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IDSP/55/STATE EPIDEMIOLOGIST/2022/NHM

Varicella Zoster (Chicken Pox) – Technical Document

Varicella zoster (chickenpox) is an acute infectious disease. It is caused by varicella-zoster virus (VZV), which is a DNA virus belonging to herpesvirus group. After the primary infection, VZV stays in the body (in dorsal root ganglia) as a latent infection. Primary infection with VZV causes varicella. Reactivation of latent infection causes herpes zoster (shingles).

A. Clinical Features

a. Incubation Period and Prodrome –

- The average incubation period for varicella is 14 to 16 days after exposure to a varicella or a herpes zoster rash, with a range of 10 to 21 days.
- A mild prodrome of fever and malaise may occur 1 to 2 days before rash onset, particularly in adults. In children, the rash is often the first sign of disease.

b. Varicella in Unvaccinated Persons –

- The rash is generalized and pruritic. It progresses rapidly from macular to papular to vesicular lesions before crusting. Lesions are typically present in all stages of development at the same time [pleomorphic rash]. The rash usually appears first on the chest, back, and face, then spreads over the entire body. The lesions are usually mostly concentrated on the chest and back. Symptoms typically last 4 to 7 days.
- In healthy children, varicella is generally mild, with an itchy rash, malaise, and temperature up to 102°F for 2 to 3 days.
- Infants, adolescents, adults, elderly, pregnant women, and immunocompromised people are at risk for more severe disease and have a higher incidence of complications.
- Recovery from primary varicella infection usually provides immunity for life. In otherwise healthy people, a second occurrence of varicella is uncommon. Recurrence of varicella can occur in those on T cell depleting chemotherapy.

Second occurrence of varicella may be more likely to occur in people who are immunocompromised. As with other viral infections, re-exposure to natural (wild-type) varicella may lead to re-infection that boosts antibody titers without causing illness or detectable viremia.

c. Varicella in Vaccinated Persons (Breakthrough Varicella)

- Breakthrough varicella is infection with wild-type varicella-zoster virus (VZV) occurring in a vaccinated person more than 42 days after varicella vaccination.
- Breakthrough varicella is usually mild. Patients typically are afebrile or have low fever and develop fewer than 50 skin lesions.
- They usually have a shorter illness compared to unvaccinated people who get varicella.
- The rash is more likely to be predominantly maculopapular rather than vesicular. However, 25% to 30% of people vaccinated with one dose who get breakthrough varicella will have clinical features similar to unvaccinated people with varicella.

B. **Transmission**

- Varicella is an air borne infection and is highly contagious. The virus can be spread from person to person by direct contact, inhalation of aerosols from vesicular fluid of skin lesions of acute varicella or zoster, and possibly through infected respiratory secretions that also may be aerosolized.
- A person with varicella is considered contagious beginning one to two days prior to rash onset until all the chickenpox lesions have crusted.
- Vaccinated people may develop lesions that do not crust. These people are considered contagious until no new lesions have appeared for 24 hours.
- About 90% of susceptible close contacts will get varicella after exposure to a person with disease.
- People with breakthrough varicella are also contagious
- Varicella is less contagious than measles, but more contagious than mumps and rubella

C. **Complications**

The most common complications from varicella are:

- In children: Otitis media, Bacterial infections of the skin and soft tissues [increased incidence of invasive group A streptococcal],myositis, necrotizing fasciitis and toxic shock syndrome, Reye's syndrome
- In adults: Varicella Pneumonia

Severe complications caused by the virus include

- Acute Cerebellar ataxia, diffuse encephalitis, aseptic meningitis, viral pneumonia, AIDP, ADEM, Transverse myelitis, vasculitis, hepatitis, DIC and hemorrhagic conditions.
- Other severe complications are due to bacterial infections and include:

- Septicemia
- Toxic shock syndrome
- Necrotizing fasciitis
- Osteomyelitis
- Bacterial pneumonia
- Septic arthritis

People at High Risk for Severe Varicella

- Immunocompromised people without evidence of immunity to varicella, such as:
  - People with leukemia or lymphoma
  - People on medications that suppress the immune system, such as high-dose systemic steroids or chemotherapeutic agents
  - People with cellular immune-deficiencies or other immune system problems
- Newborns whose mothers have varicella from five days before to two days after delivery
- Premature babies exposed to varicella or herpes zoster, specifically:
- Hospitalized premature infants born at ≥28 weeks of gestation whose mothers do not have evidence of immunity
- Hospitalized premature infants born at <28 weeks of gestation or who weigh ≤1,000 grams at birth regardless of their mothers' varicella immunity status
- Pregnant women without evidence of immunity to varicella

D) **Varicella in Special situations**

a. ***Immunocompromised People***

Immunocompromised people who get varicella are at risk of developing visceral dissemination (VZV infection of internal organs) leading to pneumonia, hepatitis, encephalitis, and disseminated intravascular coagulopathy. They can have an atypical varicella rash with more lesions, and may have prolonged illness compared to immunocompetent people who get varicella. New lesions may continue to develop for more than 7 days, may appear on the palms and soles, and may be hemorrhagic.

b. ***People with HIV or AIDS***

Children with HIV infection tend to have atypical rash with new crops of lesions presenting for weeks or months. The lesions may initially be typical maculopapular vesicular but can later develop into non-healing ulcers that become necrotic, crusted, and hyperkeratotic. This is more likely to occur in HIV-infected children with low CD4 counts.
Retinitis can occur among HIV-infected children and adolescents.
Most adults, including those who are HIV-positive, have already had varicella and are VZV seropositive. As a result, varicella is relatively uncommon among HIV-infected adults.
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c. ***Pregnant Women***

i. Pregnant women who get varicella are at risk for serious complications, primarily pneumonia, and in some cases, may die as a result of varicella.
ii. If a pregnant woman gets varicella in her first or early second trimester, her baby has a small risk (0.4 to 2.0%) of being born with congenital varicella syndrome.
iii. If a woman develops varicella rash from 5 days before to 2 days after delivery, the newborn will be at risk for neonatal varicella. The vaccine is contraindicated for pregnant women.

E. **Investigations**

Apart from routine investigations like hemogram, LFT, RFT and electrolytes, in case of severe varicella focused investigations should be done to rule out coagulopathy/DIC, pancreatitis, encephalitis etc

F. **Management of Varicella Infection**

The decision whether to initiate antiviral therapy in a patient with chickenpox depends on the patient's age, underlying medical conditions, and the risk of complications. In general, young children (under age 12 years) are at lower risk for complications than are adolescents or adults. . Benefits of antiviral therapy are minimal for healthy children presenting with greater than 24 hours of illness. Because of the greater risk of complications, antiviral therapy is appropriate for adolescents and adults with chickenpox, probably even for those presenting 48–72 hours into the course of illness. Immunocompromised patients with varicella are at significant risk for viral dissemination and visceral involvement and should always receive antiviral therapy.

a. **Children**

In healthy children, varicella is associated with low rates of morbidity and mortality. For most children, supportive care alone is sufficient. Astringent soaks, antipruritics, and antipyretics (preferably acetaminophen) improve comfort. Trimming the fingernails closely helps prevent bacterial superinfections caused by scratching. If bacterial cellulitis (especially caused by group A streptococcus) develops, antibiotics may be required. Proper hydration should be ensured. SALT RESTRICTION SHOULD NOT BE ADVISED AS IT MIGHT LEAD TO HYPONATREMIA.
Antiviral treatment with acyclovir should be initiated in children at risk of progression to severe complications.

b. **Adults**

Immunocompetent adolescents and adults with varicella can be seriously ill, with high fever, hundreds of cutaneous lesions, incapacitating constitutional symptoms, and a higher risk of complications (especially pneumonitis) and hence should be initiated on antivirals at the earliest**.**

Antivirals used for Treatment

	Drug	Dose	Major Toxicities
Immunocompetent patients			
Varicella	Acyclovir	20mg/kg (800mg max) PO 5 times daily x 5d. In adults famiciclovir and valacyclovir will also likely be effective	None, minor nausea or headache
Herpes Zoster	Acyclovir	800 mg PO 5 times daily x7-10 d	As above
	Valacyclovir	1000mg PO every 8h x 7d	None, minor nausea or headache
	Famciclovir	500 mg PO every 8 h x 7d	None, minor nausea or headache
	Brivudine	125mg PO once daily x 7d	Potentially lethal interaction with flouropyrimidines (eg.5-fluorouracil)
Immunocompromised patients			
Varicella	Acyclovir	10-15 mg/kg (or500 mg/m2) intravenously every 8h for ≥7 d	Nephrotoxicity (rare); CNS disturbances (rare)
Herpes Zoster	Acyclovir	IV therapy (as above) Mild to moderately immunocompromised patients (including most AIDS patients)can be treated with oral therapy	As above
Disseminated VZV syndromes (eg. encephalitis, pneumonitis)	Acyclovir	IV therapy (as above)	As above
Infection caused by acyclovir- resistant VZV	Foscarnet	60-90 mg/kg intravenously every 12 h until healed (≥ 10d)	Nephrotoxicity (common): electrolyte disturbances (common); seizures, arrhythmias, anaemia, genital ulcers

Note: Doses given are for adults with normal renal function

Renal Dose modification of Acyclovir

Renal impairment (IV)

- CrCl 25-50 mL/Min/1.73 m^2 : Give recommended dose q12hr
- CrCl 10-25 mL/Min/1.73 m^2 : Give recommended dose q24hr
- CrCl <10 mL/Min/1.73 m^2 : Give 50% recommended dose q24hr

Renal Impairment (PO)

- Normal dosage 200 mg q4hr or 400 mg q12hr and CrCl <10 mL/Min/1.73 m^2 : Decrease to 200 mg q12hr
- Normal dosage 800 mg q4hr and CrCl 10-25 mL/Min/1.73 m^2 : Decrease to 800 mg q8hr
- Normal dosage 800 mg q4hr and CrCl <10 mL/Min/1.73 m^2 : Decrease to 800 mg q12hr

c. **Pregnant Women**

Women who contract varicella while pregnant have an estimated 10% risk for developing severe VZV pneumonitis. Aggressive antiviral therapy is recommended for a pregnant woman with varicella who develops any evidence of pulmonary involvement, including cough, shortness of breath, or abnormal chest radiograph. Acyclovir is a Cat B drug in pregnancy .No fetal toxicity attributable to acyclovir has been demonstrated and the risk-benefit ratio clearly supports the use of acyclovir in the setting of maternal varicella pneumonia.

G. **POST- EXPOSURE PROPHYLAXIS**

Management of susceptible patients depends upon the nature of the exposure, the patient's risk of developing serious disease, and whether the patient is eligible for varicella vaccine .
Usually adopted post-exposure prophylaxis strategies are
1. Varicella vaccination.
2. Varicella Immunoglobulin.
3. Acyclovir chemoprophylaxis from 7 th day of exposure.

a. **Eligibility criteria for post-exposure prophylaxis with varicella vaccine**

After a significant exposure to VZV, susceptible adults or children should be vaccinated with monovalent varicella vaccine [live attenuated] if they are eligible.. To be eligible for vaccine prophylaxis, patients must meet all of the following criteria:

- Age ≥12 months.
- Not pregnant.
- Not immunocompromised (eg, without primary or acquired T lymphocyte immunodeficiency; without malignant neoplasm of the bone marrow or lymphatic system; not receiving immunosuppressive therapy)
- No history of severe reaction to varicella vaccine or varicella vaccine component.

Patients who received antiviral therapy with acyclovir, valacyclovir, or famciclovir within the previous 24 hours or antibody-containing immunoglobulin or blood product within the previous 3 months may have a diminished response to varicella vaccine. For such patients, individualize decisions about post-exposure vaccination after a discussion of the risks and benefits.

b) Timing

- **≤5 days after exposure** – Varicella vaccine is most effective if it is administered within five days of the exposure.
- Exposed patients ≥12 months of age who were previously unvaccinated should receive the first dose within five days of the exposure. The recommended timing for the second dose varies with age .
- Exposed patients ≥4 years of age who have only received one dose of vaccine should receive the second dose within five days after exposure to varicella provided ≥28 days have elapsed after the first dose.

b. **Passive immunoprophylaxis**

In the post-exposure setting, passive immunoprophylaxis against VZV infection typically consists of varicella-zoster immune globulin.

Target groups — Passive immunization with varicella-zoster immune globulin (eg, Varizig) is indicated for susceptible individuals after a significant exposure if they are ineligible for varicella vaccine prophylaxis, at high risk for severe infection and/or complications, **and** can receive immunoprophylaxis within 10 days of exposure
Indications for Varicella immunoglobulin

1. Immunocompromised where Varicella vaccination is contraindicated.
2. Pregnancy
3. Newborns of mothers who develop varicella five days before to two days after delivery.
4. Hospitalized premature infants born at ≥28 weeks of gestation whose mothers do not have evidence of immunity.
5. Hospitalized premature infants born at <28 weeks of gestation or who weigh ≤1000 g at birth, regardless of maternal evidence of immunity to varicella.

Dose of Varizig

Varizig is administered as a single dose intramuscularly. It is supplied in vials containing 125 international units. It is dosed according to weight as follows:
-<2 kg – 62.5 international units
-2.1 to 10 kg – 125 international units
-10.1 to 20 kg – 250 international units
-20.1 to 30 kg – 375 international units
-30.1 to 40 kg – 500 international units
-≥40 kg – 625 international units

IVIG – IVIG contains antivaricella antibody titers that vary from lot to lot. The recommended dose for varicella prophylaxis is 400 mg/kg, administered as a single dose intravenously. IVIG should be considered as an alternative therapy only, since limited data exist regarding efficacy.

c. **Role of antivirals as post-exposure prophylaxis** —

Antiviral prophylaxis with acyclovir or valacyclovir may prevent clinical varicella infection after an exposure, although efficacy data are limited. Antiviral prophylaxis is an option for patients who cannot receive varicella vaccine or immune globulin (eg, due to lack of availability, timing, or contraindications)
Anti virals as chemoprophylaxis should be initiated 7 days[dose is treatment dose] after exposure and should be continued for a week. Delaying prophylaxis until days 7 to 10 allows for the early steps of replication to occurwhich is essential for conversion of acyclovir monophosphate to triphosphate for which viral thymidine kinase is essential. Duration of chemoprophylaxis in immunocompromised may haveto be prolonged.

H. **Nosocomial Transmission of VZV**

Nosocomial transmission of VZV is well-recognized and can be life threatening to certain groups of patients. Patients, healthcare providers, and visitors with varicella or herpes zoster can spread VZV to susceptible patients and healthcare providers in hospitals, long-term-care facilities, and other healthcare settings.
In healthcare settings, transmissions have been attributed to delays in the diagnosis or reporting of varicella and herpes zoster and failures to implement control measures promptly.
Although all susceptible patients in healthcare settings are at risk for severe varicella and complications, certain patients without evidence of immunity are at increased risk:

- Premature infants born to susceptible mothers
- Infants born at less than 28 weeks gestation or who weigh ≤1000 grams, regardless of maternal immune status
- Immunocompromised people, including those who are undergoing immunosuppressive therapy, have malignant disease, or are immunodeficient
- Pregnant women

IPC precautions to be Adopted
Healthcare providers should follow standard precautions plus airborne precautions (negative air-flow rooms) and contact precautions until lesions are dry and crusted. If negative air-flow rooms are not available, patients with varicella should be isolated in closed rooms with no contact with people without evidence of immunity. Patients with varicella should be cared for by staff with evidence of immunity.

I) References
1. Chickenpox for Healthcare professionals-CDC
2. Mandell, Douglas and Bennett's Principles and practice of Infectious Diseases: Edition 10
3. Treatment of varicella zoster Infection: UpToDate
4. Red Book: American Academy of Paediatrics

Acknowledgements: State Medical Board, Kerala