Legionnaire’s Disease: History, Epidemiology; Assessment and Control of Environmental Factors leading to Outbreak Conditions

Presented at the HKIOEH Professional Development Seminar
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Outline of Presentation
- Legionaries’ Disease
  - History
  - Occurrence
  - Nature of Disease
  - Route of Infection
  - Pathogenesis
  - Diagnosis and treatment
  - Prevention of infection
  - Understanding the ecology of Legionella
  - Control Measures
  - Risk assessment / management
  - An Outbreak investigation

The First Legionnaire’s Disease outbreak
- It occurred during The 1976 American Legionnaires’ annual meeting at a hotel in Philadelphia, Pennsylvania
- Upon returning home, 221 got sick, 34 died
- Investigation revealed a responsible bacteria
- This Bacterium was named (Legionella pneumophila)
- Records reveal similar outbreaks 1947 & 1967

Since 1976 Outbreaks continue to take place all over the world
- World-wide Occurrence:
  - Range of 1 – 21 cases / million
  - Europe ~ 4.3 cases / million
  - HK ~ 3 cases / million
- Accuracy depends on efficiency of recognition and reporting!
- No evidence of transmission from person to person
- All sources are environment related

Legionella Problem in the USA
- Between 8000 to 18,000 cases reported each year
  - 10 to 20 % fatality
- ~23% are hospital acquired
- 30-40% mortality rate
- ~30,000 patients have died from hospital acquired Legionnaires’ disease in the past 25 years
The situation in HK

- cases which raised public awareness:
  - [Link](http://www.youtube.com/user/isdgovhk#p/a/u/2/wq2p0Gcns9w)
  - [Link](http://www.youtube.com/user/isdgovhk#p/a/u/0/c00s-lDH-zQ)
  - [Link](http://thesun.on.cc/channels/news/20070224/20070224020822_0000.html)
  - [Link](http://orientaldaily.on.cc/cnt/news/20111222/00176_025.html)

Legionnaires' Disease is a reportable disease in HK

**Legionella Outbreaks Continue**

Some result in Court Cases

**The France Case**

[Link](http://www.guardian.co.uk/france/story/0,11882,1118151,00.html)

**The UK Case**

[Link](http://www.thisisthelakedistrict.co.uk/farm/farming/display.var.458625.0.0.php)

**Summary of Recent Cases**

[Link](http://www.hcinfo.com/outbreaks-news.htm)

**Legionella Outbreaks Continue…**

Legionnaire’s disease victims support group

[Link](http://www.q-net.net.au/~legion/legionnaires_disease_support_group.htm)

**Characteristics of Legionella Bacteria**

- Gram negative rods
- Ubiquitous in:
  - natural water bodies
  - rivers, lakes and streams
  - soil (moist)
  - artificial water sources
  - cooling towers, evaporative coolers, hot and cold water systems, shower facilities

**Outbreak Occurrences**

- Majority found in association with:
  - Cooling towers
  - Evaporative Condensers
  - Hot and Cold Water Systems
  - Spa Pools
Outbreak Occurrences

- Also found in
  - Cutting Oil of Machine tools
  - Clinical humidifiers for respiratory therapy
  - Humidifiers in food display
  - Decorative fountains
  - Potting compost

Mist From Cooling Tower

There are 2 forms of Legionaries’ Disease

- Pneumonia
- Pontiac Fever

Legionnaire's Disease (I) – Pneumonia

- Fulminating pneumonia
- Low attack rate (< 5%)
- Relatively high fatality rate (up to 40%)
- Incubation period 2–10 days
- Symptoms include general malaise, muscle pain, cough, difficulty in breathing, headache, fever, gastrointestinal pain, diarrhea, & respiratory failure
- Higher mortality rate among immuno-compromised

Legionnaire's Disease (I) – Pneumonia

- Rarely found in people <20 years old, most patients are 40–70 years old
- Severity of symptoms is proportional to age
- Male to Female affected – 3:1
- Increased chance of developing serious illness in smokers, and in patients with chronic illnesses, renal diseases
**Legionnaire’s Disease (II) – Pontiac Fever**

- Pontiac Fever:
  - Mild infection
  - High attack rate ~80%
  - Incubation Period: 24-48 hours
  - Major symptoms is fever
  - Self limiting in 2-5 days without antibiotics
  - First discovered in Pontiac, Michigan

**Route of Infection**

- Respiratory exposure to aerosols (2-5µm) containing the Legionella bacteria
- An airborne concentration of 0.02 cfu/l has been found to be infectious
- Bacteria gain entry into alveoli

**Pathogenesis of Legionella**

- Inhalation of aerosol containing Legionella
- Damages occur in alveoli
- Legionella releases toxin & enzymes to invade tissues
- Influence operation of WBC
- Suppress biochemical function of neutrophiles
- Stop fusion of lysosome and phagosome in macrophages

**Pathogenesis of Legionella**

- Legionella releases various toxins and enzymes to invade tissue
  - Hemolysin
  - Cytotoxin
  - Endotoxin
  - Lipase
  - Protease
  - Phosphatase
  - DNase
  - Chymotrypsin

**Lung Tissue Slides**

- Gram stain from lung showing no bacteria (they stain poorly)
- Same lung tissue: deiterle silver stain showing short rod-shaped Legionella bacteria
Age distribution of cases showing a disease of the elderly

Note that 'nosocomial' means acquired in hospitals as opposed to in the community.

Treatment of Legionnaire's Disease

- Penicillin, Cephalosporin, Aminoglycosides) are ineffective
- Erythromycin – most effective
- Rifampin, Erythromycin can be used together

Ecology of Legionella Bacteria

- Enhanced growth: 20°C-45°C (70°F-110°F) water temperature
- Will not grow < 20°C water temperature
- Will not survive > 60°C water temperature
- Residues, sludge, calcification layer & other organic materials in water can serve as nutrient for bacteria

Growth rate of bacteria in water: primarily in hot water system

- Often found growing in components of water supply system
- Other water borne organisms (algae, ameba, other bacteria) can serve as nutrient source
- Affinity for living in biofilm = symbiosis (?)

What is Biofilm?

- A polysaccharide matrix containing a mixing of microorganisms (bacteria, fungi, protozoa, algae) which live together as a community
- Slimy to the touch
- Can stick to many surfaces (rubber, glass, polyurethane, copper, PVC, etc.)
- Microbes in biofilm require higher concentration of biocide and longer time to disinfect
  - 1 ppm chlorine takes 60 – 200 time longer contact time to kill bacteria hidden inside amoeba than free living ones
  - 50 ppm chlorine for 1 – 4 hours is required to disinfect water systems with biofilm
Legionella bacteria live inside protozoans.

Concentration of Legionella bacteria does vary significantly between water samples collected at different times.

Occurrence of Legionella in Water Systems

- A UK study indicates presence of Legionella in
  - 35% of hot water systems
  - 13% of cold water systems
  - 45% of cooling towers
- A 2012 screening study in HK after case in Government building in Dec 2011 indicates
  - Occurrence of 13% in domestic cold water systems

There are at least 50 species of Legionella Bacteria
18 species have been associated with respiratory illness

The Vast Majority of illnesses are caused by *L. pneumophila*

- *L. pneumophila* includes 16 serogroups
- Serogroup 1 accounts for 70 – 90% of all cases of Legionnaires’ Diseases
- Serogroup 1 has many subtypes:

  Examples:
  - Pontiac
  - Bellingham
  - Albuquerque
  - Karachi
  - Johannesburg
  - Pittsburgh
  - Longbeach

Legionella species and serogroups

- At least 50 species have been confirmed, 70 serogroups
- *L. pneumophila* - species most often associated with disease
- *L. pneumophila* - includes 16 serogroups
- *L. pneumophila* - Serogroup 1 most often associated with disease

Legionella pneumophila has 16 serogroups

- Serogroup 1 accounts for 70 – 90% of all cases of Legionnaires’ Diseases
- Serogroup 1 has many subtypes:

Culturing Legionella Bacteria

- Requires L-cysteine as added nutrient
- Grows best in High humidity plus 2 to 5% CO2
- Buffered Charcoal Yeast Extract (BCYE) culture media is readily available in the market
### Culturing of Legionella Bacteria from Water Samples
- Many microbes in water samples
- Eliminate other microbes in water sample by:
  - Acid treatment (pH 2.2 for 5 mins)
  - Heat treatment (50°C for 30 mins)
- Use selective media to culture for Legionella
- Must add an essential amino acid nutrient - cysteine
- Culturing condition: 35°C, 5% CO₂, 80% RH
- Takes 3 to 10 days to grow.
  - Appearance of colony:
    - 1 to 2mm diameter
    - White shiny surface
    - Round, smooth, raised & smooth edge
    - Gram-negative rod shape
    - 0.5-3µm x 1-3µm

### Identification of Legionella Bacteria
- At least 50 species, 70 serogroups
- Biochemical methods
- Serotyping with monoclonal antibody
- Direct fluorescent antibody test
- Polymerase Chain Reaction (PCR)

### Limitations of Various Detection Methods
- Direct immunofluorescence microscopy:
  - Unreliable
  - Monoclonal vs polyclonal antibodies
  - Cannot distinguish between live or dead cells
- Culture:
  - Often underestimates by at least 1 order of magnitude
- Polymerase Chain Reaction (PCR):
  - Cannot distinguish live or dead cells
  - May not be quantitative

*Results are highly dependent on representative sampling, sampling time, sample handling and transport.*

### Risk Assessment for an Outbreak
- Is the water system contaminated with Legionella bacteria?
- Does the condition of the water system provide favorable conditions for the survival and multiplication of Legionella bacteria? (system design, temperature, flow, nutrient, biofilm, water treatment, etc.)
- Is the Legionella infected water aerosolized into respirable droplets?
- Is there susceptible population in the vicinity of the respirable droplets? (size of the population, age, health condition, etc.)
- Are there control measures in place? How well are they implemented?

### Transmission Factors and Prevention

### Preventive Measures for Cooling Towers and Fountains
Preventing infestation of Legionella

- Prevent water temperature of 20 to 45°C wherever feasible: Legionella thrives in this temperature range
- Prevent still water (stagnation, dead end pipes, etc.) as it enhances biofilm formation which in turn enhances Legionella growth
- Prevent the use of construction material which provide nutrients for microbial growth
- Use materials that are easy to clean

- Inspect, maintain and Clean system regularly, avoid residue build up
- Add scale/corrosion inhibitors
- Disinfect system regularly to inhibit bacterial growth
  - Maintenance dose 2 - 5 ppm Chlorine at pH7
  - Disinfection dose 50 ppm Chlorine at pH7
- Culture water regularly to monitor microbial population
  - Total Bacterial Count <500,000 CFU/ml
  - Legionella count <1,000 CFU/ml
- Keep record of design, installation, maintenance, control measures and monitoring requirements

Use of other agents for controlling Legionella in Water

- Ozone
  - Corrosion to system components
  - No residue effect
- UV
  - Effectiveness depends on clarity of water
  - Effective only at point of application
  - Cannot control biofilm
  - Bacterial cell may repair itself after UV damage
- Filters
  - Only filters with 0.2 micron pore size will work
  - Slow water flow, needs frequent change

US OSHA Action Levels for Legionella Levels in Building Water Systems (After reporting of a disease case)

<table>
<thead>
<tr>
<th>Colony-Forming Units (CFUs) of Legionella Per Milliliter</th>
<th>Action 1</th>
<th>Action 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Action 1: Prompt cleaning and/or biocide treatment of the system.</td>
<td>Cooling tower</td>
<td>Domestic water</td>
</tr>
<tr>
<td>1</td>
<td>100</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>1,000</td>
<td>100</td>
</tr>
</tbody>
</table>

**Action 1:** Prompt cleaning and/or biocide treatment of the system.

**Action 2:** Immediate cleaning and/or biocide treatment. Take prompt steps to prevent employee exposure.

HK EMSD and HA Recommendation for Fresh Water Cooling Towers:

- Legionella <10 cfu/ml, Total count <100,000 cfu/ml - system under control
- Legionella ≥10 and <1,000, Total count ≥200,000 and <5,000,000 - Review operation
- Legionella >1,000, >5,000,000 - Implement corrective measures

Control droplet / aerosols

- Use drift eliminators
  - Minimizes rather than “eliminates”
  - Performance dependent on material, construction and air flow velocity

Management of Hot and Cold Water systems to prevent disease outbreak

- Design should follow specifications
- Hot water storage vessel should operate at 60 °C and all outlets should be 50 °C
- When mixing hot and cold water, mix at point of use with thermostatic mixing valves to obtain 50 °C ± 2 °C
- During commissioning of new building
  - Clean system to remove rust, sludge & sediment
  - Flush clean and disinfect (thermally and/or chemically)
Management of Hot and Cold Water systems to prevent disease outbreak

- Maintain current a mapping of water distribution system
- Identify dead legs, stagnation points, infrequently used points and redundant pipework
  - Dismantle or conduct routine flushing
  - Flush daily if in "high risk" area
  - If flushing is impractical, disinfect prior to re-occupation
- Inspect clean and drain tanks regularly to prevent contamination, rust, dirt, foreign material and biofilm buildup (scrub tank with disinfectant)
  - Hot water tank - yearly
  - Cold water tank – quarterly
  - May need more frequent cleaning depending on condition

Management of Hot and Cold Water systems to prevent disease outbreak

- May need to regularly monitor water for designated temperature targets *
- Regularly maintain thermostatic mixing valve
- May need to monitor Legionella if control levels of treatment regime are not consistently achieved *
- May need to disinfect system if it has been taken out of service for more than 1 week or has been substantially altered *
- Regular sampling in water supply system for Legionella is generally not recommended. It is done only if a confirmed case has been identified in the facility
  * More frequent for high risk areas

Maintenance of AC components

- Inspect, clean and disinfect drain trays regularly *
- Provide air duct cleaning and access panels for inspection and cleaning *
- Inspect, clean or replace air filters regularly to minimize collection of dust and microbes *

Maintenance of Humidifiers

- Use steam humidifiers instead of water spray or evaporative type wherever feasible
- For recirculation water spray humidifiers
  - Use UV to disinfect recirculating water
  - Clean unit frequently
  - Drain reservoir each day and disinfect frequently
  - Use boiled water for high risk patients

Maintenance of Drinking Water system

- Boiled water for drinking and mouth wash for high risk patients
- If point of use filters are used, use ones with 0.2 micron pore size and change filter accordingly to manufacturers’ instruction
- Do not use drinking fountains in health care facilities

Maintenance of Decorative Fountains

- Do not use in indoor environment in health care facilities
- Must have water treatment scheme (biocide, anti-corrosion, etc.)
- Frequent inspection and maintenance
- Drain and replenish small volume of water regularly
- Monitor treatment performance regularly

* More frequent for high risk areas
An Occupational Hygienist’s Role In An Epidemiological Investigation of a Legionnaire’s Disease Outbreak

A First Hand Report
By
Dr Joseph Kwan, DEnv, MPH, CIH

Events Leading to the Investigation

- Social Security Administration, Richmond, CA
- 6 Floors - 575,000 sq ft, 1200 occupants
- Sept 9, 91 - 5 cases of pneumonia (1 death), 3 of the cases involved janitorial staff at basement
- Sept 10, 91 - 2 additional cases of pneumonia, autopsy performed, outbreak suspected

Many Agencies Were Involved

- Cal/DHS, USPHS, SSA, GSA, OSHA, Cal/OSHA, CDC
- A response team was assembled: epidemiologists, occupational hygienists, facility engineers, administrators, etc
- OSHA took lead role in managing activities
- Tasks divided among different agencies

Events Leading to the Investigation

- Sept 11, 91 - OH commissioned to assist with the identification and remediation of environmental factors associated with the observed clinical illness
- USPHS and OSHA were notified
- Sept 12, 91 - Legionella isolated from lung of deceased (L. pneumophila I Knoxville-like strain)
- All Personnel were evacuated, building was closed
Roles of Occupational Hygienists

General Work Scope
- Planning and implementation of critical path
- Addressing emergencies
- Monitoring ongoing daily activities
- Collaborating with federal and state agencies

Specific Tasks
- Determining safety measures for site entry
- Cooling tower investigation
- Water systems investigation
- HVAC systems investigation
- Asbestos abatement
- Dispersion modeling

Specific Tasks
- Health and safety audit
- Air sampling for Legionella
- Review of chemical usage
- Organizing laboratory services
- Other OH consultations
Determining Safety Measures for Site Entry

Entry Requirements Established

- Secured entire perimeter, entry into parking lot by permit only
- Entrance into building locked and guarded
- Respiratory protection required for entry
- Occupational Hygienist selected appropriate respirator and performed fit testing

Cooling Tower Investigation
Cooling Tower Condition

- Mists at top drift towards air intake of bldg
- Biofilm found on surface of bricks
- No records of tower water disinfection
- Sludge found at bottom of sump tank
- Legionella bacteria isolated
- *L. pneumophila* I Bellingham strain

Need to perform remediation of the cooling towers to control Legionella infestation
Details of Water System

- Several systems: tepid, cold, drinking, kitchen
- Tepid water system maintained at 105 F
- Tepid water fed to all water closets
- Water samples were taken from all systems for Legionella investigation
- Culture + Direct Fluorescent + PCR
- Several samples from tepid water system yielded positive culture for *L. pneumophila* Knoxville-like strain (janitor's room, rest room, steam heater, humidification line)
- Other Legionella strains were isolated from other samples
**Disinfection of the Water System**

- A log of all the taps and spigots was obtained
- Disinfection by chlorination (50 ppm, 12 hours) and temperature shock treatment (140 F, 10 minutes)
- Post treatment water samples yielded no Legionella

**HVAC Systems Investigation**
Asbestos Abatement
Dispersion Modeling

Goal of Dispersion Study

- To evaluate the dissemination pattern of the Legionella bacteria from known sources to various locations within the building where clusters of Legionnaires’ disease were identified

Three Phases of Dispersion Studies

- Field assessment of air pressure regime by measuring intake and exhaust air flow at specific building locations
- Smoke release studies to visualize and confirm air flow patterns
- Tracer gas studies to re-construct possible airborne pathways of microbial spreading inside the building
Air Sampling for Legionella
Air sampling confirmed the absence of Legionella and the respiratory protection requirement was lifted

Other OH consultations
- Organizing laboratory services
- Review of chemical usage
- Health and safety audit
- Heat stress monitoring

A typical day started at dawn and ended after midnight...
Thank You

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Q and A?