A Salmonella Story – a Verified Acquired Laboratory Infection

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Overview

- Laboratory Acquired Infections - Overview
- *Salmonella* spp. – Overview
- Summary of the confirmed LAI Exposure to *Salmonella enterica* spp. – June, 2016
  - Details of the Incident
  - Identified Oversight
  - Response Overview; and
  - Remedial Actions
Laboratory Acquired Infections (LAIs)

- “All infections acquired through laboratory or laboratory-related activities regardless whether they are symptomatic or asymptomatic in nature”
- In US, approx. 500,000 lab workers are potentially exposed; most common cases of LAI involve:
  - *Brucella* spp.
  - *Shigella* spp.
  - *Salmonella* spp.
  - *Mycobacterium tuberculosis.* (Singh, 2009)
Laboratory Acquired Infections (LAIs)

- Difficult risk assessment for LAI:
  - “lack of systemic reporting”
  - “available data are limited to retrospective and voluntary postal surveys, anecdotal case reports, and reports about selected outbreaks with specific microorganism” (Singh, 2009)

What is known is only ....

“tip of the iceberg”

What remains hidden (the List of lab. Workers) .......
who contracted potentially contagious infections but did not start community outbreaks is much, much longer.........
**Salmonella enterica spp.**

- Gram negative, facultative rod-shaped bacteria (2500 serovars) and found worldwide
Salmonella infection

Almost any kind of food or beverage can carry the bacteria that causes salmonella infection, although meat and eggs the most are common sources.

How salmonella progresses

Bacteria travel to small intestine, adhere to lining; begin life cycle

In severe cases, bacteria break through intestinal wall to bloodstream; can be deadly if not properly treated

Symptoms

Within 12-72 hours
Nausea, vomiting, fever, diarrhea abdominal cramps

4-7 days Illness ranges from mild to severe; most people recover without treatment

Severe cases More likely with infants, elderly, people with impaired immune systems

Treatment

Oral or injected antibiotics, usually for 2 weeks

Source: U.S. Food and Drug Administration, Current Medical Diagnosis & Treatment, Mayo Clinic

McClatchy-Tribune
University of Saskatchewan

- Containment level 2 lab located at Vaccine and Infectious Disease Organization-International Vaccine Centre (VIDO-InterVac) (located on the VIDO side)
VIDO- InterVac

- Consists of multidisciplinary research team to study all aspects of infectious disease with the ultimate goal of developing vaccines and anti-infective compounds to alleviate disease caused by emerging and re-emerging pathogens
  - 175 employees working at facility

- Operates as a containment level 2 (CL2) and 3 (CL3) research facility.
  - *In vitro*
  - *In vivo* – Small animal, large animal and Prions
CL2 Lab Background

- Number of strains of *Salmonella* spp. are handled in the laboratory
  - Mainly works with *S. enterica* servar *typhimurium*
- Conduct microbiological work and molecular biological techniques
- Lab of good standing
- No previous incidents or non-compliances observed or from past biosafety audits and inspections
- All training, including general lab safety and biosafety, and site specific training were current
Salmonella Exposure – Incident Details

- June 3, 2016
  - Summer student working in CL2 lab reported fever, chills, and aches to principal investigator (PI), which started the evening before
  
  - Individual reported working with a strain of *Salmonella enterica serotype enteritidis* (African strain) the previous day
    - Type of African strain that causes systemic infection that is similar to, but less severe than typhoid fever
**Salmonella Exposure – Incident Details**

- **June 3, 2016**
  
  - Initiated the infectious disease exposure response plan
    
    - Notification of VIDO-InterVac senior management and InterVac Biosafety Officer (BSO)
    
    - Setting up a teleconference call to the Infectious Disease Specialist and Saskatoon Health Region (SHR) Medical Health Officer since the potential exposure was to a RG2 pathogen.
  
  - Gathered all available information on the Salmonella (PSDS) and transported the individual to hospital emergency for assessment
Salmonella Exposure – Incident Details

- June 3, 2016
  - Individual was hospitalized and examined by the Infectious Disease Specialist
    - Immediately put on antibiotics as a precaution.
  - Contacted Andrea Smida, University of Saskatchewan Biosafety Officer and informed her of the situation
  - Individual’s symptoms worsened, developed severe chest pain when breathing, and was placed on oxygen
  - Samples were taken for diagnostics.
Salmonella Exposure – Incident Details

June 3, 2016

- Initial antibiotic treatment was not continued as the supervising Physician did not believe it to be Salmonella due to the short incubation period

- Surface decontamination of work surfaces in the laboratory was carried out by a Senior Research Scientist
  - Used a freshly prepared solution of 1% bleach with a contact time of a minimum of 30 minutes.

- Lab personnel were notified of situation and copy of PHAC’s Pathogen Safety Data Sheet was provided to laboratory personnel and discussed

- All work in the lab was temporarily halted
Salmonella Exposure – Incident Details

- June 5, 2016
  - Diagnostic lab confirmed Salmonella in the stool of the individual
  - Individual was not immediately placed back on antibiotic treatment since the normal protocol for Salmonella is to not give antibiotics
  - PI alerted and argued with the physician that the individual needed 2 weeks of antibiotic treatment to both ensure that the Salmonella was cleared from the body and that it would not be passed on to the employee’s immediate contacts
Salmonella Exposure – Incident Details

- **June 5, 2016**
  - University of Saskatchewan incident report online form was completed by PI and submitted online

- **June 6, 2016**
  - Review of the all lab procedures and protocols done with *Salmonella* was initiated
  - All lab personnel were asked to list all activities done 1 week prior to reported incident
Salmonella Exposure – Incident Details

- June 7, 2016
  - Individual continued antibiotic regimen
  - *Salmonella spp.* obtained from stool specimen from SHR local lab to Health Region Provincial lab
  - Initial interview with individual done with Saskatoon Health Region Medical Health Officer notified of possible lab exposure
Salmonella Exposure – Incident Details

• June 13, 2016
  • SHR and PI received results stating salmonella typing as salmonella typhimurium and PFGE Xbal & Blnl pattern
  • PI obtained the swap of isolated Salmonella from SHR and grew the isolate on several different agar media to observe the colony morphology
Salmonella Exposure – Incident Details

• June 13, 2017
  • Determined that the colony morphology that grew from the isolate appeared to be the standard laboratory isolate S. Typhimurium (ATCC 14028s) rather than the suspected African strain

• June 14 to July 11, 2016
  • PI purified genomic DNA from isolate and sent for genome sequencing to Delta Genomics in Edmonton to determine and verify the source
  • Individual completed the antibiotic regime and recovered from illness
Salmonella Exposure – Incident Details

- June 14 to July 11, 2016

- Interviewed individual to identify potential routes of exposure
  - At time could not identify
  - Proper PPE was utilized

- List of all activities of all personnel in lab from May 25-June 2, 2016 was provided by PI to the BSO, which included:
  - Preparation of competent cells
  - Electroporation, recovery, and plating of Salmonella spp. African strain and typhoidal strains
  - Inoculation of overnight bacterial cultures
  - Plasmid minipreps (DNA extraction)
  - PCR, protein extractions and western blot assays, immunoblotting
Salmonella Exposure – Incident Details

- **July 15, 2016**
  - Final analysis stated the isolate was *Salmonella enterica serovar Typhimurium* strain (not the African strain)
  - **End result: CONFIRMED Laboratory Acquired Infection**

- **July to Sept, 2016**
  - Incident investigation continued and completed
  - Voluntarily reported LAI incident to PHAC as at time of incident no licence was issued and obligated reporting of incident not required
Identified Oversights

- From the investigation, it was determined that:
  - Identified procedure done in the lab that generated aerosols (e.g. electroporation) and carried out on bench instead of biosafety cabinet (BSC);
  - Protocols, procedures or other documents that guided the work were not followed correctly (followed as written, but not detailed enough or clear) (e.g. decontamination and hand washing); and
  - Training was inappropriate or insufficient to support adequate understanding of protocols.
Remedial Actions - Immediate

- Individual taken to emergency and implemented exposure control plan
- VIDO-InterVac Senior Management and Biosafety Officer were notified of the incident immediately and has subsequently reviewed the case and supported the corrective action plan
- Surface decontamination of all work surfaces in the laboratory
- All work with *Salmonella* was halted until potential source of exposure was identified
Remedial Actions - Long Term

- Review of current SOPs and processes to ensure proper operational processes, PPE, and safety controls are in place and followed
- All work with RG2 biological materials must be done in BSC
- Provide review and training of CL2 operational processes and BSC use to all lab personnel
- Improve communications between lab personnel, PI, and management
Conclusion – Lessons Learned

- Conduct annual review of SOPs and training
- Continue to use this case study to educate new staff and students about lessons learned
- Implement daily and continuous surface decontamination checks
- Implement conscious checks to ensure proper hand washing techniques are used
- Updated the lab’s biosafety plan, which is the lab’s documented local risk assessment
Conclusion – Lessons Learned

- Identified increased virulence risk
  - Lab research is focused on transmission of *Salmonella* and long-term persistence
  - Possible that this research initiative may have inadvertently created high risk situations where some of the Salmonella strains became more infectious.
  - Due to the identified potential higher risk of virulence, localized risk assessment was updated and recognized the need to add additional operational precautions (e.g. PPE) and procedures in working with all *Salmonella* strains.
Any questions??

Thanks!