January 2025



Note: For **Prevention and Management of Varicella Exposures in Healthcare Settings**, see pages 8-9

## Varicella-Zoster Virus (VZV) infections

In susceptible persons, VZV infection causes primary varicella (chickenpox). After initial infection, VZV remains latent and can reactivate at a later time causing herpes zoster (shingles). Shingles is characterized by grouped vesicular lesions in the distribution of 1–3 sensory dermatomes, sometimes accompanied by pain and/or itching. For more information regarding shingles, see the Zoster Quicksheet.

## Infectious period

From 1–2 days before rash onset and continuing until all lesions are crusted (usually about 5 days).

## Incubation period

10–21 days from exposure to varicella rash onset, most commonly 14–16 days. Incubation period may be up to 28 days in persons who have received varicella-zoster immune globulin (VariZIG) after an exposure and may be shortened in immunocompromised patients. Varicella can develop after birth in infants born to people with active varicella around the time of delivery; the usual interval from onset of rash in a birthing parent to onset in the neonate is 9 to 15 days.

#### Course of infection

In children, varicella lesions are often the first sign of disease. Both adults and children may have 1–2 days of fever and malaise prior to rash onset. Varicella rashes are pruritic, generalized and progress from macules to papules to vesicular lesions before crusting. Two to four successive crops of lesions will appear over several days and will be in several stages of development. Lesions may first appear on the chest, back and face and then spread over the entire body, with the highest concentration of lesions on the trunk (centripetal distribution). Typical varicella cases have about 250–500 lesions. Breakthrough varicella (infection in a vaccinated person) tends to be milder with fewer lesions (usually <50) and mild or no fever. Infants, adults, pregnant persons, and individuals with compromised immune systems are at higher risk for severe or complicated disease (see page 5).

## **Complications**

- · Bacterial infections of the skin and soft tissues
- Infection of the lungs (pneumonia)
- Infection or swelling of the brain (encephalitis, cerebellar ataxia)
- Bleeding problems (hemorrhagic complications)
- Bloodstream infections (sepsis)

## State reporting requirements

- Persons who were hospitalized or died due to primary varicella (chickenpox) infection.
- Varicella (chickenpox) outbreaks (≥3 cases).

- Single, non-hospitalized varicella (chickenpox) cases are <u>not</u> reportable unless a part of a cluster or outbreak.
- Herpes zoster (shingles) cases are <u>not</u> reportable, including disseminated herpes zoster cases.

Note: Varicella cases that are not reportable may come to public health attention because of concerns related to the setting (for example congregate, school, or healthcare setting) or because they are part of an outbreak.

# Case definition (January 2024)

## Clinical criteria

In the absence of a more likely diagnosis:

- An acute illness with a generalized rash with vesicles (maculopapulovesicular rash), OR
- An acute illness with a generalized rash without vesicles (maculopapular rash).

In vaccinated persons who develop "breakthrough" varicella more than 42 days after vaccination, the disease is almost always mild with fewer than 50 skin lesions and shorter duration of illness. The rash may also be atypical in appearance (maculopapular with few or no vesicles).

## Laboratory criteria

## Confirmatory:

- Positive polymerase chain reaction (PCR) for varicella-zoster virus (VZV) DNA, OR
- Positive direct fluorescent antibody (DFA) for VZV DNA, OR
- Isolation of VZV, OR
- Significant rise (i.e., at least a 4-fold rise or seroconversion) in VZV IgG antibody.

## Supportive:

Positive test for serum VZV immunoglobulin M (IgM) antibody.

## Epidemiologic linkage

## Confirmatory:

- Exposure to or contact with a laboratory-confirmed varicella case, OR
- Can be linked to a varicella cluster or outbreak containing ≥1 laboratory-confirmed case, OR
- Exposure to or contact with a person with herpes zoster (regardless of laboratory confirmation).

#### Presumptive:

Exposure to or contact with a probable varicella case that had a generalized rash with vesicles.

#### Healthcare record criteria

A person whose healthcare record contains diagnosis of varicella or chickenpox but no rash description.

## Case classification

#### Confirmed:

- Meets clinical evidence AND confirmatory laboratory evidence, OR
- Meets clinical evidence with a generalized rash with vesicles AND confirmatory epidemiologic linkage evidence.

#### Probable:

- Meets clinical evidence with a generalized rash with vesicles, OR
- Meets clinical evidence with a generalized rash without vesicles, AND:
  - o confirmatory or presumptive epidemiologic linkage evidence OR
  - supportive laboratory evidence OR
- Meets healthcare record criteria AND:
  - o confirmatory or presumptive epidemiologic linkage evidence, OR
  - confirmatory or supportive laboratory evidence

## Specimen collection for PCR and virus isolation

- A PCR assay can detect VZV nucleic acid in vesicle swabs, scabs, or lesions.
- For PCR, the ideal specimens include vesicles and scabs. Scrapings of maculopapular lesions
  are appropriate if vesicles and scabs are not present. In cases with neurological symptoms,
  cerebrospinal fluid can also be tested.
  - Remove several scabs (a glass slide is useful for this purpose) and place in a clean, dry container. Swab basal cells from the unroofed lesion. Place swab in clean, dry container. Swabs submitted for PCR should be sent dry rather than diluted in viral transport media (VTM).
  - See <u>VRDL specimen shipping guidelines and current submittal form</u> (navigate to "General Purpose Specimen Submittal Form (PDF)").
  - Contact VRDL for additional laboratory testing and shipping questions:
    - Email: <u>VRDL.submittal@cdph.ca.gov</u>
    - Phone: (510) 307-8585
    - Shipping address:

Viral and Rickettsial Disease Laboratory

Attn: Specimen Receiving 850 Marina Bay Parkway Richmond, CA 94804

# Varicella exposure definition

- Varicella exposure can occur from direct contact with or aerosolization of lesion material, or through respiratory aerosols from an infectious person with primary varicella.
- The CDC definition of exposure to primary varicella includes close contact with an infectious person, such as close indoor contact (e.g., in the same room) or face-to-face contact, without recommended personal protective equipment (PPE). Experts differ in their opinion about the duration of contact; some suggest 5 minutes and others up to 1 hour. Exposure does not include transitory contact.
- Persons with shingles can also transmit VZV; exposure to a person with shingles can result in primary varicella in a susceptible person. Please refer to the <u>Zoster Quicksheet</u> for shingles exposure definitions.

#### **Exposure management**

- Note: Because only a subset of varicella cases are reportable, not all varicella exposures are managed with public health input.
- Exposed persons who are known to be at high risk of severe disease (see page 5) should be contacted by phone as soon as possible.
- For all exposed persons, determine if the exposed person:
  - Has presumptive evidence of immunity (see page 4); or

- Has high-level immunosuppression (see page 5); or
- Had anyone else with them at the time of the exposure, and whether that person is high-risk, unvaccinated, or a healthcare worker.

## Recommendations for isolation, quarantine, and exclusion

- For Prevention and Management of Varicella Exposures in Healthcare Settings, see pages 8-9.
- Infectious persons should be isolated until all lesions are crusted (usually about 5 days).
- Vaccinated persons with breakthrough varicella may develop lesions that don't crust (macules/papules only). Such persons should be isolated until no new lesions appear for 24-hours.
- For healthcare personnel with varicella (chickenpox), exclude from work until all lesions have dried and crusted; or, for those who only have non-vesicular lesions that do not crust, exclude from work until no new lesions appear within a 24-hour period.
- Because of the high likelihood of infection, school exclusion of nonimmune siblings of cases from day 8 after sibling's rash onset through day 21 after the last day the sibling was infectious is reasonable.
- There are no specific public health recommendations for quarantine or exclusion of contacts to varicella cases in non-outbreak and non-healthcare settings; however, as a control measure, exclusion of unvaccinated or under-vaccinated child or adult contacts from high-risk settings can be considered.
- Exposed persons without evidence of immunity who have contraindications to vaccination (e.g., immunocompromised persons, pregnant women) should be excluded from an outbreak setting through 21 days after rash onset of the last identified case because of the risk of severe disease in these persons.
- CDC defines a varicella outbreak as ≥3 cases that are related in time and place. However, single
  cases in a high-risk setting, e.g., healthcare facility, prison/jail, or homeless shelter, should be
  investigated.

#### Varicella outbreaks in schools

- Local health jurisdictions should weigh the risks and benefits of school exclusion of nonimmune students in the context of a new or ongoing outbreak.
- CDPH does not generally recommend that healthy students without evidence of varicella immunity be excluded from school during an outbreak. CDC recommends that students who do not have evidence of varicella immunity and whose parents refuse vaccination for them be excluded from school from the start of the outbreak through 21 days after rash onset of the last identified case.

#### **Evidence of immunity**

The criteria below provide evidence of immunity to varicella for the purposes of a contact investigation:

- Documentation of age-appropriate varicella vaccination
  - children 12 months through 3 years of age: 1 dose.
  - o persons 4 years of age and older: 2 doses.
- Laboratory evidence of immunity.
- Prior laboratory confirmation of disease.

- U.S. birth before 1980 (this should not be considered evidence of immunity for healthcare personnel, immunocompromised persons, pregnant women, and persons born outside the U.S.)
- Prior healthcare provider diagnosis or verification of a history of varicella or shingles.

## Postexposure prophylaxis (PEP)

Varicella vaccine as PEP may be effective in preventing illness or modifying illness severity if given within 3-5 days after first exposure.

- A second dose of varicella vaccine can be given to patients who have received only one dose and do not have contraindications:
  - o Children <13 years of age can receive second dose >3 months after their first dose.
  - o People >13 years of age can receive second dose >4 weeks after their first dose.
- Varicella zoster immune globulin (VariZIG) should be administered as soon as possible and within 10 days of first exposure to contacts at high risk of severe varicella infection (see flowchart on page 6).
- Antiviral PEP for healthy exposed, susceptible persons is not routinely recommended, however, acyclovir as PEP may be considered.

# Contacts at high risk of severe varicella infection

- Persons with high-level immunosuppression without evidence of varicella immunity (see definition below);
- Pregnant women without evidence of varicella immunity;
- Newborn infants whose mothers had onset of chickenpox within 5 days before delivery or within 48 hours after delivery;
- Hospitalized preterm infants (28 weeks or more of gestation) whose mother lacks evidence of immunity against varicella;
- Hospitalized preterm infant less than 28 weeks gestation or birth weight 1000 g or less, regardless of maternal immunity.

Per CDC and <u>IDSA guidance</u>, patients with high-level immunosuppression include those:

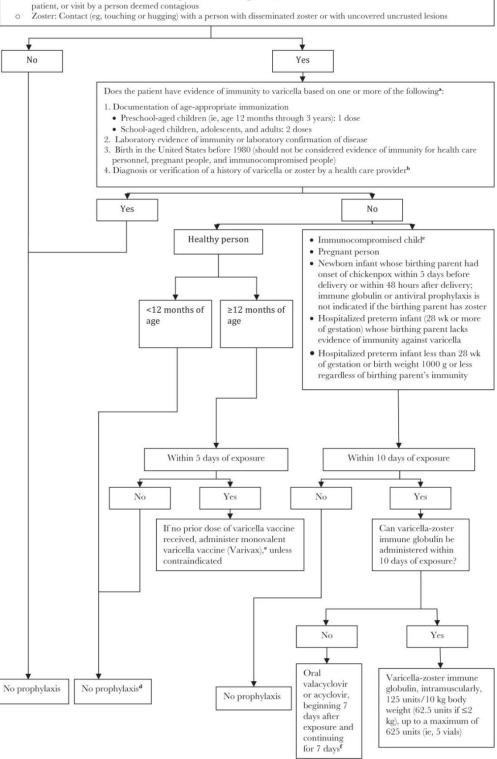
- with combined primary immunodeficiency disorder (e.g., severe combined immunodeficiency);
- who are receiving cancer chemotherapy;
- on treatment for acute lymphocytic leukemia (ALL) within and until at least 6 months after completion of immunosuppressive chemotherapy;
- within 2 months after solid organ transplantation;
- who have received a bone marrow transplant, until at least 12 months after finishing all immunosuppressive treatment, or longer in patients who have developed graft-versus-host disease;
- with HIV infection with a CD4 T-lymphocyte count <200 cells/mm³ for adults and adolescents and percentage <15 for infants and children;
- receiving daily corticosteroid therapy with a dose ≥20 mg (or >2 mg/kg/day for patients who weigh
   <10 kg) of prednisone or equivalent for ≥14 days; and</li>
- receiving certain biologic immune modulators, such as a tumor necrosis factor-alpha (TNF-α) blocker or rituximab.

# Management of Exposures to Varicella-Zoster

(From 2024-2027 AAP Red Book)

#### Significant exposure:

- · Household: residing in the same household
- Playmate: face-to-face indoor play ≥5 minutes (some experts use >1 hour)
- Newborn infant
- Hospital:
  - Varicella: In same 2- to 4-bed room or adjacent beds in a large ward, face-to-face contact with an infectious staff member or patient, or visit by a person deemed contagious



# Figure Legend

IGIV indicates immune globulin intravenous.

VariZIG is manufactured by Cangene Corporation (Winnipeg, Canada) and distributed in the United States by FFF Enterprises (Temecula, California; 800-843-7477) and ASD Healthcare (Frisco, Texas; 800-746-6273).

- <sup>a</sup> People who receive hematopoietic stem cell transplants (bone marrow transplants) should be considered nonimmune regardless of previous history of varicella disease or varicella vaccination in themselves or in their donors.
- <sup>b</sup> To verify a history of varicella vaccination in an immunocompromised child, health care providers should inquire about an epidemiologic link to another typical varicella case or to a laboratory confirmed case, or evidence of laboratory confirmation. Immunocompromised children who have neither an epidemiologic link nor laboratory confirmation of varicella should not be considered as having history of disease.
- c Immunocompromised children include those with congenital or acquired T-lymphocyte immunodeficiency, including leukemia, lymphoma, and other malignant neoplasms affecting the bone marrow or lymphatic system; children receiving immunosuppressive therapy, including ≥2 mg/kg/day of systemic prednisone (or its equivalent) for ≥14 days, and certain biologic response modifiers; all children with human immunodeficiency virus (HIV) infection regardless of CD4+ T-lymphocyte percentage; and all hematopoietic stem cell transplant patients regardless of pretransplant immunity status.
- d If the exposed person is an adolescent or adult, has chronic illness, or there are other compelling reasons to try to avert varicella, some experts recommend preemptive therapy with oral acyclovir (20 mg/kg per dose administered 4 times per day, with a maximum daily dose of 3200 mg) or oral valacyclovir (if ≥3 months of age; 20 mg/kg per dose administered 3 times per day, with a maximum daily dose of 3000 mg) beginning 7 to 10 days after exposure and continuing for 7 days. If the child is ≥12 months of age, age-appropriate vaccination still is recommended for protection against subsequent exposures, but vaccine should not be administered while antiviral therapy is being administered; if the exposure occurred during an outbreak, 2-dose vaccination is recommended for preschool-aged children younger than 4 years for outbreak control.
- e If 1 prior dose of varicella vaccine has been received, a second dose should be administered at ≥4 years of age. If the exposure occurred during an outbreak, a second dose is recommended for preschool-aged children younger than 4 years for outbreak control if at least 3 months have passed after the first dose.
- f If VariZIG and IGIV are not available, some experts recommend preemptive therapy with oral acyclovir (20 mg/kg per dose, administered 4 times per day, with a maximum daily dose of 3200 mg) or oral valacyclovir (if ≥3 months of age; 20 mg/kg per dose, administered 3 times per day, with a maximum daily dose of 3000 mg) beginning 7 to 10 days after exposure and continuing for 7 days. Preemptive oral acyclovir has only been studied in the normal host but sometimes is used in addition to VariZIG or IGIV in the immunocompromised host.

## Prevention and Management of Varicella Exposures in Healthcare Settings

## Preventing healthcare exposures

Ensure that your facility has protocols in place to:

- Utilize a phone triage to identify patients with symptoms of varicella and schedule them for care
  at the end of the day when other patients aren't present if possible.
- Promptly identify and isolate suspect varicella cases arriving at the facility who have not called ahead. Ensure that all staff have documentation of immunity to varicella.

## Infection control measures for suspected varicella patients in healthcare settings

- Do not allow patient to stay in the waiting room or other congregate areas.
- Immediately place a surgical mask on patient suspected to have varicella and place patient in an
  airborne infection isolation room (AIIR), if one is available, with the door closed. The patient may
  remove their mask only when in an AIIR with the door closed.
- If an AIIR is not available, place patient in a single person exam room with a closed door or evaluate patient in an outside location away from other patients.
- Only essential visitors and staff should be in the patient room. All staff should use personal protective equipment that includes:
  - respiratory protection (fit-tested N95 respirator or higher level of protection)
  - contact precautions (gowns and gloves)
- Use diligent hand hygiene before and after contact with the patient.
- Staff known to be susceptible to varicella should not enter the room.
- If possible, keep exam room vacant for 1 hour before using it for another patient; room can be cleaned using routine cleaning procedures. See <a href="CDC guidance">CDC guidance</a> about air changes per hour and time required for airborne-contaminant removal efficiency.
- If the patient is discharged home, advise patient to remain home until all lesions have crusted, which usually takes about 5 days.

# Hospital inpatient unit exposures

If exposure occurs in a hospital inpatient unit:

- All exposed patients without evidence of immunity should be discharged as soon as medically appropriate.
- Consider serologic testing of exposed patients whose varicella immune status is not known.
- For exposed patients without evidence of immunity who cannot be discharged, all staff should use
  personal protective equipment that includes respiratory protection (fit-tested N95 respirator or
  higher level of protection) and contact precautions (gown and gloves) from day 8 after the first
  exposure until 21 days after the last exposure to the index patient.
- Patients who receive VariZIG or IGIV should be isolated until through day 28 after the last exposure.

## Varicella contact investigation in a healthcare setting

- If the patient was not masked before or upon entry to facility and immediately placed in an AIIR, an exposure investigation should be conducted.
- Notify staff responsible for facility infection control immediately. If the exposure or response is large, facility leadership may need to be involved to facilitate response.

- Identify all potentially exposed patients, visitors, and staff based on shared airspace and/or direct contact.
  - If staff always used appropriate respiratory protection (fit-tested N95 respirator or higher level of protection) while sharing an airspace with the patient, and PPE when touching lesions, they are not considered exposed.
- Check the varicella immunity status of exposed staff; occupational health may be able to assist.
- Identify exposed patients, visitors, and staff who are non-immune or likely to be non-immune and/or who are at high-risk for severe infection (see above for discussion of high-risk individuals and PEP). Consider children who may not have yet been vaccinated as a high-yield group to review.
  - Ascertain whether immunization data are available for exposed patients. If no immunization data are in patient medical records, the California Immunization Registry (CAIR) may be queried. The local health department and CDPH can help check CAIR if the facility does not have access.
- As needed, coordinate rapid serologic testing for varicella immunity (varicella IgG) for high-risk contacts whose varicella immune status is not known.
- As needed, coordinate VariZIG or intravenous (IV) immune globulin (IG) for high-risk susceptible contacts, and/or varicella vaccine for low-risk susceptible contacts as post-exposure prophylaxis (PEP) according to recommendations.
  - o If PEP is indicated and it is within the time window for the indicated PEP, it is generally the healthcare facility's responsibility to arrange for PEP administration.
  - Healthcare facilities typically do not stock VariZIG so it may need to be rapidly ordered (see "Resources" section). Consider involving pharmacy early.
  - Primary care physicians and the local public health department may be able to assist with post-exposure vaccination.
- Contact persons with known high risk of severe disease by phone as soon as possible.
  - Determine if the exposed person (patients, visitors, and healthcare workers) meets presumption of immunity criteria (page 3):
  - Determine if the exposed person had anyone else with them at the time of the exposure, and if so, if those additional exposed individuals are high-risk, unvaccinated, or healthcare workers.
  - Arrange for serologic testing or PEP if indicated.
- Contact all other potentially exposed patients.
  - o If the number of patients is manageable, these patients can also be contacted by phone.
  - If the number of patients is too large for phone calls to be practical, a certified letter may be sent, or in some healthcare systems, an email.
  - A CDPH template letter is available upon request.

#### **Exposed healthcare workers (HCWs)**

- For asymptomatic HCWs without evidence of immunity:
  - Administer varicella vaccine as soon as possible or immune globulin if appropriate based on risk factors (page 5).
  - Exclude from work from the 8th day after the first exposure through the 21st day after the last exposure. Work restrictions are not necessary for healthcare personnel who received one dose of the varicella vaccine prior to exposure if they receive the second dose of vaccine within 5 days after exposure.
  - Implement daily monitoring for signs and symptoms of varicella from the 8th day after the first exposure through the 21st day after the last exposure. If symptoms develop, exclude from work if not already excluded.

- o If VariZIG is administered as postexposure prophylaxis, exclude from work from the 8th day after the first exposure through the 28th day after the last exposure.
- For asymptomatic HCWs with evidence of immunity (2 doses of vaccine, laboratory evidence of immunity, or prior laboratory confirmation of disease):
  - o Postexposure prophylaxis is not necessary.
  - Work restrictions are not necessary.
  - Implement daily monitoring for signs and symptoms of varicella from the 8th day after the first exposure through the 21st day after the last exposure; exclude from work if symptoms develop.

## Healthcare personnel with varicella

• For healthcare personnel with varicella (chickenpox), exclude from work until all lesions have dried and crusted; or, for those who only have non-vesicular lesions that do not crust, exclude from work until no new lesions appear within a 24-hour period.

For more information on HCWs exposed to varicella (chickenpox) and disseminated or localized herpes zoster (shingles) see: <u>Infection Control in Healthcare Personnel: Epidemiology and Control of Selected Infections Transmitted Among Healthcare Personnel and Patients.</u>

#### Resources

- Local health department contacts
- Chapter 17: Varicella | Manual for the Surveillance of Vaccine-Preventable Diseases | CDC
- AAP Redbook varicella chapter
- CDC Prevention of Varicella Recommendations of the Advisory Committee on Immunization
- <u>CDC/HICPAC Guidelines for Environmental Infection Control in Health-Care Facilities</u>
   (Table B.1. ACH and time required for airborne- contaminant removal by efficiency and Table B.2. Ventilation requirements for area affecting patient care in hospitals and outpatient facilities)
- CDC lab specimen collection guidance
- Information on VariZIG and IGIV administration is available at:
  - AAP Redbook varicella chapter
  - o Updated recommendations for the use of VariZIG United States, 2013
  - o <u>CDC Prevention of Varicella Recommendations of the Advisory Committee on Immunization Practices</u>