Bovine Leukosis Virus: Pathogenesis and Control

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Bovine Leukemia Virus

- History
  - Clinical disease recognized in 1870's
  - Viral etiology established in 1969
  - Experimental transfer of disease with lymphocytes from infect animal in 1972
  - Recognition of virus as type C oncornavirus in 1972
  - Serology test introduced in 1979

Bovine Leukemia Virus

- Bovine Leukosis

Enzootic	Sporadic
Asymptomatic	Calf form
Persistent	Thymic form
Lymphocytosis	Skin form
Lymphosarcoma	

Bovine Leukemia Virus

- BLV Clinical States
  - Lymphadenopathy (rectal)
  - Exophthalmos
  - Diffusely thickened uterus
  - Melena (ulcers, esp mid lactation)
  - Congestive heart failure - brisket and ventral edema

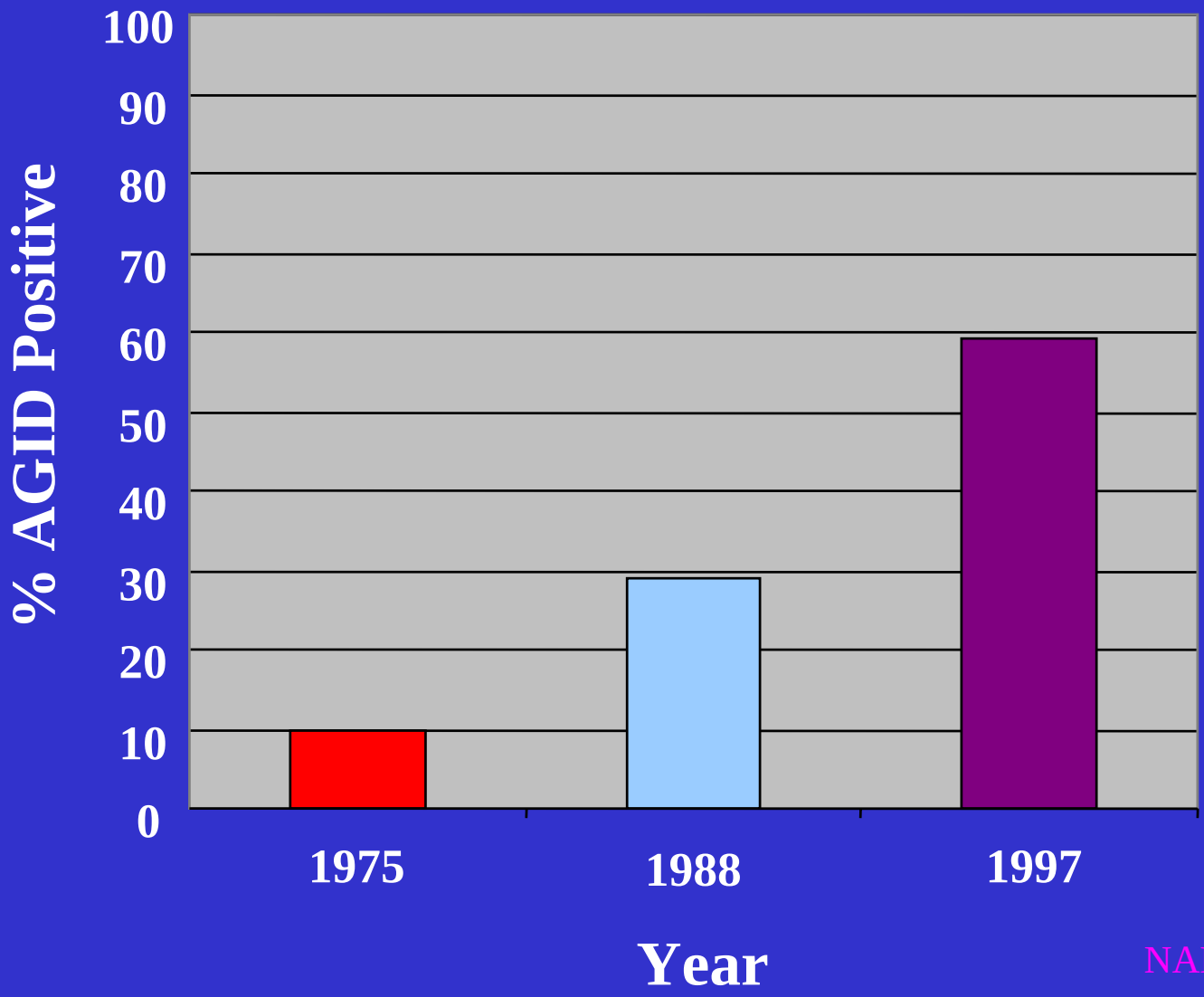
Bovine Leukemia Virus

- BLV Clinical States -con't
  - Ataxia, paresis, downer cows
  - Emaciation
  - Edema / swelling of extremities
  - Sudden death - splenic rupture

Bovine Leukemia Virus

- Prevalence
  - Worldwide distribution
    - Prevalence rates vary dramatically with country
  - Prevalence increases with age
  - Dairy cattle generally have higher prevalence rates than beef cattle
    - Management factors
    - Breed susceptibility differences?

BLV Prevalence Estimates: U.S. Dairy Cattle



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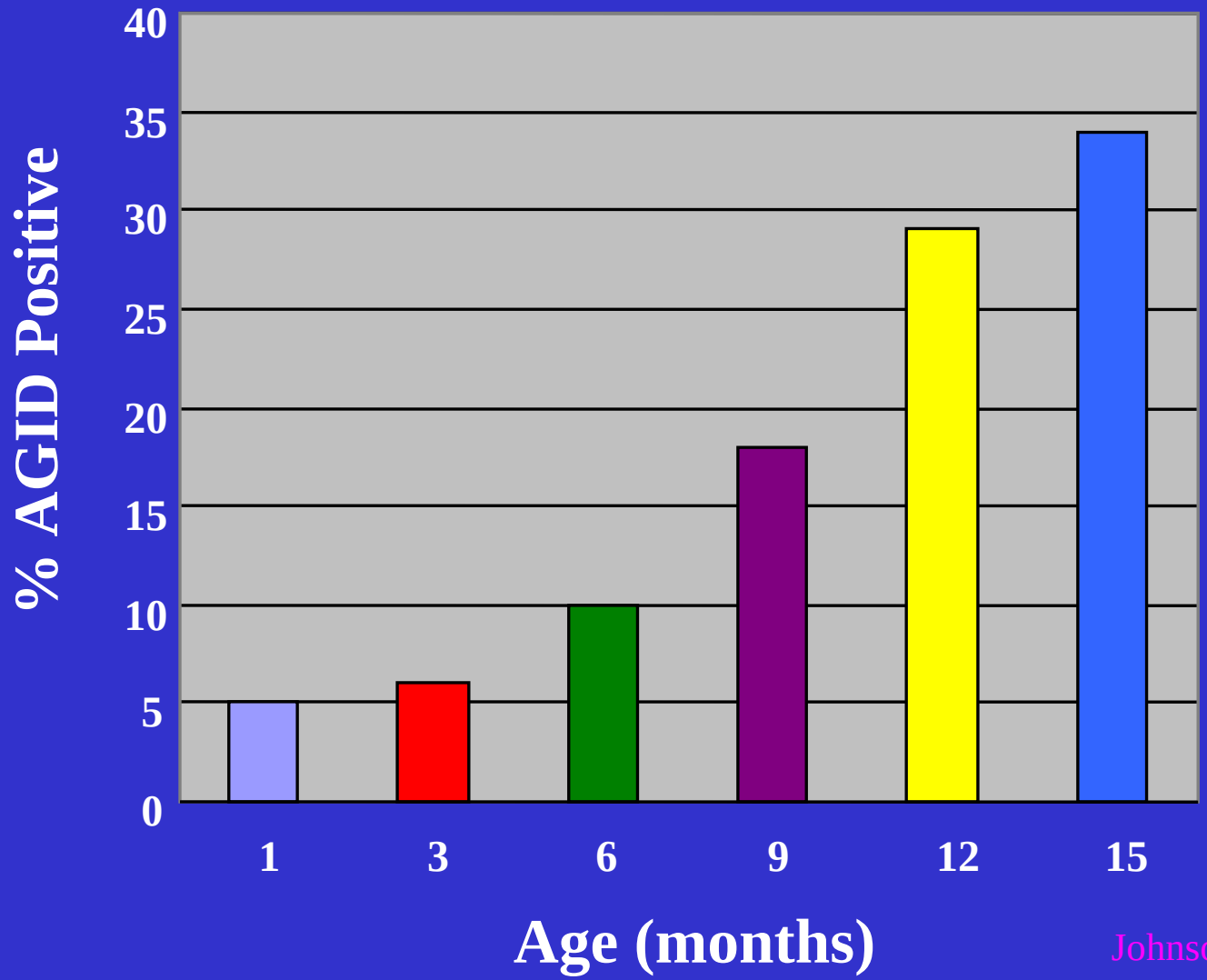
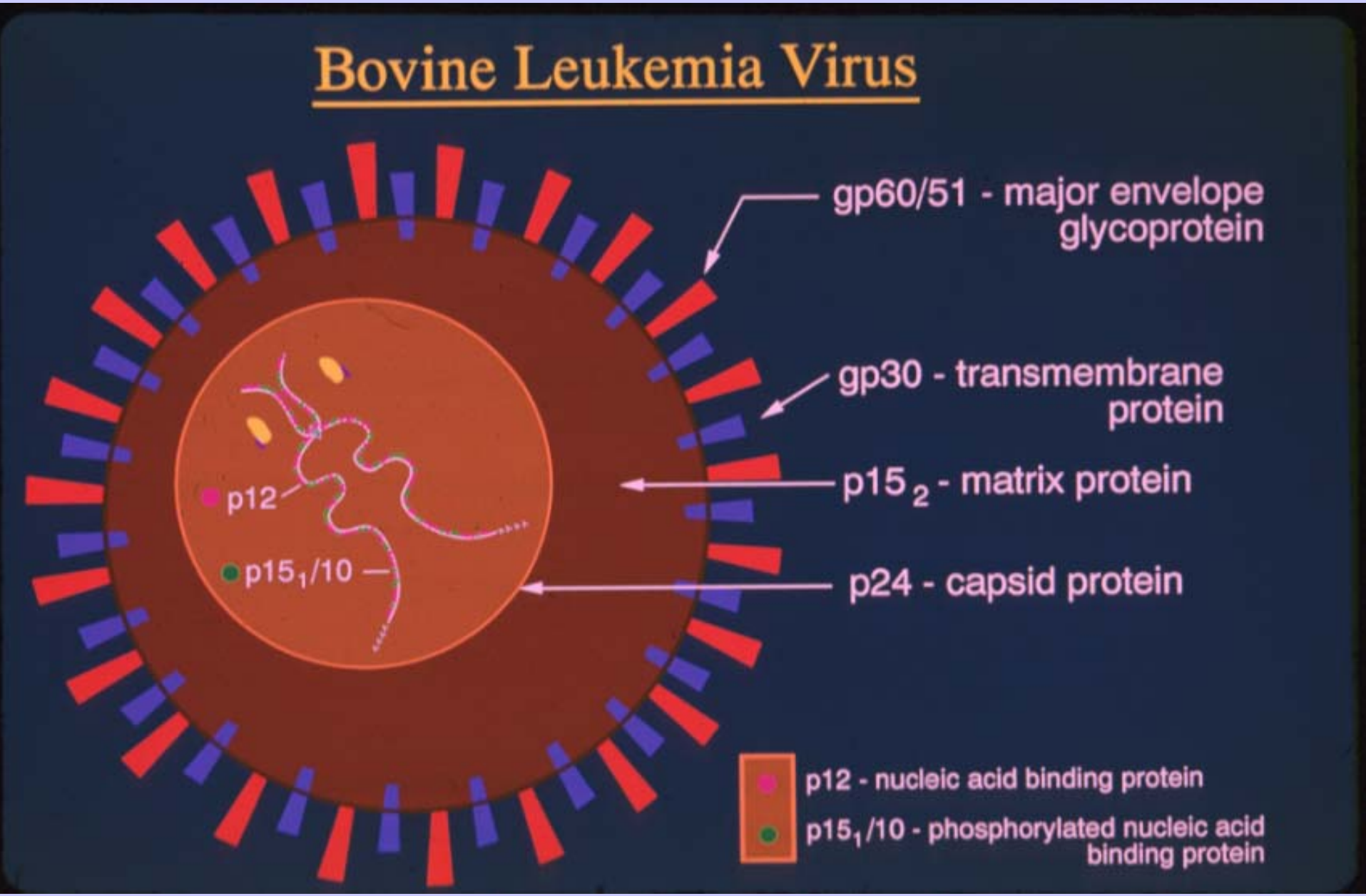
BLV Prevalence by Age Group



Johnson & Kaneene 1998

Bovine Leukemia Virus

- Bovine Retroviruses
  - Oncornavirus - Bovine leukemia virus - BLV
  - Spumavirus - Bovine syncytial virus - BSV
  - Lentivirus - Bovine lentivirus - BIV


Bovine Leukemia Virus
gp60/51 - major envelope glycoprotein
gp30 - transmembrane protein
p15 2 - matrix protein
p24 - capsid protein
p12
p15 1/10
p12 - nucleic acid binding protein
p15 1/10 - phosphorylated nucleic acid binding protein

Bovine Leukemia Virus

- Retrovirus
  - Proviral DNA integrates into the chromosome of host cell
    - Infection persists for life of cell or animal
    - Virus generally evades immune surveillance system
    - May assume control of cell division
    - Can exist in absence of viremia

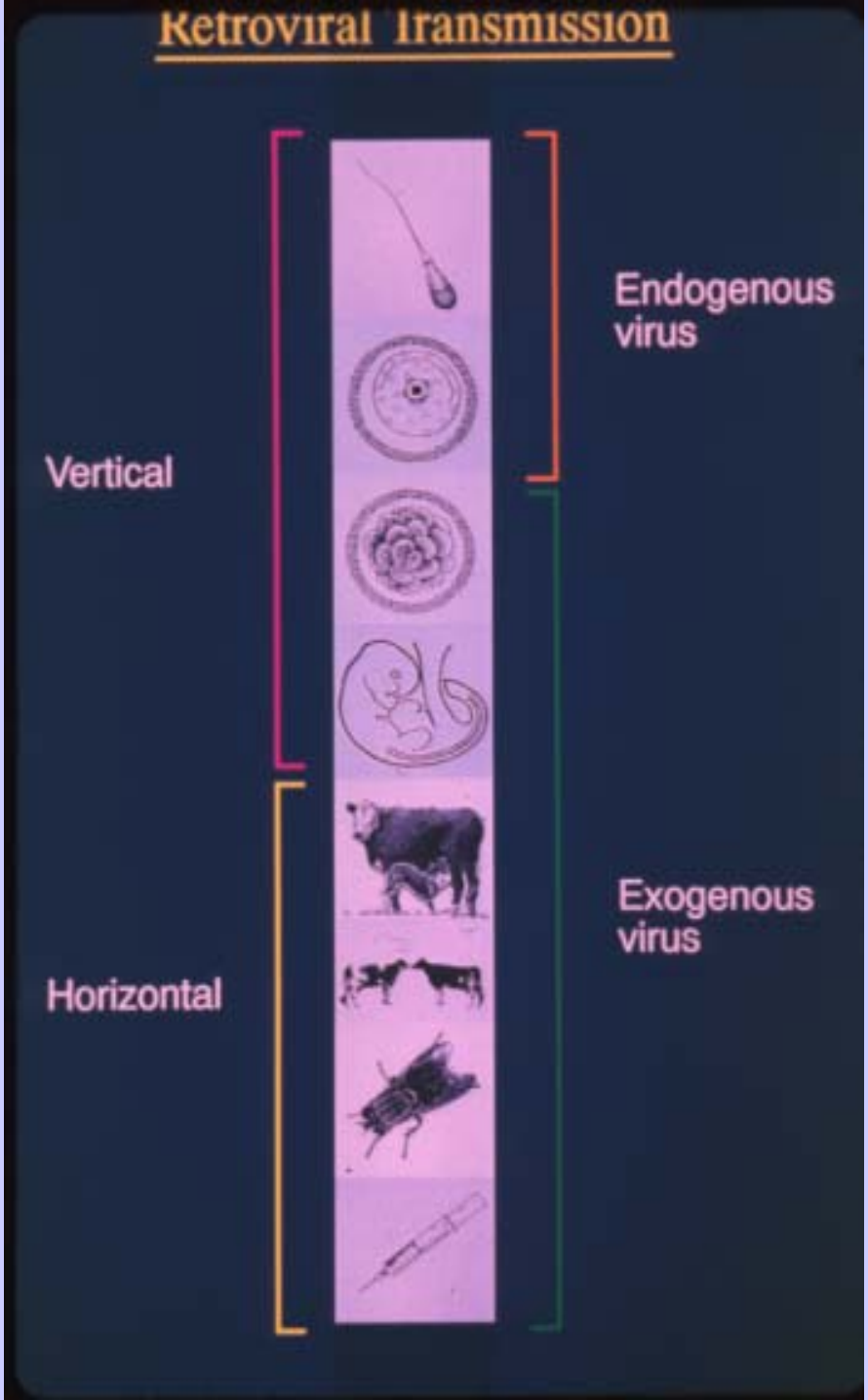
Bovine Leukemia Virus

- Detection of Infected Animals
  - Leukosis “keys”
  - Serology tests
    - Agar-gel immunodiffusion
    - Enzyme immunoassays
    - Radioimmunoassays
    - Virus neutralization

Bovine Leukemia Virus

- Detection of Infected Animals-con't
  - Virus neutralization
  - Antigen detection tests
    - Plasma Blocking Factor
  - Nucleic Acid detection tests
    - DNA probes
    - Polymerase Chain Reaction

Retroviral Transmission



Bovine Leukemia Virus

- Vertical Transmission
  - No evidence for the transmission of BLV through semen or through embryos from BLV-positive animals
  - In utero infection of the fetus does occur with variable frequency
    - Status of dam is critical factor

BLV+ calves born to all sero+ dams:

23/208= 11%; 95% CI: 7-16%

BLV+ calves born to all sero+, Non-PL dams:

13/189= 6.9%; 95% CI: 4-11%

BLV+ calves born to PL dams:

10/19= 53%; 95% CI: 30-75%

Persistent Lymphocytosis

1. **Absolute Lymphocyte count greater than three SD above the mean**

2. **Breed and Age Specific**

3. **Minimum Duration- 3 months**

Bovine Leukemia Virus

Poor transmittors	Efficient transmittors
+Gp51	+Gp51
-P 24	+ P24
Normal lymphocyte count	+Lymphocytosis

How does BLV spread?

- Transfer of blood or other body fluids with blood cells to uninfected animals

Bovine Leukemia Virus

- Horizontal Transmission
  - General
    - Viremia is non-existent or extremely transient
    - BLV infectivity is associated with the transfer of blood cells
    - Incidence of transmission is not constant
      - Widely held belief that young calves are more susceptible to infection

Bovine Leukemia Virus

- Horizontal Transmission con't
  - Direct Contact
    - In absence of viremia, physical proximity of infected and uninfected animals may be low risk
      - → Most studies fail to take into account the "range" of infectivity of BLV-positive animals
      - → Animals with lymphosarcoma and animals persistently lymphocytotic are more likely to transfer the disease
      - → Close contact does increase likelihood of transmission

Bovine Leukemia Virus

- Horizontal Transmission-con't
  - Iatrogenic
    - Multiple use of single needle
      - → Frequency of vaccination increases risk
    - Multiple use of obstetric sleeves
    - Contaminated vaccines
    - Dehorning instruments
    - Tattooing instruments

How does BLV spread?

Equipment:

- Needles
- Syringes
- Obstetrical sleeves
- Dehorners
- Tatoo pliers
- Ear taggers
- Medicine vials (oxytocin)
- Hoof knives
- Nose tongs
- Rectal ultrasound equipment
- Tail docking equipment
- Ear notchers
- Milking equipment

Bovine Leukemia Virus

- Horizontal Transmission con't
  - Insects
    - Larger insects more likely to transmit
    - No evidence for biological vector
    - Increased incidence rates in summer and fall
    - Higher prevalence in warmer climates
    - Higher prevalence in wetter areas

Bovine Leukemia Virus

- Horizontal Transmission-con't
  - Milk
    - BLV infected lymphocytes exist in milk and colostrum from BLV-positive animals
    - Bulk tank milk fed to BLV-negative calves will transmit the disease
    - Feeding colostrum from BLV-positive animals is still controversial
      - → May be protective under certain conditions

Bovine Leukemia Virus

- Direct Losses
  - Condemnation at slaughter
  - Higher culling rates
  - Decreased reproductive performance
  - Decreased milk yields
    - Most all economic analyses have failed to distinguish various clinical entities of BLV

Bovine Leukemia Virus

- Indirect Losses
  - Loss of export market
  - Loss of sales to AI industry
  - Loss of sales to embryo transfer industry
  - Loss of consumer confidence
  - Expenses involved in status testing

Bovine Leukemia Virus

Zoonotic Potential

- BLV will infect human cells
- No study has linked BLV to human disease
  - Most not willing to deny potential exists
  - Molecular technology should be able to provide definitive answer

Bovine Leukemia Virus

- Control Options

- Test and Slaughter
- Test and Segregate
- Test with Management Changes

Controlling Spread of BLV

- Critical to prevent the horizontal transmission of white blood cells from infected to uninfected animals
  - Clean maternity pen, remove calf ASAP
  - Feed colostrum from negative cows
  - If prevalence in herd is high (over 60%) freeze colostrum to destroy virus
  - Do not feed waste milk
  - Manage positive and negative groups separately

Controlling spread…cont.

- Use single-use needles
  - Discard syringes with blood contamination
  - Prevent blood contamination of medicine/vaccine vials
- Clean and disinfect equipment used between animals
- Use electric dehorners rather than cutting dehorner
- Use new OB sleeve for each cow
- Use artificial insemination

Controlling spread…cont.

- Do not over crowd animals
  - No greater than 110% in freestalls
- Implement an integrated pest management program

Is testing necessary?

- Testing can be helpful
  - Determine which animals are infected
  - Monitor progress for control or eradication
  - Determine if and where horizontal transmission is occurring in herd

Timeframe to Eradication

- Dependent upon:
  - Initial herd prevalence
    - Higher prevalence = longer time to eradication
    - Very high prevalence (60-80%) may not be able to accomplish without separation of negative and positive groups
  - Level of commitment
    - Need to implement ALL management practices
  - Ability to raise only BLV negative heifers
    - Break cycle of new infections

Timeframe to Eradication

- Dependent upon:
  - Degree of crowding and possibility of animal-to-animal contact
    - Horizontal transmission - nasal/ocular discharge
  - Feasibility of separating negative and positive groups
  - Priority given to culling BLV positive animals
  - Frequency of testing
    - Herd testing (6 months and older) every 6 months
    - Identify groups with new infections
    - Confirmation of negatives