

# Severe Fever with Thrombocytopaenia Syndrome (SFTS)

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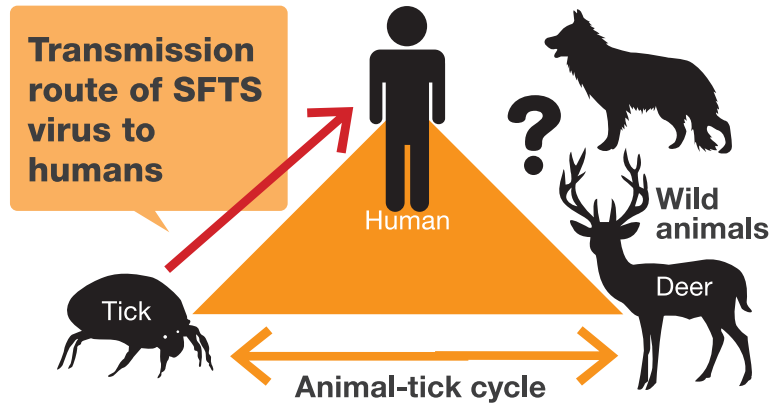
## Medical Care Handbook



| | | [Version 2.5] 2014.3.17 | |

# What is severe fever with thrombocytopenia syndrome (SFTS) ?

- SFTS is an emerging infectious disease caused by a newly identified SFTS virus (family *Bunyaviridae*, genus *Phlebovirus*), which was first reported by a researcher in China in 2011.
- In Japan, the first patient with SFTS was reported in 2013. However, a retrospective investigation revealed that a case occurred at least as early as 2005.
- SFTS is characterized by fever, leukocytopenia, and thrombocytopenia. In severe cases, it also causes bleeding tendency and multiple organ failure.
- Tick bite is thought to be a primary infection route. However, medical workers should take appropriate measures to prevent infection during medical care of patients; cases of family and occupational infections due to contact with blood and/or body fluid from the patient have been reported in China.



### How to remove a tick

Grasp the mouth parts as close to the skin's surface as possible using tweezers and slowly pull them upward from the skin surface.

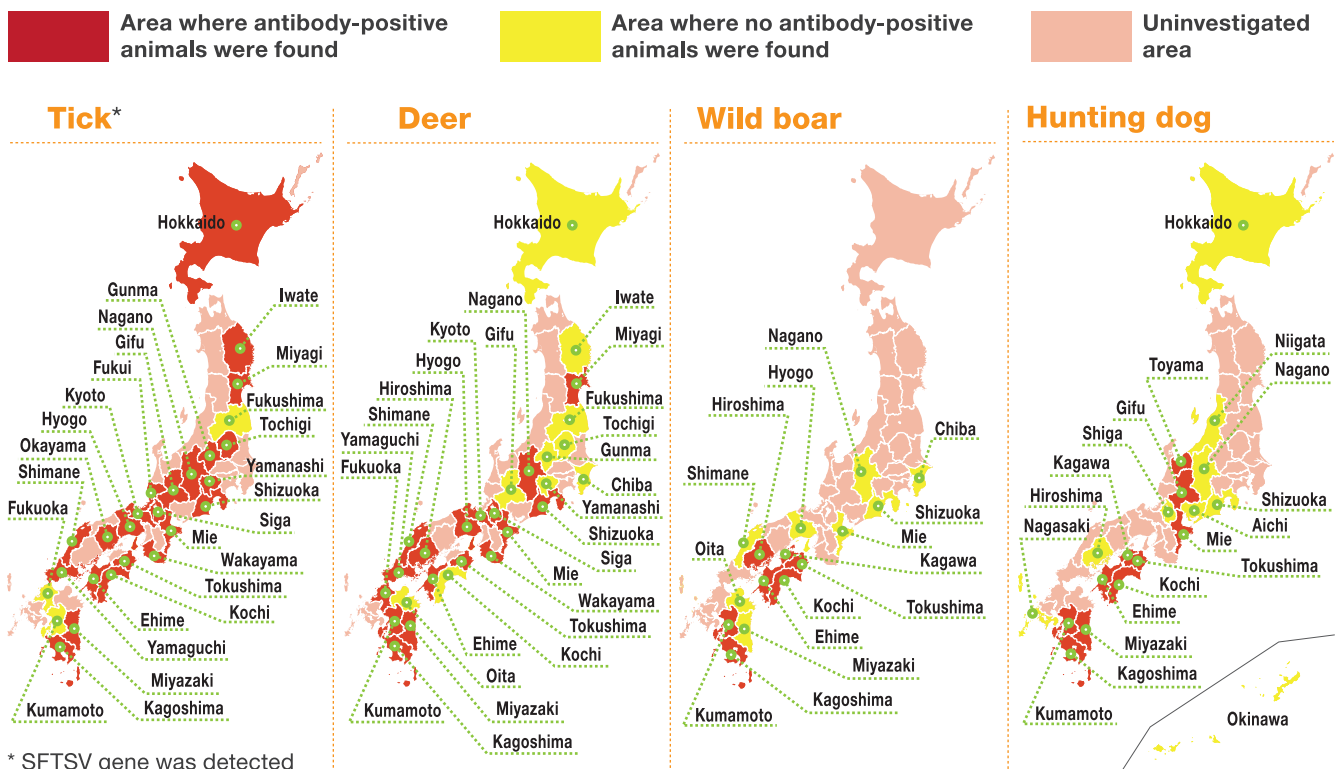
*Amblyomma testudinarium* (adult)

*Haemaphysalis longicornis* (adult)

Tick removal - Purdue University, USA

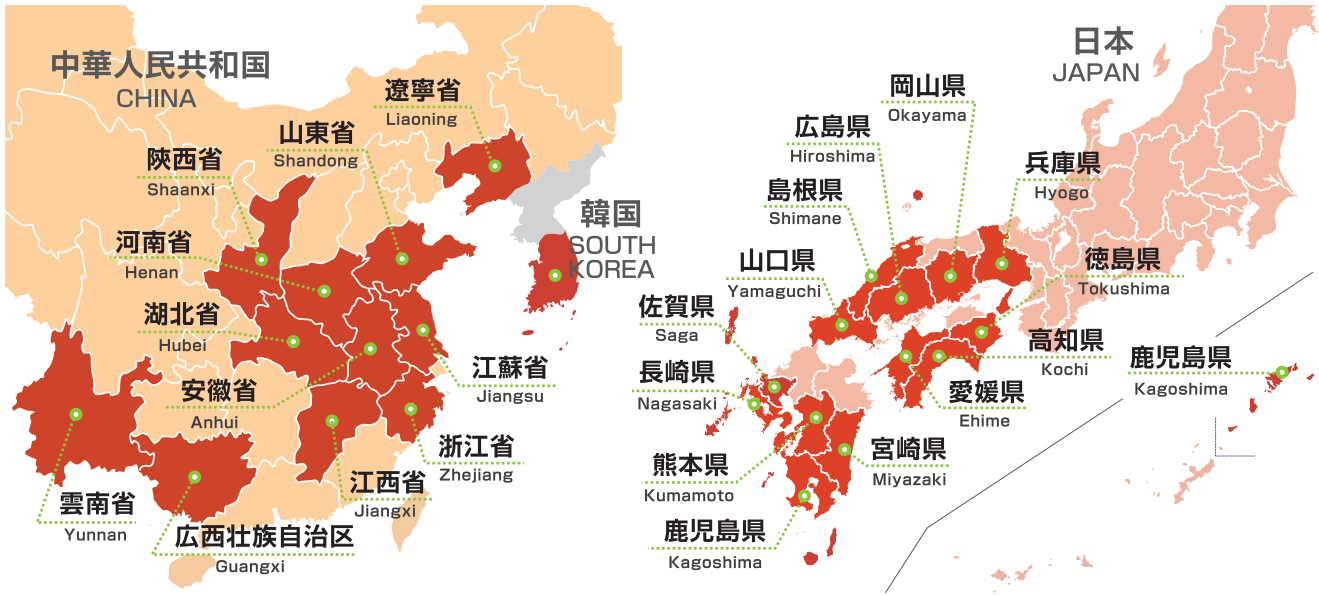
## Distribution of the SFTS virus in Japan (second report)

IASR rapid communication, February 24, 2014

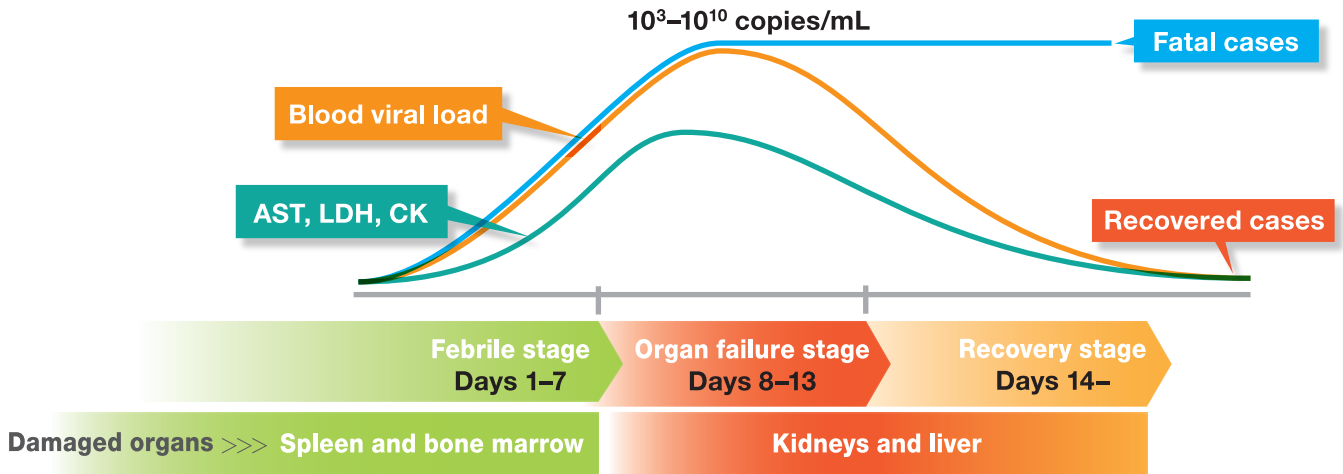


# Areas in East Asia where cases have occurred

\* As of October 2013



## Clinical course



## Epidemiology of patients in Japan (n = 40)

Patients who developed SFTS on or after January 1, 2013

### Gender ratio

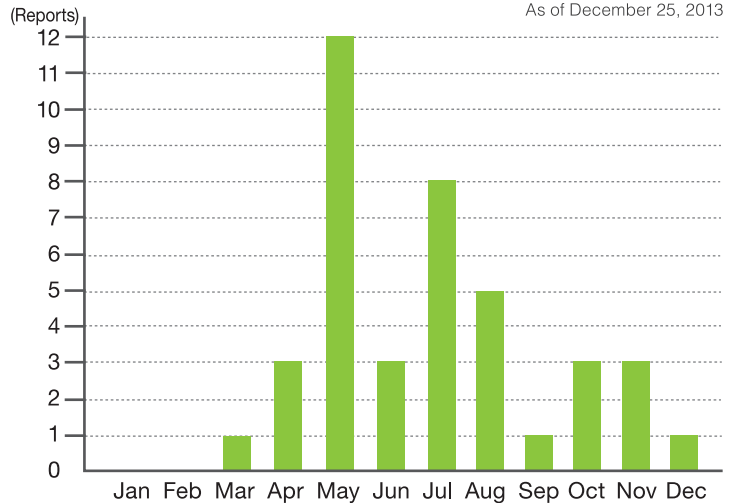
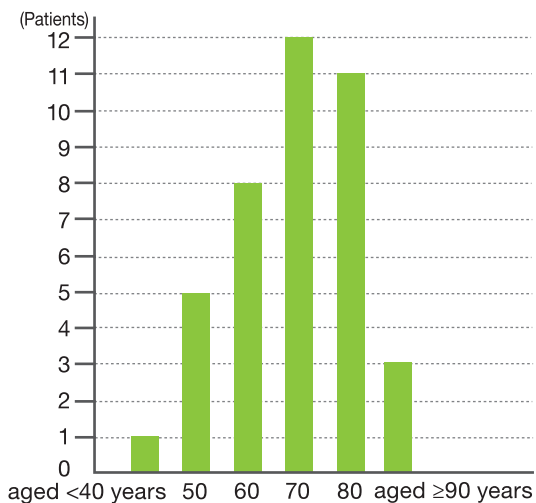
● Men: 16 ● Women: 24

### Median age

● 73 years

### Deceased

● 13 (33%)



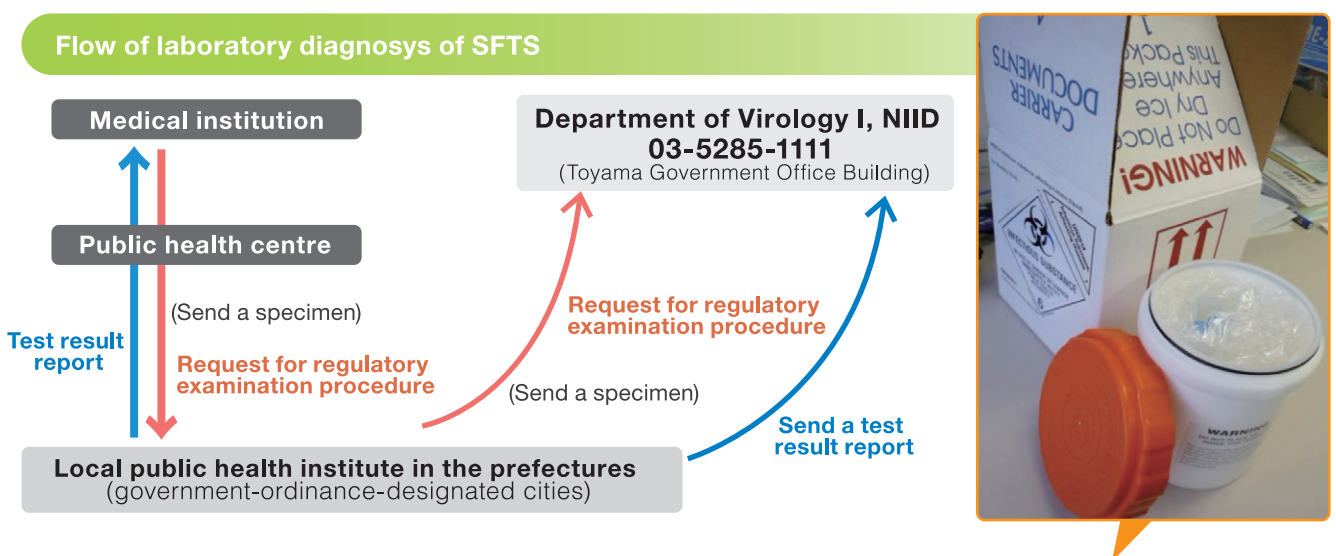
## Clinical features of SFTS

- Incubation period: 6–14 days
- Fever >38°C
- Thrombocytopenia (<100,000/mm<sup>3</sup>)
- Leukocytopenia (<4,000/mm<sup>3</sup>)
- Increase in serum enzyme levels (AST, ALT, LDH)
- Gastrointestinal symptoms (nausea, vomiting, abdominal pain, diarrhoea, melena), headache, muscle pain, neurologic manifestations, lymphadenopathy, and bleeding
- Fatality rate of approximately 10–30%

## Tests required for definitive diagnosis

Test method	Test material
Isolation of SFTS virus	Blood, throat swab, urine
Detection of SFTS virus RNA using RT-PCR	
Demonstration of IgM or rising IgG antibodies by ELISA or IFA (detection of IgM antibody, seroconversion in paired sera, or significant increase in antibody titre)	Serum
Demonstration of virus neutralization antibodies (seroconversion in paired sera or significant increase in antibody titre)	

## Regulatory examination flow



## Specimen and packaging

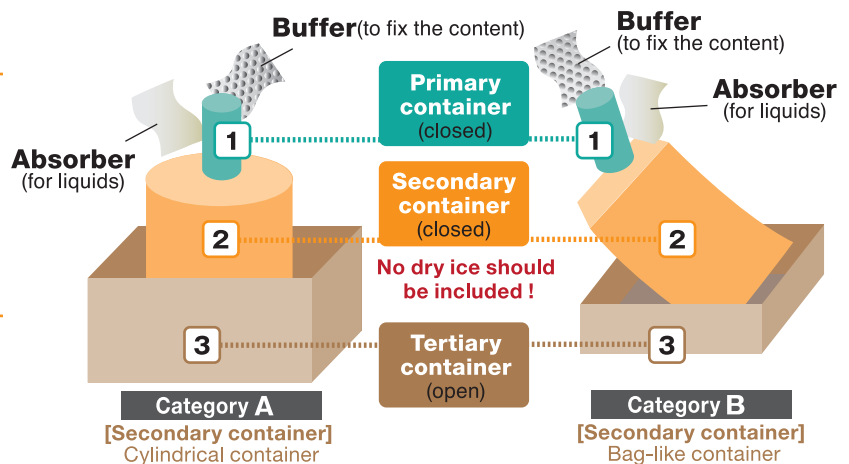
### Basic triple packaging system

#### Proper specimens

- Blood (collected in a serum Spitz tube, no need for serum separation)
- Urine (in a container with a screw cap)

#### Request for testing

- Nearest public health centre
- Use of the UN standard packaging for Category A substances is preferred (pathogen requiring BSL3)



\* When using Yu-Pack, use quaternary packaging with a duralumin case.

# Algorithm of diagnosis, treatment, and infection prevention

Summary of previously reported cases in Japan

- Primarily from western Japan
- No history of exposure to tick in some cases
- High incidence from spring to autumn
- High incidence in the elderly

## Patients with severe fever accompanied by bleeding tendency and/or gastrointestinal symptoms

### Differential diagnosis

#### ● Infectious diseases

- Toxicogenic shock syndrome
- Acute viral hepatitis
- Disseminated intravascular coagulation due to severe septicaemia
- Rickettsia, scrub typhus, Japanese spotted fever
- Leptospirosis, etc.

#### ● Non-infectious diseases

- Drug-related fever
- Haemophagocytic syndrome, etc.

#### ● Patients with a history of travelling overseas

##### ● Viral haemorrhagic fever

Dengue haemorrhagic fever, haemorrhagic fever with renal syndrome, yellow fever, Lassa fever, Crimean-Congo haemorrhagic fever, Rift Valley fever, Ebola/Marburg haemorrhagic fever, etc.

##### ● Malaria

##### ● Typhoid/paratyphoid

### Test with priority

#### Compliance with standard precaution:

- blood count,
- blood biochemical properties,
- blood culture, etc.

### Clinical characteristics considered suspicious for SFTS

#### Hospitalise the patient, as standard practice

A private ward is preferable

#### Wear personal protective equipment

Use gloves and apron and add a surgical mask and visor according to the risk of exposure to blood and/or body fluids. Wear an N95 mask during aerosol-generating techniques.

#### Request testing

Contact the nearest public health centre to request testing at a local public health institute

### Definitive diagnosis (SFTS virus is detected)

Notify an authority of the occurrence of a Category 4 infectious disease

### Treatment memo

- No effective antiviral agent for treatment is available at present
- Supportive treatment for sepsis may improve survival
- Efficacy of steroids in cases complicated with haemophagocytic syndrome is unclear



Proper personal protective equipment to use during aerosol-generating techniques

## Ensure use of personal protective equipment

- **Gloves**
- **Gown**
- **Surgical mask**
- **Face shield (goggles)**

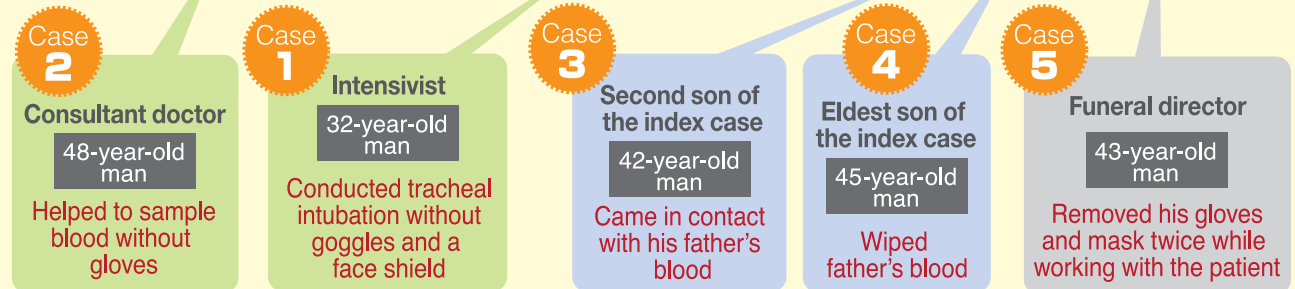
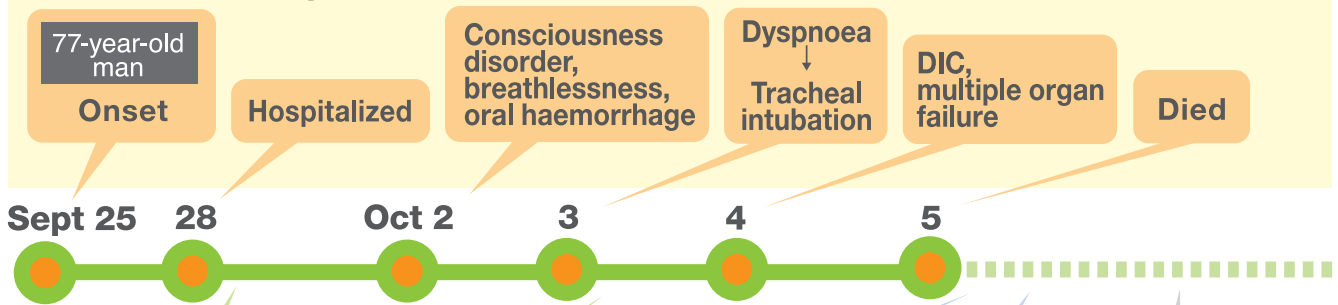
In cases with the following, use additional devices, as listed bleeding, severe vomiting/diarrhoea, aerosol-generating techniques

- **Double gloves**
- **N95 mask**

## Cases of human to human transmission (Shandong Province, 2010)

### ● Index case/77-year-old man

● Blood viral load:  $10^{10}$  copies/mL



### ● Secondary cases:

No record of the days to onset. The symptoms developed 7–15 days after exposure, but were mild in all cases. Although these are extremely rare cases, human-to-human transmission may occur in the presence of a high blood viral load.

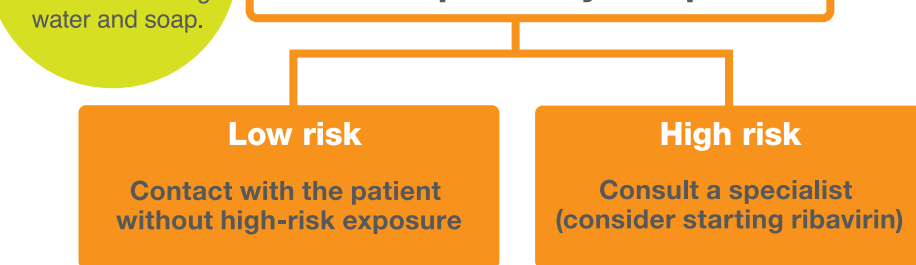
Clin Infect Dis 2012; 54:249-252.

## Management after exposure to patient's blood and/or body fluid

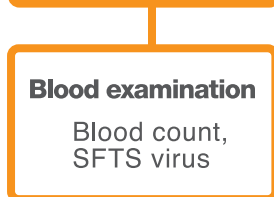
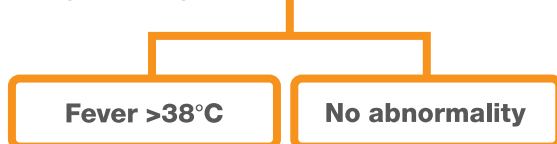
Wash off blood and/or body fluid with a large volume of running water and soap.

### Proper way to dispose of blood/body fluid, including vomit

There is a possibility of exposure



Measure temperature:  
Daily for 14 days



### High-risk exposure

- Needle-stick, mucosal membrane exposure to a splash
- Aerosol-generating technique, such as tracheal intubation, without proper personal safety devices

### When you need advice from a specialist:

- National Institute of Infectious Diseases  
Department of Virology I  
Infectious Disease Surveillance Center
- National Center for Global Health and Medicine  
Division of Preparedness and Emerging Infections,  
Disease Control and Prevention Center



Cover with a diaper or something similar and pour 0.5% hypochlorous acid on the substance from above



Dispose, while avoiding direct contact with the diaper

## Domestic (Japan) information

### Masayuki Saijo, Masayuki Shimojima, Hidenori Fukushi, et al.

General description of 8 patients with severe fever and thrombocytopaenia syndrome (SFTS) identified in Japan  
(IASR Vol. 34 p. 110: April 2013)

### Masayuki Saijo, Masayuki Shimojima, Hidenori Fukushi, et al.

Two patients that were retrospectively identified after the first identification of patients with severe fever and thrombocytopaenia syndrome (SFTS) in Japan  
(IASR Vol. 34 p. 108-109: April 2013)

### Shigeru Morikawa, Akihiko Uda, Yoshihiro Kaku, et al.

First report of the distribution of severe fever with thrombocytopaenia syndrome (SFTS) virus in Japan  
(IASR Vol. 34 p. 303-304: October 2013)

### Yoshito Honma, Koji Murakami, Chie Yamamoto, et al.

Clinical characteristics of 5 SFTS patients, including 2 patients with family-related infection  
(IASR Vol. 34 p. 312-313: October 2013)

## Government notices

Enforcement of a government ordinance that revised a portion of the Order for Enforcement of the Act on Prevention of Infectious Diseases and Medical Care for Patients with Infectious Disease  
(No. 0222-2 Proposed by Director of Health Service Bureau)

A request related to specimens for the testing of severe fever with thrombocytopaenia syndrome (SFTS) and their disposal method (testing request manual)

Department of Virology I, National Institute of Infectious Diseases

Severe fever with thrombocytopaenia syndrome (SFTS) Q&A

## Published articles

### Yu X, Liang M, Zhang S, et al.

Fever with thrombocytopenia associated with a novel bunyavirus in China. *N Engl J Med* 2011;364:1523-1532.

### Zhang Y, He Y, Dai Y, et al.

Hemorrhagic fever caused by a novel bunyavirus in China: pathogenesis and correlates of fatal outcome.  
*Clin Infect Dis* 2012; 54:527-533.

### Gai Z, Zhang Y, Liang M, et al.

Clinical progress and risk factors for death in severe fever with thrombocytopenia syndrome patients.  
*J Infect Dis* 2012;206:1095-1102.

### Gai Z, Liang M, Zhang Y, et al.

Person-to-person transmission of severe fever with thrombocytopenia syndrome bunyavirus through blood contact.  
*Clin Infect Dis* 2012;54:249-252.

### Bao C, Xi G, Qi X, et al.

A family cluster of infections by a newly recognized bunyavirus in eastern China, 2007: further evidence of person-to-person transmission. *Clin Infect Dis* 2011;53:1208-1214.

### Tang X, Wu W, Wang H, et al.

Human-to-human transmission of severe fever with thrombocytopenia syndrome bunyavirus through contact with infectious blood. *J Infect Dis* 2013;207:736-739.

### Advisory Committee on Dangerous Pathogens(ACDP).

Management of Hazard Group 4 viral haemorrhagic fevers and similar human infectious diseases of high consequence"

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**When you need advice from a specialist:**

- **National Institute of Infectious Diseases**  
Department of Virology 1  
Infectious Disease Surveillance Center

**TEL. 03-5285-1111 (main)**

- **National Center for Global Health and Medicine**  
Division of Preparedness and Emerging Infections,  
Disease Control and Prevention Center

**TEL. 03-3202-7181 (main)**

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Comprehensive Research for the Control of SFTS, Health and Labor Sciences Research Grant  
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Principal Investigator: Takeshi Kurata (Department of Pathology, National Institute of Infectious Diseases)