40th year of publication

Epidemiological News Bulletin

QUARTERLY

APRIL - JUNE 2014 VOL. 40 NO. 2 A PUBLICATION OF THE MINISTRY OF HEALTH, SINGAPORE

CONTENTS

Suggested citation:
Ministry of Health, Singapore. [Article title]. Epidemiol News Bull [Year]; [Vol]:[inclusive page numbers]

MOH Weekly Infectious Diseases Bulletin
http://www.moh.gov.sg/content/moh_web/home/statistics/infectiousDiseasesStatistics/weekly_infectiousdiseasesbulletin.html

Epidemiology of acute hepatitis C infection in Singapore, 2005-2013

Introduction

The disease burden of hepatitis C virus (HCV) is of public health concern, as chronic infection poses significant challenges with long-term medical, economic and social consequences. According to the United States Centers for Disease Control and Prevention, about 75% – 85% of individuals infected with HCV would develop chronic infection, while the remaining 15% – 25% would develop spontaneous clearance with natural immunity.[1] Of those with chronic HCV infection, 60% – 70% would develop chronic liver disease, 5% – 20% would go on to develop cirrhosis over a period of 20–30 years, and 1% – 5% would die from cirrhosis or liver cancer.

The World Health Organization (WHO) estimated that about 3 to 4 million people are infected with HCV worldwide every year.[2] An estimated 150 million people are chronic carriers, who are at risk of developing liver cirrhosis and/or hepatocellular carcinoma. More than 350,000 people die every year from HCV-related causes.[3] In April 2014, WHO issued its first guidance for the treatment of hepatitis C. These new guidelines also summarised what should be done to prevent the transmission of hepatitis C, including measures to assess the safety of medical procedures and injections in health care settings and among people who inject drugs.[4]

The HCV is most efficiently transmitted by direct percutaneous exposure to infected blood or injecting drug use. Prior to the availability of screening for HCV, the main parenteral mode of HCV transmission was through transfusion of contaminated blood or blood products.[5] Since the 1990s when widespread screening of the blood supply began,

ISSN 0218-0103
http://www.moh.gov.sg/content/moh_web/home/Publications/epidemiological_news_bulletin/2013.html

transmission currently occurs mainly through use of contaminated needles, syringes and other instruments used for injections and other skin-piercing procedures. In Singapore, screening of blood donors was introduced in December 1992.[6] The prevalence of HCV infection among the blood donors in Singapore was 0.05% between 2005 and 2012 (data not published).

Surveillance of acute viral hepatitis facilitates the monitoring of disease burden caused by these infections as well as the design and implementation of appropriate intervention activities. The objective of our study was to review the epidemiology of acute hepatitis C infection in Singapore during the 9-year period from 2005 to 2013. We examined the trends and risk factors associated with HCV transmission.

Materials and methods

Case surveillance

Acute hepatitis C is a legally notifiable infectious disease in Singapore under the Infectious Diseases Act. All medical practitioners and medical laboratories are required to notify acute viral hepatitis to the Ministry of Health (MOH) within 72 hours from time of diagnosis.

Acute HCV infection is defined by a discrete onset of symptoms, including fever, dark urine, pale stools, nausea, jaundice, and abdominal discomfort, and confirmation of the presence of anti-HCV antibody using recombinant immunoblot assay (RIBA) or the presence of HCV RNA by reverse transcription-polymerase chain reaction (RT-PCR). Notified cases are interviewed by a trained public health officer to determine the presence of known and potential risk factors for acquiring HCV.

Epidemiological data are obtained from the cases through interviews by a trained public health officer. Cases are considered to have a known or potential risk factor for acquiring hepatitis C if they report having a history of injecting drug use, sexual contact with causal partners, chronic hepatitis, blood transfusion, occupational exposure to blood, chronic hemodialysis, perinatal infection, and usage of penetrating instruments (i.e. acupuncture, tattooing and ear piercing), during their estimated exposure period. For cases who report more than one risk factor during the exposure period, a single category is assigned that represents the more likely source of infection based on the relative efficiency of the transmission route.[7]

Statistical analysis

For the analysis, the study period was divided into two periods based on notification trend: 2005 to 2007 (3 years) and 2008 to 2013 (6 years). For the calculation of annual age-specific and ethnic-specific notification rates, the denominators used were the corresponding estimated mid-year populations compiled by the Department of Statistics, Singapore. Proportions between two groups were compared using two-sample independent z-test, with standard error estimated using pooled value of the two proportions. All p values reported were 2-sided and statistical significance was taken at $p < 0.05$.

Results

During the period 2005 to 2013, there were a total of 110 notified laboratory-confirmed cases of acute HCV infection, comprising 78 cases for the 3-year period from 2005 to 2007, and 32 cases for the 6-year period from 2008 to 2013. As a proportion of all reported acute cases of viral hepatitis, acute HCV infection constituted 10.1% and 2.4%, respectively

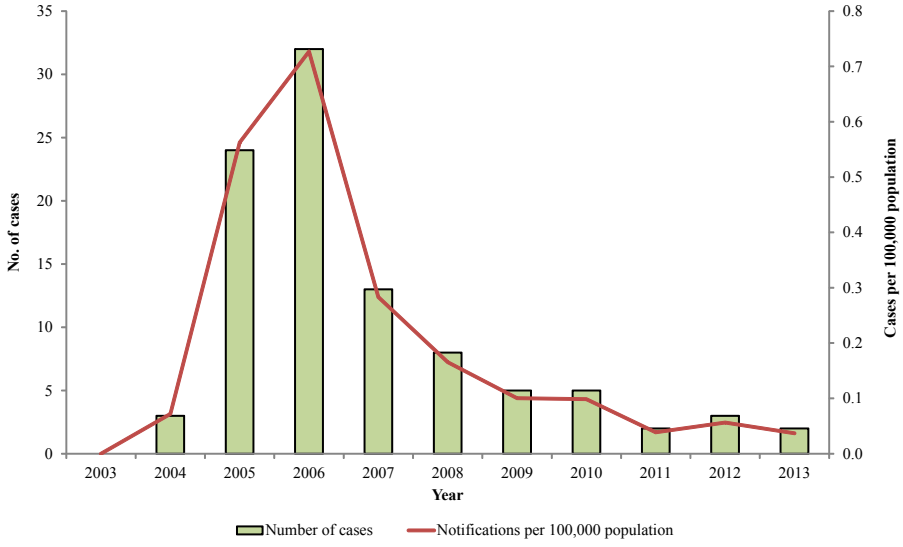
during these two periods. Over the entire 9-year period, 16 of the cases were tourists and foreigners seeking medical treatment in Singapore, and they were excluded from our subsequent analysis.

The highest annual number of acute hepatitis C cases was 32 (excluding 3 foreigners seeking medical treatment in Singapore) in 2006 (*Fig. 1*). The annual number of acute hepatitis C cases ranged from 17 to 35 cases (0.37 to 0.80 per 100,000 population) during the first period from 2005 to 2007, and dropped to a range from 2 to 8 cases (0.04 to 0.17 per 100,000 population) during the second period from 2008 to 2013.

There was no significant difference in the proportion of cases hospitalised for acute HCV infection during the two periods; 95.7% of 69 cases during the first period from 2005 to 2007, and 92.0% of 25 cases during the second period from 2008 to 2013 (p = 0.486). There were no case fatalities during the entire 9-year period. There were 4 imported cases (5.8%) during the first period, and one imported case (4.0%) during the second period. For both periods, the male to female ratio was 5:1 (*Table 1*).

During the first period from 2005 to 2007, about two-thirds of the cases (62.3%) were in the age group of 25-44 years. There was a shift in the age profile of the cases in the second period from 2008 to 2013, with about half of the cases (52.0%) in the age group of 35-54 years. The proportions of cases aged 15-24 years and those aged 55 years or older during the second period were doubled that during the first period, with no significant difference detected (p = 0.310 and p = 0.203, respectively). The age-specific mean annual notification rate was highest in adults aged 35-44 years at 0.92 per 100,000 population during the first period, while it shifted to the older age group of 45-54 years at 0.16 per 100,000 population during the second period (*Table 1*).

Figure 1
Annual notifications of acute hepatitis C cases, 2003 -2013*



* Excludes 16 tourists and foreigners seeking medical treatment in Singapore.

Table 1

Distribution and notification rate (per 100,000 population) of acute hepatitis C cases by gender, age group and ethnic group, 2005-2013*

Characteristic	2005-2007 (3 years)		2008-2013 (6 years)	
	No. (%)	Rate per 100,000 population**	No. (%)	Rate per 100,000 population***
Total	69 (100)	0.51	25 (100)	0.08
Gender				
Male	58 (84.1)	0.85	21 (84.0)	0.25
Female	11 (15.9)	0.17	4 (16.0)	0.05
Age group (years)				
0-4	0	0	1 (4.0)	0.08
5-14	0	0	0	0
15-24	6 (8.7)	0.29	4 (16.0)	0.08
25-34	21 (30.4)	0.77	3 (12.0)	0.04
35-44	22 (31.9)	0.92	6 (24.0)	0.11
45-54	15 (21.7)	0.78	7 (28.0)	0.16
55+	5 (7.2)	0.23	4 (16.0)	0.07
Ethnic group				
Singapore residents				
Chinese	21 (30.4)	0.26	8 (32.0)	0.05
Malay	44 (63.8)	2.99	10 (40.0)	0.33
Indian	3 (4.3)	0.31	2 (8.0)	0.10
Others	0	0	1 (4.0)	0.13
Foreigners	1 (1.4)	0.05	4 (16.0)	0.05

* Excludes 16 tourists and foreigners seeking medical treatment in Singapore.

** Based on estimated mid-year population of 2006 for the period 2005-2007.

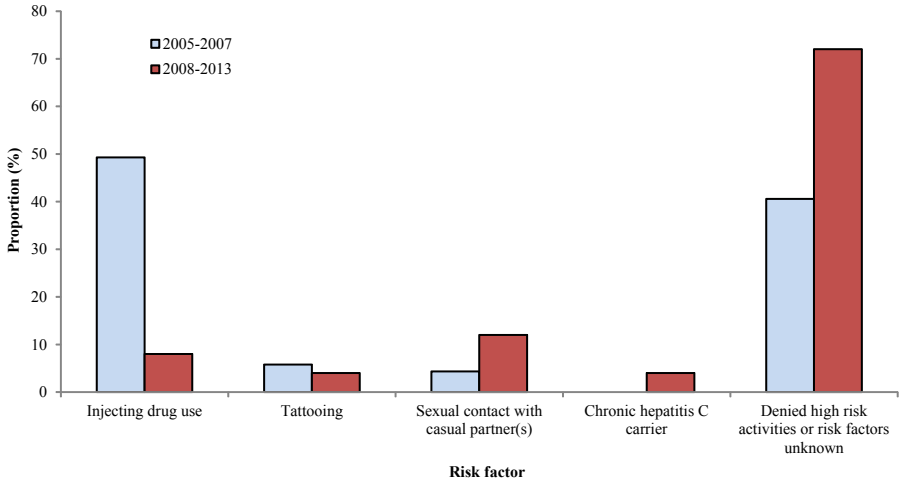
*** Based on estimated mid-year population of 2011 for the period 2008-2013.

Among the three main ethnic groups, Malays comprised majority of the cases, followed by Chinese during the two periods. The proportion of cases who were Malays was significantly higher at 63.8% during the first period, compared to 40.0% during the second period ($p = 0.039$). Malays also had the highest mean annual notification rate of 2.99 per 100,000 population and 0.33 per 100,000 population, respectively.

Of the 69 acute hepatitis C cases notified during the first period from 2005 to 2007, 28 (40.6%) either denied involvement in high-risk activities or their risk factors were unknown (*Fig. 2*). Among 41 cases with risk factors, 34 cases (82.9%) had a history of injecting drug use, majority of whom were Malays (85.3%) while the rest were Chinese. Of the remaining 7 cases with risk factors reported during the estimated exposure period, 4 had tattooing and 3 had sexual contact with casual partners.

Among the 25 acute hepatitis C cases notified during the second period from 2008 to 2013, 72.0%

Figure 2
Distribution (%) of risk factors among reported acute hepatitis C cases by two periods, 2005-2007 and 2008-2013*



* Excludes 16 tourists and foreigners seeking medical treatment in Singapore.

either denied involvement in high-risk activities or their risk factors were unknown. This proportion was almost doubled that of the first period from 2005 to 2007 (p = 0.007). Among 7 cases with risk factors, 3 had sexual contact with casual partners, 2 reported injecting drug use, 1 had tattooing and 1 was a chronic hepatitis C carrier.

Comments

After a spike in acute hepatitis C cases in 2005[8] (25 cases excluding 2 foreigners seeking medical treatment in Singapore) and 2006[9] (32 cases excluding 3 foreigners seeking medical treatment in Singapore), the number of notifications has remained at 5 or lower since 2009. However, the annual rates may be underestimated as HCV infection is usually asymptomatic and often does not come to light until some years later.[10] Nonetheless, the declining trend which we observed is valid as the proportion of undiagnosed infections had remained constant, and screening and disease reporting did not change during the study period.

In our study, we noted a male preponderance. We are aware of under-reporting of high risk behaviours. Of the 94 acute hepatitis C cases notified over the 9-year period from 2005 to 2013, about half reported engagement in high-risk activities of injecting drug use, sexual contact with casual partner and tattooing. None of the acute cases acquired HCV infection through blood transfusion. During the first study period from 2005 to 2007 when there was a higher number of acute hepatitis C cases, injecting drug abuse was the leading risk factor. Injecting drug use is one of the most commonly reported risk factors among patients with acute hepatitis C infection in developed countries including Australia[11,12], Canada[13], the United States[7] and Italy[14]. We attributed the spike in the acute hepatitis C cases during this period mainly to Subutex abuse among injecting drug users. Prompt measures taken by MOH in collaboration with other

agencies to control Subutex abuse could have contributed to the declining trend of acute HCV infection in recent years.

Subutex (or buprenorphine hydrochloride) was approved by MOH as a substitution treatment for opiate-dependent drug abusers within a framework of medical, social and psychological treatments, and it was subsequently introduced into the Singapore market in 2002.[15] A "needle injection culture", which is common among drug addicts in many other countries but never part of the local drug addiction scene, then emerged in Singapore, with increasing reports of complications of parenteral drug abuse noted by clinicians.[16] To tighten control on Subutex prescription, MOH introduced the Clinical Practice Guidelines (CPG) on "Treatment of Opiate Dependence" in November 2005, and the Central Addiction Registry for Drugs, Singapore (CARDS), a web-based system which monitors the prescription of Subutex by doctors and enables them to identify patients who obtain additional supplies from different doctors. In addition, MOH required Subutex-prescribing doctors to attend a mandatory eight-hour training course on managing opiate dependents. With effect from 14 August 2006, buprenorphine was made a Class A Controlled Drug under the Misuse of Drugs Act.

Currently, there is no vaccine for the prevention and control of HCV infection.[2] Prevention is usually targeted at those at risk of acquiring the virus. The key prevention and control efforts against HCV infection entail minimising transmission by ensuring a safe blood supply, putting in place good infection control practices in healthcare institutions and providing public education about disease transmission and preventive measures. Extra attention is warranted for populations in specific settings such as correctional institutions, drug treatment programmes, HIV counselling and testing sites, and clinics for patients with sexually transmitted infections.

(Contributed by Ang LW[1], Chan PP[2], James L[1], Cutter JL[2], Epidemiology & Disease Control Division[1], and Communicable Diseases Division[2], Ministry of Health, Singapore)

References

1. *United States Centers for Disease Control and Prevention. Hepatitis C information for the public. Available at http://www.cdc.gov/hepatitis/c/cfaq.htm (accessed 2 April 2014).*
2. *World Health Organization. Factsheet - Hepatitis C (updated 2013). Available at http://www.who.int/mediacentre/factsheets/fs164/en/ (accessed 15 August 2013).*
3. *Perz JF, Armstrong GL, Farrington LA et al. The contributions of hepatitis B virus and hepatitis C virus infections to cirrhosis and primary liver cancer worldwide. J Hepatol 2006; 45:529–38.*
4. *World Health Organization. Guidelines for the screening, care and treatment of persons with hepatitis C infection. Publication date: April 2014. Available at http://www.who.int/hiv/pub/hepatitis/hepatitis-c-guidelines/en/ (accessed 13 April 2014).*
5. *World Health Organization. Disease information - Hepatitis C. Available at http://www.who.int/ith/diseases/hepatitisC/en/ (accessed 2 April 2014).*
6. *Ong YW, Teo D, Tan HH. Hepatitis C screening in Singapore blood donors. In: Oon CJ, Aw SE, Goh KT (editors). Selected papers from the international symposia on viral hepatitis and hepatocellular carcinoma research, Singapore. Ministry of Health, 1994.*
7. *Williams IT1, Bell BP, Kuhnert W et al. Incidence and transmission patterns of acute hepatitis C in the United States, 1982-2006. Arch Intern Med 2011;171:242-8.*

8. Ministry of Health, Singapore. Communicable Diseases Surveillance in Singapore 2005. Singapore, 2006.

9. Ministry of Health, Singapore. Communicable Diseases Surveillance in Singapore 2006. Singapore, 2007.

10. United States Centers for Disease Prevention and Control. Hepatitis C Information for health professionals. Available at http://www.cdc.gov/hepatitis/hcv/hcvfaq.htm (accessed 2 April 2014).

11. Dore GJ1, Law M, MacDonald M et al. Epidemiology of hepatitis C virus infection in Australia. J Clin Virol 2003;26:171-84.

12. Iversen J1, Grebely J, Topp L et al. Uptake of hepatitis C treatment among people who inject drugs attending needle and syringe programs in Australia, 1999-2011. J Viral Hepat 2014;21:198-207.

13. Public Health Agency of Canada. Hepatitis C in Canada: 2005-2010 Surveillance Report. Available at http://www.catie.ca/sites/default/files/1109-0139-Hep%20C%20Report-EN%20FINAL.pdf (accessed 2 April 2014).

14. Spada E1, Mele A, Mariano A et al. Risk factors for and incidence of acute hepatitis C after the achievement of blood supply safety in Italy: results from the national surveillance system. J Med Virol 2013;85:433-40. Erratum in J Med Virol 2013;85:940.

15. Ministry of Health, Singapore. Press reléase: tougher action against Subutex abuse. Date of release: 11 August 2006. Available at http://www.moh.gov.sg/content/moh_web/home/pressRoom/pressRoomItemRelease/2006/tougher_action_against_subutex_abuse.html (accessed 2 April 2014).

16. Lee CE. Tackling Subutex abuse in Singapore. Singapore Med J 2006;47:919-21.

Emerging technologies in the battle against non-communicable diseases

The increasing burden of non-communicable diseases (NCDs) has accelerated a paradigm shift in healthcare from reactive 'disease treatment' to "4P's medicine" – Predictive, Personalized, Pre-emptive, and Participatory, with a focus from institutional care to a more sustainable community or home-based care for long-term chronic conditions. This new era of "4P's medicine" has been shaped by technology breakthroughs such as the emergence of cloud computing and systems biology, targeted diagnostics and stratified therapeutics, regenerative medicine and 3D organ printing. This review identifies key emerging technologies and their potential application in the healthcare sector.

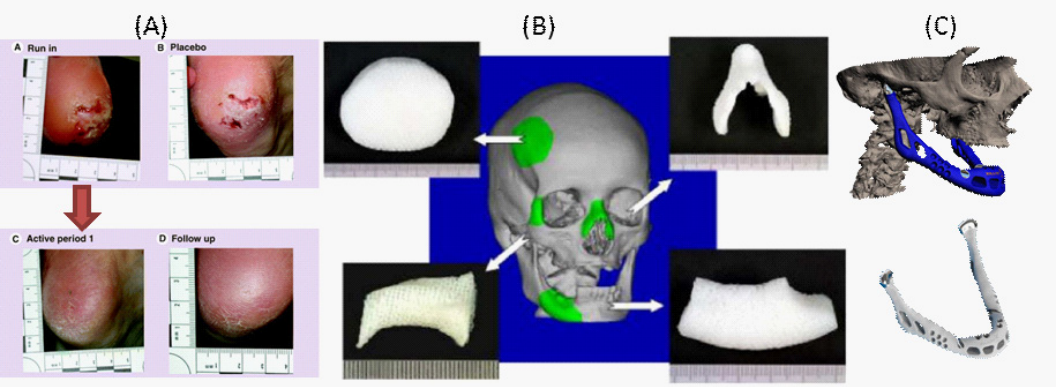
Regenerative medicine

Regenerative medicine is the process of creating living, functional tissues either by repairing damaged tissues *in vivo* via stimulating the tissues to self-heal or by replacing irreparable organs with organs grown *ex vivo*.[1] Currently, relatively simpler nonmodular tissues such as skin and bone have been created *ex vivo* and have been approved by FDA for commercialization.[2] Progress has been made towards more complex therapies, such as the generation of functional nephrons in mice from mouse embryonic cells, and the conversion of human adult pancreatic stem cells to insulin-producing cells that were functional

after transplantation in mice.[3,4] Treatment of diabetic foot ulcers using dressings loaded with autologous keratonocytes has obtained encouraging evidence of efficacy, as there had been reports of complete healing in selected patients who were subjected to the treatment (*Fig. 3A*).[5] The rapidly advancing 3D printing technology has enabled fabrication of customized prostheses and implants that mimic natural structures (*Fig. 3B* and *C*). The ultimate aim of 3D printing is the realization of bioprinters, which use "bio-ink" made of living cells to synthesize tailor-made *de novo* ultra-structures for implantation. In January 2013, scientists have demonstrated the possibility of utilising highly fragile human embryonic stem cells in 3D printing.[6] The printed cell aggregates could be made in customized and reproducible sizes, and maintained stem cell pluripotency and viability, marking the first step towards 3D-printed organs.

It is predicted that the full benefits of regenerative medicine will be realized within 20 years.[7] As a result, the United States, the United Kingdom, Europe, Australia, Japan, China, South Korea and many other countries have committed growing investments into what is perceived to be an industry of the future.[8-13] Singapore is also in the race, with on-going research efforts to understand the molecular mechanisms underpinning the process of cellular reprogramming. The Singapore Stem Cell Consortium (SSCC) was initiated by A*STAR Biomedical Research Council (BMRC) to coordinate a focused translational research and development programme in stem cells in Singapore. It has formed a collaborative partnership with REMEDiE (*Regenerative Medicine in Europe*) to exchange ideas and transfer technologies. More initiatives that focus on regenerative medicine are being set up by the National University of Singapore and the Nanyang Technological University.[14] In the area of 3D printing with biomedical applications, current R&D in Singapore mainly focus on printing absorbable 3D structures to act as temporary scaffolding for cell growth. There have been several successful

Figure 3
Applications of regenerative medicine. (A) Treatment of diabetic ulcer by dressings loaded with autologous keratinocytes (adapted from Moustafa M et al [5]); (B) 3D printed implants for cranio- and maxillo-facial reconstruction (courtesy of Professor Leong Kah Fai, Nangyang Technological University (NTU)); (C) The world's first complete patient-specific jaw successfully printed in 2012 by a Belgian company, LayerWise, and subsequently implanted in an elderly woman

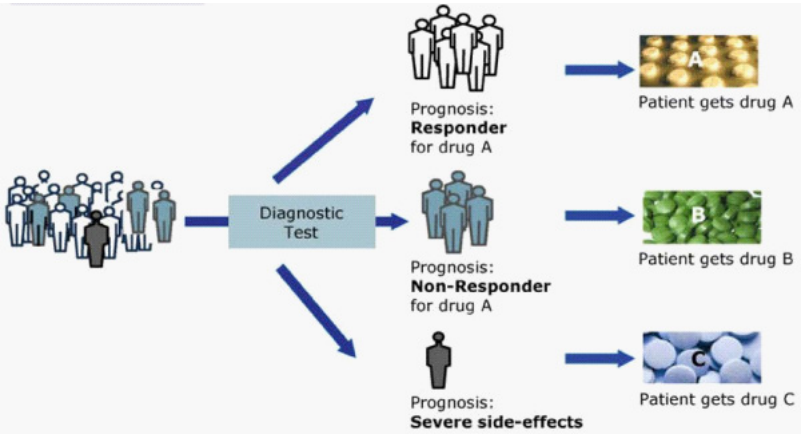


spin-off enterprises in this area. One such example is the customized scaffold bone filler made of biodegradable polycaprolactone (PCL), developed by a group of engineers and doctors from the National University of Singapore (NUS), the National University Hospital (NUH) and Temasek Polytechnic.[15] PCL, approved by US FDA for craniofacial applications, is biocompatible to both soft and hard tissues, and is degraded and assimilated over 24 months. This scaffold was first successfully tested in a 23-year-old patient who was admitted to NUH after an industrial accident.[16] A 3D PCL scaffold was fashioned following his skull's curvature and some of the patient's living bone cells were injected into the scaffold. After two years, the patient was still doing well, the scaffold fused smoothly with the surrounding tissue and his hair grew back. Similar plugs have been fitted into more than 14 patients and they all showed good integration of scaffold and growth of new bone. In addition to 3D printed scaffolds, the local researchers are closely monitoring the international development of "organ printing" and are working to develop such capabilities in Singapore.

Personalized medicine

Personalized medicine is the use of marker-assisted diagnosis and targeted therapies derived from an individual's molecular profile.[17] The ultimate goal of personalized medicine is to target preventive resources and therapeutic agents at the right population while they are still well. Current screenings including pap smear, mammogram or blood-pressure measurement are anticipated to be replaced by the molecular equivalent tests, which will define more precisely the predilection for disease development. Sequencing of entire tumour genomes will guide combinations of therapies. Directed diagnostics and therapy regimes for obesity, rheumatoid arthritis and cardiovascular diseases are also being fervently researched. In the long-term, advances in molecular technology will pave ways for risk identification and targeted treatment for neurodegenerative conditions like Parkinson's disease and Alzheimer's disease. The personalized medicine approach will help to tackle the challenge of selecting suitable drug in conventional medical approaches, by avoiding trial and error phases and the possibility of valuable drugs go to unsusceptible patients (*Fig. 4*).

Figure 4
Better patient treatments through advanced molecular diagnostics and targeted therapeutics will guide the clinical decision-making, depending on the patient's prognosis to be a responder or non-responder to a given medication (adapted from Martinez de Lecea G and Rossbach M).



Currently, 1,000 to 1,300 genetic tests are available for an estimated 2,500 conditions.[18] New tests are regularly emerging at a rate of several per month. In the US, it has been predicted that the proportion of the population that benefit from genetic tests will increase from the current 2% to over 60% in the near future.[19] In the UK, the National Health Service (NHS) launched the "UK genome plan" in December 2012 to sequence and map the genes of 100,000 Britons suffering from cancer and rare diseases. Locally, Singapore has intensive research efforts and industrial collaborations in this field. One exemplary research initiative is the Singapore Gastric Cancer Consortium (SGCC), which aims to convert the current uniform "one-size-fit-all" protocols to personalized therapeutics for gastric cancer.[20] The Roche Translational Medicine Hub is one of the several government-industrial collaborations in Singapore that focus on creating new personalized treatment modalities.[21]

The excitement generated by the promise of personalized medicine is coupled with the challenges to regulate the field. Current demand-supply has driven more commercialisation of genetic testing services both locally and globally. As a result, several developed countries have been trying to regulate genetic testing. Thus far, Germany is the only country that banned all direct-to-consumer (DTC) genetic testing. Under the law approved by the parliament in 2009, genetic tests can only be carried out by a doctor and require the full consent of all parties involved.[22] France passed laws in 2004[23] and 2011[24] to restrict the circumstances under which genetic tests may be legally performed within France, but the laws are general, open to interpretation, and do not explicitly mention DTC genetic tests. The UK Human Genetics Commission (HGC) published its "Common Framework of Principles" for DTC genetic testing services in August 2010.[25] As the HGC is not a regulatory body, the Principles only helps to identify the need for additional regulation or legislation. The US FDA is still grappling with regulations in genetic testing and it has assessed and publicly stated that it considers several specific DTC genetic tests to be medical devices, which are subject to regulation under the Federal Food Drug and Cosmetic Act.[26] In response to FDA's letters to manufacturers of genetic tests, some companies (e.g., Pathway Genomics) voluntarily removed their products while they seek to come into compliance with the relevant regulations, and others (e.g., 23andMe) have continued to offer their products directly to consumers while they negotiate with the FDA.

In 2005, the Bioethics Advisory Committee (BAC) recommended that tests that provide predictive health information should not be offered directly to the public and advertising of such direct genetic tests should be strongly discouraged.[27] Clinical genetic tests offered by healthcare institutions in Singapore are regulated by the Private Hospitals and Medical Clinics (PHMC) Act. The supply of genetic testing kits in Singapore is regulated by the Health Sciences Authority (HSA).

Big Data

"Big Data" refers to the tools, processes and procedures to create and manage extremely large data volumes at high velocities.[28] The application of Big Data in healthcare involves the combination of large dataset and scientific knowledge into valuable clinical information. A number of companies globally are building products and services that manage extreme volumes of data captured in real-time from hospitals and research institutes, as well as social media, fit-

ness devices and a multitude of other unconventional sources. Big Data has a wide variety of applications, ranging from decision-support machine that assist doctors to make faster and more accurate diagnosis and treatment,[29] to mobile and telehealth technologies that enables the management of patients with chronic diseases at home or community-based settings.[30-32] The UK Department of Health showed in 2011 that, if delivered properly, telehealth can substantially reduce mortality by 45%, decrease A&E visits by 15%, reduce the need for admissions to hospital (20% in emergency admissions and 14% in elective admissions), lower the number of bed days spent in hospital by 14% and reduce tariff costs by 8%. If scaled up, the use of telehealth across the NHS could lead up to £1 billion in annual savings with hundreds of thousands of patients' lives improved significantly[33]. Nevertheless, several hurdles remain in the way to the successful implementation of Big Data in healthcare both locally and globally, including privacy and security, regulatory labyrinth, technical and cultural barriers.

Singapore has established itself as a global leader in electronics and data storage since 1980s.[34] In terms of data analytics, the Agency for Science, Technology and Research (A*STAR) has various capability groups to deliver large-scale data analytics to lay persons, leveraging on cloud infrastructure. Some research projects in the domain of healthcare include epidemic modelling and simulation of infectious diseases, system to manage health-related misinformation over social media, and computer-aided diagnosis for cardiovascular diseases. [35] An advanced rehabilitation therapy for stroke patients based on Brain-Computer Interface developed by A*STAR and collaborators are currently undergoing randomized clinical trials.[36] According to A*STAR, it will continue working with industry partners such as HP and Rolls-Royce to generate innovations to stay abreast of the Big Data arena, with increasing focus on healthcare applications.

Conclusion

The emerging technologies reviewed in this article are exemplary but not exhaustive. Other fields such as robotic technology and nanotechnology are also transforming the way we practice medicine. Advancement in biomedical sciences has paved the way to translate research into clinical practice and health policies. However, the move towards greater technologies also comes along with challenges in a complex framework, which spans from research, regulatory to policy development. Singapore is at the early stages of exploration, development and application of these technologies in the healthcare domain. It would be necessary to monitor overseas developments to inform local practices and policy/ regulatory response to ensure safe, accessible and evidence-based application of new technologies to healthcare.

(Contributed by Public Health Intelligence Unit, Epidemiology & Disease Control Division, and Communicable Diseases Division, Ministry of Health, Singapore)

References

1. *US National Institutes of Health. Regenerative medicine: NIH factsheet. http://report.nih.gov/NIHfactsheets/ViewFactSheet.aspx?csid=62&key=R#R*

2. *Chen FM, Zhao YM, Jin Y et al. Prospects for translational regenerative medicine. Biotechnology Advances 2012;30: 658-72.*

3. Xinaris C, Benedetti V, Rizzo P et al. In vivo maturation of functional renal organoids formed from embryonic cell suspensions. Journal of the American Society of Nephrology. 2012;23:1857-68.

4. Scientists learn to regenerate insulin cells. http://www.abc.net.au/news/2012-11-14/scientists-learn-to-regenerate-insulin-cells/4370816

5. Moustafa M, Bullock AJ, Creagh FM et al. Randomized, controlled, single-blind study on use of autologous keratonocytes on a transfer dressing to treat nonhealing diabetic ulcers. Regen Med, 2007;2:887-902.

6. Faulkner-Jones A, Greenhough S, King J et al. Development of a valve-based cell printer for the formation of human embryonic stem cell spheroid aggregates. Biofabrication 2013; 5 015013 doi:10.1088/1758-5082/5/1/015013.

7. U.S. Department of Health and Human Services.2020: a new vision a future for regenerative medicine, 2005.

8. Multi-Center Fellowship in Regenerative Medicine. http://www.fda.gov/AboutFDA/WorkingatFDA/FellowshipInternshipGraduateFacultyPrograms/CommissionersFellowshipProgram/ucm116228.htm

9. REMEDiE. http://www.scoopproject.org.uk/1regenerative-medicine-in-europe-new-knowledge-for-the-challenges-ahead.aspx

10. TERM. http://www.termproject.eu /

11. StemBANCC. http://www.imi.europa.eu/content/stembancc

12. The C4C consortium announces the implementation of France's first ever facility for the industrialization of cell therapeutics and presents the five drugs under development for use in personalized medicine. http://www.businesswire.com/news/home/20121021005017/en/C4C-consortium-Announces-Implementation-Frances-Facility-Industrialization

13. The Kobe Medical Industry Development Project Outline. http://www.city.kobe.lg.jp/information/project/iryo/press/2000/20000331_e.html

14. CREATE. http://www.nrf.gov.sg/nrf/otherProgrammes.aspx?id=188

15. http://www.osteopore.com.sg/pub.htm

16. http://www.innovationmagazine.com/innovation/volumes/v4n3/features1.shtml

17. LayerWise builds the world's first patient-specific lower jaw using laser technology. http://lrd.kuleuven.be/en/news/layerwise-builds-lower-jaw

18. Ginsburg GS, McCarthy JJ. Personalized medicine: revolutionizing drug discovery and patient care. Trends in Biotechnology 2001; 19:491-6.

19. Martinez de Lecea G, Rossbach M. Translational genomics in personalized medicine – scientific challenges en route to clinical practice. The HUGO Journal 2012, 6:2 doi:10.1186/1877-6566-6-2

20. US National Institutes of Health. Database of GeneTests, http://www.ncbi.nlm.nih.gov/sites/GeneTests/?db=GeneTests

21. US Department of Health and Human Services Secretary's Advisory Committee on Genetics, Health, and Society. System of oversight of genetic testing: a response to the charge of the Secretary of Health and Human Services, 2008: 1-192.

22. Tan IB, Ivanova T, Lim KH et al . Intrinsic subtypes of gastric cancer, based on gene expression pattern, predict survival and respond differently to chemotherapy. Gastroenterology 2011;141:476-85

23. Roche establishes new biomedical research hub in Singapore. http://www.roche.com/media/media_releases/med-cor-2010-01-28b.htm

24. Ban on direct-to-consumer genetic tests in Germany. http://www.phgfoundation.org/news/4562/

25. Loi n°. 2004-800 rélative à la bioéthique. 6 August 2004.

26. Loi n°. 2011-267 d'orientation et de programmation pour la performance de la sécurité intérieure. 14 March 2011.

27. UK Human Genetics Commission. Common Framework of Principles, 2010.

28. US FDA.Letters to manufacturers of genetic tests. 2010. http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm219582.htm

29. Singapore Bioethics Advisory Committee. Genetic testing and genetic research. https://www.bioethics-singapore.org/index.php/publications/reports/171-genetic-testing-and-genetic-research

30. Big Data in Healthcare – hype and hope. Dr. Bonnie 360. http://www.west-info.eu/files/big-data-in-healthcare.pdf

31. IBM Watson: ushering in a new era of computing. http://www-03.ibm.com/innovation/us/watson/

32. mHealth: new horizons for health through mobile technologies. WHO global observatory for eHealth series 2011; Volume 3.

33. Future care: care and technology in the 21st century. Carers UK.

34. UK Dept of Health. Whole system demonstrator programme: headline findings, 2011. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/215264/dh_131689.pdf

35. Healthcare without walls: A framework for delivering telehealth at scale, 2020 Health, 2010. http://www.2020health.org/2020health/Publication/NHSit/telehealth.html

36. A*STAR Yearbook 2011-12. http://www.a-star.edu.sg/Media/Publications/A-STAR-Yearbook.aspx

37. Zhang T, Fu X, Kwoh CK et al. Temporal factors in school closure policy for mitigating the spread of influenza. Journal of Public Health Policy 2011;32:180-97.

38. Singapore ramps up biomedical sciences effort with injection of S$36m into medical technology research. http://www.a-star.edu.sg/Media/News/PressReleases/tabid/828/articleType/ArticleView/articleId/1146/Default.aspx

A global perspective on the epidemiology of foodborne illnesses

Background

The World Health Organization defines foodborne illnesses as diseases, usually either infectious or toxic in nature, caused by agents that enter the body through the ingestion of food.[1] Foodborne illnesses are increasingly recognized as an important public health issue in both developed and developing countries. In recent years, there have been significant changes in global food production, processing, distribution and preparation, which in turn contribute to the changes observed in the epidemiology of foodborne pathogens and the nature of outbreaks (from conventional locally limited outbreaks to widespread trans-regional or international outbreaks). Emerging issues such as antimicrobial resistance in foodborne pathogens as well as the rising awareness and concerns of consumers on food related illnesses have led to increasing public health focus and efforts to enhance the prevention and control of foodborne illnesses. This report identifies the key global drivers of the changing trend and epidemiology of foodborne illnesses.

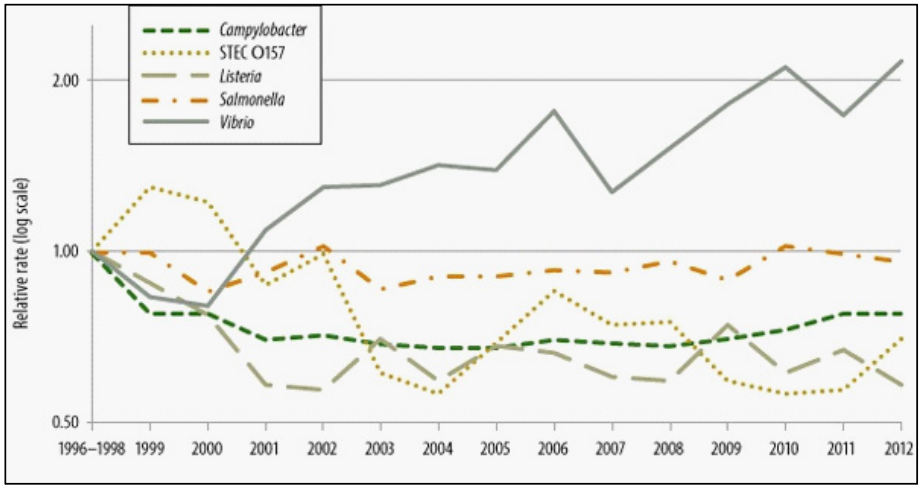
Changing trends of foodborne illnesses

The global burden and cost of foodborne illnesses is estimated to be substantial, though the exact extent of the disease burden globally is yet to be determined.[2] According to WHO's estimates, up to 30% of the population in developed countries are affected annually by foodborne illnesses.[1] Approximately one in six Americans[3] and one in eight Canadians[4] get sick from foodborne illnesses annually while reports from the United Kingdom (UK)[5] and Australia[6] estimated one million and 5.4 million cases respectively, of foodborne illnesses annually.

Major foodborne pathogens

During the past two decades, changes in the epidemiology of foodborne illnesses have been observed particularly in developed countries. Previously known foodborne illnesses such as typhoid fever, cholera and bovine tuberculosis had virtually disappeared from the developed world through better sanitation, sewage treatment, milk sanitation and pasteurization. Nonetheless, new foodborne pathogens have been described either through (a) the identification of new strains, or (b) the identification of an association of foodborne illness with existing pathogens that were not recognized as being transmitted through food.[7] In the last decades, *Campylobacter*, non-typhoidal *Salmonella*, *Listeria* and *Escherichia coli* are the major foodborne pathogens reported in developed countries. In these countries, the overall trends of the incidence of major foodborne pathogens either increased or remained unchanged during the past few years. (*Fig. 5 and 6*)

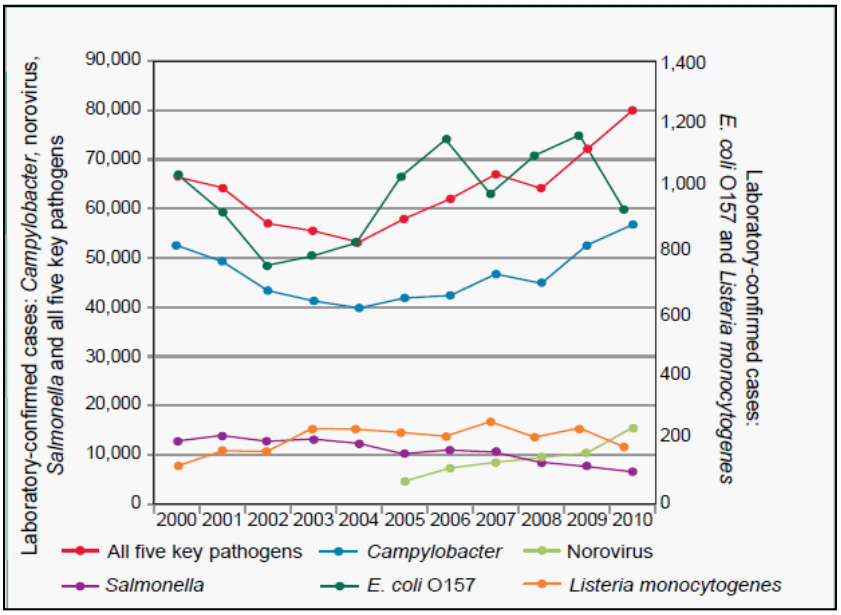
Figure 5
Relative rates of laboratory-confirmed infections with *Campylobacter*, STEC*O157, *Listeria*, *Salmonella*, and *Vibrio* compared with 1996-1998 rates, by year – Foodborne Diseases Active Surveillance Network, United States, 1996-2012^



* Shiga toxin-producing *Escherichia coli*.
^ The position of each line indicates the relative change in the incidence of that pathogen compared with 1996-1998. The actual incidences of these infections cannot be determined from this graph. Data for 2012 are preliminary.

Source: Centers for Disease Control and Prevention, United States. Foodborne Diseases Active Surveillance Network (FoodNet): Figures – 2012 Preliminary Data. Available at http://www.cdc.gov/foodnet/data/trends/figures-2012.html (accessed on 17 June 2014)

Figure 6
UK-acquired laboratory-confirmed cases of foodborne pathogens, 2000 to 2010



Source: Food Standards Agency, United Kingdom. Annual Report of the Chief Scientist 2010/11. Available at http://multimedia.food.gov.uk/multimedia/pdfs/publication/csr1011.pdf (accessed on 17 June 2014)

Scale of foodborne outbreaks

The scale of foodborne outbreaks worldwide has been changing with increasing impact. In the past, traditional foodborne outbreaks involved cases of a particular illness in a local group who were associated with the consumption of a common food and the source of contamination was usually some erratic food handling. However in recent years, foodborne outbreaks have become diffuse and widespread, involving different geographical areas of counties, states and sometimes even nations. In these highly dispersed outbreaks, the implicated food is widely distributed with low level of contamination which might have occurred anywhere along the entire farm-to-table supply chain.[7] The outbreak of *E. coli* O104:H4 in Germany and the multistate outbreak of listeriosis in the United States in 2011 highlight the emergence and importance of widespread foodborne outbreaks. Both outbreaks occurred in developed countries with well-established food safety systems, affecting many cases that were widely distributed in affected regions of the countries and resulting in significant morbidity and mortality.

Overseas, foodborne outbreaks with widespread impact have been reported to be on the rise. In the U.S., the annual reported number of multistate outbreaks stood above 10 since 2010, compared to three to six such outbreaks reported between 2006 and 2009.[8] Australia reported 154 foodborne or suspected foodborne outbreaks in 2010, compared to a 5-year mean of 127 outbreaks.[9]

Unidentified agents or pathogens

Foodborne illnesses caused by unidentified agents or pathogens constitute a substantial proportion even in developed countries and they pose a challenge in developing pathogen-specific prevention and control measures. Of approximately 48 million episodes of foodborne illness that occur in the U.S. every year, only 20% of the cases has been caused by 31 major foodborne pathogens, while unspecified agents are responsible for the other 80% of the illnesses.[10] In Australia, the unknown agents constitute 72% of foodborne illnesses in the country[11]; the UK estimates show that about 48% of foodborne illnesses in the UK are caused by unidentified agents[12].

Antimicrobial resistant bacterial pathogens

The emergence of antimicrobial resistance in bacterial pathogens in the food chain could pose a potential challenge. Infections with antimicrobial-resistant bacteria might result in increased severity of illnesses in humans. Limited antibiotic treatment options of human infections could lead to treatment delay or even treatment failure.[13] In a review done by the European Union (EU) countries in 2011, it was found that antimicrobial resistance was commonly detected in *Salmonella* and *Campylobacter* isolated from human cases as well as from food-producing animals and food. This was also the case for indicator (commensal) *E. coli* and enterococci isolated from animals and food.[14] Currently, strong evidence exists only in the association between veterinary usage of fluroquinolones and antibiotic-resistant *Campylobacter* infections in human. The general associative and causative relationship of antibiotic usage in animal husbandry and the emergence of antibiotic-resistant foodborne pathogens in humans are still to be substantiated.[15]

Drivers of the epidemiology of foodborne diseases

Multiple drivers or factors are suggested to have contributed to the changing epidemiology of foodborne illnesses globally. They could be generalised into the following four themes.

Global population growth

Global population growth together with changes in demographics, resulting in the increase in the population vulnerable to foodborne illnesses is one of the factors identified. Vulnerability arises often because of immune suppression, through either disease processes (e.g. HIV/AIDS) or the medications used to manage them (e.g. immunosuppression treatment), and at the extremes of age (age less than 5 or greater than 60 years old)[16,17] or in pregnancy. This vulnerability results in reduction in the number of organisms needed to cause disease and increased severity of the illness.[18,19]

Globalisation

Globalisation presents two challenges to foodborne diseases - travellers' diarrhoea and a global food market. Global travel has increased immensely in recently years and the number of international tourist arrivals worldwide reached 1,087 million in 2013, compared to 883 million in 2009.[20] With the increase in the global travel, more people become exposed to foodborne pathogens in parts of the world where water safety, food hygiene and food safety are inadequate. The majority of the cases of foodborne diseases reported in developed countries occur in travellers

and bacterial enteropathogens are the most common causal agents of traveller's diarrhoea[21].

Globalisation also brings about advancements in transport logistics and conditions, which have liberalised international trade of food products. While the international trade creates more food choices for individuals, it heightens the risk of widespread foodborne illnesses by facilitating rapid transfer of microorganisms across wide geographical regions, and from one country to another. In addition, the increase in the time between processing and consumption of food products provides opportunities for contamination and time / temperature abuse of food products, resulting in outbreaks that originate from a low-level contamination of a widely distributed food.

Changing human behaviours

Changing human behaviours and practices related to food is another factor identified to have contributed to the changing epidemiology of foodborne illnesses. With the economic development and modernisation of the world, the consumption pattern of humans has changed, with increasing demand for raw or lightly cooked food, and exotic food. For example, dining in restaurants and salad bars was relatively rare 50 years ago, but today, they are a major source of food consumption in many countries of the Organisation for Economic Co-operation and Development (OECD).[22] This has resulted in an increasing number of outbreaks associated with food prepared outside the home.

Moreover, farming practices, including new animal feeds and modern intensive animal husbandry, have changed greatly in the 20th century in order to maximise production of animal food at lower costs, in response to the increasing demand for high-protein foods. One of the best examples of the impact that farming practices have on human health is the detection of variant Creutzfeldt-Jakob disease (vCJD) in humans. Human cases of vCJD were linked to the bovine spongiform encephalopathy (BSE) epidemic in cattle in the UK in the 1990s, which was caused by contaminated high protein animal feeds prepared from BSE infected ruminant carcases.[23,24]

Large and intensive livestock farms also result in high stocking density, stress on animals and low level of genetic diversity, which then lead to increases in the potential for the spread of diseases amongst livestock.[25] These factory farms have given rise to increased prevalence of *Salmonella* and *Campylobacter* in herds of the most important production animals (poultry, cattle and pig).[24] The use of high levels of antibiotics in these factory farms to promote growth and prevent diseases rather than to cure existing conditions[26] may have contributed to the increased emergence of antibiotic resistant foodborne pathogens in food for humans.

The shift to free-range or organic animal production involves the use of manure and irrigation water which may contain pathogens, thus increasing the risk of food contamination and the spread of foodborne illnesses. The outbreak of shiga toxin-producing *E. coli* (STEC) O104:H4 in Europe that was linked to fenugreek seeds produced in Egypt, was thought to be a result of the use of contaminated water for irrigation, or the application of improperly treated organic fertilizer, which led to the growth of the bacteria on the plants or within the production facility.[27]

Climate change, as a result of human activities in industrialisation, effects the transmission of foodborne illnesses and the evidence is shown by the sea-

sonality of foodborne and diarrhoeal diseases, changes in disease patterns that occur as a consequence of temperature increase, and associations between increased incidence of food and waterborne illness and severe weather events. For example, both salmonellosis and campylobacteriosis have been shown to increase with elevated ambient temperature,[28,29] although such effects could be mitigated by improved food handling and storage practices.

Improvement in surveillance and diagnostic capabilities

Modification of surveillance systems and advancements in the diagnostic capabilities of foodborne illnesses is another contributing factor to the rising trends in foodborne illnesses. In the last two decades, a number of developed countries have conducted studies to better understand the actual burden of foodborne illnesses,[30] and continue to improve their foodborne disease surveillance and monitoring systems, resulting in increased awareness and notifications of foodborne illnesses. During the same period, laboratory-based surveillance systems have similarly advanced, resulting in the increasing application of molecular methods to detect and characterize microorganisms. The application of new molecular subtyping methods enables the health authorities to detect clusters of foodborne illnesses, and identify the common source outbreaks for sporadic and seemingly unrelated cases that may span large geographical areas.

Summary

Foodborne illnesses represent an important public health problem globally. A good understanding of the drivers of foodborne illness is important in interpreting changing trends and epidemiology, and in formulating relevant public health response and control measures.

(Contributed by Public Health Intelligence Unit, Epidemiology & Disease Control Division and Communicable Diseases Division, Ministry of Health)

References

1. *World Health Organization. Food Safety and Foodborne Illnesses. Fact Sheet N°237. Available at http://www.who.int/mediacentre/factsheets/fs237/en/index.html (accessed on 24 May 2012)*
2. *Kuchenmuller T, Hird S, Stein C et al. Estimating the global burden of foodborne diseases – a collaborative effort. Euro surveill 2009;14:pii=19195.*
3. *Centers for Disease Control and Prevention, United States. CDC estimates of foodborne illness in the United States, 2011. Available at http://www.cdc.gov/foodborneburden/PDFs/FACTSHEET_A_FINDINGS_updated4-13.pdf (accessed on 24 May 2012)*
4. *Thomas MK, Murray R, Flockhart L et al. Estimates of the burden of foodborne illness in Canada for 30 specified pathogens and unspecified agents, circa 2006.Foodborne Pathog Dis 2013;10:639-48.*
5. *Food Standards Agency, United Kingdom. Annual Report of the Chief Scientist 2011/12. Available at http://www.food.gov.uk/multimedia/pdfs/publication/csar1112.pdf (accessed on 20 December 2012)*
6. *Hall G, Kirk MD, Becker N et al. Estimating foodborne gastroenteritis, Australia. Emerg Infect Dis 2005;11:1257-64.*
7. *Tauxe RV. Emerging foodborne pathogens. Int J Food Microbiol 2002;78:31-41.*
8. *Centers for Disease Control and Prevention, United States. List of selected multistate foodborne outbreak investigations. Available at http://www.cdc.gov/foodsafety/outbreaks/multistate-outbreaks/outbreaks-list.html (accessed on 31 March 2014)*

9. The OzFoodNet Working Group. Monitoring the incidence and causes of diseases potentially transmitted by food in Australia: Annual Report of the OzFoodNet Network, 2010. Commun Dis Intell 2012;36;e213-41.

10. Scallan E, Hoekstra RM, Angulo FJ et al. Foodborne illness acquired in the United States – major pathogens. Emerg Infect Dis 2011;17:7-15.

11. Australian Government Department of Health and Ageing. Foodborne illness in Australia. Annual incidence circa 2000. Available at http://www.ozfoodnet.gov.au/internet/ozfoodnet/publishing.nsf/Content/7BDEF9F8EC3835D9CA257165001AB31D/$File/foodborne_report.pdf (accessed on 22 March 2011)

12. Adak GK, Long SM, O'Brien SJ. Trends in indigenous foodborne disease and deaths, England and Wales: 1992 to 2000. Gut 2002;51:832-41.

13. Doyle MP, Erickson MC. Emerging microbiological food safety issues related to meat. Meat Sci 2006:74;98-112.

14. European Food Safety Authority & European Centre for Disease Prevention and Control. The European Union summary report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2011. EFSA Journal 2013;11:3196.

15. Newell DG, Koopmans M, Verhoef L et al. Food-borne diseases – the challenges of 20 years ago still persist while new ones continue to emerge. Int J Food Microbiol 2010:139;S3-S15.

16. The Foodborne Disease Working Party for the Communicable Diseases Network Australia and New Zealand. Foodborne disease. Towards reducing foodborne illness in Australia. December 1997, Technical Report Series No. 2. Available at http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-cditech-foodborne.htm/$FILE/foodbrne.pdf (accessed on 18 November 2012).

17. Levine WC, Smart JF, Archer DL et al. Foodborne disease outbreaks in nursing homes, 1975 through 1987. JAMA 1991;266:2105-9.

18, Lund BM, O' Brien SJ. The occurrence and prevention of foodborne disease in vulnerable people. Foodborne Pathog Dis 2011;8:961-73.

19. Morris JG, Potter ME. Emergence of new pathogens as a function of changes in host susceptibility. Emerg Infect Dis 1997;3:435-41.

20. World Tourism Organization, UNWTO. Press release: International tourism exceeds expectations with arrivals up by 52 million in 2013. Available at http://media.unwto.org/press-release/2014-01-20/international-tourism-exceeds-expectations-arrivals-52-million-2013 (accessed on 31 March 2014)

21. Shah N, DuPont HL, Ramsey DJ. Global etiology of travelers' diarrhea: systematic review from 1973 to the present. Am J Trop Med Hyg 2009;80:609-14.

22. Rocourt J, Moy G, Vierk K et al. The present state of foodborne disease in OECD countries. Available at http://www.who.int/foodsafety/publications/foodborne_disease/oecd_fbd.pdf (accessed on 5 March 2011)

23. Farquhar CF, Dornan J, Moore RC et al. Protease-resistant PrP deposition in brain and non-central nervous system tissues of a murine model of bovine spongiform encephalopathy. J Gen Virol 1996;77:1941-6.

24. World Health Organization. Factsheet: Variant Creutzfeldt-Jakob disease, revised February 2012. Available at http://www.who.int/mediacentre/factsheets/fs180/en/ (accessed on 27 April 2012).

25. Nathan C. Antibiotics at the crossroads. Nature 2004;431:899-902.

26. Shea KM. Antibiotic resistance: what is the impact of agricultural uses of antibiotics on children's health? Paediatrics 2003;112:253-8.

27. European Food Safety Authority. Shiga toxin-producing E. coli (STEC) O104:H4 2011 outbreaks in Europe: taking stock. EFSA journal 2011;9:2390.

28. D'Souza RM, Becker NG, Hall G et al. Does ambient temperature affect foodborne disease? Epidemiology 2004;15:86-92.

29. Kovats RS, Edwards SJ, Charron D et al. Climate variability and Campylobacter infection: an international study. Int J Biometeorol 2005;49:207-14.

30. Flint JA, Duynhoven YTV, Angulo FJ et al. Estimating the burden of acute gastroenteritis, foodborne disease, and pathogens commonly transmitted by food: an international review. Clin Infect Dis 2005;41:698-704.

An outbreak of gastroenteritis caused by *Salmonella* Enteritidis linked to a food court stall in Singapore

Introduction

Salmonella infection is a major cause of food-borne illness worldwide. In the United States, an estimated 1.4 million cases of *Salmonella* infections are reported annually with more than 500 deaths[1]. Consumption of contaminated eggs and poultry meat remains the most common risk factor for food borne salmonellosis[3, 4]. In Singapore, 1499 cases of salmonellosis were reported in 2012, of these 357 were caused by *S.* Enteritidis [2-4]. Investigations into *S.* Enteritidis outbreaks by the Ministry of Health (MOH) have implicated a variety of food items such as cream cakes, bread and tiramisu [5-8].

Notification

MOH was alerted by the National Environment Agency (NEA) on 24 Jan 2014 of an article in a local newspaper of a 4-year old Indian boy who allegedly died from food poisoning on 22 Jan 2014. The article also stated that the deceased's mother and sister had also come down with food poisoning. We describe the epidemiological, microbiological and environmental investigations and findings of this incident.

Epidemiological investigations

Epidemiological investigations were carried out as soon as the alert was received. Preliminary investigation revealed that all of them had consumed food purchased from a food court stall located in a shopping centre in Yishun, Singapore, prior to onset of symptoms.

The implicated food premise was inspected and food samples and environmental swabs were taken for testing of bacterial pathogens (*Salmonella, Staphylococcus aureus, Escherichia coli, Campylobacter, and Clostridium perfringens*). The implicated food handlers were referred to the National University Hospital and screened for enteropathogens. Genotyping of *Salmonella* isolated (determined by multiple-locus variable number of tandem repeat analysis, MLVA), was performed by the National Public Health Laboratory (NPHL).

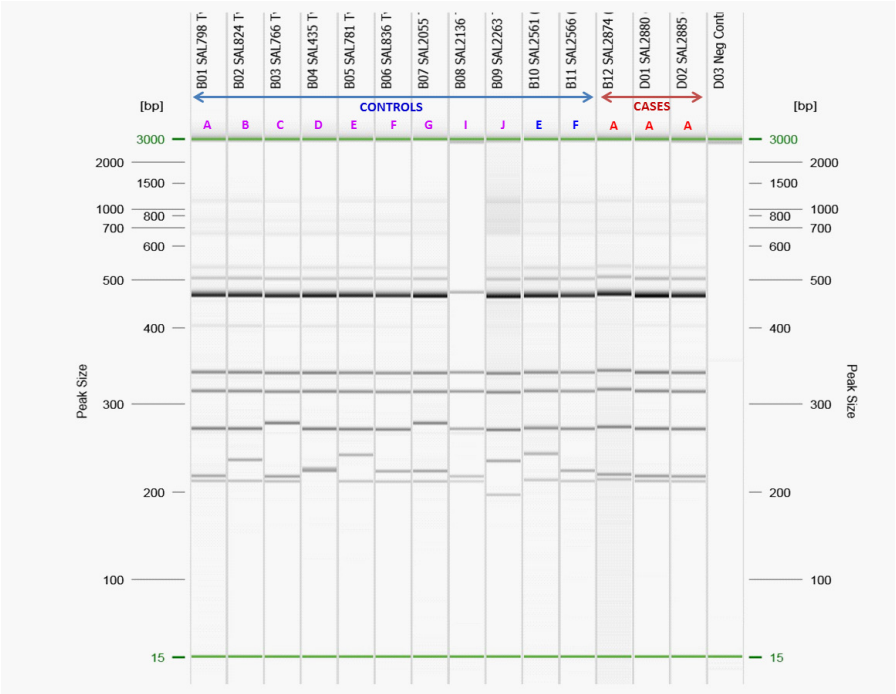
Findings

This incident was confined to the deceased, his two-year-old sister and 35-year-old mother. No other family members (the deceased's father and grandfather and the family's domestic helper) were affected as they did not eat the incriminated food. A review of the notified cases of food poisoning confirmed that there were no other reported cases linked to the implicated premises in January 2014.

The clinical features were watery diarrhoea (at least two episodes in 24 hours)(100%), fever (100%) and vomiting (100%). Symptoms developed within 24 hours of consumption of the implicated meal consisting of rice, curry chicken and begedil. The three cases could not recall the exact time of onset. Two were hospitalised and one subsequently passed away on 22 Jan 2014. The cause of death was reported as consistent with *Salmonella* septicaemia. The remaining case (33.3%) sought outpatient treatment. Stool samples from all three cases were positive for *Salmonella* Enteritidis, MLVA type A (*Fig. 7*).

Seven food samples (assam pedas fish, begedil, curry chicken, egg with sambal, scrambled egg, white rice and raw eggs) and two environmental swabs (from a pair of tongs used for cooked food and from

Figure 7
MLVA typing of *Salmonella* Enteritidis isolated from 3 cases in an outbreak of gastroenteritis, Jan 2014



a food blender) were tested negative for bacterial food poisoning pathogens. Of four implicated food handler screened, one was tested positive for norovirus genogroup I while the rest were tested negative for food-borne pathogens. Inspection of the food stall revealed that the premise was generally clean. However, we noted that ready-to-eat food items were left uncovered at ambient temperature and one of the food handlers was unregistered.

The food preparation processes for the curry chicken and begedil are summarised below:

Curry chicken

- *Fig. 8* gives a visual on the preparation of the chicken parts prior to cooking in gravy.
- Two types of chicken gravy were prepared by the stall daily, the masak merah (red) sauce and the lemak cili padi (small red chilli curry).
- Each type of gravy was prepared using a combination of spices mixed and cooked in water for approximately 30 mins (until boiling).
- After the gravy had boiled, the chicken parts were added into it. Thereafter, the mixture was heated further for another 30 mins.

Begedil

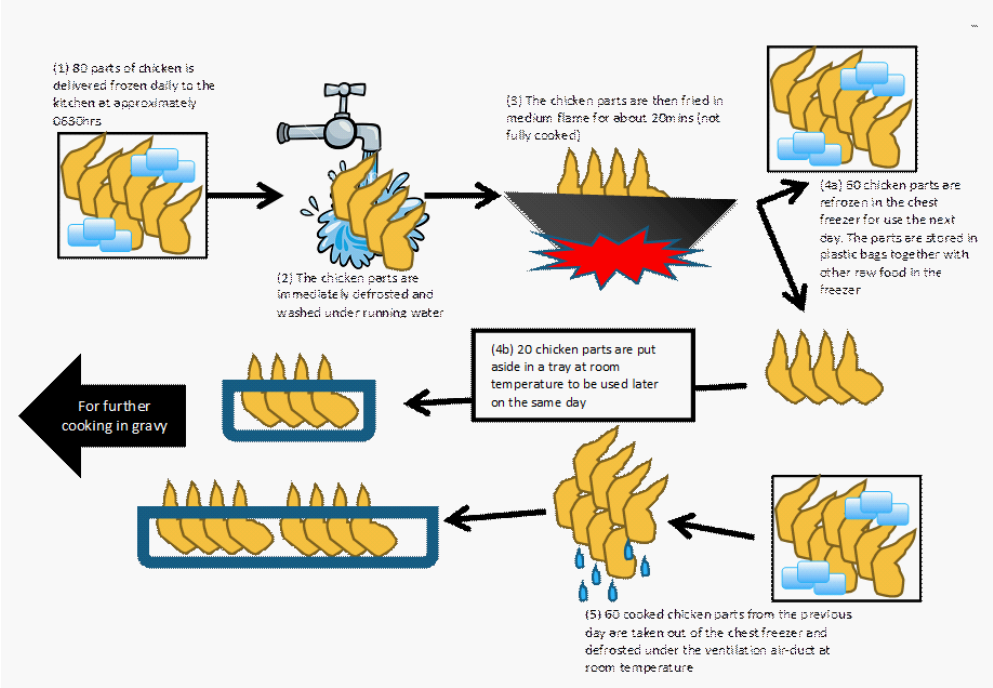
- Ingredients included potato flakes, eggs and spices
- Ingredients were mixed and moulded one day prior to cooking
- The moulded uncooked begedil were stored in the chiller until the next day
- Two batches of 30 each were prepared for cooking in the morning and afternoon

Discussion

This is a point source outbreak of salmonellosis involving three family members. One of them died . The clinical symptoms (watery diarrhoea, fever and vomiting) with an incubation period within 24 hours fit the description of *Salmonella* infection (6-72hr, usually about 12-36hr). This is further supported by the isolation of *Salmonella* Enteritidis in all three cases, all with similar MLVA type. The only food history common to the three cases but not the other family members from the same household was the consumption of food (chicken with curry, begedil and rice) purchased from the food court stall located in a shopping centre in Yishun.

We noted that for the preparation of the curry chicken, the stall had stored some of the partially cooked chicken parts (for use the next day) together with other raw food in the chest freezer for re-freezing. The practice of freezing partially cooked poultry is an unsafe practice. Partial cooking may not destroy all the pathogens which could have been present in the raw poultry. In the process of freezing it once again without the use of rapid freezing, the pathogens which had earlier persisted would continue to multiply before they could be inactivated by the low freezer temperature. Storage of the partially cooked chicken parts in the freezer together with the other raw food poses further risk of cross contamination between the raw and partially cooked food. Furthermore, the frozen partially cooked chicken parts were thawed at room temperature the next day and only warmed in gravy prior to display for sale. Slow thawing at room temperature allows further multiplication of pathogens which would not be fully eliminated if the chicken was not thoroughly cooked. Preparing food in advance of needs, improper refrigeration and inadequate heat treatment during cooking and reheating have been implicated as risk factors in bacterial food poisoning outbreaks[4,9,10].

Figure 8
Preparation of the chicken parts prior to cooking in gravy



We had advised the stall owner to cease this practice, and to ensure that raw food which has been thawed are to be thoroughly cooked on the same day to minimize cross contamination and the growth of food-borne pathogens.

(Contributed by M Fauzy, Tow C, Osman AR, Raj P, Badaruddin H and La MV Communicable Diseases Division, Ministry of Health)

References

1. *Mead PS, Slutsker L, Dietz V et al. Food-related illness and death in the United States. Emerg Infect Dis 1999; 5:607–25.*
2. *Ministry of Health, Singapore. Communicable Disease Surveillance in Singapore 2012.*
3. *Kimura AC, Reddy V, Marcus R et al. Emerging Infections Program FoodNet Working Group. Chicken consumption is a newly identified risk factor for sporadic Salmonella enterica serotype Enteritidis infections in the United States: a case-control study in FoodNet sites. Clin Infect Dis 2001; 38 (Suppl 3): 244-52.*
4. *Gillespie IA, O'Brien SJ, Adak GK et al. Foodborne general outbreaks of Salmonella Enteritidis phage type 4 infection, England and Wales, 1992–2002: where are the risks?. Epidemiol Infect 2005; 133: 795-801.*
5. *Suhana S, Chan PP, Lalitha K et al. An outbreak of gastroenteritis caused by Salmonella enterica serotype Enteritidis traced to cream cakes. Western Pacific Surveillance and Response Journal 2011; 2(1). doi: 10.5365/wpsar.2010.1.1.001*
6. *Tien WS, Toh HY, Hishamuddin P et al. Outbreaks of gastroenteritis caused by Salmonella Enteritidis linked to a bakery in Singapore. Epidemiol News Bull 2012; 38:8-12.*
7. *Tow C, Pang QY, Hishamuddin P et al. Outbreak of gastroenteritis caused by Salmonella Enteritidis associated with the consumption of food from a restaurant in Singapore. Epidemiol News Bull 2013; 39:64-9.*
8. *Lin YJ, Fauzy M, Badaruddin H et al. Outbreak of gastroenteritis caused by Salmonella Enteritidis associated with the consumption of food from a factory canteen. Epidemiol News Bull 2014; 40:13-6.*
9. *Diane R. Factors contributing to outbreaks of food poisoning in England and Wales 1970–1979. J Hygiene 1982; 89:491-8.*
10. *Bryan, Frank L, Doyle et al. Health risks and consequences of Salmonella and Campylobacter jejuni in raw poultry. J Food Protect 1995; 3: 326-44.*

The Epidemiological News Bulletin is published quarterly by the Ministry of Health, Singapore

Any comments or questions should be addressed to:

The Editor
Epidemiological News Bulletin
Communicable Diseases Division, Ministry of Health
College of Medicine Building, 16 College Road,
Singapore 169854
E-mail : Goh_Kee_Tai@moh.gov.sg
Jeffery_Cutter@moh.gov.sg