THE NORTHERN HOSPITAL

LEGIONELLOSIS

"Piece of Turf", Albrecht Durer, Watercolor and gouache on paper, 1503, Graphische Sammlung Albertina, Vienna

"A dreadful rumor, reaches us from the West. Rome is occupied: her citizens ransom their lives for gold; but no sooner are they stripped of their possessions than they are again besieged and, having already lost their goods, they must now lose their lives as well. My voice is choked with sobs as I dictate these words. The city that has conquered the universe is now herself conquered… She dies of hunger before dying by the sword - scarcely do any men survive to be led off into captivity. The fury of the starving fastens on to nourishment unspeakable, they tear each other to pieces, the mother not sparing even the infant at her own breast…"

St Jerome, Letter CXXVII, 412 AD

So wrote St Jerome in the year 412 AD on hearing of the Gothic sack of Rome. For the West this was the most catastrophic event in history. The Roman Empire had existed since time immemorial. Its capital, Rome had not fallen to the barbarian since a Gallic tribal invasion 800 years previously. With the fall of the Roman Empire the West would be plunged into what has become known to history as the "Dark Ages". For the next 700 years, the science, art and culture of the Greco-Roman tradition, kept tenuously alive only in the Arabic world, would be lost amid interminable warfare between a kaleidoscopic array of transient states and early nations and the increasingly repressive iron grip of centralized religious dogma that would stifle all scientific inquiry. Centuries of stagnation in the arts and sciences would result.

The historical record from these times is scant. No great orator, such as Cicero, no great man of science such as Pythagoras, no great artist such as the creator of the "Winged Victory" would be bequeathed to us from these centuries. Then suddenly, as if from nowhere, the flame of Art and scientific learning in the West flickered back into life to illuminate the darkness. The historian Roy Porter nominated early twelfth century Sicily as the major launching point for the West's reawakening. Certain learned men of the medical school of Salerno as well as Benedictine Monks from the nearby monastery of Monte Cassino began to take an intense interest in ancient Greek manuscripts, from the Arabic world, where vast amounts of ancient Greco-Roman literature had been preserved down through the centuries by being transcribed into Arabic. By translating the Arabic back into Latin the lost humanities and sciences were re-introduced back into Western Europe. Despite intense resistance from the church, which saw the new science as a threat to its own authority, the flicker rapidly became a raging fire, which could not be extinguished.

The ensuing centuries are now known to history as the "Renaissance", literally the rebirth of art and learning. Not only was much of the ancient arts and knowledge recovered, but it soon came to be far surpassed. The art of this period shows an increasing realism, reflecting an intense desire to study and understand nature in a scientifically rigorous manor. Previously most art was symbolic of ideas, usually of a religious or moral nature with little attempt at depicting the world as it was in true life. An example of this new scientific realism can be seen in the works of Durer, with his incredibly true to life depictions of nature including animals, even pieces of turf. "Depart not from nature..." he once wrote, in reference to his works. Once this new way of viewing the world had been firmly established the path was paved for the subsequent scientific revolutions of the "Enlightenment" of the Seventeenth and Eighteenth

centuries. Men like Newton, Boyle and Hooke took man's understanding of nature beyond anything the ancients or even Durer could possibly have imagined. A case in point was the publication of Hooke's Micrographia, which revealed to the world for the first time the previously unknown microscopic world of animals. Hooke showed that there was far more to Durer's turf than first met the eye. Within it was a whole previously unknown universe of microscopic life.

In the 21st century we are now able to see even deeper into Durer's turf than even Hooke himself could have imagined. We can see a world of microorganisms, such as Legionella pneumophila, ubiquitous within the soil. Like the hoard of ancient Goths invading Rome, this organism may invade our patients, but unlike the Romans we are able to defend ourselves and it is the legacy of the spirit of scientific inquiry of the Renaissance and the Enlightenment, which allows us to do this. The doctors of the medical school of Salerno and the Monks of Monte Cassino would have been astounded and well pleased to know where their efforts have led, some nine centuries after their own time.

"Columbine", Watercolor and gouache on paper, 1526, Albrecht Dürer, Graphische Sammlung Albertina, Vienna

LEGIONELLOSIS

Introduction

Legionella species are ubiquitous in the environment.

They are often isolated from water and wet areas in the natural environment, such as creeks, hot springs, sea water, woodchips, mulch and soil. Potting mixes are often colonized with Legionella species, particularly L. longbeachae.

Sporadic and epidemic forms of **Legionnaires'** disease occur in Australia.

Legionella infections are believed to account for 5 - 15% of community-acquired pneumonias.

Legionellosis is transmitted through inhalation of **contaminated aerosols**. Person to person transmission has **not** been recorded.

Legionellosis has two recognized presentations:

1. Legionnaires' disease:
   - This is a pneumonic form of the disease.
2. Pontiac fever.
   - This is a septicemic form of the disease.

Only Legionnaires' disease has been reported in Australia.

Early antibiotic treatment improves survival.

Untreated, there is a high mortality rate, especially in those over 50 years of age or those who are immunocompromised.

History

The first recognized cases of Legionnaires' disease occurred in 1976 in Philadelphia, Pennsylvania.

There were 2000 attendees of an **American Legion convention** (hence the name) held at the Bellevue-Stratford Hotel.

182 attendees contracted the disease and 29 of them died

Epidemiology

Sporadic and epidemic forms of Legionnaires' disease occur in Australia.

Outbreaks in Australia are generally associated with artificial water systems, including water cooling towers and spa baths.

Legionella thrive in artificial water systems if the water temperature is maintained at 20 - 43 ° C, which favours the proliferation of the bacteria.

These systems include cooling water towers associated with air-conditioning and industrial processes, spa baths and household warm water systems for bathing.

Showerheads, nebulizers, humidifiers, ultrasonic misting systems, car washes and fountains have also been implicated.

Evaporative air-conditioners, such as those commonly used for domestic cooling, are not generally associated with Legionella infections.

Legionella outbreaks due to contaminated warm water systems are **regularly** reported from other countries.

Pathology

Organism:

Legionellae are **gram-negative bacilli**.

There are currently more than 45 known species of Legionellae.

Those that are known to cause disease in Australia include:

1. **L. pneumophila**

    - This species has 16 identified serogroup subtypes.
    - **L. pneumophila serogroup 1** has been identified as the cause of over 80% of cases in Victoria, and is the most common cause of disease worldwide.

Less commonly:

3. L. longbeachae

    - In Australia Legionella longbeachae has been associated with potting mixes.

4. L. micdadei

5. L. bozemanii.

Reservoir

The organism is ubiquitous in soil and water.

- It is often isolated from water and wet areas in the natural environment such as creeks, hot springs, seawater, woodchips, mulch and soil

- Potting mixes are often colonized with legionella species

- Legionellae also thrive in man-made water systems if the water temperature is maintained at 20°C - 43°C, which favors the proliferation of the bacteria.

  Generation of aerosols by these systems (such as spas and cooling water towers associated with air conditioning and industrial processes) then readily disperses the organism into the immediate environment

  Note that evaporative air conditioners like those commonly used for domestic cooling have not been associated with Legionella infections.

Transmission

- Legionellosis is transmitted through inhalation of contaminated aerosols of water or of dust

- Person to person transmission has **not** been reported.

Incubation Period

- Legionnaire's disease:

  ♥ 2 - 10 days, (most commonly 5 - 6 days).

- Pontiac fever:

  ♥ Is rapid, at around 24 - 48 hours.

Period of communicability

- Legionella is *not* readily communicated from person to person.

Susceptibility & resistance

- There is a greater risk of more severe legionellosis in persons:

  ♥ Aged 50 years and over

    ♥♥ More than 70% of infections in the state of Victoria occur in patients over 50 years of age.

- ♥ Who are regular smokers.
- ♥ Who are immunosuppressed.

- **The disease is extremely rare in children.**
- Nosocomial infections and infections in severely immunosuppressed patients have a much higher case fatality rate (up to 40%) when compared to the 7% overall mortality rate in Victoria.
- Serological surveys identify Legionella-specific antibody in 10 - 20% of healthy adults with no history of clinical legionellosis.
- **It is unclear whether legionella specific antibodies confer protective immunity.**

Clinical Features

An acute bacterial disease with two recognized presentations:

Legionnaire's disease:

This is the pneumonic form of the illness.

Untreated this form has a significant mortality rate.

Features include:

1. Constitutional symptoms:

   There is often a severe influenza like prodrome with general systemic symptoms, including:

   - Fever
   - Anorexia
   - Malaise
   - Myalgias

2. GIT symptoms:

   - GIT symptoms may be prominent with **diarrhea**

3. Pneumonic process:

- Patients may present with any form of pneumonia, however as a group they are more likely than other community acquired pneumonias to fulfill the criteria for severe disease.

  Note that upper respiratory tract symptoms such as runny nose and sore throat are rare.

4. Multi-organ failure:

   - There may be rapid progression to multi-system involvement, including renal failure and ARDS

Pontiac fever:

A non-pneumonic form of the infection has been reported in other countries, presenting as a flu-like illness with fever and malaise lasting 2 - 3 days.

Although there is said to be a high attack rate (95%), recovery is relatively rapid with no reported deaths.

High Risk Features:

Legionnaire's Disease should be suspected:

1. On epidemiological grounds, as it often occurs in clusters / epidemics, (but sporadic cases do occur).

2. In immunocompromised patients, especially with COPD, smokers and alcoholics.

3. Following the use of potting mixes or exposure to freshly disturbed soils.

The disease is **very rare** in **children**, and **young adults < 20**, as in general these age groups are not immunocompromised.

Investigations

Blood tests

1. FBE

2. CRP

3. U&ES / glucose

   - There is frequently an associated mild **hyponatremia**.

4. Serological testing:

The utility of serological testing for Legionella is limited

- Serology: look for a 4 fold increase in antibody titre. The second specimen is best taken in 4-6 weeks (rather than the usual 4 weeks).
- Positive Legionella antibody results (both IgG and IgM) are common in healthy adult populations
- The presence of antibodies is not necessarily indicative of recent infection, especially in acute phase sera.

CXR

There are nearly always radiographic changes on CXR at the time of presentation.

There can be a diffuse bilateral alveolar infiltrate, or a more "typical" picture lobar consolidation.

Blood cultures

Usual aerobic and anaerobic bottles to rule out *other organisms.*

Legionellae are fastidious organisms and will not grow on conventional culture media. Culture for *Legionella* must be specifically requested if the illness is suspected

Yield is low (unless the patient is very unwell / septicaemic).

Sputum

If sputum is present, it will give far better yield than blood cultures.

Culture remains the gold standard and the only method by which human specimens can be compared to environmental samples.

In contrast to urinary antigen studies it will pick up all legionella species.

Urinary antigen testing:

Urine for **Legionella antigens**:

- This test can be performed within several hours, if a result is needed urgently.
- It is currently specific for **legionella pneumophila serotype I**, (by far the most common infecting agent world wide).
- The Legionella urinary antigen test is the most rapid and sensitive test currently available

Note however that if this test is negative it does not necessarily rule out legionella, as

- Infection could be different legionella species / serotype
- it may be too early in disease process, (it may take up to **5 days** into the disease process to become positive)
- The antigen load may simply not have been great enough at the time of testing.

PCR:

PCR testing of **respiratory** specimens is available if required.

It is useful for unwell patients whose urinary Ag test is negative.

Exact serotyping is also useful for important epidemiological studies.

In urgent cases a result can be obtained within 24 hours.

Serology:

Positive Legionella antibody results (both IgG and IgM) are common in healthy adult populations.

The presence of antibodies is not necessarily indicative of recent infection, especially in acute-phase sera.

Diagnosis is made by the observation of a significant fourfold increase in antibody titre between sera taken in the acute phase and during convalescence, 3 - 6 weeks after the first specimen.

Management

Prevention:

There is currently no vaccine available for legionellosis.

To minimize the risk of infection through **potting mix**, gardeners should be advised to:

- Open the bag with care to avoid inhaling airborne potting mix
- Moisten the contents to avoid creating dust
- Wear gloves and an appropriate mask
- Wash hands after handling potting mix, even if gloves have been worn.

The same measures are also advisable when handling other gardening material, such as compost.

Treatment:

In general terms:

1. Supportive care as required:

   - Oxygenation and ventilatory support as clinically indicated, as for any pneumonic process.

2. **IV Antibiotic therapy:**

   Early antibiotic treatment improves survival.

   - **IV Azithromycin** 500 mg IV daily

     Give daily until significant improvement, then change to azithromycin 500 mg orally, daily.

     Alternatively:

   - Erythromycin 500 mg to 1 gram IV, 6 hourly

   And

   - IV cefotaxime 1-2 grams should be added empirically in first instance (to cover other non-legionella organisms)

   The *optimal duration* of treatment for severe Legionella pneumonia is uncertain. International guidelines recommend 7 - 10 days (IV + oral) treatment, though prolonged treatment may be required for immunocompromised patients - seek expert advice.

   If cases are severe the following can also be added:

   - Ciprofloxacin 400 mg IV, 12-hourly

   Or

   - Rifampicin 300 mg IV, 12 hourly.

3. **Oral antibiotics therapy:**

   For **less severe disease** oral therapy may be sufficient:

   Options include:

- Azithromycin 500 mg orally daily for 5 - 7 days

Or

- Doxycycline, 100 mg orally, 1 hourly for 14 days.

See latest Antibiotic guidelines for full prescribing details.

Notification

Legionellosis (Group A disease) must be notified immediately by telephone or fax followed by written notification within five days.

This is a Victorian statutory requirement.

School exclusion:

Primary school and children's services centers exclusion for legionellosis is not required.

Disposition

Most suspected cases of Legionella should be admitted to hospital in the first instance.

Treatment may be considered on an outpatient basis, providing:

- Patient is well.
- Without significant co-morbidity.
- Not immunocompromised.
- < 50 years of age.

Close follow up however will be essential.

Outbreak measures:

- Although there is no risk of person-to-person transmission, an active search for other people who may have been exposed to the same environmental source is commonly undertaken as part of the investigation of cases.
- When two or more cases are linked in time and place, an investigation is generally undertaken to identify likely Legionella sources in the common area.

  Environmental sources sampled during the department's investigations, such as cooling towers and spa baths, are generally requested to be disinfected as a precaution while laboratory testing is conducted.

References

1. The Blue Book Website, Accessed November 2017.

2. eTG - July 2017

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