PHA 5128

Exam 2

Spring 2013

1 Carbamazepine (5 points)
2 Theophylline (10 points)
3 Gentamicin (10 points)
4 Drug-drug interaction (5 points)
5 Lidocaine (5 points)
6 Cyclosporine (5 points)
7 Phenobarbital (5 points)
8 Renal Disease (5 points)
9 Basic PK (5 points)
10 Methotrexate (10 points)
11 Bioavailability (5 points)
12 Procainamide (10 points)
13 Phenytoin (10 points)
14 Digoxin (10 points)

Total Points: 100
Problem 1 (5 points)

Carbamazepine is a lipid soluble anti-epileptic drug that has a large volume of distribution in obese patients. Which of the following statements is true of the expected carbamazepine disposition in obese patients?

A. The elimination half-life in obese patients is expected to be decreased.

B. The elimination half-life in obese patients is expected to be increased.

C. As a result the elimination half-life in obese patients is expected to remain the same.

D. Its volume of distribution is expected to decrease.

E. None of the above statements is true.

Solution:

\[ t_{1/2} = 0.693 \times \frac{V_d}{CL} \]
**Problem 2 (10 points)**

Sophia is a 2-year-old, 12 kg girl in the PICU who is placed on a theophylline drip at 1 mg/kg/hr after first receiving a 5 mg/kg bolus at 10 am. The drug level was monitored and listed in the table below.

<table>
<thead>
<tr>
<th>Time</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>11 am</td>
<td>8.2 mg/L</td>
</tr>
<tr>
<td>7 pm</td>
<td>13.7 mg/L</td>
</tr>
</tbody>
</table>

What is the half-life of theophylline in this girl?

A. 1 h
B. 3 h
C. 6 h
D. 9 h
E. 12 h

Solution:

\[
CL = \frac{2 \times R_0}{(C_1 + C_2)} + \frac{2 \times Vd \times (C_1 - C_2)}{(C_1 + C_2) \times (t_2 - t_1)} = \frac{2 \times 1 \times 12}{(8.2 + 13.7)} + \frac{2 \times 0.5 \times 12 \times (8.2 - 13.7)}{(8.2 + 13.7) \times (19 - 11)} = 0.7 \, L/h
\]

\[
Vd = 0.5 \times 12 = 6L
\]

\[
k_e = \frac{CL}{Vd} = \frac{0.7}{6} = 0.117 \, h^{-1}
\]

\[
t_{1/2} = \frac{0.693}{k_e} = \frac{0.693}{0.117} = 5.9 \approx 6h
\]
Problem 3 (10 points)

C.D. is a 60 years old, 6’2” tall and 185 lbs weight male patient who suffers post-surgical wound infection and has been treated with gentamicin for several days. His serum creatinine is 1.5 mg/dL. The gentamicin is given IV infusion over 15 min with dose of 6 mg/kg once daily. Which of the following is close to the measured peak concentration that was taken 90 min after the infusion was started? (Please use $ke = CL/Vd$)

A. 30 mg/L
B. 25 mg/L
C. 20 mg/L
D. 15 mg/L
E. The information provided is not enough to calculate the peak concentration at steady state.

Solution:

$IBW = 50 + 2.3(\text{height in inches-60}) = 50 + 2.3(74-60) = 50 + 32.2 = 82.2 \text{ kg}$

$TBW = \frac{185}{82.2} \times 100\% = 102.3\% < 120\%$  TBW will be used to calculate creatinine clearance

$CL \approx CL_c = \frac{(140 - age) \times BW}{Cp_c \times 72} = \frac{(140 - 60) \times 185/2.2}{1.5 \times 72} = 62.3 \text{ ml/min} = 3.7 \text{ L/h}$

$Vd = 0.25 \text{ L/kg} \times \frac{185}{2.2} \text{ kg} = 21.0 \text{ L}$

$k_e = \frac{CL}{Vd} = \frac{3.7}{21.0} = 0.176 \text{ h}^{-1}$

$\tau = 24 \text{ h}$ and $T = 0.25 \text{ h}$
\[
C_{\text{max}} = \frac{Dose}{Vd \times k_e \times T \times (\frac{1-e^{-k_e \tau}}{1-e^{-k_e \tau}})} = \frac{6 \times 185/2.2}{21.0 \times 0.176 \times 0.25 \times (\frac{1-e^{-0.176 \times 24}}{1-e^{-0.176 \times 0.25}})} = 23.9 \text{ mg/L}
\]

t_1 = 1.25 h,

\[
C_{\text{max}}^* = C_{\text{max}} \times e^{-k_{hi}} = 23.9 \times e^{-0.176 \times 1.25} = 19.2 \text{ mg/L} \approx 20 \text{ mg/L}
\]

**Problem 4 (5 points)**

Which of the following combination is **TRUE** of triazolam metabolism and drug-drug interaction?

1) Based on the graphs above, rifampin induces the metabolism of triazolam
2) Based on the graphs above, ritonavir induces the metabolism of triazolam
3) Based on the graphs above, rifampin inhibits the metabolism of triazolam
4) Based on the graphs above, ritonavir inhibits the metabolism of triazolam
5) Metabolic enzyme inducers can increase the enzyme expression level through various mechanisms, including increasing transcription, decreasing mRNA degradation, etc.
6) There are only two types of metabolic enzyme inhibition, which are competitive and non-competitive inhibition.

A. 1, 4, 5&6
B. 2, 3, 5&6
C. 1, 4 &5
D. 2, 3 &5
E. 1&4

**Problem 5 (5 points)**

J.D, a 72 kg, 35 years old man, was admitted to the hospital for his liver cirrhosis. What is the loading IV dose of lidocaine to achieve the plasma level of 4 mg/L and what is the infusion rate of lidocaine to maintain the concentration to 4 mg/L?

A. LD is 200 mg and MD is 100 mg
B. **LD is 200 mg and MD is 120 mg**
C. LD is 170 mg and MD is 100 mg
D. LD is 170 mg and MD is 120 mg
E. LD is 100 mg and MD is 120 mg

Solution:

\[ V_c = 0.6 \times 72 = 43.2 L \]

We used the initial distribution because we are calculating the loading IV dose.

\[
LD = \frac{V_c \times Cp}{F \times S} = \frac{43.2 \times 4}{1 \times 0.87} = 198.6 mg \approx 200 mg
\]

\[
CL = 0.36 \times 72 = 25.9 L/h
\]

\[
MD = \frac{D}{\tau} = \frac{CSS \times CL}{S \times F} = \frac{4 \times 25.9}{0.87 \times 1} = 119.1 mg/h \approx 120 mg/h
\]
Problem 6 (5 points)

A 65 kg liver transplant patient was receiving 300 mg QD cyclosporine with IV infusion. His plasma concentration at steady state was 160 ng/mL. Since his hepatic function tests appear to be fine, the physician would like to change the IV infusion to oral administration and adjust the steady state concentration to be 130 ng/mL. What would be an appropriate oral dose for him?

A. 90 mg/day
B. 600 mg/day
C. 800 mg/day
D. 900 mg/day
E. 1000 mg/day

Solution:

\[
Dose_{\text{new}} = \frac{C_{ss_{\text{desired}}}}{C_{ss_{\text{current}}}} \times \frac{F_{\text{current}}}{F_{\text{new}}} \times Dose_{\text{current}} = \frac{130}{160} \times \frac{1}{0.3} \times 300 = 812.5 \approx 800 \text{ mg/day}
\]
Problem 7 (5 points)

J.D. is a 2-week-old neonate, 4 kg in weight has developed tonic-clonic seizure activity and was administered phenobarbital sodium intravenous infusion. Half-way through the dosing interval ($C_{ss,ave}$) after 8 weeks of dosing at 5.1 mg every 12 hours, his blood concentration of phenobarbital was 23 mg/L. Determine J.D.’s phenobarbital clearance. Assume that steady-state is achieved.

A. 0.89 L/hr/kg
B. 1.7 L/hr/kg
C. 0.017 L/hr/kg
D. 12 L/hr/kg
E. 0.00416 L/hr/kg

Solution:

\[
CL = \frac{S \times F \times \frac{Dose}{\tau}}{C_{ss,ave}} = \frac{0.9 \times 1 \times \frac{5.1}{12}}{23} = 0.017 \frac{L}{hr}
\]

\[
CL \text{ by weight} = \frac{0.0166 \frac{L}{hr}}{4 \text{ kg}} = 0.00416 \frac{L}{hr/kg}
\]
Problem 8 (5 points)

Which combination of the following factors makes the serum creatinine level a good choice to estimate renal function?

1) Creatinine is endogenous
2) Creatinine is only eliminated by the kidney
3) Creatinine urinary excretion rate is not affected by diseases
4) Creatinine is bound to protein in plasma
5) Creatinine is usually constantly formed by muscle

A) 1, 2 & 5
B) 1, 2, 3 & 5
C) 1, 2, 4 & 5
D) 1, 3, 4 & 5
E) All of the factors make the serum creatinine level a good choice to estimate renal function.
Problem 9 (5 points)

Select all TRUE statements.

1) Clearance can be thought of as a volume of plasma from which the drug is removed in a specific time period.

2) If elimination from the central/body compartment is first order we can assume that a one compartment pharmacokinetic model is applicable.

3) Given $C_p = C_{p0} \times e^{-kt_{\text{tot}}}$, and two data points $(t_1, C_{p1})$ and $(t_2, C_{p2})$, the elimination rate constant can be calculated as the slope equals to $-(\ln C_{p2} - \ln C_{p1})/(t_2 - t_1)$.

4) If the infusion rate constant ($k_0$) is doubled the steady state plasma concentration ($C_{pss}$) will be doubled, assuming the other parameters are unchanged.

5) Appropriate unit for AUC is mg·hr·L.

A. 1, 2, 3 & 4
B. 2, 3, 4 & 5
C. 1, 2, 3
Problem 10 (10 points)

V.A., a 25-year-old, 61-kg woman (non-obese, SCr = 1.2 mg/dL) is to receive a course of methotrexate (MTX) therapy for acute lymphoblastic leukemia. Her regimen will consist of an IV infusion of 40 mg/h for 36 hours. Calculate her anticipated MTX plasma level (in μM) 60h after the beginning of the infusion. You may assume that steady state has been achieved after 24h.

A. 0.15 μM

B. 0.25 μM

C. 0.35 μM

D. 0.45 μM

E. 0.55 μM

Solution:
\[
CL_{Cr} = \frac{(140 - \text{age})(\text{weight in kg})}{85(Scr_{ss})} = \frac{(140 - 25)(61)}{85(1.2)} = 68.8 \frac{mL}{min} = 4.1 \frac{L}{h}
\]

\[
CL_{MTX} = (1.6)CL_{Cr} = (1.6)4.1 \frac{L}{h} = 6.6 \frac{L}{h}
\]

\[
C_{36} = C_{ss,avg} = \frac{Dose}{\tau \cdot CL} = \frac{40mg}{(1h)(6.6 \frac{L}{h})} = 6.1 \frac{mg}{L}
\]

\[
6.1 \frac{mg}{L} = 13.4 \mu M
\]

Let \( t^* \) be the time (after stop of the infusion) that is required to for MTX concentration to fall to 0.5 \( \mu M \).

\[
t^* = \frac{ln\left(\frac{13.4 \mu M}{0.5 \mu M}\right)}{0.231 \frac{1}{h}} = 14.2h
\]

\[
60h - 36h - 14.2h = 9.8h
\]

\[
k_o(< 0.5 \mu M) = \frac{ln(2)}{10h} = 0.0693 \frac{1}{h}
\]

\[
C_{60} = C_{50.2}(e^{-0.0693 \cdot 9.8h}) = 0.5 \mu M(e^{-0.0693 \cdot 9.8h}) = 0.25 \mu M
\]

**Problem 11 (5 points)**

In general, what is **NOT** the reason that an oral dosage form will have <100% bioavailability:

A. Poor solubility/dissolution rate

B. First-pass effect

C. Poor permeability

D. **Low volume of distribution**

E. All above are the reasons that an oral dosage form will have <100% bioavailability.
Problem 12 (10 points)

T.H. is a 43-year-old, 45 kg weight female with serum creatinine of 1.7 mg/dL. She is hospitalized with congestive heart failure and procainamide is recommended by the physician. What is the half-life of procainamide in this patient?

A. 0.1h
B. 1.5h
C. 3h
D. 4h
E. 8h

Solution:
\[ CL_{kr} = \frac{(140 - \text{age}) \times BW}{Cp_{cr} \times 85} = \frac{(140 - 43) \times 45}{1.7 \times 85} = 30.2 \text{ml/min} = 1.8 \text{L/h} \]

\[ CL_{renal} = 3 \times CL_{kr} = 3 \times 1.8 = 5.4 \text{L/h} \]

\[ CL_{acetylation} = 0.13 \times BW = 0.13 \times 45 = 5.9 \text{L/h} \]

\[ CL_{other} = 0.1 \times BW = 0.1 \times 45 = 4.5 \text{L/h} \]

\[ CL_{total} = CL_{renal} + CL_{acetylation} + CL_{other} = 5.4 + 5.9 + 4.5 = 15.8 \text{L/h} \]

Because of CHF,

\[ CL_{total} = 15.8 / 2 = 7.9 \]

\[ Vd = 2 \times 45 = 90L \]

\[ k_e = \frac{CL}{Vd} = \frac{7.9}{90} = 0.088h^{-1} \]

\[ t_{1/2} = \frac{0.693}{k_e} = \frac{0.693}{0.086} = 7.9h \approx 8h \]

**Problem 13 (10 points)**

T.M., a 39-year-old, 60kg female, had been taking 220mg/day of sodium phenytoin; however, her dose had been increased to 300mg/day because her seizures were poorly controlled and because her phenytoin plasma concentration was only 2.6mg/L. Now she complains about minor CNS side effects and her measured plasma phenytoin concentration is 26mg/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 phenytoin concentration to drop to 15 mg/L after discontinuation of dose?

The following equation may be helpful to solve this problem:

\[ T = \left( K_M \times \ln \left( \frac{C_0}{C} \right) + \left( C_0 - C \right) \right) \times \frac{V_d}{V_{max}} \]
Problem 14 (10 points)

A.P., a 55-year-old, 90-kg man, 6’2”, was admitted with complaints of increased shortness of breath and yellow sputum production. He has a medical history of congestive heart failure. During his hospital stay, he developed atrial fibrillation and was given digoxin to slow his ventricular rate. He received 0.75-mg digoxin IV at 9pm on day 1 and was given a maintenance dose of 0.2-mg IV each morning (starting at 9am on day 2). His serum creatinine is stable at 1.7 mg/dL. Calculate his anticipated digoxin plasma concentration at 9am on day 4.

A. 1.0 μg/L
B. 1.3 μg/L

Solution:

\[ V_d = 0.65 \frac{L}{kg} * 60 \text{ kg} = 39 \text{ L} \]

\[ V_{\text{max}} = \frac{(D_1) * (D_2) * (C_2 - C_1)}{C_2 * (D_1) - C_1 * (D_2)} = \frac{220 * 300 * (26 - 2.6)}{26 * 220 - 2.6 * 300} = 313 \frac{mg}{\text{day}} \] (sodium phenytoin)

\[ K_M = \frac{C_1 * (V_{\text{max}} - D_1)}{D_1} = \frac{2.6 * (313 - 220)}{220} = 1.1 \text{ mg/L} \]

\[ T = \left(K_M * \ln \left(\frac{C_0}{C}\right) + (C_0 - C)\right) * \frac{V_d}{V_{\text{max}} * S} = \left(1.1 * \ln \left(\frac{26}{15}\right) + (26 - 15)\right) * \frac{39}{313 * 0.92} \]

\[ = 1.57 \text{ days} * 24 = 37.7 \text{ h} \]
C. 1.6 µg/L
D. 2.0 µg/L
E. 2.3 µg/L

Solution:

\[ IBW_{male} = 50kg + 2.3kg(14) = 82.2kg \]

\[ TBW < IBW \times 1.2 = 98.7kg \]

Thus, the patient is non-obese.

\[ CL_{Cr} = \frac{(140 - age)(BW)}{72(Scr_{ss})} = \frac{(140 - 55)(90)}{72(1.7)} = 62.5 \frac{mL}{min} \]

\[ VD[L] = 3.8(BW \text{ in kg}) + 3.1(CL_{Cr} \text{ in mL/min}) = 3.8 \times 90 + 3.1 \times 62.5 \approx 536 L \]

\[ CL_{CHF} \left[ \frac{mL}{min} \right] = 0.33(BW \text{ in kg}) + 0.9 \left( CL_{Cr} \text{ in } \frac{mL}{min} \right) = 0.33 \times 90 + 0.9 \times 62.5 \]

\[ \approx 86 \frac{mL}{min} = 5.2 \frac{L}{h} = 124 \frac{L}{day} \]

\[ k_e = \frac{CL}{VD} = \frac{124}{536} \frac{L}{day} = 0.231 \frac{1}{day} \]

\[ C_{Sum} = \frac{D_1}{V} e^{-k_e t_1} + \frac{D_2}{V} e^{-k_e t_2} + \frac{D_3}{V} e^{-k_e t_3} = \]

\[ \frac{750\mu g}{536L} e^{-0.231 \frac{1}{day}2.5days} + \frac{200\mu g}{536L} e^{-0.231 \frac{1}{day}2days} + \frac{200\mu g}{536L} e^{-0.231 \frac{1}{day}1day} = 1.3 \frac{\mu g}{L} \]
# Aminoglycosides

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>$V_d$ [L/kg]</td>
<td>0.25</td>
<td>Dosing Weight: if $TBW &gt; 1.2 \times IBW$, $IBW + 0.4 \times (TBW - IBW)$</td>
</tr>
<tr>
<td>$CL$ [L/h/kg]</td>
<td>$CL_{Cr}$</td>
<td>$CL_{Cr}$</td>
</tr>
<tr>
<td>$t_{1/2}$ [h]</td>
<td>2-3</td>
<td>Third Space Fluids: Add to $V_d$ (1L/kg)</td>
</tr>
<tr>
<td>% renal</td>
<td>100</td>
<td>Dettli Equation: $k = 0.00293 \times CL_{Cr} (\text{ml/min}) + 0.014$ [h$^{-1}$]</td>
</tr>
<tr>
<td>$F$</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>$S$</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>$C_{max}$ [mg/L]</td>
<td>&gt;8-10 \cdot MIC</td>
<td></td>
</tr>
<tr>
<td>$C_{min}$ [mg/L]</td>
<td>&lt;2 (G, T)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;10 (A)</td>
<td></td>
</tr>
</tbody>
</table>
## Phenobarbital

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>BW</th>
<th>TBW</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vd [L/kg]</td>
<td>0.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CL [L/h/kg]</td>
<td>0.004 (ad.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.008 (ch.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>t_{1/2} [h]</td>
<td>120 (ad.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>60 (ch.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% renal</td>
<td>25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>0.9 (sodium)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C_{max} [mg/L]</td>
<td>&lt;40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C_{min} [mg/L]</td>
<td>&gt;15</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Carbamazepine**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vd [L/kg]</td>
<td>1.4 (variable)</td>
</tr>
<tr>
<td>CL [L/h/kg]</td>
<td>0.064 (mono)</td>
</tr>
<tr>
<td></td>
<td>0.1 (poly)</td>
</tr>
<tr>
<td>t&lt;sub&gt;1/2&lt;/sub&gt; [h]</td>
<td>30 (first dose)</td>
</tr>
<tr>
<td></td>
<td>15 (mono)</td>
</tr>
<tr>
<td></td>
<td>10 (poly)</td>
</tr>
<tr>
<td>% renal</td>
<td>0</td>
</tr>
<tr>
<td>F</td>
<td>0.8 IR (0.7 XR)</td>
</tr>
<tr>
<td>S</td>
<td>1</td>
</tr>
<tr>
<td>C&lt;sub&gt;max&lt;/sub&gt; [mg/L]</td>
<td>&lt; 12</td>
</tr>
<tr>
<td>C&lt;sub&gt;min&lt;/sub&gt; [mg/L]</td>
<td>&gt; 4</td>
</tr>
</tbody>
</table>

Autoinduction

BW, TBW

f<sub>u</sub> 0.25
Phenytoin

\[
C = \frac{K_M \cdot R_0}{V_{\text{max}} - R_0}
\]

\[
R_0 = \frac{V_{\text{max}} \cdot C}{K_M + C}
\]

\[
R_0 = \frac{S \cdot F \cdot D}{\tau}
\]

\[
V_{\text{max}} = \frac{D_1 \cdot D_2 \cdot (C_2 - C_1)}{C_2 \cdot D_1 - C_1 \cdot D_2}
\]

\[
C_{\text{normal}} = \frac{C'}{(1 - 0.1) \cdot \frac{\text{Albumin}}{4.4} + 0.1}
\]

\[
\begin{align*}
Vd \ [\text{L/kg}] &= 0.65 \\
V_{\text{max}} \ [\text{mg/kg/day}] &= 7 \\
K_M \ [\text{mg/L}] &= 4 \\
% \text{ renal} &= 2 \\
F &= 1 \\
S &= 0.92 \\
C_{\text{max}} \ [\text{mg/L}] &= <20 \\
C_{\text{min}} \ [\text{mg/L}] &= >10
\end{align*}
\]

Oral Products: 30, 50, 100, 200, 300

Bid or qd (Sustained Release)
# Digoxin

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Formula</th>
<th>Clearance-Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>$V_d$ [L]</td>
<td>$3.8 \cdot IBW [kg] + 3.1 \cdot CL_{Cr} [\text{mL/min}]$</td>
<td></td>
</tr>
<tr>
<td>$CL$ [mL/min]</td>
<td>$0.8 \cdot IBW + CL_{Cr} [\text{mL/min}]$</td>
<td>Quinidine 0.5</td>
</tr>
<tr>
<td>($CHF$) $CL$</td>
<td>$0.33 \cdot IBW + 0.9 \cdot CL_{Cr} [\text{mL/min}]$</td>
<td>Amiodarone 0.5</td>
</tr>
<tr>
<td>$t_{1/2}$ [h]</td>
<td>40</td>
<td>Verapamil 0.75</td>
</tr>
<tr>
<td>$%$ renal</td>
<td>60</td>
<td>Hyperthyroidism 1.3</td>
</tr>
<tr>
<td>$F$</td>
<td>$0.7 \ (T), \ 0.8 \ (E), \ 1.0 \ (C)$</td>
<td>Hypothyroidism 0.7</td>
</tr>
<tr>
<td>$S$</td>
<td>1</td>
<td>Vol. Distribution-Factor</td>
</tr>
<tr>
<td>$C_{max}$ [ng/mL]</td>
<td>$&lt; 2$</td>
<td>Quinidine 0.7</td>
</tr>
<tr>
<td>$C_{min}$ [ng/mL]</td>
<td>$&gt; 0.8$</td>
<td>Hyperthyroidism 1.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hypothyroidism 0.7</td>
</tr>
</tbody>
</table>
# Methotrexate

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$V_d$ [L/kg]</td>
<td>$0.2$ ($V_e$)</td>
</tr>
<tr>
<td></td>
<td>$0.7$ ($V_d$)</td>
</tr>
<tr>
<td>$CL$ [L/h]</td>
<td>$1.6 \cdot CL_{Cr}$</td>
</tr>
<tr>
<td>$t_{1/2}$ [h]</td>
<td>$3 &gt; 0.5 \mu M$</td>
</tr>
<tr>
<td></td>
<td>$10 &lt; 0.5 \mu M$</td>
</tr>
<tr>
<td>% renal</td>
<td>80</td>
</tr>
<tr>
<td>$F$</td>
<td>$1 (&lt;30 mg/m^2)$</td>
</tr>
<tr>
<td>$S$</td>
<td>1</td>
</tr>
<tr>
<td>$f_u$</td>
<td>0.5</td>
</tr>
</tbody>
</table>

$\mu M = mg/L \times 0.454$

MTX

LD and 36h-Infusion

Leucovorin-Rescue

$10 \text{ mg/m}^2 \text{ Q6h for 72h or } MTX < 0.1 \mu M$

If $MTX > 1 \mu M$ at 48h, increase Leucovorin to 50-100 mg/m$^2$ Q6h

Body Surface Area

$$BSA = \left( \frac{IBW}{70} \right)^{0.73} \cdot 1.73 \text{ m}^2$$
## Theophylline

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Clearance-Factor:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vd [L/kg]</strong></td>
<td>0.5</td>
<td>Smoking 1.6</td>
</tr>
<tr>
<td><strong>CL [L/h/kg]</strong></td>
<td>0.04 (ad.)</td>
<td>CHF 0.4</td>
</tr>
<tr>
<td></td>
<td>0.08 (ch.)</td>
<td>Cystic Fibrosis 1.5</td>
</tr>
<tr>
<td><strong>t_{1/2} [h]</strong></td>
<td>8 (ad.)</td>
<td>Cirrhosis 0.5</td>
</tr>
<tr>
<td></td>
<td>4 (ch.)</td>
<td>Pulmonary Edema 0.5</td>
</tr>
<tr>
<td><strong>% renal</strong></td>
<td>18</td>
<td>Viral Illness 0.5</td>
</tr>
<tr>
<td><strong>F</strong></td>
<td>1</td>
<td>Erythromycin 0.75</td>
</tr>
<tr>
<td><strong>S</strong></td>
<td>0.8 (A)</td>
<td>Ciprofloxacin 0.7</td>
</tr>
<tr>
<td><strong>C_{max} [mg/L]</strong></td>
<td>&lt;20</td>
<td>Cimetidine 0.6</td>
</tr>
<tr>
<td><strong>C_{min} [mg/L]</strong></td>
<td>&gt;10</td>
<td>Influenza vaccine 0.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phenobarbital 1.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rifampin 1.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phenytoin 1.6</td>
</tr>
</tbody>
</table>
## Cyclosporine

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$V_d$ [L/kg]</td>
<td>4.5 L/kg</td>
</tr>
<tr>
<td>$CL$ [L/h/kg]</td>
<td>0.5</td>
</tr>
<tr>
<td>$t_{1/2}$ [h]</td>
<td>7</td>
</tr>
<tr>
<td>% renal</td>
<td>-</td>
</tr>
<tr>
<td>$F$</td>
<td>0.3</td>
</tr>
<tr>
<td>$S$</td>
<td>-</td>
</tr>
<tr>
<td>$f_u$</td>
<td>0.1</td>
</tr>
<tr>
<td>$C_{max}$ [ng/mL]</td>
<td>&lt;400</td>
</tr>
<tr>
<td>$C_{min}$ [ng/mL]</td>
<td>&gt;150</td>
</tr>
</tbody>
</table>

**Dosing Weight:** TBW

**Available oral doses:** 25 mg, 100 mg
# Lidocaine

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$V_c$, $V_d$ [L/kg]</td>
<td>0.5, 1.3 TBW</td>
</tr>
<tr>
<td></td>
<td>0.3, 0.9 (CHF)</td>
</tr>
<tr>
<td></td>
<td>0.6, 2.3 (Cir.)</td>
</tr>
<tr>
<td>CL [L/h/kg]</td>
<td>0.6 IBW</td>
</tr>
<tr>
<td></td>
<td>0.36 (CHF)</td>
</tr>
<tr>
<td></td>
<td>0.36 (Cir.)</td>
</tr>
<tr>
<td>$t_{1/2}$ [h]</td>
<td>0.1 ($\alpha$)</td>
</tr>
<tr>
<td></td>
<td>1.7 ($\beta$)</td>
</tr>
<tr>
<td>% renal</td>
<td>2</td>
</tr>
<tr>
<td>F</td>
<td>0.4</td>
</tr>
<tr>
<td>S</td>
<td>0.87</td>
</tr>
<tr>
<td>$C_{max}$ [mg/L]</td>
<td>&lt; 5</td>
</tr>
<tr>
<td>$C_{min}$ [mg/L]</td>
<td>&gt; 1</td>
</tr>
</tbody>
</table>
# Procainamide

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vd [L/kg]</td>
<td>2</td>
</tr>
<tr>
<td>CL [L/h]</td>
<td>(3 \cdot CL_{Cr} + 0.23 \cdot BW)</td>
</tr>
<tr>
<td>N-acetylprocainamide (NAPA) in CHF</td>
<td>(\downarrow(0.5))</td>
</tr>
<tr>
<td>(t_{1/2}) [h]</td>
<td>0.1 ((\alpha)) 3 ((\beta))</td>
</tr>
<tr>
<td>% renal</td>
<td>70</td>
</tr>
<tr>
<td>F</td>
<td>0.85</td>
</tr>
<tr>
<td>S</td>
<td>0.87</td>
</tr>
<tr>
<td>(C_{\text{max}}) [mg/L]</td>
<td>&lt; 8</td>
</tr>
<tr>
<td>(C_{\text{min}}) [mg/L]</td>
<td>&gt; 4</td>
</tr>
</tbody>
</table>