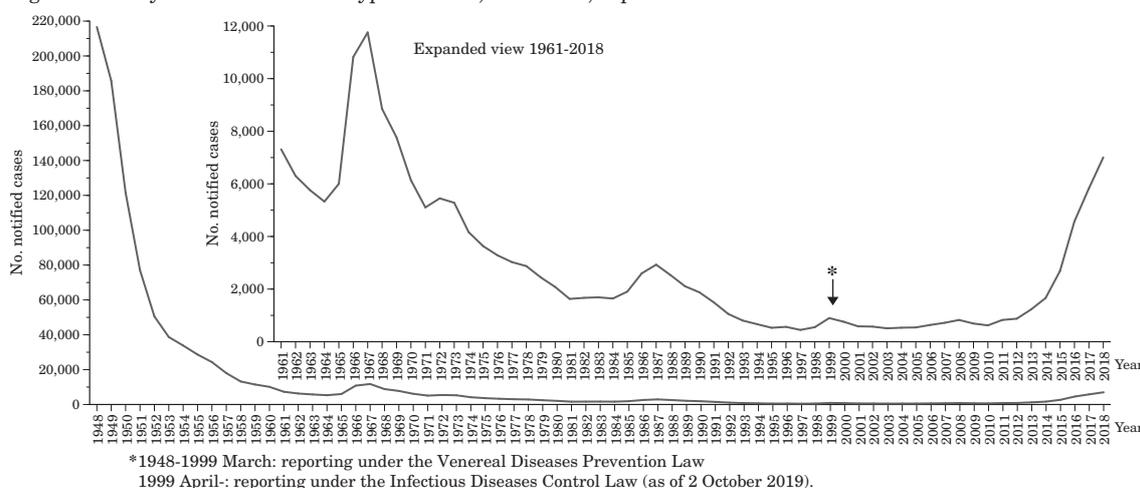


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### <THE TOPIC OF THIS MONTH> Syphilis, Japan

Figure 1. Yearly number of notified syphilis cases, 1948-2018, Japan



#### Background

Syphilis is an infectious disease caused by the *Treponema pallidum* subspecies *pallidum*. *T. pallidum* is a spirochete bacterium sized 0.1-0.2  $\mu\text{m}$  in diameter and 6-20  $\mu\text{m}$  in length. It has active motility and can be observed microscopically by staining or dark field microscopy. The mechanism of pathogenicity is poorly understood because it cannot be cultivated in vitro. *Treponema* includes species and subspecies that do not cause sexually transmitted infections, but recently, the *T. pallidum* subspecies *endemicum* (bejel) was first reported in Japan as a sexually transmitted disease (see p. 4 of this issue).

Syphilis is positioned as a disease that needs to be prioritized for public health because it is a sexually transmitted disease with a large number of patients, has relatively inexpensive diagnostic methods, and appropriate treatment of mothers with antibiotics can prevent mother-to-child transmission (MTCT). The World Health Organization (WHO) decided at the World Health Assembly to reduce the global syphilis incidence by 90% compared with 2018 and congenital syphilis incidence to less than or equal to 50 cases per 100,000 live births in 80% of countries by 2030. Currently, WHO is working to eliminate MTCT of three diseases, HIV infection, hepatitis B, and syphilis, for which similar measures can be taken from the viewpoint of maternal and child health. Many developed countries have achieved this elimination. In Asia, the number of syphilis patients in China was by far the largest, although the number of reported cases, including congenital syphilis, has been decreasing in recent years (see p. 16 of this issue).

#### Routes of infection and clinical manifestations

*T. pallidum*, which is present in exudates from the mucocutaneous lesions of the infected person, enters and infects the contacted person through small wounds in the mucous membranes or skin. In addition to vaginal intercourse, oral sex can also transmit the infection because humans are the only host and are primarily infected by sexual contact, and the lesions occur at many sites. Although transfusion-related infections originating from the blood of infectious patients was problematic in the past, no new cases caused by blood transfusion have been identified due to advances in screening techniques. Infection does not provide life-long immunity and there is a possibility of re-infection.

When *T. pallidum* invades mucous membranes and skin, after an incubation period of approximately three to six weeks, an infected person usually develops initial sclerosis and hard chancres at the site of entry (primary symptomatic syphilis), all of which are characterized by painlessness. Over the next few weeks to months that follow, *T. pallidum* spreads throughout the body via blood circulation, leading to rashes on the skin and mucous membranes of the entire body (secondary symptomatic syphilis). The rashes vary widely, and papular syphilides, psoriasiform syphilis, and roseola syphilitica are frequently observed. Primary and secondary symptomatic syphilis are collectively called "early symptomatic syphilis." Primary symptomatic syphilis resolves in a few weeks even if left untreated, and remains asymptomatic until the mucocutaneous lesions of the secondary symptomatic syphilis

(Continued on page 2')

(THE TOPIC OF THIS MONTH-Continued)

appear several months later. If untreated, “late symptomatic syphilis”, including gummas, cardiovascular, and neurological symptoms, may develop several years to several decades after infection.

If a pregnant woman is infected, the fetus can be infected through the placenta, resulting in abortion, stillbirth, or congenital syphilis. MTCT by breast-feeding usually does not occur. Congenital syphilis consists of early congenital syphilis characterized by the development of skin lesions, hepatosplenomegaly, and osteochondritis shortly after birth, and late congenital syphilis without symptoms in infancy and with Hutchinson’s triad (parenchymatous keratitis, inner ear deafness, and Hutchinson teeth) later in childhood.

#### Laboratory diagnosis and treatment

As *T. pallidum* cannot be cultured, syphilis is diagnosed by observation of *T. pallidum* from the lesion under an optical microscope or detection of antibodies against Treponemal antigens or cardiolipin in the serum of patients (see p. 5 of this issue). Detection of the *T. pallidum* gene from mucocutaneous lesions by PCR in the early stage before seroconversion has been investigated as an auxiliary means of antibody testing. Penicillin antibiotics are effective for treatment and no penicillin-resistant bacteria have been reported. However, resistance to azithromycin has been increasing. Benzathine penicillin G, the world-standard treatment, cannot be used in Japan and its supply is insufficient worldwide. In Japan, oral administration of aminobenzylpenicillin (ampicillin and amoxicillin) or potassium benzylpenicillin intravenous has been recommended as syphilis treatment by the Japanese Society for Sexually Transmitted Infections.

#### National Epidemiological Surveillance of Infectious Diseases

In Japan, notification of all diagnosed syphilis cases began in 1948 under the Venereal Diseases Prevention Law. In April 1999, syphilis was classified as a category V notifiable infectious disease under the Infectious Diseases Control Law. A physician who diagnoses a syphilis case must notify it to the nearby health center within 7 days (see <https://www.niid.go.jp/niid/images/iasr/36/420/de4201.pdf>).

Although changes in surveillance should be noted, the number of notified syphilis cases has declined significantly since 1948 (Fig. 1). The number of notifications had been on a decreasing trend as a whole, although minor epidemics that peaked in 1967, 1972, 1987, 1999, and 2008 were observed. However, the number increased after 2010 and has increased rapidly until 2018. The total number of notified syphilis cases in 2015-2018 was 20,098, which consisted of 13,641 males (68%) and 6,457 females (32%) (as of 2 October 2019). Among them, 14,017 were early symptomatic syphilis (6,924 primary and 7,093 secondary), 459 were late symptomatic syphilis, 5,568 were asymptomatic syphilis, and 54 were congenital syphilis (Table in p. 3). Since 2015, 9-17 cases of congenital syphilis have been reported annually, and the number has been increasing in recent years. The incidence rate per 100,000 population was 2.1 in 2015 and 5.5 in 2018. The average annual incidence rate by prefecture was the highest in Tokyo, followed by Osaka and Okayama (see pp. 6 & 8 of this issue).

In both men and women, early symptomatic syphilis, which reflects the trend of patients in the early stage of *T. pallidum* infection, accounted for the majority (Fig. 2 in p. 3). Regarding the reported age distribution of early symptomatic syphilis, it peaked in the 20s for females, whereas males had a broad peak in their 20s to 40s (Fig. 2 in p. 3) and increased in the same age group after 2015 (Fig. 3 in p. 3). A total of 555 patients (male: 188, female: 367) younger than 20 years were reported between 2015 and 2018. Regarding the routes of infection, for males, infections by heterosexual contact have been higher than infections by homosexual contact since 2015 and surpassed infections by homosexual contact, which had increased slightly until 2018 (Fig. 4 in p. 3). For females, the majority of infections were caused by heterosexual contact and the increase was also due to this infection (Fig. 4 in p. 3).

Effective January 1, 2019, the following were added to the survey on infectious disease outbreaks: pregnancy, HIV infection, history of syphilis infection, history of working in and using the sex industry, and presence of oral or pharyngeal lesions. Based on preliminary data, the number of notifications of pregnant syphilis cases was more than 200 per year (see p. 9 of this issue).

#### Prevention and control

Sexual contact with an unspecified number of people is a risk factor for syphilis infection and inappropriate use of condoms increases the risk (see p. 10 of this issue). It is important to educate young people about avoiding unprotected sexual contact with an unspecified number of partners. Awareness needs to be raised about the symptoms of syphilis, and the importance of suspecting and consulting syphilis, even if the lesions, such as ulcers, are painless and disappear spontaneously. It is also important for medical institutions to promote early diagnosis, early treatment, education about the prevention of sexually transmitted infections to sexual partners considered to be at high risk, and testing and treatment of syphilis. In addition, it should be disseminated that genital ulcers of syphilis increase the risk of transmission of other sexually transmitted infections such as HIV. Measures against transmission during homosexual contact among males, which is increasing slightly, need to be continued. Regarding the prevention of MTCT of syphilis, it is also important to promote prenatal examinations, including syphilis screening, provide early treatment if syphilis is diagnosed during pregnancy, promote safe sex during pregnancy, and actively test for syphilis if there are signs or suspicious symptoms during pregnancy.

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*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 Act on the Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases, and 2) other data covering various aspects of infectious diseases. The prefectural and municipal health centers and public health institutes (PHIs), the Department of Environmental Health and Food Safety, the Ministry of Health, Labour and Welfare, and quarantine stations, have provided the above data.*

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

表. 梅毒患者の届出数と病期別内訳, 2008~2019年

Table. Number of notified syphilis cases, 2008-2019, Japan

(\*: 暫定値 (provisional))

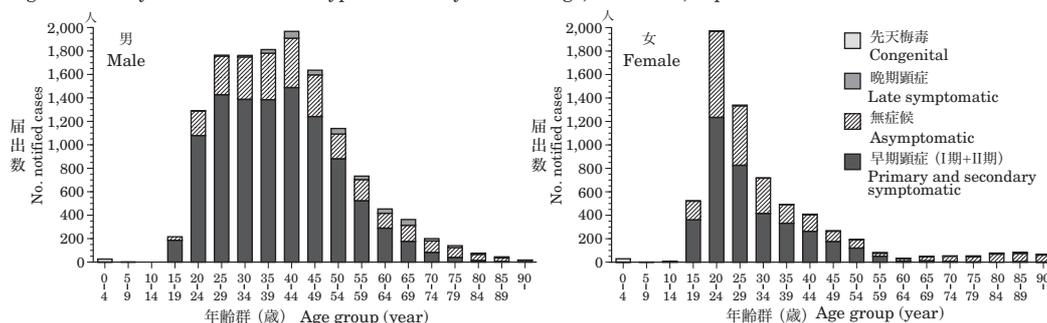
年 (Year)	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018*	2019*
総届出数 (Total)	827	691	621	827	875	1,228	1,661	2,690	4,575	5,826	7,007	3,281
早期顕症 (I期、II期) (Primary and secondary symptomatic)	454	393	341	432	475	692	957	1,758	3,179	4,123	4,957	2,240
晩期顕症 (Late symptomatic)	65	44	41	54	48	66	81	90	115	118	136	63
無症候 (Asymptomatic)	299	249	238	335	348	466	613	829	1,266	1,576	1,897	969
先天梅毒 (Congenital)	9	5	1	6	4	4	10	13	15	9	17	9

(感染症発生動向調査: 2019年10月2日現在届出数)

(National Epidemiological Surveillance of Infectious Diseases: as of 2 October 2019)

図2. 梅毒患者の病期別性別年齢群別届出数, 2015~2018年

Figure 2. Yearly number of notified syphilis cases by clinical stage, 2015-2018, Japan

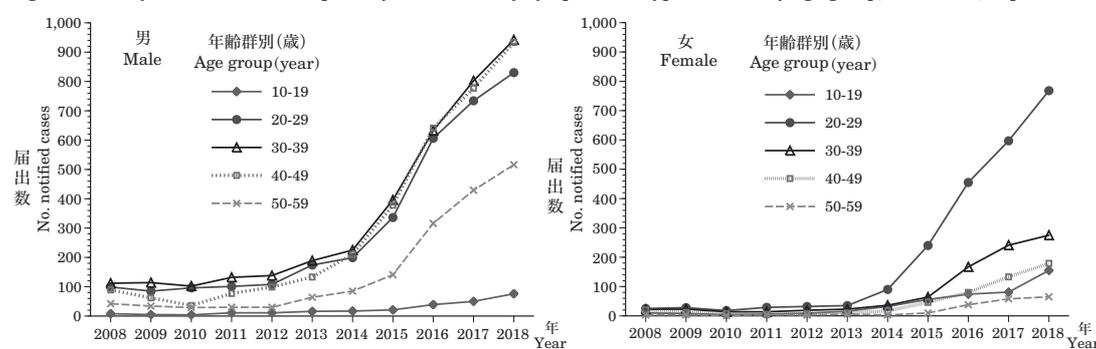


(感染症発生動向調査: 2019年10月2日現在届出数)

(National Epidemiological Surveillance of Infectious Diseases: as of 2 October 2019)

図3. 早期顕症梅毒 (I期, II期) 患者の性別年齢群別届出数, 2008~2018年

Figure 3. Yearly number of notified primary and secondary symptomatic syphilis cases by age group, 2008-2018, Japan

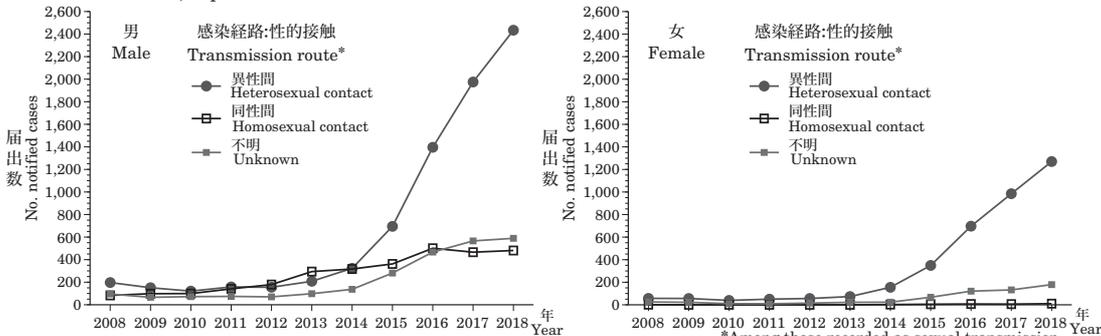


(感染症発生動向調査: 2019年10月2日現在届出数)

(National Epidemiological Surveillance of Infectious Diseases: as of 2 October 2019)

図4. 早期顕症梅毒 (I期, II期) 患者の性別感染経路別届出数, 2008~2018年

Figure 4. Yearly number of notified primary and secondary symptomatic syphilis cases by transmission route, 2008-2018, Japan



(感染症発生動向調査: 2019年10月2日現在届出数)

(National Epidemiological Surveillance of Infectious Diseases: as of 2 October 2019)