Varicella Zoster

Also known as: Chickenpox, VZV-varicella zoster virus

Responsibilities:
Hospital: Report outbreaks
Infection Preventionist: Report outbreaks
Physician: Report outbreaks
Follow-up of investigation by Local Public Health Agency (LPHA): outbreaks only

Iowa Department of Public Health
Disease Reporting Hotline: 1-800-362-2736

1) THE DISEASE AND ITS EPIDEMIOLOGY

A. Agent:

Varicella-Zoster is a member of the herpesvirus family.

B. Clinical Description

Symptoms: Primary infection results in varicella (chickenpox). A mild prodrome may precede the onset of a rash. Adults may have 1 to 2 days of mild fever and malaise. Prior to rash onset, but in children the rash is often the first sign of disease.

The rash is generalized, pruritic, and rapidly progresses from macules to papules to vesicular lesions before crusting. The rash typically consists of 250 to 500 lesions; appear first on the scalp, moves to the trunk, and then the extremities, with the highest concentration of lesions on the trunk (centripetal distribution). The vesicles are superficial and delicate; contain clear fluid on an erythematous base. Usually 2 to 4 successive crops of lesions, crops appear over several days, with lesions present in several stages of development. The rash is self-limited, generally lasting 4-5 days.

The clinical course in normal children is generally mild, with malaise, pruritus, and fever up to 102^{o} F for 2-3 days. Adults may have more severe disease and have a higher incidence of complications. Respiratory and gastrointestinal symptoms are absent.

Complications: The risk of complications from varicella varies with age. Children with lesions due to varicella are at greater risk for secondary bacterial infections. Complications are infrequent among healthy children. They are much higher in persons > 15 years and infants < 1 year of age. Adults account for only 5% of reported cases of varicella, but account for approximately 35% of mortality.

Complications include bacterial superinfection of the skin lesions, pneumonia (viral or bacterial), thrombocytopenia, arthritis, hepatitis, cerebellar ataxia, encephalitis, meningitis, and glomerulonephritis. Reye Syndrome can follow some cases of chickenpox, although the incidence of Reye Syndrome has decreased dramatically with decreased use of salicylates during varicella or influenza-like illnesses. Severe and even fatal varicella has been reported in otherwise healthy children receiving intermittent courses of corticosteroids for treatment of asthma and other illnesses.

The hospitalization rate is 3 per 1000 cases. Death rate 1 per 60,000 cases.

Outcome: Recovery from primary varicella infection usually results in lifetime immunity. In otherwise healthy persons, a second occurrence of chickenpox is uncommon, but may occur, particularly in immunocompromised persons.

The virus establishes latency in the dorsal root ganglia during primary infection. Reactivation results in herpes zoster "shingles". Grouped vesicular lesions appear in the distribution of 1 to 3 sensory dermatomes, sometimes accompanied by pain localized to the area. The immunologic mechanism that controls latency of VZV is not well understood. Approximately 15-30% of the population will experience zoster during their lifetimes. Factors associated with recurrent disease include aging, immunosuppression, intrauterine exposure to VZV, and varicella at a young age < 18 months. Post herpetic neuralgia is defined as pain that persists after resolution of the rash, may last as long as a year after the episode of zoster.

Herpes Zoster Vaccine
Zoster vaccine (licensed in 2006 Zostavax) is a live attenuated vaccine approved for persons 60 years of age and older. ACIP (Advisory Committee on Immunization Practices) recommends a single dose of zoster vaccine for adults 60 years of age or older whether or not they report a prior episode of herpes zoster. Persons with a chronic medical condition may be vaccinated unless a contraindication or precaution exists for the condition.
For more information on zoster vaccine, visit:
www.cdc.gov/vaccines/vpd-vac/shingles/default.htm#clinical
The vaccine should be stored frozen at an average temperature of +5°F (-15°C) until it is reconstituted. Read and follow the package insert for storage and reconstitution instructions.
A person should not get shingles vaccine who:

- •has ever had a life-threatening allergic
  - reaction to gelatin,
  - the antibiotic neomycin,
  - or any other component of shingles vaccine.
- has a weakened immune system because of
  - HIV/AIDS or another disease that affects the immune system,
  - treatment with drugs that affect the immune system, such as steroids,
  - cancer treatment such as radiation or chemotherapy,
  - a history of cancer affecting the bone marrow or lymphatic system, such as leukemia or lymphoma.
  - has active, untreated tuberculosis.

C. Reservoirs

Humans are the only source of infection for this highly contagious virus.

D. Modes of Transmission

Spread: The varicella zoster virus enters the body through the respiratory tract and conjunctiva. The virus is believed to replicate at the site of entry in the nasopharynx and regional lymph nodes. Primary viremia occurs 4-6 days after infection, which disseminates the virus to other organs, such as the liver, spleen and sensory ganglia. A secondary viremia occurs with viral infection of the skin.

Person-to-person transmission occurs by airborne spread from respiratory tract secretions and by direct contact with drainage from lesions in patients with varicella. Patients with zoster spread disease primarily by direct contact with drainage from zoster lesions. Transmission may also occur by respiratory contact with airborne droplets or by direct contact or inhalation of aerosols from vesicular fluid of skin lesions of acute varicella or zoster. Patients with disseminated zoster may also transmit disease via the airborne route. In utero infection also can occur as a result of transplacental passage of virus during maternal varicella infection.

E. Incubation period:

The incubation period is from 14 to 16 days from exposure with a range of 10 to 21 days. Incubation may be prolonged in immunocompromised patients.

F. Period of Communicability or Infectious Period:

Patients are most contagious from 1 to 2 days before to shortly after onset of the rash. Contagiousness persists until crusting of the lesions.

G. Epidemiology:

Varicella is highly infectious, with secondary infection rates in susceptible household contacts approaching 90%. Secondary family cases may have more severe disease than that in the index case.

In temperate climates varicella is a childhood disease with a marked seasonal distribution with peak incidence during winter and early spring. In tropical climates, the epidemiology of varicella is different; acquisition of disease occurs at later ages, resulting in a higher proportion of adults being susceptible to varicella compared with adults in temperate climates.

In the prevaccine era (prior to 1995), most cases of varicella in the United States occurred in children younger than 10. With the implementation of universal immunization, a higher proportion of cases are expected to occur among adolescents and adults. As vaccine coverage increases and the incidence of wild-type varicella decreases, a higher proportion of varicella cases will occur in immunized people as break-through disease. In sites conducting active surveillance, cases of breakthrough disease have increased as a percentage of all cases from 4% in 1995 to 25% in 2000. This should not be confused as an increasing rate of breakthrough disease or as evidence of increasing vaccine failure.

H. Bioterrorist Potential:

None - differentiate from smallpox.

2) DISEASE REPORTING AND CASE INVESTIGATION

A. Purpose of Surveillance and Reporting:

Varicella is not currently a nationally notifiable disease, and surveillance data are limited.

B. Laboratory Criteria for Diagnosis:

- Positive serologic test for varicella-zoster immunoglobulin M (IgM) antibody.
- Isolation of varicella-zoster virus (VZV), demonstration of VZV antigen by direct fluorescent antibody (DFA), or by polymerase chain reaction (PCR) tests from a clinical specimen.
- Significant rise in serum varicella immunoglobulin G (IgG) antibody level by any standard serological assay.

C. Local Public Health Agency Follow-up Responsibilities

Outbreak Investigation:

A parent letter and varicella outbreak worksheet is available to help in an outbreak response.

Case investigation of all suspected cases of varicella is not feasible or necessary. Reporting of varicella outbreaks (child care centers, schools, institutions etc.) will facilitate public health action.

In addition, in certain high-risk settings (e.g., hospitals and other health-care settings) rapid case identification and public health action are important to prevent infection of susceptible persons at high risk for serious complications of varicella, such as immunocompromised persons and susceptible pregnant women.

Pre-licensure vaccine efficacy studies ranged from 70-90% for all disease and > 95% for severe disease while mild "breakthrough" varicella may be expected to occur in 10-20% of vaccinated children. The rate of varicella (mild or severe) among vaccinated children should be monitored; if the rate of breakthrough disease is higher than expected (e.g., $\geq$ 30%) the cause of the problem should be investigated.

"Breakthrough disease" is defined as a case of wild-type varicella infection occurring more than 42 days after vaccination. The disease is almost always mild with fewer than 50 skin lesions. Rash may be atypical maculopapular with few or no vesicles. Breakthrough disease is contagious.

3) CONTROLLING FURTHER SPREAD

A. Isolation and Quarantine Requirements:

Isolation (exclusion) or cohorting of individuals with varicella until all of their lesions have crusted is routinely recommended for outbreak control. However, because substantial transmission of chickenpox occurs before rash onset, exclusion may have limited value as an outbreak control measure.

Quarantine measures: none.

Exclusion is also recommended for exposed susceptible individuals, who may be in contact with persons at high risk of serious complications (e.g., health-care workers, family members of immunocompromised persons). In these situations, exclusion is required for the duration of the period of communicability (i.e., from the 10th until the 21st day post-exposure).

B. Protection of Contacts of a Case:

Epidemiologic and serologic studies confirm that greater than 90% of adults are immune to VZV. Rates of immunity may be lower for adults who were raised in certain tropical or subtropical areas.

Vaccination for Outbreak Control:

During a varicella outbreak, persons who have received one dose of varicella vaccine should, resources permitting, receive a second dose provided the appropriate vaccination interval has elapsed since the first vaccine. (Three month interval for persons 12 months through 12 years of age and at least a 28 day interval for persons 13 years of age and older.) Varicella vaccine, if administered within 72 hours and possibly up to 120 hours following varicella exposure, may prevent or significantly modify disease. If exposure to varicella does not cause infection, post-exposure vaccination with varicella vaccine should induce protection against subsequent infection. If the exposure results in infection, the vaccine may reduce the severity of the disease. There is no evidence that administration of varicella vaccine during the incubation period of illness increases the risk for vaccine-associated adverse events.

Antivirals may be considered for persons at increased risk of moderate to severe disease. The decision to use antiviral therapy and the route and duration of therapy should be determined by specific host factors, extent of infection, and initial response to therapy.

Antiviral drugs have a limited window of opportunity to affect the outcome of Varicella-zoster infection. In immunocompetent hosts, most virus replication has stopped by 72 hours after onset of rash; the duration is extended in immunocompromised hosts. Oral acyclovir is not recommended for routine use in otherwise healthy children with varicella. Administration within 24 hours of the onset of rash results in only a modest decrease in symptoms. A 7-day course of acyclovir may be given to susceptible adults beginning 7 to 9 days after varicella exposure if vaccine is contraindicated or more than 72 hours has elapsed from the time of exposure. (Most adults with no or uncertain history of chickenpox are nonetheless immune).

Oral acyclovir should be considered for people at increased risk of moderate to severe varicella, such as people older than 12 years of age, people with chronic cutaneous or pulmonary disorders, people receiving long-term salicylate therapy, and people receiving short, intermittent, or aerosolized courses of corticosteroids. Some experts also recommend use of oral acyclovir for secondary household cases in which the disease usually is more severe than in the primary case. Oral acyclovir is not recommended routinely for pregnant women with uncomplicated Varicella, because the risks

and benefits to the fetus and mother are unknown. Intravenous acyclovir is recommended for the pregnant patient with serious complications of varicella.

Children with varicella should not receive salicylates or salicylate-containing products, because administration of salicylates to such children increases the risk of Reye syndrome. Acetaminophen may be used for control of fever.

Varicella zoster immune globulin (VariZIG):

This is recommended for post-exposure prophylaxis of susceptible persons who are at high risk for developing severe disease and when varicella vaccine is contraindicated. VariZIG is most effective in preventing varicella infection when given within 96 hours of varicella exposure; for maximum effectiveness it should be given as soon as possible after exposure. The decision to administer VariZIG to a person exposed to varicella should be based on 1) whether the person is susceptible, 2) whether the exposure is likely to result in infection, and 3) whether the patient is at greater risk for complications than the general public.

Such groups include:

- Newborn infants whose mothers developed varicella around the time of delivery (< 5 days before to 2 days after delivery),
- Immunocompromised children without history of varicella or varicella immunization.
- Susceptible pregnant women,
- Hospitalized premature infants > 28 weeks gestation whose mother had no history of varicella, and
- Premature infants < 28 weeks gestation, regardless of the mother's history of varicella.

VariZIG can be ordered from the distributor (FFF Enterprises, Inc., Temecula, CA) by calling 800-843-7477. VariZIG is given by intramuscular (IM) injection and contains between 10% and 18% Globulin and does not contain thimerosal. One vial (approximate volume, 1.25 ml) containing 125 U is given for each 10 kg of body weight and is the minimal dose. The suggested maximal dose of VariZIG is 625 U (i.e., 5 vials). For more information, visit:
www.cdc.gov/mmwr/preview/mmwrhtml/mm6112a4.htm

C. Managing Special Situations

- **Prenatal & Perinatal exposure:**
  Women should be assessed prenatally for evidence of varicella immunity. Upon completion or termination of their pregnancies, women who do not have evidence of varicella immunity should receive the first dose of vaccine before discharge from the healthcare facility. The second dose should be administered 4 to 8 weeks later at the postpartum or other healthcare visit.

  Prenatal infection is uncommon because most women of childbearing age are immune to VZV. Fetal infection after maternal varicella during the first or early second trimester of pregnancy occasionally results in varicella embryopathy, which is characterized by limb atrophy and scarring of the skin of the extremities (congenital varicella syndrome). Central nervous system and eye manifestations also can occur. The incidence of congenital varicella syndrome among infants born to mothers with varicella is approximately 2% when infection occurs before 20 weeks of gestation.

  Children exposed to varicella-zoster virus in utero during the second 20 weeks of pregnancy can develop inapparent varicella and subsequent zoster early in life without having had extra uterine varicella.

  Varicella infection can be fatal for an infant if the mother develops varicella from 5 days before to 2 days after delivery.

When varicella develops in a mother more than 5 days before delivery and gestational age is 28 weeks or more, the severity of disease in the newborn is modified by transplacental transfer of varicella-zoster virus (VZV) specific maternal IgG antibody of the parent.

- **Hospitalized Patient**:
  In addition to Standard Precautions, Airborne and Contact Precautions are recommended for patients with varicella for a minimum of 5 days after onset of the rash and as long as vesicular lesions are present, which in immunocompromised patients can be a week or longer. For exposed susceptible patients, Airborne and Contact Precautions from 10 until 21 days after exposure to the index patient also are indicated; these precautions should be maintained until 28 days or longer after exposure for those who received VariZIG.

  Immunocompromised patients who have zoster (localized or disseminated) and immunocompetent patients with disseminated zoster require Airborne and Contact Precautions for the duration of illness. For immunocompetent patients with localized zoster, Contact Precautions are indicated until all lesions are crusted.

- **Healthcare worker**:
  The Advisory Committee on immunization Practices recommends that all healthcare workers be immune to varicella, either from a reliable history of disease or from vaccination. In a health-care institution serologic screening of personnel who have a negative or uncertain history of varicella is likely to be cost effective.

  All susceptible exposed personnel should be furloughed or excused from patient contact from day 10 to day 21 after exposure to an infectious patient. The interval should be extended to 28 days or longer for people who have received VariZIG.

  Varicella immunization is recommended for susceptible personnel if varicella does not develop from the exposure. Serologic testing for immunity is not necessary for personnel who have been immunized, because 99% of adults are seropositive after the second vaccine dose.

- **Outbreaks involving children covered by childcare or school requirements**:
  Unvaccinated children with no history of varicella disease should be instructed to be vaccinated immediately or excluded from school for the duration of the period of communicability (i.e., from 10-21 days post exposure or for the duration of the outbreak.

- **Outbreaks in child care centers or schools**: The public health response includes informing parents and caregivers of the outbreak, providing them with information on varicella and its potential to cause complications, and providing information about the availability of vaccine. Children with uncomplicated chickenpox who have been excluded from school or child care may return when the rash has crusted, or in immunized people without crusts, when lesions have faded or new lesions have appeared in the last 24 hours.

- Exclusion of children with zoster whose lesions cannot be covered is based on similar criteria. Children who are excluded may return when lesions are crusted. Lesions that are covered seem to pose little risk to susceptible people.

- **Institutional outbreaks or outbreaks involving adolescents or adults**: Vaccination of susceptible persons should be strongly considered because it is likely to limit or control the outbreak by interrupting transmission. Outbreak control should be considered at any stage of an outbreak if there are remaining susceptible persons.

D. Preventive Measures:

Vaccination

The Oka/Merck attenuated varicella vaccine was licensed in the United States in 1995. Because of the thermolability of the vaccine, the manufacturer's requirements for maintaining the cold chain must be followed strictly. Vaccine that is not stored properly before administration could have reduced potency.

- Recommendations for the use of varicella virus vaccine:
    - Routine administration of live attenuated varicella virus vaccine for all children 12-18 months of age. On June 2006 ACIP recommended a routine 2 dose varicella vaccine schedule for all children less than 13 years of age, with the first dose administered at 12-15 months of age and the second dose at 4-6 years of age (i.e., before a child enters kindergarten). The second dose can be administered at an earlier age provided the interval between the first and second dose is at least 3 months. However, if the second dose is administered at least 28 days following the first dose, the second dose does not need to be repeated
    - A second dose catch-up varicella vaccination is recommended for children, adolescents, and adults (without evidence of immunity) who previously had received only one dose, to improve individual protection against varicella and for more rapid impact on school outbreaks. The minimum interval between vaccine doses is 28 days. Catch-up vaccination can be implemented during routine health care provider visits.

- Children with a reliable history of typical chickenpox can be assumed to be immune to varicella. Serologic testing of such children prior to vaccination is not warranted because the majority of children between 12 months and 12 years of age without a clinical history of chickenpox are not immune. Serologic testing of adolescents and adults with an uncertain or negative history is likely to be cost-effective because 70%-90% of these individuals are likely to be varicella-immune.
- Serologic testing for varicella immunity following two doses of vaccine is not necessary because 99% of persons are seropositive after the second dose.

Transmission of varicella vaccine virus

- Available data suggest that transmission of vaccine virus is a rare event. It appears that transmission occurs mainly and perhaps only, when the vaccinee develops a rash. If a vaccinated person develops a rash, it is recommended that close contact with persons who do not have evidence of varicella immunity and who are at high risk of complications of varicella, such as immunocompromised persons, be avoided until the rash has resolved.

- **Varicella Vaccine Contraindications and Precautions**:
    - Severe allergic reaction to vaccine component or following a prior dose
    - Women known to be pregnant or attempting to become pregnant should not receive varicella vaccine. Pregnancy should be avoided for 1 month following receipt of varicella vaccine
    - Immunosuppression due to disease or medication
    - Moderate or severe acute illness
    - Recent blood product

See **www.cdc.gov/mmwr/preview/mmwrhtml/00042990.htm** for more information.

- Varicella vaccination is contraindicated for all persons with moderate or severe cellular immunodeficiency due to human immunodeficiency virus (HIV) infection and is not recommended for adults who are HIV infected. However, vaccination should be considered for HIV-infected children if they have asymptomatic or mildly symptomatic HIV infection, in CDC class N, A, or B CD4+ T-lymphocyte percentage of $\geq$ 15% and without evidence of varicella immunity should receive two doses of single antigen varicella vaccine at a minimum interval of three months.

See **www.cdc.gov/mmwr/PDF/rr/rr4806.pdf** for more information.

4) ADDITIONAL INFORMATION

The Council of State and Territorial Epidemiologists (CSTE) surveillance case definitions for Varicella can be found at: www.cdc.gov/osels/ph_surveillance/nndss/phs/infdis.htm#top

CSTE case definitions should not affect the investigation or reporting of a case that fulfills the criteria in this chapter. (CSTE case definitions are used by the state health department and the CDC to maintain uniform standards for national reporting.)

Comment: Two probable cases that are epidemiologically linked are considered cases, even in the absence of laboratory confirmation.

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