FRI Briefings

Emergence of a Highly Virulent Strain of *Salmonella typhimurium*

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British cattle farmers have enough to worry about with bovine spongiform encephalopathy (BSE) and the recent outbreak of *E. coli* O157:H7 in Scotland. Now, a dramatic increase in *Salmonella typhimurium* isolates that are resistant to 5 or more antibiotics is adding to their problems. Since 1993, 65% of all *Salmonella* species cultured from cattle in the UK have been identified as a strain of *S. typhimurium* DT104, resistant to ampicillin, chloramphenicol, streptomycin, sulfonamides, and tetracycline (*1*). Some strains are also resistant to trimethoprim, spectinomycin and/or ciprofloxacin (*2*). Antibiotic-resistant DT104 were first observed in 1984 but remained an infrequent isolate until 1990.

An increasing percentage of *S. typhimurium* isolates from humans in England and Wales have also been identified as DT104. This strain accounted for 70% (2700) of all reports of *S. typhimurium* during the first 8 months of 1996 and for 55%, 52%, and 32% of isolates in 1995, 1994, 1993, respectively. Although *S. enteriditis* PT4 continues to be the most commonly isolated species of *Salmonella, S. typhimurium* DT104 is now in second place (*3*). Foodborne *Salmonella* infections are usually not severe. However, 34 of 83 DT104 cases studied in a 1993 epidemiological study required hospitalization and 10 died. The very young and the very old were most susceptible to serious complications (*4*).

Foodborne transmission of DT104 has been documented for several outbreaks; suspected vehicles included roast beef, ham, pork sausage, salami sticks, "cooked meats," chicken legs, and unpasteurized milk (*5–9*). Analyses of 786 samples of fresh and frozen sausages in England in 1994 demonstrated that 17% were contaminated with *Salmonella* spp., including *S. typhimurium* DT104 (*10*). This indicates that these bacteria are commonly present in some types of meats and pose a significant risk if such foods are not cooked and handled properly.

In contrast to *S. enteritidis*, which is associated primarily with poultry and eggs, DT104 is most commonly detected in cattle. Some sheep, pigs, goats, chickens, and turkeys are also infected. A majority of recent bovine salmonellosis cases investigated in England were caused by DT104, and 15 of 16 new outbreaks of bovine salmonellosis in Scotland, in March 1996, were caused by DT104 (*1,11*). These bacteria cause diarrhea in cattle and may persist in the animals for up to 6 months after recovery. A number of farm families appear to have acquired DT104 infections while caring for sick farm animals (*12,13*). Household pets may also be a source of infection. Of 110 *Salmonella* spp. isolated from sick house cats in England in 1991–1994, 40 were *S. typhimurium* DT 104 resistant to 5 antibiotics (*14*).

Where has this multiply resistant strain of *S. typhimurium* come from? Plasmids containing drug resistance genes are well known in bacteria and can be transferred among different species of enteric bacteria. However, most of the genes coding for resistance to these antibiotics in DT104 are located on chromosomal, rather than plasmid, DNA. Some interesting recent research reported a relatively high frequency of hypermutable strains among pathogenic *E. coli* and *Salmonella* spp. (*15*). When compared to standard strains of these bacteria, isolates associated with some foodborne outbreaks produced mutant cells resistant to rifampin at a 1000-fold greater frequency. These increased rates of mutation were associated with the presence of mutant genes coding for enzymes involved in the recognition of foreign DNA and DNA repair. Defects in one of these repair systems, the methyl-directed mismatch repair, were found in many pathogenic mutator strains. Hypermutability will, of course, produce many nonviable cells but also greatly increases the likelihood that advantageous mutations will occur. Such mutations in DNA repair systems also facilitate the acquisition of plasmid DNA containing antibiotic resistance genes from other species of bacteria.

Under the selective pressure of antibiotics, the growth of resistant organisms is favored. Some evidence indicts the increased use of veterinary drugs as a factor in the dramatic increase in drug resistance. Resistance to ciprofloxacin in DT104 isolates has increased from 1% in 1994 to 6% in 1995, coincident with the licensing of this drug for veterinary use in the UK in 1994 (*2*). Resistance to trimethoprim (present in 27% of DT104 isolates) may have been acquired in response to the use of this drug to combat bovine infections with DT104 resistant to other drugs. Surveys of *S. typhimurium* isolates from cattle and humans in Australia (*16*), France (*17*), Hong Kong (*18*), and Spain (*19*) all reveal an increased incidence of resistance to multiple antibiotics in this organism.

As yet, there have been no reports of *S. typhimurium* DT104 in the USA, but the rapid rise of this organism in the UK warns us in the USA to be vigilant. Increasing resistance to so many different antibiotics makes it very difficult to treat severe cases of human salmonellosis.

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Additional information

"Multidrug-resistant *Salmonella* serotype typhimurium – United States, 1996. Center for Disease Control and Prevention, *MMWR* 46(14):308–310 (April 11, 1997): http://www.cdc.gov/epo/mmwr/preview/index97.html

return to top

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