that the clearance of foscarnet by hemodialysis was about 89 ml/minute.

Alexander *et al.* (1996) studied the disposition of foscarnet during continuous cyclic and continuous ambulatory peritoneal dialysis in a single patient. Foscarnet plasma half-lives during these two types of dialysis were 41 and 45 hours, respectively, much longer than the plasma half-life observed by the same investigators in patients with normal renal function (4.5 hours) and half that seen in anuric patients at a time when they were not on dialysis. The authors suggested that foscarnet dosing needed to be individualized during peritoneal dialysis.

5e. Drug interactions

Because the kidneys are the main target of foscarnet toxicity, giving foscarnet with other drugs known to be nephrotoxic (e.g. aminoglycoside antimicrobials, amphotericin, parenteral pentamidine) substantially increases the risk of decreasing renal function (and thereby increasing serum foscarnet concentrations). Close monitoring of renal function is generally required in patients receiving foscarnet, and co-administration with effective doses of other nephrotoxic drugs usually mandates daily renal function testing.

No drugs should be infused simultaneously with foscarnet. Ganciclovir and foscarnet co-therapy do not alter the plasma clearance or volume of distribution of either drug (Aweeka *et al.*, 1995). However, these drugs are not compatible and cannot be infused together.

Two studies showed that zidovudine and didanosine have no interactions with foscarnet and vice versa (Aweeka *et al.*, 1992; Taburet and Singlas, 1996); this limited evidence suggests that foscarnet therapy would not alter the pharmacokinetics of nucleoside antiretroviral drugs, nor would they alter foscarnet pharmacokinetics. Information on other classes of antiretroviral drugs is absent.

Foscarnet should not be given to patients receiving intravenous pentamidine because both drugs may cause hypocalcemia and renal insufficiency. The concomitant administration of intravenous pentamidine and foscarnet has been associated with severe, potentially fatal hypocalcemia (Youle *et al.*, 1988). Similarly, there is a recommendation that foscarnet should not be given to patients receiving amphotericin B, because of a potential increased risk of renal impairment (Reusser *et al.*, 1992). Liposomal amphotericin has not been studied.

6. ADVERSE REACTIONS AND TOXICITY

The major toxicities of foscarnet are summarized in Table 219.14. A review of 63 patients who had received reduced-dose foscarnet for CMV infections in the context of cord blood transplantation summarizes most of the data on foscarnet toxicity (Narimatsu *et al.*, 2007).

6a. Nephrotoxicity

The most common and usually the most clinically significant adverse effect of foscarnet therapy is nephrotoxicity, with up to 25% of patients developing dose-limiting renal impairment (Jacobson, 1992b; Narimatsu *et al.*, 2007). Continuous infusion is associated with a higher risk of nephrotoxicity than intermittent (twice or three times daily) administration (Chrisp and Clissold, 1991). Nyberg and colleagues (1989) described five renal transplant patients with nephrotoxicity due to foscarnet, which was associated with high fever in all cases. The temperature normalized quickly when foscarnet was withdrawn, but the serum creatinine continued to rise for a further 3 days or so. Foscarnet-induced renal impairment

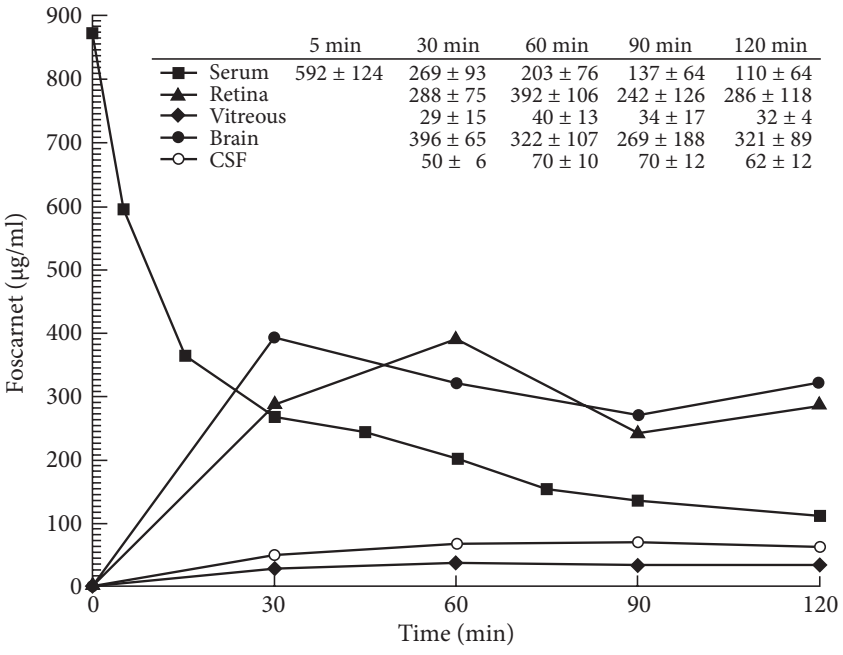

Figure 219.2. Foscarnet concentrations in plasma and ocular tissues and fluids after intravenous administration to rabbits. A single dose of foscarnet was administered to 32 rabbits, and fluids and tissues were assayed at the times shown (1 μM is approximately equal to 0.3 μg/ml). (Redrawn with permission from López-Cortéz *et al.* (2000).)