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Salmonella surveillance: a global survey of public health serotyping

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SUMMARY

To better understand the global epidemiology of salmonellosis and the national surveillance programmes used for salmonella infections in humans, we conducted a global survey of the 191 WHO Member States. We gathered information on the total number of salmonella isolates serotyped, and the 15 most commonly isolated serotypes from humans in 1990 and 1995. Of the 104 countries that responded, 76 (73·1%) conducted public health surveillance for salmonella and 69 of these (90·8%) conducted serotyping as part of the surveillance. Fifty-nine countries (56·7% of those responding) provided information about the most commonly isolated serotypes in 1995. Three serotypes, Enteritidis, Typhimurium and Typhi accounted for 76·1% of all isolates reported in 1995. One of these three was the most common serotype identified in 93·2% of countries reporting data for that year. In 1995, Enteritidis was the most frequently isolated serotype in 35 countries, followed by Typhi (12 countries) and Typhimurium (8 countries). The global pandemic of *Salmonella* Enteritidis continued to expand. The mean national proportion of all salmonella isolates that were Enteritidis increased globally from 25·6% in 1990 to 36·3% in 1995. Serotyping is a frequently used component of a public health response to the global challenge of salmonellosis. Support for serotyping as part of national salmonella surveillance, and for rapid international communication of the results via a new WHO electronic website will help target future prevention strategies.

INTRODUCTION

Foodborne infectious diseases have emerged as an important public health problem in many countries in the last decade [1, 2]. The global appearance of enteric pathogens such as *Salmonella* Enteritidis means that similar foodborne diseases may challenge many countries at once. Understanding the global nature of these problems is important to developing surveillance and control strategies for them. To better understand the global epidemiology of salmonellosis and the prevalence of national surveillance programmes for salmonella infections in humans, the World Health Organization (WHO) jointly with the United States Centers for Disease Control and Prevention (CDC), as the WHO Collaborating Center for Foodborne Disease Surveillance, have conducted a global survey of national public health laboratories to learn about current practices regarding salmonella serotyping and to determine the most commonly isolated salmonella serotypes from humans in 1995 and 1990. This is the first such global summary to be published.

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Fig. 1. World map showing countries that provided information about salmonella surveillance practices.

METHODS

A questionnaire was sent through the WHO to the WHO member states in February 1997. Each country was requested to give information about whether or not the country had public health surveillance for salmonella infections (typhoid and/or nontyphoid) and whether or not serotyping of salmonella isolates was performed as a part of the surveillance. We also requested information about the sources of reagents used for salmonella serotyping, the total number of human salmonella isolates in 1990 and 1995, and a list, by serotype and number of isolates, of the 15 most commonly isolated salmonella serotypes from humans in 1995 and 1990. The questionnaires were then returned to CDC for entry and analysis. After entry, data were sent to the responding countries for verification.

The questionnaire was sent to 191 countries in the 6 WHO regions; 45 in the African region, 35 in the American region, 23 in the Eastern Mediterranean region, 50 in the European region, 11 in the Southeast Asian region and 27 in the Western Pacific region.

The results from this survey are based on replies received by August 1998.

RESULTS

Of 191 countries surveyed, a completed questionnaire was received from 104, an overall response rate of 54·5% (Fig. 1). The regional response rates were: African region 60·0%, American region 34·3%, Eastern Mediterranean region 69·6%, European region 50·0%, South-East Asian region 81·8%, and Western Pacific region 55·6%. We received two different responses from four countries (South Africa, Mexico, Uruguay and India). For these countries we merged the responses and treated them as one response for the analysis of serotypes. The first response was received at CDC in March 1997 and the last response was received in August 1998. The number of responses received at CDC peaked in the period May–July 1997 (61%).

Of 104 responding countries, 76 (73·1%) reported conducting public health surveillance for salmonella

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(typhoid and/or nontyphoid). All of the European but only 40% of the responding countries in the Western Pacific region had such surveillance (Table 1). Among countries that performed salmonella surveillance, 69 (90·8%) of 76 reported they conducted serotyping as a part of surveillance. The national laboratories used typing reagents from a variety of sources (Table 1). Among these, 83·8% used commercial sources entirely or in part. Of the 104 responding countries 54 (51·9%) provided information about the most commonly isolated serotypes in 1990 and 59 (56·7%) for 1995.

Of the 104 reporting countries, 57 (54·8%) reported the total number of human salmonella isolates in 1990 and 61 countries (58·7%) in 1995 (Table 1). The total number of human isolates serotyped in these countries was 271440 in 1990 and 290092 in 1995. In 1995 the numbers by region were 730 for Africa (0·3% of the total that year), 52045 for the Americas (17·9%), 3623 for the Eastern Mediterranean (1·3%), 215590 for Europe (74·3%), 9249 for Southeast Asia (3·2%), and 8855 for the Western Pacific (3·1%).

Enteritidis was the most frequently isolated serotype in both 1990 and 1995, followed by Typhimurium and Typhi (Table 2). One of these three was listed as the most commonly isolated serotype in 89·0% of the countries in 1990 and in 93·2% of the countries in 1995. The number of countries reporting Enteritidis as the most commonly isolated serotype increased from 26 in 1990 to 35 in 1995. Significant regional differences were observed. In 1995, Enteritidis was found as the most frequently isolated serotype in 88·0% and 87·5% of the countries in the European and the American regions respectively, but in none of the countries in the African region. Typhi, on the other hand, was the most frequently isolated serotype in 62·5% and 66·7% of the countries in the African and Southeast Asian countries respectively, but in none of the countries in the American, European, or Western Pacific regions. Between 1990 and 1995, the number of countries reporting that Enteritidis was the most commonly isolated serotype, increased in the American, Eastern Mediterranean, Western Pacific and European regions. Aggregating the data globally, Enteritidis and Typhimurium were reported as the two most frequently isolated serotypes in 1995 with a total of 176256 and 40982 isolates respectively (Table 2), followed by Hadar (4756 isolates), Infantis (4701 isolates), Newport (3787 isolates), and Typhi (3572 isolates). All of them were reported among the top 15 serotypes in countries in at least 4 of the regions.

Table 1. Salmonella *surveillance and serotyping, by regions**

Region	Number of responses	Have salmonella surveillance (% of responses)	Serotyping conducted (% of responses)	Source of reagents (% of those providing information about origin of reagents)				Provided information about most common serotypes and numbers (% of responses)		Provided information about the total number of salmonella isolates (% of responses)	
				Own	Other non-commercial	Commercial	Both own and commercial	1990	1995	1990	1995
African	27	16 (59·3)	15 (55·6)			15 (100·0)		7 (25·9)	8 (29·6)	7 (25·9)	8 (29·6)
American	12	10 (83·3)	9 (75·0)	3 (33·3)	1 (11·1)	2 (22·2)	3 (33·3)	8 (66·7)	8 (66·7)	9 (75·0)	9 (75·0)
Eastern Med.	16	12 (75·0)	10 (62·5)			10 (100·0)		4 (25·0)	8 (50·0)	6 (37·5)	9 (56·3)
Europe	25	25 (100·0)	25 (100·0)	7 (29·2)		13 (54·2)	4 (16·7)	25 (100·0)	25 (100·0)	25 (100·0)	25 (100·0)
Southeast Asia	9	7 (77·8)	6 (66·7)		1 (16·7)	4 (66·7)	2 (33·3)	6 (66·7)	6 (66·7)	6 (66·7)	6 (66·7)
Western Pacific	15	6 (40·0)	4 (26·7)			4 (100·0)		4 (26·7)	4 (26·7)	4 (26·7)	4 (26·7)
Total	104	76 (73·1)	69 (66·4)	10 (14·7)	2 (2·9)	48 (70·6)	9 (13·2)	54 (51·9)	59 (56·7)	57 (54·8)	61 (58·7)

* World Health Organization regions [1].

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Table 2. *Number of specific serotypes reported in 1995, by region*

Serotype	Number of isolates	Countries and regions with the serotype listed among the 15 most common serotypes (number of countries with the serotype listed as the most common serotype)						
			Region†					
		Countries*	AF	AM	EM	E	SA	WP
Enteritidis	176256	48 (35)	x	x (7)	x (3)	x (22)	x (1)	x (2)
Typhimurium	40982	47 (8)	x (2)	x (1)	x	x (2)	x (1)	x (2)
Hadar	4756	31	x	x		x	x	x
Infantis	4701	34 (1)	x	x	x (1)	x	x	x
Newport	3787	27		x	x	x		x
Typhi	3572	30 (12)	x (5)	x	x (3)	x	x (4)	x
Agona	3284	32 (1)	x	x		x (1)	x	x
Virchow	3268	26	x			x	x	x
Heidelberg	3227	21	x	x		x		x
Derby	1722	25		x	x	x	x	x
Weltevreden	1202	3					x	x
Thompson	1167	7		x		x		x
Montevideo	1127	13		x	x	x		x
Stanley	1034	12		x		x	x	x
Muenchen	1020	11	x	x		x		x
Braenderup	997	8		x		x		x
Anatum	993	17		x		x	x	x
Paratyphi A, B or C	888	19 (1)	x (1)	x	x	x	x	x
Javiana	854	4		x				
Bovismorbificans	845	14			x	x	x	x
Brandenburg	824	10				x		x
Oranienburg	805	9	x	x		x	x	
Bredeney	748	9				x		
Panama	714	10		x		x	x	
Poona	531	1		x				
Blockley	482	11	x	x		x		x
I 4, 5, 12:i:-	422	1					x	
Saint-paul	409	15		x		x	x	x
Goldcoast	342	6				x		
Livingstone	330	4			x	x		
Senftenberg	253	6	x	x		x	x	x
Tennessee	247	6		x		x		
Rissen	222	1					x	
Ohio	185	6	x		x	x	x	
Cholerasuis	142	2		x			x	
Krefeld	135	1					x	
Mbandaka	130	7	x	x		x	x	x
Hvittingfoss	125	1					x	
Bareilly	118	4				x		x
Moscow	3	1 (1)			x (1)			
Other	2369							
Total	264195							

* Number of countries listing the serotype among the 15 most prevalent.

† World Health Organization regions: AF, African region; AM, American region; EM, Eastern Mediterranean region; E, Europe; SA, Southeast Asia; WP, Western Pacific region.

x = serotype listed among the 15 most common serotypes.

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The three serotypes Enteritidis, Typhimurium and Typhi predominate in all regions and accounted for 76·1% of all salmonella isolates reported from 1995. The mean proportion of all salmonella isolates that were Enteritidis increased globally from 25·6% in 1990 to 36·3% in 1995. This increase was observed in most regions (American 11·3% in 1990/42·6% in 1995, Eastern Mediterranean 2·8%/16·0%, European 47·2%/58·6%, Western Pacific 8·9%/32·3%, African 7·1%/9·6%), but not in the Southeast Asian region (11·9%/2·6%). The trends in the proportion of isolates that were Typhimurium were more variable. This decreased in the American (20·8%/8·0%) and European region (20·2%/17·6%), and increased in the Southeast Asia (9·5%/19·6%), Eastern Mediterranean (4·5%/4·9%), Western Pacific region (17·4%/26·0%), and African region (12·9%/15·9%) between 1990 and 1995. Over the same time interval, the global proportion of isolates that were Typhi decreased 15·3% in 1990 to 12·1% in 1995, and sharp decreases were observed in the American (13·4%/1·9%), Eastern Mediterranean (36·1%/18·9%), and Western Pacific regions (11·8%/2·5%), compared to the African (34·5%/34·2%), European (0·8%/1·3%), and the Southeast Asian region (37·8%/39·1%).

Many countries reported a limited number of serotypes, suggesting a shortage of reagents. For 12 countries, less than three different serotypes were isolated in 1995. Ten of the countries also listed salmonella isolates by serogroups for 1995 in addition to specific serotypes. Of the countries that reported that serotyping was part of their salmonella surveillance, two listed only salmonella serogroups and no specific serotypes for 1995 and eight countries reported neither specific serotypes nor serogroups for 1995. Surveillance was limited in time or scope for some countries. Equatorial Guinea had just established routine salmonella serotyping in 1996. The serotypes reported from Germany are based on isolates from 6 of the 16 Federal states in Germany. Only these six states had a system of reporting salmonella-cases differentiated by serotype. General surveillance for salmonella in South Africa stopped in 1992. The most common serotypes reported for 1995 for that country are based on a limited survey, and *Salmonella* Typhi isolates are not included. Gambia reported that surveillance for salmonella was limited to the Western Region of Gambia and that serotyping was limited to the serotypes Typhi, Paratyphi A, B and C, Typhimurium and Enteritidis).

DISCUSSION

Salmonellosis is a global challenge to public health. This survey indicates that many countries have already established surveillance for salmonellosis for their own public health purposes, and illustrates the practical reality of serotyping as a universal language for laboratory isolate-based surveillance. Almost all countries that performed surveillance for salmonella infections also conducted serotyping as part of that surveillance. It means that useful information is available at regional and global level to describe and address this public health problem. This also means that a global market exists for high quality typing antisera.

Three specific serotypes, Enteritidis, Typhimurium and Typhi accounted for more than 76% of all isolates reported in 1995. One of these three was the most common serotype in 93% of countries reporting data for that year. They thus dominate the epidemiology of salmonellosis in general, and probably represent global phenomena. Among the three, Enteritidis is rapidly increasing in relative prevalence, and in 1995 represented more than 60% of all reported isolates. The global pandemic of Enteritidis infection noted in 1988 is continuing and expanding [3]. Further attention to this particular serotype is warranted in many countries, if the overall burden of salmonellosis is to be reduced. In many countries, Enteritidis infections have been documented to be foodborne, transmitted to humans through eggs or meat from reservoirs in chickens [4]. Efforts to better define the global distribution of subtypes of Enteritidis, the proportion of cases related to egg, poultry or to other sources, and the impact of targeted control measures are needed.

A second nontyphoidal serotype, Typhimurium is already prevalent in Europe and the Americas, and is of growing importance in the Southeast Asian, Western Pacific and African region. It is unclear whether this regional increase reflects the spread of the multiply resistant phage type called definitive type 104, which has emerged as an important zoonotic infection in the United Kingdom and the United States [5, 6]. Further assessment of the geographic distribution of subtype and source is needed to better define the global nature of this problem. Typhimurium is present among many animal species, and like other nontyphoidal salmonella serotypes is most likely to infect humans through contaminated foods of animal origin [7]. However, the appearance of Typhimurium

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as the most common serotype in two African countries is noteworthy, and may be related to the phenomenon of nosocomial transmission of multi-resistant strains of Typhimurium, particularly among persons with impaired immunity [8, 9].

Salmonella Typhi, which causes typhoid fever, is distinct from nontyphoidal salmonella in that it has a human reservoir, and is most common in countries with limited sanitary infrastructure. The decrease in the proportion of salmonellosis that is caused by *Salmonella* Typhi between 1990 and 1995 may indicate that some progress is being made in preventing this infection, perhaps as a welcome consequence of economic development in some parts of the world. The challenge of *Salmonella* Typhi infections is increased by the emergence of increasingly resistant strains, as recently reported from the Indian subcontinent, Southeast Asia and elsewhere [10–12].

This survey has several important limitations. Many countries did not respond, including both developed and developing nations. However, the response rate was generally similar among regions, being lowest in the Americas, owing to the inclusion of the large number of small Caribbean nations in the denominator. Least developed nations might be expected to be less likely to conduct serotype-based surveillance, and thus to be systematically under represented in the results of serotyping. This economic bias means that the proportion of infections due to Typhi may be underestimated. The circumstances of isolate collection are likely to vary widely from one country to another or from one year to another, depending on the availability of laboratory diagnosis, the use of sentinel hospitals and reporting regulations. As the observed changes in serotype frequency may have several explanations, epidemiological studies are needed to clarify them. While the relative frequency of a serotype remains a useful comparative index, the lack of known population denominators means that these isolate data should not be used to calculate incidence. Finally, standardized quality control procedures would be needed to be sure of the interlaboratory comparability of these results. For Enteritidis and Typhimurium, deployment of standard subtyping strategies that could be reproducibly and inexpensively applied in national public health laboratories around the world would be an important advance. For example, bacteriophage typing systems for the serotypes Typhi, Typhimurium and Enteritidis have been developed by the WHO Collaborating Centre for Enteric Phage Typing (London, UK). These systems are used worldwide (they identify PT 4 of *Salmonella* Enteritidis and DT 104 of *Salmonella* Typhimurium) and help to subdivide these three common serotypes. In the United States, molecular subtyping using pulsed field gel electrophoresis is being implemented at all State Health Department laboratories for salmonella and other foodborne pathogens [13, 14].

The broad range of serotypes identified in many countries reflects the multifaceted challenge of salmonellosis and its control. Serotyping is a common procedure that is now in widespread use. Its use in public health laboratories permits rapid detection of clusters and outbreaks, and rapid communication of the results [15]. Investigating such outbreaks provides critical information about how to control them, and how to prevent similar events in the future. Because outbreaks are typically caused by contamination of food or water with a single serotype, routine serotyping of a meaningful sample of clinical salmonella isolates can provide information useful to public health efforts in an individual country. It is the essential starting point for epidemiologic investigations into the source of infections, it supports identification of specific points of contamination, and is needed to monitor the effectiveness of control measures. Serotyping thus represents a critical component of a national public health response to salmonellosis. It is the basic substrate for more detailed laboratory based surveillance strategies, including subtyping and antimicrobial resistance monitoring. It is also the gold standard against which the development of more advanced molecular strategies for subtyping salmonella will be measured.

International outbreaks of salmonellosis have been recognized and successfully investigated as a result of serotyping and rapid communication. For example, in 1996, an outbreak of *Salmonella* Stanley infections affecting Finland and the United States simultaneously was traced to alfalfa sprouts produced from alfalfa seeds obtained from a third country [16]. An outbreak of *Salmonella* Agona infections affecting the United Kingdom and the United States was traced to a peanut snack imported from Israel; notification of Israel led to recognition and control of a nationwide epidemic in Israel caused by this product [17, 18]. The original global dissemination of *Salmonella* Agona was documented in the 1970s following the use of contaminated fishmeal from Peru in chicken feed around the world [19]. The ability to recognize and ultimately to control such outbreaks depends on the coordinated communication as well as common

serotyping language. Efforts to develop such electronic communication links, such as the European EnterNet, the Public Health Laboratory Information System in the United States, or the informal net of collaborators who responded to this questionnaire are likely to identify more such outbreaks in the future [20, 21]. When identification is linked to appropriate actions to investigate and control the source, the result will be improved global public health.

Because of the global interest identified in this survey, the World Health Organization has launched a new web-based surveillance network for salmonella infections, called Global SalmSurv. This is happening with the partnership of CDC and the Danish Veterinary Laboratory to extend the global use of serotyping for salmonella. The WHO *Salmonella* Reference Centre at the Pasteur Institute in Paris is a central laboratory for defining new serotypes [22]. Participating national public health laboratories are joining an e-mail listserv to exchange technical information, and are able to post the annual results of serotyping on a public website (www.who.int/salmsurv). To increase the use of serotyping Global SalmSurv members can participate in an external quality assurance system and regional training course in laboratory methods, organized by WHO. In future, we hope that this simple global surveillance will improve collaboration and communication about the continuing challenges posed by salmonellosis.

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