**Team Case Assignment: Clinical Pharmacokinetics P-313**

**March 19, 2013**

1. MS is a 60 year-old male, 85kg (6 Ft 1 in) with very severe COPD admitted to TUH medical ICU for respiratory failure and placed on mechanical ventilation.

PMH: COPD, HTN, hypercholesterolemia , diabetes mellitus and cirrhosis SH: quit smoking 2 yrs ago

Meds PTA: Theo-24 100mg daily, lisinopril 20mg daily, pravastatin 10mg daily, lactulose 30 gms BID, Lantus 30 units AM and insulin lispro 12 units TID with meals, Fluticasone/ salmeterol 250/50 1 puff every 12 hours, tiotropiuim 18 mcg inhale 1 cap daily, albuterol 1 puff prn

His current theophylline concentration is 3 mcg/ml.

The medical team asks you to calculate a loading dose and maintenance dose of theophylline intravenous (mg/hr) to obtain a goal serum concentration of 8 mcg/ml. In addition, calculate an infusion rate for the theophyllne infusion (conc. 400 mg/500 ml) maintenance dose (ml/hr).

Assume the patient has been compliant on his home theophylline dose.

2. CN is a 21 yr-old woman who was diagnosed with her first manic episode six months ago. She was hospitalized at that time, treated with lithium 600 mg po bid (serum concentrations 0.8 mg/dL while in the hospital). She did not keep her follow-up appointment with her psychiatrist and presents to the ER today at the request of her mother. She is kicking wildly while being pulled from the car and can be heard screaming “The FBI is after me, Mom! I would have made it out of the country if you hadn’t gotten in the way! I was going to marry Prince William and be the next Queen of England!”

Upon exam, she is irritable and is pacing around the room. She is dressed in a short skirt, high heels and is wearing an excessive amount of make-up and costume jewelry. Her mother reports that she “lost” her prescription within days of being discharged and has stopped attending classes at the local community college. She has started staying out late and has exhibited reckless driving habits, finally hitting the side of the garage while parking early this morning.

1. What is CN’s goal lithium serum concentration and why?
2. When can her mother expect to see changes in CN’s behavior, assuming she is compliant with her treatment?
3. When should her next lithium level be drawn?

3. One day, CN’s mother calls, concerned that her daughter has been complaining of nausea, vomiting, and diarrhea for several days. Over the past few hours, CN has become confused and has developed a coarse tremor and slurred speech. It has been 4 months since her last lithium level, at which time her lithium level and laboratory panel were normal. The only change is that CN has recently starting taking Advil regularly for tension headaches.

a. What is the likely cause of her symptoms? What action should be taken?

**Question 1:**

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| Loading dose:  Vd= 0.5L/kg \* 85 kg = 42.5 L  LD= (40 L) (8mg/L-3 mg/L) = 212.5 mg loading dose   1. (1)- b/c we are giving IV theophylline   LD= 212 should round to 215 mg  New dose:  MD= (Css)(Cl)(τ)  (F)(S)  Rearrange the formula to solve for Cl  Cl= Dose (F)(S) = (100mg-dose pt on at home) (1)(1- on theophylline at home salt=1)  (Css)(τ) (3mcg/ml)(24 hours)  Actual theophylline clearance = 1.4 L/hr  Using this clearance we need to calculate a new dose to achieve a goal serum concentration of 8 mcg/ml using theophylline infusion  Ko= Css (Cl) = 8 mg/L (1.4 L/hr) = 11 mg/hr  S F (1) (1)-for theophyllne  Infusion rate: 400 mg/500 ml= 0.8 mg/ml  1 ml x 11 mg = 13.75 round to 14 ml/hr  0.8 mg hr |

**Question 2:**

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| a.**Goal:**  0.8-1 mmol/L because CN is experiencing an acute manic attack. Mania can increase lithium clearance by as much as 50%, which decreases lithium concentrations. A higher dose may be needed to achieve therapeutic goals.  **b. Behavioral changes:** onset of action is generally 1-2 weeks; however, a 4-6 week period may be necessary to assess complete response to lithium therapy  **c. Lithium levels:** Steady-state is reached in 3-5 days. The level should be measured just before the first morning dose (which ideally should be 12 hours after the last evening dose). Once the manic phase resolves, levels should be checked again and the therapeutic goal should be adjusted to 0.6-0.8 mmol/L. This may require a dose reduction as lithium clearance should return to baseline once mania is resolved. |

**Question 3:**

a. **Cause:** Possible lithium toxicity (N/V, diarrhea, confusion, tremor, slurred speech) – likely moderate toxicity given symptoms. This is most likely due to CN’s *regular* use of ibuprofen. NSAIDs have been shown to decrease lithium clearance and thereby increase lithium concentrations 🡪 toxicity.

**Action:** Measure serum lithium concentration and relevant laboratory data (Na, Mg, K, Scr, BUN, K, WBC). Hold lithium until CN’s symptoms resolve and lithium level is in the therapeutic range. DC ibuprofen. Consider acetaminophen for headache relief.