Erythema infectiosum (Human parvovirus B19 infection)

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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.niid.go.jp/niid/images/iasr/37/431/de4311.pdf](http://www.niid.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), 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; [https://idsc.niid.go.jp/iasr/19/217/tpc217.html](https://idsc.niid.go.jp/iasr/19/217/tpc217.html)). In the 2015 season, the epidemic that started in the 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).

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 prod-ucts were reported. In 2008, the CLEIA method (chemiluminescent enzyme immunoassay), whose sensitivity was as high as 106 copies/ml, 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.