Chapter 3

Drug Action across the Life Span

Lesson 3.1

Objectives

- Explain the impact of the placebo effect and nocebo effect.
- Identify the importance of drug dependence and drug accumulation.
- Discuss the effects of age on drug absorption, distribution, metabolism, and excretion.
- Explain the gender-specific considerations of drug absorption, distribution, metabolism, and excretion.

Placebo and Nocebo

- Placebo effect: A patient's positive expectation can positively affect the outcome
- Nocebo effect: A patient's negative expectations can result in a less-than-optimal outcome
- Ethical concerns for both

Drug Dependence

- Person is unable to control his/her ingestion of drugs
  - Physical: person develops withdrawal symptoms if drug withdrawn
  - Psychological: a person is emotionally attached to a drug

Drug Accumulation

- Drug accumulation occurs when the next dose is given before the previously given drug has been metabolized or excreted
- May result in drug toxicity

Factors Affecting Drug Action

- Absorption
  - Process by which drugs are absorbed in the body; most common is via GI tract; other routes are parenteral and topical
- Premature
  - Slower gastric emptying time may allow increased absorption

Factors Affecting Drug Action (cont.)

- Neonates
  - IM absorption erratic, reduced gastric acidity
- Infants
  - Topical absorption increased

Factors Affecting Absorption

- Geriatric patients
  - IM absorption erratic
  - Reduced salivary flow makes swallowing difficult
  - Transdermal absorption hard to predict
  - Timed-release/enteric-coated tablets cannot be crushed
  - Reduced GI acidity affects absorption
  - Slower gastric emptying time
  - Decreased GI motility and blood flow

Factors Affecting Distribution

- Ways in which drugs are transported to site of action
- Depends on pH, body water concentrations, fat tissues, protein binding, cardiac output, and blood flow
- Infants
  - Higher total body water content, requiring higher dose on mg/kg basis
  - Lower body fat
  - Reduced protein binding in neonates

Factors Affecting Distribution (cont.)

- Geriatric patients
  - Total body water content decreases
- Gender
  - Total body fat higher in females

Factors Affecting Metabolism

- Process whereby the body inactivates medications; primarily occurs in the liver
- Infants
  - Enzymes take several weeks to a year to develop
- Older adults
  - Liver cells decrease, blood flow decreases
- All ages
  - Genetics, smoking, diet, other medications, liver disorders

Excretion

- Drug metabolites and the drug itself are excreted from the body
- Preterm infants have 15% of the renal capacity of the adult
- Neonates have 35%
- Full adult function occurs at 9 to 12 months

Excretion (cont.)

- Geriatric
  - Decreased renal blood flow
  - Reduced cardiac output
  - Loss of glomeruli
  - Decreased tubular function
- Serum creatinine levels give estimate of renal function

Therapeutic Drug Monitoring

- Measurements of drug concentration in blood sample
- Very essential in neonates, infants, children
- Dosage and frequency of medications can be adjusted to maintain therapeutic level of potentially toxic drugs

Pediatric Patients

- Dosage adjustments expected during growth
- Measure liquid medications using mL
- Use appropriate dilution
- Verify dosage prior to giving
- Aspirin use linked with Reye's syndrome
- Allergic reactions occur rapidly in children

Geriatric Patients

- Complete a thorough drug history, including prescription, OTC, herbal medications, and nutritional status
- Evaluate vision and motor skills
- When evaluating a new symptom, determine whether it was induced by a medication already prescribed
- Start with smaller doses and gradually increase

Geriatric Patients (cont.)

- Keep multidrug regimen simple
- Review if any medications can be discontinued
- Assess ability to pay for medications
- Polypharmacy: multidrug therapy

Potentially Inappropriate Medications for Geriatric Patients

- Includes medications that should be avoided and those that are rarely appropriate
  - Some barbiturates, benzodiazepines, and some narcotics
- Some are considered appropriate to give only with certain indications but may have potentially adverse reactions

Audience Response Question 1

- Which patient has the greatest percentage of body water?
  - A. Older adult
  - B. Middle-aged person
  - C. Infant
  - D. Toddler

Audience Response Question 2

- Which type of topical drug is more readily absorbed by infants?
  - A. Fat-soluble
  - B. Water-soluble
  - C. Emollient
  - D. Protective

Audience Response Question 3

- Which form of medication is more easily administered for the toddler who requires a course of antibiotics?
  - A. Enteric
  - B. Capsules
  - C. Tablets
  - D. Liquid

Audience Response Question 4

- Therapeutic levels of drugs are important to maintain in order to avoid the complications of being over- or undermedicated. If a drug level of 0.5 to 2 ng/mL is considered therapeutic, a drug level of 0.45 ng/mL is considered to be what?
  - A. Toxic
  - B. Therapeutic
  - C. Subtherapeutic
  - D. Tolerant

Audience Response Question 5

- Due to the decreased protein-binding capacity in preterm infants, what adjustment in dosage of protein-binding drugs would need to made?
  - A. The dosage should be decreased.
  - B. The dosage should be increased.
  - C. The dosage should be kept at the same levels.
  - D. Protein-binding drugs are not administered to infants.

Gender and Absorption

- Females
  - Stomach empties more slowly
  - Gastric pH greater
  - Alcohol absorbed faster

Gender and Metabolism

- CYP3A4 component more active in women

Lesson 3.2

Objectives

- List the definitions of the use-in-pregnancy categories A, B, C, D, and X.
- Discuss the impact of pregnancy and breastfeeding on drug absorption, distribution, metabolism, and excretion.
- Discuss the role of genetics and its influence on drug action.

Pregnant Patients

- Fetus exposed to substances in mother's blood
- Teratogens
  - Drugs that cause abnormal development of fetal tissues

Use in Pregnancy Categories

- A—Adequate, well-controlled studies in pregnant women have not shown an increased risk of fetal abnormalities
- B—Animal studies have revealed no evidence of harm to the fetus; however, there are no adequate and well-controlled studies in pregnant women OR animal studies have shown an adverse effect, but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus

Use in Pregnancy Categories (cont.)

- C—Animal studies have shown an adverse effect, and there are no adequate and well-controlled studies in pregnant women OR no animal studies have been conducted, and there are no adequate and well-controlled studies in pregnant women
- D—Studies: adequate, well-controlled, or observational; in pregnant women have demonstrated a risk to the fetus. However, the benefits of therapy may outweigh the potential risk

Use in Pregnancy Categories (cont.)

- X—Studies: adequate, well-controlled, or observational; in animals or pregnant women have demonstrated positive evidence of fetal abnormalities. The use of the product is contraindicated in women who are or who may become pregnant

Use of Monitoring Parameters: Pregnant Women

- Avoid drugs if at all possible
- When taking woman's history, be alert to possibility of pregnancy
- Instruct patient to avoid drugs, alcohol, and tobacco
- Try nonpharmacologic treatments before using medicines
- Avoid herbal medicines

Drugs Known to be Teratogenic

- Drug classifications known to be teratogenic
  - Androgenic and estrogenic hormones
  - ACE inhibitors, ethanol, tetracycline
  - Thalidomide, vitamin A, warfarin
  - Angiotensin II receptor antagonists
  - Anticonvulsants, antimanic agents, antithyroid
  - Chemotherapy, statins, cocaine

Use of Monitoring Parameters: Breastfeeding Infants

- Some drugs are known to enter breast milk and harm the nursing infant
- Discuss all medications with physician
- Take medicine immediately after breastfeeding or just before infant's longest sleeping period

Genetics

- Study of how living organisms inherit the traits of their ancestors, including function of metabolic pathways
- Pharmacogenetics: study of how drug response may vary according to inherited differences
- Significant differences can occur among racial and ethnic groups