Neonatal Pharmacology

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Conflict of Interest

The speaker has no actual or potential conflicts of interest to disclose.

The speaker may discuss some off-label uses of medications.

Objectives

- Define common terminology associated with neonatal pharmacology
- Identify key differences that affect medication absorption, distribution, metabolism, and elimination in neonatal patients
- Discuss medications most commonly utilized in neonatal patients and specific considerations for each
- Review nursing responsibilities related to medication administration in neonatal patients

Common Terminology

Pharmacology: the study of medication properties and their effects on the body

Pharmacotherapy: the administration of medication to a patient

Medication: any substance intended to cure, mitigate, or prevent disease

Bioavailability: the portion of an administered drug that reaches the site of action in the body

Therapeutic range: range in which the probability of seeing the desired outcome is high, while potential for toxicity is low

Common Terminology

Therapeutic Drug Monitoring (TDM): measurement of plasma medication concentrations to optimize therapy

Steady State: point in which amount of medication administered is equal to amount eliminated – plasma concentrations are steady

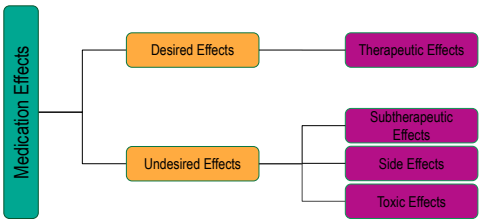
Half-life: time required for plasma concentration to decrease by half

Levels:

- **Peak Level**: level drawn after the dose and after distribution
- **Trough Level**: level drawn just prior to the next dose
- **Random Level**: level drawn anytime after a dose is given

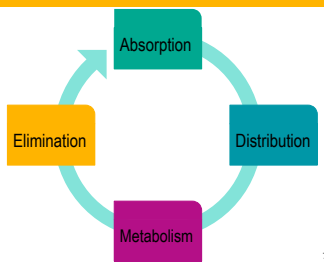
Pharmacodynamics

- What the **drug does** to the body



Pharmacokinetics

- What the **body does** to the drug



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Absorption

Movement from the site of administration into the bloodstream

- Largely dependent on the **site of administration**
- Active and Passive

Intravascular
★ Direct administration into the bloodstream

Extravascular
★ Enteral
★ Rectal
★ Topical / Percutaneous
★ Intramuscular

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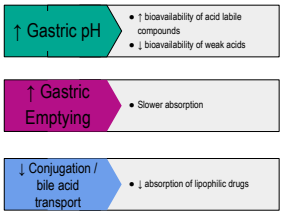
Absorption: Enteral

- Most common route of administration
- Pros:
  - Lower infection risk
  - Lower cost
  - Increased convenience



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Distribution

Movement of medication through the body compartments

- Dependent on multiple factors

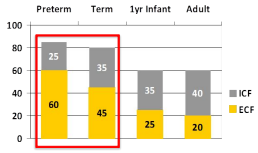
Blood Flow **Medication Solubility** **Molecule size**

Protein binding **Site of action**

Distribution: Total Body Water (TBW)

Volume of Distribution (Vd):
- volume of body fluid required to dissolve a medication

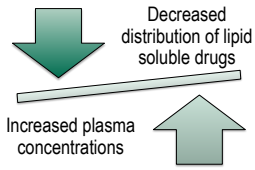
* TBW to body mass ratio ↓ with ↑ age



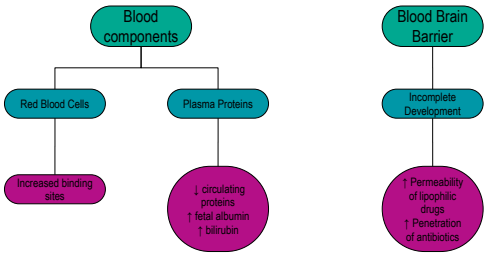
Distribution: Fat

Neonates have **widely variable** body fat percentages

- **1%** of total body mass **at 28 weeks** vs. **15% at term**



Distribution: Blood components & Blood Brain Barrier



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Metabolism

Chemical change of a medication from one form to another

- Primary site → **Liver**
- Generally **increases water solubility**
- Can result in **active** or **inactive** metabolites

Phase I
CYP enzymes
(oxidation, reduction, hydrolysis, demethylation)

Phase II
(acetylation, methylation, or conjugation)

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Elimination

Elimination of the medication from the body

- Primary Site → **Kidneys**
- Minor pathways:

★ **Salivary glands** ★ **Sweat glands** ★ **Mammary glands**

★ **Lung** ★ **Liver** ★ **GI tract**

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Elimination: Renal

- Renal function is significantly **decreased** in neonates compared to older patients

Glomerular Filtration Rate (GFR)	• Directly related to GA • Rapidly increases in the first 2 weeks of life • Adult values by 8 - 12 months
Tubular Secretion	• Dependent on efficiency of tubular function • Adult values by 1 year

Common Neonatal Medications

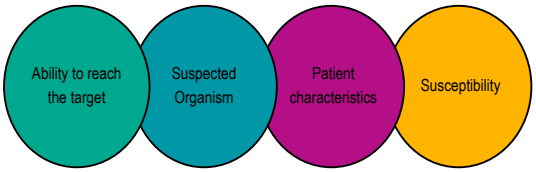
Antimicrobials

Any agent that either kills or inhibits growth of microorganisms

- Bacterio**static** → **inhibits** growth
- Bacteri**cidal** → **kills** microorganism

Concentration Dependent	Time Dependent
Goal: **maximize peak** serum levels **Dose** is key!	Goal: **maximize time** above the MIC **Frequency** is key!

Antimicrobials: Choice of Agent



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Antimicrobials: Choice of Agent

Infection	Common Organisms	Common Antimicrobials
Early Onset Sepsis (EOS)	• *Group B Streptococcus* (GBS) • *Escherichia coli* • *Listeria monocytogenes*	• Ampicillin • Gentamicin • Cefepime
Late Onset Infections	• EOS organisms • *Staphylococcus* spp. • *Enterococcus* spp. • *Enterobacter* spp. • *Klebsiella* spp. • *Pseudomonas aeruginosa*	• **Nafcillin** / oxacillin • Vancomycin • Gentamicin • Piperacillin/tazobactam • Cefepime
Viral	• Herpes simplex virus	• Acyclovir
Fungal	• *Candida* spp. • Most common → *Candida albicans*	• Amphotericin B • Fluconazole

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Cardiovascular Agents

* Medications that affect regulation, inhibition, or stimulation of the cardiovascular system

Vasopressors & Inotropes | **Antihypertensives & Vasodilators** | **Antiarrhythmic Agents**

- **Vasopressors** ↑ vascular **tone**
- **Inotropes** ↑ myocardial **contraction**
- **Chronotropes** ↑ heart **rate**

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Cardiovascular Agents: Vasopressors / Inotropes

Agent	Receptors		Action
Dopamine	Low dose (2 - 5 mcg/kg/min)	DA_1 / DA_2	↑ renal and mesenteric blood flow
	Intermediate dose (5 - 10 mcg/kg/min)	β_1 / β_2 Some α_1	↑ myocardial contractility ↑ heart rate
	High dose (> 10 mcg/kg/min)	α_1	↑ systemic vascular resistance
Dobutamine	2 - 20 mcg/kg/min	α_1 / β_1 / β_2	↑ myocardial contractility ↑ heart rate +/- systemic vascular resistance
Epinephrine	Low dose (0.01 - 0.1 mcg/kg/min)	β_1 / β_2	↑ heart rate ↑ myocardial contractility Peripheral vasodilation
	High dose (> 1 mcg/kg/min)	α_1	↑ vasoconstriction ↑ heart rate

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Cardiovascular agents: Antihypertensives & Vasodilators

Class	Mechanism	Effects	Examples
Beta Blockers	Competitively block β-receptors	↓ heart rate, ↓ contractility, ↓ cardiac output	**Propranolol** Esmolol
Diuretics	Generally ↑ excretion of Na and water along with other electrolytes	↓ Intravascular volume	Furosemide Hydrochlorothiazide Spironolactone
Angiotensin Converting Enzyme (ACE) Inhibitors	Prevent conversion of angiotensin I to angiotensin II	↓ systemic vascular resistance Prevents deterioration of cardiac function	Captopril Enalapril
Vasodilators	Direct vasodilation of arterioles	↓ systemic vascular resistance	Hydralazine

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Cardiovascular agents: Antiarrhythmic Agents

Agent	Mechanism	Key Points
Adenosine	Slows conduction through the AV node Interrupts re-entry pathways in the AV node	Used for treatment of SVT Extremely short $t_{1/2}$ (< 10 seconds)
Digoxin	Direct suppression of the AV node ↑ refractory period	Can be pro-arrhythmic with excessive dosing Electrolyte imbalances increase the risk of toxicity
Esmolol	Competitively block β-receptors	May potentiate hypoglycemia

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Central Nervous System (CNS) Medications

Anesthetic agents:
Medication that removes the pain sensation

Analgesic agents:
Medications that produce decreased sensation to pain

Sedative-hypnotic agents:
Medications that provide mood alteration in patients with anxiety

- Do **NOT** provide pain relief

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CNS Medications: Analgesics

Non-Opioid Agents

- **Acetaminophen** (APAP)
- MOA: Inhibition of prostaglandin synthesis
- Mild - moderate pain
- Adverse effects: hepatotoxicity

Opioid Agents

- **Morphine** & **Fentanyl**
- MOA: Block μ-receptor activation
- Moderate - severe pain
- Adverse effects
  - respiratory depression
  - chest wall rigidity (fentanyl)
  - dependence

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CNS Medications: Sedative-hypnotics

Barbiturates

- **Phenobarbital & Pentobarbital**
- MOA: depresses the sensory cortex, decreases motor activity, alters cerebellar function
- Adverse effects:
  - Dose dependent respiratory depression
  - Bradycardia / hypotension

Non-barbiturates

- **Benzodiazepines (midazolam, lorazepam)**
- MOA: enhance the inhibitory effect of GABA
- Adverse effects
  - respiratory depression
  - hypotension

Dexmedetomidine	
Mechanism	α2-adrenergic receptor agonist
Adverse effects	Bradycardia, hypotension/hypertension
Administration & Dosing	Continuous infusion: 0.1 - 0.3 mcg/kg/hr (max: 1.5 mcg/kg/hr)

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Withdrawal

Tolerance
Need for larger doses and higher concentrations to achieve the same effect

Dependence
Continued administration is required for **physiologic well being**

Addiction
Changes in lifestyle as the result of dependence

Withdrawal
Clinical symptoms related to abrupt discontinuation in a dependent person

Withdrawal: Treatment

Non-pharmacologic
- Supportive Care
- Swaddling, minimal stimulation, quiet environment

Pharmacologic
- Not appropriate for all patients
- Utilize a **similar agent** to what is causing withdrawal
  - Opiate: morphine, methadone
  - Benzodiazepine: lorazepam
  - Adjunct: clonidine, phenobarbital

CNS Medications: Stimulants

Caffeine Citrate

Indication	Treatment of **apnea** of prematurity
Mechanism	**↑ levels of cyclic AMP** ↑ sensitivity to CO2 ↑ diaphragmatic contraction Stimulation of the respiratory drive
Key Points	**Long half-life** (72 - 96 hours) Adverse effects: **tachycardia**, irritability

Immunizations

- Goal is to prevent viral or bacterial infections

Active Immunity
Produced by the body
Disease or vaccine

Passive Immunity
★ Mother to child immunity
★ Antibody administration

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Immunizations

Inactivated
Contain pathogens inactivated by heat or chemicals
- **Cannot cause disease**

Live Attenuated
Contains modified or weakened pathogens
- Should not be given while inpatient

Resources:
- Vaccine Adverse Event Reporting System (VAERS)
- CDC Website

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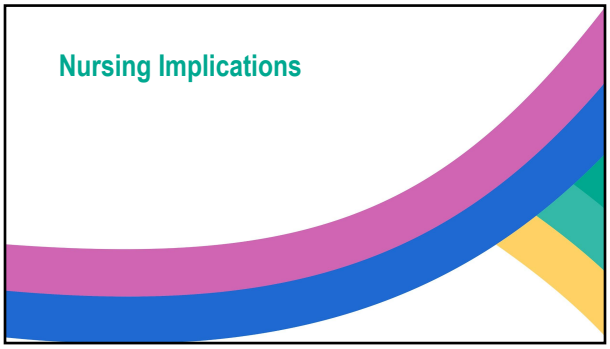
Nursing Implications



Implications for Nursing

Bedside nurses are very valuable resources in many areas and functions.

Medication Administration & Documentation
- ★ Incompatibilities

Monitoring
- ★ Clinical response
- ★ Levels
- ★ Toxicity

Dose Double Check
- ★ mg/kg doses
- ★ Rate checks
- ★ Volume checks

Questions

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