Theophylline Peripheral Brain

## Important Formulas:

- **$Ke = \frac{Cl_T}{V_d}$**
- **$T_{1/2} = \frac{0.693}{Ke}$**
- **$C_{ss} = \frac{(S)(F) \cdot \text{Dose}}{CL(\tau)}$**
- **$C_{ss} = C_{desired} - C_{current} = \frac{(S)(F) \cdot \text{Dose}}{V}$**
- **$C_{1} = C_{ss} \left(1 - e^{-ke \tau}\right)$**
- **$C_{2} = C_{1} \times e^{ke \tau}$**

### IV intermittent infusion formulas:

- **$C_t = \frac{(S)(F)(\text{Dose}/T) \cdot (1-e^{-ke T}) \cdot \left(e^{-ke t'} + \frac{t}{T}\right)}{CL \cdot \left(1-e^{-ke \tau}\right)}$**
- **$C_t = C_1 \times e^{-ke t}$**

### IV infusion formulas:

- **$R = \frac{(2 \times S \times R)/(C_1 + C_2) + \{2V(C_1 - C_2)/\{C_1 + C_2\}(\Delta t)\}}{\Delta t}$**
- **$R = \frac{(2 \times S \times R)/(C_1 + C_2)}{\Delta t}$**

## Salt Factors (S):

- Aminophylline dihydrate (inj): 0.79
- Theophylline anhydrous (inj, oral soln 80mg/15ml): extended release (100,200,300,400,450,600): 1.0

## Bioavailability (F):

- Liquid: 1.0
- Most extended release: 0.9 - 1.0
- May vary with meals or preparation

## Time to Peak:

- Sustained Release: varies w/ formulation = 4-8h
- Immediate Release: 1-2 h

## Volume of Distribution – Loading dose should be based on TBW and administered over 30’ (NOTE: some authors recommend IBW)

- Neonates (0-4 weeks): 0.7-0.8 L/kg
- Infants (4wk – 1 yr): 0.5-0.7 L/kg
- Children and Adults: 0.5 L/kg (Range: 0.3-0.7 L/kg)
- Elderly – lower end of range
- Cirrhosis, malnutrition, CF – higher end of range

## Elimination:

- Liver: 90% liver 1° by CYP1A2 to inactive metabolites in pt > 3yo
- 10% to caffeine (accumulates in neonates)

## Kinetics:

- Linear in most “normal ranges”; non-linear in upper normal and toxic ranges; non-linear kinetics impossible to predict

## Half-life:

- Term Infant: 11-25 h – dependent upon gestational and postnatal age
- Child (1-17yo): 4 ± 2 h
- Adult (16—60yo): 8 ± 2 h
- > 60 yo: 10 ± 2 h (variable)
- Adult Smoker: 5 h
- Adult Liver Disease (Child Pugh Score > 8; Class B or C): 24 h
- Adult Mild CHF NYHA I or II (severe NYHA III or IV): 12 h (24 h)

## Clearance (use Ideal BW when calculating MD):

- **Variable** – varies 15 - 30% in same individual
- **Obese** – clearance = non-obese if IBW is used

### Increased clearance:

- Smoker (varies w/amount): 1.57
- Passive Smoker: 1.5
- Phenobarbital: 1.2 - 1.34
- Phenytin: 1.6
- Rifampin: 1.3 - 1.8
- Cystic fibrosis (14-28 yo): 2

### Decreased clearance:

- Cirrhosis (Child-Pugh Class A) or acute hepatitis: 0.5
- Cirrhosis (Child-Pugh Class B or C): 0.2 – 0.3
- CHF with edema (SEVERE – NYHA III or IV): 0.43
- Fever associated with acute viral illness in children (9-15yo): 0.5
- Acute Pulmonary Edema: 0.5
- Pneumonia: 0.4
- COPD – stable, elderly, nonsmoker ≤ cor pulmonale: 0.8
- Sepsis with multiorgan failure: 0.7
- Elderly (>60 yo): 0.625
- Ciprofloxacin 40 – 74% decrease: 0.26-0.6
- Diltiazem: 0.88 (0.77- 0.92)
- Verapamil: 0.77-0.80
- Erythromycin: 0.82 (0.6 – 0.85)
- Oral Contraceptives: 0.7

## Other Cl Alterations ... and there are many more:

- ↑Cl - low CHO, high protein diet, parenteral nutrition, ketoconazole, carbamazepine, hyperthyroidism
- ↓Cl – Cimetidine, propranolol (↓Cl 30-50%), steroids, allopurinol > 600mg/day, fluvoxamine, hypothyroidism

Revised 04 2014sgt
Levels:

**Efficacy:** ↑ level → ↑ efficacy  
Asthma/COPD:  10 – 15 mg/L  
Anti-inflammatory:  5– 10 mg/L  
Apnea of Prematurity:  5 – 13 mg/L  (weaning from ventilator may require ↑ levels)

**Toxicity:** not highly associated with level – SEIZURES can occur at any level in upper range (unlikely < 8 – 12 mg/L)  
> 20 – N/V, HA, irritability/insomnia, SVT, v-arrhythmias  
> 40 - ↓ K, ↑ Glucose, ↑WBC, ↑ Ca, ↓P, ↓Mg, metabolic acidosis w/resp compensation (β-system)  
> 50 – tx w/ charcoal hemoperfusion or oral charcoal  
Neonates:  failure to gain wgt, ↓ sleep, irritability, diuresis, dehydration, ↑ reflexes, jitteriness

**Assay Information:**
EMIT – no significant interferences  
Spectrophotometric methods:  may be falsely elevated by furosemide, sulfathiazole, phenylbutazone, probenecid, theobromine, caffeine-containing beverages, chocolate, and acetaminophen – check institutional assay used