1. Basic Principles of Drug Action
   a. Drug Administration
      Ingestion (oral route)
      Injection (SC, IM, IV)
      Inhalation
      Absorption through mucous membranes
      Transdermal

   b. Drug Distribution
      Must enter bloodstream
      Must pass blood-brain barrier (non-ionized, lipid soluble molecules)
      Distributes to all the body cells

   c. Drug Metabolism (liver enzymes)
   d. Drug Elimination (kidney, urine; other routes)
   e. Drug “half-life”
   f. Mechanisms of Drug Action (in NS is synapse, receptor sites)

   g. Drug Tolerance
      Shifts dose-response curve to the right
      Takes more of drug to get same result as before
      Not all drugs exhibit tolerance
      Can develop tolerance to some, but not all, of a drug’s effect
      Mechanisms: e.g. liver enzyme induction, changes in RSs

   h. Drug Withdrawal Effects & Physical Dependence
      Exposure to a drug produces compensatory changes in NS that offset
      the drug’s effects and produce tolerance
      Rapid/abrupt D/C of drug vs. gradual tapering off of drug
      Is not the same as addiction (cravings, concentrated focus, reward)
      “Conditioned” tolerance (conditioned stimuli --- compensatory
      bodily changes), role in drug ODs
2. **Drug Addiction (p.2)**

a. **Biopsychological Theories of Addition**
   “older” physical-dependence theories
   do not adequately describe the data on addition
   addicts that do not exhibit withdrawal effects still crave
   relapse occurs without dependence/withdrawal
   addiction does not occur even with dependence/withdrawal

   **“newer” positive-incentive theories of addiction**
   addict uses drug in order to re-experience the positive incentive
   (“pleasure”, “release” from tension effects)
   to stop the “cravings” from the drug
   “pleasure” vs. “intense focus/attention on” experiencing the drug

b. **Brain areas involved in “pleasure/focus”**
   intracranial self-stimulation studies (septal/lateral hypothalamus)
   mesotelencephalic **dopamine** system
   cell bodies in midbrain (substantia nigra & **ventral tegmental area**)
   axons project to telencephalon (forebrain), including prefrontal ctx,
   limbic ctx (**cingulated gyrus**, **olfactory bulb**, **amygdala**, **septum**,
   dorsal striatum (caudate nucl. & putamen),
   & **nucleus Accumbens**
   (2 pathways using dopamine, one for motor control via the
   basal ganglia, and one for “reward” via forebrain & limbic
   structures)
   “**mesocorticolimbic pathway**”

   **dopamine agonists are likely to be very addictive**
   e.g. cocaine, methamphetamines, nicotine
   drugs that are dopamine antagonists or that have no effect on dopamine
   are not addictive

   **nucleus Accumbens** may not actually mediate the reward/pleasure
   experience per se; but does attach “meaning” to a stimulus (e.g. a
   drug) that signals **that “reward” is imminent**, stimulus becomes the
   **focus of attention**, S will try to get the stimulus, will “crave” it, will
   seek it to the exclusion of all other stimuli… “addiction”