

Changing epidemiology of human salmonellosis in Hong Kong, 1982-93

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SUMMARY

A comprehensive analysis of the epidemiology of salmonellosis in a major hospital in Hong Kong from 1982-93 is reported. The trend of salmonella isolations over the past 12 years and changes in the occurrence of individual serotypes are delineated. A total of 5328 isolates were analyzed. Groups B (*Salmonella typhimurium* and *S. derby*) and E (*S. anatum*) were the commonest serogroups isolated from the intestinal tract in all age groups. A significant increase in the isolation of group D salmonellae has been observed since 1989. This is accounted for by a substantial rise in *S. enteritidis* isolation as seen in Western countries, despite a concomitant decrease of *S. typhi*. The extraintestinal isolation index (EII) is proposed as an index of the virulence potential of individual serotypes and serogroups. Group D salmonella was found to be the most invasive serogroup. While group D was the predominant serogroup isolated from extraintestinal sites in patients older than 1 year, group B serotypes (especially *S. typhimurium*) were more frequently seen in infants younger than 12 months.

INTRODUCTION

Salmonellosis remains a major public health problem in many parts of the world despite the general improvement in sanitary conditions. Although the incidence of typhoid fever has been decreasing over the years [1, 2], human infections due to nontyphoidal salmonellae has been on the rise in many areas [3-6]. Many countries witnessed a dramatic rise in the isolation of *S. enteritidis* over the past 8 years [7]. In certain countries, *S. enteritidis* has become the commonest serotype isolated [7]. A pandemic of *S. enteritidis* is considered by some authorities to be afoot, but information on this trend is still scanty in this part of the world.

Salmonellosis is still prevalent in Hong Kong with around 2000 reported cases per year (40 cases per 100 000 population). Hong Kong presents a unique setting in this changing pattern of salmonellosis. Within the past four decades, Hong Kong has evolved from a developing area into a highly urbanized city. It is therefore not surprising to conjecture that similar changes in the serotype prevalence might have occurred in Hong Kong as in other developed countries. Increasing tourism and immigration into this locality (over 60 000 immigrants into Hong Kong in the year 1992 from neighbouring countries) may also alter the local

epidemiology of salmonellosis. Furthermore, over 60% of the total food supplies of Hong Kong came from China, where the prevalence of salmonellosis is still relatively high. The local pattern of salmonellosis could therefore be affected by these multiple factors.

Salmonella infection is assuming an increasingly important place in acquired immunodeficiency syndrome (AIDS) patients, in whom it carries significant mortality and poses a particular problem in management. There are currently over 400 HIV-positive patients in Hong Kong [8], and the number is increasing steadily. Hence it would be important to summarize local data on salmonellosis in view of the aforementioned changes. In this paper, we present our experience of human salmonellosis in Hong Kong over a period of 12 years in a major teaching hospital. We also compare the changes in epidemiology with previous reports from the same locality and the virulence potential of various serogroups.

MATERIALS AND METHODS

Records of salmonella isolations by the clinical laboratory of the Department of Microbiology in Queen Mary Hospital from 1982-93 were reviewed. This is a 1350-bed major tertiary care and university teaching hospital serving a regional population of 1.3 million. Repeated isolation of the same serotype from the same site in the same patient was counted as one isolate only. There were no major changes in the culture and identification methods over the period. Stool or rectal swabs were cultured routinely on MacConkey agar, deoxycholate citrate agar (DCA), and xylose lysine deoxycholate (XLD) agar (Oxoid) for the isolation of enteric pathogens. Selenite F broth was also used. Specimens from other sites were cultured using standard procedures [9, 10]. Suspected colonies were identified by standard biochemical method [11]. The identity of isolates from blood culture and from sterile body sites was further confirmed by the AMS GNI card system (AutoMicrobic System, Vitek Systems). Salmonella isolates were serotyped using standard antisera (Wellcome) according to the Kauffmann-White classification scheme (World Health Organization, 1982).

RESULTS

A total of 5328 salmonella isolates from 1982-93 were analyzed, comprising 122 different serotypes. The male to female ratio was 1.09:1. The mean age of the patients was 18 years and the median age was 5 years (range: less than 1 month to 96 years). The highest occurrence was in infants less than 1 year of age, followed by patients in the first decade of life (Table 1). Among those patients aged less than 12 months, the peak occurrence was seen at the twelfth month, which differed from the pattern observed in other countries. A smaller rise in incidence was also noted in the third decade of life. The peak season of isolation has consistently been between July and October every year (figure not shown). 86.9% of the 5328 specimens were cultured from stool (Table 2). The commonest site of extraintestinal isolation was from the blood stream (9.5%), followed by the urinary tract (1.2%), the hepatobiliary system (0.6%) and other sterile body fluids (0.4%).

Table 1. Number of salmonella isolates in different age groups, 1982-93

Age groups (years)	Year																								Total
	1982		1983		1984		1985		1986		1987		1988		1989		1990		1991		1992		1993		
	EI	GI	EI	GI	EI	GI	EI	GI	EI	GI	EI	GI	EI	GI	EI	GI	EI	GI	EI	GI	EI	GI	EI	GI	
< = 1	7	150	7	140	10	216	7	224	15	158	13	106	15	146	18	195	9	155	6	155	10	154	16	242	2174
> 1 to < = 10	13	35	5	40	6	51	14	39	4	45	12	49	5	107	10	78	4	80	3	65	4	58	5	62	794
> 10 to < = 20	11	19	7	15	11	10	6	23	8	19	6	7	7	28	8	28	2	16	3	20	3	18	5	30	310
> 20 to < = 30	15	100	11	71	31	61	13	55	11	25	7	28	8	57	9	56	6	48	4	47	12	41	8	65	789
> 30 to < = 40	4	25	6	25	0	12	6	15	5	19	3	11	9	34	7	29	8	27	7	56	1	37	10	55	411
> 40 to < = 50	5	13	5	17	5	4	0	17	3	10	2	7	3	24	3	14	2	15	4	12	6	20	4	24	219
> 50 to < = 60	8	9	3	14	1	6	2	16	2	12	2	5	1	23	1	26	7	17	5	23	2	19	5	10	219
> 60 to < = 70	8	12	2	8	2	4	3	4	1	9	5	6	1	11	3	18	8	10	4	13	7	16	1	19	175
> 70	7	9	3	7	8	10	3	6	4	8	3	6	4	28	9	16	11	19	14	16	2	19	8	17	237
Grant total	78	372	49	337	74	374	54	399	53	305	53	225	53	458	68	460	57	387	50	407	47	382	62	524	5328

Table 2. *Isolation of salmonella from various body sites*

Specimen	Others						Total
	A	B	C	D	E	Others	
Stool	4	2073	1070	358	1071	54	4630 (86.9%)
Blood culture*	19	110	55	309	9	2	504 (9.5%)
Urinary tract	0	33	12	10	6	1	62 (1.2%)
Hepatobiliary system†	2	2	0	29	0	1	34 (0.6%)
Sterile body fluids‡	1	8	2	7	2	0	20 (0.4%)
Cerebrospinal fluid§	0	1	2	4	1	0	8 (0.2%)
Respiratory secretions	0	3	0	0	0	0	3 (< 0.1%)
Platelet concentrate	0	0	0	2	0	0	2 (< 0.1%)
Genital tract specimens	0	2	0	0	0	0	2 (< 0.1%)
Surgical specimens¶	0	22	14	19	7	1	63 (1.2%)
Total	26	2254	1155	738	1096	59	5328

* Including three isolates cultured from bone marrow.

† Including bile (30), liver biopsy tissue (1), and liver abscess aspiration (1).

‡ Including joint fluid (3), peritoneal dialysate (2), pericardial fluid (1), peritoneal fluid (9) and pleural fluid (5).

§ Including one from subdural fluid.

|| Including a high vaginal swab (1) and endocervical swab (1).

¶ Including aspiration from various abscesses, catheter tips, lymph node biopsies and wounds.

The annual number of salmonella isolates over the 12-year period remained steady (Table 1). The frequency of isolation of groups B, C and E salmonellae over the period did not change significantly. The occurrence of *S. typhimurium* and *S. derby*, the two commonest serotypes overall, remained stable. The most important change occurred in serogroup D in which there was a significant increase over this period. *S. typhi* (286 isolates from extraintestinal and 65 from intestinal sites) and *S. enteritidis* (47 from extraintestinal and 215 from intestinal sites) together made up 83% of all group D isolates. The trends of *S. typhi* and *S. enteritidis* isolation are shown in Fig. 1. Among intestinal isolates, *S. enteritidis* has far exceeded *S. typhi* in recent years as the commonest group D isolate. In the case of extraintestinal isolates, a rising trend for *S. enteritidis* was also seen, which in 1993 approximated *S. typhi* in terms of frequency of isolation. The frequency of extraintestinal isolation of *S. typhi*, on the other hand, showed a declining trend over the years, though a smaller decline in intestinal isolations was also observed.

The frequency of isolation of individual serogroups from intestinal and extraintestinal sites is shown in Fig. 2. Group B salmonella was the commonest serogroup isolated from all sites combined and from the intestinal tract, accounting for 42.2% and 44.7% respectively. Groups A and D were recovered from extraintestinal sites more frequently than from intestinal sites. In particular, group D salmonellae alone accounted for 54.4% of all extraintestinal isolates, of which 75% of the extraintestinal group D isolates were *S. typhi* (286 isolates). Despite the well-recognized virulence of group D salmonellae, a very different pattern of isolation was observed in infants when compared with the older individuals. In infants, group B salmonellae predominated, accounting for 45.2% and 39% of intestinal and extraintestinal isolations respectively.

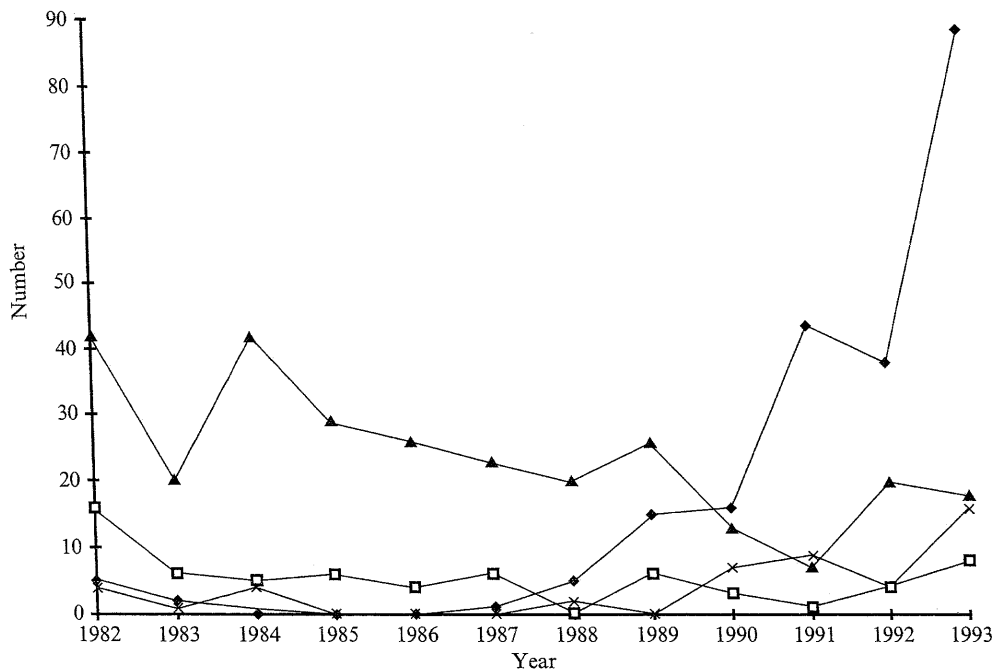


Fig. 1. Comparison of the frequency of isolation of *S. typhi* and *S. enteritidis* from intestinal (GI) and extraintestinal (EI) sources, 1982-93. x, *S. enteritidis* (EI); ◆, *S. enteritidis* (GI); ▲, *S. typhi* (EI); □, *S. typhi* (GI).

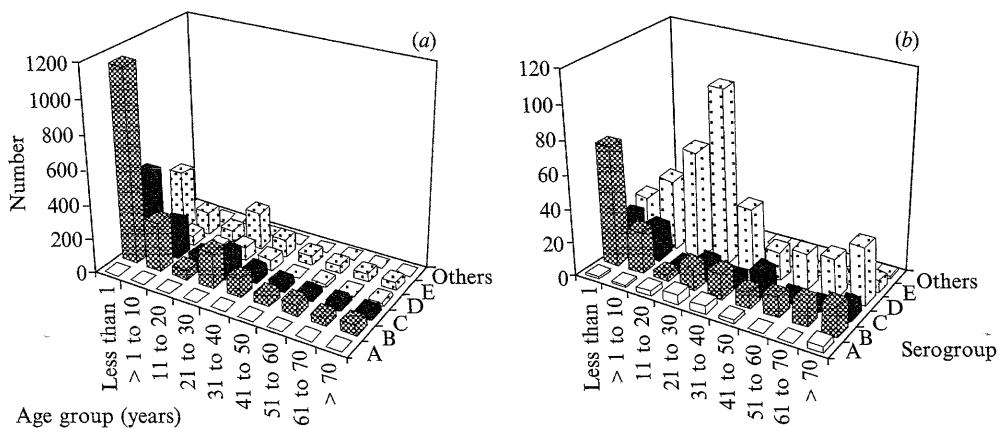


Fig. 2. Intestinal (a) and extraintestinal (b) isolation of various salmonella serogroups.

S. typhimurium, *S. derby* and *S. saintpaul* were the commonest serotypes encountered in both categories. *S. anatum* was another common serotype of intestinal source. The second commonest extraintestinal serotype isolated in infants was *S. panama* (6%), while *S. choleraesuis*, *S. newport*, and *S. typhi* ranked third (4.5%).

In patients older than 1 year, group B salmonellae remained the commonest intestinal isolates (20.9%, accounted for by *S. derby* and *S. typhimurium*). Group

E (*S. anatum* and *S. london*) was the second commonest, the third being *S. enteritidis* (7.5%). For extraintestinal isolates, the five commonest serotypes were *S. typhi* (49.6%), *S. typhimurium* (13.3%), *S. enteritidis* (7.4%), *S. choleraesuis* (6.1%), and *S. paratyphi A* (3.7%).

DISCUSSION

Continuing three decades of surveillance of human salmonellosis in Hong Kong [1, 2, 12, 13], we now describe the changing epidemiology of salmonella infections in the Hong Kong Island district over the past 12 years. Though there might have been changes in the catchment population and patterns of referral over that period, the isolation of non-typhoidal salmonellae has not changed significantly (Table 1). The seasonal trend and age distribution of salmonella-infected individuals was similar to that of other countries [3-5, 14, 15]. Infants were most susceptible to salmonella infection (Table 1). This high incidence continued into the first decade of life. Among those younger than one year, the peak incidence was observed in the twelfth month of life, rather than in the second and third months as reported elsewhere [3-5, 15].

Compared with previous reports [1, 2, 12, 13], there have been significant changes in the epidemiology of human salmonellosis in Hong Kong over the past 40 years. The incidence of typhoid fever has been decreasing since the 1950s [1, 2]. In the 1953-62 period, *S. typhi* and *S. choleraesuis* were the two commonest serotypes isolated. The prevalence of *S. typhi* in intestinal isolation persisted up to the early 60s, when group B salmonellae (mainly *S. derby* and *S. typhimurium*) became the predominant serogroup seen in intestinal isolates up till the present. There has not been any significant change in the frequency of *S. derby* and *S. typhimurium* isolation in the period of the current review. The large number of *S. johannesburg* isolates in 1973-4 was the result of an epidemic due to this serotype in Hong Kong during that period. Subsequent isolation of this serotype has been sporadic. Extraintestinal isolations were still dominated by group D salmonellae, with *S. typhi* heading the list. For non-typhoidal salmonella bacteraemia, *S. typhimurium* since 1973-82, had superseded *S. choleraesuis* as the most frequent blood culture isolate; this trend was still apparent in the period 1982-93.

A pandemic of *S. enteritidis* has been observed worldwide since 1986 [7, 16-18], affecting North America, Britain, continental Europe including Scandinavia, and many other parts of the world. In certain areas, *S. enteritidis* has replaced other serotypes as the most frequently isolated serotype. We have documented similar changes in the isolation of *S. enteritidis* in Hong Kong (Fig. 1). Since 1989 there has been a dramatic rise in *S. enteritidis* isolations in intestinal isolates, a trend which continues. A similar increase has been observed in the extraintestinal isolation of *S. enteritidis*, albeit less marked than for intestinal isolates. In the present review, *S. enteritidis* was the third commonest serotype isolated from extraintestinal sources after *S. typhi* and *S. typhimurium*. If this worldwide trend continues, *S. enteritidis* is very likely to become a major serotype in extraintestinal salmonellosis.

The reason for the surge in *S. enteritidis* isolation in Hong Kong is not yet defined. Studies from North America and Europe indicate that raw or lightly-

cooked eggs or egg products as well as chickens are the most important vehicles in outbreaks of *S. enteritidis* [7, 19-22]. The traditional rearing of poultry in Southern China had been on a small scale with flocks reared by individual peasants. Intensive rearing of flocks started in this region only about 10 years ago. The breeding stocks for layers and broilers of local farms are mostly imported from overseas, chiefly North America (personal communication). Under such circumstances, any prior infection of poultry stocks with salmonella would rapidly disseminate among the flocks.

An important difference in the prevalence of individual serogroups in different age groups was observed for extraintestinal isolations (Table 3). In infants, group B was the most frequently isolated serogroup from extraintestinal sites. Important serotypes included *S. typhimurium*, *S. saintpaul* and *S. derby*. In individuals older than 1 year, *S. typhi* was consistently the commonest extraintestinal serotype isolated. The reason for the difference is not known, though it may be explained by the differences in the feeding habits of infants. It is customary for Chinese parents to feed infants around 1 year of age with congee mixed with minced pork or beef. Raw or undercooked eggs or poultry are not important dietary components of infants. Hence, group D non-typhoidal salmonellae, such as *S. enteritidis*, are less prevalent among infants. Other serotypes, being prevalent in other livestock, would assume greater importance. The adult pattern of exposure, and therefore serotype prevalence, would be established soon after the children take up adult feeding pattern. The predominance of group B salmonellae in infants was also seen in the United States where surveys revealed that *S. heidelberg*, another group B salmonella, was the commonest serotype found in paediatric patients with bacteraemia [23-25].

The ten commonest serotypes accounted for 59.1% of all salmonella isolates (*S. typhimurium*, *S. derby*, *S. typhi*, *S. anatum*, *S. enteritidis*, *S. london*, *S. saintpaul*, *S. manhattan*, *S. blockley*, and *S. agona*, in descending order). The frequency of occurrence of individual serogroups in intestinal and extraintestinal sites (Table 4) agrees with the clinical experience of that certain salmonella serogroups (groups A and D) and serotypes are relatively more invasive. We proposed the term extraintestinal isolation index (EII), which is measured by the number of extraintestinal isolates of a particular serogroup or serotype relative to the total number of isolates from all sites. We believe that the EII is a useful indicator of the invasive potential of a particular serotype or serogroup. We have deliberately included isolates from other extraintestinal sites (such as urine, sterile body fluid and tissues) rather than limiting ourselves to bacteraemic cases in the calculation of EII values. Although bacteraemia accounted for the largest proportion of extraintestinal isolation of salmonella, it would be more representative if salmonella isolations from other sites were considered as well. This is because the bacteraemic phase (which may only be transient) may not always be detected in the investigation of patients with extraintestinal complications of salmonellosis. The EII values confirmed the impression that particular serotypes do have a much higher invasive potential. However, more severe disease was more likely to result in submission of a specimen and the identification of an organism, and the possibility of the index reflecting ascertainment bias in addition to the true severity of disease has to be considered.

Table 3. *Commonest salmonella serotypes in different age groups*

All age groups	No. (%)	Age ≤ 1 year	No. (%)	Age > 1 year	No. (%)
Intestinal	4630 (86.9)	Intestinal	2041 (93.9)	Intestinal	2589 (82.1)
<i>S. typhimurium</i>	658 (14.2)	<i>S. typhimurium</i>	397 (19.4)	<i>S. derby</i>	280 (10.8)
<i>S. derby</i>	565 (12.2)	<i>S. derby</i>	285 (14.0)	<i>S. typhimurium</i>	261 (10.1)
<i>S. anatum</i>	345 (7.5)	<i>S. anatum</i>	107 (5.2)	<i>S. anatum</i>	238 (9.2)
<i>S. london</i>	223 (4.8)	<i>S. saintpaul</i>	93 (4.6)	<i>S. enteritidis</i>	195 (7.5)
<i>S. enteritidis</i>	215 (4.6)	<i>S. london</i>	75 (3.7)	<i>S. london</i>	148 (5.7)
Extraintestinal	698 (13.1)	Extraintestinal	133 (6.1)	Extraintestinal	565 (17.9)
<i>S. typhi</i>	286 (41)	<i>S. typhimurium</i>	24 (18)	<i>S. typhi</i>	280 (49.6)
<i>S. typhimurium</i>	99 (14.2)	<i>S. saintpaul</i>	16 (12)	<i>S. typhimurium</i>	75 (13.3)
<i>S. enteritidis</i>	47 (6.7)	<i>S. derby</i>	12 (9)	<i>S. enteritidis</i>	42 (7.4)
<i>S. choleraesuis</i>	38 (5.4)	<i>S. panama</i>	8 (6)	<i>S. choleraesuis</i>	32 (6.1)
<i>S. derby</i>	24 (3.4)	<i>S. choleraesuis</i>	6 (4.5)	<i>S. paratyphi A</i>	21 (3.7)
		<i>S. newport</i>	6 (4.5)		
		<i>S. typhi</i>	6 (4.5)		

Table 4. *Intestinal and extraintestinal isolation of different salmonella serogroups*

Serogroup	Extraintestinal	Intestinal	Total
A	22	4	26
B	181	2072	2253
C	85	1070	1155
D	380	358	738
E	25	1072	1097
Others	5	54	59
Total	698	4630	5328

Group D remained the most invasive serotype (Table 5). This is true even when only non-typhoidal group D salmonellae (EII = 0.24) were considered. A few serotypes, such as *S. sendai*, scored an EII of 1.00, though there were fewer than 10 isolates in total. Of other major serotypes, the five most invasive serotypes were: *S. choleraesuis* (0.95), *S. paratyphi A* (0.85), *S. typhi* (0.81), *S. panama* (0.27), and *S. enteritidis* (0.18). This finding agreed with the results seen in some other studies in that *S. choleraesuis* was considered a highly invasive serotype with over 70% of its isolates coming from blood cultures [26]. At the other end of the spectrum, group E salmonellae are probably the least invasive of all major serogroups, having an EII of only 0.02.

Three groups of salmonellae may thus be distinguished based on their calculated invasive potential (Table 5): (a) high invasiveness (EII ≥ 0.50 –1.00): including *S. typhi*, *S. sendai*, *S. paratyphi A*, and *S. choleraesuis*; (b) moderate invasiveness (EII ≥ 0.10 –0.50): including *S. panama*, *S. enteritidis*, *S. typhimurium* and *S. saintpaul*; (c) low invasiveness (EII < 0.10): other salmonella serotypes such as groups E and C salmonellae (with the exception of *S. choleraesuis*).

The EII is important in both epidemiological and clinical terms. Although virtually any salmonella serotype is capable of causing extraintestinal disease, this is much more likely for certain serotypes. Since it is impossible to know exactly which patient suffering from intestinal salmonellosis will develop systemic complications, the identity of the isolate may help one to predict such risks. The invasive potential of a particular isolate may be a useful guide to the clinician as

Table 5. *Extraintestinal isolation index (EII) of several important serogroups and serotypes*

By serogroup			By invasive potential	
Serogroup	Serotype	EII	Invasiveness (EI/total)	EII
A	—	0.85	High* (352/423)	≥ 0.50-1.00
	<i>S. paratyphi A</i>	0.85	<i>S. sendai</i>	1.00
B	—	0.08	<i>S. choleraesuis</i>	0.95
	<i>S. typhimurium</i>	0.13	<i>S. paratyphi A</i>	0.85
	<i>S. derby</i>	0.04	<i>S. typhi</i>	0.81
	<i>S. saintpaul</i>	0.12		
	<i>S. agona</i>	0.05	Medium* (176/1232)	≥ 0.10-0.50
	<i>S. stanley</i>	0.05	<i>S. panama</i>	0.27
C	—	0.07	<i>S. enteritidis</i>	0.18
	<i>S. mahattan</i>	0.02	<i>S. typhimurium</i>	0.13
	<i>S. blockley</i>	0.05	<i>S. saintpaul</i>	0.12
	<i>S. infantis</i>	0.06		
	<i>S. newport</i>	0.08	Low*† (109/3157)	< 0.10
	<i>S. choleraesuis</i>	0.95	Other serotypes, e.g.	
D	—	0.51	<i>S. derby</i>	0.04
	<i>S. typhi</i>	0.81	<i>S. newport</i>	0.08
	<i>S. enteritidis</i>	0.18	<i>S. london</i>	0.03
	<i>S. panama</i>	0.27	<i>S. anatum</i>	0.01
	<i>S. sendai</i>	1.00		
	Group D non-typhoidal salmonella	0.24		
E	—	0.02		
	<i>S. anatum</i>	0.01		
	<i>S. london</i>	0.03		
	<i>S. weltevreden</i>	0.08		
	<i>S. krefeld</i>	0.03		
	<i>S. senftenberg</i>	0.05		

* Statistically significant difference between intestinal and extraintestinal isolations of these 3 groups ($P < 0.001$, χ^2 test). EI = number of extraintestinal isolates, total = total number of isolates from all sites.

† Includes only those serotypes with a total number of isolates ≥ 30.

to whether or not a case of intestinal salmonellosis should be treated with antibiotic. It is generally stated that antibiotic treatment of non-typhoidal salmonella gastroenteritis is not warranted in most cases. Nonetheless in our opinion antibiotic therapy should probably be considered if the intestinal isolate is a relatively invasive serotype, such as *S. enteritidis*. This should also raise one's suspicion to look out for extraintestinal complications. Conversely, when infection is due to certain serogroups such as group E, which are relatively non-invasive, expectant management would probably be appropriate under most circumstances unless there was definite evidence of systemic disease.

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