Pharmacology Module

Date	Session	M&M Chapters	Speaker
Nov-23	Pharmacologic Principles	7	Saddawi-Konefka
Nov-30	Inhalational Agents	8	Ishizawa
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Dec-14	Analgesics	10	Vazquez
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Contents

Pharmacologic Principles

Pre-Reading

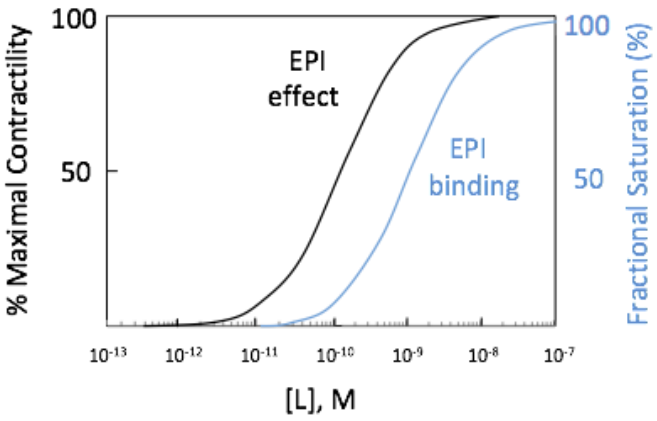
- Morgan & Mikhail, Chapter 7

Content outline

- Mechanisms of Action
- Potency, Efficacy -> EC50
- Receptor Affinity vs Drug Effect -> Kd
- Distribution vs elimination
- Compartments and “volume” of distribution
- Elimination
- First order versus zero order kinetics
- Absorption / bioavailability
- Biotransformation
- Clearance
- Context-sensitive half-times

Questions

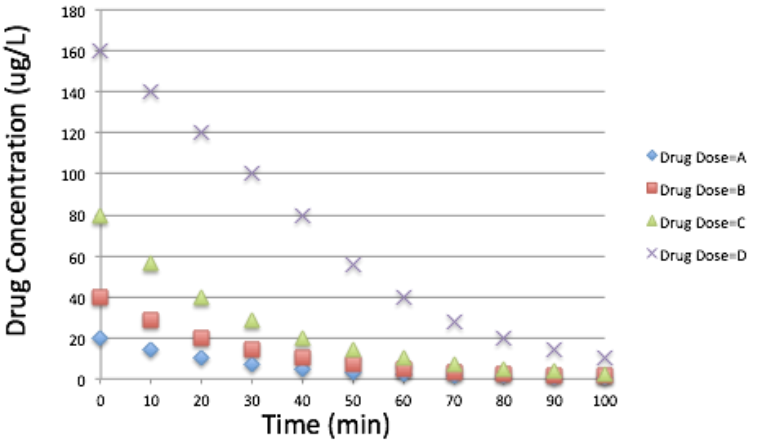
1. Receptor downregulation can occur with continuous stimulation of GPCRs (desensitization). How would the two curves below change as the system becomes progressively desensitized?



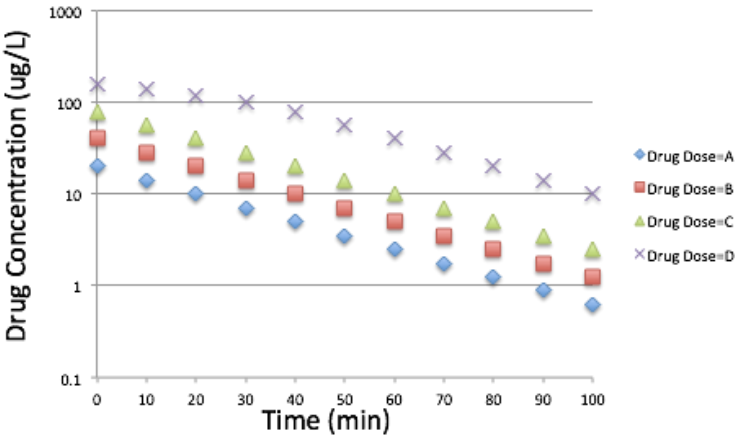
2. *** NOTE: FOR THIS QUESTION, ASSUME THAT DISTRIBUTION HAS ALREADY HAPPENED AND YOU ARE ONLY SEEING ELIMINATION IN THE GRAPHS. ***
   Four mice were given one i.v. injection of an experimental sleep medicine, at one of 4 different doses. Like propofol, this new drug is distributed and then cleared by hepatic metabolism. But unlike propofol, awakening does not occur until the elimination phase, when the drug concentration has reached 10 ug/L. The graphs plot the plasma drug concentration as a function of time for each mouse. The drug is distributed very rapidly so the distribution phase is not evident on the graph. The drug has a volume of distribution of 10 L.
   a) Calculate the 4 drug doses
   b) How long do the animals stay asleep at each dose?

c) What is the half-life of the drug?
d) What is the relationship between the drug dose, length of effect, and the half life?

Linear scale

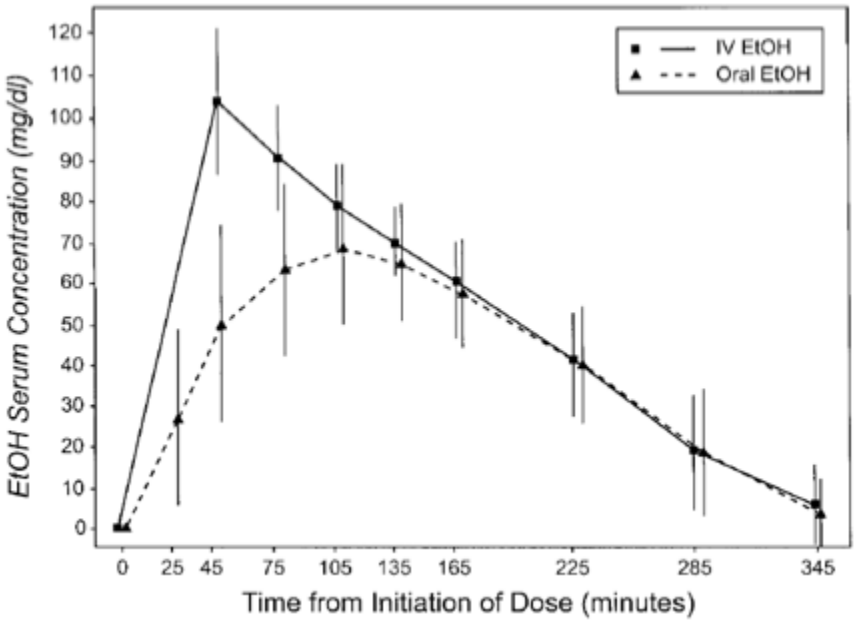


Log scale



3. The following graph shows serum ethanol concentrations from a single dose of ethanol (700 mg/kg) administered orally or by intravenous administration to 20 male volunteers.
   a) How do you explain the difference in the shape of the curves?
   b) For the elimination phase, is the shape of the curve consistent with first-order kinetics? (Note that this NOT a semilog plot). How does this relate

to the idea that we can typically metabolize about one drink per hour?



Inhalational Agents

Pre-Reading

- Morgan & Mikhail, Chapter 8

Content outline

- Volatile effects on body (e.g., CNS [concept of MAC], CV, Resp, NM function, etc)
- Brief uptake kinetics and relevant patient factors (e.g., cardiac output effect on induction)
- Delivery systems and vapor pressure
- Comparative properties of volatile anesthetics (main differences between volatiles - focus on isoflurane, sevoflurane and desflurane)

Questions

- Imagine you are delivering isoflurane in a variable bypass vaporizer with the dial set to 2%. How would delivering it in Boston compare to delivering it in Denver (barometric pressure = 630mmHg). What differences would you expect in your patient (and how clinically meaningful would you expect these differences to be)?
- You “MacGyver” a way to fill the sevoflurane vaporizer with isoflurane. Assuming no end-tidal monitoring (i.e, you set the dial to what you want), what would you be delivering? Would your patient end up at a higher or lower MAC than you were hoping?
- You are providing anesthesia for a patient with end-stage liver disease and poor pulmonary gas exchange. Describe how these each would contribute to the speed of inhalational induction (this is hypothetical). What could you do to increase the speed of induction?

IV Agents and NMBs

Pre-Reading

- Morgan & Mikhail, Chapters 9, 11, 12

Content outline

- Advantages/disadvantages of each hypnotic for induction of anesthesia (cardiovascular effects, duration of action, effects on seizure threshold, off-target effects (PONV, adrenal suppression))
- Other (non-induction) uses do each of these agents have (sedation/MAC drugs, amnestic, analgesic, delirium(?))
- Depth of neuromuscular blockade and reversal agents
- Residual neuromuscular blockade—prevalence, clinical manifestations (pharyngeal weakness/obstruction/aspiration), costs and outcome

Questions

- In hemodynamically unstable patients requiring emergency surgery, what are the safest strategies for induction of anesthesia?
- Describe how to use a quantitative train of four monitor.
- What are the most common clinical signs of residual neuromuscular blockade? How would you treat these?

Analgesics

Pre-Reading

- Morgan & Mikhail, Chapter 10

Content outline

- Anatomy and physiology of nociception
- Opioids (mechanisms and side effects)
- Non-opioid analgesics
    - NSAIDs
    - Alpha-2 agonists
    - NMDA antagonists
    - Gabapentinoids
    - Glucocorticoids

Questions

- The first case assigned to your room is a healthy 38-year-old woman coming in for an elective laparoscopic cholecystectomy. She is scheduled for same day discharge and has no allergies. What would be your plan for intraoperative and post-operative analgesia?
- Your second case of the day is also an elective laparoscopic cholecystectomy, this time in a 58-year-old man with a history of chronic pain. His home pain regimen includes a fentanyl patch (125mcg/hr) plus as needed oxycodone. How will you change your management for this patient?
- You are scheduled as the anesthetist for a multilevel decompression and spinal fusion. The case is expected to be 8-10 hours. Your patient is an otherwise healthy 47-year-old man with a history of anaphylaxis to IV morphine and IV hydromorphone. His allergist assures you that he is able to take all other drugs, including other opioids. How will you manage this man's pain?

Local / LAST

Pre-Reading

- Morgan & Mikhail, Chapter 16

Content outline

- Properties of local anesthetics: structure, mechanism of action + clearance, pKA
- Non-LAST toxicity: allergy, local tissue toxicity, methemoglobinemia
- LAST: clinical picture and treatment (including doses)

Questions

- You are on the block team and are planning to perform a block as the primary anesthetic for a transmetatarsal amputation in a patient with severe COPD and chronic pain. Which local anesthetic(s) would you choose?
- A patient endorses an allergy to lidocaine. What else do you want to know? How would you proceed?
- In the treatment of LAST, it is advised that you avoid vasopressin, calcium channel blockers, and beta blockers and that you reduce your epi doses. Why do you do each of those things?