1. A 42-year-old, 60 kg female with a serum creatinine of 1.2 mg/dL, is to receive 12 g IV methotrexate infused over four hours. Calculate the methotrexate concentration 12 hours after the end of the infusion.

\[
\text{Cl}_{\text{cr}} = \frac{(140 - \text{age}) \times \text{weight}}{85 \times \text{SeCr}} = \frac{(140 - 42) \times 60\text{kg}}{85 \times 1.2\text{mg/dL}} = 57.6(\text{ml/min}) = 3.46(\text{L/h})
\]

\[
\text{Cl} = 1.6 \times \text{Cl}_{\text{cr}} = 1.6 \times 3.46 = 5.54(\text{L/h})
\]

\[
\text{Cp}_{(12\text{h})} = \frac{\text{Dose}}{\text{Cl} \times T} \times (1 - e^{-kT}) \times e^{-ke_t}
\]

\[
= \frac{12000\text{mg}}{5.54\text{L/h} \times 4\text{h}} \times (1 - e^{-0.231^4}) \times e^{-0.231^{12}}
\]

= 20.42 mg/L

\[
\text{Cp}_{(12\text{h})} = \text{Cp (mg/L)} / 0.454 = 20.42 / 0.454 = 45(\mu\text{M})
\]

2. A 23 year old female patient weighing 60 kg, has been taking uncoated (rapidly absorbed) theophylline tablets, 200 mg q 6 hr, with satisfactory response. Recently, steady-state theophylline plasma concentrations were determined to be 16.0 mg/L 1 hour after administration (peak) and 8.0 mg/L 6 hours after administration (trough). Please estimate the average steady-state theophylline concentration with this regimen. (For this case, assume that F=1.)

\[
k = -\frac{\ln C_2 - \ln C_1}{t_2 - t_1} = -\frac{\ln 8.0 - \ln 16.0}{6 - 1} = 0.138(\text{h}^{-1})
\]
\[
C_1 = \frac{D}{V} * \frac{1}{1 - e^{-k*\tau}} * e^{-k*t_1}
\]

\[
16\text{mg/L}= \frac{200\text{mg}}{V} * \frac{1}{1 - e^{-0.138*6}} * e^{-0.138*1}
\]

\[V=19.34(\text{L})\]

\[C_l= k*V=0.138*19.34=2.67(\text{L/h})\]

\[C_{ss} = \frac{D * F}{\text{Tau} * C_l} = \frac{200 * 1}{6 * 2.67} = 12.48(\text{mg/L})\]

3. Please mark the CORRECT statements about Digoxin.
   1) Digoxin is a PGP-substrate.
   2) Digoxin follows a one compartment body model.
   3) Digoxin levels are increased in patients with hyperthyroid function.
   4) Digoxin distributes rapidly into the myocardial tissue.
   5) Digoxin is only renally eliminated

A. 1, 3, 4  
B. 2, 3, 5  
C. 1, 2, 3, 4  
D. 1, 2, 4, 5  
E. None of the above

4. In the hospital, a 55 year old liver transplant patient received 300 mg cyclosporin once a day as an iv infusion which resulted in a trough level of 175 ng/ml. After he is discharged, he is to be started oral cyclosporine treatment. Please make a dose recommendation for him to keep the equivalent therapeutic effectiveness.
Dose_{new} = \frac{F_{current}}{F_{new}} \times Dose_{current} = \frac{1}{0.3} \times 300mg = 1000mg \text{ (day)}