

# Legionnaires' Disease: Laboratory Diagnosis, Epidemiology and Outbreak Response



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## Outline

- Diagnosis of LD and case definitions
- LD epidemiology in SA: past and present
- LD outbreaks:
  - Public health response
  - Travel-associated LD
- Future of LD in SA?

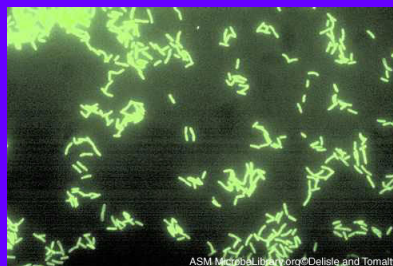
## Diagnosis of LD

- **Culture**

- Gold standard
- 100% specific
- Technically difficult: specialised culture media, technical skill
- Slow to grow (>5 days)
- Detects all species and serogroups
- May be affected by antibiotic therapy
- Specimens: respiratory secretions, lung biopsies
  - LD very rarely bacteraemic



- **DFA** (direct fluorescent antibody) staining of pathologic specimens
  - 95% specific; 25-75% sensitive
    - Technical skill required
  - Require representative tissue biopsies – invasive, not frequently performed
  - Rapid result



- **Serology**

- Prior to urinary antigen test –most commonly used diagnostic test
- Range of available serological tests on the market
  - Detection of Legionella spp vs *L. pneumophila* vs *L. pneumophila* sg1.
  - Different formats: e.g. IFA, ELISA
  - Wide variability in performance of individual tests
- For diagnosis of LD: require a fourfold ↑ titre in specimens obtained 3-6 weeks apart (may take up to 9 weeks to 'seroconvert')

- For seroconversion (4fold ↑titre):
  - Specificity 95-99%
  - Sensitivity 70-90%
- A single high titre is NOT diagnostic of LD!
  - Background seroprevalence in general population must be known to guide cut-off values
    - Cut-off values are test-dependant
    - Denmark: 23% healthy blood donors pos titres of up to 1:128
  - No internationally validated cut-off values

- Retrospective diagnosis (until second sera tested) delays public health response
- Not affected by antibiotic therapy
- Can detect infection due to non-sg1 and non-pneumophila spp



#### - **Urinary antigen test (UAT)**

- Most commonly used and recommended diagnostic test presently (except for SA!)
- Easy to perform, rapid results (15 min – 3hr)
- Specifically for LP sg1
- Not affected by antibiotic therapy
- Remains positive for days to weeks after infection
- Specificity 99-100%
- Sensitivity for LP sg 1: ~95%
- Sensitivity for other LP sg: 13-45%

- Rapid result: timely public health response



- **PCR**

- Current data insufficient for reliable estimate of sensitivity/specificity values
- Current PCR tests and protocols not standardised and not well validated

- Potential advantages:

- Rapid test
- May detect all LP serogroups or even all Legionella species



## LD case definitions

- WHO: confirmed case
  - Clinical/radiological evidence of pneumonia
  - PLUS  $\geq$  one of:
    - Isolation of Legionella from respiratory specimens
    - Positive UAT
    - Positive DFA
    - Fourfold  $\uparrow$  titre of specific serum Ab titre to LP sg1

- US CDC: confirmed case
  - Clinically compatible case
  - PLUS  $\geq$  one of:
    - Isolation of Legionella from respiratory specimens/lung tissue/pleural fluid/other normally sterile fluids
    - Positive UAT
    - Fourfold  $\uparrow$  titre of specific serum Ab titre to LP sg1

- ELDSNet confirmed case:
  - Acute LRTI with focal signs of pneumonia on clinical examination and/or radiological evidence of pneumonia

PLUS  $\geq$  one of:

  - Isolation of Legionella from respiratory secretions/lung specimens/blood
  - Positive UAT
  - Fourfold  $\uparrow$  titre of specific serum Ab titre to LP sg1

- Case definition consensus:
  - Community acquired LD: a person with LD does not meet criteria for nosocomial or TALD
  - Nosocomial LD: LD in a person who was hospitalised for  $\geq 10$  days prior to onset of illness
  - TALD: LD in a person who in 10 days prior to onset of illness visited/stayed in an accommodation site

## What diagnostic tests are available and used in SA?

- Culture
  - Most micro labs could perform culture but lack experience
  - Specialised culture media requirements: not detected by routine 'MCS' on respiratory secretions; need to request specifically from the lab
- DFA
  - Not routinely offered

- Serology
  - Offered by all private labs, some NHLS labs
  - Problems:
    - Labs don't specify which test is performed (i.e. Legionella spp vs LP all serogroups vs LP sg1)
      - Tests have variable sens/spec
    - No background seroprevalence data for SA (or even Africa) is available to guide cut-off values
    - Paired sera hardly ever submitted; cannot make a diagnosis on a single specimen!!



- PCR
  - Offered by a few major private labs in SA
  - None of the currently available PCR tests are accredited/endorsed by CDC, WHO, ELDSNet etc due to lack of validation and standardisation
- UAT
  - Offered by NHLS (at ICSL)
  - Not yet offered by any private labs

## Epidemiology of LD in SA: The past



- C. Kaplan, et al. Legionnaires' Disease in Johannesburg. SAMJ, July 1980
  - First two cases reported in SA. A male, 52, diabetic, recovered and a female 48, smoker, recovered. No possible sources of infection discussed.
- T.W. Randall, et al. Legionnaires' Disease in Port Elizabeth. SAMJ, July 1980
  - Eight sporadic cases discussed, age range 21-51, all recovered.

## Legionnaires' disease in a Johannesburg teaching hospital

### Investigation and control of an outbreak

P. M. STREBEL, J. M. RAMOS, I. J. EIDELMAN, LYNNE TOBIANSKY,  
H. J. KOORNHOF, H. G. V. KÜSTNER

#### Summary

During the period 11 November 1985 - 21 February 1986, 12 cases of Legionnaires' disease were identified at a Johannesburg teaching hospital. Only 2 patients definitely acquired the disease in hospital.

Although *L. pneumophila* was cultured from the hospital hot-water system, there was no association between the location of patients and culture-positive water sites. Cases were clustered in the medical and surgical intensive care units. Being on a ventilator was a significant risk factor for acquiring Legionnaires' disease (relative risk 18,4; 95% confidence interval 2,4 - 142,2). The potential role of ventilators in the transmission of the disease is discussed

## Epidemiology of LD in SA: the present



- LD is **notifiable** but no reliable data on case numbers or trends
- Why so few cases identified, notified and investigated?
  - Not perceived by healthcare sector or general public as a disease that occurs in SA or is of relative importance
  - Lack of awareness of disease by HCW for both community acquired and nosocomial LD
  - Lack of awareness of testing modalities
  - High background rates of other respiratory pathogens
  - Inability of routine microbiology investigation on patients with pneumonia to detect LD

## LD Outbreaks in SA: Public health response

- Response to single cases and outbreaks requires multisectoral teamwork (the relevant outbreak response team):
  - DoH Communicable Diseases Co-ordinate
  - DoH Environmental Health
  - Dept of Water Affairs
  - NHLS (incl NICD)
  - Other stakeholders.

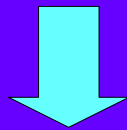
- Challenges and obstacles
  - Delayed notification of LD by HCW
    - May not be notified at all
  - Notified 'cases' need verification due to problems with diagnostic modalities used, especially serology (pseudo-cases/outbreaks)
  - Investigation of possible exposure sources is labour-intensive and costly
    - Requires specific risk assessment approach and specific sampling methods – not all EHPs are experienced in this



- Zululand observer, 21 June 2010 reports:
  - ‘4 employees of a bank in a Richards Bay mall ill with severe flu symptoms associated with LD’
  - Bank closed as a result
  - Air-conditioning thought to be cause of LD; noted to be malodorous since May
- Panic ensues
  - GPs and physicians overwhelmed
  - One patient hospitalised
  - Many persons tested for Legionella...

- Private lab does Legionella serology testing; 'positive' results for 5 patients
- Outbreak investigation: DoH, FELTP, NICD, others
  - Legionella guidelines and fact sheets distributed
  - None of the 'cases' had pneumonia (incl the hospitalised person)
- The bank, the mall and various other companies etc contract a number of water treatment companies to conduct water testing

- 6 urine specimens sent to ICSL, NHLS: negative
- 2 sputum specimens sent to ICSL: negative
- Results from water testing: reported as negative by all clients



PSEUDO-OUTBREAK!!

### Shut down bank remains off-limits

STORY: Ronelle Ramsamy

#### *All eyes on outcome of investigation into possible Legionnaires disease threat*

Investigations are still underway to ascertain the root of the problem which led to four Richards Bay bank employees displaying severe flu symptoms associated with Legionnaires' disease. First National Bank at the Boardwalk

### Legionnaires' disease mystery

STORY: Ronelle Ramsamy

The exact source of the Legionella bacteria that infected staff members at a Richards Bay bank last month remains a mystery. Latest test results at the First National Bank (FNB) at the Boardwalk Inkwazi Shopping Centre proved negative relating to the prevalence of the bacteria. FNB, Boardwalk and the KZN Department of Health, in conjunction with the City of uMhlatuze, had all conducted tests after five people were exposed to the bacteria, with one patient being hospitalised. Results released this week could not pinpoint how employees could have contracted the bacteria. Allegations that Legionella could have spread from the air-conditioning unit have been ruled out. Four FNB staff members displayed severe flu symptoms associated with Legionnaires

## Pseudo-outbreaks...

- 2010: the year for LD pseudo-outbreaks:
  - June 2010: Bank, Richards Bay (air-con)
  - October 2010: Bank, Johannesburg (air-con)
  - October 2010: Private Hospital, Mpumalanga (air-con)
  - September 2010: GP, Oudtshoorn (heard about LD at Fancourt...)
- Why?
  - 'Google' air conditioning and illness = LD
  - HCW not cognizant of the clinical features of LD and test indiscriminately
  - Serology testing only

Serology result for patient in Richards Bay seen by GP with nonspecific URT symptoms, not requiring admission to hospital.

LEGIONELLA ANTIBODIES (SEROTYPES 1-14)

- > Legionella Screen
- > Legionella IgM
- > Legionella IgG
- > Comment

Positive	*
1:100	* < 1:100 titre
1:200	* < 1:100 titre

The serological findings demonstrated a positive IgG & IgM antibody titre for Legionella. This is indicative of an acute legionella. However, false border positive values may be seen during the acute phase of a disease due to cross reactive antibodies/proteins. If the clinical findings are suggestive of legionella, suggest that the patient should be treated. According to our experience, the serological response of acute legionella is usually slow. Depending on the clinical findings, we suggest the antibody titre for legionella should be repeated after 10-14 days or a sputum (from bronchial origin) can be submitted for a legionella PCR confirmatory test.

Case 1 – Oudtshoorn (May 2009)  
70 yrs male; presented with bronchitis  
No extrapulmonary complications etc

----- P.K.R. DEPARTEMENT -----  
Toets Resultaat Wyser Verwysing

PKR RESPIRATORIESE VIRUS PANEEL

> PKR RESP BAKTERIEE PANEEL

POSITIEF

Daar is vir die volgende bakteriee getoets:

- Mycoplasma pneumoniae
- Legionella pneumophila
- Streptococcus pneumoniae
- Haemophilus influenzae
- Bordetella pertussis
- Chlamydia pneumoniae

Die volgende bakteriee is waargeneem:

- Legionella pneumophila
- Haemophilus influenzae

Case 2 – Oudtshoorn (July 2010)  
 58 yrs male; presented with sepsis  
*Staph aureus* on admission blood culture with  
 subsequent multifocal metastatic disease

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----- SEROLOGIE -----
Toets                               Resultaat Wyser Verwysing
LEGMONELLA                          POSITIEF H
  > LEGMONELLA IPA

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LEGMONELLA KOMMENTAAR
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:
:1. Ongeveer 25% van pasiënte toon serokonversie in die
: eerste week van siekte, 50% teen die tweede, 75% teen
: die derde en 90% teen die vierde week van siekte. Die
: oorblywende 10% ontwikkel antiliggamme gedurende die
: sesde tot negende week.
:2. 'n Viervoudige titer styging vanaf die akute tot herstel
: fase dui op 'n onlangse infeksie.
:3. 'n Enkele titer van >= 256 is verenigbaar met die
: afwesigheid van siekte, vorige siekte of huidige
: siekte. Terwyl 'n enkele titer van >= 1024 suggestief
: is van huidige infeksie.
:4. Weens die stadige antiliggamme respons mag dit nodig wees:
: om seriele monsters oor 'n 6-9 weke periode serologies
: te ondersoek.
:5. Aangesien IgM antiliggamme vir 'n geruime tyd mag
: persister, is dit nie moontlik om huidige van vorige
: siekte te onderskei op grond van IgM antiliggamme titers
: nie.
:

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## Travel-associated LD in SA

- TALD increasingly recognised worldwide
  - EU: at least 20% LD cases are TALD
  - US: similar
- Why?
  - Increasing numbers of travellers
  - Increasing numbers of travellers with underlying risk factors for LD
  - High index of suspicion in EU and US so cases detected



## Holiday hell cash payout

Jan 26 2009 (<http://www.birminghammail.net/news/top-stories/2009/01/26/>) by [Allison Dayani](http://www.birminghammail.net/authors/alison-dayani/) (<http://www.birminghammail.net/authors/alison-dayani/>), Birmingham Mail

A MIDLAND postman has won a five-figure payout from a travel giant after a last-minute holiday left him fighting for his life with deadly Legionnaires' disease.

Father-of-two David Higgs, from Smethwick, was hoping to recharge his batteries in Tenerife when it turned into a holiday from hell.

Just one day into the seven-day getaway, booked with First Choice, to the Orlando Club Resort, in Playa de las Americas, David and his daughter Leah fell violently ill after they both used the shower in their apartment.



tuesday, 12 april 2011

## Starwood faces a US \$16.7 million Legionella Lawsuit

The suit claims that Thomas Boyle, from Britain, and Elodie Nogues, from France, contracted Legionnaires after staying at the Dubai Westin Mina Seyahi in January and February of 2009. The health of the pair deteriorated rapidly and resulted in hospital stays. A third guest, BBC radio commentator Bill Frindall, 69, passed away as a result of contracting the disease.

## Fentons Solicitors is one of the country's leading claimant personal injury firms

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Keep 100% of your compensation.  
24 hr Freephone  
0808 1493 029

In order for a holidaymaker to make a claim for personal injury against the hotel or tour operator for legionnaires disease, the source of the infection needs to be established. In most cases the incubation period for legionnaires disease is 2-10 days.

If you booked a package holiday you may be able to bring a claim under the Package Travel Regulations 1992 against the tour operator. This has the advantage of bringing the claim under

### “legionnaires disease – what the holidaymaker should know”

27 February 2007

## Possible Legionnaires' Disease Outbreak Associated with the EPIC Hotel in Miami, Florida

Attorney Fred Pritzker has successfully represented victims of Legionnaires' disease outbreaks associated with hotels. He has been interviewed and quoted by *The New York Times*, *The Wall Street Journal*, *USA Today*, *Lawyers USA* and other publications. To contact a [Legionnaires' disease lawyer](#), please call 1-888-377-8900 (toll-free), [email Attorney Fred Pritzker](#), or submit our [free case review form](#).

**European Guidelines for  
Control and Prevention  
of Travel Associated  
Legionnaires' Disease**

**Produced by members of the European  
Surveillance Scheme for Travel Associated  
Legionnaires' Disease and the European  
Working Group for Legionella Infections**



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## **ELDSNet (previously EWGLINET) protocols**

- All TALD are reported to the ELDSNet co-ordinator/s in the country where the illness was contracted
- When 2 or more cases are reported that have been to the same accommodation site in the 10 days before the onset of illness, within a 2 year period, it is called a cluster outbreak
- The ELDSNet co-ordinator/s then inform and send the ELDSNet guidelines to the accommodation sites.
- The co-ordinator then arranges for a risk assessment and Legionella sampling of the implicated facility.

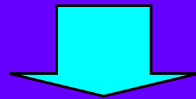
- Samples taken during the risk assessment and any follow-up samples must be processed according to ISO/DIS:11731 method
- Once the risk assessment is completed, Form A is submitted to ELDSNet. This should be sent within 2 weeks of notification.
- Once suitable control measures are in place, Form B is submitted to ELDSNet. This should be sent within 6 weeks of notification.
- If the above 6-week deadline is not adhered to, the name of the accommodation establishment is posted for public access on the ELDSNet website.
- The day after the country is notified of a cluster, EU tour agencies are also notified by ELDSNet.



**21<sup>st</sup> January 2010**

- EWGLINET notifies WHO of cluster of LD cases with travel history to the same hotel/golf resort in the W. Cape
- Report sent to Infection Control Services Lab and to NICD
- EWGLINET already sent out travel alert to all travel agencies in Europe; many block bookings cancelled

- **Case 1:** 65 yr male Norwegian national
  - Travelled to SA; departed 15/11/2008
  - Date of illness onset: 17/11/2008
  - Dx: UAT.
  - Patient very ill, requiring prolonged hospitalisation but recovered
- **Case 2:** 48 yr British national
  - Stayed at resort 23/11/2009 to 06/12/2009
  - Returned to England; became ill on 07/12/2009
  - LD diagnosed on urinary antigen
  - Patient ill, requiring hospitalisation



2 cases in a 2 year period = a cluster of LD: requires environmental investigation for possible source

- Numerous risk factors detected
- Costly interventions
- LP sg 2-14 isolated from water samples

European Legionnaires' Disease Surveillance Network (ELDSNet)  
European Centre for Disease Prevention and Control (ECDC)  
SE 171 83 Stockholm, Sweden

## 20<sup>th</sup> December 2010

- ELDSNet issues a Cluster alert of travel-associated LD cases with recent visit to SA
  - Both had stayed at 5 hotels/guest houses in Eastern and Western Cape
- ELDSNet forwards cluster alert to travel operators
  - tour operators forward to SA partners on 19 January
- Change in reporting policy for non-EU countries: report to WHO Geneva who then cascade to WHO country level etc – report only given to DoH by WHO on 8<sup>th</sup> February.

- Case 1:
  - 69-yr-old female resident of Netherlands
  - Travelled to SA; departed 31 Jan 2010
  - Date of illness onset 31 Jan 2010
  - Dx: urinary antigen
  - Recovered
- Case2:
  - 64-yr-old female resident of Netherlands
  - Travelled to SA; departed 8 Dec 2010
  - Date of illness onset 10 Dec 2010
  - Dx: urinary antigen
  - Recovered



## Cluster investigation...

- All establishments contacted on 9 Feb to notify them, and with advice on procedure for ELDSNet-acceptable risk assessment and water testing
- Problems:
  - No awareness of Legionella, and possible repercussions
  - Water treatment companies offer variable levels of risk assessments and offer suboptimal rapid tests for Legionella in water specimens ('dipslide' tests)
  - Private labs that offer Legionella water testing use non-validated tests
  - Risk assessments are costly
  - Legionella water testing
    - Only ICSL offer ISO/DIS:11731 method testing
    - Costly
    - Specimens need to be couriered to ICSL for prompt processing

## 17 March 2011

- ELDSNet issues a cluster update – cluster now a complicated cluster as a further case has been reported!
  - 68-yr-old male resident of Netherlands
  - Travelled to SA; departed SA on 16 Feb
  - Date of illness onset: 21 Feb
  - Dx: urinary antigen
  - Recovered
- This third case had stayed at the 5 hotels, and an additional hotel in Oudtshoorn (which one of the other cases also visited)...

## Progress to date...

	Graaf-Reinet	Port Elizabeth	Plettenberg Bay	Somerset West	Cape Town	Oudtshoorn
Risk assessment	✓	✓	✓	✓	✓	✓
ICSL water testing	✓	✓	✓	✓	✓	✓
Form A	✓	✓	✓	✓	✓	✓
Form B	✓	No	✓	✓	No	No
Problems identified at risk assessment?	✓	✓	✓	✓	✓	✓
Interventions in place?	no	no	no	no	no	no
Positive ICSL water test results?	No	✓ sg 1	✓ sg 1	✓ sg 2-14	✓ sg 1	No

## 21 April 2011



**European Legionnaires' Disease Surveillance Network (ELDSNet)**

European Centre for Disease Prevention and Control (ECDC)  
SE 171 83 Stockholm, Sweden

### Notification of a single case of Legionnaires' disease: 2011

The European surveillance scheme has been informed of a confirmed case of Legionnaires' disease in a 88 year old male resident of the United Kingdom (EAW111502), whose illness may be associated with travel to **Durban, South Africa**.

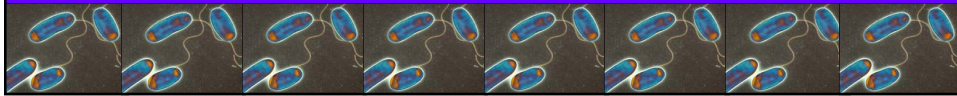
The reported date of onset was 14/03/2011, and the patient died. Legionella infection was diagnosed by urinary antigen detection.

Comment: Case lived 6 months in UK & 6months in South Africa. Returned to UK permanently on 10/03/2011. Case used a communal swimming pool at his home in S. Africa & at the B&B.



## The future of LD in SA?

- Promote awareness of LD in healthcare sector, and travel tourism sector
- Urge laboratories to offer UAT and review serology testing offered
- Legionella surveillance programme?
- Legionella working group?



## Acknowledgements

- DoH, members of Outbreak Response Unit and FELTP, NICD
- Mr Rob Stewart (ICSL, NHLS)

