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Biosafety Tips

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Biosafety Tips brings you practical approaches to biosafety or “news you can use.” If you are looking for a useful and sensible solution to a biocontainment problem or perhaps a reference to help convince a skeptical researcher of the need for caution, this is the place to look. In this column I will share some biosafety insights for managing a variety of workplace situations. I welcome feedback or suggestions for future topics. Please e-mail any comments or suggestions to karen_byers@dfci.harvard.edu or to Co-Editor Barbara Johnson at barbara_johnson@verizon.net.

Outbreak in a Poultry Vaccine Plant

When two staff members from the same poultry vaccine plant had confirmed cases of salmonella, the Maine Department of Public Health (MDPH) conducted an investigation. The 74 staff who worked at the plant were interviewed; 21 staff members reported symptoms of salmonel-la infection during the previous 1-month period. Seven stool cultures were available for analysis; five were positive for Salmonella enteritidis. The S. enteritidis isolated from the stool cultures submitted by workers at the vaccine plant had the same phage type as the poultry vaccine. During the same time period, there were eight cases of salmonel-la infection from different locations in the state with no connection to the plant; the isolates from cases with no connection to the production plant had different phage types. Careful analysis of the work assignments of the staff with symptoms showed a strong association between infection and work in Room A. One month prior to the first case, on a routine walkthrough of the fermentation tank room, a production plant employee discovered a 1 to 1.5 liter spill of S. enteritidis culture on the floor (CDC, 2007). Wearing appropriate personal protective equipment (PPE), described as a “biohazard suit, hat, boots, mask, and gloves,” a plant worker cleaned up the spill using a mop with a 5% bleach solution and also a disinfectant. The mop was then transported 30 feet to Room A, where it was auto-

Lessons Learned from Laboratory-acquired Salmonella Infections

The Centers for Disease Control and Prevention estimates that, in the United States, approximately 1.2 million Salmonella infections occur annually (CDC, 2012). Approximately 400 fatalities per year in the general U.S. population result from Salmonella infections; reactive arthritis also occurs in a small fraction of infections (CDC, 2012). Since there is no national reporting system for laboratory-acquired infections (LAI), the incidence of Salmonella (LAI) is not known. Reviewing the actual case reports described below and discussing the “lessons learned” from these events may be an effective training tool to illustrate the modes of transmission and the hazards of non-compliance.
claved prior to disposal. The next day, the plant worker who cleaned up the spill had mild diarrheal symptoms, but reported to work.

The MDPH conducted surface sampling in the fermentation tank area and in Room A 3 weeks after the first infection, but routine cleaning and disinfection had occurred and none of the samples were positive. However, MDPH observed lapses in PPE and handwashing during routine operations in Room A. The MMWR report (CDC, 2007) also notes that person-to-person transmission in this Salmonella outbreak could not be ruled out, since a symptomatic staff member reported for work.

The MDPH issued the following recommendations for prevention of occupationally acquired Salmonella infections in staff at the poultry vaccine plant:

- Reinforcement of handwashing practices
- Development of a written spill procedure
- Use of PPE in Room A
- Advising staff to stay home when ill

Fortunately, in the vaccine plant outbreak described above, no secondary infections occurred in family members of staff who worked at the poultry vaccine plant or others in the outside community, and all workers recuperated fully. An additional lesson from this outbreak is the need to develop and communicate a policy for reporting symptoms that may be associated with occupational exposures. To prevent the spread of Salmonella, if symptoms develop, staff must be advised to stay home, focus on careful handwashing after use of the bathroom, and abstain from food preparation.

Secondary Transmission from a Clinical Laboratory

A chilling description of secondary transmission of Salmonella was described by Blaser in 1981. In June 1980, the microbiology laboratory director of a 500-bed hospital was subculturing the laboratory stocks, performing biochemical testing to confirm the identity of the strains, and then re-culturing the stocks on a slant. He did 3-5 subcultures per day in June and provided several strains to a clinical laboratory student intern to work up as unknown samples. Two of the strains provided to the student to identify were S. typhi and S. agona. The resistance pattern for S. agona was well characterized since it had been used in a national proficiency testing exercise. These strains were worked with for several days by both the student and the director. After work, the laboratory director went home to prepare and share dinner with his wife, son, and daughter. On June 24, the wife was hospitalized; her stool and blood cultures were positive for S. typhi. Subsequent blood cultures were also positive for S. agona. Unfortunately, the wife died from the infections. On July 5, the son became ill with a temperature of 40.6°C, malaise, and diarrhea. He was hospitalized on July 8, and blood cultures were positive for S. agona. The son recuperated completely from the infection.

Neither the wife nor the son had ever visited the lab. How did they become infected? The obvious link is the laboratory director, but what was the breach in laboratory containment practice? Gloves in the microbiology laboratory were not mentioned in this 1980 account. Could the lab director have neglected to perform handwashing? Could a residual dose have been left on his hands after handwashing? Or did the student inadvertently contaminate surfaces that the lab director touched after handwashing? The actual mode of transmission is not known. The five other microbiologists who also worked in that laboratory, the student intern, and the director never developed symptoms. Stool and blood samples obtained from the director were negative. The director had received typhoid immunization in 1964; perhaps that protected him? The authors speculate that passive secondary transmission occurred, since bacteriophage typing results left little doubt that the laboratory was the source of the S. typhi and S. agona secondary infections (Blaser & Lofgren, 1981). A more recent report of secondary transmission is available on the web (Showman, 2012). The college roommate of a microbiology student was infected with the same strain of Salmonella that was used in the college microbiology laboratory. The brief news report includes a quote from the Clark County Public Health Department review of the college laboratory practices:

“One of the big recommendations we made involved taking personal items in and out of the lab,” … “Often, students will bring pens and pencils from home and use them in the laboratory, and what we’ve recommended, is that [the college] actually purchase pens and pencils and keep them in the lab and not have students take them back and forth.”

This recommendation is congruent with current CDC recommendations (CDC, 2011).

Outbreaks Associated with Teaching Laboratories

In 1980, CDC reviewed 24 Salmonella laboratory-acquired infections that occurred over a 33-month period (Blaser, 1980). Obvious breaks in technique were found to be the cause of infection for 7 of the 24 infected students. Another 5 never handled the Salmonella cultures; they merely sat in the laboratory to take a class later in the day. Contaminated bench tops are assumed to be the fomite that transmitted infection to the hands of those students. Laboratory practices included mouth pipetting, and that is no longer an acceptable routine practice. But the 24 cases demonstrate how easily the bacterial inoculum can be delivered to the student host in a laboratory environment.

Two student cases with serious complications from Salmonella LAI have been described. Typhoid fever with serious complications developed 3 weeks after the student participated in a classroom exercise involving S. typhi. Surgical drainage of an abdominal abscess, an ileostomy, and then reversal of the ileostomy were required for recovery (Hoerl et al., 1988). Another student developed enteritis associated with erythema nodosum and reactive arthritis caused by a strain of S. typhimurium used in her microbiology class (Steckelberg, 1988).
On April 28, 2011, CDC published preliminary results of an investigation of a *Salmonella typhimurium* outbreak associated with clinical and teaching microbiology laboratories. The final update to the report on laboratory-acquired infections was published on January 12, 2012. This outbreak was identified by *PulseNet*, a national network of public health and food regulatory agency laboratories coordinated by the U.S. Centers for Disease Control and Prevention. One hundred and nine infections with *S. typhimurium* strain X were documented, resulting in four hospitalizations and one death. Thirty-two individuals answered in-depth interviews; 60% had exposure to a clinical microbiology or teaching laboratory the previous week. Four children of students in microbiology teaching labs were infected (Gaines, 2012). One result of the CDC investigation was the development of specific preventive advice for clinical laboratory instructors and for students that is available online (CDC, 2011). The report also has a compelling message for biosafety training programs. In comparing laboratories where the infections occurred and laboratories that had had students handling *Salmonella* strain X without LAI, CDC made the following observations.

“Laboratory practices and settings appear to be largely similar across both groups, but several differences were found. Staff working at laboratories that were associated with illness were less likely to have knowledge of biosafety training materials. In comparison, staff working in laboratories that were not associated with illness were more likely to train students and staff on the signs and symptoms of infection with *Salmonella* when conducting safety training. Similar safety policies were in place across the different laboratories. However, some policies appeared to be more difficult to monitor and enforce, such as not allowing the use of handheld devices (e.g., cell phones or music players) at the laboratory work space.” (CDC, 2011)

Useful references for symptoms of infection with *Salmonella* or other pathogens include the Pathogen Safety Data Sheets and Risk Assessments produced by the Public Health Agency of Canada (PHAC, 2011) and the FDA *Bad Bug Book* (FDA, 2012).

There are numerous “lessons learned” from the case studies described above, including the importance of surface decontamination, personal protective equipment, and prevention of secondary transmissions.

An important component of training programs is a description of the symptoms and potential consequences of infection. The infective dose of non-typhoidal *Salmonella* (caused by strains other than *S. typhi* and *S. paratyphi*) may be as low as 100 bacteria; the infective dose of typhoidal strains is 1,000 bacteria (FDA, 2012). The consequences of infection differ. Infection with non-typhoidal *Salmonella* is a self-limiting illness in those with a healthy immune system, but may cause fatalities in the young, the elderly, and the immunocompromised. Infection with typhoidal *Salmonella* has a 10% mortality rate if treatment is not initiated promptly. These facts should motivate compliance with the established laboratory procedures. However, training programs must also include information about a non-punitive system for reporting exposures and LAI to reduce the potential for spread and to provide insights into improvements in laboratory practice.

**References**


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