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National Institute of Infectious Diseases and Tuberculosis and Infectious Diseases Control Division, Ministry of Health, Labour and Welfare

<THE TOPIC OF THIS MONTH>
Syphilis 2008-2014

Syphilis is a bacterial infectious disease caused by *Treponema pallidum*. *T. pallidum* is a highly motile spirochete bacterium sized 0.1-0.2 μm in diameter and 6-20 μm in length. It can be observed microscopically by staining or by using dark field microscopy. The pathogenicity of *T. pallidum* has not been fully elucidated.

In Japan, notification of all detected syphilis cases began in 1948 under the Venereal Diseases Prevention Law. In April 1999, syphilis was classified as 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 http://www.nih.go.jp/niid/images/iasr/36/420/de4201.pdf for notification criteria).

Routes of infection and clinical manifestations: Generally, the infection is acquired through sexual contact with a person in the early stage of syphilis. Transmission occurs when *T. pallidum* present in lesion exudate penetrates the skin through mucous membrane or damaged skin. Placental infection of a fetus from the infected mother causes abortion, stillbirth or congenital syphilis. There is no evidence of transmission of syphilis through breast-feeding.

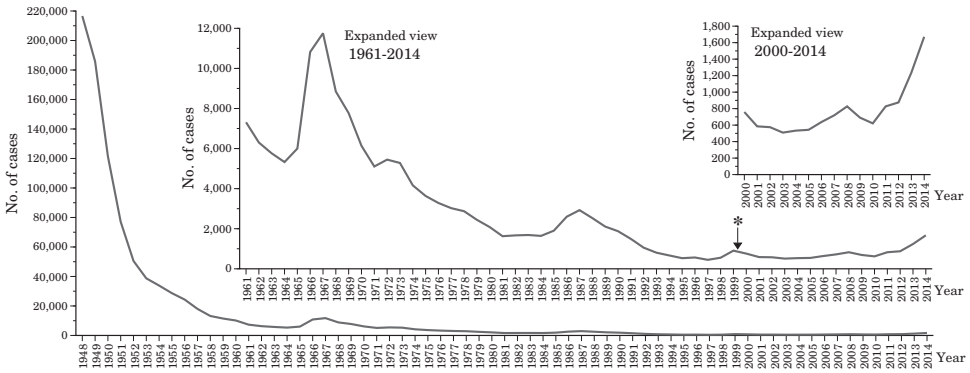
Three to six weeks after infection, an infected person usually develops initial sclerosis and hard chancres at the infected sites (primary symptomatic syphilis). During the latency period of a few weeks to months that follows, the bacteria spreads via blood circulation, and the infection becomes generalized giving rise to rashes appearing on the skin or on the mucous membrane (secondary symptomatic syphilis). Primary and secondary symptomatic syphilis are collectively called "early symptomatic syphilis". A few years to some decades after infection, gummas, cardiovascular and/or neurological symptoms characteristic of "late symptomatic syphilis" appear. Infected persons are often asymptomatic during the period between the early and late symptomatic phases, which often results in delayed diagnosis and treatment.

Congenital syphilis consists of early and late congenital syphilis. Early congenital syphilis is characterized by development of skin lesions, hepatosplenomegaly and osteochondritis, shortly after birth. After a latent period without clinical manifestations, late congenital syphilis, characterized by development of Hutchinson's triad, parenchymatous keratitis, inner ear deafness and Hutchinson teeth, appear during childhood.

Laboratory diagnosis and therapy: Laboratory diagnosis consists of direct identification of the causative agent, *T. pallidum*, under an optical microscope and/or detection of antibodies against Treponemal antigen or cardiolipin antigen (see p. 20 of this issue). PCR detection of the bacterial genome from skin lesions is used as a test to supplement the antibody tests when the patients have yet to seroconvert (see p. 21 of this issue). Penicillin is the first choice for therapy, and no penicillin-resistant strains have been yet reported.

National Epidemiological Surveillance of Infectious Diseases: The law governing surveillance of syphilis was switched from the Venereal Diseases Prevention Law to the Infectious Diseases Control Law in April 1999 (indicated by an asterisk in Fig. 1). Overall, the number of reported syphilis cases continuously decreased from 1948 until 2010, though with slight fluctuations (Fig. 1). Since 2010, however, notification has been on the rise (Fig. 1). The total number of reported syphilis cases in 2008-2014 was 6,745, which consisted of 5,262 males and 1,483 females (as of 15 January 2015). Among them, 3,740 were early symptomatic syphilis (1,290 primary and 2,450 secondary; average annual notification rate: 0.42 per 100,000 population), 399 late symptomatic syphilis, 2,567

Figure 1. Number of reported syphilis cases by year, 1948-2014, Japan



*1948-1999 March: reporting under the Venereal Diseases Prevention Law;
1999 April-: reporting under the Infectious Diseases Control Law (As of January 15, 2015).

(Continued on page 18′)

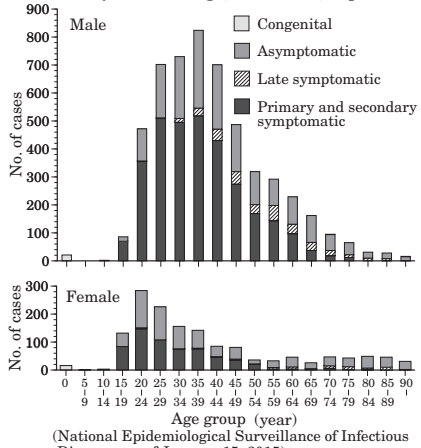
(THE TOPIC OF THIS MONTH-Continued)

Table1. Number of reported syphilis cases, Japan, 2008-2014

Year	2008	2009	2010	2011	2012	2013	2014
Total	831	691	621	828	875	1,228	1,671
Primary and secondary symptomatic	456	393	341	433	475	692	950
Late symptomatic	66	44	41	54	48	66	80
Asymptomatic	300	249	238	335	348	466	631
Congenital	9	5	1	6	4	4	10

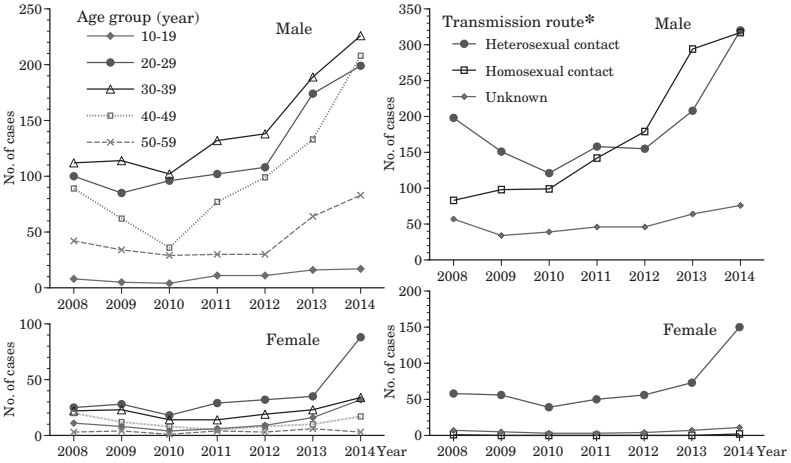
(National Epidemiological Surveillance of Infectious Diseases: as of January 15, 2015)

Figure 2. Age distribution of syphilis cases by clinical stage, 2008-2014, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of January 15, 2015)

Figure 3. Reported number of primary and secondary symptomatic syphilis cases by age group & transmission route, 2008-2014, Japan



*Among those recorded as sexual transmission

(National Epidemiological Surveillance of Infectious Diseases: as of January 15, 2015)

asymptomatic syphilis, and 39 congenital syphilis (Table 1). The average annual notification rate of total syphilis cases in 2008-2014 was 0.75 per 100,000 population. Cases from Tokyo, Osaka, Aichi, Kanagawa and Fukuoka prefectures occupied 62% of cases (Table 2 in p.19).

Fig. 2 shows the age distribution of cases. The age distribution of early symptomatic syphilis showed a broad range from 20 years to 44 years. Among the early symptomatic syphilis cases, the number of male patients in their 20's-40's increased from 2012 to 2014, while the number of female patients, particularly in their 10's-20's, doubled from 2013 to 2014 (Fig. 3 left). The number of early symptomatic syphilis cases under the age of 18 years was 57 from 2008 to 2014 (14, 4, 5, 4, 6, 10, and 14 in respective years); among them 21 were males and 36 females. As for transmission routes, among males, there was a notable increase in cases associated with homosexual contact since 2008, though heterosexual contact have also been increasing; among females, the main transmission route was heterosexual contact (Fig. 3).

In 2014, the incidence of congenital syphilis (per 100,000 live births) was 1.0, which was the highest in the last 7 years (Table 1). From 2008 to 2013, the annual incidence was 0.8, 0.5, 0.1, 0.6, 0.4 and 0.4 per 100,000 live births, respectively (birth data derived from Vital Statics, the Ministry of Health, Labour, and Welfare's demographic survey; 2014 data based on tentative estimate).

Reported number of asymptomatic syphilis increased, which was detected during such times as clinical consultations on ailments related to other sexually transmitted diseases, blood testing before blood donation, prenatal checkups, and laboratory tests before surgical operations (Table 1).

Prevention and control: Frequent sexual contact with casual partners, particularly without using condoms, is a high risk behavior. Genital ulcers caused by syphilis increase the risk of infection by other sexually transmitted diseases including HIV. The co-infection of HIV and syphilis enhances the progress of both infections (see p. 22 of this issue). Infection through blood transfusion, which was a serious problem in the past, has almost disappeared owing to the advancement of blood screening technology. Needle-stick injury- or laboratory-acquired infection risks persist, however.

The risk of congenital syphilis increases when a fetus is infected after the formation of placenta, i.e., the 16th week of gestation. It is therefore important to instruct expectant mothers to receive a syphilis test in the early stage of pregnancy, and receive appropriate therapy if she is found to be infected. It is also important that women take measures to prevent syphilis infection during pregnancy (IASR 34: 113-114, 2013).

In recent years, increase in asymptomatic and early symptomatic syphilis have been reported not only in Japan but also from abroad (see p. 24 of this issue). Providing young and sexually active people with appropriate information is a crucial public health measure. Such information should include: (i) transmissibility of syphilis through oral or anal sex (see p. 23 of this issue); (ii) absence of life-long immunity to syphilis; and (iii) progression of the disease when the infected are not treated during the asymptomatic phase between the early and late symptomatic phases. Physicians who have diagnosed syphilis should not only notify and treat the case but also educate and/or test his/her sexual partner(s). National guidance on the prevention of sexually transmitted infections emphasizes the importance of early detection and early treatment as effective measures for preventing infection and spread of sexually transmitted diseases.

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.

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

表2. 都道府県別梅毒患者報告数, 2008～2014年

Table 2. Syphilis cases, by prefecture, 2008-2014

都道府県	Prefecture	早期顕症(I期・II期) Primary and secondary symptomatic		晩期顕症 Late symptomatic	無症候 Asymptomatic	先天性 Congenital		総数 Total	
		報告数 Cases	人口10万対* Rate*	報告数 Cases	報告数 Cases	報告数 Cases	出生10万対** Rate**	報告数 Cases	人口10万対* Rate*
北海道	Hokkaido	79	0.20	11	67	2	0.7	159	0.41
青森県	Aomori	10	0.10	2	12	–	0.0	24	0.25
岩手県	Iwate	2	0.02	2	7	–	0.0	11	0.12
宮城県	Miyagi	71	0.43	5	61	3	2.2	140	0.85
秋田県	Akita	8	0.11	5	15	–	0.0	28	0.37
山形県	Yamagata	6	0.07	4	15	–	0.0	25	0.31
福島県	Fukushima	25	0.18	3	13	–	0.0	41	0.29
茨城県	Ibaraki	65	0.31	10	61	1	0.6	137	0.66
栃木県	Tochigi	28	0.20	12	53	1	0.9	94	0.67
群馬県	Gunma	27	0.19	4	30	1	0.9	62	0.44
埼玉県	Saitama	114	0.23	12	82	–	0.0	208	0.41
千葉県	Chiba	132	0.30	30	111	6	1.7	279	0.64
東京都	Tokyo	1,212	1.32	73	749	7	0.9	2,041	2.22
神奈川県	Kanagawa	221	0.35	19	132	2	0.4	374	0.59
新潟県	Niigata	21	0.13	2	18	1	0.8	42	0.25
富山県	Toyama	23	0.30	4	22	–	0.0	49	0.64
石川県	Ishikawa	17	0.21	5	12	–	0.0	34	0.42
福井県	Fukui	18	0.32	–	9	–	0.0	27	0.48
山梨県	Yamanashi	7	0.12	1	4	–	0.0	12	0.20
長野県	Nagano	20	0.13	1	26	–	0.0	47	0.31
岐阜県	Gifu	33	0.23	5	28	1	0.8	67	0.46
静岡県	Shizuoka	94	0.36	3	72	2	0.9	171	0.65
愛知県	Aichi	207	0.40	26	184	1	0.2	418	0.81
三重県	Mie	42	0.32	6	25	–	0.0	73	0.56
滋賀県	Shiga	21	0.21	3	10	–	0.0	34	0.34
京都府	Kyoto	38	0.21	9	18	–	0.0	65	0.35
大阪府	Osaka	473	0.76	33	264	2	0.4	772	1.24
兵庫県	Hyogo	81	0.21	20	66	1	0.3	168	0.43
奈良県	Nara	23	0.23	1	15	–	0.0	39	0.40
和歌山県	Wakayama	18	0.26	4	17	–	0.0	39	0.56
鳥取県	Tottori	6	0.15	–	7	–	0.0	13	0.32
島根県	Shimane	3	0.06	2	8	–	0.0	13	0.26
岡山県	Okayama	27	0.20	11	27	–	0.0	65	0.48
広島県	Hiroshima	37	0.18	6	21	1	0.6	65	0.32
山口県	Yamaguchi	17	0.17	4	10	–	0.0	31	0.31
徳島県	Tokushima	6	0.11	2	5	–	0.0	13	0.24
香川県	Kagawa	30	0.43	6	20	–	0.0	56	0.80
愛媛県	Ehime	20	0.20	3	3	–	0.0	26	0.26
高知県	Kochi	16	0.30	6	14	1	2.6	37	0.69
福岡県	Fukuoka	224	0.63	16	87	2	0.6	329	0.93
佐賀県	Saga	10	0.17	1	7	–	0.0	18	0.30
長崎県	Nagasaki	28	0.28	1	12	–	0.0	41	0.41
熊本県	Kumamoto	54	0.42	4	52	2	1.8	112	0.88
大分県	Oita	18	0.21	1	17	2	2.8	38	0.45
宮崎県	Miyazaki	37	0.47	2	18	–	0.0	57	0.72
鹿児島県	Kagoshima	29	0.24	8	26	–	0.0	63	0.53
沖縄県	Okinawa	42	0.43	11	35	–	0.0	88	0.90
総計	Total	3,740	0.42	399	2,567	39	0.5	6,745	0.75

(感染症発生動向調査：2015年1月15日現在報告数)

*人口は2010年国勢調査, 年平均罹患率

**出生は2010年人口動態統計, 年平均報告数

(National Epidemiological Surveillance of Infectious Diseases: as of January 15, 2015)

* Per 100,000 population (2010 Population Census of Japan)

**Per 100,000 live births (Vital Statistics of Japan in 2010)