



New York State Cattle Health Assurance Program
Salmonellosis Module
*Usefulness of Vaccination and Vaccine for
Control of Salmonellosis*

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Summary Points:

1. Few well designed vaccine studies have been published evaluating salmonella vaccines in adult cattle or calves. Studies involving vaccines on the market in the US are equivocal.
2. Only one controlled adult cow study has been reported using a modified live vaccine (*S. Cholerasuis*):
 - (See USAHA, 2000 Salmonella Committee Report , House, Dueger et al at <http://www.usaha.org/reports/reports00/r00sal.html>).
 - Serogroup specific protection measured by reduced fecal shedding in calves and adults; no reductions were seen in other serogroups.
3. Results from vaccine studies in calves have been equivocal
 - Protection, if present, is short lived if delivered by passive (colostral) immunity in calves

See also Point 6 from WSU materials

▪ **Key Points from point 6 of the WSU Document**

- ... *S. Typhimurium* sends a protein signal through the wall of a nearby intestinal cell of the host.Salmonella and other pathogens are able "trick" the intestinal mucosal M cells into ingesting them, which gives the bacteria direct access to the reticuloendothelial system but are protected from it.
- ..this protein signal is only produced when the salmonella is near an enteric cell and is not produced during laboratory fermentation.
- ...bacterins simply targeted at producing antibodies against antigens produced during standard laboratory fermentation are not likely to be highly efficacious. Other than anecdotal experience, little empirical evidence suggests that current commercial *bacterins* are or are not beneficial and good clinical trials are needed in this area (House and Smith, 1997).

- Bacterins, or *deletion mutants*, targeted at specific parts of this relationship, such as blocking the Type III signaling, are more likely to provide protection.
- For more information on vaccination as an option for control - see also - Evaluation of Bovine Salmonella Vaccines (JK House, BP Smith) <http://www.usaha.org/speeches/bosava97.html>.

***** Added Notes from Cornell**

Vaccines are of two major types:

1. Live attenuated bacterial vaccines

examples are the *aroA* mutants developed for *S. Dublin*;

2. Whole cell bacterins (killed or inactivated), or core, or subunit (e.g., flagellar or OMP) vaccines

-these bacterins may be a commercially available product containing 1 or more serotypes of *Salmonella*

- Examples are the Colorado Serum Co.'s combined *S. Dublin*/ Typhimurium bacterin, or the gram negative core antigen bacterins such as ENDOVAC-Bovi (*Salmonella* Minnesota core mutant) or the J5 or JVAC (*E. coli* core mutant)
- **ENDOBAC-Bovi**: this is a commercially made bacterin composed of a mutant strain of *Salmonella* Typhimurium which lacks the polysaccharide repeat units of the LPS that confer serotype specificity on the *Salmonella*, i.e., it is a LPS core product.
 - Claims are made for this product to provide cross protection (because of similarities in the gram negative LPS) against *E. coli* mastitis, and other endotoxin-mediated diseases such as *Salmonella*, *Pasteurella multocida*, and *Manheimia hemolytica*.
 - Such a product would be expected to protect against the systemic effects of endotoxin/LPS. Such a product would not be expected to prevent colonization of the gut mucosae by *Salmonella* or to provide specific serotype immunity via activated macrophages such as would be elicited by a live attenuated infection with *Salmonella*. [note: Endobac-bovi has an proprietary Aimmune enhancer@ added to the bacterin for which claims are made that it elicits humoral and CMI responses; this provide additional protection against the clinical effects of systemic disease].
- **J5-VAC and J-5**: these are two commercially available *E. coli* LPS core antigen bacterins made from mutant strains of *E. coli*. Claims have also been made with these types of products to protect cattle against the effects of endotoxemia associated with gram negative diseases including *E. coli* and *Salmonella* Typhimurium. Similar discussion about the ability to protect cattle against salmonellosis may be found above under Endobac-bovi.

3. An autogenous bacterin (usually whole cell) is defined as a bacterin made from the serotype isolated from the herd of cattle under study. The difference between a core LPS bacterin and another bacterin (such as an autogenous bacterin) made from non-mutant whole cells would be that the non-mutant whole cell would have polysaccharide repeat units that would evoke serotype specific antibody that might provide more efficient or quicker phagocytosis of *Salmonella* that found their way into the bloodstream

What constitutes protective immunity in the cow against salmonellosis?

- it is thought that immunity to salmonella infection requires both a humoral (antibody) and a cellular (CMI) immune response which are both elicited following a natural infection;

- vaccination with a live attenuated vaccine is thought to stimulate the immune system in such a way that occurs following a sublethal infection with a wild-type strain, whereas vaccination with a killed bacterin product is thought to confer only humoral immunity.
- To really evaluate accurately the efficacy of vaccines and the purported roles of CMI and humoral immunity in cattle (versus the mouse model) we must:
 - evaluate the vaccination and infection in the target animal, i.e., the cow or calf
 - use a natural route of infection, i.e, oral
 - assess protection at the intestinal mucosae level (local mucosal immunity)
 - assess protection at the reticuloendothelial level (systemic immunity)
- the various roles, if any, in immunity ascribed to whole cells, or just the LPS, or OMP, or other cell wall components needs to be determined; few well controlled studies have been reported in calves or adult cattle.

Potential Uses for Vaccination:

- a.) the passive immunity/protection of the calf afforded by the colostrum from a cow vaccinated during the dry period has been shown to be of value; usually killed (often autogenous) bacterins are used. This approach probably provides specific antibody to prevent colonization of the calf's gut, and also some systemic antibody that may serve to protect the calf against the effects of endotoxin/LPS if the *Salmonella* were to become bacteremic. This sort of immunity could easily be overcome with an overwhelming challenge dose from the environment. This type of immunity also appears to be quite short lived (first week of life). (see House, J et al "Prevention of Salmonellosis in Dairy Cattle" Proceedings 18th ACVIM, Seattle, WA 2000.)
- b.) Calves and adult cattle have been protected by vaccination with live attenuated vaccines against challenge with the same serogroup; (for an abstract of this report -see <http://www.usaha.org/reports/reports00/r00sal.html>).

The problem is that not all attenuated live vaccines are equal in protection, some cause morbidity, and most are not commercially available in this country. Although not known, this vaccine approach may prevent colonization or even spread of the *Salmonella* beyond the mucosal defense mechanism in the gut.

***Salmonella* serotype Dublin:**

- **BEWARE** of literature you read on salmonellosis, i.e., there may be serotype dependent clinical presentations. For example, *Salmonella* Typhimurium (mild to severe enteric signs versus *S. Dublin*'s septicemia/meningitis/pneumonia in calves.
- ***Salmonella* Dublin has emerged as a problem in parts of the Northeast USA; this has tremendous herd and public health significance.**
- ***S. Dublin* is host adapted to cattle, therefore, there is potential for establishing a chronic carrier state in cattle after infection and subsequently the potential for establishing endemic infections at the herd level. (McDonough et al, J Clin Micro; Aug 1999, 2418)**
 - Most *S Dublin* infections were identified in veal and dairy beef operations in NY and PA between 1988-1995. No isolates have been identified in NY since then.
 - Contaminated trucks were considered a major risk for infection.

CLINICAL SIGNS - CATTLE - spectrum of disease (subclinical, clinical case: acute/chronic, carriers)

1. **peracute disease**: colostrum- deprived or -deficient calf most commonly affected; fever (105-107 F); diarrhea (yellow with or without flecks of blood and mucus); rapid dehydration, prostration and death occurring within 24-48 hours due to fulminating septicemia. Mortality high.

NOTE: many veal calves and dairy beef have a different presentation when infected with *Salmonella* Dublin - 8 to 10 week old calves go off feed, have fevers, show clinical signs of pneumonia/septicemia, diarrhea may or may not be present. Morbidity in affected units is high as is mortality in untreated calves.

2. **acute enteritis**: most common form in adult cattle and many times is precipitated by some stress factor(s). Affected cattle rapidly contaminate their environment. Clinical signs include: fever (104-106 F) followed by anorexia, depression and a foul-smelling diarrhea with varying amounts of blood, mucus, fibrinous casts, and shreds of intestinal mucosa. In milking animals there is a severe drop in milk production. Abortion sequels are not uncommon. Dehydration varies with the severity of disease. Temperatures rise 24 hours before the onset of diarrhea and may drop off again with the onset of diarrhea. Mortality rates vary depending on the serotype of salmonella involved. The time course of clinical infection is usually 7-10 days with recovery in 2 to 3 weeks. Some animals may never resume full production. Acute cases that recover may become carriers that shed *Salmonella* for varying periods of time (e.g., *S. Typhimurium* from 3 to 6+ months versus *S. Dublin* = lifelong carriers).
3. **chronic cases**: preceded by the acute form of disease. Fever (103-104 C) is intermittent and watery diarrhea persists resulting in progressive dehydration and weight loss. Recovery may be slow and mortality rates are difficult to predict; cattle are often culled due to unthriftiness and poor condition.
4. *S. Dublin* specific serology (ELISA) has been developed and is offered by referral laboratories for identification of chronic carriers.