered, except in Cases, for example, 10 and 11, in which the therapy did not yield any favorable results.

SUMMARY

Streptomycin is effective for the prompt improvement of typhoid and paratyphoid fever, when it is given in the early stage of disease, at the latest within 10 days. The above fact was verified in 13 out of 17 cases of typhoid and paratyphoid fever, in 3 cases of which the treatment was commenced in the later stage of disease without success.

REFERENCES