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<THE TOPIC OF THIS MONTH>

Scrub typhus and Japanese spotted fever in Japan 2007-2016

Rickettsiosis in Japan is largely represented by two diseases, scrub typhus (*tsutsugamushi* disease) and Japanese spotted fever. Their vectors are mites and ticks, respectively. Fever, rash and eschar at the site of the bite form the diagnostic triads. They are category IV infectious diseases that require reporting of all cases under the Infectious Diseases Control Law (criteria for notification: <http://www.nih.go.jp/niid/images/iasr/38/448/de4481.pdf>, <http://www.nih.go.jp/niid/images/iasr/38/448/de4482.pdf>). Their differential diagnosis is difficult without laboratory diagnosis.

Scrub typhus: The causative agent is *Orientia tsutsugamushi* (*Ot*), and are transmitted via trombiculid mites, *tsutsugamushi*. The incubation period is 5-14 days. The main serotypes of *Ots* found in Japan include the “standard” serotypes of Kato, Karp and Gilliam, along with and 3 others, namely Kawasaki, Kuroki and Shimokoshi. Geographical and seasonal distribution of disease occurrence is variable depending on the *tsutsugamushi* species, their geographical distribution, and larvae’s active seasons. *Leptotrombidium akamushi*, which carry Kato type *Ot*, is restricted to the northern part of Japan; *L. pallidum*, found throughout Japan, carry Karp type and Gilliam type *Ots*; and *L. scutellaris*, found from the Southern part of Tohoku to Kyushu, carry Kawasaki (Irie) type and Kuroki (Hirano) type *Ots*.

Cases reported: In 2016, 505 scrub typhus cases were reported (as of April 27, 2017) (Fig. 1a). During 2007-2016, a total of 4,185 scrub typhus cases were notified; suspected place of infection was Japan for 4,163 cases, overseas for 17 (e.g. 6 cases in Republic of Korea, 3 cases in Cambodia, 2 cases in Malaysia), and unknown for 5 cases. Prefectures with the largest number of cases notified were Kagoshima (average of 58.7 cases/year) followed by Fukushima, Miyazaki and Chiba (average notifications/year exceeded 30 cases for all three prefectures) (Fig. 2a and Table 1 in p.111 of this issue). Although infection occurred within the reporting prefecture for majority of the cases, the patient reported from Hokkaido in 2008 was suspected to have been infected in Tokyo. In 2008, Okinawa reported scrub typhus for the first time, and Akita reported patients infected with Kato type *Ot* for the first time in 15 years; occurrence in both prefectures have continued since then (see pp.120 & 113 of this issue).

Case notifications, based on month of diagnosis, show two seasonal peaks, in May-June and November-December (Fig. 3 in p.110). In regions where cold-tolerant *L. pallidum* is prevalent, overwintering larvae cause spring peaks, whereas in regions where *L. scutellaris* is prevalent, peak disease season occurs from autumn to early winter.

Sex and age distributions: During 2007-2016, 2,277 cases were male (54%) and 1,908 were female (46%). Patients in their 60s and 70s were frequent (median 68 years, 66 years for males and 71 years for females) (Fig. 4a in p.110).

Signs and symptoms: According to the written notification records of 4,185 cases, frequently reported symptoms/signs were fever (95%), rash (86%), eschar (dark scab) (85%) and headache (40%). There were 115 pneumonia (3%) and 31 encephalitis cases (0.7%). Twenty cases were dead at the time of notification (case fatality rate 0.48%); among them, 15 were reported from the Tohoku area where *L. pallidum* is the major vector (Table 1 in p.111 of this issue).

Figure 1. Annual reported number of scrub typhus and Japanese spotted fever cases, 1990-2016*, Japan

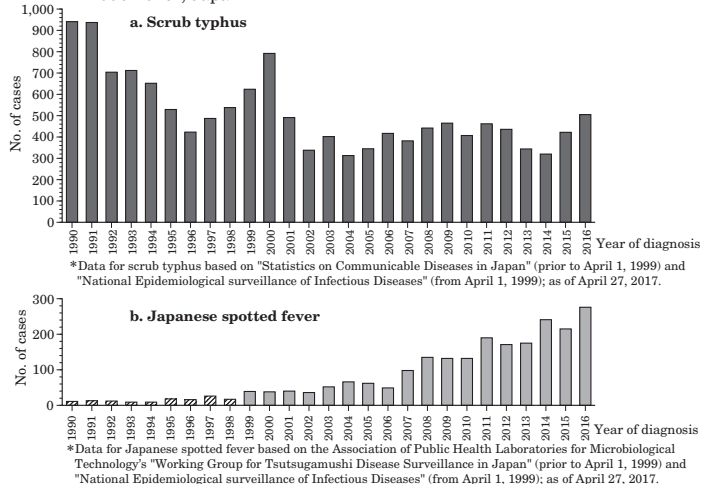
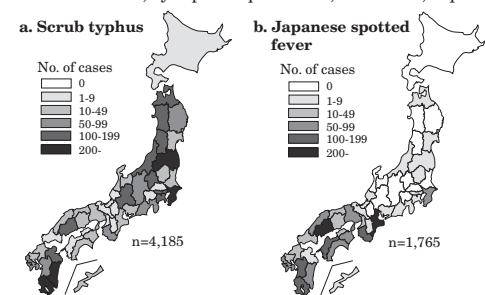


Figure 2. No. of scrub typhus and Japanese spotted fever cases, by reported prefecture, 2007-2016, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of April 27, 2017)

(THE TOPIC OF THIS MONTH-Continued)

Laboratory diagnosis: Among 4,185 cases notified, 3,553 were diagnosed by serum antibody detection (85%); 806 by pathogen genome detection by PCR (19%) from blood (574 cases), pathological (e.g., scab) (391 cases) or other specimens; and 217 by pathogen isolation (5%) from blood (202 cases) or pathological specimens (23 cases) (includes cases diagnosed by more than one method). Indirect fluorescent antibody technique (IFA), using antigens from the 3 standard serotypes, is covered by national health insurance, and can be conducted at commercial laboratories. IFA using antibodies for detection of the locally prevalent *Ot* serotype(s) is also conducted at some prefectural and municipal public health institutes (PHIs). PCR detection of *Ot* genome is becoming increasingly common.

Japanese spotted fever (JSF): The causative agent is *Rickettsia japonica*, which is transmitted by ticks. Incubation period is shorter than that of *Ot* and 2-8 days. The rash appears first in the extremities and then spreads to the trunk. The eschar is smaller than that of *Ot*. Patients developing acute infectious purpura fulminans have been reported (IASR: 31: 135-136, 2010).

Cases reported: In 2016, 276 JSF patients were reported (as of April 27, 2017), the largest annual number of notifications reported to date (Fig.1b). A total of 1,765 cases were reported in 2007-2016, and all were infected in Japan. Many notifications were from Western Japan, and prefectures that reported the largest number of cases were Mie (average of 34.9 cases/year), followed by Hiroshima, Wakayama, Kumamoto, Kagoshima, and Ehime (average notifications/year exceeded 10 cases for all five prefectures) (Fig. 2b, Table 2 in p.112 of this issue). However, more recently, Tochigi and Niigata also reported JSF cases believed to have been infected there. It is believed that, with nationwide increase in the reported number of patients, there has been expansion in the geographic area of infection. Notifications of JSF were found to increase from May to October, temporally correlated with the tick's active season (Fig. 3).

Sex and age distributions: Among the cases notified during 2007-2016, 806 were male (46%) and 959 were female (54%). Majority of cases were aged >60 years (median 70 years, 68 years for males and 72 years for females) (Fig. 4).

Signs and symptoms: According to the written notification records of 1,765 cases, frequently reported signs/symptoms were fever (99%), rash (94%), liver dysfunction (73%), eschar (66%, in contrast to 85% in scrub typhus), headache (31%) and DIC (20%). Sixteen cases were dead at the time of notification (case fatality rate 0.91%) (Table 2 in p.112 of this issue).

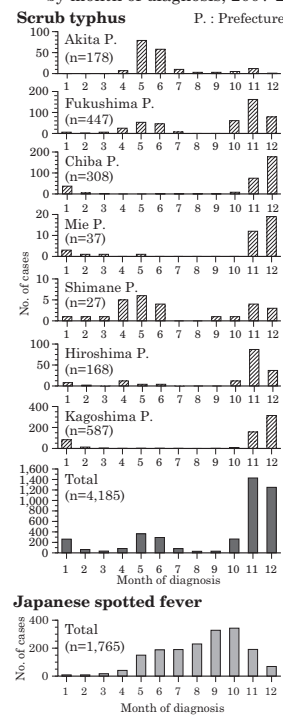
Laboratory diagnosis: Among 1,765 cases notified, 1,084 were diagnosed by serum antibody detection (61%); 787 by PCR (45%) from blood (437 cases) or skin biopsy specimens from the site of the tick bite (548 cases); and 62 by pathogen isolation from blood (54 cases) or tissue specimens (10 cases) (includes cases diagnosed by more than one method). Though the laboratory methods used for JSF are similar to those used for scrub typhus, there are no laboratory tests covered by the national health insurance and facilities capable of conducting tests for JSF are limited in number. National Institute of Infectious Diseases and some PHIs conduct laboratory tests upon request from physicians who suspect JSF in a patient.

Treatment: Tetracycline-line antibiotics are remarkably effective for rickettsial infections. When rickettsia infection is suspected in a patient, prompt administration of antibiotics is advised.

Other rickettsiosis: Other rickettsioses, including various spotted fever group rickettsioses such as Far-Eastern spotted fever, and flea-borne murine typhus, have been reported in Japan (IASR 31: 136-137, 2010 & 34: 313-314, 2013). As imported rickettsiosis, African tick bite fever and other spotted fever group rickettsioses have been reported (IASR 27: 41-42, 2006 & 31: 120-122, 2010). Imported cases of murine typhus (see p. 121 of this issue, IASR 27: 42-44, 2006) and Queensland tick typhus (see p. 123 of this issue) were recently reported for the first time in Japan.

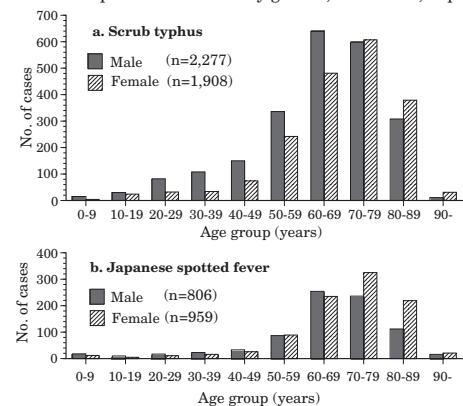
Additional remarks: Scrub typhus and JSF have continued to be reported in Japan; the geographic distribution of patients and vectors have often overlapped (see pp. 114, 116 & 118 of this issue). Fatal cases have continued to be reported despite the availability of effective antimicrobial drugs (see p. 124 of this issue). Furthermore, since 2013, 50-60 cases of severe fever with thrombocytopenia syndrome have been reported every year, mostly from Western Japan (IASR 37: 39-40, 2016). In 2016, a fatal case of tick-borne encephalitis was reported from Hokkaido for the first time since 1993 (see p. 126 of this issue). These circumstances indicate the need for comprehensive differential diagnosis based on clinical symptoms, place of infection and patients' behavioral information (see p. 117 of this issue). There is a need to understand clinical and epidemiologic aspects regarding various tick/mite-borne infections; strengthening and sustaining surveillance systems, laboratory capacity and risk communication are necessary to enable more effective responses from the medical and public health sectors.

Figure 3. Scrub typhus and Japanese spotted fever cases, by month of diagnosis, 2007-2016, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of April 27, 2017)

Figure 4. Age distribution of scrub typhus and Japanese spotted fever cases by gender, 2007-2016, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of April 27, 2017)

The statistics in this report are based on 1) the data concerning patients and laboratory findings obtained by the National Epidemiological Surveillance of Infectious Diseases undertaken in compliance with the Law Concerning the Prevention of Infectious Diseases and Medical Care for Patients of Infections, and 2) other data covering various aspects of infectious diseases. The prefectural and municipal health centers and public health institutes (PHIs), the Department of Food Safety, the Ministry of Health, Labour and Welfare, and quarantine stations, have provided the above data.

(特集つづき) (THE TOPIC OF THIS MONTH-Continued)

表1. 年別都道府県別つつか虫病患者報告数, 2007~2016年
Table 1. No. of reported scrub typhus cases, by year and prefecture, 2007-2016

| 都道府県 Prefecture | 診断年 Year of diagnosis | | | | | | | | | | 合計 Total | 人口100万対 Per 1,000,000† | |
|--------------------|-----------------------|---------|---------|---------|---------|---------|---------|---------|---------|---------|-------------|---------------------------|------|
| | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016* | | | |
| 北海道 | - | 1 | - | - | - | - | - | - | - | - | - | 1 | 0.02 |
| 青森県 | 12 | 17 | 16 (1) | 11 | 20 (2) | 15 | 20 (1) | 13 | 8 | 9 | 141 (4) | 10.27 | |
| 岩手県 | 1 | 4 | 8 | 4 (1) | 10 | 7 (2) | 7 (1) | 5 | 7 | 3 | 56 (4) | 4.21 | |
| 宮城県 | 2 | 5 | 4 | 6 | 2 | 4 | 3 | 5 (1) | 4 | 5 (1) | 40 (2) | 1.70 | |
| 秋田県 | 10 | 15 | 14 | 25 | 29 | 20 | 28 (1) | 21 | 13 | 3 | 178 (1) | 16.39 | |
| 山形県 | 8 (1) | 10 | 9 | 4 | 24 | 18 | 3 | 3 | 8 | 5 | 101 (1) | 8.64 | |
| 福島県 | 44 | 67 (1) | 96 (1) | 60 | 38 | 32 | 31 (1) | 25 | 26 | 28 | 447 (3) | 22.03 | |
| 茨城県 | - | 3 | 7 | 1 | 4 | 7 | 5 | 3 | 5 | 12 | 47 | 1.58 | |
| 栃木県 | 2 | 1 | 1 | 4 | 3 | 1 | 6 | 4 | 9 | 1 | 32 | 1.59 | |
| 群馬県 | 7 | 15 | 21 | 11 | 11 | 14 | 9 | 13 | 18 | 24 | 143 | 7.12 | |
| 埼玉県 | 1 | 1 | 2 | - | 1 | 2 | - | 1 | - | 1 | 9 | 0.13 | |
| 千葉県 | 46 | 34 | 42 | 36 | 31 | 25 | 12 | 21 | 27 | 34 | 308 | 4.95 | |
| 東京都 | 15 | 18 | 14 | 16 | 11 | 19 | 13 | 17 | 14 | 7 | 144 | 1.09 | |
| 神奈川県 | 27 | 12 | 22 | 21 | 29 | 13 | 11 | 12 | 12 | 15 | 174 | 1.92 | |
| 新潟県 | 6 | 16 | 13 | 18 (1) | 27 | 26 | 11 | 6 | 6 | 3 | 132 (1) | 5.56 | |
| 富山県 | - | 2 | 4 | 1 | 2 | 2 | 3 | 4 | 4 | 11 | 33 | 3.02 | |
| 石川県 | - | 3 | 1 | 2 | 5 | 4 | 4 | 3 | 1 | 2 | 25 | 2.14 | |
| 福井県 | 1 | - | - | - | 1 | 2 | - | - | 2 | - | 6 | 0.74 | |
| 山梨県 | 2 | 2 | 2 | - | - | - | - | - | - | - | 6 | 0.70 | |
| 長野県 | 4 | 1 | 3 | 3 | 6 | 12 | 10 | 8 | 6 | 1 | 54 | 2.51 | |
| 岐阜県 | 28 | 23 | 19 | 17 | 18 | 16 | 14 | 9 | 16 | 27 | 187 | 8.99 | |
| 静岡県 | 11 | 11 | 5 | 11 | 9 | 13 | 13 | 5 | 6 | 8 | 92 | 2.44 | |
| 愛知県 | 4 | 6 | 5 | 2 | 4 | 2 | 4 | 2 (1) | 2 | 3 | 34 (1) | 0.46 | |
| 三重県 | - | 5 | 8 | 5 | 3 | 2 | 3 | 2 | 3 | 6 | 37 | 1.99 | |
| 滋賀県 | - | - | - | 2 | 1 | 1 | - | - | - | 1 | 5 | 0.35 | |
| 京都府 | - | - | - | - | 1 | 1 | 1 | - | - | - | 2 | 0.08 | |
| 大阪府 | - | - | - | 1 | 1 | - | 1 | 1 | - | 1 | 4 | 0.05 | |
| 兵庫県 | 3 | 1 | 1 | 4 | 2 | 2 | 2 | 3 | 5 | 9 | 32 | 0.57 | |
| 奈良県 | - | - | - | 2 | - | 1 | - | - | - | - | 3 | 0.21 | |
| 和歌山県 | 12 | 4 | 7 | 15 | 6 | 5 | 10 | 10 | 7 | 12 | 88 | 8.78 | |
| 鳥取県 | 2 | 2 | 3 (1) | - | - | 2 | - | 1 | 3 | 4 | 17 (1) | 2.89 | |
| 徳島県 | 3 | 2 | 5 | 1 | 2 | 5 (1) | - | 3 | 4 | 2 | 27 (1) | 3.76 | |
| 岡山県 | - | - | 1 | 1 | 3 | 2 | - | 2 | 1 | 2 | 12 | 0.62 | |
| 広島県 | 15 | 16 | 11 | 11 | 13 | 15 | 15 | 12 | 21 | 39 | 168 | 5.87 | |
| 山口県 | - | 1 | - | 1 | - | - | - | - | - | - | 2 | 0.14 | |
| 徳島県 | 1 | - | 3 | 1 | - | 1 | 1 | 1 | 1 | 2 | 11 | 1.40 | |
| 香川県 | - | - | - | - | - | 1 | - | - | 3 | - | 4 | 0.40 | |
| 愛媛県 | - | - | 1 | 3 | - | 2 | - | - | 1 | 2 | 9 | 0.63 | |
| 高知県 | 2 | 5 | 4 | 2 | 5 | 8 | 3 | 3 | - | 4 | 36 | 4.71 | |
| 福岡県 | 1 | 2 | 1 | 2 | 4 | 4 | 2 | 3 | 2 | 4 | 25 | 0.49 | |
| 佐賀県 | 1 | 1 | 4 | 1 | 5 | 5 | 5 | 3 | 6 | 9 | 40 | 4.71 | |
| 長崎県 | 6 | 10 | 6 | 6 | 10 | 11 | 6 | 6 | 4 | 12 | 77 | 5.40 | |
| 熊本県 | 9 | 6 | 11 | 11 | 8 | 7 | 9 | 9 | 11 | 20 | 96 | 5.28 | |
| 大分県 | 12 | 17 | 16 | 7 | 11 | 12 | 8 | 13 | 22 | 33 | 12.20 | 12.20 | |
| 宮崎県 | 25 | 38 | 20 | 24 | 29 | 47 | 23 | 27 | 61 | 52 | 346 | 30.48 | |
| 鹿児島県 | 59 | 72 | 59 | 53 | 73 | 48 | 38 | 38 | 70 | 77 | 587 | 34.40 | |
| 沖縄県 | - | 1 | - | 1 | 2 | - | 1 | 2 | 4 | 10 (1) | 21 (1) | 1.51 | |
| 総数 | 382 (1) | 442 (1) | 465 (3) | 407 (2) | 462 (2) | 436 (3) | 344 (4) | 320 (2) | 422 (0) | 505 (2) | 4,185 (20) | 3.27 | |

()内は死亡数, *2016年は暫定値, †人口は2010年国勢調査を基にした年平均報告数
Nos. in parenthesis denote the no. of reported fatal cases. *Provisional data †Per 1,000,000 person-year (2010 Population Census of Japan)

(感染症発生動向調査: 2017年4月27日現在報告数)
(National Epidemiological Surveillance of Infectious Diseases: as of April 27, 2017)

(特集つづき) (THE TOPIC OF THIS MONTH-Continued)

表2. 年別都道府県別日本紅斑熱患者報告数, 2007~2016年
Table 2. No. of reported Japanese spotted fever cases, by year and prefecture, 2007-2016

| 都道府県 Prefecture | 診断年 Year of diagnosis | | | | | | | | | | | 合計 Total | 人口100万対 Per 1,000,000† | |
|--------------------|-----------------------|------|------|------|------|------|------|------|------|-------|-------|-------------|---------------------------|------|
| | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016* | | | | |
| 北海道 Hokkaido | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 青森県 Aomori | 1 | - | - | - | - | - | - | - | - | - | - | - | 1 | 0.07 |
| 岩手県 Iwate | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 宮城県 Miyagi | - | 1 | - | - | - | - | - | - | - | - | - | - | 1 | 0.04 |
| 秋田県 Akita | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 山形県 Yamagata | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 福島県 Fukushima | - | - | - | - | 1 | - | - | - | - | - | - | - | 1 | 0.05 |
| 茨城県 Ibaraki | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 栃木県 Tochigi | - | - | - | - | - | - | - | - | 1 | - | - | - | 1 | 0.05 |
| 群馬県 Gunma | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 埼玉県 Saitama | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 千葉県 Chiba | 1 | 7 | 6 | 5 | 3 | 4 | 4 | 6 | 5 | 10 | 5 | 51 | 0.82 | |
| 東京都 Tokyo | - | - | 1 | 1 | 1 | - | - | - | 1 | - | 3 | 3 | 0.02 | |
| 神奈川県 Kanagawa | - | 1 | - | - | - | - | - | 1 | - | - | 2 | 2 | 0.02 | |
| 新潟県 Niigata | - | - | - | - | - | - | - | 1 | - | - | 1 | 1 | 0.04 | |
| 富山県 Toyama | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 石川県 Ishikawa | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 福井県 Fukui | - | - | - | - | - | - | - | 1 | - | - | - | 2 | 0.25 | |
| 山梨県 Yamanashi | - | - | - | - | - | - | - | - | - | 1 | - | - | - | - |
| 長野県 Nagano | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 岐阜県 Gifu | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 静岡県 Shizuoka | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 愛知県 Aichi | - | - | 1 | - | 3 | - | - | - | - | 2 | 2 | 5 | 5 | 0.13 |
| 三重県 Mie | 20 | 34 | 36 | 26 | 37 | 38 | 51 | 34 | 25 | 48 | 349 | 5 | 0.07 | |
| 滋賀県 Shiga | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 京都府 Kyoto | - | - | - | - | 1 | - | - | 1 | 2 | - | - | 4 | 0.15 | |
| 大阪府 Osaka | - | 1 | - | 1 | - | - | 1 | 5 | 1 | - | 14 | 14 | 0.16 | |
| 兵庫県 Hyogo | 4 | 4 | 5 | 1 | 1 | 1 | 5 | 11 | 9 | 13 | 54 | 54 | 0.97 | |
| 奈良県 Nara | - | - | - | - | - | - | - | 1 | - | - | 1 | 1 | 0.07 | |
| 和歌山県 Wakayama | 16 | 16 | 11 | 20 | 21 | 24 | 18 | 34 | 17 | 17 | 194 | 194 | 19.36 | |
| 鳥取県 Tottori | 1 | 2 | - | - | 3 | 1 | 2 | 2 | 10 | 10 | 31 | 31 | 5.27 | |
| 島根県 Shimane | 10 | 13 | 3 | 3 | 11 | 8 | 4 | 6 | 10 | 15 | 83 | 83 | 11.57 | |
| 岡山県 Okayama | - | - | 2 | - | 3 | - | 2 | 4 | 3 | 4 | 18 | 18 | 0.93 | |
| 広島県 Hiroshima | 5 | 4 | 17 | 16 | 20 | 25 | 27 | 30 | 45 | 36 | 225 | 225 | 7.87 | |
| 山口県 Yamaguchi | - | - | - | 1 | - | - | 1 | 2 | 2 | 4 | 10 | 10 | 0.69 | |
| 徳島県 Tokushima | 2 | 2 | 3 | 5 | 10 | 1 | 2 | 13 | 6 | 6 | 50 | 50 | 6.37 | |
| 香川県 Kagawa | - | - | - | - | 1 | 7 | 1 | 7 | 9 | 7 | 25 | 25 | 2.51 | |
| 愛媛県 Ehime | 4 | 5 | 10 | 17 | 13 | 7 | 5 | 12 | 14 | 13 | 100 | 100 | 6.99 | |
| 高知県 Kochi | 1 | 6 | 6 | 7 | 15 | 4 | 1 | 7 | 4 | 13 | 64 | 64 | 8.97 | |
| 福岡県 Fukuoka | - | - | - | - | 2 | 2 | 3 | 2 | - | 6 | 15 | 15 | 0.30 | |
| 佐賀県 Saga | - | - | - | - | 1 | 1 | 1 | 5 | 3 | 8 | 19 | 19 | 2.24 | |
| 長崎県 Nagasaki | 2 | 2 | 2 | 3 | 9 | 6 | 2 | 14 | 13 | 8 | 61 | 61 | 4.28 | |
| 熊本県 Kumamoto | 11 | 18 | 16 | 8 | 20 | 22 | 20 | 18 | 11 | 19 | 163 | 163 | 8.97 | |
| 大分県 Oita | - | - | - | - | - | - | - | 2 | 3 | 2 | 7 | 7 | 0.59 | |
| 宮崎県 Miyazaki | 4 | 8 | 5 | 6 | 4 | 9 | 10 | 7 | 9 | 6 | 68 | 68 | 5.99 | |
| 鹿児島県 Kagoshima | 16 | 11 | 9 | 11 | 9 | 17 | 14 | 14 | 11 | 22 | 134 | 134 | 7.85 | |
| 沖縄県 Okinawa | - | - | - | 1 | 1 | 1 | - | - | - | - | 3 | 3 | 0.22 | |
| 総数 Total | 98 | 135 | 132 | 132 | 190 | 171 | 175 | 241 | 215 | 276 | 1,765 | 1,765 | 1.38 | |

()内は死亡数, *2016年は暫定値, †人口は2010年国勢調査を基にした年平均報告率
Nos. in parenthesis denote the no. of reported fatal cases. *Provisional data †Per 1,000,000 person-year (2010 Population Census of Japan)
(感染症発生動向調査: 2017年4月27日現在報告数)
(National Epidemiological Surveillance of Infectious Diseases: as of April 27, 2017)