



衛生防護中心  
Centre for Health Protection

## Scientific Committee on Vector-borne Diseases

### Prevention of Rickettsioses Commonly Occurring in Outdoor Settings

#### Purpose

The rickettsioses (rickettsial diseases) are diseases caused by a group of Gram-negative obligate intracellular bacteria in the family *Rickettsiaceae* (1). They encompass a range of human systemic infections often characterized by fever and rash. These diseases are primarily transmitted by the bite or faeces of infected arthropod vectors such as ticks, mites, lice, and fleas. Certain rickettsioses occur mainly in outdoor settings.

2. This paper examines the main features of the rickettsial diseases that commonly occur in outdoor settings and recommends on the prevention approaches.

#### Scope

3. Rickettsiae are obligatory intracellular parasites that infect the endothelial cells of blood vessels. They replicate by binary fission inside the host cells, and result in heavy damage and hence vasculitis.

4. The taxonomic classification of the genus *Rickettsia* has been constantly changing. Recent developments in molecular methods have resulted in the reclassification of the Rickettsiales under which 3 groups of diseases are still commonly called rickettsioses (2). They include scrub typhus, spotted fever group, and the typhus group comprising of epidemic typhus and endemic (urban / murine) typhus.

5. The spectrum of vectors, causative agents, epidemiological risk factors and the associated diseases are summarized in Table 1. Among the rickettsioses, scrub typhus and spotted fever are well known to occur in outdoor settings (3, 4, 5). Though the causative



agent of scrub typhus has been reclassified as a distinct genus called *Orientia* (6), it has been conventionally grouped under Rickettsiosis as prevention and control measures are similar.

## **Clinical features of scrub typhus and spotted fever**

### Scrub typhus

6. Scrub typhus, caused by *Orientia tsutsugamushi*, is also known as tsutsugamushi disease, a disease found mainly in the Asia-Pacific region (5). The disease is transmitted through the bite of the infected larval trombiculid mites.

7. The incubation period is 10 to 12 days. The disease is characterised by a primary skin ulcer, an eschar, corresponding to the site of attachment of the infected mite, which may be present in around 50% of patients (3). An acute febrile illness follows within a few days, along with headaches, chills, conjunctival injection and lymphadenopathy. A maculopapular rash may develop on the trunk, extending to the extremities. A pneumonitis may also develop. Reported fatality rate for untreated case is between 1% and 60%, depending on the strain of the infectious agent and previous exposure (7).

### Spotted fever

8. The spotted fever group (SFG) comprises more than 30 species in the genus *Rickettsia* (see Table 1). It is commonly transmitted by the Ixodid tick and brown dog tick, although fleas and mites may also be responsible for transmission of other species (e.g. *R. felis*). Each member of the SFG has a different geographical distribution, therefore practically the distribution is worldwide.

9. The clinical symptoms of spotted fever group rickettsioses generally begin 6 –10 days after the arthropod bite and typically include fever, headache, muscle pain, rash, local lymphadenopathy, and a characteristic inoculation eschar (“tache noire”) at the bite site. However, the main clinical signs vary depending on the species involved (8).

10. The most extensively studied member among the SFG is Rocky Mountain Spotted Fever (RMSF), caused by *R. rickettsii*. RMSF causes a severe disease which is characterized by sudden onset of moderate to high fever, malaise, chills, myalgia, severe headaches, and conjunctival injection. A maculopapular rash, which occurs in up to

90% of patients, first appears on the cooler parts of the body such as the distal extremities, including the palms and soles on the 3<sup>rd</sup> to 5<sup>th</sup> day, and spreads in a centripetal fashion to the rest of the body. A petechial exanthem may also occur in 40-60% of patients. An eschar is not typical. Reported fatality rates among untreated cases ranged from 13% to 25%, which can be substantially reduced through prompt recognition and treatment (3, 7).

11. Japanese spotted fever is less severe compared to RMSF. It was first described in 1984 in Japan (9, 10) and later cases were described in Korea as well (11). Symptoms resemble that of RMSF which include high fever and rash on the extremities. An eschar may also be present but is generally smaller than that of scrub typhus.

## Diagnosis

12. Apart from epidemiological and clinical features, definitive diagnosis of scrub typhus and spotted fever requires laboratory studies.

13. The mainstay for laboratory confirmation is serology, which requires acute and convalescent sera from patients. Positive cases are characterised by a four-fold or higher rise in antibody titres against the scrub typhus or spotted fever group. However, cross-reactivity between the typhus and spotted fever groups may occur, complicating the diagnosis. Another limitation of serology tests is the inability to diagnose early infections due to delayed antibody response, which may also be affected by treatment.

14. Recent advance in molecular techniques has improved the diagnosis of rickettsial diseases especially in early disease. Prompt detection is possible by means of PCR amplification of target genes in leucocytes or serum. To enhance sensitivity, blood samples should be collected preferably within the first week of illness onset and sent in EDTA bottles for molecular testing in all suspected cases (12).

15. PCR followed by DNA sequencing can be used to differentiate the *Rickettsia* species, which is useful to delineate the epidemiological pattern of rickettsiosis especially the SFG. Nevertheless, since the treatment for all rickettsial diseases are similar, species differentiation may not affect treatment.

## Local epidemiology of scrub typhus and spotted fever

### Scrub typhus

16. The number of scrub typhus cases dropped from 14 in 1999 to 2 in 2000, and then rose steadily to 12 cases each in 2003 and 2004.

The number of cases which occurred in the first seven months of 2005 has already exceeded the total in 2004, and it is the highest number recorded for the past 6 years (Figure 1).

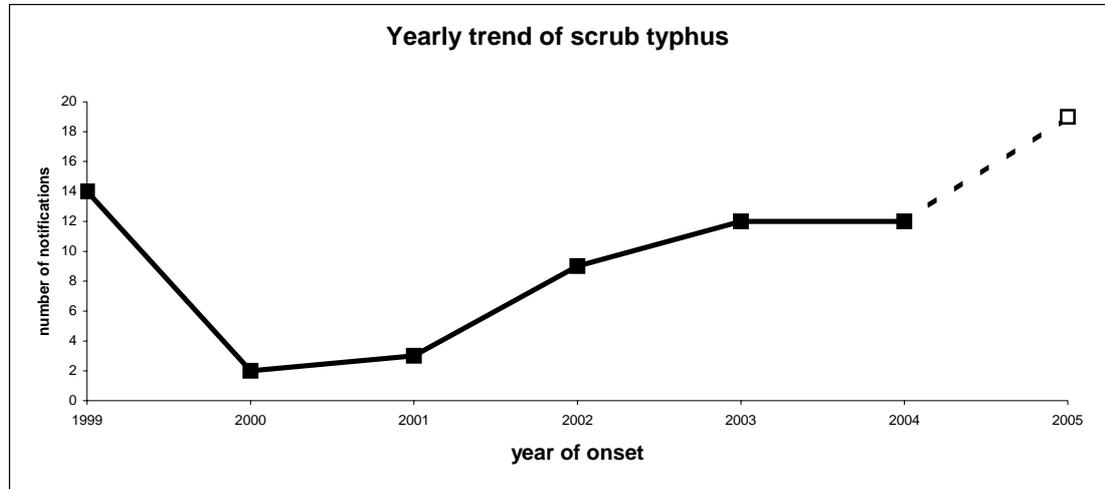


Figure 1. The number of scrub typhus cases by onset dates: 1999 – July 2005

17. As for the seasonality, more cases seemed to occur in summer and fall (Figure 2). Between 1999 and 2004, the number of cases with onset dates from July to October constituted 67% of all cases.

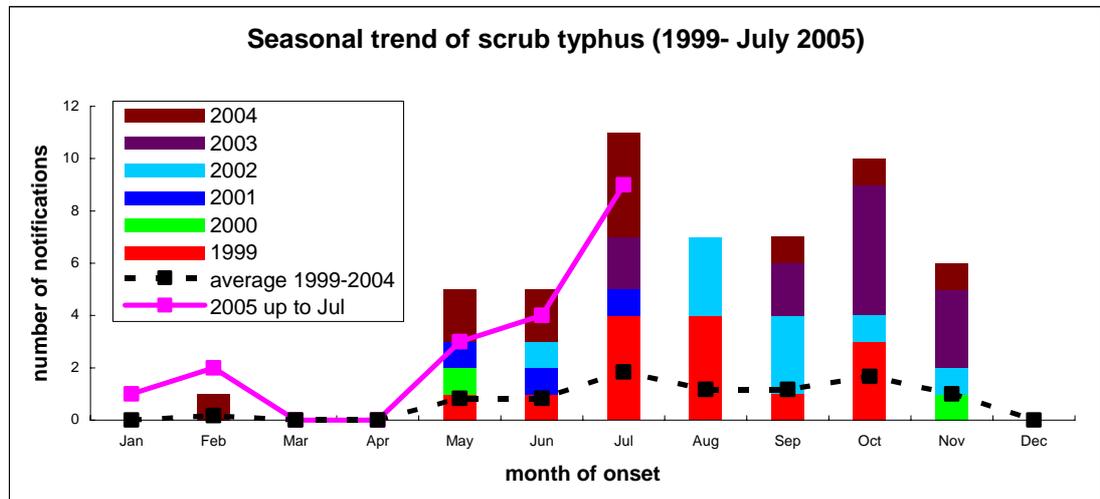


Figure 2. The number of scrub typhus cases by month of onset: 1999 – July 2005

18. A total of 31 scrub typhus cases with onset dates between January 2004 and July 2005 were recorded. One case in 2004 was an imported case. An analysis was conducted among the 30 local cases (Table 2). There was no epidemiological linkage among cases.

19. Among the 30 local cases, the male to female ratio was 1.7 to 1. The median age was 47.5 years. As regards the clinical presentations, all patients had fever and 43% had a rash. Eschars were

found in 53%, which is consistent with the rates reported in the literature (13). 97% of cases had deranged liver function tests. 93% were hospitalised, with a median length of stay of 8 days (range: 3-46 days). The median interval between onset of disease and hospital admission was 6 days. Four patients developed complications, such as septicaemia and renal failure but there were no fatalities.

20. Epidemiological investigation found that 90% had a history of exposure to vegetated areas during hiking, at work, or near their homes. Only 10% of cases had a clear recollection of being bitten by arthropods during the incubation period. For all cases, field investigations were conducted by the Pest Control Advisory Section (PCAS) of Food and Environmental Hygiene Department (FEHD). It was found that hiking places were the most likely place of contracting the disease and was reported in 14 patients.

21. Of the remaining 16 cases without a history of hiking, 8 were considered to have contracted the disease around their homes. PCAS investigation showed that 7 cases had vegetation near their homes which were suitable for harbouring mites, 2 of which were flower beds, which are found commonly in Hong Kong. Vector surveys were carried out among these vegetated areas near human residents but no vector was found.

### Spotted fever

22. A voluntary disease registry has been maintained by the Centre for Health Protection (CHP) on spotted fever. Between 1999 and 2003, an average annual number of 8.2 cases of spotted fever were reported to the CHP. However, the number of cases reported has risen to 17 in 2004 (Figure 3). For 2005, a total of 6 cases with onset dates between January and July have been reported.

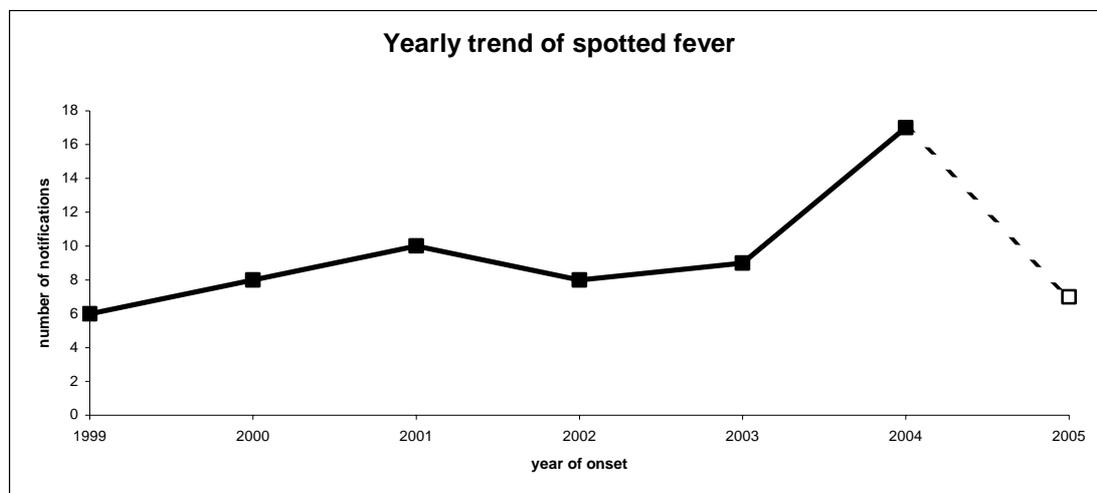


Figure 3. The number of cases of spotted fever by onset dates: 1999 – July 2005

23. More cases were observed in June and November while no case was observed in February (Figure 4). Again, we conducted a detailed analysis on the 24 cases (Table 2) with onset dates between 2004 and July 2005. All occurred locally, except for one unclassifiable case in 2004.

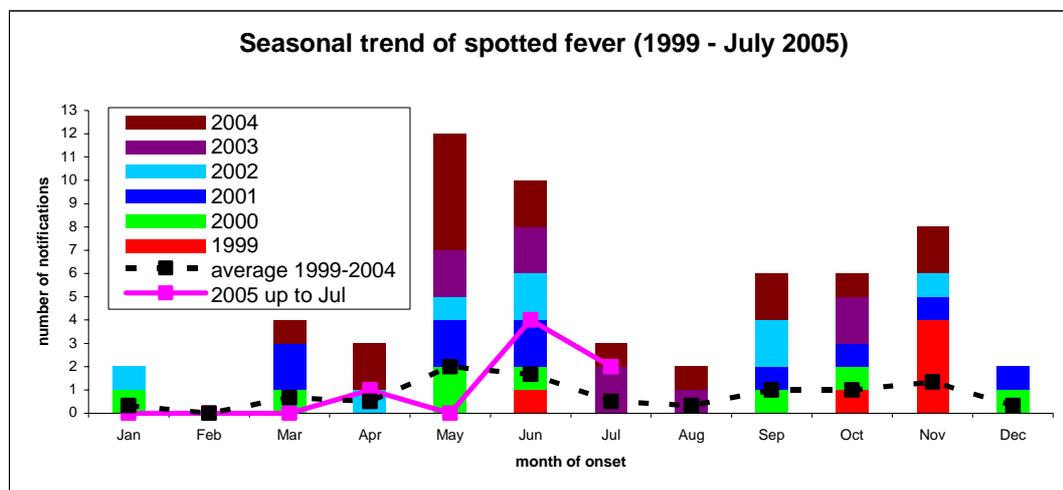


Figure 4. The number of spotted fever cases by month of onset: 1999 – July 2005

24. Among the 23 local cases, the median age was 51 years. The male to female ratio was 1.6 to 1. All cases had fever and rash. Eschars were found in 48% of patients. 74% of cases had deranged liver function tests. All cases were hospitalised with a median length of stay of 7 days (range: 2-25 days). The median interval between onset of disease and hospital admission was 4 days. One patient developed hepatic failure, but later recovered. There were no fatalities.

25. As regards the exposure history, 26% of cases had a history of being bitten by arthropods during the incubation period. This is slightly higher when compared with scrub typhus. This might be due to the fact that a tick is larger than a larval mite.

26. Exposure to vegetated area and animals (pets, stray dogs, rodent) were common (Table 2). Hiking places was considered as the probable place of infection in 10 (43%) cases. On the other hand, 7 cases were thought to have contracted the disease in areas around their homes. 6 of these patients' home areas have dense vegetation nearby where subsequent vector surveys conducted by PCAS identified ticks in 2 of these areas. 6 kept pet dogs at home. In 2005, adult ticks belonging to genus *Haemaphysalis* had been collected at Kadoorie Farm & Botanic Garden in Tai Po. Testing conducted by the Public Health Laboratory Services Branch (PHLSB) of CHP, DH revealed that the tick collected at Kadoorie Farm & Botanic Garden was *Rickettsia* positive.

27. The PHLSB reported that, among 25 serologically positive serum samples, 4 were PCR-positive and subsequently identified to be *R. japonica* by DNA sequencing (12). *R. japonica* has also been detected from ticks harvested by the Agriculture, Fisheries and Conservation Department. These seem to suggest that *R. japonica* could be one of the prevalent agents for the SFG in Hong Kong.

### **Treatment and prognosis**

28. Doxycycline is the most effective drug whereas all beta-lactams and aminoglycosides are not effective. However, its use is limited by its contraindication in pregnant women and young children. A shorter course regimen of doxycycline could be an effective and safe alternative for children. The newer azithromycin could be an option for pregnant women.

29. The susceptibility of the host, the virulence of the infecting strain and the time of administration of appropriate antibiotic produce wide range of severity of illness. Old age and alcoholism have been associated with more severe disease. For causative factors, some Rickettsia species have more severe potential, such as *R. rickettsii*, *R. prowazekii*, and *O. tsutsugamushi*. Generally, Japanese spotted fever causes less severe disease. For severe cases, a multiple organ dysfunction syndrome can be observed that usually leads to a fatal syndrome. Therefore, early administration of doxycycline before definite diagnosis is made is critical.

### **Environmental factors and vector ecology**

30. The chance of infection is affected by the interplay between human behaviour and the seasonal abundance and activity of the arthropod vectors, which modify the risk of disease exposure.

#### Mites and scrub typhus

31. Trombiculid mites, *Leptotrombidium akamushi* and *Leptotrombidium deliense*, are the vectors for scrub typhus. Only mites in the larval stage feed on animal hosts. The free-living nymphs and adults of *Leptotrombidium* genera have specialized ecological requirements. Mites prefer warm, moist, and shady places. Human behaviours like travelling to or working in outdoor settings like banks of rivers/streams, swamp, grasslands, shrubby areas, and border areas of forests and farmlands would be a risk (3, 4, 14).

32. Since larval mites must feed on animal hosts for survival, rodents infested sites have a higher chance of harbouring mites. Rodents provide body fluid to the growth of larval stage of mites. Wild rats of the genus *Rattus*, subgenus *Rattus*, are very important hosts of

*Leptotrombidium*. Therefore, living areas with stagnant water, vegetation, and mismanaged food remnant and refuse, will support the harbourage of rodents and hence mites.

33. The habitat must be one in which host animals such as rodents regularly traverse so that the larvae will have chance of attaching themselves to their hosts. Larval mites prefer to clump in large number and wait for passing hosts on leaves or grass close to the ground. Human can be bitten by larval mites when they are directly exposed to infested vegetations, or if the mites were attached on their belongings like cloths and bags placed on these vegetations. The life cycle of mites usually takes about two to three months. In the tropics, the mite could have more than one generation per year.

34. The mites infested spots are usually isolated and small in size (termed “mite island”). As a result, travelling collaterals of scrub typhus patients may not be affected. Larval mites are less than 1/60<sup>th</sup> cm in size and would be very difficult to be spotted by the naked eye. Mite bites are neither painful nor itchy. Mite activity and abundance are higher in the wetter months (15).

#### Tick vectors, other animal hosts, and spotted fever

35. Ixodid ticks, which are considered as the vectors of spotted fever, are found in similar habitats as mites, where dense vegetation and suitable host animals are found. The exact seasonality of the host-seeking activity depends on the kind of habitats and species of tick. In general, tick activities are lowest in colder months (16). The species collected locally are listed in table 3.

36. For spotted fever, human may also be exposed to ticks through transport hosts. Larvae and nymphs of many ticks seem to have a predilection for small animals, such as rodents, cats, and dogs, and ground-inhabiting birds, whereas adults seem to prefer to feed on cattle, horses and a variety of large animals. These hosts, usually rodent, pet dogs or stray dogs, may carry the infected ticks from its original habitats to other sites. In addition to tick bite, transmission of spotted fever is also by contact of the hands with skin and eyes after accidental crushing of ticks removed from dogs. Similarly, cat fleas, which transmit *R. felis*, can also be brought into contact with human by pet cats and dogs.

### **Recommendations on prevention and control**

37. As effective vaccines are not available for scrub typhus and spotted fever, control strategies should target at primary prevention through raising public awareness and enhancing early disease detection,

building upon the current information on local epidemiology, possible risk factors, and the clinical features and symptomatology of the diseases. The following highlights five recommended areas of strengthening of control.

#### Enhancing clinical suspicion

38. The classical symptoms of fever, headache, lymphadenopathy, eschar, and rash should prompt physicians to consider the diagnosis of scrub typhus and spotted fever. An eschar found in the groin and axillary regions (17) is typical of scrub typhus. For spotted fever, the tache noire is commonly found on the lower limbs, groin, or lower abdomen of adults, where for infants, the scalp is a common location (3). However, different species of ticks could have different preference for site of attachment (18). Thus, clinicians should also examine other areas not normally examined, such as scalp, back of buttocks, scrotums, or under the foreskin in search for eschars in suspected cases.

39. Clinical presentations may sometimes be non-specific and difficult to be differentiated from other febrile illness. The eschar may also be absent or in a location difficult to be noticed (19). Medical practitioners should therefore be advised to include these rickettsial diseases in their list of differential diagnosis for febrile illnesses, particularly when the patient has exposure to vegetated areas either in the countryside, near their residences, or at work.

40. In view of the relative high fatality rate of untreated cases, early detection and provision of treatment is important. In order to enhance clinical suspicion of the disease, a factsheet for medical practitioner was developed for the purpose (Appendix).

#### Reducing risk of exposure

41. Places like backyards and campsites can be cleaned of bushes and weeds. Grass can also be cut close to the ground. This will make the area less survivable for ticks and mites. If removal of vegetation is not possible, insecticide can be applied (14). Sitting, lying, or putting personal belongings in damp grass or on damp logs should be avoided.

42. If necessary, vector populations can be controlled by applying insecticide with residual action to sites of rat infestation, followed by the removal of potential breeding sites of rodents. This sequence of actions prevents the vector from switching from rodent hosts to human. Food source should be removed and holes in walls and

ceilings should be sealed. A dry and clean environment will also prevent the survival of vectors.

#### Enhancing personal protection

43. The awareness of the general public should be improved through targeted messages. When visiting vegetated areas, long-sleeve clothing of light colour should be worn to improve protection against vector attachment, as ticks are easier seen.

44. High risk locations and densely vegetated areas should be avoided. Bush or shrubby vegetation that might harbour ticks or mites should be avoided. One should also avoid touching stray dogs, rodents, livestock. For pet owners, preventive measure like ticks/fleas repellent collar should be used.

45. One should apply insect repellents (Meta-N,N-diethyl toluamide, DEET) to skin and clothing at regular intervals according to the supplied instruction. The area of exposed skin can also be minimized by tucking the pants inside the socks.

46. When visiting high risk area, travellers should perform regular self-checking for vector attachment or for sign of insect/arthropod bite. This is also necessary for pet owners and for people exposed routinely to animal in their work environment.

47. A soapy shower is advisable after visiting a high risk area to remove mites from the skin (20). Washing the clothes afterwards is also a good preventive measure. It is a good practice to wash hands after dealing with dogs and removing ticks from dogs.

#### Encouraging patients to seek early medical attention

48. If bitten, one should apply proper wound care and refrain from scratching the bite area so as to prevent secondary infection. An attached tick should be removed as soon as possible by grasping it close to the skin with a pair of forceps and pulling it slowly upward with steady pressure, at the same time avoiding twisting, crushing, or breaking off its mouthparts (21, 22).

49. Medical attention should be sought as soon as possible should one develop fever after visiting risk areas. Patients should report their travel histories and relevant exposure histories to animals, and histories of arthropod bites. Studies suggest that doxycycline in weekly 200 mg-dose provides effective chemoprophylaxis for scrub typhus if it is started before exposure to infection and continued for six weeks after exposure (23, 24). Although study suggests post-exposure

treatment with doxycycline is effective for some other tick-borne diseases such as relapsing fever (25), little studies focus on the effect of post-exposure prophylaxis for “rickettsiosis”. The use of prophylaxis may be beneficial for person with high risk of infection. Health care providers may determine whether the advantages of prescribing antibiotics after tick bite outweigh the disadvantages.

#### Enhancing the knowledge base through additional studies

50. The epidemiological picture of rickettsial diseases can be better understood through serological studies in humans and animals. These studies are particularly useful in uncovering sub-clinical cases (26), and cases where empirical treatment have resulted in cure before a definitive diagnosis has been made.

51. Seroprevalence study in rodents, pets, and stray dogs/cats will provide an assessment of the current risk, such as the distribution and prevalence of the causative agent (27).

52. The simultaneous collection of fleas, lice, ticks, mites from these hosts, to estimate their number (mite/flea index), seasonal pattern, types, and to study the presence of rickettsiae in them would yield additional valuable information (28). A study of the number and types of ticks and mites over the territory may help to locate high risk areas in Hong Kong.

#### **Advice sought**

53. Members are invited to note the content of the paper and comment on the proposed recommendations.

**Surveillance and Epidemiology Branch**  
**Centre for Health Protection**  
**December 2006**

The copyright of this paper belongs to the Centre for Health Protection, Department of Health, Hong Kong Special Administrative Region. Contents of the paper may be freely quoted for educational, training and non-commercial uses provided that acknowledgement be made to the Centre for Health Protection, Department of Health, Hong Kong Special Administrative Region. No part of this paper may be used, modified or reproduced for purposes other than those stated above without prior permission obtained from the Centre.

## References

1. Todar K. The Rickettsiae. In *Todar's Online Textbook of Bacteriology*. [online] [access 2005 Aug]. Available from URL <http://textbookofbacteriology.net/Rickettsia.html>
2. Rolain JM, Jensenius M, Raoult D. Rickettsial infections--a threat to travellers? *Curr Opin Infect Dis*. 2004 Oct;17(5):433-7.
3. Angeloni VL. Chapter 11, Rickettsial diseases. In *Military Dermatology*. Washington: TMM Publications; 1994. p213-254
4. Washington State Department of Health. *Reporting and Surveillance Guidelines*. 2002.
5. Watt G, Parola P. Scrub typhus and tropical rickettsioses. *Curr Opin Infect Dis*. 2003 Oct;16(5):429-36.
6. Tamura A, Ohashi N, Urakami H, Miyamura S. Classification of *Rickettsia tsutsugamushi* in a new genus, *Orientia* gen. nov., as *Orientia tsutsugamushi* comb. nov. *Int J Syst Bacteriol*. 1995 Jul;45(3):589-91.
7. Heymann DL. *Control of communicable diseases manual*. 18th ed. United States of America: American Public Health Association; 2004.
8. Parola P, Davoust B, Raoult D. Tick- and flea-borne rickettsial emerging zoonoses. *Vet Res*. 2005 May-Jun;36(3):469-92.
9. Araki M, Takatsuka K, Kawamura J, Kanno Y. Japanese spotted fever involving the central nervous system: two case reports and a literature review. *J Clin Microbiol*. 2002 Oct;40(10):3874-6.
10. Noji Y, Takada N, Ishiguro F, Fujino S, Aoyama T, Fujita H, Yano Y, Shiomi S, Mitsuto I, Takase K, Haba T, Mabuchi H. The first reported case of spotted fever in Fukui Prefecture, the northern part of central Japan. *Jpn J Infect Dis*. 2005 Apr;58(2):112-4.
11. Jang WJ, Kim JH, Choi YJ, Jung KD, Kim YG, Lee SH, Choi MS, Kim IS, Walker DH, Park KH. First serologic evidence of human spotted fever group rickettsiosis in Korea. *J Clin Microbiol*. 2004 May;42(5):2310-3.
12. Yeung EYH, Cheng PKC, Lo JYC. LABORATORY DIAGNOSIS OF SPOTTED FEVER AND TYPHUS. *Public Health & Epidemiology Bulletin*. 2005 Mar; 14(1):5-7.
13. Jensenius M, Fournier PE, Raoult D. Rickettsioses and the international traveler. *Clin Infect Dis*. 2004 Nov 15;39(10):1493-9.
14. WHO. Mites. In *Vector control – Methods for use by individuals and communities*. 1997. [online] [access 2005 Aug]. Available from URL [http://www.who.int/docstore/water\\_sanitation\\_health/vectcontrol/ch27.htm](http://www.who.int/docstore/water_sanitation_health/vectcontrol/ch27.htm)
15. Frances SP, Watcharapichat P, Phulsuksombati D, Tanskul P, Linthicum KJ. Seasonal occurrence of *Leptotrombidium deliense* (Acari: Trombiculidae) attached to sentinel rodents in an orchard near Bangkok, Thailand. *J Med Entomol*. 1999 Nov;36(6):869-74.
16. EUROPEAN UNION CONCERTED ACTION ON LYME BORRELIOSIS. *BIOLOGY: The Tick: Seasonality*. [online] [access 2005

Sep]. Available from URL [http://www.oeghmp.at/eucalb/biology\\_the-tick-seasonality.html](http://www.oeghmp.at/eucalb/biology_the-tick-seasonality.html)

17. Hahn JD, and Ascerno ME. Control of scabies and chiggers on humans. [online] [access 2005 Aug]. Available from URL [www.extension.umn.edu/distribution/housingandclothing/DK1035.html](http://www.extension.umn.edu/distribution/housingandclothing/DK1035.html)
18. Felz MW, Durden LA. Attachment sites of four tick species (Acari: Ixodidae) parasitizing humans in Georgia and South Carolina. *J Med Entomol.* 1999 May;36(3):361-4.
19. Lau SM, Yu WL, Wang JH. An unusual site of chigger bite in a patient with scrub typhus. *Diagn Microbiol Infect Dis.* 1999 Oct;35(2):159-61.
20. Goddard J. In *Infectious diseases and arthropods.* Humana Press; 2000. p151-173.
21. Samlaska CP. Chapter 9, Arthropod infestations and vectors of disease. In *Military Dermatology.* Washington: TMM Publications; 1994. p183-196.
22. Torres M, Carey V. Review of public health advice about ticks. *N S W Public Health Bull.* 2004 Nov-Dec;15(11-12):212-5.
23. Twartz JC, Shirai A, Selvaraju G, Saunders JP, Huxsoll DL, Groves MG. Doxycycline prophylaxis for human scrub typhus. *J Infect Dis.* 1982 Dec;146(6):811-8.
24. Olson JG, Bourgeois AL, Fang RC, Coolbaugh JC, Dennis DT. Prevention of scrub typhus. Prophylactic administration of doxycycline in a randomized double blind trial. *Am J Trop Med Hyg.* 1980 Sep;29(5):989-97.
25. Hasin T, Davidovitch N, Cohen R, Dagan T, Romem A, Orr N, Klement E, Lubezky N, Kayouf R, Sela T, Keller N, Derazne E, Halperin T, Yavzori M, Grotto I, Cohen D. Postexposure treatment with doxycycline for the prevention of tick-borne relapsing fever. *N Engl J Med.* 2006 Jul 13;355(2):148-55.
26. Marshall GS, Stout GG, Jacobs RF, Schutze GE, Paxton H, Buckingham SC, DeVincenzo JP, Jackson MA, San Joaquin VH, Standaert SM, Woods CR. Tick-Borne Infections in Children Study Group. Antibodies reactive to *Rickettsia rickettsii* among children living in the southeast and south central regions of the United States. *Arch Pediatr Adolesc Med.* 2003 May;157(5):443-8.
27. Siritantikorn S, Sangkasuwan V, Eamsila C, Singchai C, Kantakamalakul W, Puthavathana P. Seroprevalence of rickettsial infection in commensal rodents and shrews trapped in the Bangkok Metropolitan Area. *J Med Assoc Thai.* 2003 Jun;86(6):516-21.
28. Blair PJ, Jiang J, Schoeler GB, Moron C, Anaya E, Cespedes M, Cruz C, Felices V, Guevara C, Mendoza L, Villaseca P, Sumner JW, Richards AL, Olson JG. Characterization of spotted fever group rickettsiae in flea and tick specimens from northern Peru. *J Clin Microbiol.* 2004 Nov;42(11):4961-

Table 1. Geographical distribution of the rickettsioses and their causative agents.

Group	Species	Geographical region	Corresponding disease	Risk groups / factors
Scrub typhus group	<i>Orientia tsutsugamushi</i>	Asia, northern Australia, Pacific Islands	Scrub typhus	Exposure to vegetated area
Spotted fever group	<i>Rickettsia rickettsii</i>	US, and in North America, Central America, and South America.	Rocky Mountain spotted fever	Male, children, exposure to dogs, rodents, and wooded/grassy area
	<i>Rickettsia conorii</i>	Mediterranean countries, Africa, India, Southwest Asia	Mediterranean spotted fever (Boutonneuse fever)	Exposure to dogs and vegetated area
	<i>Rickettsia sibirica</i>	northern provinces of China, Siberia, Mongolia	Siberian tick typhus	Exposure to vegetated area
	<i>Rickettsia japonica</i>	Japan, Korea, Hong Kong	Japanese spotted fever	Exposure to vegetated area
	<i>Rickettsia australis</i>	Australia	Australian tick typhus	Exposure to vegetated area
	<i>Rickettsia akari</i>	US, former Soviet Union	Rickettsialpox	Exposure to vegetated area
	<i>Rickettsia felis</i>	California, Texas, Louisiana, and New York, Europe	Cat flea transmitted urban typhus like disease	Exposure to pets
Typhus group	<i>Rickettsia typhi</i>	Worldwide	Urban typhus	Exposure to rodent/rodent-infested area.
	<i>Rickettsia prowazekii</i>	South America, Africa, US	Epidemic typhus and Brill-Zinsser disease	Exposure to louse.

Table 2. Summary of local scrub typhus and spotted fever cases occurred from Jan 2004 to Jul 2005.

	Scrub typhus	Spotted fever
Cases	30	23
Age range	5-79	9-78
Median age	47.5	51
Bite history		
Yes	3 (10%)	6 (26%)
No	19 (63%)	9 (39%)
Unknown	8 (27%)	8 (35%)
Clinical features		
Fever	30 (100%)	23 (100%)
Rash	13 (43%)	23 (100%)
Headache	13 (43%)	12 (52%)
Lymphadenopathy	7 (23%)	4 (17%)
Conjunctivitis	4 (13%)	2 (9%)
Myalgia	20 (67%)	11 (48%)
Eschar	16 (53%)	11 (48%)
Liver function test derangement	29 (97%)	17 (74%)
Complications		
Yes	3 (10%)	1 (4%)
No	22 (73%)	22 (96%)
Unknown	5 (17%)	0 (0%)
Exposure to vegetated area	27 (90%)	21 (91%)
Hiking	14 (47%)	13 (57%)
Occupational	6 (20%)	4 (17%)
Near home area	7 (23%)	7 (30%)
Outdoor recreational area*	2 (7%)	2 (9%)
Exposure to pets/rodents/stray dogs		
Yes	17 (57%)	19 (83%)
No	4 (13%)	4 (17%)
Unknown	9 (30%)	0 (0%)
Probable place of infection		
Hiking places	14 (47%)	10 (43%)
Rural workplace	5 (17%)	4 (17%)
Urban workplace	2 (7%)	1 (4%)
Near home area	8 (27%)	7 (30%)
Outdoor recreational area*	0 (0%)	0 (0%)
Uncertain/Unknown	1 (3%)	1 (4%)
Hospitalized	28 (93%)	23 (100%)
Length of hospitalization (days)		
Range	3-46	2-25
Median	8	7
Interval between onset and admission (days)		
Range	1-27	0-22
Median	6	4

\* Outdoor recreational area includes park, theme park, and golf course.

Table 3: Ixodid ticks found in Hong Kong

Family	Genera	Species
Ixodidae 硬蜱	<i>Haemaphysalis</i> 血蜱屬	<i>Haemaphysalis birmaniae</i> 緬甸血蜱
		<i>Haemaphysalis doenitzi</i> 鈍刺血蜱
		<i>Haemaphysalis verticalis</i> 草原血蜱
		<i>Haemaphysalis hystricis</i> <i>supino</i> 豪豬血蜱
		<i>Haemaphysalis formosensis</i> 台灣血蜱
	<i>Rhipicephalus</i> 扇頭蜱屬	<i>Rhipicephalus sanguineus</i> (Brown Dog Tick) 血紅扇頭蜱
		<i>Rhipicephalus pumilio</i> 短小扇頭蜱
	<i>Hyalomma</i> 璃眼蜱屬	<i>Hyalomma</i> species 璃眼蜱

**Title**

1. Fact sheet on rickettsial infections commonly occurring in outdoor settings

**Background**

2. *Rickettsiae* are small bacteria that are obligate intracellular parasites. They are maintained in nature through cycle involving reservoir mammals and arthropod vectors. The severity of disease can range from mild to multi-organ failure and even fatal outcome. See Table 1 for a description of their epidemiological characteristics.

**Table 1. Epidemiological and Clinical Characteristics of Rickettsial Infections**

	<b>Spotted Fever</b>	<b>Scrub Typhus</b>
<b>Causative agents</b>	It comprises a large group of tick- and flea-borne infections, e.g. <i>R. rickettsii</i> , <i>R. japonica</i> , <i>R. conorii</i> , <i>R. felis</i>	<i>O. tsutsugamushi</i>
<b>Major vectors</b>	Ticks and fleas	Larval stage (chigger) of trombiculid mites
<b>Major reservoirs of vectors</b>	Rodents and domestic dogs	Small rodents
<b>Geographic distributions and transmission</b>	Different parts of the world for different species	Asia and Pacific region
<b>Average incubation period</b>	6 to 10 days	10 to 12 days
<b>Symptoms</b>	Fever, headache, muscle pain, rash, local lymphadenopathy, and eschar	Fever, headaches, chills, conjunctival injection, lymphadenopathy, rash, and eschar
<b>Fatality rate for untreated case</b>	13 to 25 % (depends on causative agent)	1 to 60 %

In Hong Kong, majority of the reported cases contracted the diseases locally, in which half of them were related to outdoor activities, such as hiking or camping in rural areas.

### **Pathogenesis and Clinical Features**

3. At the site of bite, organisms localize in endothelial cells and entry into the cells is by receptor mediated mechanism and phagocytosis. A papule may be formed which later ulcerates in the central. It is called eschar. The organisms released from the infected cells can infect endothelial cells in the blood vessels throughout the body via lymphatic vessels. The rickettsaemia causes generalized vasculitis affecting every organ in the body. See Table 1 for the clinical features of rickettsial infections.

### **Clinical Suspicion and Diagnosis**

4. Diagnosis of rickettsial infection relies upon a combination of clinical, epidemiology and laboratory findings. Eschar could be absent or in locations difficult to be noticed, like scalp, back of buttocks, scrotum, or under the foreskin. Medical practitioners should therefore be advised to include rickettsial diseases in their list of differential diagnoses for febrile illnesses, particularly when the patient has exposure to vegetated areas either in the countryside, near their residences, or at work.

Culture for these organisms is not usually undertaken in clinical laboratories, and diagnosis mainly relies on serology. Indirect immunofluorescence assay (IFA) is regarded as the standard serological test because of its superior sensitivity and specificity. Antibody titres specific to either spotted fever group or scrub typhus are determined. Positive cases are characterized by a significant (four-fold or more) increase in titres in the specific group. However, cross-reactivity between the typhus and spotted fever group may occur. Furthermore, serological assay cannot be relied upon to diagnose early infections due to delayed antibody response, which may also be blunted by antibiotic treatment. In Hong Kong, requests for specific assays for rickettsial infections are processed by the Virology Division, Public Health Laboratory Services Branch, Centre for Health Protection of the Department of Health.

## Treatment

5. Doxycycline is the most effective drug. The usual adult oral dose of doxycycline is 100 mg twice daily for 7–14 days. The use of tetracycline is limited by its contraindication in pregnant women and young children. Short course regimen (1-2 days course) of doxycycline may represent an effective and safe alternative in children, preventing the occurrence of tooth discoloration. Azithromycin, a newer macrolide, is an alternative to doxycycline for rickettsial infection in pregnant women.

## Prognosis

6. The susceptibility of the host, the virulence of the infecting strain and the time of administration of appropriate antibiotic produce wide range of severity of illness. Old age and alcoholism have been associated with more severe disease. For causative factors, some *Rickettsia* species have more severe potential, such as *R. rickettsii* and *O. tsutsugamushi*. Generally, Japanese spotted fever causes less severe disease. For severe cases, a multiple organ dysfunction syndrome can be observed that usually leads to a fatal syndrome. Therefore, early administration of doxycycline before definite diagnosis is made is critical.

## Prevention and Control

7. Public is encouraged to observe personal protection measures while doing outdoor activities, especially in rural areas. The preventive measures include wearing protective long sleeved clothes and trousers, and insect repellents (DEET, N,N-Diethyl-m-toluamide) on exposed skin as well as on clothes. Animals like rodents and dogs are reservoirs for these vectors. Thus, proper control of these animal reservoirs is useful to reduce the infection rate. Studies suggest that doxycycline in weekly 200 mg-dose provides effective chemoprophylaxis for scrub typhus if it is started before exposure to infection and continued for six weeks after exposure. Few studies focus on the effect of post-exposure prophylaxis for “rickettsiosis”. The use of prophylaxis may be considered for person with high risk of infection. Health care providers may determine whether the advantages of prescribing antibiotics after tick bite outweigh the disadvantages.

## Notification

8. Both scrub typhus and murine typhus are notifiable diseases. While spotted fever is not notifiable, prompt report of this disease to the DH is encouraged

## References

1. Mahara F. Japanese spotted Fever: Report of 31 cases and Review of the Literature. *Emerging Infectious Disease* 1997;3:105-11.
2. Chung PH. Epidemiology of Spotted Fever, Scrub Typhus and Murine Typhus in Hong Kong, 1995-2004. *Public Health and Epidemiology Bulletin* Mar 2005, 1-5.
3. Yeung EYH, Cheng PKC, Lo JYC. Laboratory Diagnosis of Spotted Fever and Typhus. *Public Health and Epidemiology Bulletin* Mar 2005, 5-7.
4. Mandell GL, Douglas RG, Bennett JE. *Principles and Practice of Infectious Diseases*. 6th ed. Churchill Livingstone 2005
5. Yu VL, Weber R, Raoult D. *Antimicrobial Therapy and Vaccines Vol I: microbes*. 2nd ed. Apple Trees Productions 2003