

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

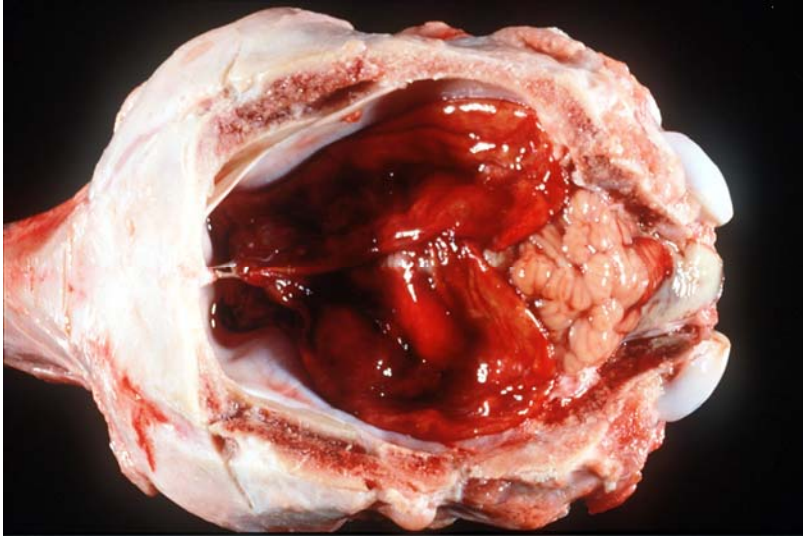
Vaccines

- **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

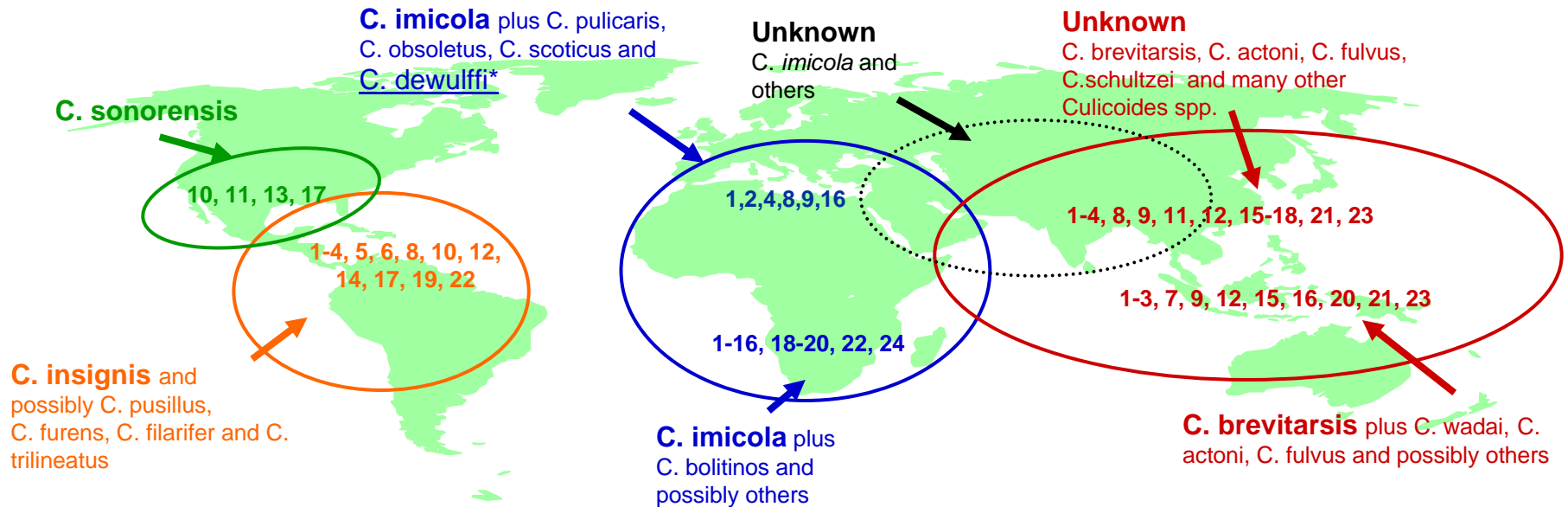
Potential Issues Pertaining to MLV BTV Vaccines: Experiences in California

- **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)

BLUETONGUE GLOBAL ECOSYSTEMS



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