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ANIMAL AND HUMAN HEALTH PREVENTION OPPORTUNITIES

Brucella abortus strain RB51 vaccine — a cattle vaccine with human health implications

Brucella spp. is a Gram-negative coccobacilli that causes disease in livestock and humans. Brucellosis is a disease of both animal health and public health importance. Infection causes abortions in cattle and other ungulates, such as bison and elk. Cattle are natural hosts for *B. abortus*; this organism causes debilitating illness in humans and is categorized as a potential bioterrorism agent. Since 1993, almost 2000 human brucellosis cases have been reported in the U.S.

To prevent abortions in cattle and resultant economic losses, the United States Department of Agriculture recommends vaccinating at-risk cattle with the *B. abortus* attenuated strain RB51 vaccine. The RB51 vaccine has been available for use since 1996 and replaced the older Strain 19 vaccine. RB51 vaccine was developed primarily because it does not produce an antibody response measurable by standard assays, and thus does not interfere with diagnostic testing. Each year in Montana, an estimated 200,000 RB51 vaccinations are administered to cattle. While the RB51 vaccine helps protect cattle from brucellosis, human exposure to the vaccine can result in systemic disease. This issue of *Montana One Health* describes human health implications associated with using RB51 vaccine and instructions for its proper use.

Veterinarians and other persons exposed to RB51 vaccine are at-risk for developing disease. High-risk exposures to RB51 vaccine predominantly occur through unintentional needlestick injuries, or splashes to the eyes or face. Based on estimates of needlestick injuries among veterinarians (1 per 1000 injections), 200 human exposures to RB51 vaccine likely occur each year in Montana. Illness can also result from exposure to RB51-infected calves or placentas at the time of delivery to a previously vaccinated heifer. Many cases of human illness from RB51 exposure have been detected through nationwide voluntary passive surveillance. However, high-risk exposures to RB51 are typically not reported to public health and clinical illnesses resulting from these exposures are likely under-recognized and under-reported. Despite the likelihood of human exposures occurring in Montana each year, no vaccine exposures or human illnesses related to RB51 vaccine exposure have been reported to Montana DPHHS since at least 2002.

Table. Local and systemic adverse events reported among persons (n=26)[a] unintentionally exposed to RB51 vaccine[b]

Adverse event	N	Percent
Local		
Induration	14	54
Erythema	12	46
Systemic		
Fatigue	9	35
Chills	7	27
Arthralgia	6	23
Fever	6	23
Myalgia	5	19
Headache	4	15
Sweats	4	15
Persistent local	4	15
Persistent systemic	6	23
Hospitalized	2	8

[a]Seven of the 26 persons exposed reported no adverse events
[b]Table adapted from Ashford, et al. (see references)

Clinical signs and symptoms caused by RB51 exposure are similar to acute brucellosis illness (Table). Acute brucellosis often goes undetected because the clinical presentation is non-specific, flu-like, and similar to other illnesses. Signs and symptoms often include fever, chills, fatigue, malaise, weight loss, and other non-specific signs and symptoms. Without adequate treatment, approximately 15% of patients will develop chronic illness, often with severe and long-term sequelae. The case-fatality rate is less than 1%.

Persons suffering a high-risk exposure to RB51, including needlesticks and face splashes, should be offered post-exposure prophylaxis (PEP) and monitored for development of disease. The preferred PEP following RB51 exposure is doxycycline 100 mg orally twice-daily for at least 21 days. Persons who have contraindications to receiving doxycycline should instead be treated with trimethoprim/sulfamethoxazole. Women who are pregnant should consult with their obstetrician before beginning a PEP regimen. Rifampin should not be used for PEP or treatment of acute illness following RB51 vaccine exposure. The RB51 vaccine was created through selection on rifampin-enriched media and is therefore resistant to rifampin.

Following a high-risk exposure to RB51, patients should be followed for the development of fever for 4 weeks following the event, and for other clinical signs and symptoms of brucellosis for six months, including headache, back pain, joint pain, malaise, muscle pain, neck pain, and sweats. Because RB51 was developed to not interfere with serologic testing, infection with RB51 does not result in a measurable antibody response; consequently, testing serial serum specimens for antibody response does not provide a useful indicator of infection. Patients suffering illness following exposure to RB51 and despite PEP will likely require additional antibiotic treatment and should be treated in consultation with infectious disease specialists.

RB51 vaccine should be administered properly to prevent disease. The following practices should be used when handling and administering the RB51 vaccine.

- Only properly trained personnel should handle and administer RB51 vaccine
- Always plan for safe handling and disposal before using RB51 vaccine
- Always use personal protective equipment, including gloves and face shield (when practical), when reconstituting, handling, or administering RB51 vaccine
- Minimize risk for injury by practicing proper animal restraint
- Avoid recapping needles
- Dispose of used syringes and needles promptly in appropriate sharps disposal containers

RB51 vaccine exposure warrants immediate attention and healthcare provider consultation. These procedures should be used after a high-risk exposure to RB51 vaccine.

- Wash needlesticks and cuts with soap and water
- Flush splashes to the nose, mouth, or skin with water
- Irrigate eyes with clean water, saline, or sterile irrigants
- Report the exposure to your supervisor
- Immediately seek medical treatment for evaluation for PEP and monitoring for signs and symptoms of acute brucellosis

Healthcare providers are encouraged to consult with public health officials regarding known occupational exposures to RB51 vaccine. Suspected human brucellosis cases, including those resulting from RB51 exposure, are required to be reported immediately to the local public health department.

RB51 VACCINE KEY SAFETY POINTS

Animal Health

- Veterinarians and other animal care personnel should use proper personal protective equipment and safe needle handling practices when handling and administering the RB51 vaccine
- Persons suffering a high-risk exposure to RB51 vaccine should seek healthcare evaluation

Human Health

- Patients suffering a high-risk exposure to RB51 vaccine should receive doxycycline 100 mg orally twice-daily for at least 21 days and be monitored for fever for 4 weeks following exposure and signs of systemic illness for 6 months following exposure
- Consult with public health regarding exposures to RB51 vaccine and report vaccine-associated illness immediately to public health

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