Question #1
H.J, a 75 kg male, was admitted to the hospital with seizures. A loading dose of sodium phenytoin was given to achieve 15 mg/L, and then a maintenance dose was given 300 mg daily. After a week, a steady-state concentration was measured at 9 mg/L. The physician decided to increase the maintenance dose to 350 mg daily. After another week, the concentration of phenytoin at steady-state was at 22 mg/L, which is too high. The following dose was discontinued until the concentration has dropped to 15 mg/L. How long will it take to achieve this drop from 22 mg/L to 15 mg/L? (3 points)

Question #2
A patient (35 years old, 65 kg) is to be started on intravenous phenobarbital sodium. The therapeutic range is 10-30 mg/L. A loading dose is given so as to yield a Cp₀ of 30 mg/L. Calculate this loading dose and the daily maintenance dose to produce an average steady state phenobarbital concentration of 20 mg/L. (Dose in phenobarbital sodium) (2 points)

Question #3
What is his expected trough concentration in this the following case:
R.M, a 10 year old 30 kg male receives 250 mg valproic acid every 12 hours for his absence seizures. But his seizures are only partially controlled. He reports no adverse effects at this dosing, and his renal and hepatic functions are normal. (2 points)

Question #4
A recent study was performed to investigate the effects of ketoconazole and carbamazepine on the pharmacokinetics of Drug 5128. Drug 5128 was given to the subjects alone, or concomitant administration of ketoconazole or carbamazepine with Drug 5128. The results are presented in the following Figures. Which of the following statement is FALSE? And WHY (Use one sentence)? (2 points)

Figure 1. Drug 5128 concentration-time profiles
Left Panel (Drug 5128 alone (close circles), concomitant administration of ketoconazole and Drug 5128 (open circles)); Right Panel (Drug 5128 alone (close circles), concomitant administration of carbamazepine and Drug 5128 (open circles)
A) In this study, ketoconazole increased mean Drug 5128 plasma $C_{\text{max}}$ significantly; and carbamazepine decreased mean Drug 5128 plasma $C_{\text{max}}$ dramatically.

B) Cytochrome P450 3A4 is a primary enzyme responsible for the metabolic clearance of Drug 5128.

C) Ketoconazole is the strong inhibitor of CYP3A4, and carbamazepine is the strong inducer of CYP 3A4.

D) Other drugs and ingested natural products that strongly modulate the activity or expression of CYP3A4 would be predicted to change exposure to Drug 5128.

E) Clearance of Drug 5128 is increased by ketoconazole; and decreased by carbamazepine

**Question #5**
Which combination of the following pharmacokinetic changes best describes the elderly and neonates? (These groups share similar PK characteristics.) *(1 point)*

1). Longer half-lives
2). Low metabolic clearance
3). Relatively less body water
4). Low renal clearance
5). Decreased protein binding