



Emerging TTIs – How Singapore secure its blood supply

Ms Sally Lam

Acting Division Director | Blood Supply Management | Blood Services Group | Health Sciences Authority

Outline

- Risk Mitigation Strategies to secure blood supply
- Singapore's experience in securing blood supply against emerging TTIs
 - Malaria, Zika, Dengue, Hepatitis E

Emerging Infections

- *Climate Change*
- *Global travel*
- *Urbanization*
- *Population change*
- *Tourism*

NYID

Dengue Virus

Chikungunya Virus

Yellow Fever

Zika

Trypanosoma cruzi

Influenza A (H5N1) and (H7N9)

SARS-CoV

Hepatitis E Virus

MERS-CoV

Risk Mitigation Strategies

- Determine efficiency of transmission, risk of infection
- Look back and trace back studies
- Minimise contamination of blood supply through collection of blood from asymptomatic donors
- Donor deferral based on infection risk - symptoms, exposure
- Review regularly
- Stop collections
- Continue collections but quarantine blood and components till infection status clarified
- Screening of blood supply
- Pathogen reduction

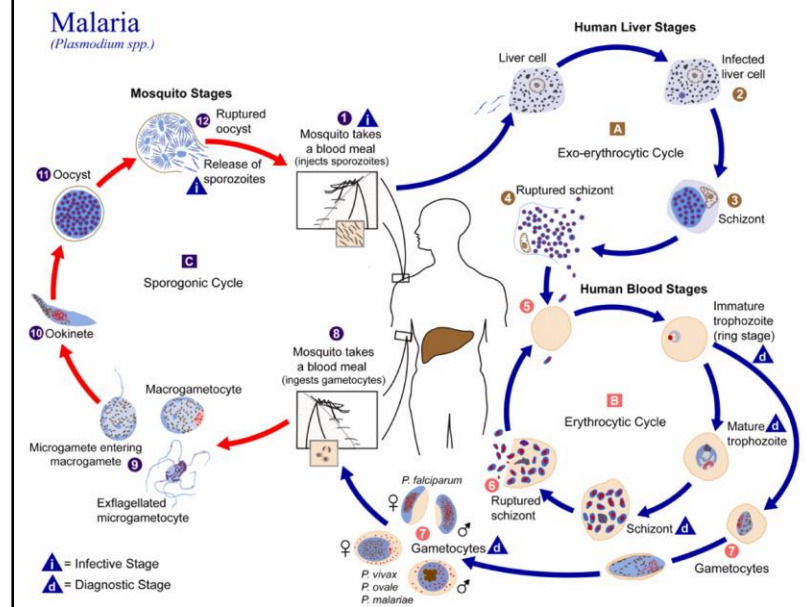
Determining Appropriate Measures for Blood Supply

- Prevalence of infection in population
- Prevalence of infection in donor population
- Effectiveness of existing strategies
- Effectiveness/availability of testing/ pathogen reduction
- Impact on blood supply availability
- Clinical importance in transfusion recipients
- Cost effectiveness in reducing disease morbidity in relation to overall health situation in the country

Singapore's experience in securing blood supply against emerging TTIs

- Malaria,
- Zika,
- Dengue
- Hepatitis E

Malaria



- A Plasmodium parasites
- *P. Falciparum*, *P. Vivax*, *P. Malariae*, *P. Knowlesi*
- Primary vector female *Anopheles* mosquitoes
- Potentially life-threatening disease
- Mainly in African (90%) and South-East Asia regions (7%)
- Singapore is not endemic for malaria but is surrounded by malaria-endemic countries
 - All imported cases
- Low parasite level in treated and fully recovered patients

Management of Malaria in Blood Supply

- Prior to 2002, donor deferral approach based on donors' risks of malaria exposure and estimated incubation periods according to their travel history and use of anti-malaria prophylaxis
- Since 2004, included malarial PCR test to enable donors with a history of travel to malaria endemic areas to donate blood
- In 2011, 2 confirmed malaria-TTI cases from a donor with history of residing in a malaria endemic region and whose implicated donation was non-reactive for malaria PCR
- Malarial antibody test included after a comprehensive risk reduction strategies review conducted
- 10% of donations screened for malarial antibody and PCR tests
 - 97.4% screened released for use = about 10,000 donations

Zika

For anyone who plans to travel to **Zika-affected areas**, avoiding mosquito bites is the best way to avoid exposure to the virus.

Zika virus is primarily spread through the **BITE OF INFECTED MOSQUITOS**.

MOTHER-TO-BABY & SEXUAL ACTIVITY

If a pregnant woman is bitten by an infected mosquito, the infection can cross the placenta, infecting the fetus.

The virus can also be transmitted sexually.

TRANSFUSION

The virus can also be transmitted through blood transfusion or laboratory exposure.

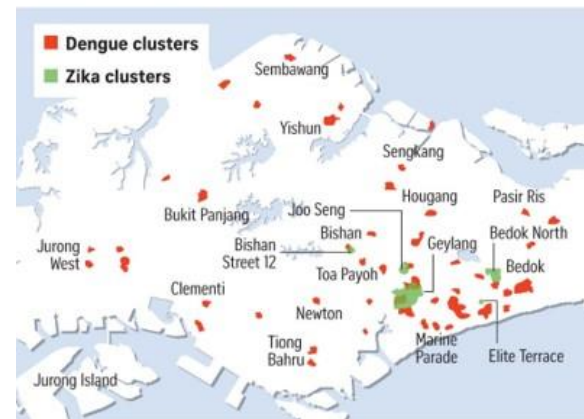


- A Flavivirus
- Primary vector *Aedes aegypti* mosquito
- 80% is asymptomatic and the clinical course of cases is self-limited
- More serious complications: Microcephaly in the fetus and other poor pregnancy outcomes; Adults such as the Guillain–Barré syndrome
- To date, there are no vaccines or specific treatments for the disease

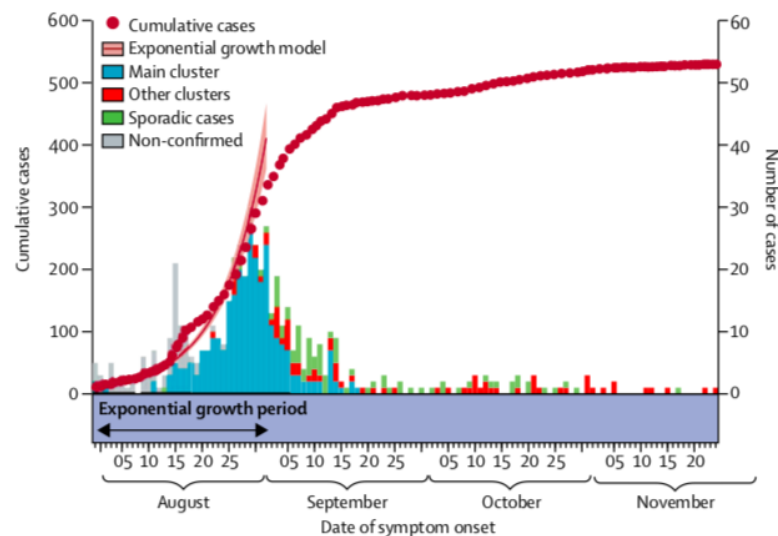
Zika Outbreak in Singapore

- Jan 2016 - 27 countries or territories reported autochthonous transmission of ZIKV
- May 2016 – 1st imported Zika case. Visited Sao Paulo, Brazil 5 days earlier. Patient recovered & no follow up cases found
- 27 Aug 2016 – MOH announced 41 cases of confirmed local Zika cases
- 17 Zika positive pregnancies, 3 pre-matured termination (not Zika related), the rest are normal with no evidence of congenital Zika Syndrome
- 2016 – total of 458 clinical Zika cases reported
- 2017 – 63 Zika clinical cases reported
- 2018 – 1 Zika clinical case reported

Where the mozzies are



Zika clusters:
Aljunied Crescent/Sims Drive/Kallang Way/Paya Lebar Way, Bedok North, Joo Seng, Bishan Street 12



Lancet Infect Dis 2017; 17: 813–21

Management of Zika in Blood Supply

- Risk Mitigation Measures 1 (Feb 2016)
 - **Pre-donation screening of at risk donors**
 - Defer blood donors who have travelled to countries with ongoing active Zika virus transmission for 28 days
 - Defer blood donors who had ZIKV infection for 28 days
 - Recall of non-transfused products collected in the 14 days before the onset of symptoms, in the event of a post-donation report of a confirmed case of ZIKV infection
- Risk Mitigation Measures 2 (Jun 2016)
 - **Provision of Zika-tested blood supply for at-risk pregnant women**
- Risk Mitigation Measures 3 (Jan 2017)
 - **Universal ZIKA NAT Screening of blood donations**
 - MOH mandated as concern on national fertility rate and population

Management of Zika in Blood Supply

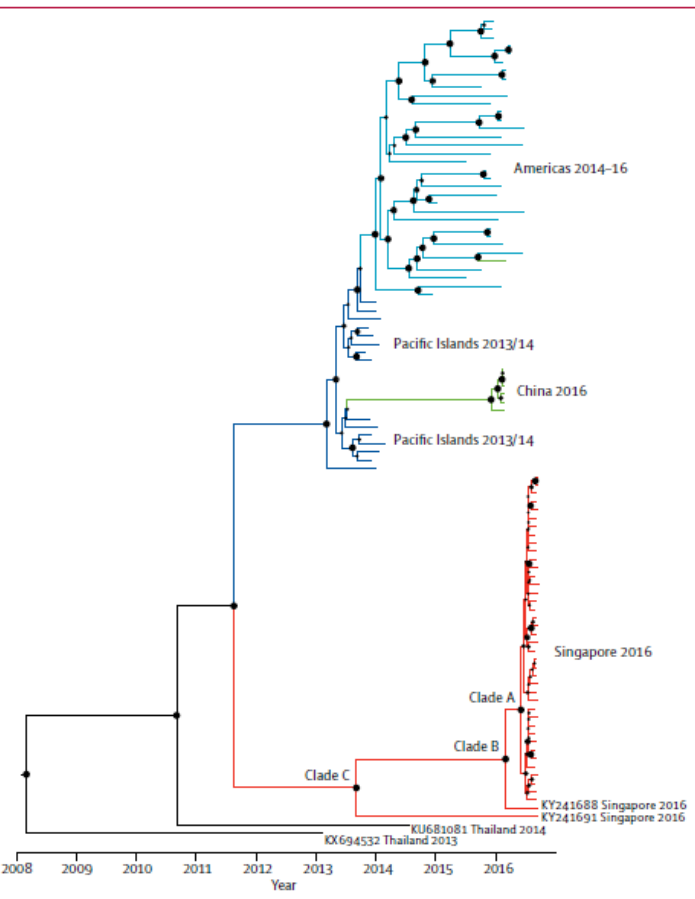
ZIKA prevalence in Singapore blood donations (Dec 2016 to Dec 2018)

= 1 in 93,684 donations

A seroprevalence study was conducted on 3,491 residual blood donor samples collected from December 2013 to February 2014 (Unpublished data)

- ZIKV IgG seroprevalence among residents aged 16-60 years was **4.88%** (0.92% - 11.67%)

**To stop or to continue
ZIKV NAT screening?**



The virus is related to the South-east Asia (Thailand) strain



Dengue

- A Flavivirus
- Primary vector : *Aedes aegypti* mosquito
- 4 main serotypes : Den-1, Den-2, Den-3 & Den-4
 - Den-5 announced in 2013 when detected in the Sarawak state of Malaysia during 2007 outbreak
- Infection with any one serotype confers lifelong immunity to that serotype
- 75% asymptomatic ; severe illness leading to Dengue Hemorrhagic Fever (DHF)
- Dengvaxia vaccine by Sanofi Pasteur available in 2016, only recommended for 9 – 45 yo with prior exposure in endemic areas

FROM WEST TO EAST

Aug 29 to Sept 20

Aug 17 to Sept 11

Aug 4 to Oct 2

8 of the 12 infected workers were bitten here and returned to their quarters at the Livia condominium construction site.

13 breeding habitats with 345 larvae were found at three of seven sites under M's Olayas Corporation.

49 others were infected by mosquitoes which had bitten the eight workers.

32 breeding habitats and 500 larvae, including a plastic pail with 60 larvae, were found.

10 subunits were found at the mall, including on canvas sheets and in drains.

30 people have been infected at these places.

32 breeding habitats have been found.

Elias Mall (near Pasir Ris Dr 3)

Pasir Ris St 52 and 53, Elias Road

Dengue up: Over 160 hit each week

NEA traces how it spread from University Town to Pasir Ris

By SAHMA KHALIK
HEALTH CORRESPONDENT

DENGUE cases are on the rise again, with more than 160 people a week coming down with it over the past three weeks - the highest weekly numbers over the past 21 months.

One of the biggest outbreaks involves more than 60 people.

It occurred when dengue first struck foreign workers at the construction site of University Town in the west, then spread to other workers living in dormitories in Pasir Ris over in the east, then to households in that area.

More cases were reported yesterday.

The workers at University Town were employed by a subcontractor, BHC Construction Pte Ltd, which was also a subcontractor in the Livia condominium site in Pasir Ris Grove.

Twelve foreign workers at University Town were bitten by infected Aedes mosquitoes between Aug 23 and Sept 14.

Following this outbreak, the National Environment Agency (NEA) swung into action and found mosquito larvae at three of the seven construction sites there.

The main contractor at these three sites, Olayas Corporation, was ordered to stop all work between Sept 23 and 29 to clean up the place.

But by then, the virus had headed east with eight of the infected workers who lived at the Livia construction site.

The other four workers live in Woodlands and did not spread the disease.

Other workers living at the Livia site started falling ill from Aug 4.

By Sept 23, a whopping 40 more people were down with the disease.

Said an NEA spokesman: "The purpose and repeated breeding found at the Livia construction site at Pasir Ris Grove would be the key reason for the quick transmission of cases."

Many went to see a doctor, whose clinic at Elias Mall is not air-conditioned.

The NEA believes that while there, these workers were bitten by female Aedes mosquitoes, which continued the spread of the virus in Pasir Ris.

Said an NEA spokesman: "It is unlikely that the mosquitoes were infected by other sources because there were no other reported cases in the area."

It is compulsory for doctors to report dengue cases to the Health Ministry. The information is passed to the NEA, which then tries to find and destroy mosquito breeding grounds so that the infection does not spread.

By the time the NEA was told of the cases at Pasir Ris Grove, 20 workers had already been infected.

The NEA has fined the contractors involved between \$1,000 and \$5,000 while households found breeding mosquitoes were fined \$200.

Many went to see a doctor, whose clinic at Elias Mall is not air-conditioned.

The NEA believes that while there, these workers were bitten by female Aedes mosquitoes, which continued the spread of the virus in Pasir Ris.

Said an NEA spokesman: "It is unlikely that the mosquitoes were infected by other sources because there were no other reported cases in the area."

It is compulsory for doctors to report dengue cases to the Health Ministry. The information is passed to the NEA, which then tries to find and destroy mosquito breeding grounds so that the infection does not spread.

By the time the NEA was told of the cases at Pasir Ris Grove, 20 workers had already been infected.

The NEA has fined the contractors involved between \$1,000 and \$5,000 while households found breeding mosquitoes were fined \$200.

Its officers found and destroyed 12 breeding sites there containing about 500 larvae, but it was too late for the other 23 workers who fell sick within the next 10 days.

By Oct 6, NEA was confident that the cluster at the construction site was no longer active.

But by then, the virus had already moved farther - to residents at Pasir Ris streets 52 and 53 and Elias Road.

So far, more than 30 people living in several UEDB blocks along these roads have fallen sick.

The NEA has fined the contractors involved between \$1,000 and \$5,000 while households found breeding mosquitoes were fined \$200.

It is also taking at least two companies to control over their role in the spread of the disease in this cluster.

NEA has 24 officers scouring the area daily for mosquito breeding sites.

Contractors there have been told to keep infected workers in air-conditioned rooms so they would not be bitten by other mosquitoes, in order to cut the cycle.

It has also appealed to residents to keep their homes free of stagnant water.

It takes only a teaspoon of water for mosquitoes to breed. In the first eight months of the year, 14,533 breeding sites were found, compared to 10,260 in the same period last year.

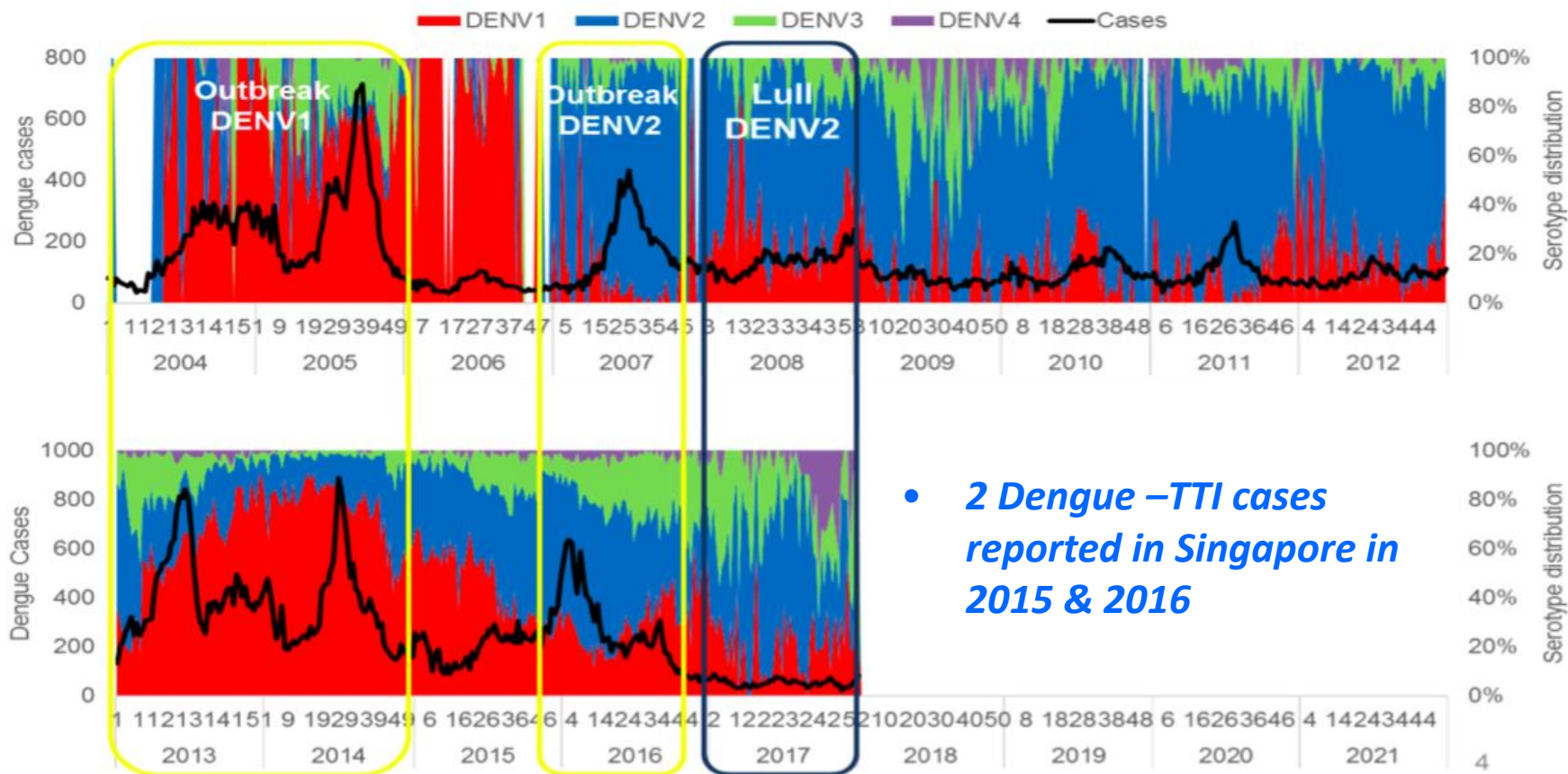
For the trans-valued cluster, larvae was found in pails, toilet bowls, tent canvas, and even in puddles on the ground.

To date, more than 4,100 people have been infected with dengue this year - about 400 more than last year.

Those infected usually get a high fever which is often coupled with a severe headache, rash, joint and muscle ache, and in some cases, pain behind the eyes and mild bleeding of the nose and gums.

suburghigh.com.sg

Weekly serotype distribution and number of dengue cases in Singapore, 2004 to 2017



ENB Quarterly | Vol 44 (2)

Dengue in Donor Population

Geographic Location	Available Data	Source
Guangdong Province, China	Dengue IgG ~ 2.49%	Gou, 2014
Hong Kong	Dengue IgG ~ 2.25%	Kwan, 2017
Tainan, Taiwan	Mean daily prevalence of asymptomatic dengue viremia in blood donors was 15.0 (95% CI, 12.3-17.7) per 10,000 (TMA NAT)	Chien, 2017
Queensland, Australia	Dengue IgM ~1 in 7,146 donations	Faddy, 2013
<i>Singapore</i>	<i>1 in 6,270 donations (2017) by TMA NAT</i>	<i>Unpublished data</i>

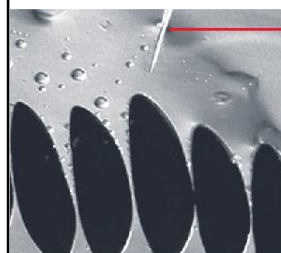
Management of Dengue in Blood Supply

- No testing for dengue in blood donations till date
- Deferral of donors by fever symptoms or exposure
- Contact 'Call-back' line for post donation fever symptoms
- To deploy resources for national vector control programs

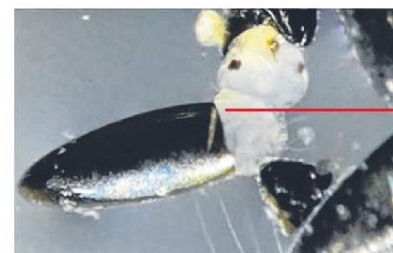


Using Wolbachia to fight dengue

The National Environment Agency will launch a small-scale field study of releasing Wolbachia-carrying male *Aedes aegypti* mosquitoes into the wild at the end of the year. The Straits Times takes a look at how this technology works.



1 The bacteria are extracted from the eggs of Wolbachia-carrying insects such as the *Aedes albopictus*, and then introduced into the eggs of the *Aedes aegypti* mosquitoes via micro-injection. This micro-injection is carried out by Associate Professor Xi Zhiyong at the Michigan State University in the United States.



2 Female Wolbachia-infected mosquitoes that emerge from these eggs will then pass on the bacteria to their offspring. They are then used to rear subsequent generations of Wolbachia-carrying mosquitoes.



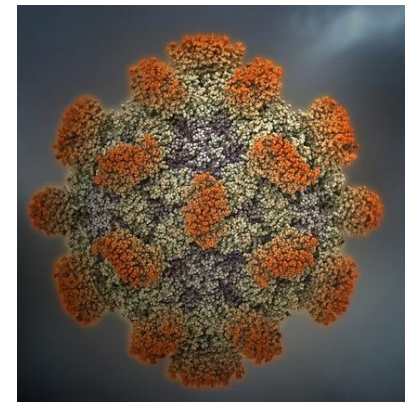
3 The female Wolbachia-infected *Aedes aegypti* are regularly screened for the bacteria and only eggs that have the highest density of the bacteria are kept at NEA's Environmental Health Institute.



4 Only male *Aedes aegypti* which carry Wolbachia will be released during the field study. Male mosquito pupae are smaller than female pupae and hence can be separated by size.

Source and Text: NEA PHOTOS: NEA, PROF XI ZHIYONG, MICHIGAN STATE UNIVERSITY, STRAITS TIMES GRAPHICS

HEPATITIS E



- A Hepevirus, non-enveloped RNA virus
- 4 major genotypes:
 - Genotypes 1 & 2 : through contaminated water & fecal-oral routes
 - Genotypes 3 & 4 : through consumption of undercooked porcine and shellfish
- Genotypes 3 & 4 infection in humans are usually asymptomatic
- Reports of transfusion-transmitted HEV infections have been documented in Europe and Asia
- Current pathogen reduction technologies generally ineffective for non-enveloped viruses
- Immunosuppressant recipients are at risk of chronic liver diseases

Management of Hepatitis E in Blood Supply

- Prevalence study conducted in 2017/2018 on donor population using HEV NAT
 - **0.14% , mainly Genotype 3**
 - % RR highest in Chinese donors.
 - No Malay donors are tested RR for HEV NAT
- Formation of Risk-Based Decision Making Workgroup to put up paper on 'Risk Mitigation Strategy for minimising risk of Transfusion-transmitted Hepatitis E virus infection Singapore'
- Reviewed by HSA Blood Advisory Committee & MOH
 - High HEV NAT prevalence but no reported HEV-TTI cases till date
 - Conduct HEV seroprevalence study on donor population
 - Pending review by MOH after looking at probability of local HEV infection through transfusions versus diet

HEV Testing in Blood Supply

Region	Country	Donor HEV RNA-positive rates	Sampling year	Reported TTHEV	Screening of blood donations
Asia Pacific	Australia	1:14,799 (IDT)	2014	Yes	Not recommended
	Japan (Hokkaido)	1:8173 (MP of 50 donors)	2005-2015	Yes	Implemented in Hokkaido (planning to implement nationwide)
North America	Canada	0:13,993 (MP of between 48 & 100 donors)	2013-2015		Not recommended
	USA	1:9500 (IDT)	2013		In evaluation
Europe	Denmark	1:2331 (IDT)	2015		Not recommended
	England	1:2848 (MP of 24 donors)	2012/13	Yes	Implemented
		1:1365 (MP of 24 donors)	2016		
	France	1:2218 (MP of 96 donors); 1:1000 (MP of 6 donors)	2012/13	Yes	Under consideration
	Germany	1:1240 (MP of 6 donors)	2011	Yes	Under consideration (Universal screening implemented in some blood establishments)
	Ireland	1: 5000 (IDT)	2013-2014		Implemented
		1:2778 (IDT)	2016		
	Netherlands	1:2671 (MP of between 48 & 480 donors)	2011/12		Implemented
	Spain	1:3333 (IDT)	2013		In evaluation

MP = mini pooled donation nucleic acid testing (NAT); IDT = Individual donation NAT
In evaluation: collecting more data

Factors Influencing HEV Strategy in Singapore

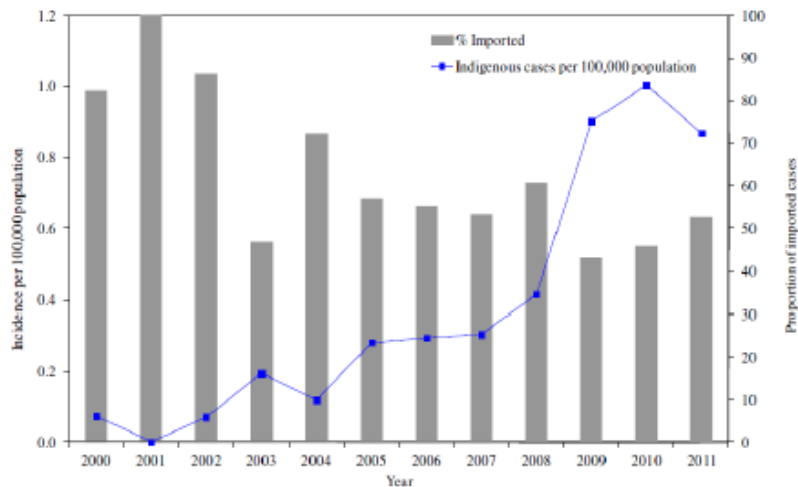


Figure 1 Incidence (per 100,000 population) of reported indigenous acute hepatitis E cases and proportion (%) of reported cases which were imported, 2000–2011*. *Excluded 59 foreigners and tourists seeking medical treatment in Singapore.
Tan et al. *Journal of infection* (2013) 66, 453–459

To do HEV
NAT screen?
HEV RNA in
donors :
0.14%



Impact on patient groups
➤ Transplant patients or more

AVA's messages



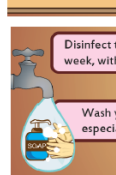
Cook Your Food Well





Separate Raw Food From Cooked Food





Disinfect tea towels or dishcloths regularly, once a week, with either chlorine or hot water.

Wash your hands before and after handling food, especially raw meat and seafood.



Ensure the centre of meat and poultry are well-cooked.

Cook food at high temperatures (above 75°C).



Bring food like stews, soups and curries to boiling temperatures when cooking.

Take special note when cooking minced meat or meat patties as mince meat becomes more exposed to bacteria during the mincing process.



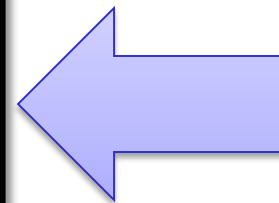
FOOD SAFETY IS A SHARED RESPONSIBILITY!



Imported pork products
HEV RNA in pork liver :

- Hong Kong :1%
- Japan : 2 - 5%
- Thailand : 0.3%

Pavio et al. *Vet Res* (2017) 48:78



Securing Blood Supply against TTIs

- Risk stratification
- Risk- based decision making
 - Logical & Evidence based approach
- Most often determined by
 - Public
 - Political
 - Media
 - Cost effectiveness

Thank You !

