

**MELIOIDOSIS**



*"Sherlock Holmes", (Actor, William Gillette), Men of the Day No.1055, lithographic print, SPY, Vanity Fair, 27 February 1907.*

*Dr Watson has been urgently summoned by Holmes, as he has become extremely ill and fears the worst! Dr Watson bursts through the door and is horrified at what he sees!*

*He was indeed a deplorable spectacle. In the dim light of a foggy November day the sick room was a gloomy spot, but it was that gaunt, wasted face staring at me from the bed which sent a chill to my heart. His eyes had the brightness of fever, there was a hectic flush upon either cheek, and dark crusts clung to his lips; the thin hands upon the coverlet twitched incessantly, his voice was croaking and spasmodic. He lay listlessly as I entered the room, but the sight of me brought a gleam of recognition to his eyes. "Well, Watson, we seem to have fallen upon evil days," said he in a feeble voice, but with something of his old carelessness of manner.*

*"My dear fellow!" I cried, approaching him.*

*"Stand back! Stand right back!" said he with the sharp imperiousness which I had associated only with moments of crisis. "If you approach me, Watson, I shall order you out of the house!"*

*Sherlock Holmes then asks Dr Watson a most unexpected favor - to immediately fetch Mr Culverton Smith - an amateur microbiologist, who spent many years in Sumatra and was well acquainted with exotic tropical diseases! The request is unexpected as Holmes had been investigating Culverton Smith for the suspected murder of the man's nephew - but had not been able to prove anything to date!...But he was a very great microbiological expert. Convinced Holmes is dying Dr Watson rushes to Culverton Smith to seek his assistance.*

*"Have you come from Holmes?" he asked.*

*"I have just left him".*

*"What about Holmes? How is he?"*

*"He is desperately ill. That is why I have come".*

*The man motioned me to a chair, and turned to resume his own. As he did so I caught a glimpse of his face in the mirror over the mantelpiece. I could have sworn that it was set in a malicious and abominable smile. Yet I persuaded myself that it must have been some nervous contraction which I had surprised, for he turned to me an instant later with genuine concern upon his features.*

*"I am sorry to hear this", said he. "I only know Mr. Holmes through some business dealings which we have had, but I have every respect for his talents and his character. He is an amateur of crime, as I am of disease. For him the villain, for me the microbe. There are my prisons", he continued, pointing to a row of bottles and jars which stood upon a side table. "Among those gelatine cultivations some of the very worst offenders in the world are now doing time".*

*Culverton Smith, with a strange glint in his eye, agrees to "assist". Watson rushes back before him to tell Holmes he will be coming - but then Holmes tells Watson not to question him, but simply to hide himself before Culverton Smith arrives! Dr Watsons hides just in time, before Culverton Smith arrives. Culverton Smith begins to interrogate Holmes:*

*"Listen now! Can you remember any unusual incident in your life just about the time your symptoms began?"*

*“No, no; nothing”*

*“Think again”.*

*“I’m too ill to think”.*

*“Well, then, I’ll help you. Did anything come by post?”*

*“By post?”*

*“A box by chance?”*

*“I’m fainting--I’m gone!”*

*“Listen, Holmes!” There was a sound as if he was shaking the dying man, and it was all that I could do to hold myself quiet in my hiding-place. “You must hear me. You SHALL hear me. Do you remember a box--an ivory box? It came on Wednesday. You opened it--do you remember?”*

*“Yes, yes, I opened it. There was a sharp spring inside it. Some joke--”*

*“It was no joke, as you will find to your cost. You fool, you would have it and you have got it. Who asked you to cross my path? If you had left me alone I would not have hurt you”.*

*“I remember”, Holmes gasped. “The spring! It drew blood. This box--this on the table”.*

*“The very one, by George! And it may as well leave the room in my pocket. There goes your last shred of evidence. But you have the truth now, Holmes, and you can die with the knowledge that I killed you. You knew too much of the fate of Victor Savage, so I have sent you to share it. You are very near your end, Holmes. I will sit here and I will watch you die!”*

*And with that confession - Holmes suddenly reveals that he is not sick at all! - He was only faking it with cleverly applied make up that made him look very ill! He gets up and tells Culverton Smith he is under arrest for murder and attempted murder! Culverton Smith simply laughs saying that it is a matter of Holmes’s word against his as there are no witnesses, whereupon, to Culverton Smith’s complete horror, Dr Watson with a grim look on his face, emerges from his hiding place - case solved!*

*Excerpts: “The Adventure of the Dying Detective”, Sir Arthur Conan Doyle, 1913*

*Before Sir Arthur Conan Doyle turned to full time writing, he was a medical practitioner, with a keen interest in Tropical Medicine. Like H.G Wells he was up with the very latest in modern developments. At the time Britain ruled the waves over a vast Empire upon which the sun never set. London was the seat of all cutting edge knowledge from around the globe. The very first description of Melioidosis by Whitmore reached London in 1912. Conan Doyle wrote the “The Adventure of the Dying Detective”, the following year in 1913. An immense amount of speculation has since followed concerning the precise nature of the deadly tropical disease that the dastardly Culverton Smith used to murder his nephew and then attempted to murder Sherlock Holmes who was investigating him. Anthrax, plague, typhus, diphtheria have all been put forward as the possible*

*microbial agent of death, but the most compelling argument of all, espoused by Drs Sodeman and Vora, points to Burkholderia pseudomallei - the agent of melioidosis - as the murder weapon! Melioidosis is a tropical disease found in Sumatra, especially the rice paddies, Culverton Smith knew so well. He knew it could be inoculated through broken skin. It could easily be cultured on gelatin plates - "...Among those gelatine cultivations some of the very worst offenders in the world are now doing time" - but most importantly its kill rate, (in a pre-antibiotic age) via direct inoculation, was such that it would have made a most reliable agent of murder, compared to several of the other postulated organisms. Like his great colleague H. G Wells, Conan Doyle gave us one of the first descriptions of the vision of the terrifying possible future consequences of the very latest scientific discoveries. The theory of the microbial cause of infectious disease had been well established by 1913. Conan Doyle, although of course not the first to suggest the possibility of biological warfare, was the first to describe it with a modern understanding of the science behind how it could work!*



*"Morning in the Tropics", oil on canvas, c. 1858, Edwin Fredrick Church*

# MELIOIDOSIS

## Introduction

**Melioidosis** is a bacterial infection endemic in **South East Asia** and **Northern Australia**.

It is a **potentially severe disease**. In a 10 year prospective study in the Northern Territory 252 cases were identified, with a case fatality rate of 19%.<sup>3</sup>

It can present with a range of clinical presentations, but most commonly this will be as a **pneumonia**. Severity can range from mild to severe to life-threatening.

**The disease can be acute in onset, delayed in onset, relapsing or re-activated.**

It is now recognised in the northern areas of the Northern Territory as the most common cause of *fatal community-acquired bacteraemic pneumonia*.<sup>3</sup>

It is also the most common cause of severe *community acquired sepsis* in Thailand<sup>3</sup>

Melioidosis has also been identified as a **potential bioterrorism** agent.

## History

Captain **Alfred Whitmore** first described melioidosis as a disease of opium eaters in Rangoon in 1912. It was originally called **Whitmore's disease**.

It had also been described as the "**Vietnamese Time-bomb**" (due to all the seropositive Veterans of that conflict).

Melioidosis was first described in *Australia* in an outbreak in sheep in 1949 in north Queensland. Human melioidosis was first described in Australia from a case in Townsville in 1950.<sup>4</sup>

*B. pseudomallei* was previously classed as part of the *Pseudomonas* genus and until 1992, it was known as *Pseudomonas pseudomallei*.

It is phylogenetically related to *Burkholderia mallei* which causes glanders, an infection primarily of horses, donkeys and mules.

The name Melioidosis is derived from the Greek *melis* meaning "a distemper of asses" with the suffixes -oid meaning "similar to" and -osis meaning "a condition", i.e a condition similar to glanders.

## Epidemiology

Melioidosis is found in tropical areas throughout the world, but particularly in:

- South East Asia
- Northern Australia.

In Australia cases typically occur in the:

- Top End of the Northern Territory:
  - ♥ Although, occasional cases have been found in the NT as far south as the Tennant Creek region.
- Far North Queensland
- The Kimberley region of Western Australia.

The majority of cases in northern Australia occur during the **wet season** in November to April.

Disease can affect all ages but is more common in adults and predominantly occurs in males and indigenous Australians.

### Pathology

#### Infectious Agent:

- **Burkholderia pseudomallei.**

This is a small gram-negative, aerobic bacillus.

*(It was previously named Pseudomonas pseudomallei or Whitmore's bacillus).*



*Wrinkled colonies of B. pseudomallei on horse blood agar after five days of incubation, also showing pronounced haemolysis, (Life in the fast Lane Website).*

## Mode of Transmission

Infection is thought to be acquired through:

- Percutaneous inoculation, (via wounds, cuts, scratches, abrasions etc.)
- Inhalation
- Ingestion, (contaminated water).

People with occupational (e.g rice paddy farmers) or recreational exposure to moist soil or surface water are at greatest risk.

The disease is only *very rarely* transmitted person to person.

## Reservoir

- The soil and water in tropical regions of Northern Australia and South East Asia.

The bacteria essentially live below the soil's surface during the dry season but after heavy rainfall are found in surface water and mud and may become airborne.

## Incubation Period

- The incubation period is uncertain, but Australian data suggests a period ranging from 1 - 21 days.
- This period can be more prolonged in infections which initially become latent.

## Susceptibility and resistance

- Disease in humans is uncommon even among people in epidemic areas who have close contact with soil or water containing the infectious agent.
- Approximately two thirds of cases have either a predisposing medical condition or have a reactivation in asymptomatic infected individuals.

## Clinical Features

**A history of travel to northern Australia or tropical regions of South East Asia should be determined.**

**The disease can be acute in onset, delayed in onset or relapsing or reactivated.**

Melioidosis can present with a range of clinical presentations, including:

1. Pneumonia:
  - Pneumonia is the most common clinical presentation of melioidosis.

- Severity can range from a mild respiratory illness to a severe pneumonia with septicaemia, with a mortality rate of over 50 %.

*Other less common presentations can include:*

2. Fulminant septicaemia:

- This can be a rapidly fatal, illness without evidence of pneumonia
- It can also recur after several days or even weeks of *apparently adequate* intravenous antibiotic treatment.
- Occasionally cases may be seen many **years** after initial exposure

3. Skin involvement:

- This can be in the form of abscesses or ulcers

4. Internal focal infection, (abscesses):

- Here symptoms come on much more insidiously, with weight loss, intermittent fever, and generalized “constitutional symptoms.
- Focal infection may involve a wide range of organs including:
  - ♥ Prostate/ kidney/ spleen/ liver/ osteomyelitis and/or septic arthritis.
- These subacute focal infections can also act as a source for subsequent systemic bacteraemia.

5. Neurological illnesses including:

- Brainstem encephalitis
- Acute flaccid paralysis.

*Additionally:*

6. **Asymptomatic infection can also occur:**

- As evidenced by seroconversion.

7. Re-activation:

In a small proportion of cases can **re-activate** from a **latent** form, many **years** later, during times of immunosuppression.



### Risk factors:

Risk factors for disease include:

- Diabetes
- Chronic lung disease
- Renal disease
- Excess alcohol consumption.
- Immunosuppression in general.

### Investigations

A **definitive** diagnosis of melioidosis can only be made by **culture** of the organism or **PCR testing** from biological samples taken from the respiratory tract, blood or other sites.

The likelihood of a bacterial diagnosis is increased by:

- Using **selective culture media** - modified Ashdown's broth. This medium contains gentamicin to suppress the growth of other bacteria. (*Burkholderia pseudomallei* is resistant to gentamicin).
- Frequent sampling (sputum, throat, rectal and ulcer swabs) and collection of blood cultures.

### Blood tests:

These should include:

1. FBE
2. CRP
3. U&Es/ glucose
4. LFTs
5. Coagulation profile
6. Blood cultures

**Serological antibody** tests are also available.

### Microscopy and culture:

Samples can be taken from:

- Throat
- Ulcerations, where present.
- Rectal, where relevant
- Urine

#### CXR:

- Lung involvement is the most common presentation.

#### MRI:

- This will be required for suspected neurological involvement.

**Others investigations are done as clinically indicated.**

#### Management

Initial intensive antibiotic therapy usually consists of:

- **Trimethoprim - sulfamethoxazole**

*Plus*

- **Ceftazidime or meropenem, or imipenem.**

**G-CSF** may be added if criteria for **septic shock** are present. <sup>3</sup>

The trimethoprim/sulfamethoxazole component is usually continued for **three months** to **ensure eradication**.

**Follow-up of cases and adherence to eradication therapy are critical to prevent relapse, which can be fatal.**

See latest Antibiotic [Therapeutic Guidelines](#) for full prescribing details.

#### Disposition:

**All patients should be admitted to hospital initially.**

**Specialist infectious disease advice should be sought for all cases.**

#### Immunization

- There is currently no vaccine available

School exclusion:

- School exclusion is not required.

Notification:

- Notification is not currently required although it is *recommended* that cases of melioidosis with a history of travel to northern Australia be reported to public health units in the relevant state or territory.
- Melioidosis has also been identified as a **potential bioterrorism agent**.

Any case or cases presenting *without a clear history of exposure in an endemic area* should be reported to the Department of Health for further investigation.

## References

- 1 The Blue Book Website, 10 February, 2007.
- 2 eTG - July 2014.
- 3 Bart J. Currie et al. Endemic Melioidosis in Tropical Northern Australia: A 10 Year Prospective Study and Review of the Literature. *Clinical Infectious Diseases* 2000; 31: 981 - 6
- 4 Bart J. Currie et al. The epidemiology of melioidosis in Australia and Papua New Guinea. *Acta Tropica* 74 (2000) 121-127.

### Further reading:

Sodeman W.A. Sherlock Holmes and Tropical Medicine: A Centennial Appraisal. *Am. J. Trop. Med. Hyg.* 50 (1), 1994, p. 99-101

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