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CONTENTS

Congenital rubella prevention in Singapore: a success story

Introduction

Rubella is a mild febrile viral disease caused by a *Togavirus* of the genus *Rubivirus* and is spread through droplets or by close contact with nasopharyngeal secretions of an infected person.

The major complication of rubella is its ability to produce anomalies in the developing foetus especially during the first trimester. The virus can be transmitted to the foetus through the placenta and is capable of causing serious congenital defects, abortions, and still-births.

The immunisation programme for rubella in Singapore started in 1976 with mass immunisation of female primary school leavers (> 11 years)[1]. This was extended to include male primary school leavers and national servicemen in 1982. In 1990, the trivalent MMR (measles, mumps, rubella) vaccine was introduced to children at 1 year of age. The monovalent rubella vaccine given to primary school leavers was replaced by the second dose of MMR vaccine in 1998 (*Fig 1*).

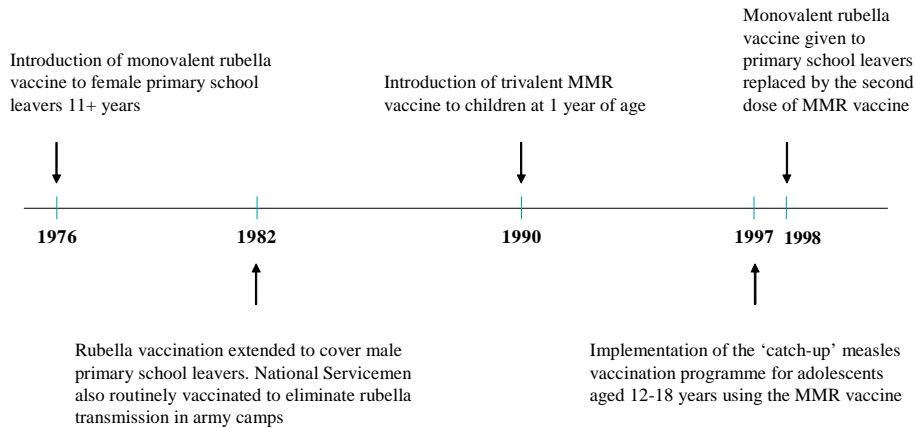The MMR immunisation coverage among children aged 2 years and below has been maintained at over 90% in the past 7 years. During the same period, the immunisation coverage for school leavers has been over 92%.

A study was conducted to assess the burden of rubella infection in Singapore and to monitor the impact of rubella vaccination programme on the incidence of maternal and congenital rubella infection.

Figure 1
Rubella immunisation programme in Singapore, 1976-2005

Introduction of monovalent rubella vaccine to female primary school leavers 11+ years

Introduction of trivalent MMR vaccine to children at 1 year of age

Monovalent rubella vaccine given to primary school leavers replaced by the second dose of MMR vaccine

1976   1982   1990   1997 1998

Rubella vaccination extended to cover male primary school leavers. National Servicemen also routinely vaccinated to eliminate rubella transmission in army camps

Implementation of the 'catch-up' measles vaccination programme for adolescents aged 12-18 years using the MMR vaccine

Materials and methods

We carried out a 10-year systematic review of epidemiological data obtained from the mandatory notification system from 1996 to 2005. To measure the burden of rubella infection in Singapore, we also analysed the annual MMR immunisation coverage obtained from the national immunisation registry from 1999 to 2004 and the rubella seroepidemiological data obtained from the national seroprevalence study (NSS) conducted by the Ministry of Health in 2005.

To assess the impact on the congenital rubella prevention programme, we studied reported cases of congenital rubella from 1982 to 2005 and the proportion of termination of pregnancy (TOP) due to maternal rubella infection from 1983 to 2004.

Results

Incidence

The incidence of clinical rubella had dropped from 13.3 cases per 100,000 population in 1996 to 3.2 cases per 100,000 in 2005. Further analysis indicated a significant decline in the incidence of rubella per 100,000 population in the past 7 years ($p<0.01$). The incidence of clinical rubella cases has stabilised at about 3.5 per 100,000 population since 2002 (*Fig 2*).

In 1983, there were 68 TOP due to maternal rubella infection representing 0.36% of the total annual number of TOP. The proportion had decreased gradually over the years and there had been no requirement for TOP for maternal rubella infection since 2002.

A similar declining trend was observed for the number of reported congenital rubella cases. From the 10 cases reported in 1983, the number had dropped to only 1 case over the past 3 years (*Fig 3*).
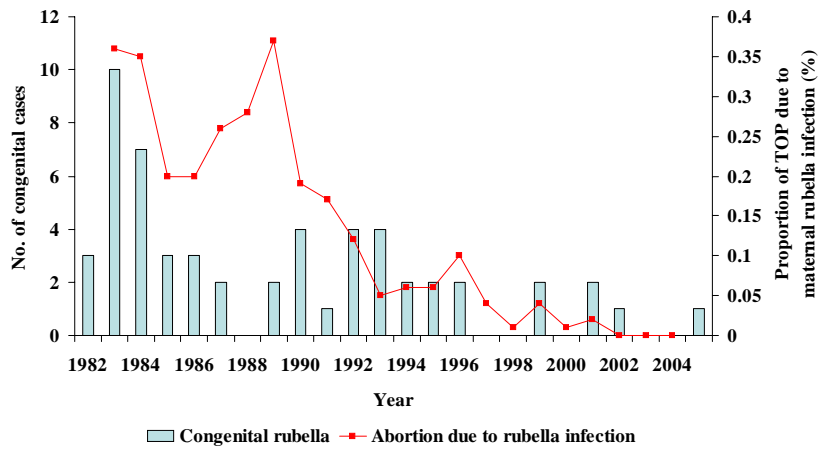
National seroprevalence study 2005

From the NSS conducted in 2005, the prevalence of antibody against rubella was 87.4% in the Singapore population (95% CI: 86.4% - 88.4%).

Figure 2
Incidence of reported rubella cases, 1996 - 2005
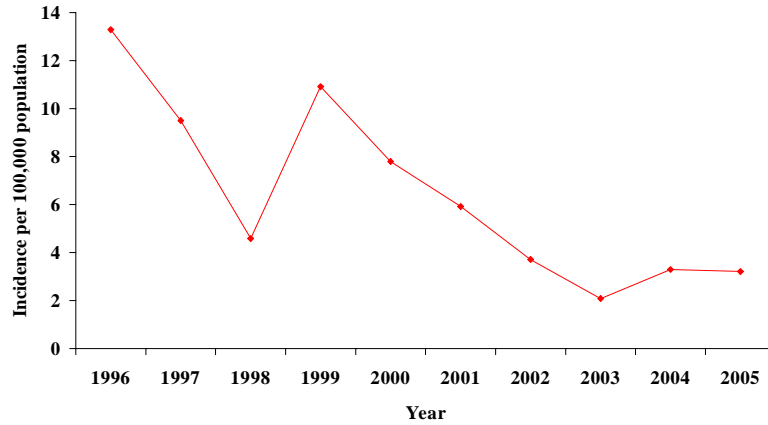
Figure 3
Proportion of TOP due to maternal rubella infection and number of congenital rubella cases from 1983 - 2005

The findings showed that 12.0% of females in the reproductive age group of 18 - 44 years remained susceptible to rubella infection (*Fig 4*). The study results did not detect any ethnic differences in susceptibility in this age group.

Comments

The childhood rubella vaccination programme and active screening programme for rubella infection in pregnant women have effectively reduced the bur-

Figure 4
Age-specific incidence of reported rubella cases and prevalence of anti-rubella IgG in females
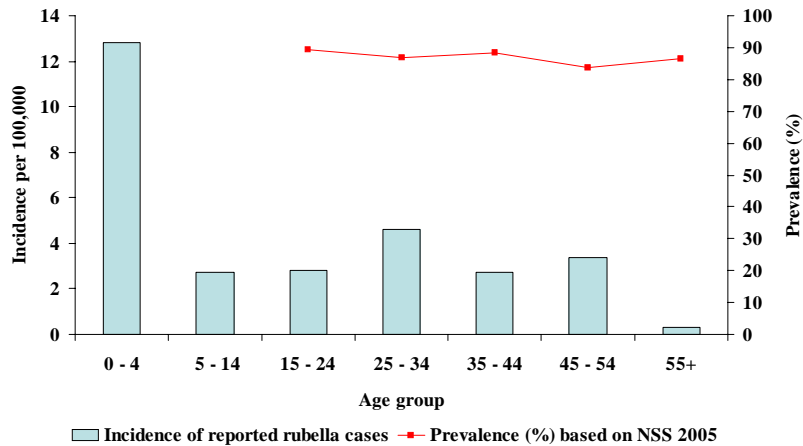
A case of congenital rubella

One case of congenital rubella was reported in 2005. The mother of the infant had an antenatal history of rubella infection at her 7th week of gestation but she decided not to terminate the pregnancy. She delivered a baby with congenital rubella syndrome at 35th week of gestation. The baby's congenital defect at birth included low birth weight of 1,055 gram, bilateral grade 1 intra-ventricular haemorrhage, large patent ductus arteriosus (PDA) of 2.4 millimetre and arterial septal defect (ASD)/ patent foramen ovale (PFO) of 1.36 millimetre. The mother had no documented history of MMR or rubella vaccination.

den of rubella infection and congenital rubella cases in Singapore.

However, we should be vigilant in preventing any unfortunate occurrence of rubella infection among pregnant women, as the NSS 2005 revealed that 12.0% of women in their reproductive age did not have rubella immunity, although the level of immunity had continued to increase from 56% in 1975-79[2] to 72% in 1985 and 85% in 1987[3]. It is advisable that unvaccinated women in the reproduction age group be immunised against rubella at least 3 months prior to conception.

(Reported by Low YJ, Ye T, Chow A, Ang LW, Chew SK, Communicable Diseases Division, Ministry of Health)

References

1. *Goh KT. The national childhood immunisation programme in Singapore. Sing Med J 1985;26:225-42.*

2. *Doraisingham S, Goh KT. The rubella immunity of women of child-bearing age in Singapore. Ann Aca Med Singapore 1981; 10:238-41*

3. *Committee on Epidemic Diseases. Efficacy of the rubella immunisation programme. Epidemiol News Bulletin 1988; 14:64*

Evaluation of a rapid diagnostic test kit for malaria screening in Singapore

Introduction

Malaria is a parasitic disease that is a major cause of sickness in many tropical and subtropical areas of Southeast Asia and the Indian sub-continent[1]. Despite our malaria-free status since 1982, Singapore continues to be receptive and vulnerable to the re-introduction of malaria because of the presence of *Anopheles* mosquitoes and continuous influx of a pool of infected people from malarious countries, respectively[2]. The Ministry of Health conducts malaria screening of high-risk populations in malaria-receptive areas to minimize the risk of local transmission. Conventional light microscopy of thick blood films stained with Giemsa, Wright's or Field's stain is used as the screening method. This method has a lower detection limit of 0.001% parasitemia and is still considered the universal "gold standard" for detecting and identifying malarial parasites[3]. However this method is not ideal for outbreak control as laboratory results are usually ready only 3 to 5 days after screening[4]. The development of rapid diagnostic tests (RDT) would allow suspect cases to be isolated and treated quickly[5,6] and lower the costs of screening (up to a reduction of S$5.50 for each sample screened). In this study, we have selected one such malaria RDT, the Binax NOW® Malaria RDT to assess its suitability for malaria screening in Singapore.

Materials and methods

The Binax NOW® Malaria RDT[7] is a 10-minute immuno-chromatographic assay which can detect circulating *P. falciparum* antigen and an antigen that is common to all four species of malaria; viz. *P. falciparum*, *P. vivax*, *P. ovale* and *P. malariae*. This test is thus able to differentiate between *P. falciparum*, non-*P. falciparum* and mixed (*P. falciparum* and non-*P. falciparum*) infections (*Fig 1*). However, it is not

Figure 5
Results interpretation from Binax NOW® Malaria RDT

RESULTS INTERPRETATION

Positive Test Result

P.f. infection: A positive test result is indicated by any visible line in the test window next to T1 together with a line in area C.

P.f. infection or mixed infection (P.f., P.o., P.m., P.v.): A positive test result is indicated by any visible line in the test window next to T1 and T2, together with a line in area C.

P.v., P.m., P.o. or a mixed infection of all three: A positive test result is indicated by any visible line in the test window next to T2, together with a line in area C.

Negative test result
The test is negative if only the C line appears.

Invalid test result
The test is invalid if the **C** line does not appear. If this occurs, the test should be repeated using a new card.

able to differentiate infections caused by the remaining three forms of malarial parasites (*P. vivax, P. malariae* and *P. ovale).*

The study comprised two phases in which the sensitivity and specificity of the RDT for *P. falciparum* and *P. vivax* were evaluated using conventional light microscopy of thick blood smears as the gold standard. Binax NOW® Malaria RDT was not tested for the detection of *P. malariae* and *P. ovale* because infections by these malarial parasites are exceedingly low (four imported *P. malariae* cases reported from 1999 to 2005). In Phase 1, a study was conducted with mixed community controls and *P. falciparum*-positive laboratory samples, while in Phase 2, negative laboratory controls and positive *P. vivax* blood samples from the patient bank in the National Malaria Reference Centre of the National University of Singapore were used. Community controls were incorporated in Phase 1 to evaluate the ease of use of the RDT in an actual malaria screening exercise and this was not repeated in Phase 2. 2x2 tables were constructed to calculate the sensitivity and specificity using the formulae:

	Thick blood smears	
RDT	Positive	Negative
Positive	A	B
Negative	C	D

Sensitivity = A / (A+C) x 100%
Specificity = D / (B+D) x 100%

Results

A total of 383 blood samples was used in the study (*Table 1*). *Tables 2* and *3* show the comparison of the RDT versus the thick blood smears for detection of *P. falciparum* and *P. vivax* and the cal-

culated sensitivity and specificity. There were six (1.6%) failed test kits out of the 383 Binax NOW® Malaria RDT used. The Binax NOW® Malaria RDT demonstrated a lower sensitivity for *P. vivax* (75%) than for *P. falciparum.* However when the sensitivity of Binax NOW® Malaria RDT was stratified by parasite load of *P. vivax*, the sensitivity increased to 92.1% for parasitemia of 0.01% and above.

Discussion

Sensitivity is the proportion of true positives that are correctly identified by a test while specificity is the proportion of true negatives that are correctly identified by a test. Hence a diagnostic test is valid if it detects most people with the disease (high sensitivity) and excludes most people without the disease (high specificity). The results of the study illustrated that the Binax NOW® Malaria RDT has a high sensitivity and specificity for *P. falciparum* and this finding is comparable to studies conducted in other countries with its demonstrated high sensitivity (100% and 89% for *P. falciparum* and *P. vivax,* respectively) and specificity (96% and 98% for *P. falciparum* and *P. vivax,* respectively)[8,9]. The Binax NOW® Malaria RDT was able to differentiate between *P. falciparum,* non-*P. falciparum* and mixed infection with high specificity.

A reason for our lowered sensitivity results for *P. vivax* could be the use of thawed blood samples which affected the pick-up rate of the malarial antigens by the RDT. In other studies, fresh patient blood was used for testing and this could have affected the sensitivity of the RDT. To understand the limitations of reduced sensitivity to *P. vivax*, especially at very low parasite load of 0.005%, we reviewed the parasitemia of reported malaria cases. From 1999 to 2005, *P. falciparum* and *P. vivax* infections accounted for 1,412 (93%) of 1,422 in-

Table 1

Breakdown of blood samples used in Phase 1 and 2 studies

	Phase 1	Phase 2
Total no. of samples	323	60
No. of positive controls	80 (parasitemia of 0.001%, 0.005%, 0.01%, 0.05%, 0.1%, 0.25%, 0.5% and 1%)	50 (parasitemia of 0.005%, 0.01%, 0.05%, 0.1% and 0.5%)
No. of negative controls	5	10
No. of community controls	238	-

Table 2

Comparison of thick blood smears vs. Binax NOW® Malaria RDT for detection of *P. falciparum*

	Thick blood smears		
Binax NOW® Malaria RDT	Positive	Negative	Total
Positive	80	6	86
Negative	0	232	232
Total	80	238	318

Sensitivity = 80/80 x 100% = 100%
Specificity = 232/238 x 100% = 97%

Table 3

Comparison of thick blood smears vs. Binax NOW® Malaria RDT for detection of *P. vivax*

	Thick blood smears		
Binax NOW® Malaria RDT	Positive	Negative	Total
Positive	36	0	36
Negative	12	11	23
Total	48	11	59

Sensitivity = 36/48 x 100% = 75%
Specificity = 11/11 x 100% = 100%

fections (31% *P. falciparum*, 65.9% *P. vivax* and 2.4% mixed infections)[10]. Of the *P. vivax* cases, only 1.2% (12 out of 937) presented with parasite load of less than 0.01%. Hence 98.8% of the cases would theoretically have been detected by the Binax NOW® Malaria RDT during screening.

Based on our findings, we recommend:

● Single use of Binax NOW® Malaria RDT for screening in clearcut *P. falciparum* cases/outbreaks due to the high sensitivity and specificity of the RDT in detecting this infection,

● Dual use of thick blood smears and Binax NOW® Malaria RDT for cases/outbreaks where a risk of *P. vivax* infection exists so that the lower sensitivity of the RDT for *P. vivax* is compensated for by the thick blood smears and the concurrent use of the RDT will allow for timely treatment for cases which can be detected on-site, and

- Single use of thick blood smears for routine screening, as there should be a higher level of sensitivity to increase the chances of detection from random screening. While the RDT provides the advantage of quick on-site diagnosis, dual use of RDT and thick blood smears is not economical and will lead to doubling of routine screening costs in the absence of cases/outbreaks.

Future replacement of thick blood smears by the Binax NOW® Malaria RDT in malaria screening would be contingent on improved sensitivity of the RDT in detecting *P. vivax* infection.

(Contributed by Lim J, Han HK, Lim S, Ooi PL, Disease Control Branch, Communicable Diseases Division, Ministry of Health)

References

1. *Heymann D. Control of Communicable of Diseases Manual, 18th Edition, 2004.*
2. *Ministry of Health. IRIS: Infectious Diseases Reporting and Investigation System.*
3. *Moody A. , Rapid diagnostic tests for malaria parasites. Clin. Microb. Reviews. 2002;15 : 66-78.*
4. *Makler M et al, A review of practical techniques for the diagnosis of malaria. Ann Trop Med Parasitol. 1998; 92: 419-33.*
5. *Palmer C et al. Multicentre study to evaluate the OptiMAL test for rapid diagnosis of malaria in U.S. hospitals. J. Clin. Microbiol. 2003; 41: 5178-82.*
6. *Ndao M et al. Comparison of blood smear, antigen detection and nested-PCR methods for screening of refugees from regions where malaria is endemic after a malaria outbreak in Quebec, Canada. J. Clin. Microbiol. 2004; 42: 2694-700.*
7. *Binax NOW® Malaria test kit product information sheet. Available from BINAX Inc (URL: http://binax.com/uploads/malaria_card_multilingual_pi_06_pdf.pdf)*
8. *Walter Reed Army Institute of Research, Maryland USA. Preliminary evaluation of the NOW® ICT malaria P.f./P.v. rapid diagnostic device for the detection of* Plasmodium falciparum *and* Plasmodium vivax. *Am. J Trop Med. Hyg. 2001; 65(3 Suppl.):320-1.*
9. *Wongsrichanalai C et al. Rapid diagnostic devices for malaria: Field evaluation of a new prototype immunochromatographic assay for the detection of* Plasmodium falciparum *and non-*Plasmodium falciparum*. Am. J Trop Med. Hyg. 2003 ; 69: 26-30.*
10. *Ministry of Health, Singapore. Communicable Diseases Surveillance in Singapore 2001 – 2005.*

The influenza epidemics in 1918, 1957 and 1968, Singapore

Three influenza pandemics occurred during the last century. The first was the 1918 Spanish influenza (H1N1) which resulted in more than 40 million deaths worldwide. This was followed by the Asian (H2N2) influenza in 1957 and the Hong Kong (H3N2) influenza in 1968, the combined death toll was two million.

A review was carried out to determine how badly was Singapore affected during these three pandemics.

The 1968 epidemic

The epidemic occurred in August when the attendances at the outpatient dispensaries were noted

to increase over a 2-week period. At the peak, there was a 65% increase in the daily attendances (from 6,052 to 9,966)[1]

At the University Health Clinic, 522 students and 443 members of the non-academic staff, their wives and children were seen and treated during the period from early Aug to early Sept 1968. The main clinical features were fever (100%), cough (88%), headache (85%), body ache (80%), nasal catarrh (79%), lassitude and lethargy (78%). None was required to be hospitalised. The overall attack rate was 19.2%. (The attack rate was 36.4% for non-academic staff and 17.6% for their children, compared with 16.8% for male university students and 12.8% for female students)[2]

The 1957 epidemic

The epidemic was recognised in early May, reached its peak about the middle of the month and thereafter, there was a gradual decline. By the last days of May, the epidemic came to an end. A total of 77,211 flu cases (comprising 47.6 % of all attendances) and 28 deaths from flu and complications of flu (pneumonia, 22 cases; myocarditis/ heart failure, 6 cases) were recorded in Government and City Council clinics. The peak flu attendance was 5528 cases per day. General Practitioners' clinics were reported to be extremely busy.

The illness tended to last 2-4 days, and in practically all cases, patients recovered in one week. There was no predilection for any age group.

One airline and one shipping line requested health checks for outward passengers from Singapore. Sea passengers from Singapore were subject to quarantine examination in India and Australia.

Schools were closed for about 2 weeks from 8 May to 20 May. The public was warned to keep away from crowded places through the media. There was a fall in attendances in cinemas during the peak of the outbreak. Elective surgery was reduced to a minimum. Additional outpatient treatment centres in school health and maternal and child health clinics, and voluntary clinics were set up[3].

Based on an investigation on 298 patients with influenza admitted to the Asian hospital in Naval Base, the mean duration of hospital stay was 5.3 days, with a mean duration of pyrexia 2.4 days. The predominant symptoms were fever (100%), headache (64.8%), sore throat (45.3%) and cough (31.2%).Complications, mainly seen in the old and young children, were recorded in 13%. The important complications were bronchitis (5.7%) and pneumonia (5.0%). The overall attack rate in Naval Base was 27.6%, with the attack rate of Asians (28.8%) more than 4 times higher than that of Europeans (6.4%). Clerical indoor workers and Europeans had lower attack rates, suggesting the role of social-economic factors in susceptibility to infection[4]

In a study on 250 children admitted to the paediatric unit of Singapore General Hospital during the flu epidemic, the maximum incidence occurred in the 1-5 year age group. No discrepancy in the gender distribution was noted. Vomiting was common in younger children and fits were reported in 44% of the cases. Hyperpyrexia (40.6 - 41.7°C) was not unusual. Bronchitis and brochopneumonia occurred in a third of the cases. In infants, vomiting of feeds was common and associated with parenteral diarrhoea in some cses. Older children (5-10 years) often complained of headache and general body ache. Constipation and profuse sweating were common[5].

The 1918 epidemic

The Straits Settlements (Singapore, Penang, Malacca and Labuan) were hit by the influenza pandemic in 1918. The 1921 Straits Settlements Report stated that "The highest death rates in the past 10 years were 46.46 per thousand in 1911, a very malarious year, **and 43.85 per thousand in 1918 when the influenza epidemic struck the country."**

Influenza vital statistics reported in the annual reports of the Straits Settlement from 1915-1921 are shown in Table 4[6].

There was an obvious excess in the number of deaths of more than 6,000 in 1918. Influenza was stated to be the cause of death in 3500 persons in same year. However, the number of deaths from pneumonia was not stated. A number of pneumonia deaths can be attributed to influenza. This was stated in the 1919 Vital Statistics report. The 6,000 excess deaths in 1918 represented 0.7% of the population in the Straits Settlements then (827,000). There could have been as many as 8,000 excess deaths in 1918 as the total number of deaths fell back to around 28,000 per year from 1919 - 1921 despite an increasing population. The 8,000 figure would represent nearly 1% of the population.

In the 1921 report, Singapore's census population was stated as 417,859 (47.4%) out of a total 881,939 in the Straits Settlements. Assuming that there were equal mortality rates throughout the Straits Settle-

Table 4
Vital statistics for influenza, Straits Settlement, 1915-1921

Year	Population	Deaths	Death rate per thousand	Principal causes of death
1915	776,444	22,633	29.15	Infantile convulsions (4017) Malaria (2929) TB (2580)
1916	797,739	24,371	30.55	Infantile convulsions (3735) Malaria (3346) TB (1870)
1917	809,869	29,950	36.98	Infantile mortality (7571) Malaria (3766) TB (3084)
1918	**827,719**	**36,294**	**43.85**	Infantile mortality (6009) Malaria (4783) **Influenza (3500)** TB (2536) Pneumonia (not recorded)
1919	846,083	27,957	33.04	Infantile mortality (5848) Malaria (4623) TB (1778) Influenza (176) Pneumonia (1415)*
1920	864,858	28,710	33.20	Deaths from influenza (362) Pneumonia (1966)
1921	881,939	28,000	31.79	Deaths from influenza (262) Pneumonia (1702)

* The report stated that "it is probable that many of the deaths were due primarily to Influenza"

ments, and applying the 47.4% proportion onto an excess deaths figure of between 6,000 to 8,000, the number of excess deaths in Singapore in 1918 could be between 2844 and 3792. Rounding off, the number of excess deaths in Singapore in 1918 was estimated to be between 2800 and 3800 deaths (0.7% - 1.0% of the population).

Comments

Although not much information was available for the 1918 epidemic, it was the worst to hit Singapore in the last century. The 1968 epidemic was the least severe and comparable to some of the seasonal influenza caused by the H3N2 variant (A/Victoria/3/75) in 1976, and the H1N1 variant (A/USSR/90/77) in 1977[7]. The 1957 and 1968 epidemics swept through the country and subsided very rapidly, within 4-6 weeks.The overall attack rates based on records in two settings was between 19% (in the University Health Clinic in 1968) and 28% (in the Naval Base in 1957). The duration of illness lasted for about a week. Pneumonia was the main cause of death.

References

1. *Ministry of Health, Singapore. Annual Report, 1968*

2. *Kadri ZN. An outbreak of 'Hong Kong Flu' in Singapore. Part 1: clinical study. SMJ 1970; 11:30-2.*

3. *Ministry of Health, Singapore. Annual Report, 1957*

4. *Lim KA et al. Influenza outbreak in Singapore. Lancet 1957 ;ii :791-6.*

5 *Yeoh OS, et al. Influenza epidemic in Singapore children. BMJ 1957; ii: 1523-5.*

6. *Straits Settlements. Annual Reports, 1915-1921.*

7. *Goh KT. Surveillance of communicable diseases in Singapore. Southeast Asian Medical Information Center, Tokyo, 1982, pg 170-4.*

Travel characteristics and health practices among travellers at the Travellers' Health and Vaccination Clinic in Singapore

Introduction

The South-east Asian region has seen recent increases in travel, and pre-travel health advice is important in protecting these travellers from risks.[1] Travellers now travel to destinations with high disease risk, and may import these infectious diseases back to their country of residence. Travellers from the Asia-

Pacific region have been shown to have poor travel health-seeking behaviour, with only 31% having sought travel health advice, and only 4% having visited a travel health specialist.[1]

This study surveyed the travel health practices and behaviours among visitors to a travel health clinic in Singapore, to determine the characteristics of travellers visiting a travel health clinic in Singapore by their demographic and travel patterns, and to identify the travel health-seeking behaviour among travellers. The findings were compared with a previous airport survey amongst Asians.[1]

Materials and methods

This study was a cross-sectional survey conducted at the Traveller's Health and Vaccination Centre (THVC) at Tan Tock Seng Hospital from 1 September to 30 November 2002. All prospective travellers visiting the clinic during the study period were given a standardised questionnaire on individual demographic and medical information, proposed travel itinerary, previous immunisation status, previous travel history and practices, and health-seeking behaviour. Post-travel individuals, pilgrims, and those who visited the clinic to obtain vaccinations for purposes other than travel were excluded.

Factors associated with the current visit to the THVC and those associated with previous pre-travel health-seeking behaviour were analysed. The factors associated with the current visit were analysed by Pearson's chi-square tests and Fisher's exact tests. Univariate and multivariate analysis with logistic regression models were then performed to determine the demographic groups and travel patterns that were more likely to result in previous visits to travel health

clinics. All analyses were performed using the statistical software Stata version 8.2, with the level of significance set at p<0.05. National demographic data were obtained for comparison.[2]

Results

During the study period, 669 eligible travellers visited the travel health clinic. Of these, 495 (74%) responded to the questionnaire. For 419 (85%) of the respondents, this was their first visit to a travel health clinic, while 433 (89%) indicated that this was their first visit to the THVC.

Demographic and travel patterns

Compared to the racial distribution in Singapore, Malays were significantly underrepresented in the survey (p<0.01) while Caucasians and Eurasians were significantly overrepresented (p<0.01). Compared to the national age distribution, there were higher proportions in the 20 to 30 years (p <0.01) and 30 to 40 years (p=0.03) age groups visiting the travel clinic than in the general population (*Table 5*).

However, there were lower proportions in the < 20 years and > 60 years age groups visiting the clinic (p<0.01 in both groups).

Among the respondents, 66% were travelling for leisure, 25% were going on business trips, while 21% were embarking on mission work. The majority planned to stay in hotels or hostels during their trip (69%), 15% with friends and relatives whom they were visiting, while 11% would be staying on campsites. The median duration of travel was 16 days, with 62% of travellers planning to travel for more than 2 weeks. Those who travelled for mission/relief work stayed less often in hotels (p<0.01), compared

Table 5

Demographic and travel patterns of travellers visiting the Traveller's Health and Vaccination Centre

Variables	Frequency (%)
Gender	
Male	50
Female	59
Race	
Chinese	74
Malay	2
Indian	11
Caucasian and Eurasian	13
Nationality	
Singaporean	81
Other Asian	12
Non-Asian	7
Age Group	
Less than 20 years	13
20 to 30 years	26
31 to 40 years	24
41 to 50 years	20
51 to 60 years	11
More than 60 years	6
Occupation	
PMEB*	22
Students	25
Blue collar	4
White collar	30
Others	19
Income	
No income	22
Up to $2000	23
$2000 to $4,999	34
$5000 to $9999	14
$10000 or more	6
Purpose of travel†	
Leisure	66
Business	25
Mission work	21
Education	9
Accommodation during travel†	
Hotel / hostel	69
Relative / friend	15
Campsite	11
Own	9
Food during travel†	
Local (non-hotel)	48
Hotels	42
Self cooked	22
Others	13
Duration of travel	
<1 week	8
1 week to <2 weeks	30
2 weeks to <4 weeks	37
4 weeks or more	25

* Professionals, managers, executives, and businessmen

† The percentages do not sum to 100% because of multiple answers per individual

to those travelling for business or leisure, but more often in hostels and with the local population (p <0.01).

The proposed and previous destinations by those who had never previously sought travel health advice at a travel clinic are shown in *Table 6*. Travellers were more likely to visit travel clinics for the first time when travelling to the Indian subcontinent, South America and Africa (p >0.01 for these destinations), compared to their previous travels. Correspondingly, visitors were less likely to visit the clinic for the first time when travelling to the rest of Asia, Europe, and South America (p >0.01 for these destinations) compared to their previous travel.

Travel health seeking behaviours

Table 7 shows the travel health-seeking behaviour among clinic visitors. Half had learned about the clinic through friends, while the media, the internet,

and travel agents each influenced less than 5% of visitors. Ninety-four percent had previously travelled outside Singapore but among them only 20% had previously consulted a doctor before travel. In addition, less than 70% of those who had consulted a doctor before travel had received vaccinations or preventive advice. Only 18% had previously had a pre-travel general health examination.

For post-travel health-seeking behaviour, the majority (80%) would first consult a general practitioner or the polyclinic if they fell ill during or after travelling. Of those with previous travel history, 7% had had a general health examination performed post-travel.

Previous travel health-seeking behaviours

From the univariate analysis, Caucasian and Eurasian travellers were significantly more likely to have previously sought travel health advice compared to Chinese (OR 3.8). Non-Asians were significantly

Table 6

Proportion of travel to proposed destinations compared to previous destinations among first time visitors to travel health clinics*

Destination	Proposed visit to destination n=418 %	Previous visits to destination for first time travel health advice seekers n=326 %	p-value
Indochina	26	34	0.07
China	14	24	<0.01
Japan, Korea, Taiwan	0	11	<0.01
Indonesia, Malaysia, Philippines	8	38	<0.01
Indian subcontinent	26	10	<0.01
Oceania	1	23	<0.01
Europe	4	16	<0.01
Middle East	3	3	0.52
Africa	21	4	<0.01
Central America	1	1	1.0
South America	7	0	<0.01
North America	3	14	<0.01

* The percentages in the columns do not sum to 100% because of travel to multiple locations per individual

Table 7

Travel health seeking behaviour among visitors to the Traveller's Health and Vaccination Centre

Variables	Frequency (%)
Knowledge about Traveller's Health and Vaccination Centre	
Newspaper	4
Polyclinics	6
General practitioners	11
Media (television, radio, magazines)	3
Travel agents	4
Friends	50
Travel clinic pamphlets	3
Internet	3
Others	25
First consult if ill during or after travel	
General practitioners	66
Polyclinics	14
Emergency department	9
Traveller's Health and Vaccination Centre	4
Communicable Diseases Centre	6
Others	2
Previous travel outside Singapore	94
Ever consulted doctor before travel*	20
The main driver for consult†	
Own accord	74
Advice of travel agency	2
Advice of friends	13
Internet	0
Media advertising	0
Others	7
Received pamphlet or booklet on travel health†	43
Received advice on prevention of travellers' diarrhoea†	62
Received advice on prevention of malaria†	65
Satisfied with advice given†	84
Received travel vaccinations†	69
Ever visited/had a general health examination pre-travel*	18
Ever visited/had a general health examination post-travel*	7
Brought a personal first aid kit for travel*	49

* These questions were posed only to those who had previous travel outside Singapore

† These questions were posed only to those who had previous travel outside Singapore and had consulted a doctor prior to travel

more likely to have previously sought travel health advice compared to Singaporeans (OR 4.2). Those above 30 years of age were more likely to have previous travel health-seeking behaviour compared to those below 20 years of age (OR >2). Professionals, managers, executives, and businessmen (PMEBs) and those who had travelled 4 or more times were 1.7 times more likely to have previous travel health-seeking behaviour than other occupations and less frequent travellers, respectively. From the multivariate analysis, only Caucasians and Eurasians were significantly more likely to have had previous travel health-seeking behaviour (OR 6.6).

Vaccinations

Table 8 summarises previous vaccination history and the vaccines given during the visit to the travel clinic. Forty-eight percent had previously had hepatitis B and 21% had had a hepatitis A vaccination within the last 10 years. More than half received ty-

phoid (81%), hepatitis A (77%), and diphtheria and tetanus (57%) vaccines at the current visit.

Discussion

This study provided an overview of the demographics, travel patterns, and travel health-seeking behaviour among travellers in Singapore. Travel within Asia is the most common travel destination, Caucasians and Eurasians were overrepresented at our travel health centre, whereas Malay were significantly underrepresented compared to the other races in Singapore. It is possible that Malays travel less, or prefer to seek advice from Malay-speaking Muslim centres. The Hajj pilgrimage is one of the main travel destinations for Malays, and pilgrims prefer to consult Muslim centres for pre-travel advice.[3]

A large proportion (89%) experienced their first visit to a specialised travel clinic, although almost all had extensive previous travel experience. For those

Table 8

History of vaccinations in the last 10 years and vaccinations given to visitors at the travel clinic (n=495)

Vaccines	% previously immunized	% vaccinations recommended and given during the visit
Diphtheria / tetatnus	28	57
Cholera	5	1
Hepatitis A	21	77
Hepatitis B	48	21
Hepatitis A & B	2	6
Influenza	3	18
Japanese B encephalitis	1	1
Meninigococcal	5	15
Mumps, measles rubella	16	9
Polio	18	13
Rabies	1	1
Typhoid	17	81
Varicella	2	2
Yellow fever	4	27
Pneumococcal	0.2	0.2

with previous travel history, only 20% had sought pre-travel medical advice prior to the current visit. This is lower compared with travellers from other regions. Caucasians and Eurasians were 6.6 times more likely to have previously sought pre-travel advice compared to the other races. In addition, non-Asians had increased pre-travel health-seeking behaviour compared to Singaporeans and other Asians. PMEBs and frequent travellers were also more likely to have had previous travel clinic visits, although higher rates of travel may have been a contributing factor.

Among first-time travel clinic visitors, there were more travellers to Africa, South America and the Indian subcontinent compared to these visitors' previous travel destinations. This suggests that visitors perceived the destination-specific risk of Africa, South America and the Indian subcontinent as higher and therefore sought specialist travel health advice, whereas travel to Asia, Europe or North America was not perceived as high risk. This may be due to the perceived health risk in certain regions by local travellers. The lack of perception of risks associated with travel within Asia is similar to our previous study amongst Asians, which documented shortcomings in knowledge, attitude and practices in Asian travellers.[1] There is a need to increase awareness among Asians about the risk of travel within Asia.

In terms of travel health-seeking behaviour, half of all visitors to the THVC had heard about the clinic from their friends, and 75% of travellers who consulted a physician before travel had done so out of their own accord. The internet, media advertising, and travel agents played a muted role in encouraging travel clinic consultations. However, there are now numerous media publicly available as sources of travel health advice in addition to travel clinics. Among those who had pre-travel consultations, less than half received reference materials and less than two-thirds received advice on important diseases such as travellers' diarrhoea and malaria. Better coverage of the risks and possible interventions may increase the effectiveness of travel healthcare.[4] Most travellers also consulted a primary healthcare physician if they fell ill during or after travel. Continuing education for physicians should include travel health to enable them to more effectively address travellers' needs.[5]

The percentage of previous immunisations versus vaccinations given at the clinic also indicates the need for further education. Vaccinations provided at the travel clinic indicate the risks posed by those diseases during travel. Local travellers need to be aware of the risks and to seek advice since Asian travellers have lower rates of travel vaccination compared to non-Asian travellers.[1] This is true for even common illnesses such as influenza, where travellers may not be aware of the risks in tropical regions.[6] It is important to emphasise that risks can be lowered by seeking proper travel health advice, intervention and preparation.[7]

There are some limitations to the study. We conducted the survey on all eligible visitors to the THVC during the study period, to increase the sample size and reduce biases. However, the three month study period may have introduced biases as travel patterns may differ from other periods of the year. Due to the need for informed consent, we could not collect information on the non-respondents (26% of all visitors). Future studies should sample visitors throughout the year, and provide demographic estimates of non-respondents for comparison.

As travel becomes more frequent amongst Asians, travel education is needed to understand the risks involved and to enable better preparation. Travellers also need to be educated on the presence of specialist travel clinics through different modalities, to allow them to seek appropriate travel healthcare.

(Reported by Lee VJ, Department of Clinical Epidemiology and Wilder-Smith A, Travellers' Health & Vaccination Centre, Tan Tock Seng Hospital. The full article can be obtained in the October issue of the Annals Academy of Medicine, Singapore)

References

1. *Wilder-Smith A, Khairullah NS, Song JH, Chen CY, Torresi J. Travel health knowledge, attitudes and practices among Australasian travellers. J Travel Med 2004;11:9-15.*

2. *Demographics of Singapore residents. Statistics Singapore. Available at http://www.singstat.gov.sg/keystats/people.html#demo. Accessed in 10 Nov 2005.*

3. *Wilder-Smith A. W135 meningococcal carriage in association with the Hajj pilgrimage 2001: the Singapore experience. Int J Antimicrobial Agents 2003;21: 112–5.*

4. *Spira AM. Preparing the traveller. Lancet 2003;361:1368-81.*

5. *Ropers G, Krause G, Tiemann F, van Beest Holle Mdu R, Stark K. Nationwide survey of the role of travel medicine in primary care in Germany. J Travel Med 2004;11:287-94.*

6. *Mutsch M, Tavernini M, Marx A, Gregory V, Lin YP, Hay AJ, et al. Influenza virus infection in travelers to tropical and subtropical countries. Clin Infect Dis 2005;40:1282-7.*

7. *Sanford C. Pre-travel advice: an overview. Prim Care 2002;29:767-85*

Chikungunya virus disease

Introduction

Chikungunya virus belongs to the family *Togaviridae*, genus *Alphavirus*.[1] It is an arthropod-borne infection transmitted to humans by the bite of infected *Aedes* mosquitoes.[2] Epidemics are sustained by human-mosquito-human transmission; the epidemic cycle is similar to that of dengue and urban yellow fever.[3]

The word "chikungunya" comes from the Makonde language of the northern Mozambique/south-east Tanzania region, meaning "that which bends up," in reference to the stooped posture of patients afflicted with the severe joint pain associated with this disease.[4]

Chikungunya fever is characterised by sudden onset of chills and fever, headache, nausea, vomiting, arthralgia, and rash. The incubation period is usually 3-7 days (range 2-12 days).[2] In contrast to dengue, chikungunya fever is characterised by a briefer febrile episode and by persistent arthralgia in some cases. However, similarities between clinical appearances of the two diseases probably account for misclassification and some underreporting of chikungunya fever in areas with endemic dengue.

Infection with chikungunya virus is thought to confer life-long immunity.[5]

Laboratory diagnosis is by detection of viral RNA by PCR or positive viral culture during the first few days of illness. In later stages when the disease becomes more classical and viraemia would have ended with antibodies formed, serology (IgM) is the mainstay of diagnosis. No vaccine or specific antiviral treatment for chikungunya is available and treatment is symptomatic.

Epidemiology

Chikungunya virus disease was first documented in East Africa in 1952-1953.[6] Since 1954, the virus has been implicated as the cause of epidemics in a number of Asian countries including the Philippines, Thailand, Cambodia, Vietnam, India, Myanmar, and Sri Lanka.[7] Chikungunya virus has been isolated from humans and mosquitoes in both Africa and Asia. Below is a brief summary of the situation in the region.

Indonesia:

Cases of chikungunya virus disease were first reported in 1973 in East Kalimantan, followed by Jambi province in 1980 and Yogyakarta, Martapura and Ternate in 1983 - 1984.[8] After a period of absence, outbreaks were again reported in Yogyakarta in 1999.[9] From September 2001 to March 2003, 24 distinct outbreaks were reported throughout Indonesia, of which 11 were laboratory confirmed.[10] Outbreaks have been reported almost on a yearly basis since 2001.[8]

Malaysia:

High seropositivity rates were documented in serological studies conducted during 1965 to 1970.[11,12] Its first recorded outbreak was in 1998 – 1999 in Port Klang.[13] Since then, outbreaks have been reported in Petaling Jaya in 1999, and most recently in Perak where more than 200 chikungunya cases, including seven hospitalized cases, were reported in April 2006.[13,14]

Thailand:

Chikungunya was first reported in 1958.[15] The disease was implicated in 15% of paediatric haemorrhagic fever cases in Bangkok from 1962 to 1977.[15] It also accounted for 1.1% of acute febrile illness seen in Thai hospitals from 1991 to 1993.[16] In a seroprevalence survey performed on a rural Thai village population, the prevalence of chikungunya virus antibody was 50% at about age 45.[17] In another survey conducted in north-west province of Prachinburi, 24% of children (ages 10 to 14) and 36% of adults were seropositive.[15]

Chikungunya outbreak in Reunion

Since March 2005, the largest documented outbreak of chikungunya has been occurring on the islands of the south-west Indian Ocean.[18] On the island of Reunion (a French overseas territory), 266 000 cases of chikungunya virus disease were estimated to have occurred from March 2005 to June 2006.[19] The number of estimated cases peaked at 45 000 in week 5 of 2006 followed by a decline with the estimated weekly figure of around 400 in June 2006.[20] The estimated weekly figures were based on the combination of surveillance data and a mathematical model.

The surveillance system was based on notifications from a network of sentinel physicians, hospital admissions for chikungunya virus disease symptoms in hospital emergency departments, microbiology laboratories, and self declarations. The surveillance system also included data on cases with severe clinical presentations. Death certificates with chikungunya virus disease mentioned as a diagnosis were also studied.

A suspected case was defined as 'a patient with a rapid onset of fever over 38.5°C with incapacitating joint pain'.[20] Laboratory confirmation was by the detection of anti-chikungunya virus IgM and/or detection of viral RNA by RT-PCR or virus isolation.[20] The main clinical features presented were: fever, joint pain, muscle pain and headache; almost a quarter of the patients had haemorrhagic symptoms, such as bleeding from the nose or gums.[20]

Of the laboratory confirmed chikungunya virus disease cases who were admitted to hospital intensive care units, clinical manifestations included meningoencephalitis, acute liver failure and multi-organ failure.[21] Serious infections were also notified among newborns, acquired either by mother-to-baby transmission or by mosquito bites.[21] A total of 213 deaths were associated with the disease.[22]

During the 2005 – 2006 period, epidemics were also reported in Comoros, Madagascar, Mauritius, Mayotte, Seychelles, and various states of India.[23] Imported cases from known outbreak areas were reported in Europe (Belgium, Czech Republic, France, Germany, Italy, Norway, Switzerland and United Kingdom), USA, Canada, the Caribbean (Martinique), and South America (French Guyana).[3,22,24]

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Editorial comments

Chikungunya virus infection is uncommon in Singapore. In a serological study conducted on 531 young healthy adults at the Defence Medical and Environmental Research Institute (DMERI) in 2002-2003, 2 (0.3 %) were tested positive for antibodies against chikungunya virus. A few clinical cases imported from Indonesia had also been tested seropositive. (Dr Ooi EE, personal communications). A high degree of vigilance over the disease situation is maintained in Singapore. Suspected cases of chikungunya fever may be laboratory confirmed at the Environmental Heath Institute, National Environmental Agency and DMERI.

References

1. *Khan AH, Morita K, Parquet Md Mdel C, Hasebe F, Mathenge EG et al. Complete nucleotide sequence of Chikungunya virus and evidence for an internal polyadenylation site. J Gen Virol. 2002;83:3075–84.*

2. *Centers for Disease Control and Prevention,USA. Chikungunya fever fact sheet [cited 2006 May 10] Available from: http://www.cdc.gov/ncidod/dvbid/Chikungunya/chickvfact.htm*

3. *Centers for Disease Control and Prevention, USA. Chikungunya fever diagnosed among international travelers — United States, 2005—2006. MMWR 2006;55:1040-2.*

4. *Dorland's Illustrated Medical Dictionary. 30th ed. Philadelphia: Saunders; 2003.*

5. *Jupp PG, McIntosh BM. Chikungunya virus disease. In: Monath TP (ed). The arboviruses: epidemiology and ecology (vol 2). Boca Raton, Florida: CRC Press; 1988:137—57.*

6. *Robinson MC. An epidemic of virus disease in Southern Province, Tanganyika Territory, in 1952-1953. I. Clinical features. Trans Royal Society Trop Med Hyg 1955;49:28-32.*

7. *Centers for Disease Control and Prevention, USA. Chikungunya fever among U.S. Peace Corps volunteers – Republic of the Philippines. MMWR 1986;35:573-4.*

8. *ProMED-mail. Chikungunya - Indonesia: background. ProMED-mail 2006; 08 Sep: 20060908.2554. <http://www.promedmail.org>. Accessed 11 October 2006.*

9. *Porter KR, Tan R, Istary Y, Suharyono W, Sutaryo, Widjaja S et al. A serological study of Chikungunya virus transmission in Yogyakarta, Indonesia: evidence for the first outbreak since 1982. Southeast Asian J Trop Med Public Health 2004 ;35:408-15.*

10. *Laras K, Sukri NC, Larasati RP, Bangs MJ, Kosim R, Djauzi et al. Tracking the re-emergence of epidemic chikungunya virus in Indonesia. Trans R Soc Trop Med Hyg 2005 ;99:128-41.*

11. *Bowen ET, Simpson DI, Platt GS, Way HJ, Bright WF, Day J et al. Arbovirus infections in Sarawak, October 1968-February 1970: human serological studies in a land Dyak village. Trans R Soc Trop Med Hyg 1975;2:182-6.*

12. *Marchette NJ, Rudnick A, Garcia R. Alphaviruses in Peninsular Malaysia: II. Serological evidence of human infection. Southeast Asian J Trop Med Public Health 1980 11:14-23.*

13. *Lam SK, Chua KB, Hooi PS, Rahimah MA, Kumari S, Tharmaratnam M et al. Chikungunya infection—an emerging disease in Malaysia. Southeast Asian J Trop Med Public Health 2001;32:447-51.*

14. *ProMED-mail. Chikungunya - Indian Ocean update (14): Malaysia, India. ProMED-mail 2006; 05 Apr: 20060405.1024. <Http://www.promedmail.org>. Accessed 10 May 2006.*

15. *GIDEON. Distribution of Chikungunya in Thailand. GIDEON <http://www.gideononline.com>. Accessed 11 October 2006.*

16. *Leelarasamee A, Chupaprawan C, Chenchittikul M, Udompanthurat S. Etiologies of acute undifferentiated febrile illness in Thailand. J Med Assoc Thai 2004 ;87:464-72.*

17. *Johnson DE, Scott RM, Nisalak A, Kennedy RS. Togavirus infection in rural Thailand. Southeast Asian J Trop Med Public Health 1980 ;11:184-8.*

18. *Hochedez P, Jaureguiberry S, Debruyne M, Bossi P, Hausfater P, Brucker G, et al. Chikungunya infection in travelers. Emerg Infect Dis [serial on the Internet]. 2006 Oct [Cited 2006 Oct 06]. Available from http://www.cdc.gov/ncidod/EID/vol12no10/06-0495.htm*

19. *Cire la Réunion-Mayotte, Institut de veille sanitaire. Epidémie de chikungunya à la Réunion. Point au 13 juillet 2006. http://www.invs.sante.fr/surveillance/chikungunya/default.htm*

20. *Paquet C, Quatresous I, Solet J, Sissoko D, Renault P, Pierre V et al. Chikungunya outbreak in Réunion: epidemiology and surveillance, 2005 to early January 2006. Euro Surveill 2006;11(2):E060202.3. Available from: http://www.eurosurveillance.org/ew/2006/060202.asp#3*

21. *Cordel H and the Investigation Group. Chikungunya outbreak on Réunion: update. Euro Surveill 2006;11(3):E060302.3. Available from: http://www.eurosurveillance.org/ew/2006/060302.asp#3*

22. *Depoortere E, Coulombier D, ECDC Chikungunya Risk Assessment Group. Chikungunya risk assessment for Europe: recommendations for action. Euro Surveill 2006;11(5):E060511.2. Available from: http://www.eurosurveillance.org/ew/2006/060511.asp#2*

23. *Krastinova E, Quatresous I, Tarantola A. Imported cases of chikungunya in metropolitan France: update to June 2006. Euro Surveill 2006;11(8):E060824.1. Available from: http://www.eurosurveillance.org/ew/2006/060824.asp#1*

24. *Pfeffer M, Loescher T. Cases of chikungunya imported into Europe. Euro Surveill 2006;11(3):E060316.2. Available from: http://www.eurosurveillance.org/ew/2006/060316.asp#2*