At the end of the instructional unit the student should be able to:

1. Describe the bioavailability, volume of distribution, protein binding, elimination pathways and clinical effects of digoxin.

2. Discuss how renal dysfunction affects loading and maintenance doses of digoxin.

3. In addition to plasma concentrations, describe other parameters that should be monitored for a patient receiving digoxin.

4. Determine a dosing regimen when given patient specific information.

5. Calculate an estimated steady state plasma concentration of digoxin given when given patient specific information

**Digoxin**

**Indications:** Supraventricular arrhythmias and systolic dysfunction

**Bioavailability:** 75-85% (80%) elixir
70-80% (75%) conventional tablets
90-100% (95%) Lanoxicaps (but digoxin content is lower)
Some metabolism may occur within the GI tract

**VD:** The alpha distribution phase is slow (35 minutes)

serum sample: 4 hrs after IV dose, or 6 hours after po dose
VD =7.3L/kg
is decreased in CRF (4-5 L/kg)
VD is larger in children and neonates
Digoxin does not distribute into adipose tissue.

**Protein binding:** 20-30% to albumin

**Elimination:** 75-85% excreted unchanged by the kidney
Half-life: 36 hours with normal renal function (adults and neonates)

**Active metabolites:** some
Major route of elimination is renal, however metabolism becomes increasingly important as a route of elimination in the setting of renal dysfunction. Enterohepatic cycling occurs.
Adjust dose in renal dysfunction: Yes
Digoxin is poorly removed by hemo and peritoneal dialysis.
Tubular secretion is inhibited by hypokalemia, spironolactone, quinidine, verapamil, and amiodarone

Effects on electrocardiogram:
increased PR interval
increased automaticity

Dosing:
Load 10-15 mcg/kg load based on ideal body weight, with a normal Vd
chronic dosing (see below)

Toxicity:
GI (anorexia, nausea, vomiting, diarrhea)
CNS (headache, fatigue, confusion, delirium, psychoses, visual disturbances)
Cardiac (ventricular ectopy, AV block)
Toxicity is more common in the setting of: metabolic alkalosis (intracellular K+ depletion), hypokalemia, hypomagnesemia, hypercalcemia (at very high digoxin levels), underlying heart disease, chronic pulmonary disease, hypothyroidism

Drug Interactions
Cholestyramine, antacids and metoclopramide reduce digoxin bioavailability by 20-35%
Propantheline may increase bioavailability
Verapamil increase digoxin levels by 70%
Amiodarone and Quinidine increases digoxin levels approximately 2 fold

Plasma levels: 0.5-2 ng/ml, however most HF trials demonstrate no additional benefit with Cp >1.2 ng/ml
Higher serum concentrations are commonly sought for control of ventricular rate however, increasing the digoxin dose and increasing serum digoxin concentrations may not necessarily result in a further reduction in ventricular response. Digoxin is not particularly effective in controlling ventricular response in the setting of AF and hyperthyroidism, sepsis, post-thoracotomy, hypoxemia

DLIS (digoxin like immunoreactive substances) common in: patients with renal failure, hepatic failure, low renin HTN, third trimester pregnancy, neonates, and infants.
Loading Doses

most reasonable indication is for ventricular rate control in a patient where verapamil and beta blockers are contraindicated

Adults:  1 mg commonly given in divided doses
         or more specific is to give a weight based dose
         10-15 mcg/kg in divided doses (50%, then 25%, then 25%)

Children: 20 mcg/kg premature infants
         30 mcg/kg full term neonates (< 2 months of age)
         40-50 mcg/kg infants (< 2 years of age)
         30-40 mcg/kg children (> 2 years of age)

or most specific is to calculate a loading dose based upon an estimate of the Vd

\[
\text{Loading dose} = \frac{(Vd) \times (Cp)}{(F)}
\]

Vd equations

\[
Vd = (3.8 \text{ L/Kg}) (\text{wt in Kg}) + (3.1)(\text{CrCl}) \quad (\text{The resulting answer is in liters.})
\]

\[
Vd = 7.3 \text{ L/Kg}
\]

\[
Vd = \text{approximately 4 L/Kg in the presence of HF and renal insufficiency}
\]

Calculate the IV loading dose for a 70 yo, 70 kg adult male with normal renal function (SrCr 1.0), if the desired Cp of 1.5 ng/ml

Calculate the oral loading dose for a 70 yo, 70 kg female with normal renal function (SrCr 1.0), if the desired Cp is 1.0 ng/ml
Calculate the oral loading dose for a 70 yo, 70 kg adult male with a serum creatinine of 3.0, if the desired Cp is 1.0 ng/ml.

Calculate the Cp if a 70 yo, 70 kg man with a serum creatinine of 3.0 is given a 1 mg IV loading dose of digoxin.

\[
\text{Maintenance} = \frac{(\text{Cl}) (\text{Cp}) (t)}{\text{(F)}}
\]
\[
\text{Dose} = \frac{(\text{F}) (\text{dose} / t)}{\text{Cl}}
\]
\[
\text{Cp} = \frac{(\text{F}) (\text{dose} / t)}{\text{Cl}}
\]

Cl equations for digoxin

Digoxin Clearance (no CHF) = (0.8 ml/kg/min) (wt in Kg) + CrCl

Digoxin Clearance (pts with CHF) = (0.33 ml/kg/min) (wt in Kg) + (0.9) (CrCl)

RB is an 84 year old male who developed atrial fibrillation with a rapid ventricular rate (125 beats/minute). The patient was in good health and has no other medical problems. He is on no other medications and has no known allergies.

PE:  BP 130/88, Pulse 125 irregularly irregular Height 5’10” weight 145 lbs.
Lab:  Electrolytes WNL, BUN 20, Creatinine 1.9

1) Calculate RB’s creatinine clearance.

2) Recommend an IV digoxin loading dose for RB (desired Cp 1.5 ng/ml).
3) Give specific recommendations regarding the administration of the drug.

4) If the intern wants to draw a digoxin plasma concentration, when would you recommend it being drawn?

5) Calculate a digoxin maintenance dose to achieve a steady-state digoxin plasma concentration of 1 ng/ml.

CL is a 72 year old female diabetic patient with CRI. She is admitted to the hospital with pulmonary edema
PMH: CAD, DM, CHF
weight 73 kg
Labs on admission BUN 89, Na 131, K 5.6, Cl 97, C02 20, Cr 5.6, Ca 8.3, P04 5.9
Meds PTA: ASA 325 mg QD
enalapril 10 mg P0 bid
digoxin 0.125 mg PO qd
lasix 80 mg PO bid
insulin 70/30 20u qAM and 5u q PM
calcium acetate 667 mg PO tid

Calculate an estimated steady state digoxin serum concentration.

After a week in the hospital, CL’s renal function worsens. Labs are now: BUN 98, Na 134, K 4.1, Cl 94, C02 26, Cr 9.5, Ca 8.2, P04 7.5
Recalculate an estimated steady state digoxin serum concentration.
How would you adjust her dose?

KJ is a 70 yo WM (57 kg) admitted for chest pain of 7 hours duration and SOB. His PMH is significant for:

- DM controlled by diet
- Paroxysmal atrial fibrillation
- Hypertension
- Peripheral Vascular Disease
- Coronary Artery Disease
- Chronic Renal Insufficiency
- Systolic Dysfunction (EF 35%)
- S/P subdural hematoma

Meds | PTA
--- | ---
benazepril 20 mg po qd
amlodipine 10 mg po qd
digoxin .125 mg po qod
aspirin 325 mg qd
amiodarone 200 mg po qd

| 133 | 101 | 99 |
| 4.4 | 20 | 2.7 |

Estimate his serum digoxin concentration.