

# Clinical Focus on Primary Immune Deficiencies

ISSUES AND INFORMATION ON CURRENT TOPICS

Volume 1 Issue 3 December 1999

**Editor:**  
Howard Lederman, MD, PhD

**Medical Advisory Committee**

**Jerry Winkelstein, MD**  
*Chairman*  
Johns Hopkins University School of Medicine  
Baltimore, MD

**Douglas J. Barrett, MD**  
University of Florida, Gainesville, FL

**R. Michael Blaese, MD**  
National Center for Human Genome Research  
Bethesda, MD

**Rebecca H. Buckley, MD**  
Duke University School of Medicine  
Durham, NC

**Mary Ellen Conley, MD**  
St. Jude Children's Research Hospital  
Memphis, TN

**Max Cooper, MD**  
University of Alabama School of Medicine  
Birmingham, AL

**Charlotte Cunningham-Rundles, MD, PhD**  
Mt. Sinai Medical Center  
New York, NY

**Erwin W. Gelfand, MD**  
National Jewish Center For Immune and Respiratory Medicine  
Denver, CO

**Robert Good, MD, PhD**  
University of South Florida All Children's Hospital  
St. Petersburg, FL

**Richard Hong, MD**  
University of Vermont School of Medicine  
Burlington, VT

**Richard B. Johnston, Jr., MD**  
National Jewish Medical & Research Center  
Denver, CO

**Alexander R. Lawton, III, MD**  
Vanderbilt University School of Medicine  
D3237 Medical Center North, Nashville, TN 37232

**Stephen Miles, MD**  
All Seasons Allergy, Asthma & Immunology Center  
Woodlands, TX

**Hans D. Ochs, MD**  
University of Washington School of Medicine  
Seattle, WA

**Fred Rosen, MD**  
The Center for Blood Research  
Boston, MA

**Andrew Saxon, MD**  
UCLA School of Medicine  
Los Angeles, CA

**William T. Shearer, MD**  
Texas Children's Hospital  
Houston, TX

**E. Richard Stiehm, MD**  
UCLA School of Medicine  
Los Angeles, CA

**John L. Sullivan, MD**  
University of Massachusetts Medical Center  
Worcester, MA

**Diane W. Wara, MD**  
UCSF Medical Center  
San Francisco, CA

## Treatment and Prevention of Viral Infections in Patients with Primary Immunodeficiency Diseases

*Walter T. Hughes, M.D.*  
*Emeritus Member,*  
*Department of Infectious Diseases*  
*St. Jude Children's Research Hospital and*  
*Professor of Pediatrics and Preventive*  
*Medicine, University of Tennessee*  
*College of Medicine*  
*Memphis, TN*

Within recent years several important developments have provided new approaches to the diagnosis, prevention and treatment of viral infections in the immunocompromised, as well as the immunocompetent host. These advances have been late in coming and are far from ideal, in comparison to the antibacterial armamentarium. Nevertheless, the morbidity and mortality rates for many of the viral infections may now be reduced in individuals with immunodeficiency disorders.

Patients with certain primary immunodeficiency disorders have a predisposition for severe life-threatening viral infections. Although persons with any profound immunodeficiency may acquire viral infections, those with T-lymphocyte defects and impaired cell-mediated immunity are most susceptible. Individuals with only humoral immunodeficiency have little difficulty with most viral infections, although cases of severe rotavirus and enteroviral infections have been reported. Individuals with primary phagocyte and complement disorders have not been noted to have unusual susceptibility to viral infections. The treatment of some primary immunodeficiency disorders with hematopoietic tissue transplantation may add to the risk of serious viral

infection. It must be kept in mind that the immunocompromised host is also at risk for all of the infections commonly acquired by normal children.

The viruses that infect individuals with primary immunodeficiency disorders are precisely the same as those that infect otherwise normal people (Table 1).

**Table 1:**  
**Causes of Serious Viral Infections in Patients with Major Immune Deficiency Disorders**

Respiratory Viruses:	Respiratory syncytial virus
	Influenza A and B viruses
	Parainfluenza viruses
	Adenoviruses
	Rhinoviruses
Enteroviruses:	Echoviruses
	Coxsackieviruses
	Poliovirus
	Enteroviruses (numbered)
Hepatitis viruses:	Hepatitis viruses A, B, C, and others
Herpesviruses:	Cytomegalovirus
	Herpes simplex virus
	Varicella-zoster virus
	Epstein-Barr virus
	Human Herpes Viruses 6, 7, and 8.
Rotavirus	

**Immune Deficiency Foundation**, the national nonprofit organization devoted to research and education for the primary immune deficiency diseases, publishes other materials for physicians and healthcare professionals (eg. Physician's Primer and Guide for Nurses) and for patients (eg. Patient and Family Handbook, Our Immune System, and Newsletter). For information about our programs, patient groups and publications, call 1-800-296-4433.

**Immune Deficiency Foundation** - 25 West Chesapeake Avenue, Suite 206, Towson, MD 21204 • (800) 296-4433 • (410) 321-6647 • Fax: (410) 321-9165

supported by an educational grant from **ICN Pharmaceuticals**



**Immune Deficiency Foundation**  
25 West Chesapeake Avenue  
Suite 206  
Towson, MD 21204

The clinical manifestations are also similar. Generally, the difference is in the severity and/or duration of the infection. The herpesviruses, including cytomegalovirus (CMV), herpes simplex virus, varicella-zoster virus (VZV) and Epstein-Barr virus, are predominant causes of serious systemic viral infections. In recent years infections from the respiratory syncytial virus (RSV) and other common respiratory viruses have been recognized as causes of potentially fatal infections in the immunocompromised host. Rotavirus, measles virus, hepatitis virus and enterovirus infections may have severe and prolonged courses. Live-attenuated virus vaccines, especially polio, have caused serious disease in a few people with severe immunodeficiency. Because of the relatively low prevalence of congenital immunodeficiency disorders, data on the incidence and courses of many of the associated infections are lacking. However, extensive studies have been done in patients with immunodeficiency induced by human immunodeficiency virus (HIV), cancer chemotherapy and suppressive regimens for organ transplantation. Interpolation from these studies must sometimes be made for the primary congenital disorders when specific information on the latter is not available.

The aim of this review is to focus on the major viral infections confronting patients with primary immunodeficiency disorders and to include only those for which some established therapeutic or prophylactic intervention is generally available. An attempt will be made to mention promising drugs or biologicals currently FDA approved or in late stages of research.

## RESPIRATORY VIRUS INFECTIONS

The prominence of respiratory viral infections in recent years is due in great part to new and improved molecular diagnostic methods. This has allowed a greater understanding of the epidemiology and outcome of these infections in immunocompromised patients. New test batteries, such as a multiplex reverse-transcriptase polymerase chain reaction enzyme hybridization assay, can be used to detect influenza A and B, RSV, and parainfluenza viruses (PIV) 1, 2 and 3. It has been estimated that 20 to 30% of bone marrow transplant (BMT) recipients with acute respiratory symptoms are infected with a respiratory virus and that about one-half the cases have pneumonia with a mortality rate of 50%.

In most cases of viral pneumonia in the immunosuppressed host, CMV, RSV, influenza and PIV are the causes.

In a study of a heterogeneous group of 785 immunocompetent patients suspected of respiratory tract infections, 199 viruses were isolated from 182 (23%) of 785 bronchoalveolar lavage specimens. The isolates were: cytomegalovirus in 131 patients, herpes simplex virus from 32, and conventional respiratory viruses from 37 patients.

### **Table 2:** **Prevention of Respiratory Syncytial Virus Infection in Immunocompromised Patients**

1. Avoid exposure:
  - a. Community: home alone versus day-care center
  - b. Hospital: strict enforcement of hospital infection control policies and visitation rules.
2. Seasonal immunoprophylaxis\* with RSV antibody for select\*\* cases:
  - a. Palivizumab 15 mg/kg/ dose i.m. monthly, starting in October or November and continuing through March or April (5 doses).
  - b. Alternative choice: RSV-IGIV 750 mg/kg monthly, intravenously, for same months as above.

\* No controlled studies for efficacy, dose and safety in immunocompromised host.

\*\* High risk = < 2 yr. old; impaired pulmonary or cardiac function; frequent exposure in home (siblings) or day care center; complicated BMT; profound immunodeficiency (eg. SCID).

### **Respiratory Syncytial Virus (RSV)**

The single stranded RNA respiratory syncytial virus is the leading cause of lower respiratory tract infection in normal infants and children, infecting about 65% in the first year of life. The most severe disease ( pneumonia and bronchiolitis) in normal infants occurs between 2 and 6 months of age. Reinfection is common throughout life but affects primarily the mucosa of the upper respiratory tract. Most infections occur during the winter months from November to May in temperate zones. Infants with congenital or acquired immunodeficiency due to major impairment of T-cell function are at high risk for the development of severe and prolonged bronchopulmonary disease and in some cases the development of giant cell pneumonia with

extramucosal spread of the virus. The mortality rate in BMT recipients with RSV pneumonia demonstrable by radiograph has been estimated to be between 50 and 75 %.

#### **Treatment:**

RSV infection must be considered a potentially life-threatening disease in immunocompromised patients. Infected patients should be managed aggressively by early diagnosis, continuous evaluation and, in many cases, specific antiviral therapy.

The only drug available for treatment of RSV infection is ribavirin, a synthetic nucleoside (Tables 2 and 3). The dose of 6.0 grams in 300 mL sterile water must be administered as an aerosol for 12 to 18 hours per day, delivered by a small particle aerosol generator, SPAG-2, using a solution of 20 mg ribavirin per mL of sterile water. Intravenous administration is not recommended. Although controlled studies are lacking for use of ribavirin in immunocompromised patients, data from comparative studies in infants as well as observational studies in adults and children without immunocompromising diseases, provided a basis for working recommendations. It must be appreciated that the degree of efficacy of ribavirin for RSV disease remains controversial.

Because of the high mortality rate with lower respiratory tract RSV disease (pneumonia, bronchiolitis) in the severely immunocompromised host, treatment with ribavirin is recommended for cases documented by positive RSV antigen detection and/or culture. The duration of treatment may be determined by the patient's tolerance of the drug, clinical improvement and clearance of RSV antigen. To be effective, ribavirin must be started as early as possible. In one study the mortality rate in BMT recipients was 25% if started on day one, and 86% if started 3 or more days after the diagnosis.

In RSV infections limited to the upper respiratory tract, the role of ribavirin is less well defined. With the exception of certain cases with extensive immunological and pulmonary compromise or when progression to lower respiratory tract involvement is likely, ribavirin is not necessary for upper respiratory tract infections.

#### **Prevention:**

Many RSV infections are acquired in the hospital from patient-to-patient, visitor-to-patient and staff-to-patient transmission. Strict adher-

ence to hospital infection control practices should be mandated to protect the compromised host while in the hospital (Table 2).

Seasonal prophylaxis has been effective in small infants with pulmonary compromise through the use of monthly infusions of RSV-polyclonal antibody (RSV-IGIV) or the injection of RSV humanized monoclonal antibody (palivizumab). Small uncontrolled studies suggest this approach may have merit for immunocompromised patients, but definitive controlled studies have not been done.

Both RSV-IGIV and palivizumab are relatively safe, however, cost may be a limiting factor in their use for older children and adults. For example, the cost of the drug alone for a four-dose course of RSV-IGIV or palivizumab in a 5.0 kg infant is approximately \$3,000. Thus, cost, as well as the quantity of drug required for a 10 kg one-year old, a 20 kg six-year old patient, or a 70 kg adult becomes extreme. Despite these problems and because of the high morbidity and mortality rates from RSV, it seems reasonable to consider RSV antibody prophylaxis for selected cases of infants and small children with profound immunodeficiency, and complicated BMT recipients, especially if any concomitant pulmonary or cardiac impairment exists. Other risk factors include frequent exposure from siblings at home or from day-care centers.

In general, palivizumab is preferred because of easier administration (i.m. versus i.v.), lack of interference with routine immunizations, fewer complications and lower cost than RSV-IGIV. However, RSV-IGIV may provide additional protection from other respiratory viral infections.

### **Influenza Virus:**

Four drugs are available for consideration in the treatment of influenza virus infection. They are amantadine, rimantadine, ribavirin and zanamivir. Unfortunately, there are no adequate comparative studies and there is also a lack of studies of any type in patients with primary immunodeficiency disorders. The following recommendations come from a composite of published studies in other patient populations.

### **Treatment:**

Zanamivir has recently been approved by the FDA for the treatment of influenza A and B in

patients 12 years of age and older. This neuraminidase inhibitor is administered twice daily for five days using a breath-activated plastic device called a Diskhaler.

Amantadine or rimantadine may be given orally early in the course for influenza type A infections, but are not effective for influenza type B.

Ribavirin aerosol has reduced symptoms in some patients with influenza, type A or B infections.

Salicylates should be prohibited during influenza infection because of the risk for Reye syndrome.

The drugs mentioned have limited effects on the infection and have been found to primarily reduce the symptoms and shorten the course of the disease.

### **Prevention:**

For compromised patients exposed to influenza A virus infection, prophylaxis should be instituted using either amantadine, rimantadine or zanamivir. For those exposed to influenza B, only zanamivir is recommended, using one dose daily during the exposure period. For infants and small children who cannot use the Diskhaler, only amantadine or rimantadine are available for influenza A infections.

**Table 3:**  
**Antiviral Agents Available for the Treatment and Prevention of Respiratory Virus, Enterovirus, Rotavirus and Herpesvirus Infections**

Infection	Prevention	Treatment
Respiratory Syncytial Virus	*Palivizumab RSV-IGIV	*Ribavirin aerosol
Influenza Virus	*Vaccine (Pre-exposure) *Zanamivir (A)(B) Amantadine (A) Rimantadine (A)	*Zanamivir (A)(B) Amantadine (A) Rimantadine (A) Ribavirin
Parainfluenza Viruses	None	?Ribavirin aerosol
Adenoviruses	None	?Ribavirin IV
Rhinoviruses	None	?Experimental Pleconaril
Enteroviruses	None	?Experimental Pleconaril
Cytomegalovirus	*Ganciclovir CMV-IgG	*Ganciclovir CMV-IgG Foscarnet Cidofovir Formivisen
Herpes simplex Virus	*Acyclovir	*Acyclovir Famciclovir Valacyclovir
Varicella-zoster Virus	*VZIG *Vaccine (competent host)	*Acyclovir Famciclovir Valacyclovir
Epstein-Barr Virus	None	None
Rotavirus	None	?Oral immunoglobulin

\* = Preferred for initial use.

(A) = influenza virus A; (B) influenza virus B

RSV-IGIV = respiratory syncytial virus immunoglobulin intravenous

? = data inconclusive

Prior to the influenza season, household members of the immunocompromised patient should be immunized against the virus. If the patient is capable of an adequate immune response, pre-season immunization of the patient is also indicated.

### **Parainfluenza Virus (PIV)**

Parainfluenza viruses cause upper respiratory infections, laryngotracheobronchitis, bronchiolitis and pneumonia. PIV type 3 is the most frequent cause of infection in immunocompromised patients in whom disease is more severe and virus excretion more prolonged than in the immunocompetent patient. Reinfection is common with PIV infections.

#### **Treatment:**

Ribavirin aerosol has been used successfully for the treatment of severe PIV disease in some children with severe immunodeficiency, but studies are inadequate to establish efficacy.

#### **Prevention:**

No specific prophylaxis is available.

### **Adenovirus Infections:**

Usually, adenovirus upper respiratory infection in the immunocompromised host is self-limited but in some cases will progress to severe infections with bronchiolitis, pneumonia, hepatitis, hemorrhagic cystitis and disseminated multi-organ disease. It has been roughly estimated that one in 10 adenovirus infections in BMT recipients will progress to serious or fatal disease.

#### **Treatment:**

Intravenous ribavirin has been used with successful responses in some cases published in the literature. A loading dose of 30 mg per kg per day in three doses was followed by a maintenance dose of 15 mg per kg per day. No controlled study is available.

#### **Prevention:**

No specific prophylaxis is available.

### **Rhinovirus:**

The common rhinovirus infections of the upper respiratory tract may progress to fatal pneumonia in immunocompromised patients. In 22 hospitalized blood and BMT recipients with rhinovirus infection, 7 (32%) developed fatal pneumonia.

#### **Treatment:**

Currently, there is no treatment of proven efficacy. Early studies with a broad-spectrum capsid-binding agent, Pleconaril (VP 63843), given orally shows promise for therapy. The drug is available on a compassionate protocol use.

#### **Prevention:**

No specific prophylaxis is available.

## **ENTEROVIRUS INFECTIONS**

The enteroviruses include Echovirus, Coxsackievirus, Poliovirus, and numbered Enteroviruses. Clinical syndromes that may occur in immunocompetent patients are persistent aseptic meningoencephalitis, poliomyelitis (oral polio vaccine-associated), hemorrhagic conjunctivitis, myocarditis, dermatomyositis and febrile episodes with or without a rash.

#### **Treatment:**

No proven treatment has been established. However, some evidence for therapeutic efficacy in enteroviral aseptic meningoencephalitis has been described for Pleconaril (mentioned above for rhinovirus infections).

#### **Prevention:**

No specific prophylaxis has been established. Immune globulin has been used for the prevention and treatment of enteroviral infections but the results are equivocal. It is of interest to note that since intravenous immune globulin replacement therapy has been used for patients with antibody immunodeficiency, the incidence of persistent meningoencephalitis has decreased.

## **VIRAL HEPATITIS**

At least five hepatitis viruses, of different families, are known to cause inflammatory disease in the livers of humans (hepatitis viruses A, B, C, D, and E). Some modes of intervention are available for the first three of these viruses and have been summarized in Table 4.

## **HERPESVIRUSES**

The human herpesviruses have been the major causes of viral infections in immunocompromised hosts with primary or secondary immunodeficiencies, with or without BMT. These include cytomegalovirus, herpes simplex virus, varicella-zoster virus, Epstein-Barr virus and human herpesviruses 6, 7 and 8. Disease

results from acute de novo infection or activation of latent infection.

### **Cytomegalovirus (CMV):**

CMV infection or reactivation is associated with clinical disease almost exclusively in patients with impaired cell-mediated immunity. Overt CMV disease is associated with high levels of CMV in blood or urine. The lungs and gastrointestinal tract are the major sites of disease among patients with primary immunodeficiency disorders. The use of blood transfusion or BMT enhances the risk of CMV disease. The risk correlates strongly with the donor and recipient's CMV antibody status. In a recent study of 562 patients receiving placental-blood transplants, including children with primary immunodeficiency disorders, 23 % of CMV seropositive recipients and 3 % of seronegative recipients developed CMV infection. This risk may be enhanced in recipients when the donor is CMV seropositive.

#### **Treatment:**

With rare exceptions, the asymptomatic carrier state of CMV infections, even in the immuno-

**Table 4:**

### **Preventive and Therapeutic Interventions for Viral Hepatitis**

#### **Hepatitis A Virus:**

Treatment: no specific therapy

Prevention:

- Before or within 2 wks. of exposure: 0.02 mL/kg Immune Globulin, i.m.
- Pre-exposure: Hepatitis A Vaccine to hosts capable of response.

#### **Hepatitis B Virus:**

Treatment:

- Acute hepatitis: none
- Acute fulminant hepatitis: Orthotopic transplant
- Chronic hepatitis: Lamivudine or interferon alpha-2b.

Prevention:

- Pre- and post-exposure prophylaxis: Hepatitis B Vaccine; in some special cases give vaccine + Hepatitis B Immune Globulin.

#### **Hepatitis C Virus:**

Treatment:

- Acute hepatitis: none
- Chronic hepatitis: interferon alpha-2b; or, interferon alpha-2b plus ribavirin.

Prevention: no specific measures

compromised host does not require treatment. Once clinical evidence of organ involvement (pneumonitis, hepatitis, retinitis, etc.) is recognized, specific treatment should be instituted.

The drug of choice with which to initiate therapy is ganciclovir. This virostatic drug is given in the dose of 5.0 mg per kg twice daily, intravenously, for a period of 2 to 3 weeks. Then, a maintenance regimen of 5.0 mg per kg daily for 5 to 7 days a week is continued until the disease and infection have cleared and host immunity is restored. When host immunity is not restored, ganciclovir may need to be continued indefinitely in some cases, depending on the underlying defect and the location and extent of the CMV disease. Recent studies with CMV in AIDS patients show that oral ganciclovir can be used successfully for the maintenance phase of treatment.

CMV cultures and CMV-DNA detection methods are used for monitoring response. Note that CMV DNA may be detected in blood and urine samples for months after clinical and viral responses are complete.

The addition of intravenous immunoglobulin or CMV-hyperimmunoglobulin has been investigated scantily, with the impression that for CMV pneumonitis the combination with ganciclovir results in a survival advantage over historical controls treated by other regimens.

Ganciclovir is myelosuppressive and neutropenia is common. For patients who cannot tolerate, or who fail to respond to ganciclovir, foscarnet is a useful alternative. This DNA polymerase inhibitor is nephrotoxic. It may be used alone or in combination with ganciclovir and intravenous CMV-immunoglobulin. A new drug, cidofovir, now approved for CMV retinitis, may be also considered as an alternative therapy for CMV disease. Formivirsin has recently been approved by the FDA for use in CMV retinitis in AIDS patients. Promising new agents in development include lobucavir, 1263W94, adefovir-dipovoxil (bis POM-PMEA) and antisense nucleotides.

#### **Prevention:**

For the immunocompromised host that is CMV-seronegative, intensive effort should be made to prevent CMV infection, especially if the patient is to receive blood or BMT. The following approaches to prophylaxis are available for consideration:

1. Use only CMV-seronegative blood products. If CMV negative donors are not available, use frozen deglycerolized red blood cells and leukocyte-depleted blood.

2. Passive immunoprophylaxis with immunoglobulin or CVM-hyperimmunoglobulin preparations.
3. CMV-seronegative donor for transplantation.
4. Prophylaxis with antiviral drugs, such as ganciclovir.

The most practical opportunity for CMV prophylaxis with antiviral drugs and passive immunization is for those patients with primary immunodeficiency disorders who are to receive BMT. In light of the high frequency of CMV disease if the donor or recipient is seropositive, an aggressive prophylaxis regimen is warranted. The following approach is suggested: ganciclovir, administered intravenously from engraftment to day +100 post BMT. An alternative approach is a pre-emptive strategy using ganciclovir for those patients who show evidence of CMV infection after transplantation. Recipients are screened with sensitive CMV detection methods at least weekly from day +10 to day +100 post transplantation. With the detection of CMV virus or antigen, ganciclovir is started and continued to at least 100 days post transplantation.

The concomitant use of intravenous immunoglobulin or CMV-hyperimmunoglobulin; or the use of oral ganciclovir or valganciclovir; foscarnet; cidofovir or other drugs in development, has not been adequately studied to make recommendations at this time. Adoptive transfer of CMV-specific CD8<sup>+</sup> cytotoxic T-cell clones from the donor to the recipient offers intriguing possibilities to be investigated further.

#### **Herpes simplex virus:**

One of the most remarkable features of herpes simplex virus infections is that in most cases it remains localized to skin and mucous membranes despite severe immunocompromise and high virus load in the host. Systemic dissemination occurs infrequently.

#### **Treatment:**

With shallow lesions of limited extent, in the absence of severe neutropenia and deep tissue or organ involvement, no systemic treatment may be needed. In other cases acyclovir is the drug of choice. Famciclovir or valacyclovir, given orally, are effective alternatives.

#### **Prevention:**

In selected patients with frequent and severe recurrences, acyclovir prophylaxis may be used. Some physicians recommend acyclovir prophylaxis for Herpes simplex virus-seropositive, allogeneic transplant recipients during the early post-transplantation period.

#### **Varicella-zoster virus (VZV):**

Varicella may be fatal in severely immunocompromised patients, especially those with defects in cell-mediated immunity. Varicella pneumonia, with or without other organ involvement, occurs in about one-third of cases with a 7% fatality rate (based on leukemic children on chemotherapy). Thus, the earliest onset of varicella in the compromised host demands immediate treatment with an antiviral drug. Zoster is less hazardous, but fatal cases occur and all cases of zoster in compromised patients should be treated with antiviral drugs.

#### **Treatment:**

Intravenous acyclovir is the drug of choice and should be administered at least five days and until no new lesions appear. Oral famciclovir and valacyclovir have been used successfully for the treatment of zoster in compromised adults.

Salicylates are contraindicated during varicella-zoster virus infections because of the risk for Reye syndrome.

#### **Prevention:**

1. Passive immunization: susceptible, VZV-seronegative compromised patients with close exposure to patients with varicella or zoster should be given VZV-immune globulin (VZIG) within three days after exposure.
2. Active immunization: susceptible members of families of immunocompromised hosts should be actively immunized with live-attenuated varicella-zoster virus vaccine. CAUTION: vaccinees should avoid contact with the compromised patient.
3. In areas where VZIG might not be available, exposed susceptibles may be given acyclovir or famciclovir prophylactically immediately after exposure and continued for 10 to 14 days. Also, standard intravenous immunoglobulin (IVIg) at the dose of 400 mg per kg provides about the same quantity of antibody as a dose of VZIG. Be aware that VZIG is the only approved agent for varicella-zoster prophylaxis and is always the preferred choice.

#### **Epstein-Barr Virus (EBV)**

Infection of the severely immunocompromised host with EBV may be complex. In addition to typical and atypical signs and symptoms of infectious mononucleosis, some patients may acquire life-threatening lymphoproliferative diseases, B cell lymphoma and possibly other malignancies attributable to EBV. Children with the X-linked lymphoproliferative syndrome, severe combined immunodeficiency syndrome, common variable immunodeficiency, Chediak-Higashi syndrome, Wiskott-Aldrich syndrome, BMT and ataxia telangiectasia have been

## 6

reported to have severe problems with EBV infection.

### **Treatment:**

No effective treatment has been established. The use of anti-B Cell monoclonal antibodies, infusions of irradiated donor leukocytes and infusions of donor derived, EBV-specific cytotoxic T lymphocytes have offered some promise in the management of the lymphoproliferative syndromes of EBV infection.

### **Prevention:**

No proven method for prevention is known. The use of donor derived EBV-specific cytotoxic T lymphocytes for BMT recipients at high risk for lymphoproliferative disease has been promising in early studies.

### **Human Herpesviruses (HHV)**

#### **6, 7, and 8:**

Much is yet to be learned about these recently recognized viruses. HHV-6 causes roseola (exanthem subitum) in normal children and also in immunocompromised hosts. Severe hepatitis and possibly encephalitis have been described in compromised patients with HHV-6 infection. HHV-7 may be a cause of roseola-like symptoms and DNA fragments of HHV-8 have been found in Kaposi sarcoma cells.

### **Treatment:**

Treatment is not probably not necessary for most cases, but little data are available. HHV-6 is susceptible to ganciclovir in vitro.

### **Prevention:**

No method to prevent these infections is known.

### **ROTAVIRUS:**

Rotavirus infection can cause severe diarrhea, particularly in the host with defective T cell function, and the infection may spread to the liver and kidneys.

### **Treatment:**

No established therapy is available. The administration of human milk with rotavirus antibody, oral doses of human immune globulin, and milk or colostrum from rotavirus immunized cows, have been tried with some evidence of success in limited studies.

### **Prevention:**

No method for prevention is available. A new attenuated rotavirus vaccine has been withdrawn from the market due to the excess occurrence of intussusception after its use.

## **CONCLUSIONS:**

Currently, several rapid diagnostic tests, antiviral drugs and immunological agents are available for the management of life-threatening viral infections in immunocompromised host. The suggestions made in this review must be taken as general and need to be considered wisely when applied to a specific patient. New studies are forthcoming in this field and those who manage immunocompromised patients must stay abreast of developments that may or may not render these current recommendations obsolete.

## **REFERENCES:**

- DeJong MD, Galasso GJ, Gazzard B, et al. Summary of the II International Symposium on Cytomegalovirus. *Antiviral Research* 1998; 39: 141-162.
- De Vincenzo J. Prevention and treatment of respiratory syncytial virus infections. *Adv Pediatr Infect Dis* 1997; 13: 1-47.
- Koff RS. Advances in the treatment of chronic viral hepatitis. *JAMA* 1999; 282: 511-2.
- Monto AS, Fleming DM, Henry D, et al. Efficacy and safety of the neuraminidase inhibitor zanamivir in the treatment of influenza A and B virus infections. *J Infect Dis* 1999; 180: 256-61.
- Ogra PL, Patel J. Respiratory syncytial virus infections in the immunocompromised host. *Pediatr Infect Dis* 1988; 7: 246-249.
- Rooney CM, Smith CA, Ng CYC, et al. Infusion of cytotoxic T cells for the prevention and treatment of Epstein-Barr virus-induced lymphoma in allogeneic transplant recipients. *Blood* 1998; 92: 1549-1555.
- Rotbart HA, O'Connell JF, McKinley MA. Treatment of human enterovirus infections: a mini review. *Antiviral Research* 1998; 38: 1-14.

to receive your **FREE** subscription to *Clinical Focus on Primary Immune Deficiencies*, send your mailing address with your request to:

Immune Deficiency Foundation • 25 West Chesapeake Avenue • Suite 206 • Towson, Maryland 21204

NONPROFIT ORG  
U. S. POSTAGE  
PAID  
ELLICOTT CITY, MD  
PERMIT NO. 70

Immune  
Deficiency  
Foundation



25 West Chesapeake Avenue  
Suite 206  
Towson, Maryland 21204