INFECTIOUS DISEASES AND SINGAPORE

PAST, PRESENT AND FUTURE

HSU Li Yang & Vincent PANG Junxiong
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Foreword

This is a truly remarkable and fascinating book charting the history and impact of infectious diseases on Singapore and the great contribution the country has made and continues to make to the national and global prevention, control and treatment of these infections. It has been put together by an outstanding group of dedicated clinicians committed to learning the lessons of history and applying those lessons to the challenges and opportunities of the 21st century. It is true in medicine as in every other walk of life that “those who do not learn from history are doomed to repeat it”. So often over the last fifty years many learned individuals have argued that infectious diseases have been defeated. These predictions have all proved wrong, and will always prove to be wrong, infectious diseases may change, but they will always be with us. The terrifying rise of drug-resistant infections, the on-going pandemic of HIV, the devastating epidemics of Nipah, SARS, Bird Flu and most recently Ebola and the continued challenge of tuberculosis, influenza and dengue remind us just how vulnerable we remain to endemic pathogens and to the emergence of new infections. With globalization, faster and greater movement of people, trade and urbanisation set to continue and expand this century, we will face new challenges. Infectious diseases do not respect borders and no country can control the threat of infections on its own, we are all inter-dependent and that should force us to work in partnership with our immediate neighbours and with the broader global community to ensure that we all remain safe. What happens today in Freetown, in London, or Riyadh, Jakarta, New York, or Shanghai may affect Singapore tomorrow, and vice versa. It is only by continuing to invest in people, in research and in public health and clinical infrastructure and by working with colleagues in the region and globally can we hope to prevent and control the threat posed by infectious diseases.

I am also thrilled and honoured to read and contribute to this superb book because of my own very personal connection to Singapore in the past and I hope in the future. I was born at the 'old' Changi Hospital, Netheravon Road and my first memories are of Singapore in the early and mid 1960s, when the shops on Orchard Road ended at Tangs with only rice fields beyond, of house-boats permanently berthed along the Singapore River, no skyscrapers, of Change Alley, and amazing holidays at Fairwinds Hotel in Port Dixon. But also sad family memories of a friend of my parents being in an 'iron lung' and subsequently dying of polio
In 1962 and I being one of the children to benefit from Singapore’s remarkable and brave decision to start nationwide polio vaccination that lead to the eradication of the infection from the island as documented so well in this book. Singapore has remained very close to my heart and I am honoured to have had so many wonderful colleagues and friends there throughout my eighteen years living and working in Ho Chi Minh City, Viet Nam (1995-2013) and now through my work with the Singapore Government as a member of the Singapore Biomedical Sciences International Advisory Council.

Singapore is truly world leading in many areas of infectious diseases, it has a fabulous human resource talent base, extremely high quality young graduates and mid-career and senior health professionals. As this book so superbly demonstrates Singapore must continue to invest in research, clinical and public health to address the on-going challenge of infectious disease, which remain endemic in the region. It also has a unique opportunity to provide a leadership role to counter the threat of epidemic infections of importance to Singapore, to the region and globally and thereby keep the citizens of Singapore, the region and the world safe.

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Introduction

Infectious diseases, according to the World Health Organization (WHO), are caused by pathogenic microorganisms such as bacteria, viruses, parasites, or fungi; they can spread from one person—directly or indirectly—to another.¹ The history of the world is inextricably tied with infectious diseases and humanity’s attempts at overcoming them. Singapore—a small island country in Southeast Asia—is no different. Our country’s modern history started with the arrival of Sir Stamford Raffles and the establishment of a British East India Company trading post on the island in 1819. Throughout the major events of the past, including the days of the Straits Settlements, the Japanese occupation during Second World War, independence in 1965, and the years of nation building afterwards, the people of Singapore have struggled against infectious diseases.

The infectious diseases that most affected the people of Singapore prior and immediately post-independence were those that are associated with poor hygiene and crowding. These included diarrhoeal diseases such as cholera; transmissible diseases such as typhoid fever and tuberculosis; and the vaccine-preventable diseases of childhood such as smallpox, polio and measles. Other infectious diseases that were prevalent in the region such as plague and malaria were also present in Singapore during that period.

Postcard reproduction. 1900’s view along Collyer Quay, looking north towards Johnston’s Pier, with the Exchange Building standing out at the far end. (Credit: courtesy of the National Archives of Singapore)
Prior to the advent of effective antimicrobial therapy and vaccination, quarantine was one of the most important ways of preventing the importation of infectious diseases and for limiting their spread. The Quarantine Ordinance—perhaps the earliest precursor of our current Infectious Diseases Act—was approved in 1868 to “make provision for the better prevention of the spread of contagious diseases”. St. John’s Island was a well-known quarantine centre for immigrants with symptoms of plague and cholera in the late 18th century, and also housed patients with other diseases such as leprosy until the mid-20th century.

The various governments of the day in Singapore had a common determined drive to improve the socioeconomic conditions of the people. Their efforts at providing clean water and food, as well as removing waste efficiently, directly led to the decline of many infectious diseases. The incidence of most of these diseases fell even before definitive medical therapy became available—a trend seen in the history of all developed countries. The small size of Singapore was also an important factor for our early successes in controlling infectious diseases. Outbreaks could be detected relatively quickly and measures to control them implemented swiftly. Socioeconomic progress and modernisation was also relatively homogeneous for the local population.

Providing clean water and food, as well as removing waste efficiently, directly led to the decline of many infectious diseases.
Medical progress, along with our continued investments in providing good public health, healthcare, health education, and biomedical research, was complementary to socioeconomic improvement in controlling infectious diseases locally. Singapore has always been at the forefront of introducing new vaccines for her people through immunisation programmes, from smallpox, Bacille Calmette-Guérin (against childhood tuberculosis) and Sabin (oral polio) vaccines pre-independence, to hepatitis B, MMR (measles, mumps and rubella), and pneumococcal vaccines post-independence. Antimicrobial agents for common pathogens have generally been made available for the local public soon after they have been launched commercially worldwide, at affordable prices via prescription-based systems.

These efforts have paid off handsomely. The last local outbreak of smallpox took place in Kampong Alexandra in 1959, involving 10 persons and 2 deaths. The last local case of wild-type paralytic polio occurred in 1978, while Singapore was declared malaria-free by WHO in 1982. Typhoid and cholera outbreaks decreased dramatically in frequency and scale, with the last large typhoid fever outbreak (Salmonella paratyphi linked to imported de-shelled coconut) occurring in 1996, whereas the last cholera outbreak involving more than twenty residents took place in 1998.

The cause of cholera—which typically presents as severe watery diarrhoea (also called “rice water stool” because of its consistency) that can result in death from dehydration—is the bacterium *Vibrio cholerae*. There have been seven cholera pandemics to date, and Singapore regularly had large outbreaks until 1928. The images show yellow colonies of *V. cholerae* on thiosulfate citrate bile salts sucrose (TCBS) agar [upper], and its microscopic appearance as typical comma-shaped Gram-negative rods [lower] (Credit: Diagnostic Bacteriology, Singapore General Hospital [SGH]).

Singapore has always been at the forefront of introducing new vaccines for her people through immunisation programmes.
Chlorination of ponds in Potong Pasir during the sterilisation campaign against cholera in 1963.
(Credit: Ministry of Information and the Arts collection, courtesy of the National Archives of Singapore)

Blood film showing falciparum malaria trophozoites within red blood cells. Malaria is caused by parasites with a life cycle that takes place between two hosts—human and Anopheles mosquitoes. As human infection progresses, infected red cells are destroyed or—in the case of Plasmodium falciparum—also become sticky and block small blood vessels, resulting in the clinical manifestations of the disease. Malaria is prevented and can be eradicated basically by interrupting mosquito-borne transmission of the parasite. But this requires considerable political will and financial commitment over a protracted period of time.
Eliminating malaria on Pulau Tekong

Although Singapore was declared malaria-free by WHO in 1982, Pulau Tekong—a small forested island housing a large military training facility located offshore—remained malaria-receptive because of the high prevalence of Anopheles mosquitoes. Visitors and military personnel regularly took malaria chemoprophylaxis in addition to other protective measures such as the use of insect repellent and bed nets while on the island, despite which small malaria outbreaks continued to occur up to the early 2000s. In December 2006, the Singapore Armed Forces embarked on an ambitious integrated vector-borne disease management programme, comprising:

- Screening of foreign workers involved in construction projects on the island for carriage of malaria parasites.
- Environmental and infrastructural work to reduce Anopheles breeding sites.
- Conventional outdoor fogging with insecticides to reduce the adult mosquito population.
- Indoor residual spraying to reduce the exposure of military personnel to mosquitoes.
- Targeting mosquito larva through the use of Bacillus thuringiensis israelensis (Bti) larvicide via ultra-low volume mist fogging throughout the island. Bti is a bacterium that produces toxins that kill the larva of several flying insects, including mosquitoes. It is used as a biological control agent for these insects globally.

Before and after photos documenting improvements to drainage and clearance of vegetation in order to reduce water pooling and build up of Anopheles breeding sites, carried out in 3-monthly cycles on Pulau Tekong. (Credit: Ministry of Defense, Singapore)
Intensified mosquito fogging on Pulau Tekong. (Credit: Ministry of Defense, Singapore)

Indoor residual spraying at the barracks. (Credit: Ministry of Defense, Singapore)
Since 2007, malaria chemoprophylaxis has not been required on Pulau Tekong, with the risk of malaria virtually eliminated.
We remain vulnerable to the threat of emerging infectious disease epidemics in view of the increasingly inter-connected nature of the world. Nonetheless, many infectious diseases, old and new, continue to plague the people of Singapore. We also remain vulnerable to the threat of emerging infectious disease epidemics in view of the increasingly inter-connected nature of the world. Singapore has accomplished much in the area of infectious diseases, although the lessons from our experiences and the stories of those who have worked to control infectious diseases are not well known. In subsequent chapters, we explore in greater detail the more important infectious diseases of the past and present, as well as how the people and government of the country have worked to eliminate or contain these threats. Finally, we also attempt to forecast—tapping on the perspectives of a large panel of experts—the possible infectious disease threats to Singapore in the future.
In 2010, access to clean water and sanitation was recognised as a basic human right by the United Nations General Assembly. But it has long been known that clean water, waste disposal and good hygiene are fundamental to public health and the prevention of many infectious diseases. When Dr John Snow persuaded the Board of Guardians of St James’s parish to remove the public water pump handle on Broad Street on 7 September 1854, he ended the cholera outbreak in Soho, London—providing both a model of epidemiological investigation as well as a much publicised link between sanitation and health prior to the development of germ theory (Louis Pasteur was to propose this in 1861).

During the 19th and early 20th centuries, water and foodborne diseases such as cholera, typhoid and other diarrhoeal diseases were rampant and of major public health concern in Singapore. This was largely due to the lack of clean water—Singapore is a water-scarce country with limited land area for collecting and storing rainfall—as well as an effective sewage, drainage and disposal system. The situation was worsened by rapid population growth and urbanisation, as well as burgeoning trading activities along the Singapore River and Kallang Basin from the early 20th century. A night soil bucket system was used for human waste disposal; garbage, pig and human excrement, and oil spillage were common in the vicinity.

During the 19th and early 20th centuries, water and foodborne diseases such as cholera, typhoid and other diarrhoeal diseases were rampant and of major public health concern in Singapore.
heavily polluted river water; and basic sanitation and hygiene awareness was limited in the community.

Singapore’s quest for water self-sufficiency is well documented. Via an integrated, holistic and long-term approach that combines demand- and supply-side management with political will as well as research and development, safe water that is “fit to drink from the tap” is cheap and accessible to all on the island. The quality of drinking water in Singapore is available as an extensive and regularly updated report from the website of the Public Utilities Board (PUB)—the national water agency responsible for the collection, production, distribution and reclamation of water in Singapore.

The management of used water and waste in Singapore progressed slowly at first. The night soil bucket system was inadequate on its own because there was no satisfactory way to dispose of the night soil after collection. Municipal engineer James MacRitchie’s experimental poudrette (dried night soil used as a fertiliser) plant in 1898 failed as it was too expensive to maintain and was closed in 1903. Sanitary engineer G. Midgeley Taylor was engaged by the municipal commissioners to report on the disposal of sewage in Singapore in 1909, and he recommended a system of underground sewers with a pumping station and purification works that would then send processed sewage into the sea via an outfall main pipe. His proposal dovetailed with a municipal enquiry commission’s report that heavily criticised the Singapore municipality’s failure at creating an organised sewage system, and the government responded.
by building the first sewers locally by 1917, with processed sewage discharged into the Singapore River.\textsuperscript{12, 13} However, night soil would still have to be collected from homes before being discharged into the sewers at central locations in the municipality.

More sewers were subsequently built, albeit in a piecemeal and protracted manner because of a variety of reasons, including lack of water and costs. It was only in the 1960s, especially post-independence, that a massive expansion of the sewer system was undertaken, with the building of Bedok, Kranji, Seletar, and Jurong Sewage Treatment Works between 1979 and 1985. This resulted in every residential household being connected to the sewage system and the last night soil bucket being returned to the PUB on 24 January 1987.\textsuperscript{13}

Workers in a 2000-feet long and 7.5 feet by 7.5 feet gravity-driven sewage tunnel (gravity sewer) along Braddell Road to Bartley Road Sewage Pumping Station, 1963. (Credit: Ministry of Information and the Arts Collection, courtesy of National Archives of Singapore)

Mr Tan Gee Paw, current chairman of PUB. “We recognised that we could not continue with the night soil bucket system. From the environmental and public health point of view, it would be a disaster. We were building housing board flats, all very compact, in a densely populated city, and therefore night soil inside the house was just impossible for us from the environmental and public health point of view. It was simply an imperative that we should get rid of it and lay sewers to every home in Singapore. Human waste when it is produced must be removed from the home as soon as it possibly can. We embarked on a massive program starting from the 1960s, and succeeded in the late 1980s when the last night soil bucket came back to us.”
The current sewage system is designed based on a 'separate system' whereby used water is collected separately in a network of underground sewers that lead to a treatment plant whereas storm water and surface runoff are collected in open drains and channelled to rivers and reservoirs. This helps to prevent any potential bacterial and viral cross-contamination between the used water and potential potable water. In the 1990s, a superhighway for used water management, the Deep Tunnel Sewerage System (DTSS), was conceived by the PUB. The concept of the DTSS is to use deep tunnel sewers to convey used water by gravity to centralised water reclamation plants (WRPs) located at the coastal areas. The used water will then be treated and further purified into clean, high-grade reclaimed water called NEWater, or discharged to the sea through the outfalls. The first phase of DTSS was completed in 2008, with the second and final phase pending completion by 2024.
Of the many examples of Singapore’s efforts to improve sanitation and hygiene, three in particular stand out. These are:

- The cleaning up of the Singapore River and Kallang Basin.
- The formation of the hawker centres.
- The phasing out of pig farms.

They were all multi-sectoral efforts, and had salutary effects beyond just improving the overall sanitation in Singapore, as any visitor to the Singapore River and hawker centres can attest.

Cleaning up Singapore’s rivers

In 1977, Prime Minister Lee Kuan Yew called for the cleaning up of Singapore’s rivers. The former chairman of the PUB and Environment Ministry Permanent Secretary Mr Lee Ek Tieng spearheaded this effort with the aid of a dedicated team, including the current PUB chairman Mr Tan Gee Paw. The clean up involved a massive relocation of about 4,000 squatters into public housing areas, along with hawkers and vegetable sellers into hawker centres. The Port of Singapore Authority moved hundreds of bumboats ferrying goods between warehouses along the river and cargo ships out at sea to a new anchorage at Pasir Panjang. Foul-smelling soil had to be dredged from the banks and the bottom of the river, with large amounts of debris and other rubbish cleared. The project was completed on time in 1987, earning Mr Lee, Mr Tan and eight others on their team gold medals from PM Lee.
Singapore’s hawker centres

Hawker centres, and hawker food, are beloved by both the locals and tourists to the country. They are iconic features of Singapore, and part of our cultural heritage. Hawker centres are a relatively recent phenomenon, however, with the first—Yung Sheng Food Centre at Jurong (currently Taman Jurong Market and Food Centre)—being built only in 1971. In the past, all hawkers were street hawkers, plying their trade where space was available. By the time of the 1950 Hawkers Inquiry Commission, street hawkers were perceived negatively by government officials and others, suspected of causing cholera and typhoid outbreaks, generating filth and pests such as flies and rats, blocking vehicle and pedestrian traffic, and rendering street cleaning difficult.
Attempts at licensing street hawkers generally failed, and the government only seriously attempted to re-settle the hawkers after 1971, when it felt that it had created enough jobs to "enforce the law and reclaim the streets". The government’s hawker resettlement programme finally moved the last street hawker into hawker centres with piped water supply, sewage and garbage disposal in 1986.

Dr Edmund Monteiro, former director of the Communicable Diseases Centre, Tan Tock Seng Hospital (retired). “One of the hawkers responsible for the 1965 typhoid outbreak (at Chung Cheng High School; 90 cases) was an itinerant hawker, and he sold cold drinks, so you can see the capacity for mischief was tremendous!”
Infectious Diseases and Singapore

Phasing out pig farms

Pig farming was common in Singapore pre- and immediately post-independence. By the end of the 1960s, there were more than 10,000 farms located all over the island, with more than 715,000 pigs.17 In 1974, the government set aside 2.5 km² of land in Punggol as an experiment to relocate traditional pig farms to high-rise intensive pig farm units. Although the performance of the settled pig farmers at Punggol exceeded expectations for pig production, pollution proved to be a bigger issue than anticipated.17 In January 1984, Dr Goh Keng Swee took over the Primary Production Department (the current Agri-Food and Veterinary Authority) and began the process that gradually phased out pig farms, culminating in the cessation of all pig farming in Singapore in November 1989. This also resulted in the virtual elimination of Japanese encephalitis—a viral brain infection—from the island, as pigs are the main amplifying hosts for this particular virus.

Mr Tan Gee Paw. “Pigs are very pollutive animals. One pig will produce five times the waste that a human being does, in high concentration. The pig farmers have no means of treating the pig waste—every morning they flush the pig waste into the drains straight into the rivers, and we were going to put up dams at the ends of the rivers to create reservoirs.”
Other government bodies supporting public health and hygiene standards in Singapore besides the Ministry of Health (MOH) and PUB include:

- The Agri-Food and Veterinary Authority (AVA)—restructured as a statutory board from the Primary Production Department in 2000 to ensure a constant and stable supply of safe food in addition to animal and plant health in Singapore among its many functions.
- The Health Promotion Board (HPB)—formed in 2001 to serve as the main driver for national health promotion and disease prevention programmes.
- The National Environmental Agency (NEA)—formed in 2002 for the purposes of improving and sustaining a clean and green environment in Singapore.
- The Public Hygiene Council—launched in 2011 to promote greater multi-sectoral partnership in support of public and personal hygiene.

These organisations have served and will continue to serve an important role in the early aspects of infectious diseases management—prevention of infection is better than cure.
Tuberculosis

Tuberculosis (TB) is an ancient disease of the human race. It is believed that the bacterium that causes tuberculosis—*Mycobacterium tuberculosis*—has been around for more than 6,000 years, with humans acquiring it in Africa before spreading it to the rest of the world via trade routes, although human-to-animal-to-human transmission may also play a role. It is hypothesised, for example, that seals may have transmitted tuberculosis to the native South Americans that hunted them thousands of years before the first Europeans set foot on the continent.\(^\text{18}\)

TB has acquired many names throughout history, including consumption, the white plague, and scrofula. Its names in other languages, 肺结核 (fèi jí hé), batuk ker-

ing, and ကြား နွာ် (kāca nōy) depict the infection as one involving the lungs, and spreading by coughing. John Bunyan memorably described it in 1680 as “the captain of all these men of death”\(^\text{19}\). Although no longer the killer it was in the 16th to 19th centuries, there are still approximately 9 million people infected each year, with 1.5 million deaths globally.\(^\text{20}\) Effective treatment exists for this disease, but TB-infected patients will have to take at least 6 months of a regimen that involves multiple pills to achieve cure, and up to 1.5 years or even longer if the germ is resistant to the first-line medications. A live vaccine—the Bacille Calmette-Guérin or BCG for short—is available, but is not effective after the childhood years.\(^\text{21}\)
A preserved lung specimen, showing cavity formation and destruction of the lung by TB.

The iconic SATA mobile X-ray van in 1956. (Credit: Ministry of Information and the Arts collection, courtesy of the National Archives of Singapore)
TB has been recognised as a major public health problem in Singapore since her founding in 1819, and was probably the most important cause of death locally in the 1940s. It was extremely common in children then, with half of all children infected by the age of 7 years. After the Second World War, both the public and the government worked together to come up with initiatives to control TB in Singapore. Two notable examples were the foundation of the Singapore Anti-Tuberculosis Association (SATA) as a charity organisation in 1947, and the establishment of the Tuberculosis Clinic at Tan Tock Seng Hospital (TTSH) in 1948.

Although supported by the government of the day in principle, no further aid was provided to SATA. Nonetheless, the organisation was very successful in raising funds through charity events, with many prominent businessmen and organisations also donating cash or even land outright. These donations were largely channelled into the development of diagnostic and treatment facilities, including the iconic SATA mobile X-ray and treatment vans, which were launched in 1955.

The Tuberculosis Clinic at TTSH was also known as the Rotary Clinic because the Rotary Club of Singapore funded its con-
In its heyday, it was the main TB treatment centre in Singapore, with more than 300 patients passing its doors each day. In the 1960s, it was also the local coordinating centre for TB research, working in collaboration with the British Medical Research Council (MRC) on chemotherapy trials for close to 30 years before it was finally demolished in the 1990s.

Three other major events occurred in the mid-1940s to 1950s. From 1945, active anti-TB drugs started becoming available in Singapore. Streptomycin, an intramuscular injectable drug, had to be specially flown in to treat selected patients in 1945, but had become widely available for prescription by local doctors by 1949, eventually ending the black market in the drug that had arisen as a result of its scarcity. In subsequent years, new anti-TB drugs were also intro-

The Tuberculosis Clinic at TTSH was the main TB treatment centre in Singapore, before it was finally demolished in the 1990s.

Foundation plaque of the Rotary Clinic, now available for viewing at the TTSH Museum.
In 1951, the BCG vaccine was introduced in Singapore by UNICEF/WHO. This significantly contributed to the dramatic decline in mortality from tuberculosis in young children. In 1951, the BCG vaccine was introduced in Singapore soon after they became commercially available—isoniazid was the second drug that became available from 1951. In 1951, the BCG vaccine was introduced in Singapore by UNICEF/WHO, with a mass newborn vaccination campaign at Kandang Kerbau Hospital (subsequently renamed KK Women’s and Children’s Hospital, or KKH for short) in 1957. This significantly contributed to the dramatic decline in mortality from tuberculosis in young children from the 1960s. In August 1958, notification of TB was made compulsory under the Quarantine and Prevention of Diseases (Amendment) Ordinance No. 19, with the Central Tuberculosis Registry established to manage the notifications and statistics. This registry was placed under a new unit—the Tuberculosis Control Unit (TBCU)—which still continues to operate from its original Moulmein Road location today. The TBCU at its inception also served to support contact tracing (i.e. location of persons who might have been exposed to TB because of their proximity to patients with pulmonary disease) and case finding through mass chest X-ray exercises, eventually taking over outpatient management of patients with pulmonary TB via its implementation of the Directly Observed Therapy Short-Course (DOTS) programme.
TBCU at its refurbished colonial building today.

The Contact Clinic can be found just beside TBCU on Moulmein Road. It also completed renovations in 2015.
Sputum collection from a patient at the TBCU at TTSH in 1964.
(Credit: Ministry of Information and the Arts collection, courtesy of the National Archives of Singapore)

Ward 75, a nightingale ward within the Communicable Diseases Centre compound at Moulmein Road where TBCU’s inpatients with TB are housed today.
Directly observed therapy, short-course (DOTS) is the tuberculosis control strategy advocated by WHO. Most in Singapore, including patients and doctors, view it as just having to take TB treatment under the observation of a polyclinic or TBCU nurse (note: the “patient” is actually a student volunteer), but it actually comprises five elements:

1. Political commitment with increased and sustained financing.
2. Case detection through quality-assured bacteriology.
3. Standardised treatment, with supervision and patient support.
4. An effective drug supply and management system.
5. Monitoring and evaluation system, and impact measurement.

Patients with TB need to take many different pills for a prolonged period of time. The picture shows a typical single day’s pills for the intensive phase of TB treatment, which has to be taken for two months, before stepping down to the continuation phase with reduced pill count for a further four to seven months.
By the 1980s, Singapore’s efforts at TB control had become multi-faceted and established, and comprised:

- **Surveillance**—mandatory notification of all cases of TB in Singapore and evaluation of the distribution and trends of TB locally.
- **Case finding**—rapidly detecting new cases of TB, and incorporation of the latest laboratory technologies for TB diagnosis.
- **Treatment**—with the majority of TB cases since 1997 placed under the DOTS programme implemented at the polyclinics and the TBCU.
- **Prevention**—incorporation of the BCG vaccine into the national childhood immunisation schedule as well as tracing the contacts of infectious TB cases and offering treatment to infected contacts from 1998 onwards.
- **Health education**—of both healthcare workers and the general public.
- **Research** into TB in Singapore and the region, and training of healthcare workers with respect to TB control and treatment.

As a result of the improvement of the general socioeconomic status and hygienic conditions in Singapore, as well as the country’s aggressive efforts at TB control, the rates of TB fell dramatically...
Ms Tiffany Tan, senior registered nurse at the TBCU. “Community support is critical to remove the stigma of tuberculosis and improve on TB care and control in Singapore.”

Prof Sonny Wang, emeritus consultant and director of TBCU since 1995, reviewing a case of pulmonary tuberculosis with a medical officer in the background. “We need many agencies and advocates in the community to keep the awareness of TB alive... Adherence of any medication given for a prolonged period of time, if it is left to the patient, is around 50% on average. In the case of diabetes, hypertension and other chronic diseases, no one else suffers if the patient is non-compliant. It is your own funeral in a way. In TB, you make other people suffer with you. If you do not take the medicines properly, you continue to be a threat to the community. Society must be interested in making sure that the patient takes the medicine so that society is safe.”
Progress against TB in Singapore has slowed, with recent reversals including a rise in the incidence of new TB cases since 2008. The former is largely due to changes in the population demographic, including an ageing local resident population as well as an influx of foreigners from countries with high TB burdens into Singapore to live and work over the past decade. The latter is symptomatic of the global trend of increasing drug resistance in the TB germ. These highlight again the difficulty in dealing with infectious diseases that are able to adapt and evolve with humans. More hard work, collective will, community support and innovations are required in order to keep on track Singapore’s battle against this ancient scourge of man.

Anonymous patient with multidrug-resistant TB, interviewed in October 2015. “I was thinking that TB only needs medical treatment, like maybe 6 months, so I was thinking it is only 6 months, it is okay. As the results came back one by one—it took quite long to come back—I was thinking why would it be me? Why is everything coming back resistant? Normally when you start the medicine, you will just have less and less medicine, but now I have more and more—it was a shock. Also, my parents and family were quite worried, seeing me taking more and more medicines.”
Vaccines

Vaccination has proven to be a remarkably effective tool against certain infectious diseases. Vaccines are substances—either killed or attenuated live microbes, or synthetic parts of microbes—that can provoke a lasting immune response, thereby making the vaccinated person safe from that particular infectious disease. The term “vaccine” actually comes from the Latin word for cow, “vacca”, because of Edward Jenner’s use of the cowpox virus to prevent smallpox.\(^3\)

Singapore has always been at the forefront of introducing new vaccines for immunisation, although the reasons for each vaccine being introduced may vary. In this chapter, we focus on three diseases and their respective vaccines—polio, hepatitis B and pneumococcal vaccine—as there is a unique Singapore story as to how each of these was introduced into our national childhood immunisation schedule.

Singapore has always been at the forefront of introducing new vaccines for immunisation.
Infectious Diseases and Singapore

Poliomyelitis

The word poliomyelitis is derived from the Greek words for ‘grey’ (polios) and ‘marrow’ (myelon). There are three subtypes of polioviruses, which belong to the genus Enterovirus (other members of this genus cause human hand foot and mouth disease as well as the common cold). In approximately 1%-5% of those infected by a poliovirus, the virus enters the central nervous system, causing neurological symptoms—paralysis occurs in a very small fraction of this latter group. Poliomyelitis used to be a very common childhood disease in Singapore, and was recognised as a major public health problem in the immediate post-Second World War period.33 Singapore was among the first countries in the world to introduce live oral poliovirus vaccine (OPV) on a mass scale in 1959. It was not an easy decision to make, because of the lack of scientific data about OPV. There were also concerns over the safety of available polio vaccines due to the Cutter incident of 1955, in which inadequate inactivation of the injectable inactivated polio vaccine (IPV) led to an epidemic of poliomyelitis in the United States.34 Prof ES Monteiro (Dean of the Faculty of Medicine and Professor of Clinical Medicine, University of Malaya, Singapore) and Professor JH
Hale (Head, Department of Bacteriology, University of Malaya, Singapore) supported the decision to use OPV-2 (there were no trivalent oral poliovirus vaccines available then) to try and stop the 1958-1959 epidemic that was caused by poliovirus-1. The controversial decision proved successful, and the epidemic was brought under control.

The poliomyelitis epidemic was brought under control

Dr Edmund Monteiro, former director of the Communicable Diseases Centre, and son of Prof Ernest Steven Monteiro. “I was a medical student at that time. We were having a polio outbreak with poliovirus-1. Prof Hale told us that Singapore had been in touch with Prof Sabin about the situation, and he recommended that we use OPV-2 to try to stem the outbreak. He explained that if we used OPV-1 in an outbreak situation, we won’t know what was causing what. We went to the Singapore Medical Association meeting, and when this topic was discussed, the room was divided... Of course, things have changed since then. We hardly use the OPV anymore, we use IPV for the simple reason that excretion of poliovirus is zero.”

A life-sized figure of Prof Ernest Steven Monteiro, available for viewing at the SGH Museum at Bowyer Block.
The government formed a committee on poliomyelitis in 1959, with Prof Lim Kok Ann—then a member of the WHO Expert Advisory Panel on Virus Diseases—serving as advisor. While there were initial hopes that poliomyelitis could be eradicated with the vaccination of a large enough proportion of the community, periodic epidemics still continued to occur. The committee concluded that poliomyelitis eradication would only be possible when the herd immunity of the population could be raised and sustained through a comprehensive and structured childhood immunisation programme. This led to the first phase of the poliomyelitis immunisation campaign among children between the ages of 6 months and 5 years, which began in March 1962, using the newly available trivalent OPV administered in 2 doses. The incidence of paralytic poliomyelitis had reduced significantly by the end of 1962.35

MOH then inaugurated a routine programme of immunisation against poliomyelitis on a voluntary basis from March 1963, using OPV. Infants aged 3 to 4 months were offered three doses of OPV at monthly intervals when they turned up for vaccination against diphtheria. The immunisation programme, implemented by the government-run Maternal and Child Health Services and School Health Services, as well as registered private medical practitioners, was further expanded in 1976 to include primary school and secondary school leavers. This resulted in the incidence of paralytic poliomyelitis dropping sharply from 74 cases in 1963 to 4 cases in 1968 and only 5 cases from 1971 to 1973. No further indigenous poliomyelitis cases were reported from 1978 onwards, and Singapore was finally certified poliomyelitis-free by the WHO on 29 October 2000, together with 36 other countries in the Western Pacific Region.
Hepatitis B

The hepatitis B virus (HBV) is spread through infected blood and body fluids, and commonly transmitted from mother to child during childbirth in this region. It affects the liver, with acute and chronic phases—the latter in particular can result in cirrhosis (hardening of the liver) and liver cancer. The annual acute hepatitis B infection rate in Singapore was 10.4 per 100,000 population and the case-fatality rate was 2.0% in the mid-20th century. About 6%-8% of adult males and 4% of adult females in Singapore were HBV carriers during that period. In addition, an estimated 1.9 million persons had no immunity to HBV and were at risk of acquiring the infection from the large pool of carriers then. The key to the prevention and control of viral hepatitis B has been and remains immunisation. The main strategy of hepatitis vaccination was to immunise infants and young children in order to prevent acquisition of the virus from birth.

Dr Oon Chong Jin, medical oncologist, and pioneer of hepatitis B vaccination in Singapore. “Singapore was chosen by the WHO for the hepatitis B vaccination study because it was a small country, had a tracer system through our NRIC, had a National Cancer Registry which was linked to IARC (International Agency for Research in Cancer)/WHO, had strong government support and research facilities, and it was also possible to monitor the changing trends of the infectious disease by periodic blood samples.”
Hepatitis B vaccination was started in mid-1983 in Singapore, supported by the WHO. It was the first country in Asia to start a hepatitis B vaccination clinical study. The study—which was linked to the hepatitis B immunisation programme—started with the immunisation of healthcare workers on a voluntary basis. Immunisation of babies born to carrier mothers was not started until 1 October 1985, when laboratory facilities for the routine screening of pregnant women became available. Before the programme was implemented, an intensive health education campaign in the mass media was put forward to educate the public on the importance of HBV infection, its mode of transmission, and its prevention. Because of the high cost of the vaccine, the programme was implemented in phases and targeted at population groups with the greatest risk of acquiring HBV. Priority was given to children, especially babies born to carrier mothers. Adults who were at risk of the infection, such as healthcare workers...
and contacts of acute hepatitis B cases and carriers, were also included. On 1 September 1987, the programme was extended to include all newborns to prevent any form of vertical and horizontal transmission—the first country in the world to do so.

The successful implementation of the national childhood hepatitis B immunisation program over the last two decades has resulted in a low prevalence of HBV infection among children and adolescents. By 2010, Singapore had already achieved the WHO Western Pacific Region's goal of reducing the prevalence of chronic HBV infection to below 2% among children aged 5 years and older by 2012 and below 1% by 2017.19

Nursing officers of SGH receiving the hepatitis B vaccine, observed by Dr Maurice Hilleman, pioneer in the development of the vaccine, April 1983. (Credit: Dr Oon Chong Jin)

The successful implementation of the national childhood hepatitis B immunisation program over the last two decades has resulted in a low prevalence of HBV infection among children and adolescents.
Infectious Diseases and Singapore

**Pneumococcus**

*Streptococcus pneumoniae* or the pneumococcus is the major cause of community-acquired pneumonia, meningitis and otitis media (infection of the middle ear) in adults and children worldwide. It is a Gram-positive coccoid bacterium, often seen in pairs or chains under the microscope, and it was discovered independently in 1881 by two microbiologists—George Miller Sternberg, who subsequently became the U.S. Surgeon General from 1893 to 1902, and the great Louis Pasteur from France.

The pneumococcus. Colonies on a blood agar plate, showing alpha haemolysis (upper). Light microscopic appearance as a spherical bacterium in pairs and chains (lower). (Credit: Diagnostic Bacteriology, SGH)
Transmission of the pneumococcus occurs through direct contact or via airborne droplets and is facilitated by overcrowding, socioeconomic factors and antibiotic use. Colonisation begins within a few months of birth, reaching a peak of up to 55% at around 3 years of age before declining to approximately 8% by the age of 10 years, and falling further in adulthood. The probability of adult colonisation is related to the presence of younger children in the household that are colonised with the pneumococcus, with studies suggesting rapid recirculation within the family. The disease-causing ability of the bacterium is largely attributed to the presence of a polysaccharide capsule that envelops the microbe. There are more than 90 distinct capsules (and therefore serotypes), although only about 20 are associated with the majority of human disease, especially in children, offering a unique opportunity for prevention via immunisation.

The pneumococcal polysaccharide vaccine was the first vaccine derived from capsular polysaccharide—subsequently similar technologies were employed to develop vaccines against typhoid, the meningococcus, and Haemophilus influenzae type b—with the latest iteration being the 23-valent (i.e. targeting 23 different capsular serotype) pneumococcal polysaccharide vaccine (PPV-23). It was launched in 1983 and became available in Singapore in 1988 after Health Sciences Authority (HSA) approval. Pneumococcal polysaccharide vaccines, however, are not immunogenic in infants and young children, and therefore not effective at preventing colonisation and disease in these most susceptible age groups. A breakthrough occurred in 2000 with the licensing—in U.S.—of the protein conjugate heptavalent pneumococcal vaccine (PCV-7), which was far more effective in infants and young children. It was licensed by HSA for prescription in Singapore, but somewhat unusually, was only included in the national childhood immunisation schedule in 2009. Invasive pneumococcal disease was made a legally notifiable disease under the Singapore Infectious Diseases Act in 2010 for the purposes of monitoring the efficacy of the vaccine.
Much of the credit for the inclusion of pneumococcal vaccination into the national childhood immunisation schedule must go to the paediatric infectious diseases team at KKH, who had shown in a series of studies the burden of pneumococcal disease among children in Singapore. An “upgraded” 13-valent conjugate vaccine (PCV-13) was licensed in 2010 globally, including Singapore, and was rapidly introduced into the local childhood immunisation schedule by December 2011. In an updated economic evaluation, pneumococcal vaccination was still found to be moderately cost-effective taking into account the effects of herd immunity.

Studies linking childhood vaccines with autism, despite having been discredited, continue to influence and worry parents today, who fear for the safety of their children. News reports of rare illnesses and deaths caused by vaccines do not help. Singapore has been remarkably progressive over the years in being an early adopter of the various vaccines, and some credit for this must surely go to local doctors and public health officials who have done the hard work and crunched the data to show that these vaccines will actually help protect the public. Public education efforts on vaccines and vaccine safety are necessary and key to continued community support for immunisation.
From her founding in 1819 until the present day, Singapore has been a major transport and travel hub for both the region and the world. Such interconnectedness has been a boon for the economy and our own access to foreign goods and ideas. Nonetheless, it has also made us vulnerable to infectious disease epidemics from across the world. Infectious diseases can either spread rapidly or slowly, with the rate and extent of spread determined by the characteristics of the pathogen (and its vector in the case of vector-borne diseases) and the number of susceptible individuals exposed to the disease over time. Globalisation and the ease of air travel have greatly facilitated the spread of infectious diseases, as infected persons and vectors can be transported enormous distances in a very short period of time into regions where these diseases are rare or non-existent, creating the potential for outbreaks. Technically, an epidemic is defined by a significant rise in incidence of a disease above its baseline rates. Thus, a few cases of a rare disease (such as Ebola or the Middle East Respiratory Syndrome) spreading within Singapore would be considered an epidemic, whereas a huge number of cases of influenza or hand, foot and mouth disease (HFMD) occurring within a short period of time is required to be accorded similar status.
Infectious Diseases and Singapore particularly MERS-CoV in view of the many local people that go to the Middle East for business or for the Haj and Umrah pilgrimages. This has resulted in fairly extensive local news coverage especially during the peaks of each epidemic. The various waves of antimicrobial-resistant bacteria—a collective example of epidemics that spread more slowly—have seldom featured in the local news even as each pathogen emerged and spread around the world, including Singapore.

Infectious Agents Causing Epidemics

All the diseases mentioned above—except for tuberculosis and antimicrobial-resistant bacteria—are caused by viruses. H1N1 is an influenza virus, and pandemics arise when influenza viruses of humans and animals (such as pigs and birds) merge or re-assort (mixing of genetic material of the viruses into new combinations), forming novel influenza viruses that we lack immunity against. SARS and MERS are caused by coronaviruses that likely originated from bats and were subsequently transmitted to humans. A unique and deadly virus that so far is only found in Africa, and is also likely to have originated from bats, causes Ebola. These are examples of zoonotic diseases, the term meaning infectious diseases that spread from animals to humans. The HIV virus is different from the other viruses listed above in that it spreads via sexual intercourse or contaminated blood products, and the disease often takes years to manifest. The dengue viruses are also unique in that an insect vector—the *Aedes aegypti* mosquito—is necessary for it to spread, and the scale and success of the dengue outbreak is tied to the survival and spread of its mosquito vector.

Each type of epidemic offers unique lessons and experiences. Many people in Singapore still remember the SARS outbreak in 2003, and probably the novel influenza A(H1N1) pandemic in 2009. HIV or TB troubles us less today, and dengue does not make it to the news very often. Nonetheless, the last three originated from epidemics and have subsequently become endemic in Singapore, precisely because they have been relatively difficult to contain, albeit for different reasons. Three epidemics—SARS, dengue and HIV—will be described in greater detail below, whereas TB is the subject of an earlier chapter.
SARS

The severe acute respiratory syndrome (SARS) outbreak in 2003 was probably the defining epidemic for Singapore since independence. Much has already been written about this first zoonotic novel virus outbreak of the 21st century, although no one is really sure of the actual events that resulted in the transmission of a coronavirus present in Chinese horseshoe bats to civet cats and then to humans in the animal markets of Guangdong, or how it mutated to become capable of human-to-human transmission.

The Singapore side of the epidemic started when three friends returned from Hong Kong in late February 2003, after staying at the Metropole Hotel at the same time period as Dr Liu Jianjun, an elderly doctor who had treated patients with SARS—including the index case nicknamed the “Poison King”—during the initial outbreak in Guangdong in early February. All three young women fell ill with respiratory symptoms. One recovered without requiring hospitalisation, a second was warded but did not infect anyone else, and the last triggered the entire SARS epidemic in Singapore that lasted four and a half months, from 1 March to 16 July. Although there were only 238 cases and 33 deaths, the impact was tremendous, with one hospital (TTSH) closed, the healthcare system almost brought to a standstill, and the economy of Singapore experiencing a GDP growth contraction of 7% during that quarter.

SARS changed forever the way emerging infectious diseases and respiratory virus epidemics was viewed in Singapore, transcending the ability of a single ministry, or even a primary ministry supported by other relevant agencies, to cope with the epidemic. It resulted in the revamp of Singapore’s Homefront Crisis Management System into its current whole of government inter-agency structure. It also resulted in greater investment in healthcare infrastructure and capability in dealing with future outbreaks, which stood Singapore in good stead during the influenza A(H1N1-2009) pandemic six years later.
The initial transmission tree of SARS in Singapore, precipitated by the index patient who was warded at TTSH after returning from Hong Kong. (Credit: TTSH)
Living through the SARS epidemic

A/Prof Jeffery Cutter, Director, Communicable Diseases Division, MOH.

It was quite challenging because in the first month or so there were no diagnostic tests. We erred on the side of safety—if we really suspected someone of being a case, we would just isolate him first and not take chances... It was everyone’s efforts and together we contained SARS.

A/Prof Brenda Ang, Senior Consultant, Department of Infectious Diseases, TTSH.

SARS was a completely new, novel pathogen and we had to scramble to come up with our own protective recommendations before there were any international guidelines. We had to go with the greatest protection that was practical, and that was something we could roll out immediately.

A/Prof Raymond Lin, Director, National Public Health Laboratory (NPHL), MOH.

PCR was not a standard laboratory technique at that time, and SARS was the first time that PCR was used here as a diagnostic technique in an infectious diseases outbreak. For some hospitals, the machines had just been delivered and were brand new and had never even been tested out.

Prof Lee Hin Peng, Professor, Saw Swee Hock School of Public Health,
National University of Singapore.

We were all traumatised by this epidemic. I was at that time the Master of a Hall of Residence. We had one case of fever in a Hall of 500 students, and it was a very trying time to make sure that this boy was properly investigated, isolated and all the measures that were required was taken.
A/Prof Tan Ban Hock, Senior Consultant, Department of Infectious Diseases, SGH.

It was the first big outbreak that I personally faced, and also for the hospital (SGH) and Singapore, and so everybody was grappling for a solution. The uncertainties we faced and the turmoil we went through came from the fact that we had to scramble for answers. There was no certainty that any of the solutions will be the correct one.

A/Prof Koh Tse Hsien, Senior Consultant, Department of Pathology, SGH.

Anyone who didn’t live through SARS would find it hard to appreciate what the fuss was about. But it was real and people that were otherwise healthy died of SARS. In fact, two of our family friends and a work colleague died of SARS, and we didn’t even attend their funerals because at that time there was so much fear about cross-transmission. But at the same time, we could see that there was a lot of selflessness and courage being displayed by frontline healthcare workers. So I think on the whole Singapore did pretty well during the SARS outbreak.

Dr Ling Moi Lin, Director, Infection Control, SGH.

As a microbiologist, I will say it is fascinating to see new organisms emerge all the time. As an infection control professional, it really brought about the recognition of infection control and prevention in the world—for the first time, people woke up and realised its importance.
Tribute from Singaporeans to healthcare workers and TTSH during the SARS outbreak in 2003. (Credit: TTSH).
Infectious Diseases and Singapore

HIV

The human immunodeficiency virus (HIV), responsible for HIV infection and acquired immunodeficiency syndrome (AIDS), probably evolved from a virus infecting chimpanzees in Africa (simian immunodeficiency virus cpz strain, or SIVcpz), and it made the transfer between chimpanzees and humans sometime in the 1930s. However, it was only in 1981 that the epidemic was first noticed, when gay men in the United States presented with rare infections such as Pneumocystis jiroveci pneumonia and Kaposi sarcoma that had previously been seen only in severely immunosuppressed patients. In 1982, the term “acquired immunodeficiency syndrome” was used for the first time, and the retrovirus that causes HIV/AIDS was discovered in 1983.

Within a few short years, HIV became an international crisis as persons with HIV infection were discovered in virtually all countries where testing was performed. In 1987, the first antiretroviral drug zidovudine (AZT) was approved by the U.S. Food and Drug Administration (FDA), but it was quickly discovered that monotherapy led inevitably to antiviral resistance and subsequent treatment failure. Relentless research into intensive combination antiretroviral cocktails using newly developed antivirals from 1995 onwards successfully changed HIV from a fatal disease to a chronic disease requiring lifelong medications. Today, with the right treatment, a patient with HIV might reasonably expect to have the same life expectancy as any other person without the disease, which is a remarkable achievement by any measure.

The first two cases of AIDS were diagnosed in Singapore in 1985. There was a subsequent steep climb in the number of cases diagnosed each year until 2008, when the rates of HIV infection appear to have plateaued.
HIV medications usually become available in Singapore soon after approval by the FDA. But the local issue in the past has been the cost of these medications, which in the long term was unaffordable by many HIV patients. It was only in November 1998 that Medisave withdrawals up to a total of $500.00 per month (currently $550.00 per month) was permitted for antiretrovirals—which if purchased in Singapore at that time cost upwards of $800.00 each month55—and a further twelve years before Medifund assistance was extended to include needy Singaporeans requiring HIV treatment.56 At the end of 2015, Medishield Life will finally provide insurance coverage for patients with existing HIV infection, albeit at higher premiums. The availability of HIV medications for many local patients in the past has been due to the activities of Action for AIDS Singapore (AFA) among other organisations, an informal “buyer’s club” that purchases generic antiretroviral medications from Thailand and India and unofficially imports them into Singapore, and to a lesser extent, doctors—especially those from the Communicable Diseases Centre (CDC)—enrolling patients in international trials of HIV therapy (trial subjects get free state of the art antiretroviral therapy).

Social attitudes towards HIV have also improved due to educational efforts by AFA as well as other activists and physicians, although there is still a way to go before the stigma of HIV is removed and the disease is viewed as just another chronic medical condition.
Specialist outpatient clinic J within the CDC compound, where patients with HIV were treated and followed-up since the start of the HIV epidemic in Singapore. It remains the clinic with the largest number of HIV outpatients locally.

Mr Harbhajan Singh, emeritus fellow and senior nurse manager, CDC. “In the 1980’s, when HIV was first detected, people were fearful to come here (CDC) to work. We had problems posting nurses here to work, because they had a fear of HIV. The fear of HIV went off (eventually) through public education and training courses. Today, the nurses do not have any fear of nursing HIV patients.”
Action for AIDS Singapore

AFA is a non-governmental organisation that was set up in 1988 by Prof Roy Chan to provide education about HIV to the population, change local attitudes towards HIV, and advocate for HIV-infected persons and high-risk groups. It raises funds to help pay for HIV treatment and other basic preventive therapies for patients who are not able to pay, and advocates for making HIV treatment more accessible. Operated from Prof Chan’s clinic at the National Skin Centre in its early years, the AFA office is currently at 9 Kelantan Lane.

Prof Roy Chan, founding president of AFA, and former director of the National Skin Centre.
“We continue to push for the rights of infected persons as human beings and (for them) not to be considered as criminals or lepers.”

The Dr Lee Jong-Wook Memorial Prize for Public Health, awarded by the WHO to AFA in 2010.
Anonymous HIV patient, interviewed at the Patient Care Centre at CDC in September 2015.

I understand this infection doesn’t spread through food. But I impose this thing on myself where I don’t share. Some people will say they don’t mind sharing, but perhaps subconsciously they have this fear. I just want to make them feel that it is okay to hang out with me.

The easily recognisable Mobile Testing Service van belonging to AFA. It provides anonymous HIV testing at a number of locations in Singapore.
Dengue

Dengue, the most rapidly spreading mosquito-borne viral infection, is prevalent in the tropical and subtropical regions of the world, including Singapore. It is a very old disease, with the earliest record of a clinical compatible disease found in a Chinese encyclopaedia first published during the Jin Dynasty (265-420 A.D.) and edited in 992 A.D. (Northern Sung Dynasty), where it is described as "water poison" and associated with flying insects.\(^5^7\) It probably had a wide geographic distribution before the first known epidemic of dengue-like illness occurred in Philadelphia in 1780.\(^5^7\)

The most effective vector for dengue, the *Aedes aegypti* mosquito, originated in Africa, but the slave trade brought it to the New World, where it became adapted to humans and urban environments, with subsequent spread throughout the tropics via sailing ships,\(^5^7\) including to Singapore. It is postulated that the ecologic disruption in Southeast Asia and other Pacific countries following World War II resulted in conditions that increased the transmission of mosquito-borne diseases, and started a dengue pandemic that continues to this day, expanding globally over the past decades.\(^5^7\)

There are four dengue serotypes (DEN-1 to DEN-4). Infection results in self-limiting but debilitating disease in most cases. Severe complications can occur in about 1% of the cases, very rarely resulting in death. Treatment is supportive—there is no specific drug or vaccine commercially available at this time. The frequency and magnitude of dengue epidemics have increased significantly over the past 40 years in Singapore, even though the *Aedes aegypti* mosquito density has remained low. This is largely due to rapid urbanisation and increasing population growth, and to a smaller extent, climate change resulting in increased ambient temperature.\(^5^8\)
Number of dengue cases notified and dengue incidence in Singapore, 1976-2014 (Source: MOH). There have been several dengue epidemics since the 1960s, with the largest occurring in 2013 (22,170 cases with 8 deaths).
During a dengue epidemic, many stakeholders are involved in controlling the spread of the disease. They include MOH, NEA, the Singapore Police Force, the primary healthcare network, and the general community. Public health officers will conduct household inspections and cluster investigations to quickly identify the potential breeding grounds, with the power to enter vacant premises under the Control of Vector and Pesticide Act. Early recognition of dengue clusters is critical for control of spread as well as for early clinical management. With the right knowledge and attitude for dengue prevention, the general community can also do their part to minimise further transmission of dengue in Singapore.

Dr Ng Lee Ching, director of the Environmental Health Institute.

Singapore has a comprehensive dengue control program and has done very well in bringing down the vector population. We brought the house index (number of homes found breeding mosquitoes for every 100 homes checked) in Singapore down from 50% in the 1960s to about 1% today. The credit goes to the community. NEA does a lot of campaigning and providing evidence and knowledge, but the activity has to be done by the community.

Dengue seroprevalence in Singapore has been shown to increase with age. The overall seroprevalence in children and adolescents has remained low, while the overall dengue seroprevalence in adults was 56.8% in 2010. As such, the paradoxical effect of the successful implementation of a comprehensive nationwide *Aedes aegypti* surveillance and control programme since the 1970s is that a large proportion of the Singapore resident population remains susceptible to dengue infection.
Public Health Lessons from SARS and other Epidemics

Prof David Heymann, Chairman, Public Health England, United Kingdom.

Borders cannot stop infectious diseases; no country can fortify itself against the entry of infectious diseases, no matter how hard it tries in the world today.

Prof Wang Linfa, Director, Emerging Infectious Diseases Program, DUKE-NUS, Singapore.

These emerging infectious disease events show the importance of early warning.

Prof Chia Kee Seng, Dean, Saw Swee Hock School of Public Health, National University of Singapore.

Three Cs: the need for Coordination, Competence, and the ability to Concentrate.

Prof Annelies Wilder-Smith, Director, Vaccinology and Global Health Programme, Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore.

Singapore is, and will always be, vulnerable to the importation of infectious diseases, being such a travel hub. What we need to learn is that we need to be prepared for more to come.

LTC (A/Prof) Vernon Lee, Head of Biodefence Centre, Singapore Armed Forces, Ministry of Defence (Singapore).

The Singapore Armed Forces (SAF) is part of a whole of government approach to dealing with national emergencies and threats under the Home Front Crisis Management system. The SAF also supports the government quarantine facilities and augments national resources in times of need.
Infectious Diseases as a Medical Specialty

Recognition and development of infectious diseases as a medical specialty is a relatively recent phenomenon worldwide. Possibly the first country to do so was the United States, where growing interest by physicians and scientists in infectious diseases led to the formation of the Infectious Diseases Society of America in 1963, with the American Board of Internal Medicine recognising infectious diseases as an independent clinical subspecialty soon after. In Europe, approval of a Section for Infectious Diseases in the European Union of Medical Specialties (UEMS) occurred only in 1996, with a European-wide training programme approved 3 years later. This was because a sufficient number of member countries recognising infectious diseases as a specialty was required before an application to UEMS could be made.

The late Prof Edward H. Kass, founding member and first president of the Infectious Diseases Society of America, had previously written a thoughtful piece on how infectious diseases came to be a medical specialty comprising a subgroup of physicians with especial knowledge about the field. He felt that in the early days of modern medicine, infectious diseases was such a large part of life as well as ordinary medical practice, and the number of specific interventions was so limited, that there was no need for infectious disease specialists, because every physician had to deal with infections by necessity. Subsequent advances in both medical care and public health resulted in greater complexity of medical care, coupled with a situation where the prevalence and consequences (both to the individual and to society at large) of infections had fallen considerably. Other than the commonest infections, broad and deep knowledge for managing infections was no longer critical (or possible) for every doctor. Thus, there was a niche created for physicians who were interested in the management and study of infectious diseases.

Recognition of the need for physicians knowledgeable in infectious diseases is a consistent feature of all countries, particularly the developed countries. However, formal recognition in the form of an accredited medical specialty occurs at different speeds in different countries, likely due to a combination of cultural or health system reasons. In several European countries,
In the early decades post-independence, infectious diseases was common and every doctor managed patients with infections as part of their daily routine. Clinical microbiologists filled the need by developing more clinically oriented training, although this approach was ultimately limited by the lack of general internal medicine training as well as the challenges of managing complex infections in haematology or transplant units. In Spain, the rise of the HIV epidemic was the catalyst that drove the recognition for the infectious diseases specialty.

Singapore was little different in this regard. Pre- and in the early decades post-independence, infectious diseases was common and every doctor managed patients with infections as part of their daily routine. With the rise of medical specialisation, the surgeons and physician specialists actively managed the infections peculiar to their respective disciplines. There was a Government Infectious Disease Camp built in 1907 along Balestier Road that served as a quarantine facility for patients with certain infectious diseases such as cholera, polio and typhoid. This was relocated in 1913 to Moulmein Road and re-named the Infectious Disease Hospital, which was again renamed Middleton Hospital in 1920 in appreciation of its first director, Dr William Robert Colvin Middleton. This subsequently became the CDC in 1985, with Dr Edmund Monteiro serving as director. But none of the physicians of this facility up to the late 1980s truly considered themselves as “just” infectious diseases physicians, nor was there a formal medical specialty as such in Singapore.
By the late 1980s, there was a recognised and mounting need for infectious diseases physicians in the acute care hospitals in Singapore. Funding for overseas specialist training in infectious diseases was made available via the Human Manpower Development Programme (HMDP)—launched in the 1980s by MOH to provide local specialists the opportunity to train and work at renowned healthcare institutes worldwide. Dr Brenda Ang (TTSH) and Dr Helen Oh (Changi General Hospital) were the first to receive HMDP awards to train in infectious diseases. The first practising infectious diseases physician locally was Prof Ti Teow Yee (retired), who eventually joined the Department of Pharmacology at the National University of Singapore.

But in order to accelerate the development of the infectious diseases specialty in Singapore, Dr David Allen, a (then) young American infectious diseases physician who had trained in New York, was invited by MOH to work and promote the specialty in Singapore. He arrived in 1989, laid the groundwork for formal infectious diseases training in Singapore, and became the founding head of the Department of Infectious Diseases at TTSH in 1992 before returning to his practice in Texas in 1994. By then, he had successfully laid the foundation for the infectious diseases specialty in Singapore, alongside his trainees and those who had returned after training abroad, including Dr Ang, Dr Oh and Dr Paul Tambyah.

Dr David Allen successfully laid the foundation for the infectious diseases specialty in Singapore

A close-up of Dr David Allen in Singapore in the 1990s. (Credit: Dr David Allen)
Formal recognition of the specialty in Singapore still took time, however. Mirroring events in the United States, the Society of Infectious Diseases (Singapore) was founded in 1990, and the specialist accreditation board for infectious diseases—constituting formal recognition of the specialty with an approved local specialist training programme—was set up in 1998.

Since then, the specialty of infectious diseases has grown and thrived. The need for infectious diseases specialists locally was made more acute by the ever-increasing complexity of medical care and by the SARS and pandemic influenza A(H1N1)-2009 epidemics. At the time of writing, there are 67 infectious diseases physicians registered with the Singapore Medical Council, and many of these physicians have started to pursue subspecialty interests in diverse areas such as travel medicine, transplant-related infections, and intensive care-related infections among others. Some have contributed in terms of internationally recognised research in the field, and others have stepped up to provide public health support.
Snapshot of the minutes of the inaugural meeting of the Society of Infectious Diseases (Singapore) on 12 January 1990.
(Credit: Dr Brenda Ang)

Dr David Allen with Prof Feng Pao Hsii at the 5th Western Pacific Congress on Chemotherapy & Infectious Diseases in 1996—the first large regional infectious diseases conference held in Singapore. Prof Feng, a prominent physician and rheumatologist, is also the founding president of the Society of Infectious Diseases (Singapore). (Credit: Dr Brenda Ang)
Infectious diseases is also recognised as a subspecialty of paediatrics locally—there is a formal fellowship programme at KKH, with infectious diseases services at both Paediatric Departments in KKH and NUH—although the subspecialty does not have its own accreditation board at this point in time. Other healthcare professions have also started recognising specialist tracks in infectious diseases: it was recognised as a specialty for pharmacists locally in 2011, with nine registered pharmacist specialists at the time of writing, whereas the first advanced practice nurse in infectious diseases, Ms Zuraidah Sulaiman, completed her internship in 2012.

Dr Shawn Vasoo (TTSH) and A/Prof Tan Thuan Tong (SGH), two of many infectious diseases physicians attending the Infectious Diseases Grand Rounds held at the National University Hospital in September 2015.
A/Prof Chong Chia Yin—director of Clinical Quality and Patient Safety at KKH, and a senior paediatric infectious diseases physician.

A/Prof Andrea Kwa—pioneer ID pharmacist specialist in Singapore.

Advanced practice nurse (APN) Zuraidah Sulaiman, who currently works at CDC at TTSH, managing patients with HIV and other infections.
What are the hallmarks of an infectious diseases physician?

Dr David Allen
“Skilled communicators, diplomats, and debaters on occasion.”

A/Prof Brenda Ang
“A broad understanding of many diseases.”

Dr Wong Sin Yew
“A person of science who treats patients humanistically.”

Prof Leo Yee Sin
“You have to be really hardworking.”

Prof Paul Tambyah, Professor of Medicine, Yong Loo Lin School of Medicine, National University of Singapore
“Flexibility, ability to cover a wide range of topics; you have to learn how to talk to surgeons.”

A/Prof Tan Ban Hock
“Being available and affable, and being a good all-rounder.”

Dr Shirin Kalimuddin, Associate Consultant, Department of Infectious Diseases, SGH
“Curious and doesn’t take things at face value.”
Other physicians managing infectious diseases in Singapore

Not all infectious diseases come under the purview of infectious diseases physicians in Singapore. Family physicians and other doctors naturally still manage common infectious diseases. TBCU maintains oversight of all cases of TB in Singapore, with its physicians directly treating the majority of pulmonary TB cases via its DOTS programme. Historically, viral hepatitis was managed by the gastroenterologists and this has continued to the present day. The medical specialty of dermatology has its roots in venereal diseases, especially in Europe, in large part because of the protean skin manifestations of syphilis. Because medicine in Singapore has a British heritage, the management of sexually transmitted infections—except for HIV—is still part of dermatology training here. The current DSC (a local acronym for Department of Sexually Transmitted Infections Control) Clinic at Kelantan Lane is run by dermatologists from the National Skin Centre, and is the successor to Middle Road Hospital. The latter was also known as the Social Hygiene Hospital, and was referred to colloquially as the “skin hospital”.

The DSC Clinic at 31 Kelantan Lane, where sexually transmitted infections are treated.

Sexual health information pamphlets (and free condoms) upon entry to the DSC Clinic.
Clinical Microbiology and the Laboratory

Antonie Philips van Leeuwenhoek, Dutch tradesman and naturalist, is widely acknowledged as the Father of Microbiology. He made his own microscopes and had discovered “animalcules” in water and other substances by 1676. But it was scientists such as Louis Pasteur and Robert Koch that formally proved the relationship between germs and disease; in particular, Koch's discovery of the germ causing TB is considered one of the major events in the history of medicine, resulting in the scientific understanding of, and rational approach to, infectious diseases. Koch's postulates have stood the test of time for evaluating the causal relationship between microbes and the diseases with which they are associated, albeit modified as pathogens that could not be grown in the laboratory were discovered.

The field of microbiology advanced as techniques and new technologies—including dyes, agar-based media, microscopy, and serology—that allowed for the culture and visualisation of the microbes were developed. In the Golden Age of Microbiology that occurred after the seminal works of Pasteur and Koch, many of the microbial agents that caused disease in living things (not just humans but also animals and plants) were discovered. The invention of the electron microscope in 1931 finally permitted viruses to be seen, and methods for culturing them (other than propagating in laboratory animals) were developed, allowing for more detailed study. With the development of antibiotics, interest in predicting their efficacy resulted in a plethora of techniques being developed from the

Koch’s Postulates

- The organism must be isolated from the diseased tissues in every case of the disease.
- The organism must be grown in pure culture.
- Inoculation of a susceptible animal with the organism must reproduce the same disease.
- The organism must be recovered from the infected animal and be grown again in pure culture.
1940s, with subsequent standardisation of susceptibility testing methods and interpretation of the results.\(^7^2\)

These advances resulted in the evolution of clinical microbiology as a separate entity to address clinical needs. The nature and history of its evolution resulted in its being included under the rubric of clinical pathology along with other fields such as haematology, chemistry and serology.\(^7^1\) The field of clinical microbiology advances in tandem with technological progress, discovery of new microbial pathogens or antimicrobial agents, and the development or refinement of medical practice that creates new clinical demands on the microbiology laboratory. The clinical microbiologist is therefore a physician knowledgeable in both the laboratory and clinical aspects of infectious diseases, and who is also often called upon to support or lead infection control practices in hospitals. There is considerable overlap between the roles of infectious diseases physicians (a medical specialty with a far shorter history and cultural heritage) and clinical microbiologists, but the roles are often complementary rather than competitive, with the balance between the two clinical specialties a function of historical development. As previously mentioned, clinical microbiologists performed the role of infectious diseases physicians in several European countries, filling that niche by developing more clinically oriented training. In countries such as Australia and the United Kingdom, joint training in infectious diseases and microbiology resulting in dual certifications have become increasingly popular. Clinical microbiologists in the United States have a much smaller footprint outside the laboratory,\(^7^3\) and the role is more commonly filled by scientists rather than physicians. In Singapore, the history of clinical microbiology and the microbiology laboratories predates independence, and is intricately tied in with both public health and pathology.

The first microbiologist to work in Singapore was Dr George Alexander Finlayson, who became the Municipal Bacteriologist in 1903.\(^7^4\) This post was created in view of the frequent outbreaks of infectious diseases such as cholera, malaria and plague then. Dr Finlayson introduced bacterial cultures, routine blood microscopy for malaria parasites and the Widal test as part of laboratory services here, and also worked on a wide range of public health activities, studying mosquitoes and rats, working on water treatment with the Municipal Engineer, and demonstrating that manure used for fertilising vegetables in conjunction with the practise of washing them in side drains in the markets contributed to the high incidence of diarrhoeal diseases.\(^7^4\) He also served as pathologist to TTSH, performing histopathological examinations and post-mortem autopsies.\(^7^4\)
In part due to Dr Finlayson’s work, the government of the day established a Pathological Department in 1905, housed in a building opposite the current College of Medicine Building, and which then also worked closely with the Straits and Federated Malay States Government Medical School (predecessor of the current school of medicine at the National University of Singapore) that was set up in the same year—this close collaboration was to result in several important discoveries and initiatives in the future. In 1930, there was a separation of pathology services, and the Bacteriology Division was created. Further rapid local development of microbiology proceeded post-Second World War, with the formation of the Central TB Laboratory at TTSH in 1959 (transferred back to the Department of Pathology—a re-naming of the Pathological Department since 1947—in 1981), the Public Health Laboratory in 1960 and the Virology and Immunology Laboratories soon after. The latter three laboratories, along with others that organically developed as different needs and capabilities arose between the 1960s and 1980s, originated at the Department of Pathology, then under the charge of Dr Moses Yu—the first locally trained microbiologist in Singapore—and his successor in 1985, the microbiologist Dr Jimmy Sng Ewe Hui.

Photo of Dr Moses Yu at his home, August 2015. He was the first locally trained clinical microbiologist in Singapore. He became the assistant director of Medical Services at MOH in 1985 and was succeeded by Dr Jimmy Sng. (Credit: A/Prof Koh Tse Hsien and Dr Moses Yu)
Prof Lim Kok Ann (1920-2003) was arguably the most prominent post-War microbiologist in Singapore. His signal achievements were the discovery of the novel influenza virus responsible for the Asian flu pandemic in 1957-1958, and the development of a new and simpler way (Lim Benyash-Melnick antiserum pools, 1960) to identify forty-nine different enteroviruses that was subsequently adopted by the WHO. His other (or perhaps first) passion was chess, and he was the first Singapore champion in 1949, founded the Singapore Chess Federation, and became the Secretary-General of the World Chess Federation after retiring from the National University of Singapore in 1992.

(Credit: Mr Olimpiu G. Urcan—artwork based on a poor-quality historical photograph featured in an early 1950s’ issue of the Singapore Chess Quarterly)
Medical Technologists

Medical technologists form the backbone of any clinical diagnostic laboratory, including the microbiology laboratory. An experienced “med tech” is an invaluable—though often underappreciated—resource to the laboratory. Working in the clinical microbiology laboratory carries an additional risk in view of the infectious pathogens that are part of that work.

Ms Ong Lay Huay, a senior medical technologist at Diagnostic Bacteriology, Department of Pathology, who received her long service award (40 years) at SGH a few years ago. “I enjoy my work, I have a passion for what I do. A job assigned to me, I definitely want to make it the best. Even a ‘small issue’ like archiving a bacteria, it is an important role. Not say just keep and then ‘bo chap!’”
The Department of Pathology remained directly under MOH until 1989, when it was transferred to SGH. Microbiology services, with clinical microbiologists to lead and oversee them, became the norm at other hospitals over time. Interested readers who wish to know more about the different laboratories and dynamic changes that took place should refer to Dr Jimmy Sng’s centenary book on pathology in Singapore.74

Dr Mavis Yeo, former Head of Bacteriology section at the Department of Pathology, now retired, at her home. “Microbiologists should have the curiosity to find out the cause of infections, and interest in laboratory work. Microbiology is an interesting field that is evolving all the time. With new pathogenic organisms coming up (all the time), maybe someone can discover something new!”
The National Public Health Laboratory

Public health microbiology as a separate entity is a relatively recent concept, because the techniques and workflow for public health investigations have become different from diagnostic laboratories, using more experimental instruments and techniques. Historically, public health and clinical diagnostic work basically involved the same techniques and laboratories in Singapore, but the transfer of the Department of Pathology from MOH to SGH created a growing void in public health microbiology. This became acutely felt with each succeeding novel viral epidemic—Nipah virus in 1999 and SARS in 2003—both in Singapore—followed by the Avian influenza A(H5N1) virus appearing in Indonesia. There was growing pressure to establish a new public health laboratory that would work outside the confines of the scopes of a hospital diagnostic laboratory, and to perform its duties at a national level.

This ultimately resulted in the formation of NPHL under MOH in 2007 to provide laboratory support for outbreaks of infectious diseases and to perform continuing surveillance of various pathogens that can cause public health problems. Its role is to use the best science possible to perform studies to protect the health of the people of Singapore. The first national public health influenza laboratory was set up at TTSH in 2009, fortuitously just a month before the onset of the influenza A(H1N1)-2009 pandemic, and was able to hit the ground running. Subsequent branches of the NPHL were set up at SGH (2010), Biopolis (2014), with even a Biosafety Level (BSL)-3 unit at the new BSL-3 laboratory at NUS (2015). The NPHL may eventually consolidate and move to the new National Centre for Infectious Diseases building that will likely be operational by 2018.
A view of the Diagnostic Bacteriology laboratory at SGH.

A laboratory technician analysing the antibiotic susceptibility testing results of a clinical strain of bacteria. This particular method is the Kirby-Bauer disk diffusion method, where standard concentrations of antibiotics are impregnated onto filter paper wafers, which are then placed strategically onto an agar plate of bacteria. The antibiotics diffuse into the surrounding agar plate, and the zone diameter of bacterial growth inhibition is measured to determine whether the bacteria is susceptible or resistant to the antibiotics.
As with infectious diseases, the specialty of clinical microbiology has also grown by leaps and bounds in Singapore. The development of automated testing, rapid diagnostic tests, and molecular tests have changed the face of clinical microbiology in many ways. The availability of MALDI-TOF (matrix-assisted laser desorption/ionisation time of flight) instruments for quick identification of bacteria and fungi, and the imminent widespread use of next generation sequencing for clinical purposes, are just two of many potential tools that will further impact both the diagnostic and public health microbiology laboratories.
Dr. James Sim, a young clinical microbiologist at Diagnostic Bacteriology, Department of Pathology, SGH.

Modern diagnostic devices and systems in a clinical molecular laboratory. (Credit: Molecular Laboratory, SGH)
Future Infectious Diseases
Threats to Singapore

Despite Singapore’s successes with infectious diseases in her past and present, the threat is never far. After SARS in 2003 and the influenza H1N1 pandemic in 2009, the world has seen the emergence of the Middle East Respiratory Syndrome Coronavirus (MERS-CoV), as well as the largest Ebola outbreak to date in Africa, with cases spreading to the United States and Europe even as the struggle to end the epidemic in West Africa took place. What are the possible infectious diseases that might threaten Singapore in the future?

As Singapore is major transport and travel hub, one can perhaps be guided by what the world bodies consider as major infectious diseases threats. The World Economic Forum (WEF) defines a global risk as “an uncertain event or condition that, if it occurs, can cause significant negative impact for several countries or industries within the next 10 years”, and identify such risks each year based on a methodology combining input from members of its Advisory Board as well as views from decision makers and the WEF’s multi-stakeholder constituencies. Over the recent six years, infectious diseases has featured on every Global Risks Report, with pandemics and antimicrobial resistance appearing over multiple years.
Some of the antimicrobial-resistant bacteria causing increasing worldwide concern

Methicillin-resistant *Staphylococcus aureus* (MRSA). The organism was initially named *staphylococci* by Sir Alexander Ogston in 1882, deriving from the Greek term *staphyle* (“bunch of grapes”), with Dr Anton Rosenback subsequently adding *aureus* (from the Latin term *aurum*) in 1884 because of the golden appearance of its colonies. (left) Gram stain of MRSA viewed under light microscopy. (Credit: Diagnostic Bacteriology, SGH). (right) Transmission electron microscopy image of MRSA. (Credit: Ms Hon Pei Yun).

A close-up view of a ChromID CARBA (bioMérieux) plate with carbapenem-resistant Enterobacteriaceae, the latest “superbug” sparking concern with antimicrobial-resistant bacteria globally. (Credit: Diagnostic Bacteriology, SGH).

Helium ion microscopy image of extensively drug-resistant *Acinetobacter baumannii*, a hospital and environmental Gram-negative coccobacilli that opportunistically infects hospitalised patients who are already critically ill or whose immune systems are compromised. Rare strains in Singapore are resistant to all available antibiotics. (Credit: Ms Hon Pei Yun)
The experts interviewed for this project provided similar responses: most felt that the highest risk to Singapore in terms of impact would be a global influenza pandemic or emergence of a novel viral pathogen that spread via the respiratory route, and which is imported here. Antimicrobial resistance among bacterial pathogens, including the germ that causes tuberculosis, was acknowledged to be a major issue as well. Some felt that there was also a need to focus on current existing infectious diseases in Singapore—to control these better so that they would be less of a threat in the future.
Experts’ perceptions of potential future infectious diseases threats to Singapore

Prof David Heymann

Some of the future infectious diseases threats are already there, like dengue and antibiotic-resistant infections. Future threats are also those that are not known—those diseases which are lurking in animals that can breach the barrier between animals and humans, infect humans, and travel to Singapore causing either an outbreak or a major epidemic.

Prof Leo Yee Sin

Looking at the development of recent years, it is very clear that emerging infectious diseases will be one of the significant challenges for everyone globally.

Prof Chia Kee Seng

We will always have emerging infectious diseases, and these will always be the curveballs, and operationally we must be ready for that. But one frustration perhaps is the existing infectious diseases in Singapore—we don’t seem to have a handle on them.

A/Prof Jeffery Cutter

MERS today is the greatest threat to the world, and to Singapore, but we will continue to encounter new emerging infectious diseases.
Prof Wang Linfa

The big threat will be travel-related importation of infections.

Prof Annelies Wilder-Smith

The real current threat is MERS. There are still ongoing MERS outbreak and cases in the Middle East, which means that at any time, any day, a traveller could import MERS-CoV into Singapore.

Prof Sonny Wang

The level of multidrug-resistant TB (worldwide) is rising at a frightening rate. Treatment is very difficult, very long, very expensive, and perhaps less successful. If multidrug-resistant TB should ever become the predominant TB, then I would say that it would be almost impossible with our current strategy to control TB, ever. We must never let that day come.

A/Prof Brenda Ang

Aside from new pathogens that can strike us, what I see as possibly no less important are other diseases that are slowly taking hold in our healthcare system, such as multidrug-resistant organisms.
A/Prof Raymond Lin

Three categories: firstly, things that are catastrophic, that affect our society, economy, and the way that our country is run—the main threat is still a new influenza pandemic, followed by malicious use of biological agents or bioterrorism. Secondly, simmering and slow-moving threats like antibiotic resistance. Lastly, hopefully we don’t need to talk about it, but if there is some extreme scenario where the infrastructure of society breaks down, we will be exposed to the classical infectious diseases.

LTC (A/Prof) Vernon Lee

Singapore and the Singapore Armed Forces are part of a global community. The threats facing the world will rapidly impact Singapore. These include health security threats such as emerging and re-emerging infectious diseases, food and waterborne diseases, antimicrobial resistance, and diseases due to climate change.

A/Prof Koh Tse Hsien

Antimicrobial resistance. Some people may say that the problem has already arrived, but on the whole, we are still seeing a lot of (bacterial) colonisation rather than infection, and I think there will be a lot of difference if we find that our transplant units and ICUs have 60% of infections being untreatable.

Dr Jeremy Lim, Partner & Head of Asia Pacific Region, Health & Life Sciences, Oliver Wyman

The biggest threat facing Singapore would be that we let our guard down, and that some novel disease arises in some other part of the world, enters Singapore through our very porous borders, and we fail to detect and manage correctly, and it spreads like wildfire throughout Singapore.
Zoonotic diseases (again)

Infectious diseases that spread from animals to humans are the cause of the majority of emerging and re-emerging infectious disease outbreaks in the world. Other than the aforementioned examples, others include the avian influenza A(H7N9) epidemic in China in 2013 and the ongoing cases of highly pathogenic influenza A(H5N1) that is now endemic in Asia. Closer to home, besides SARS and influenza A(H1N1-2009), two major zoonotic disease outbreaks are the Nipah virus outbreak causing encephalitis among pig abattoir workers in 1999, and—more recently—the outbreak of Group B streptococcus linked to consumption of raw Asian bighead carp (*Hypophthalmichthys nobilis*).

Epidemics and pandemics occur when the pathogens that cause these diseases evolve such that they are also able to transmit directly between humans. This link between animals and emerging infectious diseases emphasises the need for a “one health” approach in surveillance on and research in emerging infectious diseases.

Gram stain of *Streptococcus agalactiae* (Group B streptococcus) obtained from the blood of an outbreak patient, appearing predominantly as chains of purple spherical bacteria under the microscope. (Credit: Diagnostic Bacteriology, SGH)
How should Singapore prepare against future infectious diseases threats? Views of the experts:

**Prof Chia Kee Seng**

Moving forward, yes, there will be new emerging infections. Let’s not be too caught up by them. The less “sexy” ones like food poisoning outbreaks, hand foot and mouth disease, dengue; we haven’t shown that we have a handle over all these problems yet.

**A/Prof Jeffery Cutter**

We should continue to invest in our people. Make sure that we are very well resourced at all levels from public health, from surveillance to people who conduct outbreak investigations; that we have proper systems in place to quarantine people; in the hospitals make sure we have people who can manage cases well, and also to conduct good research.

**Prof Wang Linfa**

Early warning system, and a better reporting system… I wish MOH can coordinate all the different ministries and infectious diseases units—basic research, diagnostic, emergency response, clinical/hospitals—and we can do drills… if we have 10% of the resources and effort put into the same kind of military training or drills for response to infectious diseases, then the country will be totally safe.
A/Prof Brenda Ang

(Multidrug-resistant organisms) we should probably spend no less effort and resources when compared to novel pathogens… It will be sad if we spend a lot of effort against a novel pathogen which never hits us, and forget about other things which are actually already present in our healthcare system.

LTC (A/Prof) Vernon Lee

We should adopt a flexible risk management approach so that we can prepare for all hazards, especially for new diseases that we cannot prepare for specifically in advance. This approach necessitates having a good risk assessment programme and risk management plans… It is important to exercise these plans frequently to determine gaps and areas for continual improvement.

A/Prof Koh Tse Hsien

There needs to be more formal links between the human, animal and environmental health organisations, because as you can see, a lot of the recent outbreaks have been linked to animals. The only way to sell antimicrobial resistance to the public is to increase awareness, the same way we have documentaries of whales on TV… and maybe as a subject in secondary school, so that everybody has a certain baseline knowledge.
Conclusion

Even as we acknowledge that the war with infectious diseases will never end, that new and existing viruses will continue to rise and spread in our interconnected world, and that bacterial evolution will continue to erode the effectiveness of antibiotics, we can continue to view the future with hope. Singapore’s activities in the past that have directly and indirectly controlled the spread of infectious diseases, including:

1. Continued socio-economic progress,
2. Provision of safe water, healthy living environment and efficient waste disposal,
3. Focus on surveillance and containment of outbreaks,
4. Continued building of clinical infrastructure and support of research into infectious diseases of local importance,
5. Continued maintenance and development of both regional and international infectious diseases research/surveillance networks and collaborations,

will remain a strong template for building on the gains of the past and ensuring another fifty years at least of improving our lives against infectious diseases threats. To this, we add that continued public education and communication, as well as work to reduce the stigma of certain infectious diseases such as tuberculosis and HIV, will play an ever increasingly important role in the future.
Acknowledgements

The project “Overcoming Infectious Diseases in Singapore: Past, Present & Future”, of which this book is a part, is an attempt to chronicle the major infectious diseases that have plagued Singapore throughout its history. Our country has accomplished much in the prevention and control of infectious diseases, but the lessons from our experiences are not well known. We have collected stories and records in order to document how far the nation has progressed and how hard-won is the protection from infectious diseases that we take for granted today. The project also aims to highlight some of the unsung heroes of the country, and inspire us to continue to work together—just as our predecessors had in the past—against the infectious disease threats of the future.

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• Ms Tristin Wong
• Ms Rose Wong
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• Dr Shawn Vasoo
• Ms Ang Li Wei
• Mr Pang Long
• Dr Sourav Das
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• Ms Mable Yap May Po
• Ms Chloe Ho Yin Jie
• Mr Alex Leow Shuangjie

Finally, we would like to thank our interviewees, who have all given of their time and views freely and unsparingly.

• Dr David Allen—Infectious Diseases Physician, ID Specialists, Dallas, Texas
• A/Prof Brenda Ang—Senior Consultant, Department of Infectious Diseases, Tan Tock Seng Hospital
• Anonymous person with HIV
• Anonymous person with HIV2
• Anonymous person with TB1
• Anonymous person with TB2
• Prof Roy Chan—Founder and President, Action for AIDS (Singapore), former Director, National Skin Centre
• Prof Chew Chin Hin—Former Deputy Director of Medical Services (retired), Ministry of Health
• Prof Chia Kee Seng—Dean, Saw Swee Hock School of Public Health, National University of Singapore
• A/Prof Chong Chia Yin—Senior Consultant, Department of Paediatrics, KK Women’s and Children’s Hospital
• A/Prof Jeffery Cutter—Director, Communicable Diseases Division, Ministry of Health
• Prof Goh Kee Tai—Senior Consultant, Office of the Director of Medical Services, Ministry of Health
• Ms Ha Kee Mong—Senior Medical Technologist, Department of Pathology, Singapore General Hospital
• Prof David L. Heymann—Chairman, Public Health England, United Kingdom
• Dr Shirin Kalimuddin—Associate Consultant, Department of Infectious Diseases, Singapore General Hospital
• A/Prof Koh Tse Hsien—Senior Consultant, Department of Pathology, Singapore General Hospital
• Mrs Stella Kon—Playwright, novelist, short story writer and poet
• A/Prof Andrea Kwa—Pharmacy Clinician Scientist, Department of Pharmacy, Singapore General Hospital
• Prof Lee Hin Peng—Professor, Saw Swee Hock School of Public Health, National University of Singapore
• Prof Leo Yee Sin—Director, Institute of Infectious Diseases and Epidemiology, Tan Tock Seng Hospital; Clinical Director, Communicable Diseases Centre, Ministry of Health
• LTC (A/Prof) Vernon Lee—Head of Biodefence Centre, Singapore Armed Forces, Ministry of Defence (Singapore)
• Dr Jeremy Lim—Partner & Head of Asia Pacific Region, Health & Life Sciences, Oliver Wyman
• Dr Lim Su Min—Graphic recorder; obstetrics & gynaecology specialist (retired)
• A/Prof Raymond Lin—Director, National Public Health Laboratory, Ministry of Health
• Dr Ling Moi Lin—Director, Infection Control, Singapore General Hospital
• Dr Edmund Monteiro—Former Director, Communicable Diseases Centre (retired), Tan Tock Seng Hospital
• Dr Ng Lee Ching—Director, Environmental Health Institute, National Environment Agency
• Ms Ong Lan Huay—Senior Medical Technologist, Department of Pathology, Singapore General Hospital
• Dr Oon Chong Jin—Medical oncologist, Medical and Oncology Clinic, Mount Elizabeth Medical Centre
• Mr Harbhajan Singh—Emeritus Fellow and Senior Nurse Manager, Department of Infectious Diseases, Tan Tock Seng Hospital
• Dr Sng Li Hwei—Senior Consultant, Department of Pathology, Singapore General Hospital
• Prof Paul Tambyah—Professor of Medicine, Yong Loo Lin School of Medicine, National University of Singapore
• A/Prof Tan Ban Hock—Senior Consultant, Department of Infectious Diseases, Singapore General Hospital
• Mr Tan Gee Paw—Chairman, Public Utility Board, The National Water Agency
• Ms Tiffany Tan—Senior Staff Nurse, Tuberculosis Control Unit, Tan Tock Seng Hospital
• Prof Wang Linfa—Director, Emerging Infectious Diseases Program, DUKE-NUS, Singapore
• Prof Sonny Wang—Emeritus Consultant and Director, Tuberculosis Control Unit, Tan Tock Seng Hospital
• Dr Wong Sin Yew—Infectious Diseases Physician, Infectious Disease Specialists, Gleneagles Medical Centre
• Prof Annelies Wilder-Smith—Director, Vaccinology and Global Health Programme, Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore
• Dr Mavis Yeo—Former Senior Consultant (retired), Department of Pathology, Singapore General Hospital.
• Dr Moses Yu—Former Assistant Director of Medical Services (retired), Ministry of Health
• Ms Zuraidah Sulaiman—Advanced Practise Nurse in Infectious Diseases, Tan Tock Seng Hospital
Additional Reading

This is a non-exhaustive list of works and resources that—in addition to the references—can be perused if more details are sought regarding infectious diseases and Singapore.

**General**


**Clean Water, Hygiene and Waste Disposal**


Vaccines


SARS


Infectious Diseases as a Medical Specialty

Clinical Microbiology and Public Health


Antimicrobial Resistance


**Glossary**

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td><em>Acinetobacter baumannii</em></td>
<td>A type of bacterium that causes opportunistic human infections, particularly in the hospital setting. It has tremendous propensity for developing antimicrobial resistance, and separately, also has industrial applications.</td>
</tr>
<tr>
<td><em>Alpha haemolysis</em></td>
<td>Lysis of red blood cells on an agar plate caused by certain bacteria, wherein the agar under the bacterial colony becomes dark and greenish. Also known as partial or incomplete haemolysis.</td>
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<tr>
<td><em>Antimicrobial agent</em></td>
<td>Drugs that are able to kill or inhibit the replication of microorganisms.</td>
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<td>Term</td>
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<td>-------------------------------------------</td>
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<tr>
<td><strong>Antimicrobial resistance</strong></td>
<td>A collective term for microorganisms developing resistance to antimicrobial agents.</td>
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<tr>
<td><strong>Anti-tuberculosis drugs</strong></td>
<td>Antimicrobial agents targeting <em>Mycobacterium tuberculosis</em> complex—the bacteria responsible for causing tuberculosis.</td>
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<tr>
<td><strong>Antiretrovirals</strong></td>
<td>Antimicrobial agents targeting retroviruses, which are</td>
</tr>
<tr>
<td><strong>Antivirals</strong></td>
<td>Antimicrobial agents that are designed against viruses, usually by inhibiting the replication of the virus, and less commonly by blocking access of the viruses to the target cells.</td>
</tr>
<tr>
<td><strong>Avian influenza</strong></td>
<td>Also known as “bird flu”, this term refers to influenza caused by viruses adapted to birds. Transmission from birds to humans usually results in severe disease manifestations in the latter.</td>
</tr>
<tr>
<td><strong>Bacille Calmette-Guérin (BCG) vaccine</strong></td>
<td>A live vaccine against tuberculosis using an attenuated strain of <em>Mycobacterium bovis</em>, the bovine tuberculosis bacterium. It is especially effective at preventing tuberculosis of the brain, but provides variable protection against tuberculosis affecting other parts of the body, with markedly decreased protection after childhood.</td>
</tr>
<tr>
<td><strong>Carbapenem-resistant Enterobacteriaceae</strong></td>
<td>Enterobacteriae (a family of bacteria that includes <em>Salmonella</em> species) that are resistant to carbapenems—a class of beta-lactam antibiotics once considered “drugs of last resort” for hospital-acquired infections—via production of enzymes that break down these drugs. The latest superbug.</td>
</tr>
<tr>
<td><strong>Carrier</strong></td>
<td>A person or other organism that harbours a disease-causing microorganism, but does not manifest any signs of the disease. The carrier can transmit the microorganism to others.</td>
</tr>
<tr>
<td><strong>Chemoprophylaxis</strong></td>
<td>The use of medications to prevent infection or disease.</td>
</tr>
</tbody>
</table>
**Cholera**

An acute diarrhoeal disease caused by the bacterium *Vibrio cholerae*. It is transmitted via food or water contaminated by the bacterium, and not via person-to-person contact. There are currently two inactivated (killed) vaccines available against cholera.

**Community-acquired pneumonia**

Infection of the lung originating from the community, as opposed to nosocomial or healthcare-associated pneumonia, where the infection started in or is related to healthcare settings.

**Dengue**

A debilitating but largely self-limited disease caused by any of 4 serotypes of dengue viruses, spread by the *Aedes* mosquito. A small number of vaccine candidates are undergoing clinical trials currently.

**Ebola**

A life-threatening infectious disease caused by the Ebola virus, occurring almost exclusively in Sub-Saharan Africa. The virus is believed to have originated in bats. A vaccine was very recently developed against the virus.

**Encephalitis**

Inflammation of the brain, usually caused by a virus. There is occasionally an overlap with meningitis (i.e. meningoencephalitis).

**Enterovirus**

A category (genus) of viruses with members causing a wide array of diseases, including the common cold, hand-foot-and-mouth disease, poliomyelitis, and encephalitis among others.

**Hand foot and mouth disease**

Human hand foot and mouth disease is an acute self-limiting infectious disease caused by enteroviruses, usually coxsackieviruses and enterovirus 71. It usually occurs in infants and young children, and is spread via contact. After a fever prodrome, sores can develop in the mouth, along with characteristic spots or blisters over the palms and soles.
### Haemophilus influenzae type b

*Haemophilus influenzae* are bacteria that occasionally cause severe infections, especially among infants. *H. influenzae* capsular type b appears to be responsible for virtually all cases of meningitis caused by this bacteria. A protective vaccine is available against this particular capsular type.

### Hepatitis B

An infection of the liver caused by the hepatitis B virus. The virus can cause both acute and chronic infection, with the latter potentially resulting in hardening of the liver (cirrhosis) and liver cancer. There are effective vaccines available.

### Hepatitis B vaccine

The commercially available vaccines contain a number of antigenic subunits of the virus (including viral envelope protein HBsAg) that are produced using cell factories (commonly yeast cells) where the genes have been deliberately inserted—a recombinant vaccine.

### Herd immunity

A concept wherein susceptible members of a population or community are indirectly protected from a disease when a large proportion of that population or community have become immune to it.

### HIV/AIDS

The spectrum of diseases caused by the human immunodeficiency virus (HIV) include HIV infection and acquired immune deficiency syndrome (AIDS). The virus is transmitted via sexual intercourse, and less commonly via contaminated blood products, contaminated needles, or from an infected mother to child during pregnancy, childbirth or breastfeeding. The virus targets the body’s CD4 T-cells, which are integral for coordinating and regulating the immune response.

### Hospital-acquired infection

Refers to infections that are acquired due to contact with the healthcare setting. Also known as "nosocomial infection" or "healthcare-associated infection".
<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Immunosuppressed</strong></td>
<td>Refers to a state where the immune system is suppressed, either by disease (such as HIV), drugs, or an inborn condition.</td>
</tr>
<tr>
<td><strong>Inactivated polio vaccine</strong></td>
<td>An injectable vaccine based on three inactivated virulent reference strains of polioviruses. The concept was first developed by Jonas Salk in 1952, and this vaccine is therefore also known as the “Salk vaccine”.</td>
</tr>
<tr>
<td><strong>Influenza</strong></td>
<td>Also commonly referred to as the “flu”. It is caused by influenza virus. Usually a self-limiting disease, but severe disease and death can occur in immunosuppressed persons or if a virulent strain arises (see Avian influenza)</td>
</tr>
<tr>
<td><strong>Japanese encephalitis</strong></td>
<td>A brain infection caused by the Japanese encephalitis virus. The virus is endemic in various parts of Asia, and is transmitted by <em>Culex</em> mosquitoes. The virus circulates among ardeid birds (especially herons) and pigs serve as amplifying hosts. There are effective vaccines against Japanese encephalitis.</td>
</tr>
<tr>
<td><strong>Kaposi sarcoma</strong></td>
<td>A type of tumour caused by a virus—human herpesvirus 8 (also known as Kaposi sarcoma-associated herpesvirus)—typically presented as reddish or violaceous skin nodules, although the lesions can also be found anywhere in the body.</td>
</tr>
<tr>
<td><strong>Larvicide</strong></td>
<td>Also written as “larvacide” = an insecticide directed against the larval stage of an insect. <em>Bacillus thuringiensis</em>—a soil bacterium—is one example of a biological larvicide. It produces a toxin that causes the larva of mosquitoes and some midges to starve to death.</td>
</tr>
</tbody>
</table>
Leprosy
A chronic disfiguring disease caused by the bacterium *Mycobacterium leprae*, associated with considerable stigma prior to the widespread availability of effective antimicrobial therapy. It is also known as Hansen’s disease, after physician Gerhard Armauer Hansen who first discovered the bacterium.

Malaria
A tropical febrile illness caused by any of five types of related protozoan parasites. The disease is transmitted by *Anopheles* mosquitoes, with rising antimalarial resistance in the most virulent strain, *Plasmodium falciparum*. Its name originated from the Italian words for bad air, as it was first (wrongly) associated with the miasma from swamps near Rome.

Measles
A highly infectious disease caused by the measles virus, with a characteristic rash that occurs 3 to 5 days after the onset of symptoms. There is an effective vaccine that is often combined with the vaccines for two other diseases, mumps and rubella (MMR vaccine). The MMR vaccine was fraudulently associated with autism in 1998, resulting in a strong anti-vaccination movement.

Medifund
An endowment fund established by the Singapore government to help pay the medical bills for Singaporeans who are unable to do so.

Medisave
A national medical savings scheme introduced by the Singapore government in 1984, which permits individuals to pay for future personal or immediate family’s hospitalisation, as well as a limited number of outpatient expenses.
**Medishield Life**  A national health insurance scheme for Singapore residents that covers hospitalisations and certain outpatient treatment expenses. It replaced the older Medishield scheme in November 2015.

**Meningococcus**  Another name for the bacterium *Neisseria meningitidis*, which is associated with epidemic outbreaks of meningitis. Effective vaccines are available against all serotypes of the bacterium currently.

**Meningitis**  Inflammation of the protective membrane (meninges) lining the brain, most commonly caused by microorganisms, although there are non-infectious causes such as drugs or cancer.

**Methicillin-resistant Staphylococcus aureus (MRSA)**  One of the original superbugs, a common bacterium in humans (and animals) that has acquired resistance to the beta-lactam class of antibiotics (which includes the penicillins).

**Microorganism**  An organism that can be seen only via the use of a microscope.

**Middle East Respiratory Syndrome**  An acute respiratory disease caused by the Middle East Respiratory Syndrome coronavirus (MERS-CoV). It was first reported from Saudi Arabia in 2012, and the virus is believed to have originated in bats, although camels are likely the animal host that passed the infection to humans.

**MMR Vaccine**  A live attenuated vaccine against measles, mumps and rubella. The MMR vaccine was fraudulently associated with autism in 1998, resulting in a strong anti-vaccination movement.

**Multidrug-resistant tuberculosis**  Tuberculosis caused by *Mycobacterium tuberculosis* complex that are resistant to isoniazid and rifampicin—first-line anti-tuberculosis drugs.
**Night soil**  
A euphemism for human faeces, usually collected at night in containers and buckets in the past, and used as an agricultural fertilizer.

**Nightingale ward**  
A hospital ward comprising of a large room with many beds and no subdivisions. Originally designed by Florence Nightingale.

**Nipah virus**  
A type of virus causing acute encephalitis and respiratory disease, first isolated in 1998 from Malaysia. The virus originated in bats, although pigs were the intermediate hosts in the first outbreak in Kampung Sungei Nipah, Malaysia.

**Oral polio vaccine**  
Developed in 1961 by Albert Sabin, and therefore also known as the “Sabin vaccine”. Current vaccines contain a mix of live attenuated strains of all 3 types of polioviruses. Rarely, the vaccine strains of polioviruses may mutate and regain the ability to cause infection and paralysis.

**Otitis media**  
Inflammation of the middle ear that is particularly common in childhood. It usually occurs after an upper respiratory tract infection, and is most commonly caused by viruses and bacteria, and less often as a result of allergy.

**Pathogenic**  
Capable of causing disease. Usually used in reference to a microorganism.

**Plague**  
A disease caused by the bacterium *Yersinia pestis*. The Black Death is the name given to the plague pandemic that took place in the 14th century, killing an estimated 75 to 200 million people. The bacterium is still persistent in animal reservoirs in many parts of the world today.
**Pneumococcal conjugate vaccine**

Conjugate vaccines are created by binding polysaccharide antigens to proteins (which are more immunogenic). The pneumococcal conjugate vaccines (PCVs) are therefore effective even in young children below the age of 2 years, unlikely the pneumococcal polysaccharide vaccine. There are currently three PCVs available, covering 7, 10 and 13 pneumococcal serotypes respectively.

**Pneumococcal polysaccharide vaccine**

Current iterations of this vaccine—termed PPV-23 or PPSV-23—are theoretically effective against 23 different pneumococcal capsular serotypes. Children below the age of 2 years are not able to mount an adequate immune response when injected with this vaccine.

**Pneumococcus**

Another name for the bacterium *Streptococcus pneumoniae*. It is the most common bacterial cause for lung infection (pneumonia) acquired in the community. There are currently two types of vaccines available against pneumococcal diseases, both directed against the microorganism's capsule, which helps to shield the pneumococcus from the body's immune system.

**Pneumocystis jiroveci**

Formerly known as *Pneumocystis carinii*, it is a fungus that causes life-threatening lung infections in persons with severely compromised immune systems, particularly persons with advanced HIV/AIDS.

**Polio(myelitis)**

A disease caused by polioviruses, which can affect the central nervous system and cause paralysis. There are two types of effective vaccines. The World Health Organization spearheads the Global Polio Eradication Initiative—currently, wild polioviruses are circulating only in two countries in the world, Afghanistan and Pakistan.

**Poudrette**

A fertilizer made from dried night soil and other substances.
<table>
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<tr>
<td><strong>Seroprevalence</strong></td>
<td>Number of persons that test positive for a disease within a population, based on presence of antibodies to the disease or its causative agent.</td>
</tr>
<tr>
<td><strong>Serotypes</strong></td>
<td>Groups within a single species of microorganisms, each of which can be distinguished by their distinct surface structures/antigens.</td>
</tr>
<tr>
<td><strong>Severe acute respiratory syndrome (SARS)</strong></td>
<td>An acute respiratory disease caused by the SARS coronavirus (SARS-CoV). It was first reported in southern China in 2002, before a global epidemic in 2003 brought it to the world’s attention. There have been no new cases since 2004. The virus is believed to have originated in bats.</td>
</tr>
<tr>
<td><strong>Smallpox</strong></td>
<td>A severe, occasionally fatal, infectious disease caused by the variola virus, characterised by a pustular rash. It was eradicated in 1980 following a global immunisation campaign.</td>
</tr>
<tr>
<td><strong>Smallpox vaccine</strong></td>
<td>The first successful vaccine to be developed, using the cowpox vaccinia virus to provide cross-immunity to smallpox. Although Edward Jenner was not the first to describe the use of cowpox to prevent smallpox, he is given credited for this as he was the first to publish his results and also distributed his version of the vaccine freely.</td>
</tr>
<tr>
<td><strong>Sputum</strong></td>
<td>A mix of mucous and other fluids coughed out from the lower airway of the lungs.</td>
</tr>
<tr>
<td><strong>Streptococcus agalactiae</strong></td>
<td>Also known as Group B streptococcus, this bacterium colonises and occasionally causes disease in humans, cattle and fish. Severe infections can occur in neonates and the elderly or immunosuppressed.</td>
</tr>
<tr>
<td><strong>Superbug</strong></td>
<td>A term commonly used to describe antimicrobial-resistant bacteria.</td>
</tr>
</tbody>
</table>
**Syphilis**
A disease caused by the spiral bacterium *Treponema pallidum* subspecies *pallidum*. It is spread primarily via sexual intercourse, and far less commonly from an infected pregnant woman to her foetus. It has myriad clinical manifestations and was once called “the great imitator” because its varied symptoms resemble those of other diseases.

**Tuberculosis**
A chronic infection caused by members of *Mycobacterium tuberculosis* complex, a group of closely related bacteria. The lungs are involved in the majority of cases, and it is transmitted via airborne particles, generated when persons with active pulmonary tuberculosis cough or sneeze.

**Typhoid fever**
A febrile illness caused by the bacterium *Salmonella typhi*. It is transmitted via food or water contaminated by the bacterium. Paratyphoid fever is similar in presentation, and is caused by the related bacterium *S. paratyphi*. These illnesses are collectively termed “enteric fever”.

**Vaccine**
A substance—either an attenuated live microbe or synthetic parts of microbes—that can provoke a lasting immune response, thereby making the vaccinated person safe from that particular infectious disease.

**Venereal disease**
Another name for sexually transmitted disease.

**Widal test**
A serological test for typhoid/enteric fever. It is usually combined with the Weil-Felix test for rickettsial diseases.

**Zoonosis**
A term for an infectious disease that spreads from animals to humans.
References


55. Singapore Statues. Central Provident Fund Act. Central Provident Fund (Medisave account withdrawals)(Amendment No. 2) Regulations 1998. Available at: http://statutes.agc.gov.sg/aol/search/display/view.w3p;page=0;query=Id%3A9e892848-5405-44c0-a86c-7dSeed951001%20Depth%3A0%20Status%3Apublished%20Published%3A30%20F10%2F1998;rec=0;resUrl=http%3A%2F%2Fstatutes.agc.gov.sg%2Faol%2Fsearch%2Fsummary%2Fresults.w3p%3D0%3Bquery%3DId%253A9e892848-5405-44c0-a86c-7dSeed951001%2520Depth%253A0%2520Status%253Apublished%2520Published%2520Published%253A30%2522F10%2522F1998 (Last accessed 12 Oct 2015).


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Singapore is a young nation at the crossroads of Asia and consistently faces the threat of infectious diseases. The infectious disease threats have changed with the times—it began with malaria, cholera and plague during the earliest days of the Straits Settlements; to vaccine-preventable diseases such as polio and smallpox; and now modern scourges including HIV, SARS, pandemic influenza, and antibiotic-resistant bacteria that threaten a return to the pre-antibiotic era.

Yet what is common is that the people and governments of Singapore have relentlessly worked together to overcome these diseases. Singapore has accomplished much in the arena of infectious diseases, but the lessons from our experiences and the personal stories from those who have worked to control infectious diseases are not well known. The collected stories and records in this volume will remind us how far the nation has progressed, how we have contributed to global and regional health and how hard-won is the protection from infectious diseases that we take for granted today.