CHRONIC SALMONELLOSIS

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This paper describes in 3 patients a syndrome that was associated with infection by salmonella organisms, but was different from commonly recognized salmonellosis in that the onset was protracted, medical care sought late, and the course prolonged, and there was an unusual combination of clinical and laboratory features. These 3 patients were African children aged 8, 9 and 11 years seen in two of the adult wards of a hospital accustomed to the vagaries and varieties of salmonella infection. During the year in which they occurred 52 other cases of salmonellosis were admitted to the same wards. The first of the 3 cases was so unlike known varieties that its nature was not at first recognized; but the 2 subsequent cases resembled the first sufficiently to make the diagnosis of salmonellosis suspected early.

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The cases are described, their resemblance to one another outlined and the differences from known clinical variants of salmonella infection emphasized.

CASE REPORTS

Case 1. M.M., African male aged 8 years

History. 2½ months of fever and generalized body pains, severe for 2 weeks. Swelling around the eyes and of the legs for 10 days.

Physical examination. An ill child with marked oedema of face, trunk and limbs, ascites, a fever of 102·4°F., and pale mucosae. Blood pressure (BP) 120/95 mm.Hg. Marked tachycardia, slight cardiomegaly, and a moderately loud aortic ejection systolic murmur. Jugular venous pressure raised 4 cm. above sternal angle, and the liver edge palpated 4 finger-breadths below the costal margin in the mid-clavicular line.

Initial investigations. Haemoglobin (Hb) 5·1 G.%, mean corpuscular haemoglobin concentration (MCHC) 32%, erythrocyte sedimentation rate (ESR) 80 mm. in 1 hour (Wintrobe), white blood count (WBC) 5,000/c.mm., of which

7% were eosinophils. Red cells normocytic and normochromic. Neutrophils showed toxic degranulation. Platelets present in normal numbers. Thick blood films showed no malarial parasites. Blood urea 60 mg.%, serum albumin 1·1 G.%, serum globulin 4·9 G.%, serum cholesterol 123 mg.%. The urine had a SG of 1010; it contained protein which precipitated as a thick cloud, moderate numbers of pus cells, finely granular casts, and a few red blood cells; a culture of *B. proteus* was obtained from a mid-stream specimen. The stool was free from blood and contained cysts of *G. lamblia*, ova of *Trichocephalus trichiura*, and free forms of *Trichomonas hominis*. Chest films revealed a moderately enlarged heart, prominent hilar shadows, congested lung fields, and a small left pleural effusion. The electrocardiogram (ECG) showed a marked sinus tachycardia and T-wave inversion in leads V3–6, standard leads 1 and 2. The corrected Q-T interval was 0·51 seconds.

Progress. The patient was considered to have glomerulonephritis that had begun 2½ months and become severe 2 weeks before admission. BP on the 3 days after admission was 130/95, 100/80, and 110/80 mm.Hg and thereafter remained at normal levels. He was given penicillin, 500,000 units *b.d.* Further urine specimens continued to show numbers of granular casts and pus cells; after the first week the continued presence on culture of *B. proteus*, and *B. coli*, led to the diagnosis of a complicating pyelonephritis. This was treated with oxytetracycline and then sulphatriad without change in the fever or urinary findings, but the blood urea declined 1 week after admission to 34 mg.%. The persistent anaemia needed correction by transfusion on 3 occasions. Ten days after admission the spleen became palpable. During the third week treatment was changed to chloramphenicol, 250 mg. 6-hourly for 7 days, and at this time the fever and tachycardia began to settle and the murmur waned. However, further chest films showed patchy clouding in both lung fields consistent with active miliary tuberculosis. Chest screening showed the cardiac enlargement to involve both ventricles, which pulsated poorly. Streptomycin, 0·5 G. twice daily and isoniazid 100 mg. 3 times daily, were substituted and continued for 6 weeks. The fever soon returned after the chloramphenicol was stopped and the patient at this time was still ill, the anaemia unimproved. ECG showed return of the T wave to normal only in lead 1. Difficulty with the diagnosis of miliary tuberculosis was caused by absence of response to antituberculosis treatment and by a negative response to tuberculin 1/1000. However, the urine returned to normal. Biopsy of an inguinal lymph node showed only reactive hyperplasia. When the failure to respond became evident, the following further investigations into the fever were made: Thick blood films again revealed no malarial parasites, LE cells were not found, a 24-hour specimen of urine failed to give a culture of *M. tuberculosis*, and the low serum-albumin and high globulin levels persisted. The zinc turbidity was 32 units, thymol turbidity 18 units and cephalin cholesterol ++++. The ESR remained high, and the WBC at this time was 11,000/c.mm., of which eosinophils formed 20%. Brucella agglutinins were not detected. Two blood cultures 6 weeks after admission grew *S. paratyphi A*, and the Widal reaction showed a titre of 1:1280 to *S. typhi O* and 1:640 to *S. paratyphi AH*. This titre was maintained 2 and 6 weeks later. Treatment with chloramphenicol, 500 mg. 6-hourly, was given for 8 days, again with remission of fever. For the second time, however, the fever returned, and was finally terminated by a third course of chloramphenicol 500 mg. 6-hourly for 10 days. At this time the anaemia abated as well. Stool and urine cultures were repeatedly negative. After clinical recovery chest films still showed slight enlargement of hilar glands and patchy clouding in the right middle lobe; the heart was normal in size. ECG now showed normal T waves over the left chest, and in the standard leads, but T inversion in leads V1-3. An intravenous pyelogram after recovery was normal.

Summary. An 8-year-old African child presented with a 2½-months history as a case of glomerulonephritis with a high fever, severe anaemia and hepatomegaly. The fever was thought initially to be due to complicating pyelonephritis, later to tuberculosis. Treatment for these conditions gave no improvement. Six weeks after admission, i.e. 4 months after onset, the diagnosis of paratyphoid-A septicaemia was made by blood culture and Widal reaction. Chloramphenicol in 3 courses was necessary to control the infection. Other features of the disease were severe abnormalities in the liver-function tests, changing radiological appearances in the lungs, and a mild eosinophilia developing after the start of chloramphenicol therapy. The spleen became palpable during the course of the illness.

Case 2. N.M., African male aged 11 years

History. Two months of swelling of the legs, anorexia, fever and sweating, dyspnoea on exertion, palpitations, and an unproductive cough.

Physical examination. An ill child with marked oedema of the ankles and sacrum, ascites, and pale mucosae; tongue furred, temperature 103°F. Pulse rate 120 per minute, blood pressure 120/70 mm.Hg. Jugular venous pressure slightly raised; ejection systolic murmur of moderate intensity at base of heart. Liver edge palpable 2½ finger-breadths below costal margin in mid-clavicular line, and spleen enlarged to 2 finger-breadths below left costal margin. At the lung bases dullness to percussion and fine crepitations were present.

Initial investigations. Hb. 5·8 G.%, MCHC 31%, ESR 77 mm. in 1 hour. WBC 6,000/c.mm. (10% eosinophils). The blood film showed toxic changes in the neutrophils, platelets in normal numbers, and normochromic red cells with slight anisocytosis. Thick blood films failed to reveal malarial parasites. Blood urea 56 mg.%, serum bilirubin 0·8 mg.%, serum albumin 1·7 G.%, serum globulin 6·0 G.%, serum alkaline phosphatase 7 KA units; zinc turbidity 27 units and thymol turbidity 11 units. The urine contained protein which precipitated as a moderate cloud, moderate numbers of pus cells, coarsely granular and hyaline casts, and red cells. On culture no growth was obtained. The stool was free from blood and contained ova of ascaris, *Trichocephalus trichiura* and Ancylostoma, cysts of *E. coli*, and free forms of *Chilomastix mesnili* and *Trichomonas hominis*. Chest films revealed a slightly enlarged heart and congested lung fields. ECG showed a sinus tachycardia and T-wave inversion in leads V1-2.

Progress. There was no response to treatment with penicillin, 1,000,000 units 6-hourly for 6 days, digitalis, and a mercurial diuretic. A blood culture taken on admission grew *S. paratyphi A;* when this was known a change was made to chloramphenicol, 500 mg. 8-hourly for 9 days, followed by 250 mg. 6-hourly for 27 days more. The Widal reaction at the same time showed a titre to *S. typhi O* of 1:1280, and *S. paratyphi AH* of 1:320. There was no reaction to *S. typhi H* or *S. paratyphi BH*.

Fever quickly remitted and the patient improved, but a minor pyuria continued, and *B. proteus* was cultured from the urine. Anaemia necessitated transfusion on 4 occasions, and an eosinophilia of up to 26% persisted with WBC of 10,000-18,000/c.mm. The Widal reaction to *S. typhi O* and *S. paratyphi AH* ranged up to 1:1280. Further positive blood cultures were obtained on the 1st and 21st days after starting chloramphenicol, the organism being sensitive *in vitro* to chloramphenicol, streptomycin and tetracycline. In investigating the refractory anaemia a reticulocytosis was never found, the serum bilirubin was never raised, and the direct and indirect Coombs tests were negative. The MCHC ranged between 31 and 34%. Ferrous sulphate, 15 gr. daily by mouth, had no effect. The stool contained no blood, and treatment of the intestinal parasites left the blood counts unchanged. Sternal marrow films showed slight diminution in the numbers of red-cell precursors and a slight increase in eosinophils and leucocytes. Another chest film at the end of the first course of treatment now showed patchy consolidation in the right lower lobe, and enlargement of the paratracheal glands on the right, the adenopathy still being present 2½ months later although the parenchymal changes were then absent. Fever soon returned after the first course of chloramphenicol and a second course of 500 mg. 6-hourly was given for 2 weeks more. Again the fever remitted promptly and again after the course it returned. This time, because of the pulmonary changes and a positive Mantoux reaction at 1/1000, therapy

was changed to streptomycin, 0·5 G. daily, and isoniazid, 100 mg. 8-hourly, given for 8 weeks. A mild intermittent fever up to 100°F. continued, and eventually after 6 weeks of antituberculosis treatment tetracycline, 500 mg. 6-hourly for 2 weeks, was added. The residual fever then receded and, apart from isolated minor episodes, remained absent. Nevertheless further positive blood cultures were obtained, one of which had the cultural characteristics of *S. typhi*. Moreover a growth of *S. typhi* was obtained from the urine at this time, the first in the 7 months since admission. *In vitro* tests of the organism showed sensitivity to chloramphenicol, streptomycin and tetracycline. Stool cultures were repeatedly negative. During the whole illness anaemia persisted, with mild leucocytosis and eosinophilia. The serum-albumin level, however, rose from its initial value of 1·7 G.% to 3·9 G.% 2 months after admission; the serum globulin changed little, from 6·0 to 5·1 G.%. At no time were there any bone pains or tenderness, and radiological examination of the spinal column was negative. The basal systolic murmur became insignificant when the fever remitted initially, and no further cardiac murmurs were detected. The patient was eventually discharged after 7 months in hospital. He was readmitted 6 months later, well and afebrile but still with hepatosplenomegaly. *S. paratyphi A* was cultured from the urine, and *S. typhi* from the sternal bone marrow. The urine was otherwise normal. Only *S. typhi O* agglutinated, at 1/160. Hb. 12·7 G.%. Eosinophils 2,800/c.mm. ESR 57 mm. in 1 hour. Sickling tests negative. Liver-function tests unchanged, but chest X-rays and ECG now normal.

Summary. An 11-year-old African boy had a 2-months' history of oedema, fever, dyspnoea and cough. He was found to have hepatomegaly, severe oedema and anaemia. Investigations revealed a marked normochromic anaemia and hypoalbuminaemia. There was mild uraemia and the urinary findings of glomerulonephritis. Multiple stool parasites were present. A blood culture of *S. paratyphi* and a positive Widal reaction were obtained. The fever responded to chloramphenicol in two courses, but relapsed on its cessation and was eventually cleared on streptomycin and tetracycline. *S. typhi* infection was also shown by culture of blood and urine. Chest X-rays revealed a changing picture involving parenchyma and hilar lymph nodes; moderate eosinophilia developed after beginning chloramphenicol. The total febrile course in hospital was 16 weeks; positive cultures were obtained from the blood and marrow 15 months after onset.

Case 3. A.M., African male aged 9 years

History. Six months before admission the patient became ill. He had headaches, abdominal pain, and diarrhoea without passing blood or mucus. These symptoms continued, and 4 months later he noticed gradually increasing swelling of the abdomen with a burning hypogastric pain, dysuria, and frequency of micturition associated with a phimosis. During this last 2 months before admission he had an ill-defined pain over the right scapula, constipation instead of the initial diarrhoea, and shivering attacks and sweats at night.

Physical examination. An ill child, temperature 103°F., with marked mucosal pallor. Pulse rate 130 per minute. BP 120/80 mm.Hg. A few scattered rhonchi in both lung fields and slight tenderness over the right scapula. Abdomen mildly distended; free fluid suspected. Liver edge palpable 3 finger-breadths below costal margin in mid-clavicular line. A minor phimosis was not observed to cause any difficulty.

Initial investigations. Hb. 6 G.%, MCHC 30%, ESR 72 mm. in 1 hour. WBC 9,000/c.mm. (5% eosinophils); mild anisocytosis and anisochromasia, and platelets in normal numbers. Thick blood films showed no malarial parasites. Weil-Felix reaction negative, no brucella agglutination. Serum bilirubin less than 0·8 mg.%, serum albumin 1·4 G.%, serum globulin 6·2 G.%, serum alkaline phosphatase 15 KA units, zinc turbidity 38 units, thymol turbidity 18 units. Urine normal and culture persistently negative. Stool free from blood, and found to contain ova of *Trichocephalus trichiura, Schistosoma mansoni,* and Ancylostoma. Stool culture negative. Radiological examination revealed no abnormality of lung, heart, right scapula or ribs. ECG showed deep T-wave inversion in leads V1–4, and flattened T waves in leads V5–6.

Progress. The patient was at first observed without treatment; he ran a swinging fever up to 104·8°F. and remained ill. Salmonella septicaemia was suspected, but until proof was obtained it was decided to give streptomycin, 0·5 G. daily, and isoniazid, 100 mg. 8-hourly. No effect was observed. Finally 2 weeks after admission a culture of *S. typhi* was obtained from the blood, and the Widal reaction gave a titre with *S. typhi O* of 1:1280, *S. typhi H* 1:2560, and *S. paratyphi BH* 1:40. Reaction to *S. paratyphi AH* negative. Chloramphenicol was therefore given, 500 mg. 6-hourly for 3 days, followed by 250 mg. 6-hourly to a total dose of 24 G. in 21 days. The fever resolved within 24 hours of beginning therapy and remained absent thereafter. *S. typhi* was isolated from the blood on 2 occasions subsequent to the first, both before beginning chloramphenicol, but on no occasion after beginning it. The spleen became palpable 1 week after admission, all observers having failed to feel it before that time. Attempted paracentesis abdominis failed. With clinical recovery the anaemia improved; however, the blood showed an eosinophilia increasing up to 20% of a WBC of 12,000/c.mm. A month after admission the serum albumin had risen to 3·2 G.% and the serum globulin to 6·9 G.%. Serum alkaline phosphatase now 11·9 KA units, zinc turbidity 35 units, and thymol turbidity 12·5 units. At this time (at the end of the chloramphenicol treatment) chest X-rays showed scattered patchy areas of shadowing, interpreted as bronchopneumonia, but there were no physical signs to support this. Liver and spleen remained enlarged. Repeated stool and urine cultures negative for salmonellae. The patient being well and afebrile was discharged; unfortunately he failed to attend for follow-up.

Summary. An 8-year-old African boy became ill 6 months before admission and suffered for varying periods with diarrhoea, headache, abdominal pain and distension, urinary symptoms and fever. Examination showed high fever, severe anaemia, hepatomegaly and, later, splenomegaly. There was no leucocytosis, but a marked liver-function abnormality. Multiple stool parasites were present. *S. typhi* was isolated from the blood, and the Widal reaction was positive. Response to chloramphenicol was immediate but was accompanied by moderate eosinophilia and changing radiological appearances in the lungs.

Summary of Findings in 3 Cases

The 3 patients, aged 8, 9 and 11 years, were all African males. The history of 2, 2½ and probably 6 months duration was of malaise and fever in all, and oedema in 2. One had a cough, and one dysuria and an initiating period of diarrhoea. All were found to have high sustained fever, marked anaemia, and hepatomegaly; splenomegaly was present on admission in 1, and appeared later in the other 2. Two were oedematous, with slightly raised jugular venous pressure, and one of these had an initial diastolic hypertension. All showed severe normochromic anaemia, and high ESR; eosinophils within normal limits on admission, but rising to abnormal levels after treatment was begun. There was hypoalbuminaemia, hyperglobulinaemia and disturbance of serum flocculation tests. The 2 oedematous patients had albumin, casts and cells in the urine, were slightly uraemic, and chest films showed cardiomegaly and pulmonary congestive changes; both had complicating pyelonephritis with urine cultures of *B. proteus*. The third patient complained of dysuria and frequency of micturition but the urine was normal. All had multiple intestinal parasites. They showed changing radiological appearances in the lungs—in all the development of patchy shadowing, in 2 hilar or paratracheal lymph-gland enlargement. Treatment with antituberculous drugs failed to influence the disease. In all chloramphenicol was the only drug that produced a response, but in 2 repeated courses were necessary and in one of these the bacteraemia

was not eradicated but an apparent response was obtained to streptomycin, isoniazid and tetracycline.

DISCUSSION

These cases differ from salmonella infections of known varieties chiefly in chronicity. Their features as described are met with to some extent in the known varieties; their combination in the same patients and their severity are however unusual, and some aspects are very exceptional, notably the eosinophilia.

A feature of salmonella infections that has been noted in recent years is its frequency as a complicating infection in other conditions, usually chronic.[1] It is necessary therefore to examine the possibility that in these cases the salmonellosis was incidental. This is suggested by the chronicity, the eosinophilia, the pulmonary changes, and the possible response in one case to streptomycin, isoniazid and tetracycline.

The recorded finding in typhoid fever is an eosinopenia,[2-4] whereas these cases had normal counts on admission and a later eosinophilia. The late development of the eosinophilia makes it seem unlikely that intestinal parasites were responsible. No improvement was noted in the one case in which an effort was made to eradicate all parasites; the radiological appearances in the lungs were not those of pulmonary ascariasis or schistosomiasis; nor was the clinical syndrome, allowing for superadded salmonella bacteraemia, akin to that seen with systemic parasitization. The possibility that this predisposed to salmonellosis is therefore unlikely.

The pulmonary radiological findings in cases 1 and 2 indicate the possibility that tuberculosis was the basic condition. This can reasonably be excluded in case 1 by the complete lack of response to specific therapy, and by the presence of a response to chloramphenicol. Neither patient produced sputum, and in both culture of the urine for tuberculosis was negative. Case 1 gave a negative tuberculin reaction. In case 2 the possibility remains; there was a positive tuberculin reaction and a slow response to streptomycin and isoniazid to which tetracycline was later added. The appearance and subsequent disappearance of radiological changes reinforces the possibility. However the leucocytosis, eosinophilia and refractory anaemia continued. Since the salmonella isolated was sensitive *in vitro* to streptomycin and tetracycline, the response of the fever could even be regarded as being no greater evidence for a tuberculous than for a salmonella infection.

The renal lesion, both glomerulo- and pyelonephritis, could conceivably have been the predisposing cause in the first two cases; this possibility is considerably reduced by prolongation of the salmonella infection well beyond the resolution of nephritic changes. Salmonellosis as a complication of glomerulonephritis has not been reported; glomerulonephritis and pyelonephritis as complications of typhoid are rare but well recognized phenomena.[5-8] Leptospirosis has been reported as a concomitant disease[1] but no evidence for it was found in these patients. Schistosomiasis has been reported as associated with chronic salmonellosis as the carrier state with localization in the urine. Among our 3 patients many urine cultures for salmonella were negative, only 1 positive. This was in case 2, in which no urinary schistosomiasis was discovered. Case 3, in which there were ova in the urine, had repeated negative urine cultures.

Hepatitis is a frequently reported concomitant of salmonella infection; the association is reviewed by Bennett and Hook.[1] There were marked changes in serum-protein levels and flocculation tests in cases 1 and 2 but no history of jaundice, and the serum bilirubin and alkaline phosphatase levels were normal. The albuminuria may well have contributed to the dysproteinaemia. Nutritional hypoalbuminaemia is a possibility, but no patient had signs ascribable to malnutrition other than the oedema in 2 cases and it has been shown[9] that the severe malnutrition of kwashiorkor does not lead to increased salmonella susceptibility.

Sickle-cell anaemia, malaria, relapsing fever and bartonellosis all cause predisposition to salmonella infection.[3] These conditions are reasonably excluded in all 3 patients. Of them only malaria and relapsing fever are known to occur here, both rarely, and they were excluded by laboratory test.

In summary, therefore, concomitant disease which might predispose to chronic salmonella infection is suggested by the long course of the illness, the eosinophilia, the pulmonary changes, and the indefinite response of the fever to streptomycin and isoniazid, and to tetracycline in one case. However, no other conditions were found that could reasonably be blamed for the persistent infection. If the manifestations are to be ascribed entirely to the salmonella infection, their occurrence in ordinary typhoid and paratyphoid infections needs examination.

The length of history in these cases is considerably greater than is to be expected. Of the orthodox salmonella cases seen in these wards, 1 had had symptoms for 4 weeks before admission, and 3 for 3 weeks. Among recent series, in 7,779 salmonella infections Saphra and Winter[10] describe the history as rarely having a duration of more than 2 weeks. The maximum duration reported by Stuart and Pullen[6] in 360 cases was 18 days before the patient took to bed, although one patient with endocarditis had a 25-days history before admission. None of the older clinicians, with great experience of typhoid fever, describe the long duration here observed,[5] although single cases have been described with similar features. Rabe[11] describes an 11-year-old girl who had a 6-weeks history of oedema and malaise; she was found to have albuminuria and casts in the urine at the onset. Diagnoses of pyelonephritis and nephrotic syndrome were made; staphylococci, *Streptococcus viridans* and *Salmonella bareilly* were cultured from the urine, but further details are lacking. Another case persisting for 3 months has been reported in an adult female.[12] In the septicaemic syndrome which Saphra and Wassermann[13] observed in 44% of *S. choleraesuis* infections in man, there was a duration of the fever of up to several weeks. The 3 present cases resemble *S. choleraesuis* infections in the invasiveness of the organism without gastro-intestinal infection, but lack the tendency to localize in specific organs or areas.

Anaemia is to be expected in typhoid and paratyphoid fevers. Stuart and Pullen[6] show a steady decrease in red-cell counts to the end of the third week, when the average was about 3·2 million per c.mm., and normochromic

anaemia features in all standard texts. The severe anaemia in these patients, with admission Hb. levels of 5·1, 5·8 and 6·0 G./100 ml., is therefore compatible with the infection and its duration. There was no evidence for a haemolytic process as is described by McFadzean and Choa.[14] The hookworm infestation found in case 2 cannot be held responsible for the anaemia, which was not iron-deficiency in type and which persisted after eradication of the infestation.

The eosinophilia has been discussed above and is not satisfactorily explained. The recorded finding of eosinopenia has been confirmed in our own cases of orthodox typhoid fever. On admission the counts in the 3 patients were within normal limits and they only became significantly abnormal after treatment with chloramphenicol in each case. Thus in case 1 the initial indirect counts were 350 and 480 per c.mm.; after the first course of treatment a maximum of 1,320 per c.mm. was reached and after the second course a maximum of 3,300 per c.mm. In case 2 the highest count before treatment was 700 per c.mm. and after the first course of treatment 1,900 per c.mm. They reached a maximum of 3,380 per c.mm. after the second course. In case 3 the pre-chloramphenicol count was 450 per c.mm. in a total count of 9,000 per c.mm. The maximum of 2,400 per c.mm. was reached 3 weeks after starting chloramphenicol. It is of interest that one of the cases of marrow depression associated with chloramphenicol therapy described by Wilson *et al.*[15] had an unusual number of eosinophils in the marrow. It is conceivable that the eosinophilia represents a response to the therapy or to the chronic salmonella infection but such a situation has not previously been reported. The mild leucocytosis involving the granulocytes is not an unusual finding in uncomplicated typhoid fever. On admission each did in fact have the white-cell count expected of the disease—5,000, 6,000 and 9,000 per c.mm.—the increase taking place later.

The hypoalbuminaemia and hyperglobulinaemia are to be expected in any chronic infection but seem particularly severe in these patients. In typhoid fever hepatomegaly occurred in 25% of Stuart and Pullen's 360 cases.[6] They do not give the results of liver-function tests apart from the cephalin flocculation test in 3 of 13 jaundiced patients; this gave a strongly positive reaction.

The diagnosis of glomerulonephritis seems secure in cases 1 and 2, the renal involvement being severer than in simple febrile albuminuria. Barbera[8] has recorded this complication in typhoid, and surveyed the incidence in the literature. The pyelonephritis seen in the same 2 patients is a further relatively uncommon finding in salmonellosis. It was observed in 1·94% of Stuart and Pullen's series,[6] with an additional 2·5% incidence of cystitis. Other authors[7,10] have also reported cases with pyelonephritis.

The clinical and radiological changes in the lungs in typhoid fever have been described by several authors. Stuart and Pullen[6] describe 37 radiological diagnoses of bronchopneumonia among 154 patients and 18 diagnoses of peribronchial thickening or hilar enlargement. Demonts and Seguela[16] describe their findings in 12 cases of typhoid fever—increased hilar shadows, accentuation of the bronchial markings, and in the early stages opacification of the parenchyma, especially at the bases and micronodular shadows.

The combination of cardiomegaly, cardiac murmurs, anaemia, fever, splenomegaly, leucocytosis, and urinary changes, suggests that the nature of the infection may have been subacute bacterial endocarditis. This is unlikely for several reasons: salmonella endocarditis is a highly fatal condition, only 3 recoveries having been recorded.[17] The murmurs were ejection systolic murmurs, to be expected in severe anaemia and fever, and they disappeared as these improved. Stuart and Pullen[6] report systolic murmurs in 31% of their 360 patients with typhoid fever. Cardiomegaly is adequately explained by the nephritis, and the other findings occur in ordinary typhoid infections. The cardiological findings were never disproportionate. Nevertheless subacute bacterial endocarditis was the provisional diagnosis in case 2 and was considered in case 1.

The ECG findings of T-wave inversion over the right chest in 2 patients are non-specific in African children; the inversion across the left chest in 1 patient taken in conjunction with the radiological findings may reflect a myocarditis.

Most of the features of the 3 cases can therefore be said to occur, though uncommonly, in typhoid and paratyphoid fever; the exceptions are the long duration, and the eosinophilia. These uncommon features may stem from the chronicity of the infection, or from the simultaneous operation of some underlying process which investigation failed to reveal. As discussed above, tuberculosis and tissue parasitization seem possible, but the evidence for both is poor.

SUMMARY

Three cases of chronic salmonella infection in young African males are described. The organisms were *S. paratyphi* in one, *S. typhi* in the second, while both were isolated from the third patient. The clinical picture included a high prolonged fever, nephritis in 2, pyelonephritis in 2 and possibly in all, severe normochromic anaemia, hepatosplenomegaly, hypoalbuminaemia and hyperglobulinaemia, multiple intestinal parasites, and changing radiological appearances in the lungs. Chloramphenicol was the only drug used to which the condition consistently responded and eosinophilia accompanied the response in all.

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