BLUETONGUE VACCINES IN THE UNITED STATES

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History of Bluetongue in the United States

- “Soremuzzle” in sheep after World War II
  - Hardy and Price, J Am Vet Med Assoc, 1952

- BTV serotype 10 (CA-8) isolated from sheep with soremuzzle in California in 1952
  - Serotype 11, 1955
  - Serotype 17, 1962
  - Serotype 13, 1967
  - Serotype 2, 1983
  - Serotypes 1, 3, 5, 6, 14, 19, 22, between 1999 – 2005

- First vaccines developed in 1950s for use in sheep
  - Embryonated chicken egg passaged modified live virus (MLV) vaccine to serotype 10 produced like those from Onderstepoort
    - Conscious decision to make vaccine using local virus strains of serotype 10 (CA-8) rather than import South African vaccine
Vaccines

• First vaccine was to serotype 10 using chicken embryo passaged CA-8 isolate
  – Sold until the early 1970s, but problems of teratogenicity etc resulted in required (by USDA) removal from the market

• Cell culture modified live virus (MLV) vaccines
  – Colorado Serum Company
    • USDA licensed so available throughout US
    • Serotype 10 only
  – California Wool Growers
    • California only
    • Monovalent vaccines to serotypes 10, 11, and 17
    • Only perhaps >100,000 doses sold annually
Fetal BTV Infections

• A property of laboratory adapted strains of BTV
  – Teratogenic defects in > 20% of ewes vaccinated at day 40 of gestation with the original CA-8 chicken embryo adapted MLV
  – Markedly reduced reproductive performance as well

• Defects reflect gestational age at infection
  – Cavitating encephalopathy and retinal dysplasia, leading to blind and/or “dumb” lambs that quickly die or fail to thrive
    • Unproven are arthrogryposis and other teratogenic defects
    • Myths include “excessive gingival tissue” in calves, and truly persistent postnatal infection
BTV Infection of Fetal Ruminants

- BTV infection in early gestation leads to fetal death or cerebral (and eye) malformation

- Only chicken embryo or cell culture adapted strains of BTV commonly cross the placenta to cause teratogenic defects – described where MLV vaccines are used

Potential Issues Pertaining to MLV BTV Vaccines: Experiences in California

- MLV vaccines are cheap, relatively safe if properly attenuated for target breeds, and induce long term serotype-specific immunity with 1 shot
  - Only viable strategy for a minor (orphan) species such as sheep in California

- Potential shortcomings
  - Result of inappropriate vaccination (pregnant sheep or in the face of an active outbreak)
    - Teratogenicity
      - Field viruses apparently never or very rarely cross the placenta whereas MLV vaccine viruses can – a feature of chicken embryo derived vaccines but also some cell culture MLV (Flanagan and Johnson, Aust Vet J, 1995)
    - Circulation of vaccine viruses or reassortment of genes with field strains – potential issue if introduce novel genes/viruses
      - Sporadic teratogenesis of cattle in California and South Africa where MLV vaccines are used in sheep but not cattle
      - Molecular genetic studies confirm circulation of vaccine viruses/genes
BTV Infection in the US: Current Situation

- Two distinct ecosystems
  - Southeastern US with serotypes 1 – 3, 5, 6, 10, 11, 13, 14, 17, 19, 22
  - Remainder of the US up to the “Sonorensis – line” only serotypes 10, 11, 13 and 17

- Some disease in sheep but not other species
  - Minimal use of vaccines, and only in sheep
  - Vaccines are not available to all serotypes

- Regulatory/trade issue to cattle industry, despite lack of disease in cattle
  - No use of vaccines
  - International movement and trade of cattle/germplasm an issue, less so regionally (Canada, Mexico, US)
Different species of *Culicoides* vector disseminate different serotypes of BTV in relatively distinct global ecosystems

- **Bold** indicates known or presumed principal vector

- *C. dewulffi* is a **putative** vector of BTV serotype 8 in northern Europe (2006/2007)*
Bluetongue; the Future in the US

• Recent incursion of new serotypes but no major disease issues
  – Geographically restricted and unassociated with animal movement
    – expansion of the Caribbean ecosystem?

• No perceived need for vaccination other than in sheep which are minor in US (approx. 7 million sheep vs. 100 million cattle; revenue >$1 billion vs. >$65 billion)
  – Continued limited use of MLV in sheep to prevent disease
  – No disease issue in the cattle industry currently, and no vaccination
  – Safe, new generation vaccines such as canarypox recombinant (Boone et al., Vaccine, 2006) now available but unlikely to be used unless cattle are affected