Diphtheria: Review of a long forgotten disease

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Diphtheria is an acute infectious disease caused by the bacterium *Corynebacterium diphtheriae*, which primarily affects the upper respiratory tract and occasionally the skin. Transmission usually occurs from person-to-person through respiratory droplets or less commonly, through contact with discharge from skin lesions. The disease is characterised by a mild fever, sore throat and an adherent membrane (pseudomembrane) on the tonsils and nasopharynx. Most complications of diphtheria are attributable to the effects of the diphtheria toxin and its subsequent dissemination to other organs and tissues distant from the site of infection. The most frequent complications of diphtheria are myocarditis and neuritis. Death occurs in 5 to 10% of the cases, with higher mortality rates (up to 20%) among persons younger than five and older than 40 years of age.

Diphtheria is a significant cause of childhood mortality in developing nations. In spite of the widespread use of diphtheria vaccines since the 1920s which led to a dramatic decline in morbidity and mortality worldwide, the disease remains endemic in countries with low vaccination coverage and substandard living conditions. During the 1990s, a large epidemic was reported in the former Soviet Union resulting in over 157 000 cases and 5 000 deaths due to an increasing proportion of susceptible adults, decreased childhood immunisation, suboptimal socioeconomic conditions and high population movement in the country. Globally, the World Health Organization recorded 4 530 diphtheria cases in 2015, and still the disease continues to occur in parts of South-East Asia, South America, Africa and India where immunisation is insufficient. A small resurgence was also seen in Malaysia and the Philippines in 2016 with 31 and 42 diphtheria cases recorded respectively, compared with four and nine cases in the previous year.

In Hong Kong, during the pre-vaccine era from 1928 to 1940, an average of 250 cases of diphtheria with 104 deaths was recorded annually. After the end of the Second World War, there had been a steady increase in the number of cases rising from 122 cases in 1947 to a peak of 2 087 cases in the late 1950s (Figure 1). The total registered deaths over the same period also increased from 49 to 157. The majority of infections occurred in children under ten years of age, particularly those under five. Following the introduction of mass immunisation in 1956, cases of diphtheria began to decline gradually. In mid-1959, the then Medical and Health Department further intensified the immunisation campaign against diphtheria and these efforts were reinforced annually before the arrival of each winter season (Figure 2). As a result of these continuing efforts, case count fell drastically since the 1960s from 1 450 cases to no more than two cases in the late 1970s. No diphtheria cases were recorded since the last fatal case occurred in 1982.

Diphtheria is highly preventable through routine vaccination. Completion of the 3-dose primary series with booster vaccination at appropriate intervals is essential to reduce the risk of diphtheria in all age groups. Under the Hong Kong Childhood Immunisation Programme, diphtheria toxoid vaccine is provided free to eligible children in combination with tetanus, acellular pertussis and inactivated poliovirus (DTaP-IPV) vaccines at two, four and six months of age, followed by booster doses at 18 months, Primary one and Primary six.
In addition to active immunisation, maintaining personal and environmental hygiene is important in preventing infection and spread of diphtheria. Travellers to endemic areas are advised to keep their vaccinations up-to-date and, if necessary, consult their family doctor for primary or booster vaccination before departure. Physicians are also reminded to stay vigilant in the disease diagnosis and notification of any suspected diphtheria cases. For more information on diphtheria, please visit the CHP website: [http://www.chp.gov.hk/en/content/9/24/20.html](http://www.chp.gov.hk/en/content/9/24/20.html).

### References


### Prevention Tips

#### Maintain good personal hygiene

- Wash hands frequently with liquid soap and water, especially before touching the mouth, nose or eyes, or after touching public installations such as handrails or doorknobs;
- Cover nose and mouth with tissue paper when coughing or sneezing, and wash hands thoroughly afterwards. Dispose of soiled tissue paper in a lidded rubbish bin;
- Put on a surgical mask when having respiratory symptoms. Refrain from work or school and seek medical advice promptly;
- Clean broken skin immediately and cover properly with waterproof adhesive dressings. Wash hands before and after touching wounds. Consult doctor promptly if symptoms of infection develop; and
- Maintain good environmental hygiene.

#### Maintain good indoor ventilation

- Frequently clean and disinfect touched surface such as furniture, toys and commonly shared items with 1:99 diluted household bleach (mixing 1 part of 5.25% bleach with 99 parts of water), leave for 15 to 30 minutes, and then rinse with water and keep dry. For metallic surface, disinfect with 70% alcohol; and
- Use absorbent disposable towels to wipe away obvious respiratory secretions, and then disinfect the surface and neighbouring areas with 1:49 diluted household bleach (mixing 1 part of 5.25% bleach with 49 parts of water), leave for 15 to 30 minutes and then rinse with water and keep dry. For metallic surface, disinfect with 70% alcohol.

#### Vaccination

- Active immunisation with diphtheria toxoid can provide long-lasting protection in the majority of immunised children.

### Update on yellow fever

**Reported by Dr KONG Wai-chi, Scientific Officer, Enteric and Vector-borne Disease Office, Surveillance and Epidemiology Branch, CHP.**

Yellow fever is an acute infection caused by the yellow fever virus which is transmitted via the bite of infected mosquitoes belonging to the *Aedes*, *Haemagogus* and *Sabethes* species. The majority of persons infected with yellow fever virus have no illness or only mild illness. Some people may develop sudden onset of fever, chills, headache, back pain, generalised muscle pain, weakness, fatigue, nausea and vomiting. The condition of most patients improves and their symptoms disappear after three to four days. Those who recover from yellow fever usually have lasting immunity against subsequent infection. However, a small percentage of the symptomatic cases will progress to a more severe form of the disease. The severe form is characterised by high fever, jaundice, bleeding, and eventually shock and failure of multiple organs; in some, infection may be complicated by secondary bacterial infection. Fatality rate among severe cases is about 20 to 50%.

There is no specific drug treatment for yellow fever. Management is mainly for symptomatic relief. Yellow fever is prevented by vaccination and avoiding mosquito bites.
Yellow fever is endemic in tropical and subtropical areas in Africa and South Americas (Figure 1 and 2). This article provides an update on the latest situation of the recent outbreaks of yellow fever in affected African countries, Brazil, as well as those affected countries and areas.

**Angola**

A yellow fever outbreak started in Luanda, Angola in December 2015 and spread quickly to the rest of the country. A total of 4,306 cases and 376 deaths, of which 884 cases and 121 deaths were laboratory confirmed, were reported in Angola. The last case was detected in June 2016 and Angola declared the end of the yellow fever outbreak in December 2016. Cases of yellow fever in Angola had been exported to countries including Democratic Republic of the Congo (DRC), Kenya and Mainland China. The national task force of Angola carried out emergency vaccination campaigns including mop up and preventative campaigns. As of mid-June 2016, Angola had received over 11 million vaccines from International Coordinating Group (ICG) for Vaccine Provision and almost half of the country had been vaccinated.

**Democratic Republic of the Congo (DRC)**

In March 2016, the National International Health Regulations (IHR) Focal Point of the DRC notified the World Health Organization (WHO) of cases of yellow fever in connection with the outbreak occurring in Angola. As of mid-February 2017, a total of 2,987 cases of yellow fever were reported from all 26 provinces of DRC during the outbreak, of which 81 cases had been laboratory confirmed, with 16 deaths. Most of the confirmed cases acquired the infection in Angola. The last case was detected in July 2016 and DRC declared the end of the yellow fever outbreak in February 2017.

In response to this outbreak in DRC, ICG on Vaccine Provision had released 2.2 million doses of vaccines and operational fund for the vaccination campaign. In addition, WHO also supported the Ministry of Health in DRC to vaccinate 10.7 million people in the city of Kinshasa using a dose-sparing strategy as a short-term measure.

**Brazil**

In December 2016, cases of yellow fever were reported in Minas Gerais and the outbreak extended to areas located in proximity of Minas Gerais. The outbreak is ongoing. According to the latest update in July 2017, a total of 792 confirmed cases and 274 deaths were reported from December 2016 to May 31, 2017.

With the support from WHO, The Brazilian Government stepped up yellow fever vaccination campaigns in several states. Moreover, strengthening surveillance and case management throughout the country were also enhanced since January 2017.

**Situation in Asia**

Although the vector, *Aedes* spp. mosquitoes, are present in the Asia, no autochthonous yellow fever cases are reported so far.

Mainland China, which had never had a yellow fever outbreak before, reported 11 imported cases who had returned from Angola in March and April 2016. The 11 affected persons include eight males and three females, aged from 18 to 53 years. The majority of them were from the province of Fujian (7 cases), two were from Jiangsu, and one each was from Sichuan and Zhejiang respectively. At least five of them did not receive vaccination against yellow fever before going to Angola. One case did receive yellow fever vaccine in Angola, but then developed symptoms within four days of receiving the vaccine so is likely to have acquired the infection before protection from the vaccination could develop.

**Situation in Hong Kong**

In Hong Kong, yellow fever is a notifiable infectious disease under the Prevention and Control of Disease Ordinance (Cap. 599). The last case of imported yellow fever was recorded in 1945. Despite that the vector *Aedes aegypti* is not found, the prevailing species *Aedes albopictus* had been demonstrated experimentally to be a possible vector of yellow fever, but it is not as competent and important as *Aedes aegypti*. Due to the large volume of international travel, there is risk of importation of yellow fever into Hong Kong. Although the risk for local transmission is low, members of the public should prevent yellow fever by vaccination and avoiding mosquito bites.

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1. Dose-sparing strategy (using one fifth of a regular dose of the yellow fever vaccine) would provide immunity against yellow fever for at least 12 months and likely longer. However, a yellow fever vaccine given at a fractional dose would not qualify for a yellow fever certificate under the IHR requirements.
**Vaccination**

WHO recommends immunisation against yellow fever for all travellers aged nine months and above, travelling to and from at-risk areas, unless they are contraindicated. In Hong Kong, yellow fever vaccination is available at the Travel Health Centres of Department of Health. When travellers are vaccinated against yellow fever, they will be provided with an International Certificate of Vaccination or Prophylaxis. The certificate will be effective 10 days after the date of vaccination. Following the amendment to the IHR (2005) on July 11, 2016, the certificate of vaccination against yellow fever is valid for the life of the person vaccinated, instead of 10 years.

**Avoid mosquito bites**

1. Wear loose, light-coloured, long-sleeved tops and trousers, and use DEET-containing insect repellent on exposed parts of the body and clothing;

2. Take additional preventive measures when going outdoor activities:
   - Avoid using fragrant cosmetics or skin care products; and
   - Re-apply insect repellents according to instructions.

*For more information on prevention of yellow fever, please visit the Travel Health Service website: [http://www.travelhealth.gov.hk/english/travel_related_diseases/yellow_fever.html](http://www.travelhealth.gov.hk/english/travel_related_diseases/yellow_fever.html)*

**References**


**NEWS IN BRIEF**

**Three sporadic cases of necrotising fasciitis due to Vibrio vulnificus infection**

In early July, 2017, CHP recorded three sporadic cases of necrotising fasciitis due to *Vibrio vulnificus* infection. The first patient was a 67-year-old male with underlying illnesses. He presented with fever and painful left middle finger swelling spreading towards left upper limb since July 3. He attended the Accident and Emergency Department (AED) of a public hospital on July 4 and was admitted to intensive care unit on the same day. The clinical diagnosis was necrotising fasciitis. Left above-elbow amputation was performed. Specimen of left forearm fascia taken on July 4 grew *Vibrio vulnificus*. His condition deteriorated and he passed away on July 13. Epidemiological investigation revealed that the patient had been to a wet market to buy a fish on July 2 and had prepared it with bare hands. It was not known whether he had sustained any sting injury. He had no recent travel history. He lived with his wife and two sons who remained asymptomatic.

The second patient was a 61-year-old male with underlying illnesses. He presented with chills and rigors since July 2. He developed bilateral painful lower limb swelling since July 3 with increasing severity. He attended the AED of a public hospital on July 4. He subsequently developed septic shock and was admitted to intensive care unit on the same day. The clinical diagnosis was necrotising fasciitis. Emergency debridement on bilateral lower limbs was performed. The left leg tissue specimen collected on July 6 grew *Vibrio vulnificus*. He was still in critical condition. The patient did not have recent travel history. He denied any visits to wet markets or any history of injury. He lived with his wife and daughter who remained asymptomatic. Investigation is ongoing.

The third patient was an 83-year-old male with underlying illnesses. He presented with fever, right wrist pain and swelling on July 3 and was admitted to a public hospital through the AED on the same day. The clinical diagnosis was necrotising fasciitis. Excisional debridement was performed. Specimens of blood and tissue collected on July 3 and July 4 respectively grew *Vibrio vulnificus*. His current condition was serious. Epidemiological investigation revealed that the patient swam daily in seawater from June 27 to June 30. He had history of right wrist abrasion by a door frame on June 30. There was no recent travel history. He lived with a domestic helper who remained asymptomatic. Investigation is ongoing.
**A probable sporadic case of Creutzfeldt-Jakob disease**

On July 10, 2017, the Centre for Health Protection (CHP) recorded a probable case of sporadic Creutzfeldt-Jakob disease (CJD) affecting a 64-year-old woman with underlying illnesses. She had presented with dizziness, visual disturbance and unsteady gait since April 2017. She was admitted to a private hospital in May 2017 and subsequently referred to a public hospital for further investigation. She subsequently developed progressive dementia, dysphasia and dysphagia. Her condition was serious. She had no known family history of CJD and there were no reported risk factors for iatrogenic or variant CJD. She was classified as a probable case of sporadic CJD.

**CHP recorded a domestic cluster of pertussis in July 2017, affecting a baby and his two close contacts. The baby was a one-month-old boy who had presented with cough and post-tussive vomiting since June 22. He was admitted to a public hospital on June 27. His condition was stable and he was discharged on July 6. His pernasal swab taken on June 27 was tested positive for *Bordetella pertussis*.**

Contact tracing identified four symptomatic close contacts. The baby's 33-year-old mother had cough since May 27 and her pernasal swab collected on June 30 was tested positive for *Bordetella pertussis*. The baby’s 68-year-old grandfather had cough since May 25 and his pernasal swab collected on June 30 was also tested positive for *Bordetella pertussis*. Two other close contacts (the baby's grandfather and aunt) also presented with upper respiratory symptoms while their pernasal swabs were tested negative for *Bordetella pertussis*. All symptomatic contacts were treated with a course of antibiotics and their conditions were stable all along.

They had no recent travel history. The baby was born in Hong Kong and was not yet due for the first dose of combined diphtheria, tetanus, acellular pertussis and inactivated poliovirus (DTaP/IPV) vaccine, while his mother and grandfather could not recall their vaccination history. Chemoprophylaxis and screening were also offered to other household contacts. Investigation is ongoing.

**CA-MRSA cases in June 2017**

In June 2017, CHP recorded a total of 119 cases of community-associated methicillin resistant *Staphylococcus aureus* (CA-MRSA) infection, affecting 68 males and 51 females with ages ranging from eight months to 84 years (median: 35 years). Among them, there were 87 Chinese, 10 Filipinos, 5 Pakistanis, 3 Caucasian, 3 Indian, 3 Nepalese, and 8 of unknown ethnicity.

One hundred and seventeen cases presented with uncomplicated skin and soft tissue infections while the remaining two cases had severe CA-MRSA infections. The first severe case affected a 31-month-old girl with underlying illnesses and past history of pneumonia caused by CA-MRSA. She presented with fever, cough with sputum, and vomiting on May 10. She attended the AED of a public hospital on May 18 and was admitted for management. Her chest X-ray showed right middle lobe consolidation. She was diagnosed with pneumonia. Her sputum collected on May 19 was cultured positive for CA-MRSA. She was treated with antibiotics. The patient remained stable and was transferred to another public hospital for rehabilitation on June 2. The second severe case affected a 55-year-old man with underlying illnesses. He presented with right thigh pain, fever, chills and rigors on June 7. He attended the AED of a public hospital on June 14 and was admitted for management. His blood specimen collected on June 14 was cultured positive for CA-MRSA. He was diagnosed to have right thigh abscess and sepsis. He was treated with antibiotics and incision and drainage of right thigh abscess with pus cultured positive for MRSA. He was discharged on June 30 in stable condition.

Among the 119 cases, two sporadic cases involved healthcare workers who were nurses working in two different public hospitals. Investigation did not reveal any epidemiologically linked cases. Besides, five clusters, with each affecting two persons, were identified. Four cases were household contacts and one case was a close contact of previously reported cases.

**Scarlet fever update (June 1, 2017 – June 30, 2017)**

Scarlet fever activity in June increased as compared with that in May. CHP recorded 227 cases of scarlet fever in June as compared with 207 cases in May. The cases recorded in June included 137 males and 90 females aged between nine months and 43 years (median: six years). There were nine institutional clusters occurring in seven kindergartens, a primary school and a special school, affecting a total of 21 children. No fatal cases were reported in June. Of note, a total of 1 213 SF cases had been reported to CHP in the first six months of 2017, representing a marked increase from the figures for the same period in 2016 (727 cases) and 2015 (674 cases). In view of the increase in scarlet fever activity in the recent few weeks, parents should take extra care of their children in maintaining strict personal, hand and environmental hygiene. People suspected to have scarlet fever should consult a doctor promptly. Children suffering from scarlet fever should refrain from attending school or child care setting until fever has subsided and they have been treated with antibiotics for at least 24 hours.