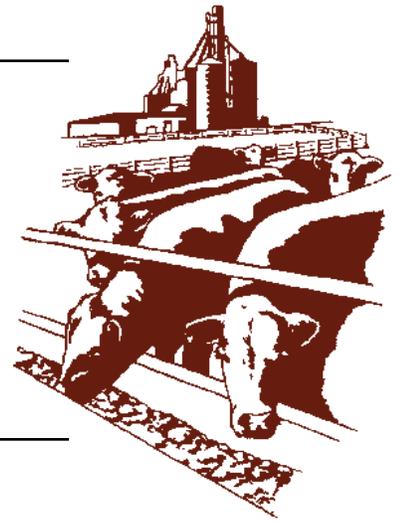




# Beef Cattle Handbook



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## Injection-site Reactions From Clostridial Vaccines: A Critical Control Point?

B. J. McFarlane<sup>1</sup>, G.L. Stokka DVM,MS<sup>1</sup>, Department of Animal Science and Industry  
Randall Basaraba DVM,PhD<sup>2</sup>, Department of Diagnostics and Pathobiology, College of Veterinary Medicine

### Abstract

One 250 kilogram steer was injected subcutaneously twice, once on each side of the neck with 5 milliliters of Ultrabac 7® clostridial vaccine with a new 16 gauge, 3/4 inch needle. The injections were given 30 days and 36 hours prior to euthanasia, at which time the resultant lesions (two) were collected. The lesions then were evaluated for possible tissue damage and physical descriptors were recorded. The 36 hour injection caused an acute lesion with higher than normal levels of neutrophils and erythrocytes in the center of the lesion. Within the surrounding skeletal muscle of the lesion, there were increased levels of fibrin and edema fluid causing separation of the muscle fibers and hemorrhaging. The 30 day injection formed a chronic lesion differing from the 36 hour lesion, primarily by the increased amounts of fibrous connective tissue forming the center of the lesion. This fibrous connective tissue also extended into surrounding skeletal muscle bundles. The surrounding skeletal muscle also showed signs of degeneration with minimal regeneration. These findings show that tissue damage can occur with a subcutaneous injection of a clostridial vaccine.

### Introduction

Livestock producers with effective herd health programs administer drugs and vaccines on a periodic basis for the prevention and/or treatment of infectious diseases<sup>1</sup> and spend millions of dollars annually<sup>2</sup>. The most effective means of building a long-lasting immunity to a particular disease is to recover from exposure to that disease<sup>2</sup>. However, the chance of risking herd infection because of

a disease outbreak is too impractical. Therefore, injections of pharmaceutical products are given, which produce immunity nearly as good as disease recovery. Many of these injections are given intramuscularly in the rump between the hooks and pins. A lack of integration and communication between the sectors of the beef industry has resulted in many animals receiving multiple injections over their lifespan; in some cases, as many as six clostridial injections<sup>17</sup>. These injections can cause severe tissue damage within the muscles of the top sirloin butt<sup>3</sup>, and a significant reduction in tenderness up to 3 inches away from the center of the lesion may result<sup>4</sup> from the increased collagen formed. The occurrence of such muscle tissue damage represents a "quality control" problem and an economic loss to the beef industry<sup>5</sup> of nearly \$55,000,000 per year<sup>4</sup>. In the face-to-face interview phase of the National Beef Quality Audit (1992), injection site-lesions ranked second, second, third, and second as major quality concerns of purveyors, restaurateurs, retailers and packers, respectively<sup>6</sup>. This is not just a problem in the beef industry. The pork industry also suffers losses in carcass trim, possible adverse publicity, and resultant decrease in consumer acceptance<sup>7</sup>.

When injections are given, either intramuscularly or subcutaneously, an acute inflammatory reaction occurs very rapidly. The severity of the reaction is dependent upon the stimulus incurred during the injection. There is very little information published on injection-sites and their effects on the beef industry. The National Cattleman's Beef Association has been responsible for the majority of this information in the literature. Therefore, our objective in this study was to collect,

evaluate (visually and histopathologically), and characterize lesions resulting from the use of clostridial vaccines in beef cattle

### Materials and Methods

One 250 kilogram steer (vaccination history not known) was injected subcutaneously twice in the neck region with 5 milliliters of Ultrabac 7® clostridial vaccine with a new 16 gauge, 3/4 inch needle. The injections were given 30 days and 36 hours prior to euthanasia. The resultant lesions were collected and evaluated at the veterinary diagnostic laboratory at Kansas State University (Manhattan, KS). The selected tissues included haired skin, subcutaneous tissue, and underlying skeletal muscle. The tissues were fixed in 10 percent neutral buffered formalin, embedded in paraffin, sectioned at 5 um (microns), and stained with hematoxylin and eosin.

### Results

Injection-site reactions were noted on the steer within 24 hours of each injection and resulted in firm, raised, circular areas visible with the naked eye (Fig. 1).

After removal of the lesions, they were evaluated histologically. The 36-hour lesions were categorized as a dermatitis/cellulitis/steatitis. It was described as an acute (intense) necrosuppurative lesion with edema (swelling), hemorrhage (bleeding), and necrosis (dying tissue). A sharp separation was visible between the affected and nonaffected tissue, evidenced by: increased edema, fibrin (building blocks for connective tissue), neutrophilic infiltrates (fight infection), and hemorrhage (Fig. 2). The normal structure of the subcutaneous tissue had become destroyed and had dense cavitations containing edema, numerous sheets of neutrophils, extravasated erythrocytes within the subcutaneous tissue, and the muscle fibers had become separated by edema fluid. An additional section composed primarily of skeletal muscle, had increased amounts of fibrin and edema fluid, was sharply demarcated, and extended into the underlying adipose tissue (steatitis). The junction between the abscess and the skeletal muscle had increased amounts of edema, fibrin, neutrophilic infiltrates, and hemorrhage. Conglomerations of neutrophils, lymphocytes, and plasma cells were found perivascular throughout the lesion. In some sections of the lesion, neutrophils and eosinophils extended into the papillary dermis.

Histologically, the 30 day lesion was characterized as dermatitis/myositis/cellulitis. It was described as chronic (persistent, lymphoplasmacytic, and fibrosing (forming connective tissue for structural support) with mineralization. The major differences from the 36 hour lesion was the increased amounts of fibrous connective tissue in the center of the lesion with alternating loose and dense accumulations of mixed inflammatory cells: lymphocytes, plasma cells, and histiocytes. The center of the lesion was composed of sheets of degenerated neutrophils (amphophilic cellular debris, i.e. greenish puss) surrounded by mixed mononuclear cells, then fibrous connective tissue with abundant neovascularization

extending outward between the muscle bundles. Scattered skeletal muscle degeneration had occurred throughout the lesion with minimal regeneration.

### Discussion

Vaccinations are a must in livestock production, both as a preventative and therapeutic means to help ensure an animal's future vitality and protect the financial investment of the owner. However, injection-site reactions vary in response with each animal. The pronounced response in this steer appears to be a response to both tissue injury brought about by irritation from the injected vaccine and a delayed-type hypersensitivity response which results from repeated exposure to a product. The lesions were comprised mainly of a dense accumulation of lymphocytes and macrophages, which are characteristic of a delayed-type hypersensitivity reaction<sup>8</sup>. Such a reaction is considered to be a classical manifestation of specific cellular immunity and can be measured quantitatively<sup>9,10</sup> to show the effectiveness of the cell-mediated response. The simplest method being an intradermal skin test similar to a tuberculin test<sup>11</sup>. The quantity of protection that an animal possesses is measured by antibody titer or the degree that the bloodstream can be diluted and still show protection toward a specific disease producing microorganism<sup>2</sup>. However, we did not utilize a measurement that would have quantified the response in this animal.

The fact that the 30 day reaction diminished over time demonstrates that injections and the resultant reactions by themselves may not be detrimental to the animal's well-being. However, they may be a critical control point in the production of high quality beef. Physical irritation causing damage in the muscle and subcutaneous tissues will initiate an inflammatory response that can leave permanent scarring in the tissues<sup>12</sup>. The appearance of the reactions in this animal indicated that the material was irritating and, if injected intramuscularly, could result in significant degeneration of skeletal muscle tissue and infiltration of fibrous connective tissue. A resultant blemish would not be revealed until later, when that part of the animal's carcass is cut into roasts or steaks, either at the packing plant, grocery store, restaurant or on your dinner plate. Although, the main objection in the meat industry to injection-site lesions has come from the purveyors who have had to absorb the financial losses of the trim-outs from carcasses and wholesale cuts.

This irritating response could also be evidence that the antigenic material was not processed properly. Antigenic material that stimulates an immune response can also cause a localized reaction at the site of injection. Irritating products such as oil of turpentine or oil adjuvant vaccines will cause more severe irritation and injection-site reactions<sup>13, 14</sup>, but the immune response may be greater. Additionally, contamination can occur through the use of "old" or dirty needles or when skin is wet and dirty. Using "old" needles (used more than 5 times) with 2 ml or 5 ml of clostridial vaccine will

increase the number of lesions and the weight of the lesions found<sup>1</sup>. It has also been reported that in cattle, a three-fold increase in bacterial numbers can occur when a "used" versus "new" needle is used<sup>15</sup>. Also, unused portions of vaccines should never be used as they are usually contaminated and can cause acute post-vaccination reactions<sup>2</sup>.

Both sterile and infected abscesses can result from injections, and if they occur in the muscle, then carcass cutouts can occur. During the most recent audit (March 1993), the incidence of injection-site blemishes in top sirloin butts was determined to be 11 percent, with an average weight per blemish of 124 grams and reported weights averaging as high as 148 grams<sup>16</sup>. It has been shown that heavier trim weights were needed when the injections were administered earlier in the animal's life<sup>1</sup>. This implies that either growth of the injection-site lesion corresponds to the animal's muscle growth or the dosage was too large on a per weight basis and the resulting reaction was more severe than normal.

### Summary

These lesions appear to have been caused by a combination of physical irritation of the injection, repeated exposure to the vaccine, and possible tissue injury by the adjuvant itself. Solutions to this problem must begin with producers and veterinarians limiting the number of clostridial vaccinations given to any one animal and controlling the route of administration (i.e., subcutaneous, intramuscular, intravenous). Oil adjuvant vaccines are more successful in stimulating antibody production<sup>7</sup>, and higher antibody titers have been associated with greater disease protection<sup>18</sup>. However, vaccines containing an oil adjuvant produce larger and more persistent lesions in the muscle than vaccines produced with aluminum hydroxide<sup>7</sup>. Producers of the biological products must produce less irritating, yet effective, adjuvants, this should diminish the chances of reactions occurring and improve our goal of decreasing the incidence of injection-site blemishes.

### Recommendations

We recommend that clostridial vaccines should be given subcutaneously in the neck with the "tenting" technique, with sterile needles and syringes (new or boiled in water for five minutes), intramuscular injections for all products should be avoided whenever alternate routes of administration are available on the label's directions, and clostridial vaccinations be limited to primary immunization<sup>19</sup>. Properly administered subcutaneous injections keep damage to nearby muscle tissue to a minimum, helping to ensure the production of high quality beef demanded by consumers<sup>20</sup>.

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Authors:

B. J. McFarlane<sup>1</sup>, G.L. Stokka DVM,MS<sup>1</sup>, Department of Animal Science and Industry  
 Randall Basaraba DVM,PhD<sup>2</sup>, Department of Diagnostics and Pathobiology, College of Veterinary Medicine

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