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## Epidemiological trends of acute hepatitis A in Singapore, 1989-2010

### Introduction

Hepatitis A virus (HAV) is a ribonucleic acid (RNA) picornavirus transmitted by the faecal-oral route, either from person to person or through contaminated food or water. The clinical manifestations vary with age, and its severity and fatality increase with age.<sup>1</sup> HAV is usually silent or subclinical in children, and on a worldwide scale fewer than 5% of infections are recognised clinically.<sup>2</sup> Asymptomatic infection is much more common in children less than six years of age compared with older children and adults.<sup>3</sup> The mean incubation period is approximately 30 days, with a range of 2 to 6 weeks. The infection usually results in an acute self-limited illness and only rarely leads to fulminant hepatic failure. Approximately 85% of individuals infected with HAV have full recovery within 3 months, and nearly all have complete recovery by 6 months.<sup>4</sup>

HAV is endemic in Southeast Asia and many parts of the world. The epidemiological patterns vary, although the differences are linked more to socioeconomic conditions than actual geographical regions. In countries where a lack of adequate sanitation and poor hygiene practices facilitate the spread of infection, subclinical childhood infection is common and most children are immune by the age of 10 years. In developed countries with high standards of hygiene or sanitation, infection is uncommon in the young and it is usually acquired during travel to endemic areas.<sup>5,6</sup> The age-specific prevalence of antibodies to HAV (anti-HAV) in developed countries therefore tends to be a sigmoid curve, with a low prevalence among children and a high prevalence among the elderly.

Singapore has experienced remarkable socioeconomic progress over the last few decades, with a corresponding rise in standards of

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sanitation and living conditions. We undertook a study to review the changing epidemiological trends of acute hepatitis A during the period 1989-2010.

## Materials and methods

The epidemiological records of all laboratory confirmed cases of acute hepatitis A maintained by the Communicable Diseases Division, Ministry of Health, during the period of review were collated and analysed. Data on deaths from acute hepatitis A were also obtained from the Registry of Births and Deaths. For the calculation of age-specific and ethnic-specific incidence rates, the denominators used were the estimated mid-year population of the corresponding years obtained from the Department of Statistics, Ministry of Trade & Industry, Singapore. A case of hepatitis A was defined as a clinically compatible disease serologically confirmed with the presence of anti-HAV IgM.<sup>7</sup> Those who had a recent travel history outside Singapore within 2 to 6 weeks prior to onset of symptoms were classified as imported cases. An outbreak was defined as a cluster of 2 or more cases epidemiologically linked by time, place, and person. Case-control studies were conducted during outbreaks to determine the vehicle and mode of transmission.

To determine the changing seroepidemiology of HAV infection in Singapore, the findings of a serological survey conducted in 1993, based on blood samples collected from apparently healthy children and adults in the community aged 6 months to over 40 years, were compared with those of earlier surveys.

Statistical analyses of the data were carried out using SPSS 17.0 (SPSS Inc., Chicago, IL). For comparison of categorical variables between groups, chi-square or Fisher's exact test was used. To estimate

the extent of risk, odds ratios (OR) and their 95% confidence intervals (CI) were computed. Linear patterns in classification (imported versus indigenous) of hepatitis A cases over the years were assessed using chi-square test for trend. In all data analyses, a *p* value of less than 0.05 was considered statistically significant.

## Results

### Epidemiological characteristics

During the period 1989 to 2010, a total of 3023 cases of acute hepatitis A were reported. There was no death from acute fulminant hepatitis. Overall, 49% of the reported cases were classified as imported, and ranged from 9.3% in 1990 to 81.8% in 2000. The incidence of indigenous cases showed a declining trend during the period of review, from 1.8 cases per 100,000 population in 1989 to 0.3 cases per 100,000 population in 2010. Two prominent spikes were observed in 1992 (7.5 cases per 100,000) and 2002 (4.1 cases per 100,000) (*Fig. 1*).

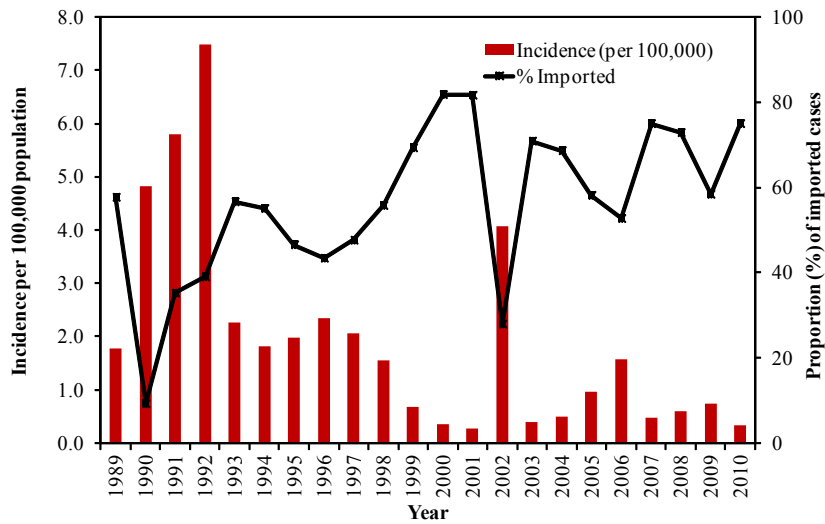
Excluding foreigners seeking medical treatment in Singapore and tourists, the mean annual age-specific incidence rate was highest in the 25 to 34 year age group with an overall male to female ratio of 2.3:1 (*Fig. 2*). Children below 5 years of age accounted for 1.1% of the reported cases.

Among the 3 major ethnic groups of Singapore residents, the mean annual incidence rate was the highest in Indians, followed by Chinese and Malays (*Fig. 3*). However, in 2002, 2006 and 2010, Chinese had the highest incidence rate.

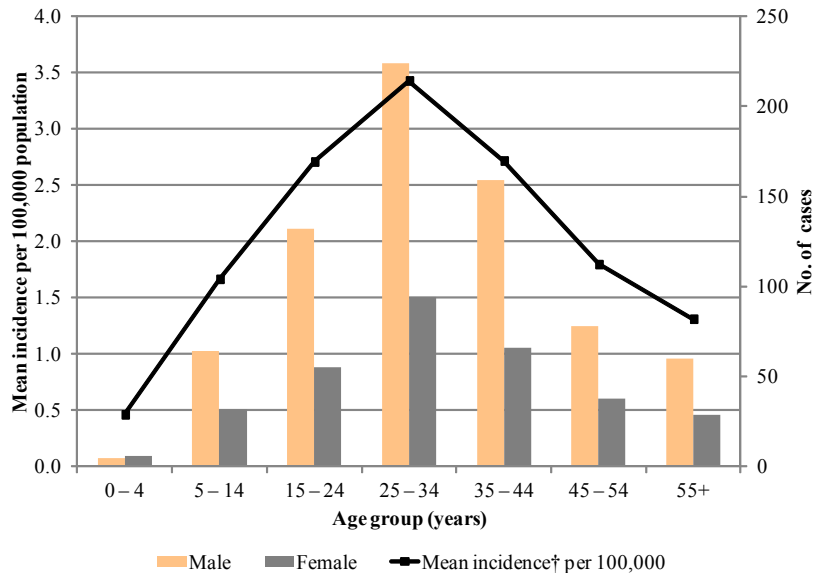
Of the imported cases, the majority were Singapore residents who had contracted the disease



**Figure 1**  
**Incidence (per 100,000 population) of indigenous cases and proportion (%) of imported cases of acute hepatitis A in Singapore, 1989-2010**



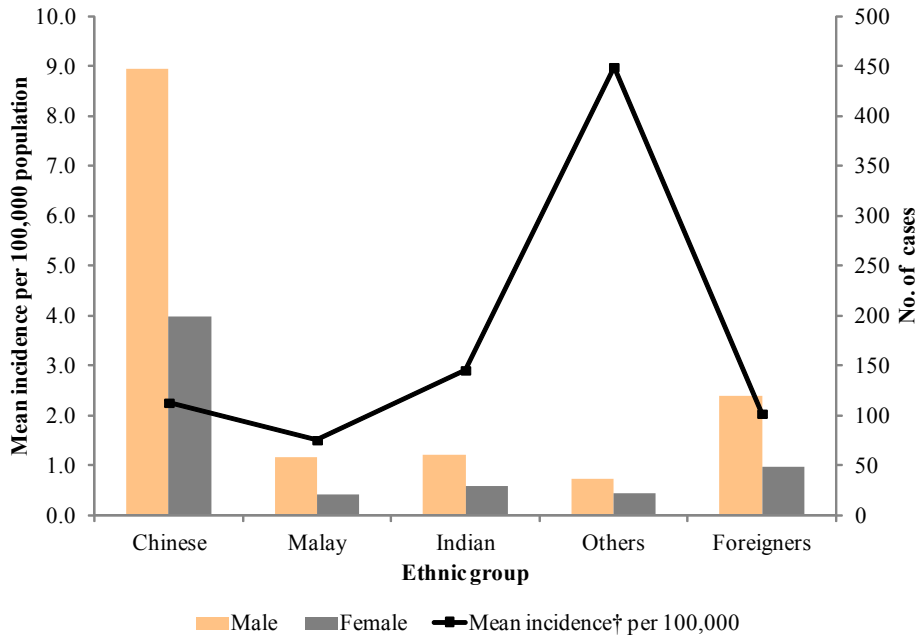
**Figure 2**  
**Age-gender distribution and age-specific incidence (per 100,000 population) of reported acute cases of hepatitis A\*, 1999-2010**



\* Exclude tourists and foreigners seeking medical treatment in Singapore.  
 † Based on estimated mid-year population, 2004.



**Figure 3**  
Ethnic-gender distribution and ethnic-specific incidence (per 100,000 population) of reported acute cases of hepatitis A\*, 1999-2010



\* Exclude tourists and foreigners seeking medical treatment in Singapore.

† Based on estimated mid-year population, 2004.

overseas during vacation/business. They accounted for between 47% and 86% of all imported cases (Fig. 4). The other categories of imported cases were work permit holders (6% to 31%), foreigners seeking medical treatment in Singapore (7% to 33%) and tourists (0% to 5%). Between 1999 and 2010, the proportion of imported cases among Singapore residents decreased significantly while that of the other categories of foreigners combined increased correspondingly ( $p < 0.05$ ). Most of the imported cases contracted the disease from Southeast Asia and the Indian subcontinent (Table 1).

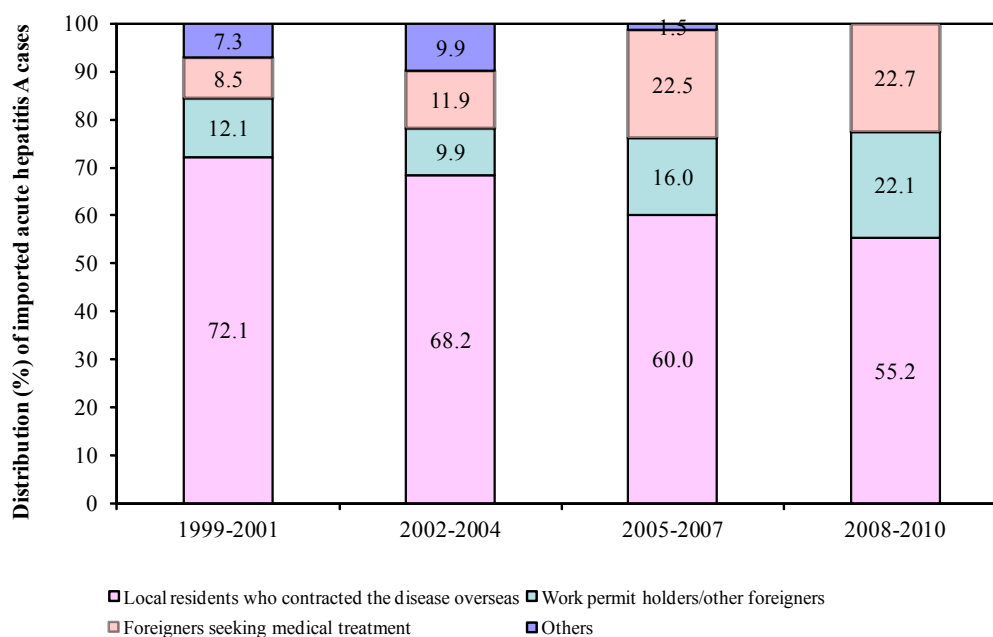
#### Shellfish-associated outbreaks

Three outbreaks occurred during the period of review. In the first outbreak in 1991, the incidence

of hepatitis A was noted to increase sharply from a weekly average of 4 to 16 cases in June. A total of 70 indigenous cases were notified between 18 June and 18 July. No icteric cases were detected through contact tracing. The attack rate was highest in the 15 to 24 (6.7 per 100,000) and 25 to 34 (4.9 per 100,000) year age groups with a male to female ratio of 2.1:1. Of the 3 major ethnic groups, Chinese had the highest attack rate (3 per 100,000), being significantly higher than that of Malays (0.3 per 100,000) ( $p < 0.05$ ). No significant difference was observed between the attack rates of Chinese and Indians (0.5 per 100,000) ( $p > 0.05$ ). Cases occurred sporadically and were not clustered in any specific geographical location by residential address or place of work. No particular food establishment was implicated. For the



**Figure 4**  
**Distribution (%) of imported acute hepatitis A cases by population group, 1999-2010**



case-control study, the cases comprised those with no recent travel history and with a compatible clinical history, raised serum transaminases, and positive anti-HAV IgM. They were interviewed regarding frequency of consumption of a variety of food items such as shellfish, raw fish, raw vegetables, iced drinks, cut fruits and ice cream, between 2 weeks and 2 months prior to onset of jaundice. Controls, matched for age, sex, and ethnicity, were chosen from family members, colleagues or neighbours who had no history of jaundice or travel outside Singapore during the preceding 3 months. Statistical analyses of the case-control study showed that the consumption of raw or partially-cooked imported cockles (*Anadara granosa*) and oysters was significantly associated with the illness (OR 4.1,  $p < 0.001$ ; OR 6.5,  $p < 0.01$ , respectively).<sup>8</sup>

In the second outbreak of 70 cases in September 1992, the epidemiological features were very similar to those of the 1991 outbreak with the highest attack rate among the ethnic Chinese in the 15 to 34 year age group and a male predominance. Case-control study showed that the vehicle of transmission was imported cockles (*Anadara granosa*) ( $p < 0.001$ ). No other types of shellfish such as oysters, crabs and prawns were implicated.<sup>9</sup>

In the last outbreak, a total of 159 indigenous cases were reported between 16 June and 16 November 2002. The epidemiological patterns were similar to those of the previous outbreaks with no clustering of cases in any locality by place of work or residence, and no specific food centre was implicated. Most of the cases (91.8%) were Chinese. The age-specific at-



tack rate was highest in the 25 to 34 year age group with a male to female ratio of 1.5:1. Case-control study showed that consumption of cockles (*Anadara granosa*) and oysters was significantly associated with the illness. Further analysis showed that cases were more likely to have consumed raw or partially-cooked cockles than non-cases after controlling for oyster consumption (OR = 6.0; 95% CI: 2.8 to 13.2). No other types of shellfish and food items were implicated.<sup>10</sup>

### Seroepidemiology

The overall prevalence of anti-HAV IgG in 1993 was 25.9%. Only 2.5% of children and young adults below 25 years of age were seropositive. The age-specific antibody positivity rate increased from 31.1% in the 25 to 34 year age group to 77.0% in the over 45 year age group (Fig. 5). No statistical significant difference in seroprevalence by gender (males 21.2% and females 29.4%) was observed. Among the three major ethnic groups, the prevalence was highest among the Chinese (29.7%) followed by Indians (23.4%) and Malays (4.3%).<sup>11</sup>

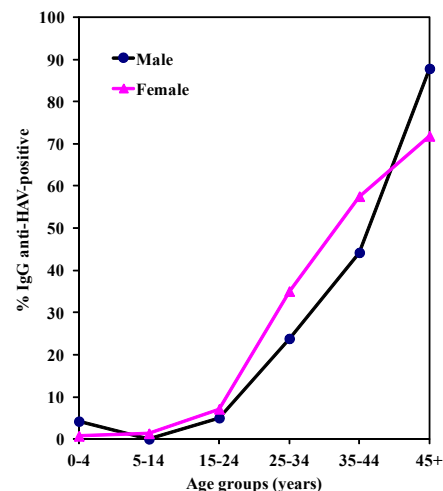
### Discussion

The incidence of indigenous acute hepatitis A cases had declined significantly from 1.8 cases per 100,000 population in 1989 to 0.3 cases per 100,000 population in 2010. Its incidence is comparable to that of other developed countries; e.g. it ranked between France (1.64 per 100,000 in 2007) and Italy (1.97 per 100,000 in 2007).<sup>12</sup> The majority (58% on average from 1999 to 2010) of the reported cases among Singapore residents were imported. This is similar to the situation in other industrialised countries, where travel accounts for a significant proportion of hepatitis A cases.<sup>13-15</sup>

**Table 1**  
Distribution (%) of imported hepatitis A cases by country of origin, 1999-2010

Country of origin	% (n=705)
<i>Southeast Asia</i>	
Brunei	0.1
Cambodia	0.4
Indonesia	27.4
Malaysia	20.1
Myanmar	1.6
Philippines	3.1
Thailand	6.2
Vietnam	0.7
<i>Indian subcontinent</i>	
Bangladesh	4.1
India	21.3
Nepal	1.6
Pakistan	2.0
Sri Lanka	0.3
<i>Other Asian countries</i>	
China	3.8
Hong Kong SAR	1.0
Japan	0.3
South Korea	0.4
Syria	0.1
Taiwan	0.4
Uzbekistan	0.1
<i>Other countries</i>	
	4.8

**Figure 5**  
Age-gender distribution of IgG antibody to HAV in Singapore, 1993



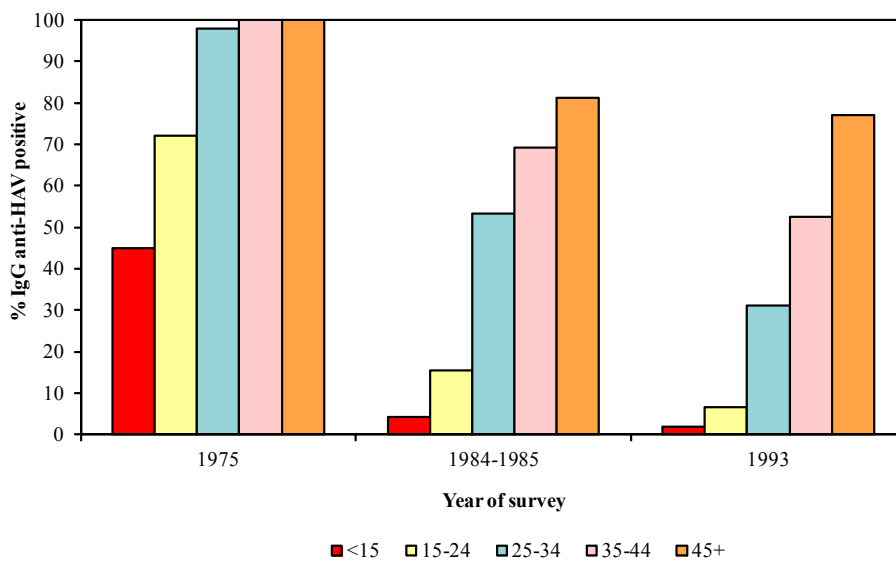
The 1993 seroepidemiological survey showed further decline in the age-specific HAV antibody prevalence when compared to previous studies conducted in 1975 and 1984/85. In 1975, 30% of children below 10 years of age were infected. The age-specific seroprevalence increased to 60% in the 10 to 19 year age group, and was higher than 80% in the 20 to 29 year age group. By the age of 30 years, virtually all were infected.<sup>16</sup> The overall prevalence of HAV infection in the population had declined from 31.8% in 1984/85 to 25.9% in 1993. This decline was seen in all age groups and was more marked in the younger age groups (<15 year olds and 15 to 24 year olds) than in the older age groups (25 to 34 year olds, 35 to 44 year olds, and >45 year olds) (Fig. 6).

The seroprevalence of HAV infection in Singapore with a very low level of transmission is similar to that of Japan (<1% in ages 0 to 19 years; 4% in ages 20 to 29 years), Australia (40% overall), New Zealand

(<20% in ages 30 to 55 years), Canada (<20% in children), the United States (30% overall), and United Kingdom (9% in ages 1 to 9 years).<sup>17,18</sup> The continuous decline in the age-specific seroprevalence over the last few decades reflects the marked improved standards of environmental hygiene and sanitation accompanying socioeconomic progress. The comprehensive disease surveillance system and measures taken against other food-borne diseases (typhoid and cholera) such as health education on personal and food hygiene had also contributed to the successful control of HAV.<sup>19,20</sup> The risk of acquiring hepatitis A in the community is very low, except for those occupationally exposed such as sewage workers<sup>21</sup> and a Gurkha community, which had a much higher seroprevalence than that of the general population in Singapore.<sup>22</sup>

As Singapore is situated in a region highly endemic for HAV infection, it is very vulnerable to the introduction of the disease because of the high volume

**Figure 6**  
Changing age-specific seroprevalence of HAV infection in Singapore, 1975, 1984/1985 and 1993



of regional travel. Indeed, over the last 8 years (2003 to 2010), the proportion of imported cases remained consistently above 50%. Pre-travel health advisory should be issued to travellers reminding them to observe good personal and food hygiene when travelling to the endemic countries, in particular, to avoid raw or partially-cooked food, especially shellfish. Vaccination against HAV infection is an important measure. Several safe and effective vaccines against HAV have been available since the first approval of the products in Singapore in 1996, such as the formalin-inactivated vaccines, HAVRIX (GlaxoSmithKline) and VAQTA (Merck & Co., Inc). A combination hepatitis A/hepatitis B vaccine consisting of HAVRIX and Energix-B (Twinrix, GlaxoSmithKline) is also commercially available.<sup>23</sup> However, Asian travellers are generally less aware of the need for pre-travel consultation and vaccination compared to their Western counterparts and pre-travel hepatitis A vaccination remains low among Singapore travellers.<sup>24</sup>

Besides the risk of travel-associated infection, sporadic and epidemic transmission of hepatitis A is also epidemiologically linked to the consumption of imported shellfish as demonstrated in the outbreaks described above. Cockles (*Anadara granosa*) and oysters are bivalve molluscan shellfish which are filter feeders and are able to accumulate and concentrate viruses and other human pathogens in an environment that is subject to chronic pollution from sewage.<sup>25</sup> They are cultivated along the muddy coastal regions in many countries in the region, where there is no sanitary control over their production and harvest. Cockles-associated outbreaks in Singapore were first reported in 1978 (57 cases), followed by other outbreaks in 1983 (161 cases between May and September),<sup>26</sup> 1985 (36 cases in October) and 1986 (37 cases in August/September). Chilled shucked oysters

imported from the Philippines were associated with a massive outbreak of 312 cases in 1980,<sup>27</sup> as well as an outbreak of paratyphoid A in 1979.<sup>28</sup> Following these outbreaks, the import of chilled shucked oysters was prohibited.<sup>27</sup> Chilled shucked oysters smuggled from other countries had also been implicated in other hepatitis A outbreaks in 1987 (30 cases)<sup>29</sup> and 1989 (4 cases)<sup>30</sup>.

The local population, especially the Chinese, prefers to consume shellfish raw or partially cooked, and this accounted for the highest attack rates in this ethnic group during outbreaks. For cockles, locally known as 'see-hum', one of the favourite methods of preparation is to pour boiling water over them till the shells are partially opened. The flesh and the gut are removed from the shell and usually eaten with chilli sauce and spices. Raw shucked cockles are also commonly added as an ingredient in food; e.g. curry noodle soup ('laksa') and fried noodles ('fried kway teow') and noodle with peanut sauce ('satay bee hoon'). In the case of oysters, they are served as oyster-omelet with the shucked shellfish added in to the fried eggs and flour just before the dish is served. These methods of food preparation are unlikely to inactivate the viruses that may be present in the core of the shellfish<sup>31</sup> as the virus may withstand boiling temperature for several minutes. Cockles commercially processed by 1 to 2 minutes of steaming to remove the shells, followed by 5 minutes boiling had been responsible for an extensive outbreak in the UK.<sup>32</sup>

The Agri-Food Veterinary Authority (AVA) is responsible for regulating the import of seafood including shellfish into Singapore. Live oysters can only be imported from countries where there is legislation for licensing of oyster farms and mandatory testing of





the microbiological quality of the oysters and of the growing water in which oysters are cultured. Under AVA's regulations, every import shipment is to be accompanied by a health certificate issued by the competent authority of the exporting country. The import of chilled shucked oysters is prohibited, and frozen oysters can only be brought in from countries with national shellfish sanitation programme approved by AVA. Imported frozen oysters from these approved countries can only be released for sale if they satisfy the established microbiological standards. A high level of vigilance is maintained to prevent shucked oysters from being illegally brought into Singapore either directly by importers or indirectly by fishermen.

Unlike oysters, cockles are of relatively lower economic value. Cockles from countries in the region which are not part of the national shellfish sanitation programme are generally grown in estuarine waters. In addition, it is difficult to prevent pollution of these estuarine waters where cockles thrive best and to relay them in clean water before export. The live shellfish are generally packed in 60 to 65 kg gunnysacks and transported by lorries from the production areas. As such, the practical approach is to educate the public through public advisories against eating raw or uncooked cockles due to the risk of food poisoning from microbial pathogens. No health certificate is required for the importation of cockles into Singapore as unlike oysters, it would not be practical or meaningful to set an acceptable standard for the import of cockles.

In recent years, there has been an increase in demand for cockle meat instead of whole live cockles due to convenience in food preparation at retail food outlets. This trend has led to a proliferation of shucking activities which were carried out illegally under unhygienic conditions. Since 1 May 2007, AVA

has implemented new regulations which only allow seafood importers with licensed cockle processing establishments to import live cockles. Previously, food service outlets (e.g. hawker stalls, restaurants) could buy live cockles and shuck these at their outlets for immediate consumption by the customers. AVA now requires that these imported cockle consignments be sent directly to the AVA-licensed processing premises upon importation and that these cockle-shucking establishments are allowed to distribute live cockles directly to retail or food service outlets only. AVA prohibits these shucking establishments from supplying the cockles to any distribution centres or wholesale markets.

About 8 to 10 tonnes are consumed by the population per day. Public health education on the risk of consuming raw and half-cooked cockles was stepped up during outbreaks and this had in some way moderated the consumption choice of this shellfish among the population. It is interesting to note that there have been no further cockle-associated outbreaks since 2002, although about 30% of the population continues to consume this shellfish in the traditional way. The reasons are not known. It is likely due to the availability of the hepatitis A vaccine and those who prefer to consume shellfish raw to partially-cooked could have been protected. However, we have no data to support this hypothesis. It could also be possible that farmers growing cockles are more aware of the risk of pollution and are growing their cockles in areas away from human settlements, thus reducing the risk of sewage contamination. Nevertheless, the public should continue to be reminded to refrain from consuming undercooked cockles, not only for the prevention of hepatitis A, but also other enteric diseases such as cholera and *Vibrio parahaemolyticus* food poisoning.<sup>33</sup>



(Reported by Lee HC<sup>1</sup>, Ang LW<sup>2</sup>, Chiew PKT<sup>3</sup>, James L<sup>2</sup> and Goh KT<sup>3</sup>, Changi General Hospital<sup>1</sup>, Ministry of Health<sup>2</sup> and Agri-Veterinary Food Authority<sup>3</sup>, Singapore)

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## Maintaining polio-free certification status in Singapore, 2010

### Background

In 1988, the World Health Assembly adopted a goal to eradicate poliomyelitis (polio) by year 2000<sup>1</sup>. In 1995, the World Health Organization (WHO) convened the first meeting of the Global Commission for the Certification of Eradication of Poliomyelitis. The Global Commission directed that the certification of polio eradication should be conducted at three levels – national, regional, and global. In each country, a national committee should be convened to review and oversee the pre-certification activities and refer their opinions to the Regional Commission as to whether the certification of polio eradication should proceed<sup>2</sup>. In keeping with the recommendations of the Global Commission, the Regional Commission for the Certification of Poliomyelitis Eradication in the Western Pacific, at its first meeting in 1996, set the polio-free certification criteria for the region as follows<sup>3</sup>:

- Absence of circulation of indigenous wild polioviruses for at least a three-year period in which surveillance activities have been maintained at the levels of performance needed for certification;
- A national certification committee in each country has validated and submitted the documentation required by the Regional Commission; and
- Appropriate measures are in place to detect and respond to any importation of wild poliovirus

In October 2000, the WHO Western Pacific Region, including Singapore, was certified polio-free. It was the second WHO region after the American Region to achieve certification.

However, polio continues to circulate in some parts of the world and the risk of importation remains. Singapore maintains high vigilance against polio,



comprising acute flaccid paralysis (AFP) surveillance system, comprehensive system of disease notification, epidemiological surveillance and response, and high immunisation coverage. This report describes the continuous effort in the maintenance of polio-free status in Singapore for 2010.

### **National Certification Committee**

The National Committee for Certification of Poliomyelitis Eradication in Singapore was formed in December 1996. The Committee continues to review the maintenance of polio-free certification status for Singapore and reports to the Regional Commission on an annual basis. The composition of the Committee was reviewed in 2010, with members comprising a public health specialist, a microbiologist and a paediatrician.

### **Poliomyelitis in Singapore**

Polio was a major public health problem in the 1950s in Singapore. With the introduction of polio vaccination in 1962, the incidence of polio declined significantly. The last indigenous case of polio was notified in 1978 and the last imported case was in 2006<sup>4</sup>.

### **Poliomyelitis surveillance**

Singapore maintains a high degree of vigilance over poliomyelitis surveillance. Notification of poliomyelitis is compulsory under the Infectious Diseases Act.

### **Acute flaccid paralysis surveillance**

In December 1995, an acute flaccid paralysis (AFP) surveillance system was set up to detect possible cases of polio as part of WHO's requirements for certification of polio eradication in Singapore. Under this system, all public acute care hospitals were required to

immediately notify the Ministry of Health (MOH) in Singapore of all cases of AFP in any child below the age of 15 years. This system was further enhanced in December 1996, when all public acute care hospitals as well as paediatricians, internal medicine specialists and neurologists in private practice were required to notify MOH of all AFP cases under the age of 15 years as well as all patients under the age of 15 years who were diagnosed with an 'at-risk' disease that could lead to AFP, regardless of whether AFP was present. This list of 'at-risk' diseases includes poliomyelitis, all forms of encephalitis, myelitis, acute infective polyneuritis, particularly Guillain Barre syndrome, mononeuritis (not due to physical causes), monoplegia, etc. The submission of monthly returns, including a 'nil' return, was required. Furthermore, a check on all hospital discharges (through public and private hospitals' computer databases) for AFP cases and cases with 'at risk' diagnosis were conducted periodically.

Following the certification in 2000, Singapore has maintained the AFP surveillance system and its performance are closely monitored and reviewed. The performance of Singapore's AFP surveillance system from January 2008 to December 2010 is summarised in *Table 2*. In 2010, the surveillance system identified 0.6 non-polio AFP cases per 100,000 population in the target population. Two adequate stool samples were collected within the specified time for 100% of AFP cases. All cases were followed up for residual paralysis at 60 days after the onset of paralysis. Details of AFP cases from January to December 2010 are listed in *Table 3*.

### **Laboratory activities**

Under the AFP surveillance system, all stool samples are sent to the Virology Section, Department



of Pathology, Singapore General Hospital. WHO has designated the Virology Section as the National Polio Laboratory (NPL) in 1995. The laboratory remains fully accredited as the designated NPL and plays a key role in the surveillance system. All test results are notified to MOH within 14 days from receipt of samples; detection of wild poliovirus is notified im-

mediately to MOH and WHO.

Besides stool specimens from AFP or suspected AFP cases, the NPL receives stool samples from other sources for poliovirus isolation. A summary of the number of specimens processed by the NPL is in *Table 4*.

**Table 2**  
Performance of the acute flaccid paralysis (AFP) surveillance system, 2008 – 2010

Year	Resident population aged < 15 years <sup>a</sup>	Expected number of AFP cases <sup>b</sup>	Total AFP cases (<15 years)	Total 'non-polio' AFP cases	Non-polio AFP rate <sup>c</sup>	AFP cases with adequate stool samples <sup>d</sup>		Cases with follow up at 60 days (%)
						No.	%	
2008	671,300	7	7	7	1.0	6	86	100
2009	667,800	7	7	7	1.0	6	86	100
2010	654,400	7	4	4	0.6	4	100	100

a Source: Population Trends 2010, Department of Statistics, Ministry of Trade & Industry, Republic of Singapore.

b Base population of 700,000 is assumed

c Per 100,000 population aged less than 15 years

d Two stool samples collected at least 24 hours apart, within 14 days after onset of paralysis, delivered to the laboratory packed in ice, with sufficient quantity for complete analysis and accompanied by proper documentation.

**Table 3**  
List of acute flaccid paralysis (AFP) cases, January – December 2010

Case #	Age	Sex	Diagnosis	Result of stool test		Follow up after 60 days (Yes/No)	Result of follow up	Final classification
				1 <sup>st</sup>	2 <sup>nd</sup>			
AFP-1001	5	F	Acute encephalopathy	Neg	Neg	Yes	Complete recovery	Non-polio AFP
AFP-1002	13	M	Guillain Barre syndrome	Neg	Neg	Yes	Complete recovery	Non-polio AFP
AFP-1003	6	M	Meningoencephalitis	Neg	Neg	Yes	Complete recovery	Non-polio AFP
AFP-1004	9	F	Influenza A encephalitis	Neg	Neg	Yes	Complete recovery	Non-polio AFP

**Table 4**  
Specimens submitted to the National Polio Laboratory for poliovirus studies, 2008 – 2010

Year	Stool specimens from AFP cases	Specimens from AFP contacts	Stool specimens from non-AFP cases	Non-stool specimens	Environment specimens*	Total
2008	10	0	253	285	47	595
2009	23	0	110	392	45	570
2010	16	0	96	361	46	519

\* Raw or treated reservoir or river water



Since 2003, the NPL has also been conducting intratypic differentiation (ITD) of poliovirus, which is used to determine whether AFP cases were associated with polio vaccination or wild poliovirus infection. *Table 5* shows the number of poliovirus-positive specimens that have undergone ITD at NPL between 2008 and 2010.

### Surveillance for vaccine-derived poliomyelitis

In 2001, one AFP case was reported involving a five month-old infant who had onset of upper limb paresis 12 days following administration of his second dose of diphtheria-tetanus-pertussis and oral polio vaccine (OPV). Two stool specimens tested were negative for polio and other enteroviruses. The upper limb paresis resolved within 60 days.

In 2004, a case of post-vaccination infantile pyrexia occurred three weeks after OPV had been given to a three month-old infant. Poliovirus 1 and 2 were isolated from the stool. The infant subsequently recovered with no permanent sequelae.

There have been no reports of such incidents involving vaccine-derived poliomyelitis since then.

### Immunisation coverage

Immunisation against poliomyelitis was first used in Singapore on a mass scale in 1958 and incorporated into the National Childhood Immunisation Programme (NCIP) in 1962<sup>5</sup>. The current poliomyelitis immunisation schedule is outlined in *Table 6*. The National Immunisation Registry of the Health Promotion Board monitors and tracks the coverage of immunisations in the NCIP among the resident children. Although OPV is used in the national programme, inactivated polio virus (IPV)-containing combination vaccines are available and widely used in both the public and private sectors for those who opt for such vaccines. From 2005 to 2009, the percentage

**Table 6**  
Polio immunisation schedule under the National Childhood Immunisation Programme

Dose	Age	Vaccine*
1 <sup>st</sup> Dose	3 months	OPV
2 <sup>nd</sup> Dose	4 months	OPV
3 <sup>rd</sup> Dose	5 months	OPV
1 <sup>st</sup> Booster	18 months	OPV
2 <sup>nd</sup> Booster	6-7 years	OPV
3 <sup>rd</sup> Booster	10-11 years	OPV

\*IPV is used in both the public and private sectors for those who opt for the combination vaccines

**Table 5**  
Polioviruses isolated at the National Polio Laboratory and subjected to intratypic differentiation, 2008 – 2010

Year	Total no. of specimens positive for polioviruses	Source of poliovirus isolates		Poliovirus intratypic differentiation (ITD) results	
		AFP cases	Oth-ers	No. of isolates sent for ITD	Results received
2008	3	0	3	3	3 <sup>a</sup>
2009	0	0	0	0	0
2010	3	0	3	3	3 <sup>b</sup>

a. All were polio type 3 Sabin-like.

b. Two isolates were polio type 1 Sabin-like and one isolate was polio type 2 Sabin-like.



of IPV-containing vaccines administered ranged from 40 to 48 percent<sup>6</sup>.

### **Response to importation of wild poliovirus and circulating vaccine-derived poliovirus in Singapore**

Singapore's national action plan for detection of and response to wild poliovirus and circulating vaccine-derived poliovirus takes into account the standing recommendations set forth by the Advisory Committee on Poliomyelitis Eradication<sup>7</sup> and the World Health Assembly resolution at the 59<sup>th</sup> session in May 2006<sup>8</sup>. Singapore is also compliant with the International Health Regulations (IHR) core capacity requirements for surveillance and response preparedness.

### **Laboratory containment**

The Communicable Diseases Division, MOH serves as the permanent focal point/office for poliovirus laboratory containment. Subsequent to an imported case of poliomyelitis reported in May 2006, the NPL had destroyed the viral samples in its possession in accordance with WHO's accreditation criteria. No other laboratories have been identified to have stored infectious or potentially infectious materials since then.

### **Comments**

This report is based on Singapore's progress report on maintaining post-certification polio-free status for 2010 submitted to the Regional Commission. The National Certification Committee stated that Singapore had maintained a robust system against the importation of poliomyelitis during the reporting period and that Singapore would continue its national

efforts to maintain a high quality AFP surveillance system and promote high level of awareness and vigilance among medical practitioners.

Following the 16<sup>th</sup> meeting on the certification of poliomyelitis eradication in the Western Pacific Region in October 2010, the Regional Commission concluded that the Western Pacific Region had remained free of circulating poliovirus during the reporting period.

However, just as the Western Pacific Region was commemorating ten years of polio-free status, a large outbreak occurred in Tajikistan in the WHO European Region – a Region which had been certified polio-free since 2002. This outbreak, following importation from India, resulted in 458 confirmed cases and 26 deaths with subsequent spread to at least three other countries in the Region<sup>9</sup>.

In August 2011, the Ministry of Health, China, informed WHO of the isolation of wild poliovirus type 1 in four cases in Xinjiang province, western China. Gene sequencing of the isolated viruses showed that they closely resembled those currently circulating in Pakistan<sup>10</sup>. As of 19 December 2011, China has reported 21 confirmed cases and two deaths, and the situation is being closely monitored<sup>11</sup>.

These events are stark reminders of the world's vulnerability to polio so long as poliovirus transmission continues in other parts of the world. Polio remains endemic in four countries (Afghanistan, India, Nigeria, and Pakistan) where transmission of wild poliovirus has never ceased previously<sup>12</sup>. Polio transmission have also been re-established for more than 12 months in Angola, Chad, and Democratic Republic of Congo, and 11 other countries are expe-



riencing outbreaks following imported polio case(s)<sup>12</sup>. Although major progress has been made in India in year 2011<sup>13</sup>, much work is needed in order to achieve Global Polio Eradication Initiative's goal of interrupting global polio transmission by the end of 2012<sup>14</sup>.

In order to promote awareness and vigilance against introduction of polio into Singapore, a circular was sent in September 2010 to all paediatricians, internal medicine specialists and neurologists in the public and private hospitals. Clinicians were updated on the performance of AFP surveillance system and reminded of various procedures and reporting requirements. A similar circular was also sent in September 2011 following the outbreak in Xianjiang province, China.

AFP surveillance can only be effective if clinicians perform the appropriate tests to rule out polio, and inform MOH promptly of all suspected cases so that control measures can be rapidly instituted. All AFP cases under the age of 15 years should be treated as suspicious for polio until that diagnosis can be ruled out. In the event that a suspected or confirmed diagnosis of polio is made, clinicians should also notify MOH using the Communicable Diseases Live & Enhanced Surveillance System (CDLENS) at <http://www.cd lens.moh.gov.sg> or by fax to 62215528 / 62215538. The MD131 can also be downloaded from the MOH website at <http://www.moh.gov.sg>. For further clarifications on AFP surveillance system, please email [moh\\_info@moh.gov.sg](mailto:moh_info@moh.gov.sg).

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## Surveillance of non-typhoidal salmonellosis in Singapore, 2010

### Introduction

Salmonellosis is one of the most common food-borne diseases in the world. An estimated number of 93.8 million cases of *Salmonella* gastroenteritis with 155,000 deaths occur annually throughout the world<sup>1</sup>. The causative agent is a gram-negative facultative rod-shaped bacterium. It consists of two species, *Salmonella enterica* and *Salmonella bongori*. *Salmonella enterica* can be divided into subspecies, serogroups and serotypes based on their antigenic formula. Under the Kauffman-White classification system, over 2,500 different serotypes have been identified so far<sup>2,3,4</sup>.

In December 2008, notification of salmonellosis became mandatory under the Infectious Diseases Act. Medical practitioners and clinical laboratories are thereby required to notify the Ministry of Health (MOH) of all clinical and laboratory confirmed cases of salmonellosis within 24 hours from the time of diagnosis<sup>4</sup>. Hence, the main source of data for the surveillance system is from the reporting of laboratory-confirmed cases from medical practitioners and clinical laboratories. Other sources include anecdotal reporting from the public regarding suspected food

poisoning incidents. From January 2010 onwards, the National Public Health Laboratory (NPHL) has started serotyping *Salmonella* positive isolates provided by clinical laboratories, to enhance public health surveillance and outbreak investigation.

We describe herein the epidemiology of the laboratory-confirmed cases of salmonellosis in 2010, including an overview of the serotype distribution and how the serotype surveillance data can be further utilized.

### Materials and methods

The demographic data of all laboratory-confirmed cases of salmonellosis notified between e-week 1 (3/1/10 to 9/1/10) and e-week 52 (26/12/10 to 1/1/11) of 2010 were extracted from the database and reviewed.

In addition, a retrospective analysis of the epidemiological data collected in 2010 for the top five most frequently detected serotypes was carried out, to identify potential clusters and trace-back clusters previously notified to MOH as food poisoning incidents via anecdotal reporting or by clinicians.



A cluster was defined as an incident involving two or more cases with onset of illness within the incubation period of salmonellosis (6 to 72 hours) and epidemiologically linked by either residential or workplace address or common implicated food establishment. If the case had a recent travel history outside Singapore three days before onset of illness, the case was considered imported.

## Results

### Distribution of cases

A total of 1480 laboratory-confirmed cases of non-typhoidal salmonellosis were reported in 2010, a 1.3-fold increase from 1144 cases reported in 2009<sup>5</sup>.

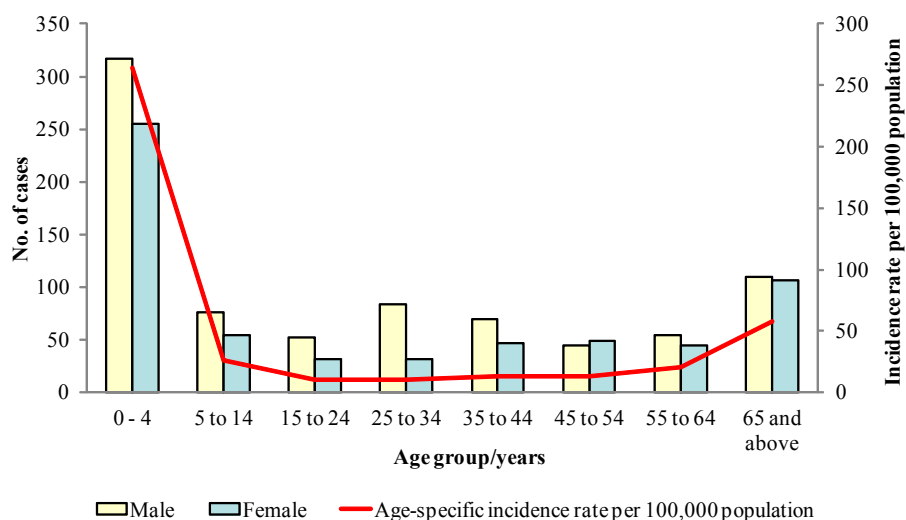
Residents constituted 76.6% of the reported cases with 96.7% locally acquired. Non-residents inclusive of tourists constituted 23.3% of the reported cases, of which 78% were locally acquired infection.

Imported salmonellosis accounted for 7.8% of all the reported cases in 2010. Out of the 115 imported cases, 38 were local residents who had reported a recent travel history to countries such as Malaysia, Indonesia, Thailand and India for leisure, business or religious purposes.

Out of these 1480 laboratory-confirmed cases, 35 were foreigners seeking medical treatment in Singapore and 21 were tourists. As this study focused on the cases who were residents in Singapore, these 56 cases were not taken into account in this analysis.

Of the remaining 1425 cases, males outnumbered females (56.6% vs. 43.4%). In both genders, the highest number of cases was in those aged less than four years, followed by those aged 65 years and above (Fig. 7). Among the three major ethnic groups, Malays had the highest incidence rate followed by Chinese and Indians.

**Figure 7**  
Age-gender distribution and age-specific incidence rate per 100,000 population of reported salmonellosis in Singapore\*, 2010



\*excluding tourists and foreigners seeking medical treatment



**Salmonella serogroups**

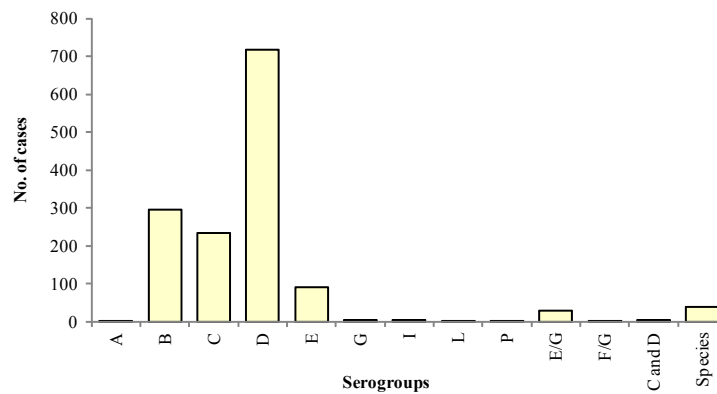
The top three most frequently isolated *Salmonella* serogroups among the 1425 cases were group D, group B and group C (Fig. 8).

A comparison between the top three most frequently occurring serogroups and the total number of notifications was carried out from January to December 2010 (Fig. 9). Pronounced peaks of cases were observed in June (n =176) and September (n =131), mostly attributed to *Salmonella* group D.

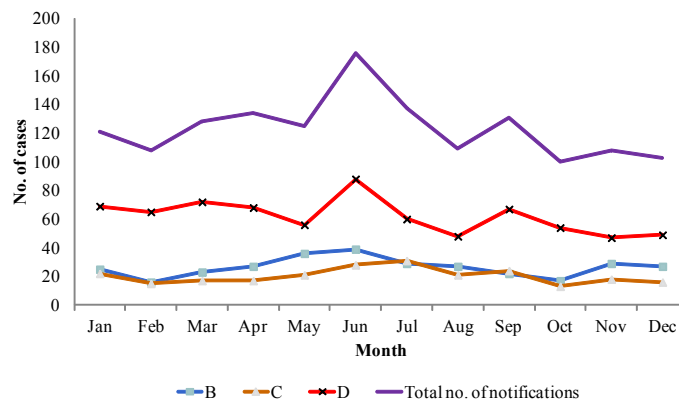
There was also a peak in the number of *Salmonella* group B cases seen in June. The peak in the number of *Salmonella* group C cases occurred only a month later compared to both *Salmonella* group B and D. However, there were no reported massive *Salmonella* outbreaks corresponding to the increase in cases during these two periods.

Of the 176 cases notified in June, 169 (96.0%) had no recent travel history. Majority (40.8%) of these cases comprised children aged 4 years and below. Similarly, 124 (94.7%) of the 131 cases notified in

**Figure 8**  
Serogroup distribution of 1425 reported cases of salmonellosis in Singapore, 2010



**Figure 9**  
Monthly distribution of 1480 reported cases of salmonellosis due to *Salmonella* group B, C, D and all serogroups in Singapore, 2010



September had no recent travel history. About one-third (33%) of these cases comprised children aged 4 years and below. Their food history included the consumption of powdered milk and home cooked meals such as porridge with minced chicken, fish and vegetables. However, the majority of their caregivers could not provide much information on their food history.

### **Salmonella serotypes**

Among the 1425 reported cases, only 545 (38.2%) were serotyped or partially serotyped (Table 7). The majority of *Salmonella* Typhi, Paratyphi A, B, C, Enteritidis and Typhimurium were serotyped in restructured hospitals' laboratories. The other isolates, which were only typed as groups A, B, C, D, and E or as ungroupable *Salmonella* by these laboratories, were sent to the NPHL for serotyping (Fig. 10).

*Salmonella* Enteritidis was the most frequently reported serotype, accounting for 54.3% of all isolates with a known serotype. The second most frequently reported serotype was *Salmonella* Stanley, accounting for 7.7% of all isolates with a known serotype. *Salmonella* Weltevreden was ranked third at 7.3%, followed by *Salmonella* Paratyphi B dT+ (var Java) and *Salmonella* Typhimurium at 4.6% and 3.1%, respectively.

### **Retrospective analysis for the top five serotypes**

Of the reported *Salmonella* Enteritidis cases, 29 (9.8%) were associated with 15 suspected food poisoning incidents reported in 2010. Nine out of the 29 *Salmonella* Enteritidis cases were food handlers, of which two were from the same caterer and with the same serotype as one of the cases in the food poisoning incident. The remaining cases were not

food handlers but were either family members or colleagues who had shared a common meal prior to onset of symptoms.

Among the 42 *Salmonella* Stanley cases, there was one workplace cluster of three asymptomatic food handlers who were tested positive during their health screening.

Of the 40 *Salmonella* Weltevreden cases, four were food handlers who were found positive after two separate, suspected food poisoning incidents involving four family members and 44 guests at a wedding buffet lunch, respectively. No stool specimens could be obtained from the cases in both incidents.

There were no known clusters of food poisoning epidemiologically associated with *Salmonella* Typhimurium and Paratyphi B dT+ (var Java).

### **Discussion**

The incidence rate of salmonellosis cases in Singapore has been increasing over the past decade, particularly from year 2008 onwards (Fig. 11). Although this could be partly attributed to enhanced laboratory testing, a greater awareness and the mandatory notification of salmonellosis towards the end of 2008, we believe that this reflects a true increase.

This trend has also been observed in countries such as the United States which has seen a 10% increase in salmonellosis incidence in 2010 compared with 2006 to 2008<sup>6</sup>. On the other hand, there has been a decrease in the non-typhoidal salmonellosis notification rates in Europe over the past three years, with the overall rate decreasing from 33.9 per 100 000 in 2006 to 29.8 cases per 100 000 in 2008<sup>7,8</sup>.



**Table 7**  
**Non-typhoidal Salmonella serotypes (n = 545) isolated at the NPHL and restructured hospitals' laboratories, 2010**

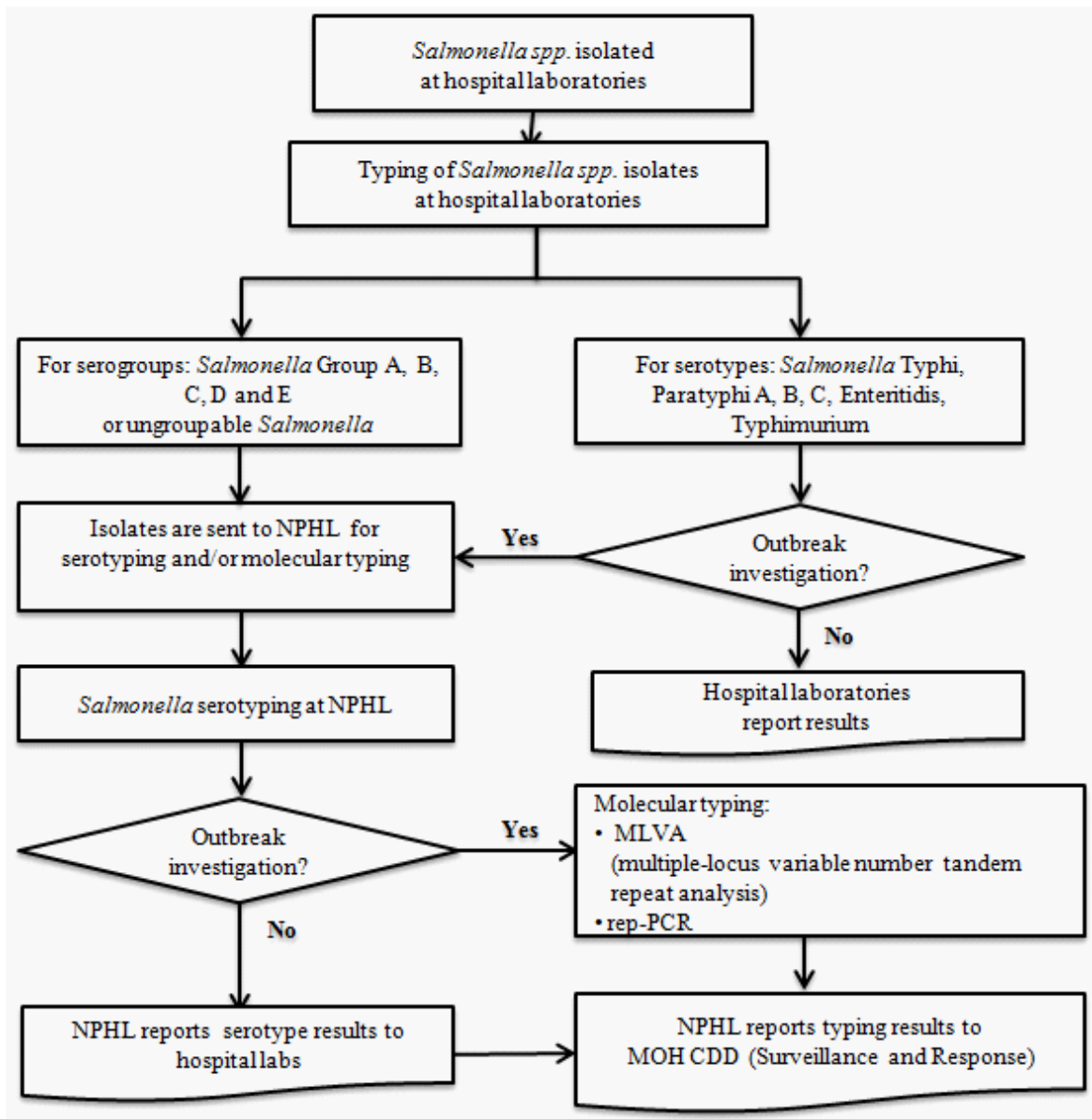
Serogroup	Serotype	No. of cases	%
B	4,5,12:d:-	3	0.6
	Agona	8	1.5
	Heidelberg	2	0.4
	Paratyphi B dT+ (var Java)	25	4.6
	Stanley	42	7.7
	Typhimurium	17	3.1
C	6,8:e,h:-	1	0.2
	6,7:e,h:-	1	0.2
	6,7,14:Poly H+	1	0.2
	Albany	12	2.2
	Altona	4	0.7
	Augustenborg	1	0.2
	Bareilly	2	0.4
	Bovismorbificans	6	1.1
	Braenderup	12	2.2
	Choleraesuis	3	0.6
	Corvallis	14	2.6
	Infantis	2	0.4
	Isangi	1	0.2
	Mbandaka	2	0.4
	Muenchen	1	0.2
	Newport	6	1.1
	Ohio	2	0.4
	Oranienburg	1	0.2
	Oslo	2	0.4
	Potsdam	1	0.2
	Richmond	1	0.2
	Rissen	4	0.7
	Singapore	1	0.2
	Tennessee	1	0.2
Thompson	1	0.2	
Virchow	1	0.2	
D	Enteritidis*	296	54.3
	Frintrop	1	0.2
	Javiana	11	2.0
	Panama	1	0.2
E	Anatum	1	0.2
	Lexington	2	0.4
	London	1	0.2
	Senftenberg	3	0.6
G	Weltevreden	40	7.3
	Okatie	2	0.4
I	16:a:-	1	0.2
	16:b:-	1	0.2
	Hvittingfoss	2	0.4
L	Ruiru	1	0.2
P	Mgulani	1	0.2
Total		545	100.0

\*4 isolates had co-infection of *Salmonella* group C and *Salmonella* Enteritidis

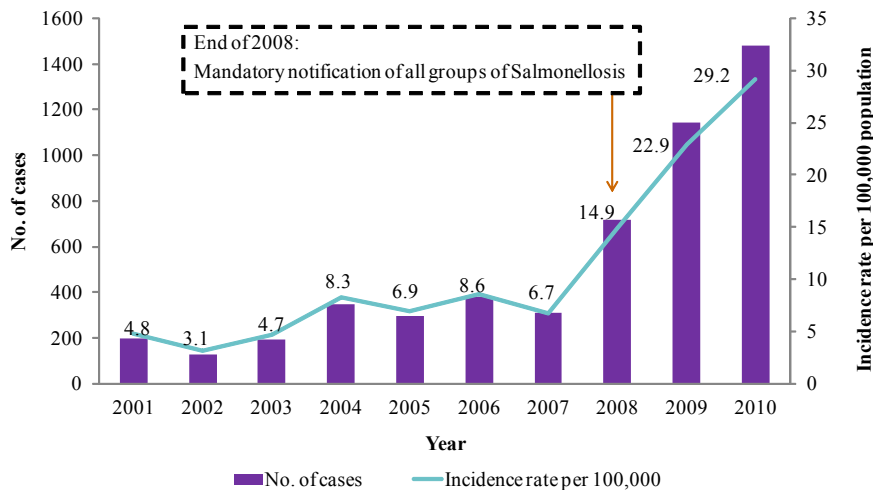


Figure 10

Workflow for *Salmonella* serotyping at restructured hospitals' laboratories and the NPHL



**Figure 11**  
Incidence rates of reported salmonellosis in Singapore, 2001- 2010.



Among the isolates, *Salmonella* Enteritidis and Typhimurium are the most common serotypes seen globally, which is within the list of the top five serotypes isolated in Singapore in 2010. The remaining top serotypes isolated in Singapore include *Salmonella* Stanley, Weltevreden and Paratyphi B dT+ (var Java). *Salmonella* Stanley is also one of the most common reported serotypes isolated in Hong Kong in 2009, under the city's *Salmonella* surveillance programme<sup>9</sup>.

Detection of outbreaks relies mainly on reporting of suspected food poisoning events by clinicians and members of the public. When *Salmonella* is detected in more than one specimen, serotyping will enable confirmation of the same serotype. Molecular typing by methods inclusive of Repetitive Extragenic Palindromic Sequence Polymerase Chain Reaction (REP-PCR) and multiple-locus variable number tandem repeat (MLVA) may be needed for further differentiation if the serotype is commonly encountered.

Monitoring for serotype distribution by routine typing of *Salmonella* isolates will give a background distribution of the serotypes. Challenges of relying on serotype distribution to actively detect outbreaks include heavy reliance on the completeness of data and the delayed dissemination of information since the time taken from onset of illness to confirmation that the case is part of an outbreak typically takes 2 to 3 weeks<sup>10</sup>. Other caveats of interpreting the data include the tendency for people to consume food at various food establishments not restricted to the area that they stay or work in. In addition, majority of the laboratories in Singapore do not conduct further test to distinguish between the serogroups or serotypes of non-typhoidal *Salmonella*, with the exception of common occurring serotypes such as *Salmonella* Typhimurium and Enteritidis as it is not necessary for clinical management. On the other hand, serogrouping the specimens may not benefit as the causative agent can fall beyond the usually recognized serogroups (A, B, C, D and E). This has been highlighted previously in our local serotype distribution for 2010.



Nonetheless, serotyping would be useful if the information is further correlated with serotypes obtained from livestock and dairy products. Detection of new or rare serotypes, or an unusual increase in one serotype, should trigger further epidemiological investigation.

#### Acknowledgements

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*(Reported by Ling VRY, La MV, Lim SK, Toh HY, Hishamuddin P, Foong BH, Lin RTP, Tay J and Ooi PL, Communicable Diseases Division, Ministry of Health)*

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## Norovirus outbreak at a primary school in Singapore

On 3 Oct 2011, the Ministry of Health (MOH) was notified of a possible gastroenteritis outbreak at a primary school, involving 148 students who had developed fever, diarrhoea and vomiting between 1 and 3 Oct 2011.

The school has a total of 1,836 students (1297 students in the morning session and 539 students in the afternoon session), with 135 teaching and non-teaching staff. The school's canteen has six food stalls and two drinks stalls.





Field investigations were carried out immediately at the school. This report summarizes the findings of the outbreak investigation.

## Methods

A case was defined as any student or staff of the primary school who developed one or more symptoms of gastroenteritis (vomiting, watery diarrhea, abdominal pain, fever and nausea) between 29 Sep and 4 Oct 2011. Cases from the school were identified and their personal particulars such as age, gender and ethnicity were recorded. Signs and symptoms of those who were ill and the types of medical treatment sought were obtained. A case-control study was conducted using a standard questionnaire to determine the vehicle of transmission by comparing the food histories of well and unwell students two days prior to the onset of symptoms.

Food and environmental samples were collected from the school canteen and sent for microbial analysis. Environmental samples from the wash basins in the school toilets and mops used for general cleaning were taken from various locations within the school premises. Food handlers from the school canteen were screened for enteropathogens (*Shigella*, *Campylobacter*, *Vibrio*, *Salmonella*, rotavirus and norovirus). A total of nine food samples, four environmental swabs and 15 food handlers from the school canteen were tested. In addition, four stool samples were collected from the affected cases and sent for laboratory testing.

Differences in attack rates between cases and controls using the chi-square or Fisher's exact test were examined first by day and then by food stalls. Differences

in food stall-specific attack rates were subsequently examined using bivariate analyses, with crude odds ratio (OR) and 95% confidence intervals (CI) computed. Statistical analyses were performed using PASW Statistics Version 18.0 (SPSS Chicago, IL). A p value of <0.05 was considered statistically significant.

## Findings

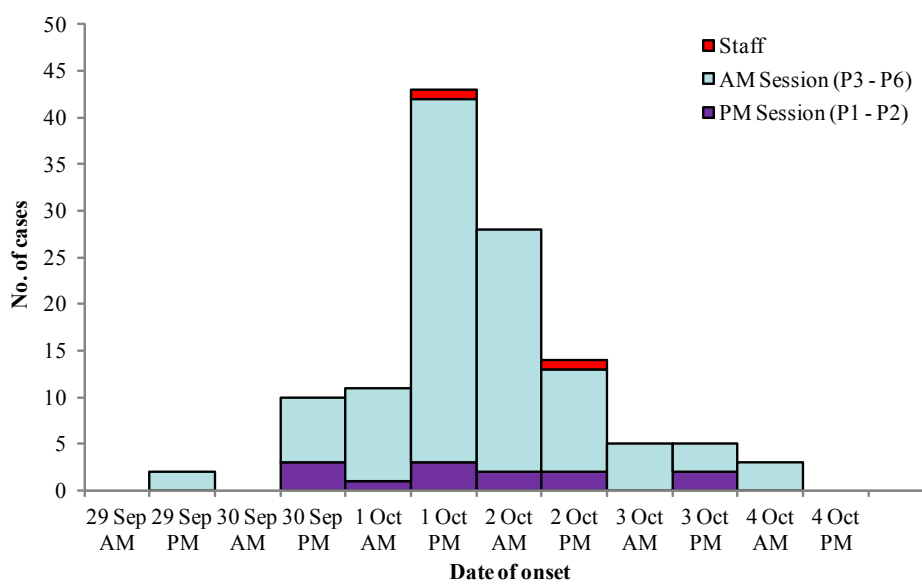
Using the case definition, a total of 121 cases, which consisted of 119 students and 2 staff, were identified, giving an overall attack rate of 6.2%. The attack rate for students was 6.5% (8.2% for morning session and 2.4% for afternoon session) compared to 1.5% for staff only. The age range for the cases was between 6 and 11 years for students and 21 and 24 for staff. The male to female ratio of the cases was 1.25:1 for students and 1:1 for staff. Their clinical features comprised vomiting (86.0%), abdominal pain (71.9%), fever (65.3%), nausea (44.6%) and watery diarrhoea (31.4%). 88 cases sought outpatient treatment (72.7%) while the rest self-medicated (19.0%). One (0.8%) was hospitalized for observation. All recovered uneventfully. The epidemic curve is shown in *Fig. 12*.

A total of 60 cases responded to the questionnaire and respondents who were asymptomatic throughout served as controls. Case-control analysis revealed no significant association between illness and consumption of food from any of the eight canteen stalls from 28-30 September 2011.

Three of the four stool samples obtained from the cases were tested positive for norovirus genogroup II. Of the 15 food handlers screened, two were tested positive for norovirus genogroup II.



**Figure 12**  
**Onset of illness of 121 gastroenteritis cases at a school in Singapore, 29 September - 4 October 2011**



One food sample taken from one of the canteen stalls was positive for *Escherichia coli* (210 MPN/g). Another food handler was found to be positive for rotavirus and *Vibrio fluvialis* (likely an incidental finding). All three food handlers who were found to be positive during screening were asymptomatic prior to this incident.

## Discussion

The epidemiological features of this gastroenteritis outbreak, with vomiting as the predominant symptom, evidence of person-to-person transmission, and absence of a food-borne vehicle, were consistent with an outbreak caused by norovirus. Noroviruses are highly contagious and are usually transmitted directly from person to person by faecal-oral spread,

and indirectly through contaminated food and water, or environmental contact. The incubation period is 12-48 hours and symptoms may last 24-72 hours<sup>1</sup>.

Our investigations revealed that a student (from a primary 2 class) had vomited in class in the afternoon of 30 Sep 2011. We believe this to be the most likely source of the outbreak, as we identified several lapses in the school's cleaning and disinfection procedures which could have directly or indirectly facilitated the rapid transmission of norovirus in the school. These lapses included not using household bleach to clean and disinfect areas contaminated by vomitus, inappropriate disinfection and storage of cleaning equipment used to clean the vomitus, and inappropriate disposal of waste materials contaminated by vomitus.



Most of the affected students were from primary 3 and 5 classes. These students had afternoon remedial or enrichment lessons on 30 Sep 2011. We hypothesized that while waiting for their afternoon lessons, the students played around the area where the vomitus was disposed of. Their close proximity to the infected vomitus may have facilitated transmission. Only a few of the primary 1 and 2 students were affected. This was because most of their classes already started before the student vomited in the afternoon of 30 Sep 2011.

The following factors could have also contributed to the explosive nature of the outbreak:

1. There was a high proportion of cases (86%) with vomiting and some of them vomited in their classrooms. Vomiting can give rise to infectious droplet aerosols and widespread contamination<sup>1</sup>.
2. The virus has a low infectious dose of 10-100 particles and could remain viable in the environment for up to five days as a consequence of inadequate environmental cleaning<sup>1</sup>.
3. The densely populated school environments and sharing of classes and facilities could facilitate transmission of the infection to susceptible population (i.e. young school children).

To prevent the recurrence of similar outbreaks, MOH has advised the school on measures to improve environmental, food and personal hygiene.

(Contributed by Ler SS<sup>1</sup>, Hishamuddin P<sup>1</sup>, Tay J<sup>1</sup> and Ooi PL<sup>1</sup>, Communicable Diseases Division<sup>1</sup>, Ministry of Health)

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