markedly improved platelet numbers in both patients. One patient was cured with foscarnet therapy but the other received a prophylactic splenectomy despite excellent platelet counts.

Congenital or postpartum CMV infections have only rarely been treated with foscarnet (Nigro *et al.*, 2004; Knorr *et al.,* 2007). Hence it is recommended that foscarnet be used in infants only if they have failed therapy with ganciclovir (Lackner *et al.*, 2008; Mareri *et al.,* 2015) or cannot tolerate that drug for other reasons (Schleiss and McVoy, 2004; Michaels, 2007).

7d. Treatment of aciclovir-resistant HSV and VZV infections

SYSTEMIC TREATMENT OF HSV AND VZV INFECTIONS

Foscarnet is useful for the treatment of mucocutaneous HSV or VZV infections in patients with HIV-infection or other immunocompromising conditions who are resistant to aciclovir or famciclovir (Safrin *et al.*, 1990; Safrin *et al.*, 1991a). Treatment should commence within 7–10 days if aciclovir-resistant infection with HSV or VZV is suspected and should continue for at least 10 days or until lesions are healed (Balfour *et al.*, 1994).

The first randomized controlled trial assessing the efficacy of any antiviral drug for treatment of a drug-resistant virus was conducted under the aegis of the AIDS Clinical Trials Group (Safrin *et al.*, 1991b). That study compared vidarabine (15 mg/kg daily) with foscarnet (40 mg/kg every 8 hours) for treatment of 14 patients with HIV-infection and aciclovir-resistant mucocutaneous herpes simplex infection, that diagnosis was assessed clinically by failure to respond to 10 days of high-dose, intravenous aciclovir. All HSV isolates were resistant to aciclovir and susceptible to both vidarabine and foscarnet by *in vitro* testing. The HSV lesions healed within 10–42 days in all 8 patients randomized to foscarnet (the investigational drug), whereas vidarabine (at the time, the only drug approved for treatment of aciclovir-resistant HSV strains) was discontinued in all 6 patients assigned to receive it, owing to lack of any clinical or virologic response (Safrin *et al.*, 1991b).

Multiple other case reports and case series have confirmed these earlier data showing the efficacy of foscarnet for the treatment of mucocutaneous infections due to aciclovir-resistant, foscarnet-susceptible strains of HSV. The clinical contexts in which this treatment has been effective include patients with HIV infection (Erlich *et al.*, 1989), bone marrow transplant recipients (Verdonck *et al.*, 1993; Reusser *et al.*, 1996), and allogeneic stem cell transplant recipients (Chen *et al.*, 2000). However, failures of therapy have occurred, even when the HSV strains were susceptible to foscarnet by *in vitro* testing (Chen *et al.*, 2000; Frangoul *et al.*, 2007). The importance of laboratory testing of HSV strains for foscarnet susceptibility was emphasized by data showing that none of seven patients infected with HSV strains dually resistant to both aciclovir and foscarnet responded to foscarnet, whereas five of seven patients with aciclovir-resistant, foscarnet-susceptible HSV strains did respond (Chen *et al.*, 2000). Similar results were reported by Danve-Szatanek *et al.* (2004), who reported that only 61% of patients with aciclovir-resistant, foscarnet-susceptible HSV lesions responded to foscarnet.

Chilukuri and Rosen (2003) recommended a staged approach to management of suspected aciclovir-resistant HSV cutaneous lesions, starting therapy by increasing the dose of aciclovir (or using valaciclovir) and then adding topical trifluorothymidine if the lesion is accessible; only if it remains unresponsive is foscarnet therapy initiated at 40 mg/kg every 8 hours.

Two cases of acute retinal necrosis (with unspecified underlying conditions) due to aciclovir-resistant HSV-2 infections have been reported in children; they responded to intravenous foscarnet with satisfactory outcomes (Khurana *et al.*, 2005).

Foscarnet-resistant strains of HSV-2 have been recovered from patients unresponsive to foscarnet therapy or in whom lesions developed while undergoing foscarnet therapy. It is interesting that in three patients, treatment with aciclovir monotherapy or in combination with foscarnet resulted in healing (Safrin *et al.*, 1994c). Topical cidofovir (see Chapter 216, Cidofovir and brincidofovir) may be of use in patients with mucocutaneous lesions due to aciclovir- and foscarnet-resistant HSV (Snoeck *et al.*, 1994).

Foscarnet-resistant multidermatomal zoster has been reported in a patient with advanced HIV infection (Fillet *et al.*, 1995). This condition often presents with atypical keratotic papular skin lesions, especially in the setting of HIV infection with significant immunosuppression (Lokke-Jensen *et al.*, 1993). An open-label study found that foscarnet was effective in the treatment of thymidine kinase-deficient or -altered strains of VZV that were resistant to aciclovir (as opposed to those with polymerase mutations) (Safrin *et al.*, 1991a). Breton *et al.* (1998) retrospectively studied 13 consecutive patients with advanced HIV infection (mean CD4 count, 20/μl) who had infections due to aciclovir-resistant VZV strains (based on clinical criteria) and who were treated with foscarnet. Complete healing was seen in 10 (77%) of these patients, but 5 relapsed at a median of 110 days after cessation of foscarnet therapy. No susceptibility testing was conducted in this study, and some of the nonresponders could have had polymerase mutations mediating dual aciclovir and foscarnet resistance.

Other case reports and case series confirm the efficacy of foscarnet for the treatment of aciclovir-resistant VZV infections in the setting of patients with immunodeficiency caused by a variety of illnesses or treatments, including hematopoietic stem cell transplantation (Hatchette *et al.*, 2008) and cancer chemotherapy with disseminated Oka-strain VZV vaccine (Levin *et al.*, 2003).

TOPICAL OR INTRAVITREAL TREATMENT OF HSV, VZV OR CMV INFECTIONS

Topical therapy of mucocutaneous HSV lesions is of questionable efficacy compared with systemic therapy, regardless