

Treatment of Calf Disease: The Next Paradigm Shift

Impact of age/disease on antibiotic distribution and efficacy in calves



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Objectives

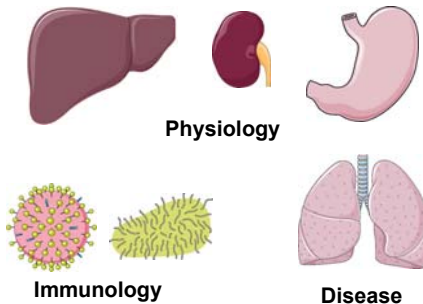
- ❖ Overview of age related changes in cattle
- ❖ Absorption, Distribution, Metabolism, Elimination
- ❖ Disease Example – Salmonella Dublin

Age is dynamic and variable

- Not just one parameter!
- Represents changes in:



Body Composition



Physiology

Immunology

Disease

Age related changes in cattle

Body Composition

- ↓ fat
- ↑ extracellular water

Physiology

- Rumen Development
- Ontogeny of metabolic pathways

Immunology

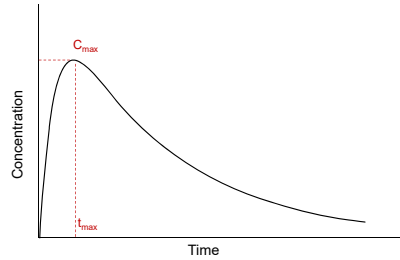
- Neutrophil function
- Immature immune system

Disease

- Different Pathogens
- Pathophysiology

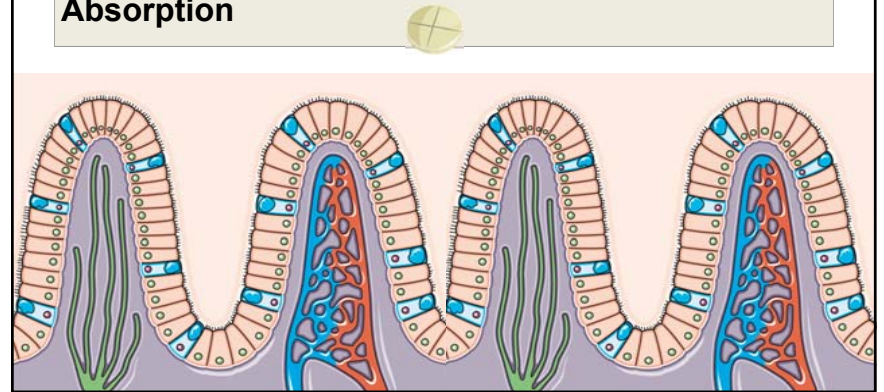


Pharmacokinetics

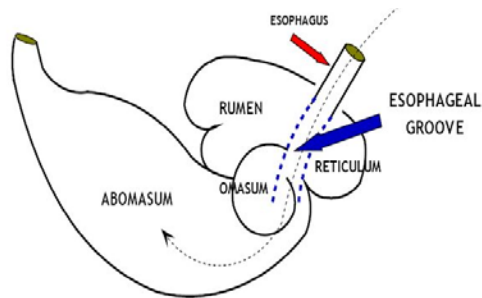


Absorption
Distribution
Metabolism
Excretion

Absorption

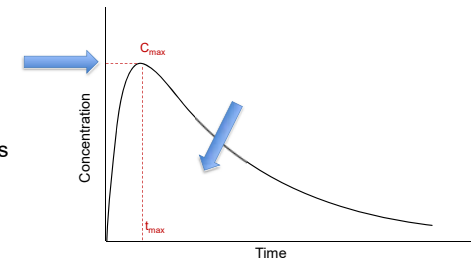


Absorption – Enteral Route



Factors that affect enteral absorption

- Gastrointestinal transit time
- Drug Properties
- Rumen Microbes
- pH of GI tract
- Binding of drug to GI contents
- Intestinal drug transporters
- Disease
 - Gut barrier function ★



Factors that affect parenteral absorption

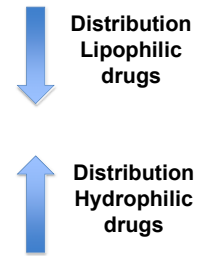
- Perfusion in area of injection
- Rate of drug penetration through capillary endothelium
- Disease
 - Hydration status ★



Distribution – Total Body Water

Body composition

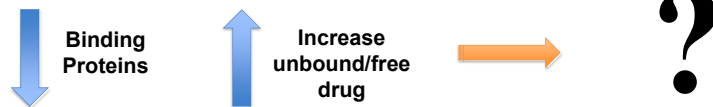
- Larger extracellular fluid volume
- Lower Body fat: Water ratios
 - Decrease in distribution of lipophilic drugs
 - Increase distribution hydrophilic drugs



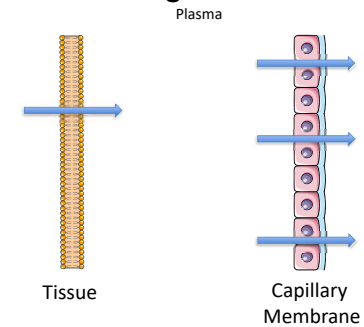
Distribution – Plasma Protein Binding

Plasma Protein Binding

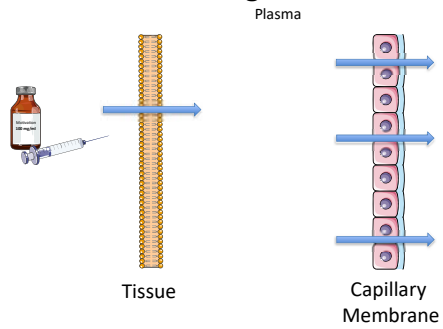
- Amount of available binding proteins (albumin, alpha1 acid glycoproteins)
- Number of available binding sites
- Affinity of the drug for the protein(s)
- Presence of pathophysiological conditions or endogenous compounds that may alter the drug-protein binding interaction ★



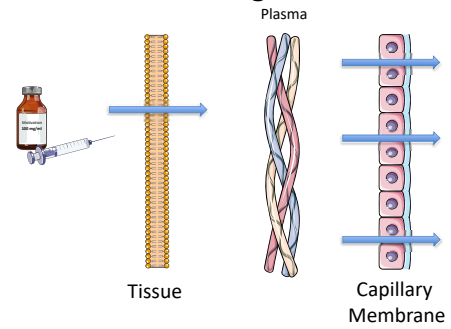
Protein Binding Effects on Distribution



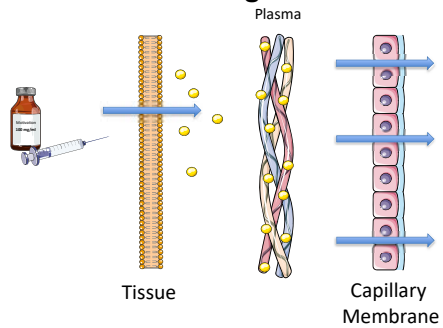
Protein Binding Effects on Distribution



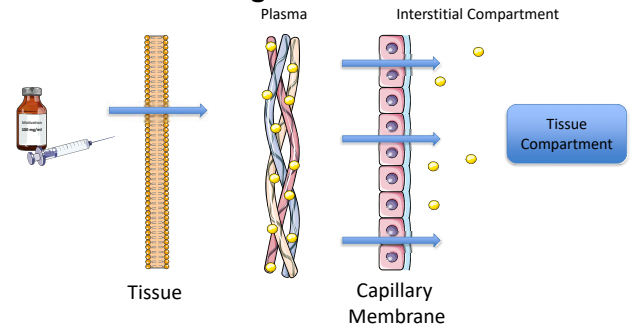
Protein Binding Effects on Distribution



Protein Binding Effects on Distribution



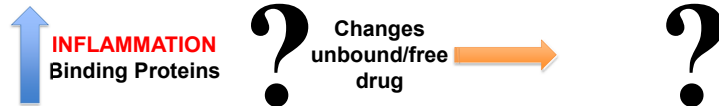
Protein Binding Effects on Distribution



Distribution – Plasma Protein Binding

Plasma Protein Binding

- Amount of available binding proteins (albumin, alpha1 acid glycoproteins)
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Metabolism/Elimination

• Hepatic Metabolism/Elimination

- Immature metabolic enzymes
- Capacity to metabolize drugs in calves may result in higher or lower drug plasma levels than those reached in adults



• Renal Elimination

- Drug excretion based on glomerular filtration (GFR), tubular secretion and reabsorption



Clinical Disease Considerations in Calves

- ★ **Dehydration:** reduction in body water, primarily from the extracellular space



Potentially Affected parameters

- **Volume of distribution** - increased concentrations
- **Clearance** - reduced GFR
- **Absorption rate constant** (subcutaneous administration)

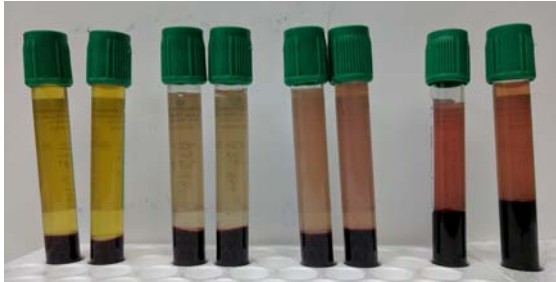
Clinical Disease Considerations in Calves


- ★ **Sepsis/Endotoxemia**
Potentially Affected parameters

- **Volume of distribution**
- **Clearance**
 - Early increase in CO, Increase CL
 - Renal dysfunction, decrease CL
- **Absorption**
 - Blood flow is directed preferentially to vital organs, decrease in absorption from SC, IM and enteral routes



Endotoxemia from P. Multocida in Calves



Maximum Plasma Concentrations 

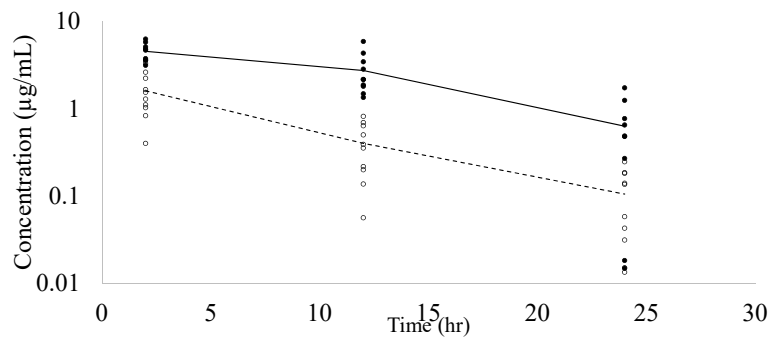
Clinical Disease Considerations in Calves

★ **Respiratory Disease**
Inflammation may impact distribution

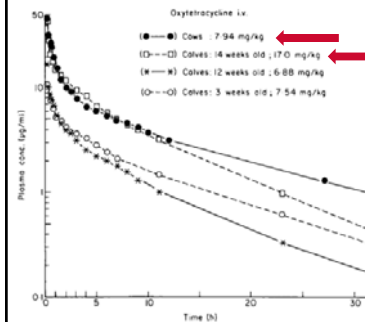
- Increase membrane permeability
- Increase phagocytes in affected tissue
 - Changed by age?
- MIC



PELF Concentrations Danofloxacin



Oxytetracycline in Calves



- Suggests calves may require **twice** the dose of cattle of oxytetracycline IM or IV.
- May be different from a tissue and residue avoidance point of view
 - Combination of decreased clearance mechanisms and increased volumes of distributions

Disease Example - Salmonellosis in Calves

Endotoxin/Fever
• ↓ Drug distribution

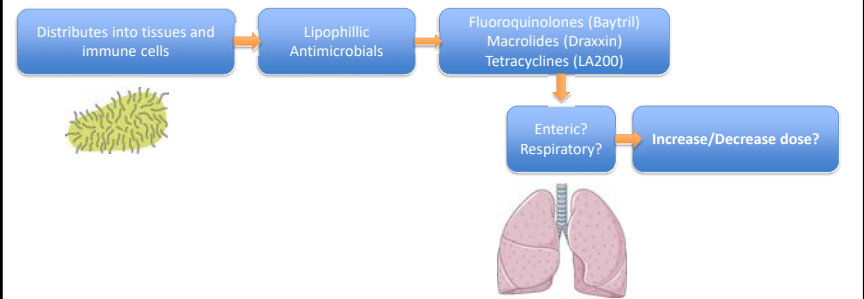


MIC of Salmonella
• Data in Calves?

Drug Concentrations
• GI Tract (local)
• Respiratory Tract (Systemic)

Immune System
• Innate Immunity
• FPT

Salmonellosis



Learning Points

- ❖ Age is Dynamic and Variable
- ❖ Pharmacokinetics can be influenced by age
- ❖ Disease can have a significant impact on drug kinetics

