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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>
Erythema infectiosum (Human parvovirus B19 infection)

Figure 1. Weekly number of reported erythema infectiosum cases per sentinel, 2010 to 2015 (until week 50), Japan
(National Epidemiological Surveillance of Infectious Diseases: as of December 16, 2015)

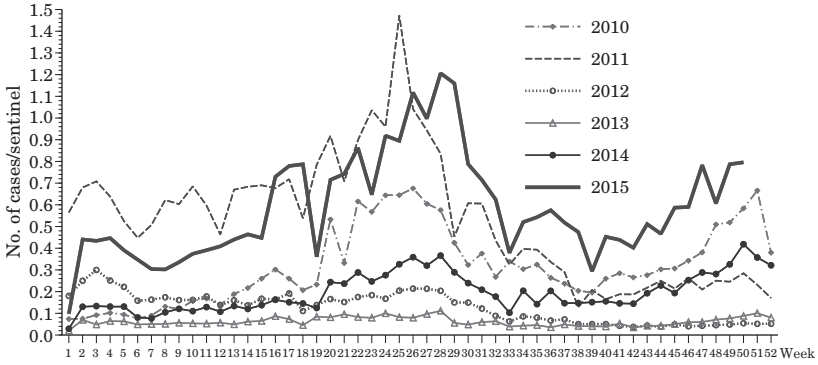
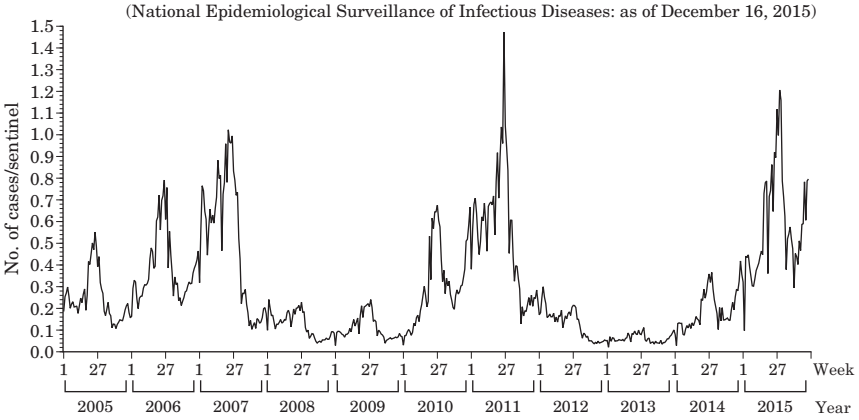


Figure 2. Weekly number of reported erythema infectiosum cases per sentinel, week 1 of 2005 to week 50 of 2015, Japan
(National Epidemiological Surveillance of Infectious Diseases: as of December 16, 2015)



Erythema infectiosum is a contagious exanthematous disease affecting mainly infants and young children. The causative agent is human parvovirus B19 (PVB19), a single-stranded DNA virus, which belongs to the genus *Erythrovirus*, the subfamily *Parvovirinae*, the family *Parvoviridae*. It is known to infect only humans. It infects the erythroid precursor cells through specific binding to the P antigen present on these cells and destroys the cells through apoptosis. The typical manifestation is butterfly-shaped erythema on the cheeks, and is thus called "apple disease" in Japan. However, the erythema, often taking lacy, mesh-like form, may extend to the extremities and the trunk (see p. 3 of this issue).

National Epidemiological Surveillance of Infectious Diseases (NESID)

Erythema infectiosum is a category V infectious disease (notification criteria are found in http://www.nih.go.jp/niid/images/iasr/37/431/de4311.pdf), and approximately 3,000 pediatric sentinel sites report patients diagnosed as erythema infectiosum on a weekly basis. The reported number of erythema infectiosum cases shows a seasonal trend in epidemic years, with a peak in June-July (Fig. 1). The annual number of patients reported from 2010 to 2014 was 50,061, 87,010, 20,966, 10,118 and 32,352, respectively. In the 2015 season, a total of 92,625 patients were reported as of week 50 (Table 1 in p.3 of this issue), the highest in the last ten years. Since the current national surveillance system was established, epidemic years (years where the peak in the weekly number of reported cases per sentinel site exceeded one) occurred in 2001, 2007, 2011, and 2015; epidemic years occurred every 4 to 6 years (Fig. 2, IASR 19: 50-51, 1998; http://idsc.nih.go.jp/iasr/19/217/tpc217.html). In the 2015 season, the epidemic that started in the

(Continued on page 2′)

(THE TOPIC OF THIS MONTH-Continued)

Kanto region spread nationwide and peaked in week 28 (Fig. 3). It then subsided but the patient number has again been increasing since autumn (Fig. 1).

Among reported cases through week 50 of 2015, those 9 years of age or under occupied 93%, and those aged 5 years made up the highest proportion (17% of total cases) (Fig. 4). Though the epidemiology of erythema infectiosum among adults is unclear as surveillance is based on the pediatric sentinel notifications, local epidemics among adults have been reported (see p. 5 of this issue). Information on the epidemiological situation abroad is limited, but outbreaks and fatal fetal cases have been reported (see p. 11 of this issue).

Figure 3. Weekly number of reported erythema infectiosum cases per sentinel by prefecture, 2015, Japan

(National Epidemiological Surveillance of Infectious Diseases: as of December 16, 2015)

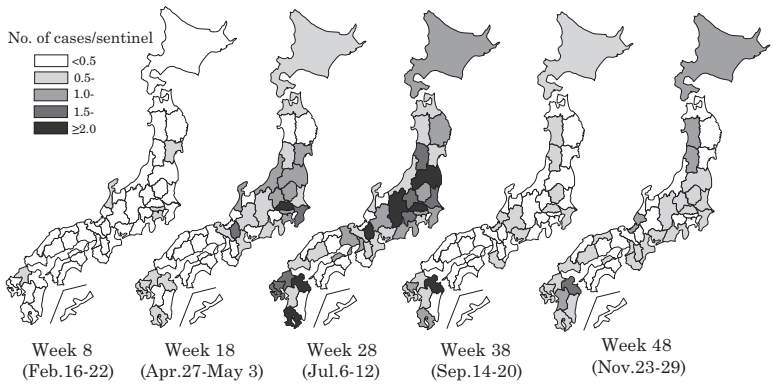
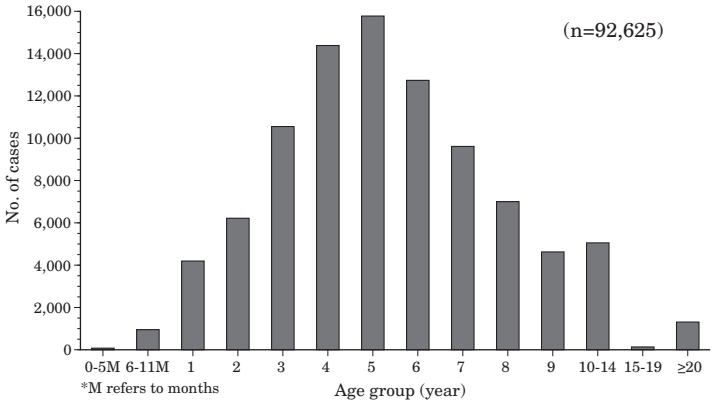


Figure 4. Age distribution of erythema infectiosum cases 2015, Japan

(National Epidemiological Surveillance of Infectious Diseases: as of December 16, 2015)



Transmission route and clinical picture

The incubation period of PVB19 is 4-15 days. It is transmitted through droplet or contact infection and is transmissible before clinical onset, but generally noninfectious post onset of the typical erythema (see p. 3 of this issue). As the blood derived from PVB19-infected patients pre-onset poses a risk for infection, raw plasma materials have been all screened for PVB19 by the agglutination method (receptor-mediated hemagglutination assay) since 1997 (IASR 19: 52, 1998). During the 11 year period till 2007, 9 infections due to transfusion blood-derived products were reported. In 2008, the CLEIA method (chemiluminescent enzyme immunoassay), whose sensitivity was as high as 10^6 copies/m*l*, was introduced, and since 2008 to 2015, only one blood product-derived infection was reported (see p. 9 of this issue).

One in four PVB19 infection cases is asymptomatic. While PVB19 infection confers lifelong immunity, the virus may cause persistent infection among immunocompromised persons.

Among adults, differential diagnosis is difficult due to variety of manifestations. In one study, about 30% of measles-suspected cases older than 20 years of age were found positive for the PVB19 genome (see p. 4 of this issue). Among adults (particularly women), PVB19 infection frequently manifests as arthritis. Other complications include transient aplastic crisis among hemolytic anemia patients and chronic anemia among immunocompromised persons.

When pregnant women are infected with PVB19, transplacental infection occurs in about 20% of the cases (see p. 7 of this issue), and about 10% of them experience miscarriage or stillbirth. Fetal hydrops is a frequent complication when mothers are infected before 20 weeks of gestation (particularly 9 to 16 weeks), but the risk decreases after 28 weeks of gestation. As transplacental infection can occur from asymptomatic cases, pregnant women who have frequent contact with children (such as those with young children or in occupational settings that involve children) should take particular care to reduce the chance of infection.

Laboratory diagnosis of PVB19

Routine laboratory diagnosis includes the titration of IgM and IgG antibodies using enzyme immunoassay and the detection of PVB19 DNA by PCR test. In case of primary infection, IgM antibody can be detected about 2 weeks post infection, when the erythema appears. IgM remains positive for about 3 months. IgG antibody is detectable a few days after the appearance of the IgM antibody, and is maintained lifelong. To determine whether an infection is primary or not, one needs to take into account the clinical picture, the PVB19 IgM antibody data and PVB19 DNA data (see p. 9 of this issue). The real-time PCR test can be used for estimating the clinical stage or the time course of infection. Utilization of a laboratory test for a "pregnant woman with erythema, who is strongly suspected of PVB19 infection" is covered by the national health insurance.

Measures to be taken against erythema infectiosum

Erythema infectiosum is generally a pediatric disease with good prognosis. However, PVB19 infection may become serious among immunocompromised persons and may cause fetal infection with serious outcome. It is important to note that preventing disease spread is challenging due to several reasons, e.g. differential diagnosis is difficult due to diverse manifestations, asymptomatic cases are infectious, and the virus is shed 1 week before the appearance of symptoms. In epidemic seasons and epidemic areas, special measures, such as intensified hospital infection control and hygienic practices in the family setting, should be implemented so as to protect persons at risk.

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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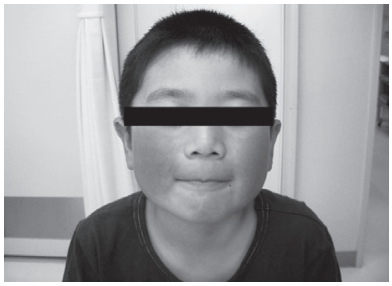
＜特集関連情報＞

小児における伝染性紅斑の概要と地域における状況

1．概念・定義

伝染性紅斑（erythema infectiosum）は，ヒトパルボウイルスB19（以下，PVB19）による感染症である。小児では頬がリンゴのように赤くなる（写真）ことから，文字通り“リンゴ病”としてよく知られる。英語でも「頬が赤くなる」との意で“slapped cheek”と称されることもあるが，“fifth disease（第5の発疹症）”の方がより一般的に用いられている模様である。



写真．6歳男児、小学1年生
両頬がやや厚みをもって赤く腫れている

2．疫　学

伝染性紅斑は，5類感染症として小児科定点報告の

(特集つづき)

表．伝染性紅斑 年別，都道府県別累積報告数・累積定点当たり報告数，2010年～2015年第50週

Table. Cumulative number of reported erythema infectiosum cases & cases/sentinel sites, by prefecture and year, 2010 to 2015 (until week 50), Japan

年 year		2010		2011		2012		2013		2014		2015*	
都道府県	Prefecture	累積 cumulative cases	定点当たり cases/ sentinel	累積 cumulative cases	定点当たり cases/ sentinel	累積 cumulative cases	定点当たり cases/ sentinel	累積 cumulative cases	定点当たり cases/ sentinel	累積 cumulative cases	定点当たり cases/ sentinel	累積 cumulative cases	定点当たり cases/ sentinel
総計	Total No.	50,061	16.53	87,010	27.77	20,966	6.67	10,118	3.22	32,352	10.29	92,625	29.43
北海道	Hokkaido	1,726	12.07	6,314	44.46	394	2.77	153	1.08	504	3.52	4,680	32.96
青森県	Aomori	1,012	24.68	602	14.68	151	3.68	80	1.95	957	23.34	956	22.76
岩手県	Iwate	89	2.23	409	10.49	871	21.78	406	10.41	760	19.00	840	21.54
宮城県	Miyagi	1,441	24.84	1,216	20.61	338	5.83	850	14.66	2,871	49.50	1,682	29.00
秋田県	Akita	1,038	29.66	625	18.38	71	2.03	72	2.12	114	3.35	859	25.26
山形県	Yamagata	772	26.62	1,465	50.52	332	11.45	46	1.59	238	8.21	1,310	45.17
福島県	Fukushima	828	17.25	2,178	50.65	672	14.00	85	1.89	718	15.96	2,214	49.20
茨城県	Ibaraki	589	7.96	1,926	25.68	192	2.56	129	1.72	555	7.40	2,549	33.99
栃木県	Tochigi	504	10.72	1,994	42.43	235	5.00	54	1.15	329	6.85	1,662	34.63
群馬県	Gunma	417	6.95	2,088	34.80	247	4.19	78	1.32	291	4.93	1,754	29.73
埼玉県	Saitama	4,317	27.85	6,109	39.16	607	3.92	514	3.32	2,118	13.66	8,368	53.30
千葉県	Chiba	4,306	33.64	3,312	25.88	717	5.52	474	3.62	1,721	13.04	5,154	38.75
東京都	Tokyo	2,929	19.93	6,317	24.30	1,626	6.28	1,608	6.23	5,069	19.65	9,909	38.41
神奈川県	Kanagawa	5,130	25.40	3,949	19.36	1,309	6.42	1,071	5.25	6,338	31.07	6,342	31.09
新潟県	Niigata	1,215	19.92	1,121	18.68	590	9.83	940	15.67	3,060	50.16	1,326	22.47
富山県	Toyama	149	5.32	192	6.62	232	8.00	807	27.83	770	26.55	192	6.62
石川県	Ishikawa	256	8.83	1,169	40.31	115	3.97	40	1.38	470	16.21	889	30.66
福井県	Fukui	782	35.55	594	27.00	91	4.14	19	0.86	76	3.45	326	14.82
山梨県	Yamanashi	486	20.25	702	29.25	70	2.92	30	1.25	36	1.50	691	28.79
長野県	Nagano	554	10.26	1,963	36.35	917	16.98	118	2.23	248	4.68	2,111	39.83
岐阜県	Gifu	160	3.08	993	19.10	812	15.62	91	1.72	89	1.71	1,438	27.65
静岡県	Shizuoka	1,327	15.80	3,231	38.46	223	2.56	121	1.38	1,012	11.50	2,531	28.76
愛知県	Aichi	1,134	6.27	6,083	33.61	1,528	8.44	335	1.84	322	1.77	3,745	20.58
三重県	Mie	1,668	37.07	1,022	23.23	156	3.47	72	1.60	154	3.42	831	18.47
滋賀県	Shiga	515	16.61	835	26.09	48	1.50	42	1.31	57	1.84	1,513	48.81
京都府	Kyoto	671	9.07	1,252	17.39	258	3.53	58	0.79	269	3.68	1,451	19.88
大阪府	Osaka	1,922	9.86	4,295	22.14	927	4.73	347	1.74	691	3.47	5,101	25.63
兵庫県	Hyogo	1,529	11.95	3,383	26.22	805	6.24	313	2.43	665	5.20	2,695	21.05
奈良県	Nara	299	8.54	919	26.26	139	3.97	32	0.94	125	3.68	466	13.71
和歌山県	Wakayama	206	6.65	1,024	33.03	147	4.74	25	0.83	21	0.68	582	19.40
鳥取県	Tottori	245	12.89	454	23.89	513	27.00	28	1.47	17	0.89	205	10.79
島根県	Shimane	82	3.57	777	35.32	459	20.86	26	1.18	22	1.00	101	4.39
岡山県	Okayama	112	2.07	502	9.47	294	5.44	80	1.48	61	1.15	595	11.02
広島県	Hiroshima	330	4.65	1,693	23.85	573	8.07	90	1.27	60	0.85	1,036	14.59
山口県	Yamaguchi	165	3.37	1,225	25.52	687	14.31	89	1.89	101	2.15	715	15.21
徳島県	Tokushima	33	1.43	729	31.70	448	20.36	19	0.86	47	2.04	174	7.57
香川県	Kagawa	68	2.43	437	14.57	278	9.27	63	2.17	44	1.52	543	19.39
愛媛県	Ehime	276	7.46	991	26.78	773	20.89	72	1.95	45	1.25	381	10.30
高知県	Kochi	249	8.30	573	19.10	820	27.33	60	2.00	42	1.40	192	6.40
福岡県	Fukuoka	5,027	41.89	4,469	37.24	185	1.54	129	1.08	530	4.42	5,079	42.33
佐賀県	Saga	423	18.39	963	41.87	41	1.86	37	1.68	127	5.52	820	35.65
長崎県	Nagasaki	1,698	38.59	721	16.39	65	1.48	42	0.95	57	1.30	1,452	33.00
熊本県	Kumamoto	1,274	26.54	816	17.00	167	3.55	77	1.54	77	1.54	1,354	27.08
大分県	Oita	700	19.44	1,065	29.58	371	10.31	59	1.64	130	3.61	2,667	74.08
宮崎県	Miyazaki	420	11.67	2,626	75.03	127	3.63	80	2.22	89	2.47	455	12.64
鹿児島県	Kagoshima	950	17.59	1,294	23.96	120	2.22	86	1.59	140	2.55	2,353	42.78
沖縄県	Okinawa	38	1.12	393	11.56	225	6.82	71	2.15	115	3.38	336	9.88

*2015年は第50週までの暫定値
*provisional number

(感染症発生動向調査：2015年12月16日現在報告数)
(National Epidemiological Surveillance of Infectious Diseases: as of December 16, 2015)