Varicella-Zoster Immune Globulin
Michelle Hudspeth and Tina L. Cheng

Pediatr. Rev. 2005;26;348-349
DOI: 10.1542/pir.26-9-348

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://pedsinreview.aappublications.org/cgi/content/full/26/9/348

Although several new antiviral agents have been released in recent years, few have been evaluated thoroughly in the pediatric population. Thus, acyclovir and ganciclovir remain two of the primary antiviral agents used in children.

Acyclovir has an excellent safety profile due to its ability to target cells infected with herpesviruses. Viral thymidine kinase phosphorylates and, thereby, activates the guanine derivative acyclovir, which subsequently suppresses viral replication through chain termination and competition for viral DNA polymerase. Acyclovir is most effective within the first 24 to 72 hours of illness.

Serious complications from acyclovir in children are uncommon. Its most frequent adverse effects are abdominal pain, nausea, vomiting, and diarrhea. For patients who have impaired renal clearance, high-dose intravenous acyclovir may induce neurologic complications, including agitation, confusion, dizziness, tremors, or seizures. Acyclovir also may exacerbate renal failure and crystallize in renal tubules of patients who have renal insufficiency. Neuropenia is a risk, especially in neonates, although it rarely is sufficient to preclude acyclovir therapy.

Acyclovir is used widely for treatment of herpes simplex virus (HSV) infections. Intravenous acyclovir is indicated for HSV encephalitis, neonatal HSV, severe primary genital HSV, HSV treatment in immunocompromised hosts, and for HSV carriers during high-risk periods (eg, immunosuppression). Oral acyclovir is recommended for HSV prophylaxis in immunosuppressed patients. In stable immunocompetent patients, oral acyclovir is appropriate for outpatient management of new-onset or recurrent genital HSV or for prophylaxis of recurrent genital or ocular disease. Topical acyclovir has no proven value in immunocompetent individuals, although it may facilitate lesion resolution in immunosuppressed patients.

Unfortunately, the limited bioavailability of acyclovir necessitates frequent administration. Oral doses of 40 to 80 mg/kg per day (maximum 1 g/d) are divided up to five times daily. Intravenous formulations are divided three times at 15 to 30 mg/kg per day in children; neonates require 60 mg/kg per day. The duration of acyclovir therapy varies with indication. If necessary, prophylaxis may be continued safely for years. Drug holidays for immunocompetent children receiving chronic prophylaxis should be considered annually to assess the frequency of HSV recurrence.

Varicella (VZV)-infected cells also are targeted effectively by acyclovir. However, healthy children who have chickenpox need not receive acyclovir. Treatment is reserved for patients who are at high risk for serious VZV sequelae. Immunocompromised patients who have VZV infection should receive acyclovir intravenously at 30 mg/kg per day for infants younger than 1 year of age or 1,500 mg/m² per day for children older than 1 year. Oral acyclovir is preferred for immunocompetent at-risk patients at 80 mg/kg per day divided every 6 hours for 5 days. Teenagers,
patients who have chronic skin conditions, patients who have chronic lung disease, and patients receiving long-term salicylates fall into this category. Patients who have VZV infection and are receiving corticosteroids, either aerosolized or as a short oral course, also may benefit from acyclovir, although this approach remains controversial in clinical practice.

Ganciclovir is a nucleoside analog that inhibits viral replication in affected cells without eradicating the infection. Although ganciclovir is phosphorylated intracellularly by multiple herpesviruses, the agent is activated preferentially in cytomegalovirus (CMV)-infected cells. Neutropenia is the most common adverse effect, occurring with both intravenous (40%) and oral (approximately 20%) therapy. Ganciclovir-induced neutropenia is reversible and apparently not dose-related. Thrombocytopenia also is common (20%). As with acyclovir, neurologic adverse effects may occur (5%). Resistance to ganciclovir increases with the duration of therapy.

Antiviral treatment for CMV is not indicated in otherwise healthy children. However, ganciclovir is essential for CMV prophylaxis and treatment in immunocompromised patients. In neonates, recent data suggest that ganciclovir effectively reduces the acoustic morbidity of congenital CMV.

Intravenous ganciclovir at 10 mg/kg per day divided twice daily is recommended for CMV therapy or for initial prophylaxis in children; 5 mg/kg daily is sufficient for prolonged prophylaxis. For neonates who have congenital CMV, intravenous ganciclovir (6 mg/kg per dose twice daily for 6 wk) is suggested. Oral ganciclovir CMV prophylaxis previously was recommended at 1 g orally three times daily, but recent studies advise 30 mg/kg three times daily. Stable oral suspensions of ganciclovir must be compounded, and noncompliance with the large volume of medication is problematic (19%).

Acyclovir and ganciclovir are effective for preventing and treating a variety of herpesvirus infections, including HSV-1 and HSV-2, VZV, and CMV. Although adverse effects always must be considered with pharmacotherapy, acyclovir and ganciclovir have yielded significantly decreased morbidity and mortality from pediatric viral infections.

In Brief

Varicella–Zoster Immune Globulin

Michelle Hudspeth, MD
Johns Hopkins Hospital
Baltimore, Md.


Varicella–zoster virus (VZV) is a highly contagious member of the herpesvirus family. It is spread when the virus comes into contact with conjunctiva or the mucosa of the upper respiratory tract. Routes of person-to-person transmission include direct contact with infected persons and aerosolized droplets from respiratory tract secretions. In addition, maternal varicella infection can lead to in utero infection through transplacental passage of the virus.

The typical incubation period for varicella disease is 14 to 16 days, but may last for up to 21 days. This period may be decreased in immunocompromised patients and can be increased to 28 days with the use of varicella–zoster immune globulin (VZIG). This timing is a critical consideration when planning airborne and contact isolation precautions in hospitalized patients who have received VZIG.

VZIG is made from the plasma of volunteer blood donors who are noted on routine screening to have high antibody titers to VZV. It contains between 10% and 18% globulins, primarily immunoglobulin G (IgG). It does not contain thimerosal and is administered by intramuscular injection.

VZIG is not indicated for treatment of varicella or zoster; rather, it is used for passive immunization in susceptible individuals considered to be at high risk for developing complications after a presumed exposure to varicella. Ideally,
it should be administered as soon as possible after the presumed exposure, but it may be effective if administered up to 96 hours after exposure.

Recommendations for the use of VZIG are based on the history of a substantial exposure to varicella or zoster in particular sets of susceptible patients. Criteria for a substantial exposure in the community include household contact and exposure to playmates through face-to-face contact during indoor play. In the hospital, a substantial exposure to varicella involves face-to-face contact with an infectious patient, staff member, or visitor. For zoster in the hospital, a substantial exposure involves intimate contact such as hugging or touching. In both the community and hospital, face-to-face contact should be nontransient, but experts differ in the duration of exposure necessary for prompt administration of VZIG.

If a substantial exposure to varicella or zoster has occurred, the following types of patients should receive VZIG: immunocompromised children who have no history of chickenpox, susceptible pregnant women, newborns of mothers who have developed varicella infections within 5 days before and 2 days after delivery, hospitalized preterm infants (≥28 weeks’ gestation) who have no reliable maternal history of varicella or serologic evidence of immunity, and hospitalized preterm infants (≤28 weeks’ gestation or ≤1,000 g) regardless of maternal status. Immunocompromised children include those who have primary immunodeficiencies, human immunodeficiency virus (HIV) infection, or cancer and those who are receiving immunosuppressive therapy.

Transplacentally acquired antibody should protect newborns whose mothers had varicella infection more than 5 days prior to the delivery as well as exposed infants of 28 weeks’ gestation or more born to immune mothers. In addition, healthy term infants who are exposed postnatally have significantly less risk of serious complications than those who are born to mothers who had varicella 5 days before to 2 days after delivery. Therefore, even if their mothers have no history of varicella infection, VZIG is not recommended for healthy term infants who have been exposed postnatally. Clinicians must judge each case individually because special circumstances may occur. For example, in the view of some specialists, a newborn who has severe skin disease and is susceptible would be a candidate for VZIG if exposed, regardless of timing.

It is unknown how long VZIG protects against varicella. Based on the half-life of IgG, however, if a second exposure occurs later than 3 weeks after VZIG is administered and no disease developed, a second dose of VZIG should be administered. For susceptible children who do not meet criteria for VZIG administration, it is recommended that varicella vaccine be administered within 72 hours of exposure.

Comment: Decisions to use VZIG should be based on: 1) patient susceptibility to varicella, 2) likelihood of exposure causing an infection, and 3) the patient’s risk for bad complications. The Advisory Committee on Immunization Practices also recommends varicella vaccine for susceptible persons after exposure. If exposure to varicella does not cause infection, vaccination can protect against future exposure. If exposure leads to infection, there is no evidence that the vaccine would influence the course of illness or adverse effects. Because varicella outbreaks can last 3 to 6 months, postexposure vaccination could facilitate the control of an outbreak.

Tina L. Cheng, MD, MPH
Associate Editor