in children, aciclovir was given (20 mg/kg for children; 800 mg for adolescents, both four times per day for 5 days commencing within 24 hours of onset of rash). Aciclovir reduced the number of lesions, reduced the time to cessation of new lesion formation and defervescence, and accelerated healing of the lesions compared to placebo. In addition there was no alteration in antibody response as a result of therapy, thereby ensuring relative immunity to future VZV infection (Dunkle *et al.*, 1991; Balfour *et al.*, 1992). In both these trials aciclovir was safe and well tolerated. Aciclovir did not decrease the risk of transmission of the virus within the household (Feldman, 1993), nor did it reduce the duration of absence from school (American Academy of Pediatrics, 2015).

In an open, noncomparative multicenter study of children with varicella aged 3 months to 2 years were given aciclovir (80 mg/kg/day in four divided doses for 4–6 days). When the therapy was started < 24 hours after the appearance of the rash, aciclovir resulted in a rapid defervescence, resolution of itch and other constitutional symptoms, and cessation of new lesions with acceleration of healing of existing lesions (Chiodo *et al.*, 1995).

For varicella cases, the American Academy of Pediatrics' Committee on Infectious Diseases recommends treatment with oral aciclovir in otherwise healthy people with increased risk of moderate to severe disease due to being > 12 years of age; having chronic cutaneous or pulmonary diseases; receiving chronic salicylate therapy to prevent of Reye's syndrome; or receiving short, intermittent, or aerosolized courses corticosteroids. Aciclovir 20 mg/kg orally given four times per day for 5 days should be initiated within 24 hours of the rash (American Academy of Pediatrics, 2015). In one nonrandomized study, postexposure prophylaxis of family members using aciclovir (40 or 80 mg/kg/day in four divided doses for 7 days) prevented or modified varicella infection, even when administered late in the incubation period. In 25 exposed children or infants who received aciclovir 7–9 days after exposure to the index case in the family, 16% developed varicella and 4% had fever, compared with 25 controls, all of whom developed disease and over two thirds developed fever; 84% of aciclovir recipients seroconverted (Asano *et al.*, 1993).

VARICELLA IN IMMUNOCOMPETENT ADULTS

Several controlled studies have found that both intravenous and oral aciclovir therapy, if commenced early following the onset of rash, can decrease the time to healing, the duration of fever, the maximum number of lesions, the virus titer within the vesicles, and the severity of symptoms of immunocompetent adults with varicella (Al-Nakib *et al.*, 1983; Feder, 1990; Wallace *et al.*, 1992). Treatment must be initiated within the first 24 hours of lesions for aciclovir to be efficacious (Wallace *et al.*, 1992).

Although there are no controlled studies to prove efficacy, treatment of adults with varicella complicated by pneumonia using intravenous aciclovir is strongly supported by case reports and uncontrolled studies (Schlossberg and Littman, 1988; Haake *et al.*, 1990). Varicella pneumonia in a pregnant woman is potentially life-threatening and must be treated with intravenous aciclovir (Boyd and Walker, 1988; Haake *et al.*, 1990; Smego and Asperilla, 1991; Arvin, 1993).

ACICLOVIR-RESISTANT VZV INFECTION

In both adult and pediatric patients with advanced HIV infection, chronic, hyperkeratotic papules due to aciclovir-resistant VZV have been reported (Pahwa *et al.*, 1988; Linnemann *et al.*, 1990; Lokke-Jensen *et al.*, 1993; Colebunders *et al.*, 1994; Lyall *et al.*, 1994). Meningo-radiculoneuritis due to aciclovir-resistant VZV has also been reported in a patient with late-stage HIV infection (Snoeck *et al.*, 1994). Foscarnet is the drug of choice for aciclovir-resistant zoster (Safrin *et al.*, 1991b). Topical trifluorothymidine alone or in combination with interferon-alpha may also be of benefit in cases of aciclovir resistance (Birch *et al.*, 1992; Rossi *et al.*, 1995); however, given the superior efficacy of foscarnet in this situation, it should be used preferably.

7c. Cytomegalovirus infections

Because CMV is less much less susceptible to aciclovir than either HSV or VZV, this drug is ineffective for treatment of CMV infections (Plotkin *et al.*, 1982; Wade *et al.*, 1982b; Wade *et al.*, 1983b; Shepp *et al.*, 1984; Table 213.3). Although some studies have shown that aciclovir prophylaxis decreases the frequency of symptomatic CMV infections after transplantation, including heart, kidney, and bone marrow (Gluckman *et al.*, 1983; Meyers *et al.*, 1988; Balfour *et al.*, 1989; Fletcher *et al.*, 1991; Elkins *et al.*, 1993; Legendre *et al.*, 1993; Mollison *et al.*, 1993; Dunn *et al.*, 1994), aciclovir failed to prevent CMV infection or disease in other studies, especially in liver transplant recipients (Bailey *et al.*, 1993; Wong *et al.*, 1993; Bacigalupo *et al.*, 1994; Singh *et al.*, 1994; Boeckh *et al.*, 1995; Winston *et al.*, 1995; Barkholt *et al.*, 1999). Aciclovir is generally considered to be markedly inferior to ganciclovir as prophylaxis against CMV infection or disease in this patient population, according to the latest guidelines from the American Society of Transplantation and American Society of Transplant Surgeons (Razonable *et al.*, 2013; Duncan *et al.*, 1994; Martin *et al.*, 1994). Valaciclovir at a dose of 2 g orally four times daily (adjusted for renal function) for 90 days reduced the incidence and delayed onset of CMV disease and reduced the incidence of acute rejection when compared with placebo treatment and in renal transplant recipients (Lowance *et al.*, 1999). Hallucinations and confusion were more common in valaciclovir recipients but were not treatment limiting. In another prospective study, both oral valaciclovir (2 g four times daily) and oral ganciclovir (1 g three times daily) significantly reduced CMV disease incidence, but the rejection rate was significantly lower in the oral valaciclovir group compared with both oral ganciclovir and deferred therapy (Reischig *et al.*, 2005). In a retrospective, nonrandomized study, there was no difference in CMV infection or acute rejection in patients treated with valaciclovir 2 g four times daily versus those treated with oral ganciclovir 1 g three times daily (Yango *et al.*, 2003). Both valaciclovir prophylaxis and preemptive therapy with valganciclovir were