THE ORIGIN OF URINARY ANTIBODIES

By G. R. E. NAYLOR* and R. A. CALDWELL

(With 5 Figures in the Text)

INTRODUCTION

Many workers have examined body fluids other than serum and lymph for the presence of antibodies. Fluids from infected organs frequently show antibody activity to the responsible micro-organism. Agglutinins for *Brucella melitensis* occur in the milk of infected goats (Zammit, 1906; Horrocks & Kennedy, 1906) and for *Rickettsia burneti* in the whey of infected cattle (Stoker & Marmion, 1952). Dysentery stools contain agglutinins for dysentery bacilli (Davies, 1922; Harrison & Banvard, 1947). Agglutinins for cholera vibrios have been demonstrated in the faeces of infected guinea-pigs (Burrows, Elliot & Havens, 1947). The urine of human beings and dogs with leptospiral infections contains agglutinins and lysins for the infecting species (van der Hoeden, 1935, 1936). Archer, Bangham, Dunbar & Ritchie (1950) demonstrated flagellar agglutinins for the carried species in the urine of two urinary enteric carriers. A virus-inactivating agent in the nasal secretion of patients convalescent from influenza was shown to possess some of the characteristics of antibody by Francis & Brightman (1941). Pierce (1947) demonstrated an agglutinin to *Trichomonas foetus* in the vaginal discharge of infected heifers. In all these observations the antibodies have been demonstrated in fluids intimately associated with an infected organ.

The site of production of these antibodies is of interest. They may be derived either from circulating antibodies due to the exudation of plasma from inflamed and damaged tissues, or from cells within the infected organ. If derived from cells in the organ, antibodies may be either produced and released in the organ, or produced elsewhere and released in the organ after transport within cells. The local production of antibody at the injection site of antigen has been demonstrated (Burnet & Fenner, 1949; Oakley, Batty & Warrack, 1951). Parallel titrations of the antibodies in serum and body fluid have shown discrepancies in the time of their appearance and of their peak titres (Horrocks & Kennedy, 1906; Pierce, 1947; Burrows *et al.* 1947) suggesting that antibody in the body fluid is independent of that in the serum. Koshland & Burrows (1950) investigated the quantitative relationship between the serum and faecal antibody response in guinea-pigs immunized with cholera vaccine, and concluded that faecal antibody behaves independently of serum antibody, and therefore is not derived from it.

The British Army, stationed in the Suez Canal Zone, employs Egyptians as cooks, waiters and kitchen boys, collectively termed foodhandlers. Foodhandlers are immunized with T.A.B. vaccine and receive a 'booster' dose annually. Enteric fever is common among the fellahin of Egypt (Miller, 1950) and foodhandlers are examined before employment and annually thereafter for urinary carriage of enteric organisms. The incidence of urinary carriers among foodhandlers tested is

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about 1% (Archer, Goffe & Ritchie, 1952). Many of the carriers continue to excrete the organism daily for periods over a year; these are chronic urinary carriers (Archer *et al.* 1952). This high incidence of urinary enteric carriage may be related to the damage to the urinary tract caused by urinary schistosomiasis which is common in Egypt.

The urine of urinary enteric carriers usually contains antibodies to the flagellar antigen of the enteric species carried (Archer *et al.* 1952). Antibodies to the flagellar antigens of enteric species may also be found in the urine of many Egyptians, who, so far as can be ascertained, are not urinary carriers. The following observations illustrate these points. Two specimens of urine from each of 781 Egyptians applying for employment as foodhandlers were cultured and examined, at a dilution of 1/2, for H agglutinins to *Salmonella paratyphi A*, *Salm. paratyphi B*, *Salm. paratyphi C* and *Salm. typhi*. Six persistent carriers were discovered, all with H agglutinins to the carried species in the urine. Of the remaining 775 men, 135 showed urinary antibodies in one or both specimens to one or more of the suspensions. Six further specimens of urine from each of the 135 men were cultured revealing one carrier of *Salm. paratyphi A* who excreted the organism intermittently. Hence, of 774 Egyptians, 134 (17%) showed H agglutinins to enteric organisms in the urine, and no salmonellae on culture of eight specimens of urine from each of them: it is unlikely that these men were urinary carriers.

Burrows & Havens (1948) report the presence of agglutinins in the urine of human volunteers following a booster inoculation of commercial typhoid vaccine, with titres up to 1/500. In view of this observation, the urine of healthy soldiers was examined, at a dilution of 1/2, for flagellar agglutinins to *Salm. paratyphi A*, *Salm. paratyphi B* and *Salm. typhi*. Urine was examined from 34 men who had received a booster dose of T.A.B. vaccine between 1 and 12 months previously, and from 22 soldiers 3, 7, 14 and 21 days after they had received a booster dose of 0·5 c.c. of phenolized T.A.B. vaccine; and from three soldiers at the same intervals after three doses of phenolized T.A.B. vaccine given at 14-day intervals. No flagellar agglutinins were detected except in one individual who had a slight postural proteinuria. Flagellar agglutinins are rarely present in the urine of healthy individuals who have been immunized with T.A.B. vaccine.

The presence of antibodies in the urine of Egyptians may be due to exudation of plasma or to bleeding into the bladder of an individual with schistosomiasis and circulating antibodies resulting from enteric fever in the past or previous immunization with T.A.B. vaccine. On the other hand they may be due, particularly in urinary carriers, to production or release of antibodies within the urinary tract. Archer *et al.* (1952) suggested that antibodies in the urine of urinary enteric carriers are produced within the urinary tract. Archer & Miller (1952) compared the agglutinin titres of serum and urine from Egyptian urinary enteric carriers with schistosomiasis, and in some instances the ratio of the urine titre to the serum titre was sufficiently low to preclude simple mechanical leakage of whole blood as the sole source of urinary antibody.

In order to elucidate the origin of urinary antibodies, serum and urine were collected at the same time from selected Egyptians, some of whom were urinary

carriers and some non-carriers. These specimens were titrated against H suspensions of various salmonellae. Specific antibodies to salmonella flagellar antigens are probably so alike in physical properties that, however plasma enters urine, the ratio of the urine titre to the serum titre is the same for each antibody. Consequently, a comparison of several serum and urinary H-antibody titres should disclose the origin of urinary antibodies. If the ratio of the urine titre to the serum titre is the same for each antibody, the urinary antibodies merely represent a dilution of plasma in urine, due to either exudation or bleeding; whereas, if one antibody has a disproportionately high titre in the urine compared with other antibodies, local production or liberation of that antibody in the urinary tract is indicated. Antibodies to salmonella H antigens were present in the serum of the Egyptians examined, due to enteric fever in the past or previous immunization with T.A.B. vaccine. In addition, two urinary typhoid carriers were immunized with a *Salm. bovis-morbificans* vaccine. Antibodies were produced and their titres in serum and urine compared with the corresponding titres for *Salm. typhi*, the carried organism.

MATERIALS AND METHODS

Selection of subjects

Serum and urine, for the comparison of antibody titres, were obtained from men selected during the routine examination of Egyptian foodhandlers at the Army Central Medical Laboratory, Fayid.

Non-carriers

During the routine examination of foodhandlers, two specimens of urine from each individual were tested, at a dilution of 1/2, against H suspensions of *Salm. paratyphi A*, *B*, *C* and *Salm. typhi*. Further specimens were examined from any man whose urine contained antibodies. Men were finally selected whose urine consistently contained antibodies to the flagellar antigens of more than one enteric species. These men had probably received T.A.B. vaccine; no salmonellae were isolated from eight specimens of urine and most of them showed ova of *Schistosoma haematobium* in every specimen of urine examined.

Urinary carriers

A small number of urinary carriers, discovered during routine investigations, were employed as labourers and visited the laboratory daily to pass a specimen of urine. These carriers were under regular surveillance for many months.

Urine culture

Urines were collected in sterile glass containers. During the investigation of all Egyptians other than known carriers, the centrifuged deposit of each urine was plated directly on MacConkey's agar. Any salmonellae isolated were identified by their biochemical and agglutination reactions. All techniques used are well recognized and are not described in detail.

The urine from urinary carriers was cultured daily. Direct plating of the uncentrifuged urine on MacConkey's agar gave a heavy growth. Each day the strain isolated was identified by its biochemical reactions and by agglutination of

a formalized broth culture to the titre of a specific H antiserum. It was usually necessary to enhance the motility of the strain by passing it through a Craigie tube.

Examination of urine deposit

The centrifuged deposit was examined microscopically for cells and *Schistosoma* ova. If no eggs could be observed microscopically, attempts were made to observe miracidia. About 1 ml. of urinary deposit was diluted at least tenfold in cool, boiled tap water and the mixture placed in a bright light at 28° C. Under these conditions, ova hatch and motile miracidia can be observed with the naked eye, or with the aid of a hand-lens, using oblique illumination and a black background.

Titration of urinary antibodies

Before titrations were performed, the pH of the urine was determined using B.D.H. universal indicator and a Lovibond comparator. By the addition of a few drops of 1 % sodium hydroxide, the pH was adjusted to 7 to conform with that of the serum. It was stored at +4° C. for ½ hr. and then centrifuged at 3000 r.p.m. for a further ½ hr. to remove insoluble material. Serial twofold dilutions of urine were prepared in saline. Titrations were performed in Dreyer tubes by the addition of 0·5 ml. of each dilution to 0·5 ml. of H suspension. Final dilutions of urine were from 1/2 to 1/256. Controls comprised urine dilutions, 1/2, 1/4 and 1/8 in saline, also volumes of each H suspension in saline. Tubes were placed in a water-bath at 52° C. for 2 hr. with the fluid column one-third immersed. Readings were taken after tubes had stood at room temperature overnight. Titres were recorded as the highest dilution of urine in which agglutination, obvious to the naked eye, and deposition occurred.

Titration of sera

Sera were titrated in the same manner as the urines, and titres expressed in the same way. The final dilutions of sera were from 1/20 to 1/20,480. Sera and urines were titrated on the day of collection.

Antisera and suspensions

Specific salmonella H antisera and H suspensions of *Salm. paratyphi A, B, C* and *Salm. typhi* were supplied by the David Bruce Laboratories. H suspensions of *Salm. bovis-morbificans* in phase 1 and of *Salm. tel-el-kebir* (the organism isolated from subject 10) in both phases, were prepared. The strains were passed through Craigie tubes containing the opposite phase antiserum, inoculated into nutrient broth, grown 6 hr. and formalized.

Preparation of Salm. bovis-morbificans *vaccine*

A recently isolated strain of *Salm. bovis-morbificans* was passed through a Craigie tube containing phase II antiserum. The strain, in phase I, was then grown in nutrient broth for 6 hr. Formalin was added and the culture stored at +4° C. for 3 days. It was then centrifuged, the supernatant discarded and the deposited organisms washed twice in saline. The organisms were finally resuspended in saline, and adjusted to a concentration of 1000 million/ml. by an opacity method, and phenol was added to a concentration of 0·5 %. The vaccine was stored in ampoules at +4° C., and tested for sterility and for susceptibility to agglutination by anti-

sera to both phases of the organism. It agglutinated to the titre of a phase I antiserum but not at all with phase II antiserum. The vaccine stimulated antibodies to antigen *r* (phase I flagellar antigen of *Salm. bovis-morbificans*) and produced no local or general reaction on subcutaneous injection.

EXPERIMENTAL RESULTS

Results of titrations of serum and urine in non-carriers

Titrations were performed on serum and urine from men whose urine regularly contained antibodies to the flagellar antigens of two or more enteric species and had shown no salmonellae on culture of eight specimens. On the day of the experiment each selected man visited the laboratory and emptied his bladder. Half an hour later a sample of blood was collected, and the urine after a further ½ hr. The urine and serum were titrated against H suspensions of *Salm. paratyphi A*, *B*, *C* and *Salm. typhi*. Results of a typical experiment are shown in Fig. 1 (subject 1).

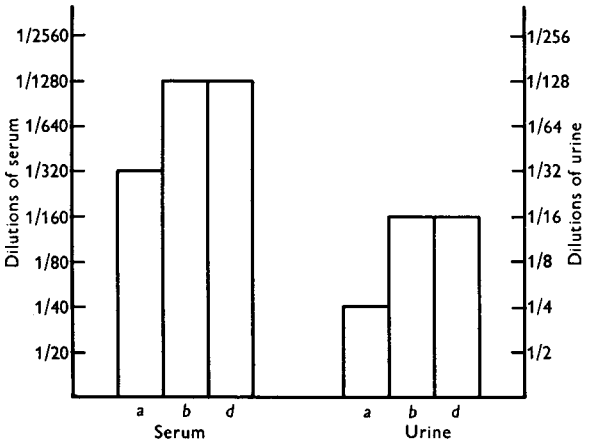

Fig. 1. Subject 1. Non-carrier. In all figures, the flagellar antigens of salmonellae are shown as in the Kauffmann-White Schema, i.e. *Salm. paratyphi A*, *a*. *Salm. paratyphi B*, *b*. *Salm. paratyphi C*, *c*. *Salm. typhi*, *d*. *Salm. bovis-morbificans*, *r*. *Salm. tel-el-kebir*, phase 1, *d*; phase 2, *e*, *n*, *z*15.

The serum contained H antibodies to *Salm. paratyphi A*, *B*, and *Salm. typhi*. Presumably the man had received T.A.B. vaccine. His urine contained H antibodies to all three species. The ratio of the urine titre to the serum titre (80 : 1) was the same for each of the H suspensions, as shown by the similar 'silhouette' of the blocks and suggested that the presence of antibodies in the urine was due to the exudation of plasma or to bleeding into the urine. The urine contained erythrocytes and leucocytes and showed ova of *Schistosoma haematobium* at each examination. Similar results were obtained on four other men (subjects 2–5). The detailed results of the titrations of serum and urine of these men (1–5) with the ratio of the urine to serum titres are shown in Table 1. For each individual the ratio of the urine antibody titre to the serum antibody titre was the same for each of the suspensions used. In these men the various antibodies had the same relation to each other in the urine as in the serum, and the antibodies in the urine probably represent a dilution of plasma in urine.

Results of titrations of serum and urine in carriers

Urinary enteric carriers were examined similarly. A sample of blood and a sample of urine were collected from each and titrated against H suspensions of the four salmonella enteric species. The results obtained in a urinary carrier of *Salm. typhi* (subject 7) are shown in Fig. 2. The serum contained antibodies to the flagellar antigens of *Salm. paratyphi A*, *B* and *Salm. typhi* and the titre to *Salm. paratyphi B* was twice that to *Salm. typhi*. Presumably the man had received T.A.B. vaccine. The urine contained H antibodies to *Salm. typhi* only: none were detectable to

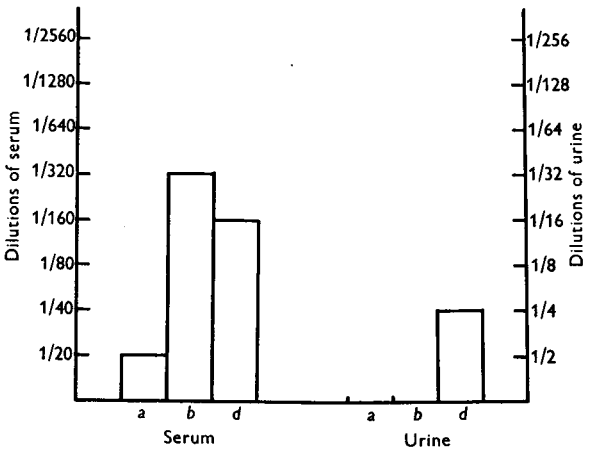

Fig. 2. Subject 7. Urinary carrier of *Salm. typhi*.

Salm. paratyphi B. This result contrasts strikingly with the results obtained in the non-carriers. The urinary antibodies to *Salm. typhi* were obviously not due to a dilution of plasma in urine because antibodies to *Salm. paratyphi B* were absent. They were therefore probably due to production or release of antibodies within the urinary tract. Any specific absorption of antibodies by organisms in the urine would tend to lower the H titre against the species carried and reduce the evidence for local production. Details of the titrations of serum and urine obtained from this subject and from another urinary typhoid carrier with similar results (subject 6) are shown in Table 1.

In non-carriers, the ratio of the urine H titres to the serum H titres is the same in each person, and, in the subjects studied, was 80 or 160. No ratios were found lower than this. On the other hand in carriers, who probably produce antibodies within the urinary tract, ratios were generally lower than this. Ratios of 20, 10 and, in one subject, 5 were observed. If antibodies are derived from the plasma, ratios of this order could only be obtained by marked exudation of plasma or gross bleeding into the urinary tract. No urines obviously contained blood. In one urinary typhoid carrier (subject 8, see Table 1), who had probably not received T.A.B. vaccine, serum and urine contained H antibodies to *Salm. typhi* only. The ratio of the urine H titre to the serum H titre was 10. His urine contained no obvious blood, and urinary antibodies were probably produced within the urinary tract, in view of the low ratio, although this could not be confirmed, in this instance, by comparison with other H antibodies.

Table 1

Subject no.	Reciprocal of serum H titres			Reciprocal of urine H titres			Ratio of urine titre to serum titre			Results of urine culture	Microscopic examination of urine deposit
	Salm. para. A	*Salm. para. B*	*Salm. typhi*	*Salm. para. A*	*Salm. para. B*	*Salm. typhi*	*Salm. para. A*	*Salm. para. B*	*Salm. typhi*		
1	320	1280	1280	4	16	16	80	80	80	Nil pathogenic isolated from 8 specimens	Ova observed at each of 6 examinations
2	640	160	2560	4	<2	16	160	>80	160	Nil pathogenic isolated from 8 specimens	Ova not found after 6 examinations
3	160	160	1280	2	2	16	80	80	80	Nil pathogenic isolated from 8 specimens	Ova observed at each of 6 examinations
4	2560	2560	2560	32	32	32	80	80	80	Nil pathogenic isolated from 8 specimens	Ova observed once in 7 examinations
5	2560	2560	1280	16	16	8	160	160	160	Nil pathogenic isolated from 8 specimens	Ova observed at each of 4 examinations
6	320	160	320	<2	<2	4	>160	>80	80	Regular urinary excretor of *Salm. typhi* for 20 months	Ova observed at 34 of 55 examinations
7	20	320	160	<2	<2	4	>10	>160	40	Regular urinary excretor of *Salm. typhi* for 12 months	Ova not found after 51 examinations. Urine contained erythrocytes and leucocytes daily
8	<20	<20	160	<2	<2	16	—	—	10	Regular urinary excretor of *Salm. typhi*	Ova observed at each of 6 examinations

Results obtained after immunization of urinary typhoid carriers with Salm. bovis-morbificans *vaccine*

Two urinary typhoid carriers were immunized with *Salm. bovis-morbificans* vaccine in order to compare the antibody titres to *Salm. typhi* and *Salm. bovis-morbificans* in both serum and urine and ascertain whether the urinary antibodies to *Salm. typhi* were produced within the urinary tract or were due to a dilution of plasma in urine. *Salm. bovis-morbificans* was selected for the immunizing salmonella because it is rarely isolated in the Suez Canal Zone and the two urinary carriers are unlikely to have been infected with it in the past.

The two urinary typhoid carriers (subjects 6 and 7) had been under surveillance for months before the experiment began. Subject 6 was known to be a regular urinary excretor of *Salm. typhi* for 16 months before the experiment began and subject 7 for 8 months. For 2 months before immunization was started, daily urine culture from these two men yielded a heavy growth of *Salm. typhi*. Urinary antibodies to *Salm. typhi* were regularly present to a titre of 1/4 or 1/8, but antibodies to *Salm. bovis-morbificans* were never observed in urine diluted 1/2. Titration of sera before immunization showed no antibodies to *Salm. bovis-morbificans* at a dilution of 1/20. Subject 6 had urinary schistosomiasis; ova were observed in 34 of 55 urines examined and his urine always contained erythrocytes and leucocytes. *Schistosoma* ova were not found in 51 urines examined from subject 7, nor were miracidia observed on attempting to hatch eggs from large volumes of urinary deposit, but his urine contained erythrocytes and leucocytes daily.

Five injections of *Salm. bovis-morbificans* vaccine were given subcutaneously at fortnightly intervals, 0·2 c.c. at the first injection and 0·4 c.c. subsequently. Both carriers were bled 10 days after the 3rd injection and 13 days after the 5th injection. Urine was collected at the same times. Daily examination of the urine during the period of immunization gave results similar to those obtained before immunization. Antibodies to *Salm. bovis-morbificans* to a titre of 1/2 were observed in the urine on two or three occasions towards the end of the immunization. This may have been due to a slight leak of plasma into these specimens.

The results obtained on titration of the serum and urine from subject 7, 13 days after the 5th injection, are shown in Fig. 3. Antibodies to *Salm. bovis-morbificans* were present in the serum to a titre of 1/1280, and to *Salm. typhi* the titre was 1/320. On the other hand, the urine titre to *Salm. bovis-morbificans* was only 1/2, whereas that to *Salm. typhi* was 1/16. There is a 32-fold difference in the ratios of urine titres to serum titres and the silhouettes of the block diagrams contrast strikingly. The urinary antibodies were not due to a dilution of plasma in urine. Presumably the antibodies to *Salm. typhi* in this man's urine were largely due to local production within the urinary tract and those to *Salm. bovis-morbificans* to a slight leak of plasma into the urine.

Similar results were obtained in subject 6. Details of the titrations and the ratios of urine antibody titre to serum antibody titre are shown in Table 2.

Table 2

Subject no.	Time of comparing serum and urine H titres		H suspensions: *Salm. para. A*	*Salm. para. B*	*Salm. para. C*	*Salm. typhi*	*Salm. bovis-morbificans*
6	Before immunization with vaccine	Reciprocal of serum H titres	320	160	40	320	< 20
		Reciprocal of urine H titres	< 2	< 2	< 2	4	< 2
		Ratio of urine titre to serum titre	> 160	> 80	> 20	80	—
	10 days after 3rd injection of *Salm. bovis-morbificans* vaccine	Reciprocal of serum H titres	320	160	40	320	160
		Reciprocal of urine H titres	< 2	< 2	< 2	8	< 2
		Ratio of urine titre to serum titre	> 160	> 80	> 20	40	> 80
	13 days after 5th injection of *Salm. bovis-morbificans* vaccine	Reciprocal of serum H titres	640	160	40	640	320
		Reciprocal of urine H titres	2	< 2	< 2	32	< 2
		Ratio of urine titre to serum titre	320	> 80	> 20	20	> 160
7	Before immunization with vaccine	Reciprocal of serum H titres	20	320	< 20	160	< 20
		Reciprocal of urine H titres	< 2	< 2	< 2	4	< 2
		Ratio of urine titre to serum titre	> 10	> 160	—	40	—
	10 days after 3rd injection of *Salm. bovis-morbificans* vaccine	Reciprocal of serum H titres	20	160	< 20	160	640
		Reciprocal of urine H titres	< 2	< 2	< 2	4	< 2
		Ratio of urine titre to serum titre	> 10	> 80	—	40	> 320
	13 days after 5th injection of *Salm. bovis-morbificans* vaccine	Reciprocal of serum H titres	20	320	< 20	320	1280
		Reciprocal of urine H titres	< 2	< 2	< 2	16	2
		Ratio of urine titre to serum titre	> 10	> 160	—	20	640

Two unusual cases

Subject 9. Titration of urine and serum from this Egyptian foodhandler gave the results shown in Fig. 4 (for details see Table 3). Antibodies to *Salm. paratyphi C* and *Salm. typhi* were present in the urine, and comparison of the serum and urine

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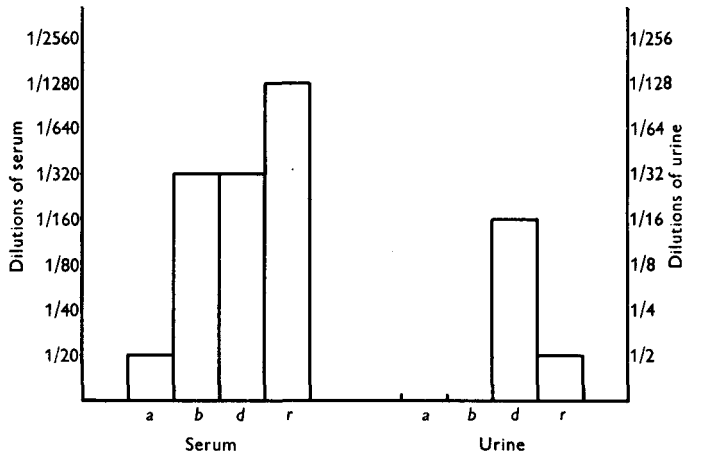

Fig. 3. Subject 7. Urinary carrier of *Salm. typhi* after immunization with *Salm. bovis-morbificans* vaccine.

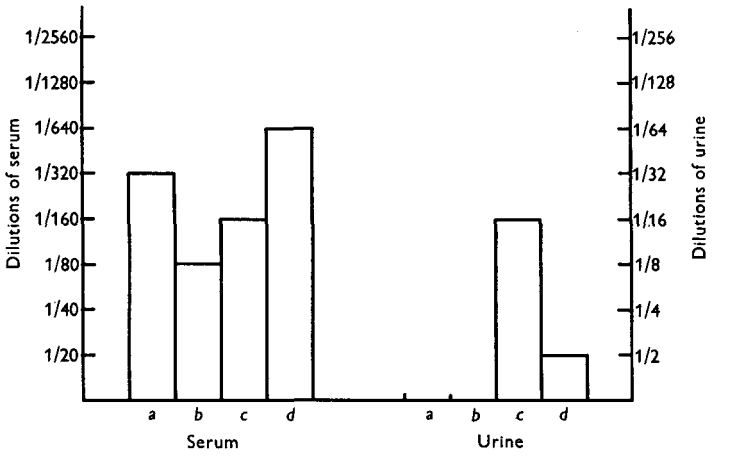

Fig. 4. Subject 9. No salmonellae isolated from eight specimens of urine. Probably a closed or recovered urinary carrier of *Salm. paratyphi C*.

Table 3

Subject no.		H suspensions			
		Salm. para. A	*Salm. para. B*	*Salm. para. C*	*Salm. typhi*
9	Reciprocal of serum H titres	320	80	160	640
	Reciprocal of urine H titres	<2	<2	16	2
	Ratio of urine titre to serum titre	>160	>40	10	320

titres shows that antibodies to *Salm. paratyphi C* were produced within the urinary tract; the presence of antibodies to *Salm. typhi* was probably due to a slight leak of plasma into the urine. *Schistosoma* ova were observed in the urine.

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Although no pathogenic organisms were isolated during the culture of eight specimens of urine, the results obtained suggest that this man either had a closed infection of the bladder with *Salm. paratyphi C* or had been a urinary carrier of *Salm. paratyphi C* in the past. He had probably been infected with *Salm. paratyphi C* in the past because he had antibodies to *Salm. paratyphi C* in his serum, and although he had probably received T.A.B. vaccine it is most unlikely that he had received T.A.B. C. vaccine. Urinary carriers of *Salm. paratyphi C* are not rare in the Suez Canal Zone.

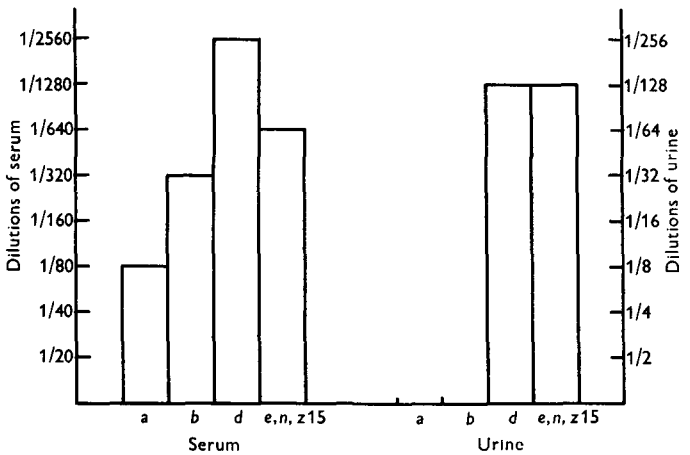

Fig. 5. Subject 10. Urinary carrier of *Salm. tel-el-kebir*.

Table 4

Subject no.		H suspensions				
		Salm. para. A	*Salm. para. B*	*Salm. para. C*	*Salm. tel-el-kebir* phase 1	*Salm. tel-el-kebir* phase 2
10	Reciprocal of serum H titres	80	320	< 20	2560	640
	Reciprocal of urine H titres	< 2	< 2	< 2	128	128
	Ratio of urine titre to serum titre	> 40	> 160	—	20	5

Subject 10. This Mauritian was a urinary carrier of a salmonella not described previously. The species has the antigenic structure XIII, XXIII, *d–e*, *n*, *z*15, and has been provisionally called *Salm. tel-el-kebir*. The results of titration of his urine and serum are shown in Fig. 5 (for details see Table 4). He had probably received T.A.B. vaccine, and scanty *Schistosoma* ova were observed in his urine. Comparison of his serum and urine titres indicates that antibodies to both phases of the carried organism were produced locally within the urinary tract, as antibodies to *Salm. paratyphi B* were not detectable in the urine at a dilution of 1/2.

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DISCUSSION

Antibodies to flagellar antigens of enteric salmonellas are found in the urine of many Egyptians. The experiments described here show that in the majority, who are not urinary carriers, the ratios of urine and serum titres of several H antibodies are the same; the urinary antibodies are simply a dilution of plasma in urine and are probably due to a leakage by exudation or bleeding into the urinary tract in individuals who have received T.A.B. vaccine and have urinary schistosomiasis. In urinary carriers of enteric organisms, antibodies to the flagellar antigen of the carried species are present in the urine and titrations of urine and serum indicate that the concentration of homologous antibody in the urine is disproportionately high when compared with the serum titre of the same antibody and the urine and serum titres of other H antibodies. This may be due to a differential leak of salmonella H antibodies from the plasma into the urine or to local production of antibodies within the urinary tract, sometimes combined with a slight, simple leak of plasma into the urine. Differential exudation of salmonella H antibodies in urinary carriers is most unlikely because salmonella H antibodies are probably very similar in physical properties and simple dilutions of plasma in urine were repeatedly found in non-carriers. It has already been pointed out that absorption of antibodies by organisms in the urine would lower the concentration of homologous antibody and decrease the evidence in favour of local production. The probable explanation of the urine and serum antibody levels found in carriers is that local production or release of antibody occurs within the urinary tract. These carriers that show local production of antibodies all have chronically infected bladders. Most of them have schistosomiasis. It is suggested that the antibodies are produced in areas of cellular infiltration within the bladder wall. This is considered to be an example of production or liberation of antibody by cells at, or close to, the site of infection.

SUMMARY

1. Antibodies to the flagellar antigens of salmonellae are frequently present in the urine of Egyptians.

2. In many individuals, who are not urinary carriers but have schistosomiasis and have received T.A.B. vaccine, these urinary antibodies are derived from the plasma due to exudation or bleeding into the urinary tract.

3. In urinary enteric carriers, the urinary antibodies are due, at least in part, to the local production or release of antibodies within the urinary tract, as shown by the ratios of urine titre to serum titre with different H suspensions.

4. The production of antibodies within the urinary tract is considered to be an example of production or liberation of antibody by cells at, or close to, the site of infection.

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