TECHNICAL REPORT

26-71

CHRONIC URINARY SALMONELLA CARRIERS WITH INTERMITTENT BACTEREMIA

By

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ABSTRACT

Fifteen Egyptian male farmers aged eight to 29 years, known urinary excreters of S. typhi or paratyphi A, were observed in hospital for periods varying between six to 18 months. Blood cultures were performed twice weekly using a Castaneda type two-phase bottle and 10 per cent ox bile. Urine samples were plated on Selenite media directly. Salmonella typhi or paratyphi A were recovered from the blood in every case though the clinical picture did not resemble typhoid fever. These bacteremic phases were transient and were in some patients accompanied by a low-grade fever with occasional spikes of high fever. All patients were malnourished, debilitated, and had an anaemia refractory to treatment with oral ferrous sulphate. Intravenous pyelography demonstrated damaged urinary tracts caused by schistosomal infection in all patients such as hydronephrosis and hydrourachy, bladder nodular filling-defects, bladder calcification stricture of the ureters, and reflux.

It is suggested that these patients harbour the salmonella organisms in the urinary tracts from which intermittently they are shed intravascularly. Treatment therefore should aim at relieving the biliary obstruction by anti-schistosomal treatment followed by treatment with either ampicillin or chloramphenicol to clear any remaining focus of infection in the kidneys.
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<tr>
<th>KEY WORDS</th>
<th>LINK A</th>
<th>LINK B</th>
<th>LINK C</th>
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<tbody>
<tr>
<td>Urinary Salmonella Carriers, Chronic</td>
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<tr>
<td>S. Typhi</td>
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<td>S. paratyphi A</td>
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<td>Recurrent bacteremic phases</td>
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<td>Urine cultures</td>
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<td>Blood cultures</td>
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<td>Ampicillin</td>
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<td>Chloramphenicol</td>
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<td>Kidney infection</td>
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<td>Egypt</td>
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CHRONIC URINARY SALMONELLA CARRIERS WITH INTERMITTENT BACTERAEMIA

from the Tropical Medicine Department,
U.S. Naval Medical Research Unit No. 3;
the Abbaseia Fever Hospital, Ministry of Public Health;
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WITH INTERMITTENT BACTERAEMIA

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The persistence of viable *Salmonella typhi* in
the human body, probably in the reticuloendo-
thelial system, for prolonged periods with
intermittent shedding of organisms into the
blood-stream has recently been described by
Watson (1967) from South Africa, and by
Neves et al. (1969) from Brazil. Watson (1967)
et al. (Lancet, 1967; Foster, 1967; Bokken- heuser et al., 1967) suggested that it would be
of interest to carry out repeated blood cultures
on known excreting carriers to determine
whether they are also intravascular shedders.

The incidence of urinary salmonella excretors
in Egypt is very high (Miller, 1950). The
condition is related to the damaged urinary
tracts caused by *Schistosoma haematobium*
infection (Miller and Floyd, 1954; Halawani and
Badran, 1958; Hathout et al., 1966). During
the past five years we were therefore easily able
to study over 40 chronic urinary enteric carriers.
Fifteen of these were followed-up in hospital
for six to 12 months and it soon became
evident that these patients not only excrete
*S. typhi* or *S. paratyphi* A in the urine but
periodically, over months, also shed the
organisms in the blood. These recurrent
bacteraemic phases were not necessarily
accompanied by fever and did not clinically
resemble typhoid fever. This paper reviews our
findings in these 15 patients.

Materials and Methods

**Patients:**
Fifteen male Egyptian farmers were from vil-
lages in the Nile Delta, mostly within 100
kilometers of Cairo. They were aged eight
to 29 years and were observed in hospital for
periods of six to 12 months in the period 1966
to 1969. All had haematuria and dysuria of
from three to 15 years' duration and all, except
four, had received previous antischistosomal
treatment. Twelve had active urinary tract
infection with *S. haematobium*. Plain x-ray
films of the bladder and intravenous py-
lography showed that all 15 patients had
damaged urinary tracts. Urines and stools were
examined routinely and haemoglobin and
haematocrits were estimated periodically in
every patient. All were repeatedly excreting
salmonella organisms in the urine. After de-
worming with bephenium hydroxynaphthoate
all patients were given 5 grains oral ferrous
sulphate three times daily.

**Bacteriology:**
*Urine Cultures*—Urine was plated directly
onto selective medium using a 5 mm platinum
loop. In addition, 5 ml of urine was added to
an equal amount of Selenite broth (Difco) and
incubated for 24 hours before plating on the
same selective media. Colony counts were made
by spreading 0.01 ml of urine from a calibrated
loop onto agar plates of Tryptose blood agar
base containing 5 per cent sheep blood and
the bacteria per ml of urine counted after 24
hours incubation. Counts of over 100,000 per
ml were considered significant of a urinary
TABLE. CLINICAL AND LABORATORY DATA.

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age (years)</th>
<th>Period (months)</th>
<th>Hb g./l (000ml)</th>
<th>Titres (multiple)</th>
<th>Blood Cultures (multiply)</th>
<th>Intravenous Pyelography</th>
</tr>
</thead>
<tbody>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>14</td>
<td>8</td>
<td>50</td>
<td>1/1280</td>
<td>S. typhi</td>
<td>Bladder nodular filling-defects.</td>
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<tr>
<td>2</td>
<td>15</td>
<td>7</td>
<td>79</td>
<td>1/1640</td>
<td>S. typhi</td>
<td>Bladder calcification; vesicoureteric reflux.</td>
</tr>
<tr>
<td>3</td>
<td>13</td>
<td>7</td>
<td>65</td>
<td>1/640</td>
<td>S. typhi</td>
<td>Bladder calcification.</td>
</tr>
<tr>
<td>4</td>
<td>15</td>
<td>6</td>
<td>74</td>
<td>1/640</td>
<td>S. typhi</td>
<td>Hydroureters; hydrenephrosis.</td>
</tr>
<tr>
<td>5</td>
<td>12</td>
<td>6</td>
<td>87</td>
<td>1/640</td>
<td>S. typhi</td>
<td>Bladder calcification.</td>
</tr>
<tr>
<td>6</td>
<td>15</td>
<td>12</td>
<td>95</td>
<td>Negative</td>
<td>S. para A</td>
<td>Bladder nodular filling-defects; vesicoureteric reflux.</td>
</tr>
<tr>
<td>7</td>
<td>20</td>
<td>12</td>
<td>57</td>
<td>Negative</td>
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<td>Hydroureters; hydrenephrosis.</td>
</tr>
<tr>
<td>8</td>
<td>13</td>
<td>9</td>
<td>95</td>
<td>1/640</td>
<td>S. para A</td>
<td>Bladder calcification.</td>
</tr>
<tr>
<td>9</td>
<td>16</td>
<td>9</td>
<td>63</td>
<td>1/320</td>
<td>S. para A</td>
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</tr>
<tr>
<td>10</td>
<td>13</td>
<td>7</td>
<td>89</td>
<td>1/640</td>
<td>S. para A</td>
<td>Bladder nodular filling-defects; vesicoureteric reflux.</td>
</tr>
<tr>
<td>11</td>
<td>29</td>
<td>6</td>
<td>96</td>
<td>1/640</td>
<td>S. para A</td>
<td>Hydroureters; hydrenephrosis; bladder calcification.</td>
</tr>
<tr>
<td>12</td>
<td>20</td>
<td>6</td>
<td>73</td>
<td>1/640</td>
<td>S. para A</td>
<td>Stricture left ureter; bladder calcification.</td>
</tr>
<tr>
<td>13</td>
<td>10</td>
<td>6</td>
<td>92</td>
<td>1/460</td>
<td>S. para A</td>
<td>Stricture right ureter.</td>
</tr>
<tr>
<td>14</td>
<td>30</td>
<td>6</td>
<td>71</td>
<td>1/320</td>
<td>S. para A</td>
<td>Bladder calcification.</td>
</tr>
<tr>
<td>15</td>
<td>8</td>
<td>6</td>
<td>56</td>
<td>1/320</td>
<td>S. para A</td>
<td>Bladder nodular filling-defects; vesicoureteric reflux.</td>
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S. para A=S. paratyphi A.

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The Widal titres were usually not markedly elevated. In two patients though the organisms were continuously cultured from blood and urine, the Widal tests were repeatedly negative. In the majority of the other patients the agglutination titres ranged from 1/320 to 1/640. The total white blood count also differed from that usually seen in typhoid and paratyphoid fevers and ranged from 6,000 to 12,000 per c.mm. Five patients were continually excreting S. typhi and 10 patients S. paratyphi A in the urine. In all patients the bacterial counts were over 100,000 per ml of urine signifying a urinary tract infection. Repeated stool cultures in all patients were always negative. Blood cultures obtained from these patients at different times during the observation period grew the same organism as was being excreted in the urine. Repeated blood cultures, however, had to be obtained and usually one out of an average of seven to eight consecutive blood cultures would be positive. A great effort was made to obtain several blood cultures during a temperature elevation, and usually we were more successful in isolating the salmonella during these brief imperceptible periods of pyrexia. All 15 patients had damaged urinary tracts caused by the schistosomal infection. Bladder nodular filling-defects were observed in four patients. Bilateral hydroureters and hydronephrosis were present in seven patients, and eight had advanced bilharzial bladder calcification. Strictures of either right or left ureters were noted in two patients and vesicoureteric reflux was diagnosed in two patients by micturating cystograms (Savage, et al., 1969). Though these patients were de-wormed and given a well balanced hospital diet plus 15 grains of ferrous sulphate daily their general clinical condition and marked anaemia hardly improved even though we observed them for over eight to 12 weeks. Following antibiotic treatment, however (chloramphenicol 50 mg. per kg body weight per day or ampicillin 100 mg per kg body weight per day for 14 days) the urine and blood cultures became negative, the refractory anaemia was corrected and their general clinical condition greatly improved. Unfortunately the majority of these patients relapsed both clinically and bacteriologically a few weeks after completing antibiotic treatment. Details of treatment using combined antischistosomal drugs and antibiotics are the subject of a separate paper (Bassily, et al. in press). Discussion

Attention has been drawn to the prevalence in Egypt of urinary typhoid and paratyphoid carriers by Neva (1949), Walton (1949), and Archer, et al. (1950). None of these authors, however, reported observing the occurrence of bacteraemia in any of their patients. Fifteen years ago, working at NAMRU-3, Miller and Floyd (1954) treated 15 Egyptian farmers with a urinary carrier history of over 12 months, and though their patients were similar to ours, these authors did not report culturing salmonella from the blood of any of their patients. Later still, Halawani, Abdalla, and Badran (1960) reported treating 36 Egyptian urinary salmonella excretors, but though these authors mention that in none of their patients was there clinical or bacteriological evidence of enteric fever at the time of admission, they did not report obtaining blood specimens for culture during the observation period prior to starting antibiotic treatment. Clearly these earlier workers were unaware of the possibility of bacteraemia occurring in their patients. By observing our patients for long periods and obtaining repeated blood specimens for culture we confirmed Watson’s findings (1967) and demonstrated that known urinary excreting carriers may also become intermittent intravascular shedders.

Diagnosis of these patients may be difficult since the clinical picture does not resemble typhoid or paratyphoid fever. A history of urinary schistosomiasis or the presence of S. haematobium eggs in the urine in a debilitated, sick, and anaemic patient not responding after de-worming to oral ferrous sulphate should arouse suspicion and lead to an active search for salmonella organisms in the urine and blood. A urine bacterial count over 100,000 per ml with a damaged urinary tract evident on intravenous pyelography practically confirms the diagnosis. Repeated blood cultures are then necessary to isolate the organisms from the blood.

We disagree with Haithout, et al. (1967) in considering bilharzial hepatic fibrosis to be the cause of the frequently associated septicaemia in these patients; and we cannot agree with Rogers (1968) who refers to these patients as cases of hepatic schistosomiasis comparing them to disseminated salmonellosis in sickle-cell anaemia, malaria, and bartonellosis. The Egyptian urinary salmonella excretor is mainly infected with S. haematobium which affects the urinary system and rarely causes severe liver fibrosis. These patients have damaged urinary tracts in which the salmonella organisms probably reside.
and from which intermittently they are shed intravascularly. We (Bassily, et al. In press) succeeded in curing some of these patients by relieving the bilharzial obstructive uropathy by giving antischistosomal treatment followed by either ampicillin or chloramphenicol treatment to eliminate remaining foci of infection in the kidneys.

Acknowledgements

This research formed part of research project MR005, 20.01-0094A of the Bureau of Medicine and Surgery, Navy Department, Washington, D.C., U.S.A. We are grateful to Dr. R. G. Petersdorf for his encouragement and helpful suggestions and to Dr. V. N. Patwardhan and Dr. W. H. Darby for discussing and reviewing the paper.

Summary

Fifteen Egyptian male farmers aged eight to 29 years, known urinary excretors of S. typhi or paratyphi A were observed in hospital for periods varying between six to 12 months. Blood cultures were performed twice weekly using a Castaneda type two-phase bottle and 10 per cent ox bile. Urine samples were plated on Selenite media directly. Salmonella typhi or paratyphi A were recovered from the blood in every case though the clinical picture did not resemble typhoid fever. These bacteraemic phases were transient and were in some patients accompanied by a low-grade fever with occasional spikes of high fever. All patients were malnourished, debilitated, and had anaemia refractory to treatment with oral ferrous sulphate. Intravenous pyelography demonstrated damaged urinary tracts caused by schistosomal infection in all patients such as hydronephrosis and hydroureters, bladder nodular filling-defects, bladder calcification, stricture of the ureters, and reflux.

It is suggested that these patients harbour the salmonella organisms in the urinary tracts from which intermittently they are shed intravascularly. Treatment therefore should aim at relieving the bilharzial obstruction by antischistosomal treatment followed by treatment with either ampicillin or chloramphenicol to clear any remaining foci of infection in the kidneys.

References