

PHA 5128 – Dose Optimization II
Case Study 4
Spring 2012

1. J.K., a 39-year-old, 75 kg male, had been taking 200mg/day of sodium phenytoin; however, his dose had been increased to 350mg/day because his seizures were poorly controlled and because his plasma concentration was only 5mg/L. Now he complains about minor CNS side effects and his measured plasma phenytoin concentration is 25mg/L. This level was decided to be too high for this patient, so the maintenance dose was discontinued. How long would it take for the concentration to drop to 15 mg/L after discontinuation of dose? Also, calculate the phenytoin loading dose required to achieve a plasma concentration 15 mg/L for this patient.

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2. L.J., a 40 year old female, was diagnosed congestive heart failure (CHF). She is 5'4" tall and weights 65 kg. Doctor would like to give her Digoxin tablets and Quinidine tablets. In order to achieve the therapeutic concentration of Digoxin (1.5 ng/mL), what would be a suggested loading and maintenance dose regimen for Digoxin? (L.J.'s serum creatinine concentration is: 1.4 mg/dL) (assuming Digoxin is rapidly absorbed)

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3. L.T., a 53-year-old, 75kg male patient (5'10", SeCr 1.3mg/dL) received a 30mg i.v. loading dose of methotrexate, followed by a 25mg/h continuous i.v. infusion over 36hours. At 36h, leucovorin rescue (10mg/m² q6h) was started. The following levels were monitored: 15μM at 36h; 0.9μM at 48h; 0.25μM at 60h. When do you expect the methotrexate levels to fall below 0.1μM?

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4. A study was conducted to assess the effect of thyroid diseases on Digoxin pharmacokinetics. Three groups of subjects received the same amount of Digoxin via intravenous administration. Group I: (Subjects with Myxedema (Hypothyroidism)); Group II: (Subjects with Euthyroid (normal) state); Group III: (Subjects with Hyperthyroidism). Serum Digoxin concentrations were measured, and concentration-time profiles were assessed. Which of following statement is FALSE?

- A) Subjects with hyperthyroidism have the highest apparent volume of distribution.
- B) If multiple doses are applied to the subjects, the time required to reach steady state will be the same for all three groups.
- C) Both clearance and volume of distribution are affected by thyroid disease.
- D) If subjects with hyperthyroidism have an increased glomerular filtration rate, and renal function is the major factor associated with digoxin clearance, patients with intrinsic renal failure will have a decreased digoxin clearance.
- E) When multiple doses are required, hyperthyroid patients will take smaller loading doses in order to achieve the same steady state concentrations as those in euthyroid state.