

Frequently Asked Questions about Multidrug Resistant Salmonella typhimurium DT104

Public and animal health agencies are becoming increasingly concerned about the occurrence of Salmonella typhimurium (definitive type (DT) or phage type) 104 that is resistant to at least 5 antimicrobics, ampicillin, chloramphenicol, streptomycin, sulfonamides, and tetracycline. One of the concerns regarding this pathogen is that it is associated with higher hospitalization and mortality rates among people than for other Salmonella infections.

What is Salmonella typhimurium DT104? Salmonella typhimurium DT104 is a subpopulation of the Salmonella serotype typhimurium which reacts in a specific way when tested against a battery of bacteriophages. A hallmark of mrDT104 is the fact that isolates are resistant to at least 5 antimicrobial drugs: ampicillin, chloramphenicol, streptomycin, sulfonamides, and tetracycline (R-type ACSSuT). Some isolates of mrDT104 in the UK have shown additional resistance to trimethoprim. For fluoroquinolones the National Committee for Clinical Laboratory Standards (NCCLS) has determined that isolates with minimum inhibitory concentration (MIC) values less than 21g/ml are susceptible to fluoroquinolones and those with MIC values of 41g/ml are considered resistant. In 1996 the MIC of some of UK human mrDT104 isolates shifted within the NCCLS susceptible range. Because the UK uses a lower MIC (0.25 lg/ml) to define resistance, 14% of mrDT104 isolates were considered "resistant" in the UK in 1996. Since fluoroquinolones are currently the drug of choice for treating highly invasive cases of Salmonella typhimurium in humans this shift in MIC values for some isolates may pose serious public health implications if they continue toward resistance.

The genes encoding antibiotic resistance in mrDT104, with the exception of trimethoprim, have been chromosomally integrated as opposed to being plasmid-mediated. Chromosomal integration is a mechanism by which bacteria can retain resistance patterns permanently, even in the absence of the selective pressure of antibiotics. Therefore, withdrawal of antibiotic agents is unlikely to have any impact of decreasing resistance. This situation would most likely limit the choices for effective drug selection among available products.

Have there been any human or animal outbreaks of DT104 in the US? There have been five reports of localized mrDT104 outbreaks in the US: humans and dairy cattle in Vermont; 2 human outbreaks in California; one in Washington; and one in Nebraska.

What are the reservoirs of DT104? Reservoirs for mrDT104 in the US are not well established. Unlike other Salmonella serotypes, such as S. enteritidis, which is associated almost exclusively with poultry and poultry products, mrDT104 has been isolated from a wide variety of animals and animal products. In the US mrDT104 has been isolated from cattle, sheep, goats, pigs, wild birds, dogs, cats, mice, and horses.

Data from the NAHMS Dairy '96 study show that Salmonella sp in general (not specifically S. typhimurium DT104) has a similar incidence as in the beef industry.

Overall, 27.5% of dairy operations and 66.7% of markets have at least one cow shedding Salmonella.

How is mrDT104 transmitted? Direct animal to animal transmission of mrDT104 is thought to occur via a fecal-oral route. Spread of infection is exacerbated by stress and overcrowded conditions during transport and in holding areas prior to slaughter at abattoirs. Indirect transmission of Salmonella can also occur by use of contaminated feed and water supplies, pasture contaminated by slurry or sewage, and wildlife vectors such as small mammals and birds. Animal feeds that contain cereal contaminated with Salmonella or byproducts of meat processing have been documented as sources of infection among animals.

Human mrDT104 infections can occur directly by contact with ill farm animals (cattle and sheep have transmitted mrDT104 infections to humans) and indirectly by consumption of contaminated foods such as beef, poultry, sausage, salami, unpasteurized milk, and meat-paste. Contamination of meat products usually occurs at slaughter processing plants where unsanitized equipment serves as a vehicle for transmission of mrDT104 from infected to noninfected carcasses. Epidemiologic studies have not identified a unique food stuff as responsible for increasing the number of human cases of mrDT104 in the UK. It is likely that human mrDT104 outbreaks have a complex etiology associated with several different kinds of foods. A portion of human infections may also be caused by direct contact with sick pets such as cats and dogs, which can also be infected with mrDT104. Salmonella has been shown to be shed in large numbers from the mouth of symptomatic cats and their grooming habits can lead to contamination of the coat of the animal. Like humans, pets probably acquire mrDT104 infection through consumption of contaminated raw meat, milk, poultry, or poultry-derived products or contacts with infected animals including wildlife.

What are the signs of mrDT104 infection? In cattle clinical mrDT104 infections usually present with fever, mental dullness, loss of condition, decreased milk production, anorexia, dehydration, and diarrhea progressing to dysentery. Carrier animals in a herd may harbor subclinical infections which do not manifest any signs commonly associated with mrDT104 infections. Furthermore, cattle have been shown to shed the pathogens in their feces for up to 18 months following an outbreak. A case of a mrDT104 infection in a domestic cat described diarrhea, pyrexia and vomiting. Specific information regarding clinical presentation of mrDT104 infections in other species is limited.

Clinical signs of mrDT104 infection in humans may include diarrhea, fever, headache, nausea, bloody stool and vomiting. A study in the UK reported severe clinical signs including septicemia, which resulted in hospitalization among 41% of the patients and death in 3% of the patients. In most healthy adult individuals, mrDT104 infections result in symptoms which are less severe and usually self-limiting.

How is mrDT104 diagnosed? The only way to definitively diagnose mrDT104 is to conduct laboratory tests on the feces of infected individuals. A positive blood culture would also be diagnostic. Such tests include culturing for Salmonella, serotyping of

Salmonella isolates to determine if they are typhimurium, phagetyping, and antibiograms to determine the pattern of antibiotic resistance.

How is mrDT104 treated? Since mrDT104 is resistant to 5 commonly used antibiotics, antibiotic treatment for this highly virulent strain poses a medical dilemma for physicians and veterinarians alike. In response to concerns about the effect of fluoroquinolone use in food producing animals on the resistance patterns of mrDT104 isolates, the FDA implemented an amendment to the Animal Medical Drug Use Clarification Act (AMDUCA) which prohibits the extra-label use of approved fluoroquinolones, among other drugs, in food producing animals.

In the case of a chronically infected cat, fecal shedding of mrDT104 persisted for 12 weeks until a 14 day course of parenteral enrofloxacin was administered. Isolates from the kitten revealed an R-type ACSSuT-Tm resistance pattern. Thus, veterinarians should consider the possibility of salmonellosis when treating cats with gastroenteritis and alert their clients to the zoonotic potential of their pets' infection.

What are effective measures to prevent mrDT104 infections? It is unlikely that eradication of salmonella in domestic animals is possible in the foreseeable future. However, efforts to reduce and control the incidence of infections in animals will be successful. Control measures should include reducing the risk of infection in food animals, reducing the risk of contamination of animal products at all stages of food processing, reducing risk for farm workers and their families, and raising awareness of measures to prevent food poisoning among food handlers and the general public, such as avoiding the consumption of unpasteurized milk or products made with it.

This information was excerpted from The Veterinarian's Role in Diagnosis, Treatment and Prevention of Multidrug Resistant Salmonella typhimurium DT104 by Dargatz DA, Wells SJ, Fedorka-Cray PJ, and Akkina J. Bovine Practitioner, 1998. The text is available in full at www.aphis.isda.gov/vs/ceah. The editor of the Colorado Dairy News appreciates the use of this information.