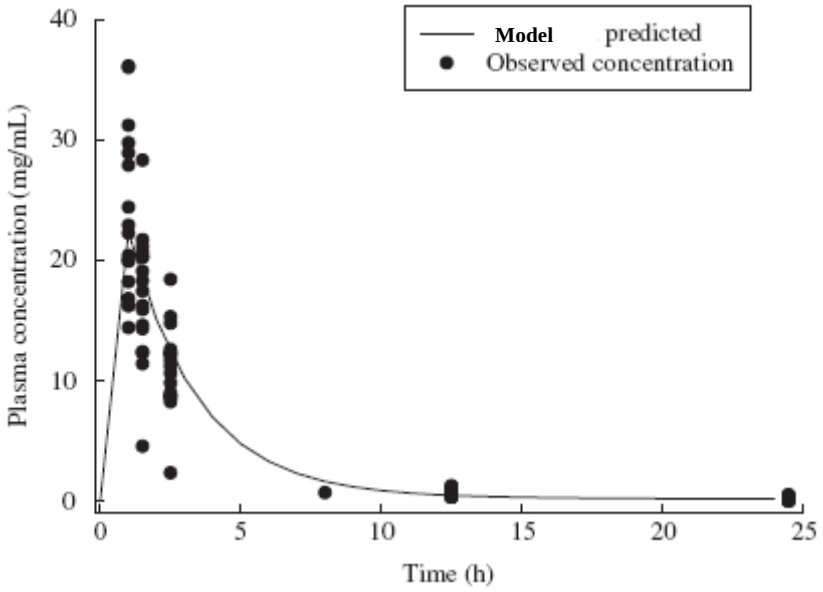
PHA 5128

CASE STUDY 3

Spring 2008

Question #1:

Aminoglycosides have a triphasic disposition, but tobramycin concentration-time profile here is described via a 2-compartment model since the alpha phase could not be characterized in the study as in the Figure. Which of the following statements is true?



A) The fast alpha phase is due to the tobramycin passive diffusion into the cells.

B) The second phase for tobramycin in this 2-compartment model represents the return from the deep compartment for aminoglycosides.

C) Patients with renal impairment will have the same profiles since tobramycin is mainly eliminated via liver.

D) Tobramycin is quickly eliminated from body as indicated by the flat second phase in the curve.

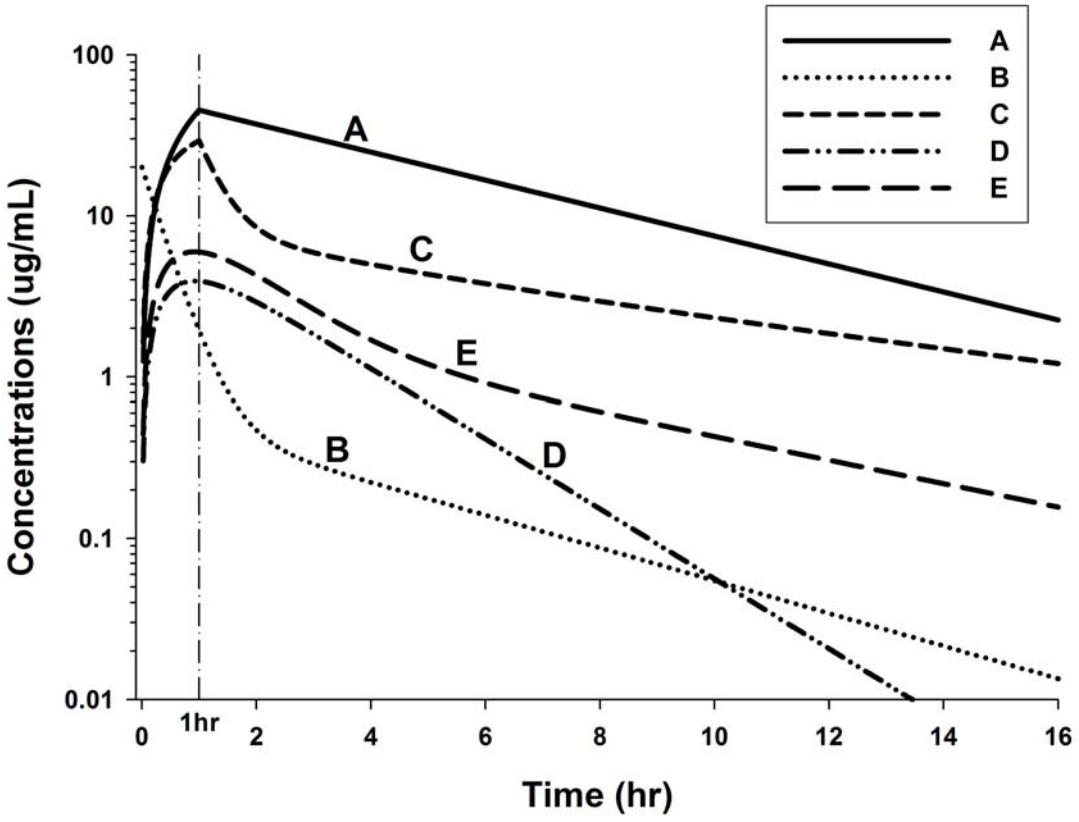
E) None of Above.

Question #2:

Discuss why the sampling time is important to monitor aminoglycoside administration. Please include why it is important for the nurse to record the exact sampling time, and when peak and trough levels should be drawn.

Question #3:

Vancomycin concentration-time profile can be described via a three compartment model. Which profile will represent a 1-hr infusion of vancomycin in the following graph?



Question #4:

GD, a 75 year old male (6'3", 94kg, Cl=30mL/min, Vd=0.7L/kg), has been empirically started on 500mg vancomycin every 8hours (multiple i.v. bolus) for the treatment of a community acquired *Streptococcus pneumoniae* infection. What would be the expected steady-state peak and trough vancomycin concentrations for GD? Discuss the results. What will be the new dose regimen to achieve expect peak concentration (26 mg/L) and tough concentration at steady-state (11 mg/L)?

Question #5:

Drug A is a basic drug. Recently, protein binding studies were performed in both *in vivo* (patients with malaria, and plasma AAG concentrations were consistently raised in acute malaria) and *in vitro*. The results were shown in Figure 1. A linear relationship between log alpha 1-acid glycoprotein (AAG) concentration and percentage of free drug A *in vivo* was identified, which was similar to that obtained by *in vitro* addition of AAG to plasma containing drug A (10 mg/L). There was no relation between plasma albumin and free fraction of drug A. Which of following statement is FALSE?

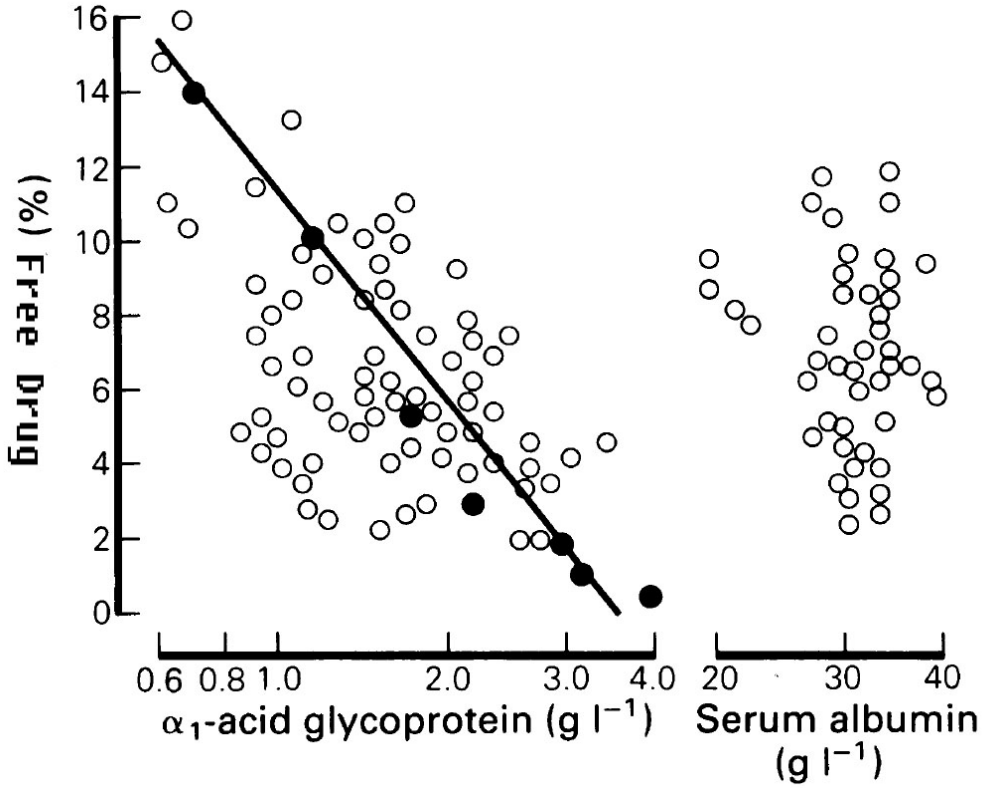


Figure 1 Relationship of drug A plasma protein binding (free/total concentrations; %) to plasma AAG concentration from *in vivo* study (open circles). The closed circles represent *in vitro* addition of AGP to a plasma sample containing drug A (10 mg/L) and AAG 0.7 g/L

A: Free drug concentrations will not be affected if drug A is a low extraction drug and protein binding changes.

B: Percent of drug A protein binding is much higher in the healthy elderly than that in the healthy young.

C: AAG is an acute phase protein, and is the principal binding protein for drug A.

D: If drug A is a high extraction drug, dose adjustment is needed for patients with higher AAG concentrations in order to achieve therapeutic effects.

E: Newborns have low protein binding of drug A because of low concentrations of AAG in plasma.