

# Australian Paediatric Surveillance Unit STUDY PROTOCOL Non Tuberculous Mycobacterial Infections

# COMMENCING July 2004

# BACKGROUND

Mycobacteria other than *Mycobacterium tuberculosis* (TB) cause a significant burden of disease in children. Non tuberculous mycobacteria (NTM) are free living soil and water organisms known to cause a spectrum of diseases including lymphadenitis, pulmonary disease, skin and soft tissue infections, ear infections, skeletal infections and disseminated infection<sup>1</sup>.

The annual incidence of NTM infections in the developed world is believed to be increasing possibly due to increasing awareness, better identification techniques and changing population groups. However, the magnitude of this problem in children is unquantified. Our study aims to expand knowledge recently gained in Australia through laboratory surveillance.

NTM infections are known to be associated with some medical conditions including human immunodeficiency virus (HIV) infection, malignancy, chronic granulomatous disease (CGD) and chronic lung disease including cystic fibrosis and bronchiectasis. However most often NTM infections occur in otherwise healthy children. Emerging data from recent studies show that even in healthy children, subtle underlying immunodeficiency or genotype differences may exist, contributing to susceptibility to NTM infection. <sup>6,7</sup>

The natural history of NTM infection has not been well described and optimal management remains unclear. There is evidence that a proportion of NTM lymphadenitis will spontaneously resolve. In children requiring intervention (e.g. due to suppurative changes) surgical clearance has been accepted as the therapy of choice. While surgery is curative in most cases, a proportion of children fail initial surgical management and may require repeated surgery or the addition of medical therapy. The role of medical therapy as first line treatment is unconfirmed. Consensus on medical treatment regimens has not been reached. Information from this study will contribute to efforts to improve the detection and the outcome of affected children.

#### STUDY OBJECTIVES

- 1. Estimate the incidence of newly diagnosed NTM infection in children seen by child health specialists in Australia
- 2. Describe the epidemiology and spectrum of disease and document known risk factors.
- 3. Describe diagnostic investigations used in Australia; frequency of use of skin testing and the clinical utility of the test, including differential skin testing.
- 4. Describe the management of NTM in Australia and the response to treatment.

## **CASE DEFINITION**

Please report any child under 15 years of age seen in the previous month newly diagnosed with:

# **1.DEFINITE NTM:**

Any child in whom a non-tuberculous mycobacterium species has been identified either by isolation on culture or by polymerase chain reaction (PCR) from a sample from a sterile site.

#### OR

#### 2. PROBABLE NTM:

A child who presents with any clinical features compatible with NTM (see below)

AND has undergone one or more of the supportive investigations (see below)

AND in whom Mycobacterium tuberculosis (TB) infection is unlikely.

Compatible clinical features	Supportive investigations (one or more)
<ul> <li>lymphadenopathy (any site)<sup>a</sup></li> <li>pulmonary disease with or without constitutional symptoms<sup>b</sup></li> </ul>	Microbiology: Acid fast bacilli (AFB) seen on sample or biopsy specimens or AFB grown from non-sterile site sample or positive AFB PCR on non-sterile site sample
skeletal infection     cutaneous infection	Histopathology: Granulomatous inflammation or caseous necrosis or AFB seen
ear disease	Skin testing: Tuberculin PPD skin testing ≥ 5mm and less than 15mm and/or Avian PPD <sup>c</sup> ≥10mm

<sup>&</sup>lt;sup>a</sup> Clinical features of NTM lymphadenitis includes typical firm LN consistency +/- overlying skin changes (e.g. violaceous hue), with no associated constitutional symptoms

<sup>&</sup>lt;sup>b</sup> constitutional symptoms referable to NTM infection include unexplained lethargy, fevers and/or anorexia and weight loss, generally only occurring with disseminated infections or pulmonary infections in chronic lung disease

<sup>&</sup>lt;sup>c</sup> Avian PPD, manufactured by Commonwealth Serum Laboratories (CSL) Limited. Intradermal dose 10 IU

# **FOLLOW-UP OF REPORTED CASES**

A brief questionnaire requesting further details will be forwarded to clinicians that report a case of NTM to the APSU.

If you have any comments or questions please contact:

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# **Collaborating investigators**

Members of the Australian Mycobacterium Reference Laboratory Network Special Interest Group in Mycobacteria – Convenor 2004, Richard Lumb, Mycobacterium Reference Laboratory Infectious Diseases Laboratories Adelaide, SA.

#### **REFERENCES**

- 1. Diagnosis and treatment of disease caused by nontuberculous mycobacteria. This official statement of the American Thoracic Society was approved by the Board of Directors, March 1997. Medical Section of the American Lung Association. *Am. J. Respir. Crit Care Med.* **156**, S1-25 (1997).
- 2. Falkinham, J.O., III. Epidemiology of infection by nontuberculous mycobacteria. *Clin. Microbiol. Rev.* **9**, 177-215 (1996).
- 3. Howell, N., Heaton, P.A. & Neutze, J. The epidemiology of nontuberculous mycobacterial lymphadenitis affecting New Zealand children 1986-95. *N. Z. Med. J.* **110**, 171-173 (1997).
- 4. Haverkort, F. National atypical mycobacteria survey, 2000. Commun. Dis. Intell. 27, 180-189 (2003).
- 5. Wolinsky, E. Mycobacterial lymphadenitis in children: a prospective study of 105 nontuberculous cases with long-term follow-up. *Clin. Infect. Dis.* **20**, 954-963 (1995).
- 6. Ottenhoff, T.H. *et al.* Genetics, cytokines and human infectious disease: lessons from weakly pathogenic mycobacteria and salmonellae. *Nat. Genet.* 32, 97-105 (2002).
- 7. Verreck, F.A. et al. Human host defense and cytokines in mycobacterial infectious diseases: interleukin-18 cannot compensate for genetic defects in the interleukin-12 system. *Clin. Infect. Dis.* 35, 210-212 (2002).
- 8. Wright, J.E. Non-tuberculous mycobacterial lymphadenitis. Aust. N. Z. J. Surg. 66, 225-228 (1996).
- 9. Wallace, R.J., Jr., Glassroth, J. & O'Brien, R. A plea for clinical trials to resolve the issue of optimal therapy in the treatment of Mycobacterium avium infection. *Am. Rev. Respir. Dis.* **144**, 3-4 (1991).