Varicella

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Key Points

- Varicella (chickenpox) is a contagious, viral disease characterized by fever, malaise, and pruritic maculopapular-vesicular rash.
- Since the introduction of the varicella vaccine in the United States in 1995, varicella cases from the wild virus have decreased dramatically. However, cases in those who have been vaccinated (breakthrough varicella) have increased.
- Before the availability of varicella vaccine, healthcare providers saw many cases of varicella and typically used clinical assessment for diagnosis. Because varicella is less common, fewer physicians have experience in diagnosis, making it a challenge.

Introduction

The Virus

- Varicella is caused by the varicella zoster virus (VZV), a DNA virus and member of the *Herpesviridae* family.
- VZV establishes latency in the sensory nerve ganglia. Primary VZV infection results in varicella. Reactivation of latent infection leads to herpes zoster (shingles).
- The virus is more contagious than mumps and rubella but not as contagious as measles.

Transmission

- Varicella is transmitted by respiratory droplets and by touching or breathing in aerosolized virus from varicella skin lesions.
- The disease can be transmitted from 1 to 2 days prior to rash onset until all lesions have crusted.
- The incubation period is 14 to 16 days after exposure (range from 10 to 21 days).
- Varicella is very contagious.
    - From 60% to 90% of susceptible persons will develop varicella after exposure.
    - If a member of a household becomes infected, usually all susceptible persons in the household become infected.
    - Transmission in pediatric healthcare facilities has occurred.
    - A child who has breakthrough varicella is about one-third as contagious as an unvaccinated child with varicella if the disease is mild (<50 lesions). A child with >50 lesions is equally contagious. (See Breakthrough in Vaccinated People.)

Epidemiology

Before the varicella vaccine was introduced, varicella was a nearly universal childhood disease in the United States. More than 4 million people acquired varicella every year, resulting in approximately 120 deaths and 10,000 hospitalizations. The introduction of the vaccine dramatically reduced the burden of disease (Table 1).

Table 1. Results of Varicella Vaccination in the United States: 1994 – 2010

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Table 1. Results of Varicella Vaccination in the United States: 1994 - 2010

	Before US Vaccination Began (1994)	After 15 Years of Vaccination (2010)
Varicella cases per year	>4 million	<350,000 (92% decrease)
Hospitalizations per year	>10,000	<1700 (84% decrease)
Deaths per year	>100	<20 (90% decrease)

Information from Chicken Pox (Varicella). Centers for Disease Control and Prevention website. http://www.cdc.gov/chickenpox/vaccine-infographic.html#text. Updated November 18, 2014. Accessed January 29, 2016.

Assessment and Diagnosis

Clinical Assessment

Clinical presentation will vary, depending on whether or not the individual has received the varicella vaccine.

Unvaccinated People

- The prodrome of varicella is characterized by fever and malaise and may occur 1 to 2 days before rash onset. In children the first sign may be rash.
- A generalized, pruritic rash appears first on the head, chest, and back before spreading to the rest of the body. The lesions progress quickly from macules to papules to vesicular lesions before crusting. Lesions appear in "crops" with stages of development varying in different parts of the body.
- The torso usually has the most lesions. A typical case of varicella has from 250 to 500 lesions but they can range from 10 to 1,500.

Breakthrough Varicella in Vaccinated People

- Varicella that develops >42 days after vaccination is called "breakthrough varicella."
- Breakthrough varicella is generally less severe and atypical in presentation:
    - Low grade or absence of fever
    - <50 lesions
    - Rash more likely to be maculopapular
    - Shorter duration of illness (4 to 6 days)
- In 25% to 30% of cases, the clinical presentation is similar to varicella in unvaccinated people.

Diagnosing breakthrough varicella is difficult. Because of the atypical presentation, varicella lesions can be mistaken for bug bites or other rashes. See Resources for help on diagnosing breakthrough varicella.

Laboratory Diagnosis

- The most frequently used laboratory tests to confirm VZV are direct antigen detection (direct fluorescent antibody [DFA]) and DNA detection methods (polymerase chain reaction [PCR]).
- The preferred specimen for confirmation of varicella disease is skin lesions.
- Serology may be used to test for varicella immunity.
- PCR is a reliable and sensitive method used to detect VZV in skin lesions. Vesicular lesions are best, but maculopapular lesions collected with proper technique can be used.
- See Resources for a link to 4-minute video that shows appropriate procedures for collecting VZV skin lesions and blood specimens.
- For a full discussion of laboratory testing for VZV, see Laboratory testing for Varicella on the CDC website.

Management

Supportive Management

Management of varicella is supportive, including the following:

- Recommend using cool compresses and trimming patient's fingernails to avoid scratching of lesions.
- Monitor for skin infections.
- Maintain hydration.
- Use antipyretics but avoid salicylates due to the risk of Reye syndrome.
- Isolate patient until complete crusting of the rash.
- Monitor for signs and symptoms of serious complications. These include altered consciousness, seizures, difficulty walking, respiratory distress, cyanosis, and low oxygen saturation. Others are prolonged or recurrence of fever and continued eruption of new lesions into the second week.

Treatment of Varicella

- Routine use of antiviral therapy in otherwise healthy children with varicella is not recommended.
- Acyclovir or valacyclovir for infants, children, and adolescents at increased risk of moderate-to-severe varicella may be indicated (Table 2).
    - Therapy should be initiated within 24 hours of onset of rash.
    - Do not use oral acyclovir to treat immunocompromised individuals with varicella because of its poor bioavailability.
- Intravenous acyclovir therapy is recommended for immunocompromised persons. Initiate therapy early, within 24 hours of rash onset, for most benefit.
- VariZIG is useful for postexposure prophylaxis. It is not recommended for use once disease has begun.

Table 2. Recommended Acyclovir and Valacyclovir Dosing

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Table 2. Recommended Acyclovir and Valacyclovir Dosing

Drug	Age	Oral Dosing	Maximum Dose
Acyclovir	Children 2 years of age and older	20 mg/kg per dose 4 times daily for 5 days	3200 mg maximum *daily* dose
	Children >40 kg and adults	800 mg per dose 4 times daily for 5 days	
Valacyclovir	Children from 2 to <18 years of age	20 mg/kg per dose 3 times daily for 5 days	Not to exceed 1000 mg 3 times daily

Complications

- The risk of severe disease and complications are increased in infants, adolescents, adults, immunocompromised persons, and pregnant women.

- The most common complications are
  - Bacterial infections of the skin and soft tissues in children
  - Pneumonia in adults
- Severe complications include necrotizing fasciitis, septicemia, toxic shock syndrome, osteomyelitis, pneumonia (bacterial and viral), and septic arthritis. Others are encephalitis, cerebellar ataxia, Reye syndrome, and hemorrhagic conditions.

Complications of Varicella in Immunocompromised People

Complications and severe disease in immunocompromised people include

- Visceral dissemination, leading to pneumonia, hepatitis, encephalitis
- Disseminated intravascular coagulopathy
- Atypical varicella rash with more lesions, which may appear on palms and soles
- Hemorrhagic lesions
- Lesion eruption continuing for up to 10 days
- Increased duration of the disease

Complications of Varicella in HIV-Infected Children

- Children with HIV infection may have
  - New crops of lesions appearing for weeks
  - Lesions that don’t heal and become necrotic, crusted, and hyperkeratotic
  - Visceral dissemination, which may occur but is less frequently observed than with other cellular immunodeficiencies
- Children receiving antiretroviral therapy or those with higher CD4 counts at the time of infection may have fewer complications.
- Retinitis can occur in children and adolescents.

Prevention

Vaccination

- Two live attenuated varicella virus vaccines are available:

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Single-antigen varicella vaccine (VARIVAX)	Licensed for use in healthy children ≥12 months, adolescents, and adults
Combined measles, mumps, rubella, and varicella (MMRV) vaccine (ProQuad)	Licensed for use in healthy children aged 12 months to 12 years

- Studies show that 1 dose of single-antigen varicella vaccine is 85% effective in preventing the disease. This was insufficient for preventing outbreaks.
- Currently, a 2-dose vaccination schedule is recommended.
- Single-antigen and combination MMRV vaccines may be given simultaneously with other vaccines recommended for children aged 12 to 15 months and children aged 4 to 6 years.
- If not administered at the same visit or as MMRV vaccine, the interval between administration of a varicella-containing vaccine and measles-mumps-rubella (MMR) vaccine should be at least

28 days.
- There is a slightly increased risk of febrile seizures associated with the higher likelihood of fever following the first dose of MMRV compared with MMR and monovalent varicella.

Vaccination Recommendations

In 2007, the Advisory Committee on Immunization Practices (ACIP) updated recommendations for varicella vaccination (Table 3).

Table 3. Varicella Immunization Recommendations

To view a larger image on your device, please click or touch the image.

Table 3. Varicella Immunization Recommendations

Varicella Immunization Recommendations		

1	**Children >13 years of age**	• Routine 2-dose vaccination of children
		  • 1st dose: 12 to 15 months
		  • 2nd dose: 4 to 6 years (before entering preschool, kindergarten, or first grade)
		• Recommended vaccination interval for children aged 12 months to 12 years is 3 months. However, if the 2nd dose was given ≥28 days after the 1st dose, then the 2nd dose is considered valid and need not be repeated.

2	**Catch up vaccination**	• Second dose catch up vaccination for children, adolescents, and adults who previously had received 1 dose. • Recommended minimum interval is 3 months for children ≤12 years and 4 weeks for persons aged ≥13 years. However, the catch-up 2nd dose may be given at any interval >minimum interval.
3	**Healthy persons ≥13 years without evidence of immunity**	• Routine 2-dose vaccination of all healthy persons aged ≥13 years without evidence of immunity. • For healthy persons aged ≥13 years, recommended minimum interval between doses is 4 to 8 weeks. If >8 weeks elapse after the 1st dose, the 2nd dose may be given without repeating the first dose. • Use only single-antigen varicella vaccine in this age group. MMRV is not licensed for use in persons ≥13 years.
4	**Prenatal assessment and postpartum vaccination**	• Prenatal assessment for evidence of varicella immunity. • Postpartum vaccination upon completion or termination of pregnancy with 2nd dose 4 to 8 weeks later. • Counsel women to avoid conception for 1 month after each dose of varicella vaccine.
5	**Use in HIV-infected persons**	• Use of the varicella vaccine for HIV-infected children with age-specific CD4+T lymphocyte percentages of 15% to 24% and adolescents and adults with CD4+T lymphocyte counts >200 cells/μL. • Eligible persons should receive 2 doses of single-antigen varicella vaccine 3 months apart.
6	**School vaccination requirements**	Required vaccination for entry to child care, school, college, and other postsecondary educational institutions.

Information from Marin M, Güris, Chaves SS, Schmid S, Seward, JF. Prevention of Varicella: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *Morb Mortal Wkly Rep.* 2007;56(RR04):1-40. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5604a1.htm. Accessed March 1, 2016.

Vaccination in People with Possible Immunodeficiency

In 2007 ACIP made the following recommendations for situations where some degree of immunodeficiency might be present in those without evidence of immunity (Table 4).

Table 4. Vaccination in Situations in Which Some Degree of Immunodeficiency Might Be Present

To view a larger image on your device, please click or touch the image.

Table 4. Vaccination in Situations in Which Some Degree of Immunodeficiency Might Be Present

Persons	Vaccination Considerations
Who have impaired humoral immunity	May be vaccinated.
Who are receiving inhaled, nasal, or topical doses of steroids	
Who are receiving systemic steroids and are not otherwise immunocompromised	• May be vaccinated if they are receiving <2 mg/kg of body weight or a total of <20 mg/kg day of prednisone or its equivalent if patient is ≥10 kg. • Consider withholding steroids for 2 to 3 weeks after vaccination if it can be done safely.
Who are receiving high doses of systemic steroids (ie, ≥2 mg/kg prednisone) for ≥2 weeks	May be vaccinated once steroid therapy has been discontinued for ≥1 month.
With leukemia, lymphoma, or other malignancies	If disease is in remission and chemotherapy has been terminated for at least 3 months, patient can receive live-virus vaccine.* *Vaccination of children with leukemia should be undertaken only with expert guidance and availability of antiviral therapy in case of complications.

Information from Marin M, Güris, Chaves SS, Schmid S, Seward, JF. Prevention of Varicella: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *Morb Mortal Wkly Rep*. 2007;56(RR04):1-40. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5604a1.htm. Accessed March 1, 2016.

Precautions and Contraindications to Varicella Vaccination

- Severe allergic reaction to a vaccine component or following a prior dose
- Persons who have any malignant condition
- Immunocompromised individuals
- Persons receiving high-dose systemic immunosuppressive therapy, including persons on oral steroids ≥2 mg/kg of body weight or a total of ≥20 mg/kg day of prednisone or equivalent for persons who weight >10 kg, when administered for ≥2 weeks
- Persons who have a family history of congenital or hereditary immunodeficiency in first-degree relatives unless immune competence has been verified
- Acute severe illness, including untreated, active tuberculosis
- Recent administration of blood, plasma, or immune globulin
- Pregnancy
- Use of salicylates (avoid using for 6 weeks after receiving varicella vaccine)

Adverse Events after Vaccination

Complications

- Severe complications caused by the vaccine virus strain are rare.
- Laboratory-confirmed complications include pneumonia, hepatitis, severe disseminated varicella infection, and secondary transmission.
- Except for the secondary transmission cases, complications only occurred in immunocompromised patients or those who had undiagnosed serious medical conditions at the time of vaccination.

Reporting

- Healthcare providers are required to report adverse events for varicella vaccines. See Resources for how to report an adverse event related to varicella vaccination.
- Healthcare providers also should obtain appropriate clinical specimens for laboratory evaluation, including strain identification. Examples are cerebrospinal fluid for encephalitis and bronchial lavage or lung biopsy for pneumonia. See Resources for contact information regarding strain identification.

Postexposure Prophylaxis

Passive Immunoprophylaxis

- VariZIG is reserved for high-risk individuals (see Indications for VariZIG).
- VariZIG should be administered as soon as possible and no later than 10 days from exposure.
    - If VariZIG is unavailable, then intravenous immune globulin (IVIG) should be used.
    - VariZIG and IVIG may prolong the incubation period of varicella.
    - Any patient receiving passive immunoprophylaxis should be isolated for 28 days and monitored for the development of signs and symptoms of varicella.

Indications for VariZIG

Indications for VariZIG are the following:

- Immunocompromised patients
- Neonates whose mothers have signs and symptoms of varicella around the time of delivery (ie, 5 days before to 2 days after)

- Premature infants born at ≥28 weeks of gestation who are exposed during the neonatal period and whose mothers do not have evidence of immunity
- Premature infants born at <28 weeks of gestation or who weigh ≤1000 g at birth and were exposed during the neonatal period, regardless of their mothers' evidence of immunity status
- Pregnant women

Dosing

- VariZIG is supplied in 125-IU vials and is administered intramuscularly (Table 5).

Table 5. Recommended VariZIG Dosing

To view a larger image on your device, please click or touch the image.

Table 5. Recommended VariZIG Dosing

Delivery	Patient Weight	Dosing	Maximum Dose
IM	>10 kg	125 IU/10 kg of body weight	625 IU (five vials)
	2.1 kg to 10 kg	125 IU (1 vial)	
	≤2 kg	62.5 IU (0.5 vial)	

Intramuscular (IM)

- If eligible, administer varicella vaccine 5 months after administration of VariZIG.
  - IVIG dosing is 400 mg/kg as a single dose.
- If VariZIG is unavailable, some experts recommend the use of acyclovir (Table 6). Therapy should begin 7 to 10 days after exposure.

Table 6. Recommended Acyclovir Dosing

To view a larger image on your device, please click or touch the image.

Table 6. Recommended Acyclovir Dosing

Delivery	Dosing	Maximum Dose
Oral	80 mg/kg/day administered in 4 divided doses for 7 days	800 mg, 4 times a day

Postexposure Varicella Immunization

Postexposure varicella immunization of susceptible person (>1 year of age) within 5 days of exposure may modify or prevent the disease.

To view a larger image on your device, please click or touch the image.

If given . . .	Vaccine is . . .
Within 3 days of exposure	≥90% effective in preventing varicella
Within 5 days of exposure	70% effective in preventing varicella 100% effective in modifying severe disease
After 5 days of exposure	Vaccination is still recommended to provide protection against future exposures.

Information from Marin M, Güris, Chaves SS, Schmid S, Seward, JF. Prevention of Varicella: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *Morb Mortal Wkly Rep*. 2007;56(RR04):1-40. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5604a1.htm. Accessed March 1, 2016.

Resources

- **Chickenpox (Varicella):** For Healthcare Professionals (CDC)
- **Breakthrough Varicella.** For help in diagnosing breakthrough varicella, see slides 6 to 11 in the following CDC slide set "Varicella and Breakthrough Varicella: To Test or Not to Test."
- Perinatal Varicella Exposure (ANGELS Guideline)
- Varicella Exposure and Treatment During Pregnancy (ANGELS Guideline)
- Procedures for Collecting VZV Skin Lesions and Blood Specimens (CDC video)
- Laboratory Testing (CDC)
- Immunization Schedules (CDC)
- **Strain Identification.**
  - Merck's VZV Identification Program—telephone: 1-800-652-6372
  - CDC's National Varicella Reference Laboratory—telephone: 404-639-0066; e-mail: vzvlab@cdc.gov
- **Adverse Event Reporting.** If you suspect an adverse event caused by varicella vaccine, report it to one of the following:
  - Vaccine Adverse Event Reporting System (VAERS)
  - MedWatch: The FDA Safety Information and Adverse Event Reporting Program
  - 24-hour VAERS information recording at 1-800-822-7967

This guideline was developed to improve health care access in Arkansas and to aid health care providers in making decisions about appropriate patient care. The needs of the individual patient, resources available, and limitations unique to the institution or type of practice may warrant variations.

References

References

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