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FEATURE IN FOCUS

Severe Fever with Thrombocytopenia Syndrome (SFTS) - A Review

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Background

Severe Fever with Thrombocytopenia Syndrome (SFTS) is an emerging infectious disease caused by a bunyavirus (SFTS virus or SFTSV in short) belonging to the genus *Phlebovirus* in the family *Phenuiviridae*, order *Bunyavirales*¹. Transmission is predominantly via bites by ticks carrying the virus. According to the Centers for Disease Control and Prevention of the United States, four tick species are known vectors for SFTSV, namely *Haemaphysalis longicornis*, *Amblyomma testudinarium*, *Rhipicephalus microplus*, and *Ixodes nipponensis*². Rarely, human-to-human transmission occurs through direct contact with or ocular exposure to blood of patients^{3,4,5,6}.

With an incubation period usually between 6 and 14 days, symptoms of SFTS include fever and gastrointestinal manifestations (e.g. nausea, vomiting, diarrhoea and tarry stool), and are sometimes accompanied by abdominal pain, muscle pain, neurological symptoms, lymph node swelling, and bleeding⁴. Patients may also present with thrombocytopenia, leukocytopenia and lymphadenopathy. Severe infections can cause haemorrhagic fever and multiple organ failure

Figure I – Image of a common vector of SFTS, Haemaphysalis longicornis⁷.

with a mortality rate of 10-30%^{1,2,4}, which is comparable to other bunyavirus infections like Crimean-Congo haemorrhagic fever and hantavirus infection that could reach a mortality rate of 35%⁸. Poor prognostic factors include older age, high serum viral loads, substantial elevation of liver enzymes, haemorrhagic symptoms, neurological manifestations, disseminated intravascular coagulation and multiple organ dysfunction⁹.

Management of patients primarily focuses on symptomatic treatment. For patients with severe SFTS, hospitalisation with supportive management is often necessary.

Global Situation

The pathogen of SFTS was first identified in Mainland China in 2010^{10,11}, but retrospective studies traced the earlier cases back to 1996 in Jiangsu of Mainland and also 2005 in the Nagasaki Prefecture of Japan^{3,11,12}. The disease was subsequently found to be endemic in several Asian countries including South Korea, Japan, Vietnam and Myanmar¹³. Thereafter, SFTS has become prevalent in the Asia-Pacific region, with cases reported annually in South Korea, Japan, Vietnam, Myanmar, Pakistan, Thailand, and the United Arab Emirates^{3,14}. Some SFTS-like cases have also been reported in the United States and Australia¹⁴.

Mainland China

In Mainland China, national data showed increasing prevalence of SFTS in the last decade. In 2011, 571 confirmed cases from 13 provinces, including 59 fatal cases were reported, the number gradually increased year by year and reached 18 902 cases, including 966 deaths (case fatality ratio (CFR): 5.1%) across more than 19 provinces by the end of 2021 11,15,16. These cases were mainly

found in the mountainous and hilly areas of Henan, Hubei, Shandong, Anhui, Liaoning, Jiangsu and Zhejiang provinces ^{17,18}. The number of SFTS cases continued to increase and the geographical distribution spread from central area to the northeast and from the west to the south ¹⁶. SFTS cases were reported all year round but majority occurred from April to October, with the incidence peaking from May to June ¹⁶. The risk of infection and mortality increased with age, with most cases occurred in age group 50-74 years (69%) and fatality in age group over 60 years (80%) ¹⁶. High-risk populations for SFTS include those who live and work in the hills, mountains and forests, as well as tourists engaging in outdoor activities in these regions, as they are more likely to get tick bites. Farmers in endemic areas and older females are also more susceptible to the infection, accounting for more than 80% of the total caseload ^{18,19}.

Japan

In Japan, SFTS was first detected and reported in 2013, though the first case could be traced back to 2005¹². Recent statistics showed an increasing trend of SFTS cases, with cases ranged from 40 to 132 per year²⁰. As of January 2024, 939 cases including 104 deaths have been reported since 2013, with CFR of 11.1%. The male-to-female ratio was 1:1, and the median age at the time of notification was 75 years. Geographically, majority of the cases were found in the western part of Japan, including Miyazaki, Hiroshima, and Yamaguchi prefectures²⁰. Notably, Japan reported a case of SFTS affecting a doctor who acquired the infection from a deceased patient in March 2024.

On March 19, 2024, Japan's National Institute of Infectious Diseases confirmed the first SFTS case of human-to-human infection in the country²¹. According to the report, a doctor attended a patient in his 90s who was later diagnosed with SFTS. On initial consultation, the doctor wore a surgical mask but performed physical examination without gloves. Subsequently, the patient's condition rapidly deteriorated and passed away. The same doctor performed various procedures on the deceased including removal of his catheter postmortem with a mask and gloves on during the procedure but reported not wearing goggles. Nine days after the patient's death, the doctor developed fever and headache, and was diagnosed with SFTS. Humanto-human transmission was confirmed after sequencing and comparing the SFTSV genes with the patient's, which were found to be identical.

South Korea

In South Korea, the first SFTS case was reported in 2013. Over the past decade, the number of patients with SFTS increased from 36 cases in 2013 to 272 in 2017, thereafter the trend remained stable in recent years with around 200 to 250 cases per year^{22,23}. Between 2013 and 2022, a total of I 697 cases and 317 deaths were reported, with a CFR of 18.7%. The older age group and those with underlying diseases were found to have higher risk of death. Most of the SFTS patients had been involved in farming (49.7%) and other outdoor activities such as hiking, walking and camping (45.1%). Geographically, most of the infections were found in the Yeongdeok-gun, Gyeongsangbuk-do, Yangyang-gun, Gangwon-do and Inje-gun, Gangwon-do regions²⁴.

Local Situation

In Hong Kong, tick-borne diseases (TBDs) including spotted fever and relapsing fever are statutorily notifiable under the Prevention and Control of Disease Ordinance (Cap 599). In the past decade (2014-2023), the CHP recorded 205 cases of spotted fever, ranging from 13 to 34 cases per year, and five deaths. Among them, 193 cases were locally acquired, three were imported and the origin of nine others was unknown. For relapsing fever, the last case was reported in 1950. Although SFTS per se is not a notifiable disease in Hong Kong, viral haemorrhagic fever (which can be a presentation of SFTS) was made notifiable on July 14, 2008. So far, there has been no confirmed case of SFTS recorded in Hong Kong.

According to the Pest Control Advisory Section (PCAS) of the Food and Environmental Hygiene Department, there have been no recorded instances of the classical vectors of SFTS being found in the environment. However, some potential vectors of Haemaphysalis sp. such as H. hystricis, H. sinesis, and Rhipicephalus sp. including R. sanguineus and R. pumillio as well as some Ixodes sp. are present.

As Hong Kong is a metropolitan city with abundant international travels, imported cases of TBDs are expected and have been recorded. Together with frequent travel of local people to Mainland China, Japan and South Korea, the wide distribution of *H. longicornis* in East Asia, and the presence of potential vectors in the locality including *Haemaphysalis sp. and Rhipicephalis sp.*, the risk of contracting SFTS remains a possibility. It is important that members of the public and healthcare professionals should take reference of health advice below for personal protection. Preventive measures are also important to avoid tick exposure when travelling abroad especially for older people, people with underlying diseases and those who would frequently engage in outdoor activities.



Prevention and Control Measures

Preventive measures should be taken when visiting rural areas to avoid being bitten by the vectors.

- ✦ Pre-visit preparation:
 - Wear loose, light-coloured, long-sleeved tops and trousers.
 - Wear shoes that cover the entire foot, avoid wearing sandals or open shoes.
 - Tuck trousers into socks or boots to prevent arthropods from reaching the skin.
 - Use DEET-containing insect repellent on exposed parts of the body and clothing.
 - Pregnant women and children of 6 months or older can use DEET-containing insect repellent.
 - Avoid using fragrant cosmetics or skin care products.
 - \$\footnote{\text{the If both insect repellents and sunscreen are used, apply insect repellents after sunscreen.}
- → During the visit:
 - Stay on footpaths and avoid walking through vegetation. Do not brush along the vegetation at the sides of footpaths.
 - Avoid resting on vegetation, or at humid and dark places.
 - Do not hang clothing on trees or vegetation.
 - Do not feed wild or stray animals.
 - * Re-apply insect repellents according to instructions.
- + After the visit:
 - Inspect body parts and clothing. Clear any attached arthropods carefully.
 - Take a soapy shower and wash the clothes.
 - Inspect and clean the bodies of accompanying pets.
- If an attached tick is found on the body:
 - Gently remove it by grasping its head with tweezers or fine-tipped forceps close to the skin, then disinfect the bite area and wash hands with soap and water
 - Do not crush or twist the tick during removal

In view of potential human-to-human transmission in nosocomial setting, healthcare workers and carers who might need to handle blood or bodily secretions of patients with SFTS are recommended to put on appropriate personal protective equipment (PPE) with eye protection and gloves.

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Updates on Infection Control Guidelines on Nephrology Services in Hong Kong

Reported by Dr Leo LUI, Associate Consultant; Mr Anthony NG, Senior Nursing Officer; Ms Jane LEUNG, Advanced Practice Nurse; Ms Candy TSANG, Advanced Practice Nurse and Dr Hong CHEN, Consultant and Head, Infection Control Branch, CHP.

Infection control in renal dialysis

Infection is a major risk factor of morbidity and mortality in renal dialysis patients because they are more vulnerable due to immunosuppression and are frequently hospitalised with an increased exposure and risk to healthcare associated infections. Haemodialysis may require prolonged period of vascular access with multiple patients receiving treatment concurrently. As a result, haemodialysis patients have a higher rate of bloodstream and other infections compared to patients not on haemodialysis. Proper infection control in dialysis setting is crucial to prevent infections before, during and after the process.

In order to identify gaps and training needs on infection control issues for public and private renal units and dialysis centres in Hong Kong, Infection Control Branch (ICB) of Centre for Health Protection (CHP) and Central Renal Committee (CRC) of Hospital Authority (HA) had launched a programme since 2008 to promote infection control in local renal units and nephrology services. The goals and objectives were to i) systematically look into the infection control context and existing practice in renal units across the territory; ii) develop and standardise guideline on infection control to safeguard patients and staff members; and iii) provide training to staff on infection control and occupational health and safety issues in renal units.

To drive the programme forward, a collaborative working group was formed consisting of the representatives from relevant parties including the CRC of HA, private nephrology specialists, hepatologist, Hong Kong Association of Renal Nurses, Hong Kong Infection Control Nurses Association, Hong Kong Kidney Foundation, Chief Infection Control Officer (CICO) office of HA, Electrical & Mechanical Services Department (EMSD) and ICB of CHP.

One of the most important deliverable of the group is to formulate infection control guideline. The first edition of the Infection Control Guidelines on Nephrology Services in Hong Kong (referred to as "the guideline" hereafter) was published in year 2010, and since then has



Figure I — Cover page of the guideline (4th edition).

become an important reference for both public and private dialysis service providers to upkeep the infection control standards in dialysis settings.

The major areas covered by the guideline include viral and bacterial infective risks, ways to prevent or minimise these risks, serology screening for bloodborne viruses (BBV), immunisations, water treatment systems, infection control practices, home dialysis, occupational safety and health, as well as surveillance and quality measures.

Guideline revision (4th edition 2023 update)

Every several years, the guideline is revised and updated according to latest local and international recommendations. The last edition (3rd edition version 3.2) was revised in October 2019 before the COVID-19 pandemic. With the infection control experience gained after the battle of COVID-19, as well as updates of major international guidelines, the working group renewed the local infection control guideline in December 2023.

The working group reviewed latest scientific evidence and discussed on areas to be revised, taking reference from international health authorities and societies including but not limited to the Centers for Disease Control and Prevention (CDC), Association for the Advancement of Medical Instrumentation (AAMI), Department of Health of the United Kingdom, Ministry of Health of Singapore, International Society of Peritoneal Dialysis (ISPD), Infectious Diseases Society of America (IDSA) and local sources such as Scientific Committee of Infection Control (SCIC) and Scientific Committee of Vaccine Preventable Disease (SCVPD) of CHP, CRC and Central Committee on Infectious Disease and Emergency Responses (CCIDER) of HA. In



Figure 2 – Home haemodialysis machine.

order to gain deeper understanding of detailed operation for haemodialysis in different settings, site visits were arranged to a haemodialysis centre in public hospital, a community haemodialysis centre and the home of a patient performing "home haemodialysis". The guideline has incorporated the observations of the practice and the review of workflow during these visits.



Major updates in the 4th edition

The revised guideline is available on the CHP website in both English and Chinese. The below highlighted the major changes comparing with the last version.

English version: https://www.chp.gov.hk/files/pdf/ic_gu_nephrology_services_in_hk.pdf
Chinese version: https://www.chp.gov.hk/files/pdf/ic_gu_nephrology_services_in_hk.pdf

- Chapter I Viral Hazards: Measures for respiratory viruses including COVID-19 e.g. placement, ventilation and isolation precautions, etc. are emphasised in the new edition. These recommendations are made in consideration of the fact that normalcy of the society has resumed, with a need to balance stringent infection control measures against practicality and disease severity of infection.
- Chapter 2 Bacterial & Fungal Hazards: Candida auris, which has caused a number of outbreaks in local hospitals and elderly homes since 2019 are included in the guideline as one of the multidrug-resistant organisms (MDROs). Medical equipment including haemodilaysis machines must be undergone proper cleaning and disinfection after use.
- ◆ Chapter 3 Prevention of Dialysis-Associated Risks: Chlorhexidine-impregnated dressings may be considered for short-term, non-tunneled central venous catheters to protect the insertion site in dialysis units with high infection rates. For prevention of peritoneal dialysis-related infections, the guideline advocates daily topical application of antibiotic cream or ointment (mupirocin or gentamicin) to the catheter exit site. Exit site should be cleaned at least twice weekly and every time after a shower or vigorous exercise.
- Chapter 4 Serology Screening for Blood-borne Viruses: Serology screening is a key issue in dialysis centre but its interpretation could be challenging. The revised edition includes a table of HBV and HCV serology interpretation and suggested actions to facilitate decision-making. Frequently-asked questions related to hepatitis serology have also been revised.
- Chapter 5 Immunisations: This chapter covers various types of vaccinations for dialysis patients. Latest recommendations from CHP regarding pneumococcal, seasonal influenza and COVID-19 have been updated according to recommendations by the CHP.
- ◆ Chapter 6 Water Treatment System: Sample collection, sampling frequency and limit levels of dialysis fluids have been updated.
- ◆ Chapter 7 Infection Control Practices in Renal Units: Minimise storage of equipment close to dialysis machines and patients. Do not handle and store medications or clean supplies in the same or adjacent area that used equipment or blood samples are handled.

- ◆ Chapter 10 Surveillance and Audit: Renal units should regularly audit the compliance of infection control practices e.g. hand hygiene using standardised methods and definitions for data collection and analysis. For example, the centre can adopt the surveillance methodology suggested by National Healthcare Safety Network (NHSN) of CDC in the United States.
- ◆ Appendix A: Frequently asked questions (FAQs) have been updated to enrich the contents on serology testing for bloodborne viruses (BBV).

Promulgation and Training Forum

To promulgate the new edition of the guideline and to enhance clinical staff's knowledge and awareness of infection control in renal dialysis, a training forum was organised by ICB on February 22, 2024 as a hybrid (in-person plus zoom) session. During the forum, Dr Lui Sing Leung (HA CRC Chairman) highlighted the rationale of updating the guideline and Prof Yuen Man Fung (Department of Medicine, HKU) explained on the topic of viral hepatitis serology testing with active discussion during the Q&A session. The forum was well received with a total of 400 attendance comprising doctors, nurses, allied health and others from both the public and private sectors. The training materials have been uploaded and all who are interested are welcome to view from the IDIC portal (https://icidportal.ha.org.hk/Trainings/View/183)



Figure 3 – Training forum organised on February 22, 2024.

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NEWS IN BRIEF

Two linked cases of listeriosis

The first case affected a 30-year-old pregnant woman with no underlying illness. She presented with vaginal bleeding, abdominal pain and decreased fetal movement on March 24, 2024. She was admitted to obstetric ward of a public hospital on the same day. Clinical diagnosis was preterm premature rupture of membrane and she had uneventful delivery on the same day. Placental swab collected on March 24 showed heavy growth of *Listeria monocytogenes*. She was given a course of oral antibiotics and was discharged on March 27. She recalled history of consumption of ice creams during pregnancy. She had no recent travel. Her home contacts were asymptomatic.

The second case affected the newborn girl who was the daughter of the first case. She was born by normal spontaneous delivery at a gestational age of 31 weeks and 4 days. Her blood collected on March 24 was cultured positive for *Listeria monocytogenes*. Clinical diagnoses were *Listeria monocytogenes* bacteremia and respiratory distress syndrome due to prematurity. She was in stable condition.

Two sporadic cases of Creutzfeldt-Jakob Disease

Centre for Health Protection (CHP) recorded two sporadic cases of Creutzfeldt-Jakob Disease (CJD) on April 2, 2024.

The first case involved a 70-year-old retired man with underlying illnesses residing in Tai Po. He presented with rapid cognitive decline in January 2024 and was admitted to a public hospital on March 18, 2024. He was found to have myoclonus and akinetic mutism. Findings of the electroencephalogram (EEG) and magnetic resonance imaging (MRI) of the brain were compatible with CJD. He was classified as a probable case of sporadic CJD.

The second case involved a 68-year-old woman with underlying illnesses. She presented with vision colour change and blurred vision, confusion and rapid cognitive decline in mid February 2024 and was admitted to a hospital in mainland in February 2024 for investigation. She was admitted to a public hospital in Hong Kong on March 30, 2024 due to persistent confusion and was found to have myoclonus and progressive dementia. She was classified as a possible case of sporadic CID.

Both cases had no known family history of CJD and no risk factors for either iatrogenic or variant CJD were identified.

A sporadic case of necrotizing fasciitis due to Vibrio vulnificus infection

On April 19, 2024, CHP recorded a sporadic case of necrotizing fasciitis caused by *Vibrio vulnificus*. The case involved a 73-year-old male with underlying illnesses. He presented with acute left leg swelling and pain on April 17, 2024 and was admitted on the same day with rapid development of erythema and bullae. The patient underwent multiple operations including wound debridement and above knee amputation. The diagnosis was necrotising fasciitis. *Vibrio vulnificus* was recovered from wound tissue and wound swab. The patient's condition deteriorated and he succumbed on April 22, 2024.

A sporadic case of brucellosis

On April 19, 2024, CHP recorded a sporadic case of brucellosis affecting a 49-year-old man with good past health. He presented with fever, headache, musculoskeletal pain, malaise and reduced appetite on March 25, 2024. He was admitted to a public hospital on April 11. His blood specimen collected on April 14 was cultured positive for *Brucella melitensis*. The clinical diagnosis was brucellosis. He was stable and discharged on April 14, 2024. He worked as a chef in mainland and handled raw sheep regularly. He injured his hand in February this year. His home contact and colleagues were asymptomatic.

World Immunization Week 2024 - Humanly Possible: Saving Lives through Immunization

World Immunization Week (WIW) is a global event held annually in the last week of April to highlight and recognise the importance of immunisation. This year's theme "Humanly Possible" celebrates the 50 years of the World Health Organization (WHO)'s Expanded Programme on Immunization (EPI) – recognising collective efforts to reach everyone with lifesaving vaccines and calling attention to the need to further protect more children, adults and their communities.

The EPI was an initiative launched by the WHO in 1974 as a global endeavor to ensure equitable access to life-saving vaccines for every child, regardless of their geographic location or socioeconomic status. Over the past five decades, EPI has saved 154 million lives and benefited people of all ages in every region. In Hong Kong, a comprehensive immunisation programme has been provided for all children for decades in line with the principles set out in the EPI. Under the Hong Kong Childhood Immunisation Programme, children receive different types of vaccines and boosters from birth to Primary Six for protection against vaccine preventable diseases including measles, poliomyelitis, and hepatitis B. In addition to the childhood vaccines, the Government also provides immunisation against influenza, pneumococcal disease and COVID-19 for populations that are considered at risk.

Immunisation is one of the safest and cost-effective public health interventions, and for decades, vaccine has been proven to be a powerful tool in reducing childhood mortality. Amid the recent resurgence of vaccine preventable diseases such as measles across the globe, parents are reminded to maintain up-to-date immunisation for their children for timely and comprehensive protection, as delays in vaccination will weaken the protection for the children against relevant infectious diseases. For more information on the WIW, please visit the CHP's thematic webpage: https://www.chp.gov.hk/en/features/107809.html.

