ISSN 0915-5813

IASR

Vol. 39 No. 8 (No. 462) August 2018
Infectious Agents Surveillance Report
https://www.niid.go.jp/niid/en/iasr-e.html

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

<THE TOPIC OF THIS MONTH>
Varicella/Herpes zoster: epidemiological trends and vaccines

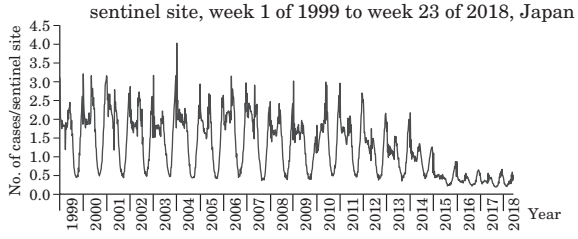
Varicella zoster virus (VZV), which belongs to the alpha herpesvirus subgenus of the herpesvirus family, is an etiologic pathogen of varicella (chickenpox) and herpes zoster (HZ). Varicella occurs in individuals infected with VZV for the first time causing maculopapular rashes to develop on all skin surfaces after the approximately 2-week incubation period (10-21 days), which then become vesicles. Varicella is characterized by the mixed presentation of macular, papular, vesicular, and encrusted lesions over the entire body and is often accompanied by fever. Varicella is a febrile rash syndrome that is common in childhood with a good prognosis. Individuals are infected with VZV through direct contact, droplet, and air-borne routes, and it is highly transmissible. Complications, such as secondary bacterial infections of the skin, pneumonia, meningitis, encephalitis, and cerebellar dysfunction, may occur. Varicella is designated as a Class II school infectious disease in the School Health and Safety Act, and school attendance is prohibited until all exanthem become encrusted. Varicella in adults is often severe, and for immunocompromised patients, it is extremely serious and can be life-threatening.

After infection, VZV establishes lifelong latency, mainly in the dorsal root ganglia (sensory ganglia including trigeminal ganglia), and can be reactivated due to aging and immunosuppression. The reactivated VZV reaches epithelial cells in skin innervated by the ganglia and causes HZ. VZV contained in vesicular fluid and respiratory tract secretions, including saliva, is infectious. Postherpetic neuralgia (PHN), a complication of HZ, is a condition in which pain persists for more than 3 months after skin lesions have healed, for which older age is an important risk factor.

National Epidemiological Surveillance of Infectious Diseases (NESID): Varicella is designated as a Category V infectious disease under the Infectious Diseases Control Law, and the number of varicella case patients is reported weekly from approximately 3,000 pediatric sentinel sites nationwide (https://www.niid.go.jp/niid/images/iasr/34/404/de4041.pdf).

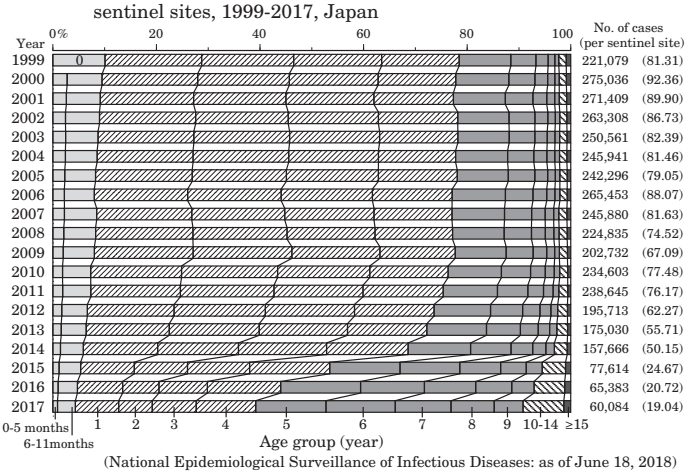
Since the Infectious Diseases Control Law was implemented in 1999, approximately 200,000 varicella cases have been reported annually from the pediatric sentinel sites, and the number of medically attended cases was estimated to be 1 million. The reported number of varicella cases from the pediatric sentinel sites was fewer than 200,000 in 2012 and it has decreased further since, reaching approximately 150,000 in 2014. The varicella vaccine was introduced into the routine immunization program for children in October 2014, after which the reported number of cases greatly decreased (Figure 1). Infants and children aged 0 to 4 years accounted for 70-80% of cases until 2014; however, their proportion has decreased since 2015, reaching approximately 40% in 2017. Although the proportion of cases aged 5 to 14 years among the total number of reported cases increased, the number of reported cases in this age group decreased (Figure 2).

Figure 1. Weekly number of reported varicella cases per pediatric sentinel site, week 1 of 1999 to week 23 of 2018, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of June 18, 2018)

Figure 2. Age distribution of varicella cases reported from pediatric sentinel sites, 1999-2017, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of June 18, 2018)

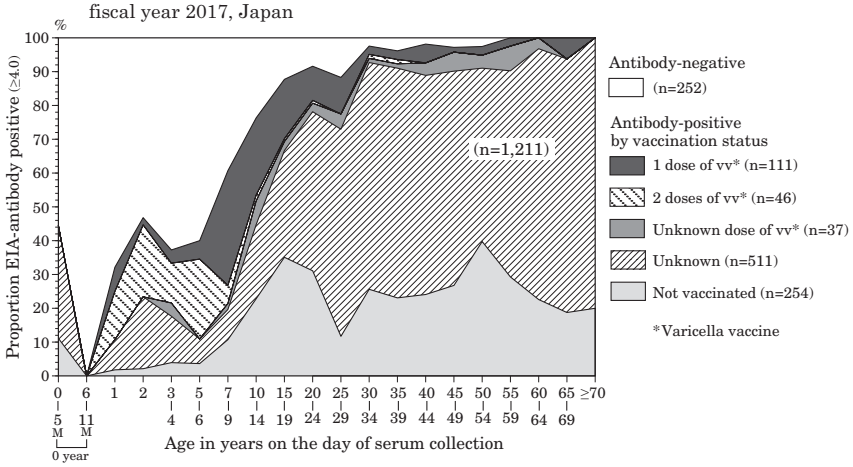
Prior to the introduction of the varicella vaccine into the routine immunization program, all varicella patients who required 24 or more hours of hospitalization were subject to notification from the 38th week of 2014 (15-21, September 2014). The notification included patients who were hospitalized for reasons other than varicella but developed varicella during hospitalization and who were hospitalized for 24 hours or more after varicella onset (https://www.mhlw.go.jp/bunya/kenkou/kekkaku-kansenshou11/01-05-140912-2.html). After the introduction of the varicella vaccine into the routine vaccination program, the proportion of children with varicella <5 years of age decreased from 34% to 11%. In 2017, 70% of hospitalized varicella patients were adults (see p. 131 of this issue).

Introduction of the varicella vaccine as a routine immunization: The varicella vaccine (Oka strain), a live-attenuated VZV vaccine that was developed in Japan in

(Continued on page 130′)

(THE TOPIC OF THIS MONTH-Continued)

Figure 3. Proportion varicella zoster virus antibody positive by age and vaccination status, fiscal year 2017, Japan



(National Epidemiological Surveillance of Vaccine-Preventable Diseases: as of March, 2018)

1974, became included in the voluntary immunization schedule in 1987, and was entered into the routine immunization program in October 2014 when varicella became a disease subject to routine vaccination (category A diseases). Varicella occurring in previously immunized individuals, known as breakthrough varicella (BV), is generally clinically mild. Therefore, it is recommended in Japan that children 12 and 36 months of age receive the vaccine twice, at least 3 months apart (6 to 12 months as a standard) between the first and the second vaccinations, to reduce the risk of BV occurrence. A study carried out in Aichi Prefecture demonstrated that the two-dose vaccination program was highly effective (see p. 132 of this issue). In the United States, the varicella vaccine has been included in the routine immunization program since 1996 and a two-dose vaccination schedule has been followed since 2006.

Seroprevalence of VZV antibody: The VZV antibody positivity in children aged 1, 2, and 3-4 years were 32.1%, 46.8%, and 37.3%, respectively, according to the National Epidemiological Surveillance of Vaccine-Preventable Diseases in FY2017 (Figure 3). Although the VZV antibody-positivity in 1-year-old children increased considerably following the introduction of the varicella vaccine into the routine immunization program, the positivity was still below 50% in children. The antibody-positivity was 95.2% for adults ≥20 years of age (see p. 133 of this issue), indicating that most adults are immune to VZV. As varicella in adulthood often becomes severe, it is recommended that those without a history of varicella or VZV vaccination be vaccinated (see p. 135 of this issue).

Herpes zoster vaccines: The HZ vaccine is effective in reducing the incidence and/or severity of HZ, and indirectly reduces the risk of PHN.

Among those such as the elderly, those who receive immunosuppressive drugs, and patients with organ transplants, VZV is reactivated from latency more frequently and the risk of HZ is higher (see p. 136 of this issue). It has been pointed out in the HZ epidemiological studies in Hyogo and Miyazaki prefectures that, due to routine varicella vaccination for children in recent years, opportunities for people to be exposed to VZV have decreased, reducing the boosting effect by natural infection. It has also been pointed out that the number of patients with HZ may increase with the aging of the population in Japan (see pp. 138 & 139 of this issue).

The freeze-dried live attenuated varicella vaccine was approved for prevention of HZ in adults ≥50 years of age in Japan in 2016. Thus, it is possible to receive the freeze-dried live attenuated varicella vaccine in order to prevent HZ (see p. 141 of this issue). However, the vaccine should not be administered to pregnant women, patients with clear indications of abnormal immune function, or those receiving immunosuppression therapy (persons considered to be inappropriate subjects for inoculation).

The freeze-dried recombinant HZ vaccine (Chinese Hamster Ovary cell origin) is a subunit vaccine with adjuvant $AS01_B$ added to recombinant glycoprotein E (gE), which was approved in the US and Canada in October 2017, and in Europe and Japan in March 2018 (see p. 142 of this issue). Efficacy of the vaccine was confirmed in large-scale clinical studies. However, it should not be used as a varicella vaccine. It should be administered intramuscularly twice, with at least 2 months between the first and second inoculations, for adults ≥ 50 years of age. Thus far, there have been no reports such as an increase in severe adverse events or autoimmune diseases due to the vaccine.

Antiviral therapy for varicella and HZ: Varicella and HZ can be treated by nucleoside analogues such as acyclovir, valacyclovir, and famciclovir. A novel drug for the treatment of HZ, the helicase-primase inhibitor amenamevir, was recently introduced as an anti-HZ drug in Japan (see p. 144 of this issue).

Laboratory diagnosis: Usually, varicella and HZ are diagnosed clinically. However, in the case of BV or atypical exanthem, virological tests are required for diagnosis. VZV DNA can be detected by PCR using specimens such as skin vesicular fluid, cerebral spinal fluid (when central nervous system infection is suspected), or peripheral mononuclear cells. The VZV antigen can also be detected. Virus isolation using vesicular fluids is also useful, although this method is more time consuming. An EIA method for the detection of the specific VZV-IgM or VZV-IgG antibody may also be used as a serological test. Details of the laboratory testing methods can be found in the laboratory manual for pathogen detection from the National Institute of Infectious Diseases (https://www.niid.go.jp/niid/ja/labo-manual.html#class5).

Summary: The reported number of varicella cases has markedly decreased due to the introduction of the varicella vaccine into the routine immunization program. On the other hand, the progressively aging population has been associated with an increase in the number of HZ patients. In the future, a high vaccination coverage for the varicella vaccine in children should be maintained, and the HZ vaccine should also be considered for prevention of HZ.

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.

Infectious Disease Surveillance Center, National Institute of Infectious Diseases
Toyama 1-23-1, Shinjuku-ku, Tokyo 162-8640, JAPAN Tel (+81-3)5285-1111