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Request for Comments on UK Standards for Microbiology Investigations (SMIs) Bacteriology document (B 40)

Response from the Institute of Biomedical Science

The Institute of Biomedical Science (IBMS) is the UK professional body for biomedical science. It represents approximately 20,000 members employed mainly in NHS laboratories, NHS Blood and Transplant, Public Health services, private laboratories, research, industry and higher education. In its capacity as a standard setting organisation, and also an HCPC approved education provider, the Institute welcomes the opportunity to contribute to the consultation on the UK SMI bacteriology document B 40.

The comments below have been compiled from those made by the members of the IBMS' Specialist Advisory Panel for Medical Microbiology:

- Safety considerations in performing MALDI-TOF analysis for the identification of any mycobacteria strains may be worth considering.

- Report time of auramine or ZN slide should be in line with Gram strain. Reporting an AFB microscopy is suggested to be within the next working day whereas a Gram strain, on a CSF for example (SMI B27) must be verbally reported within 2hrs with a hard copy available within 24hrs.

- There is the safety briefing circulated very recently by PHE regarding M.chimaera which should also be considered for inclusion in the policy. This is obviously related to a risk of post operative infections following use of by-pass machines (see attached). The organism belongs to the M. avium complex however it would seem sensible to mention it as a separate species and list the new risks related to cardio surgery.

Further comments:

In the introduction it states "The genus Mycobacterium is a member of the family Mycobacteriaceae and consists of 168 species and 10 subspecies of which a few have been reclassified to other genera within the family" Ref 3. Euzeby,JP. List of prokaryotic names with standing in nomenclature - Genus Mycobacterium.

Comment:

According to ref 3 there are 170 species and 13 sub species yet this SMI states 168 and 10 sub species. This requires some clarification to avoid confusion.

In addition, within ref 3 states "**Note:** In 2009, Leao *et al.* proposed the union of ¤ *Mycobacterium bolletii* and ¤ *Mycobacterium massiliense*, and the recognition of two subspecies within ¤ *Mycobacterium abscessus*: *Mycobacterium abscessus* subsp. *abscessus* and *Mycobacterium abscessus* subsp. *massiliense*. The proposal of *Mycobacterium abscessus* subsp. *massiliense* was not in accordance with the Rules of the Bacteriological Code, because the epithet *bolletii* has priority over the epithet *massiliense*. Consequently, the name *Mycobacterium abscessus* subsp. *massiliense* was illegitimate. In 2011 Leao *et al.* propose the correct name *Mycobacterium abscessus* subsp. *bolletii* (Adékambi *et al.* 2006) Leao *et al.* 2011."

Comment:

There are several publications that do not agree that *M abscessus* subsp *massiliense* is an illegitimate name, see references below:

a) Comparing Mycobacterium massiliense and Mycobacterium abscessus lung

infections in cystic fibrosis patients Journal of Cystic Fibrosis 2015 Jan;14(1):63-9 Anne-Laure Roux et al

b) Molecular Fingerprinting of *Mycobacterium abscessus* Strains in a Cohort of Pediatric Cystic Fibrosis Patients *J. Clin. Microbiol.* 2012, 50(5):1758.

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c) Cohort Study of Molecular Identification and Typing of *Mycobacterium abscessus*, *Mycobacterium massiliense*, and *Mycobacterium bolletii*_ JOURNAL OF CLINICAL MICROBIOLOGY, July 2009, p. 1985–1995 Vol. 47, No. 7 Adrian M. Zelazny,1,2* Jeremy M. Root,2 Yvonne R. Shea,1 Rhonda E. Colombo,2 Isdore C. Shamputa,3Frida Stock,1 Sean Conlan,4 Steven McNulty,5 Barbara A. Brown-Elliott,5 Richard J. Wallace, Jr.,5Kenneth N. Olivier,2 Steven M. Holland,2 and Elizabeth P. Sampaio

In the section Non-Tuberculous Mycobacteria (NTM) it states " NTM are ubiquitous in nature, have a varied spectrum of pathogenicity for humans, are not transmitted from person to person and are often resistant to classical anti-tuberculous chemotherapy41,42.

Comment:

While this may be true of most NTM there are several publications confirming the transmission of *M abscessus* complex, in particular *M massiliense* in the CF population but also in other clinical settings: see references below

d) The growing threat of nontuberculous mycobacteria in CF Journal of Cystic Fibrosis (2014) Volume 14, Issue 1, Pages 1–2 R. Andres Floto * Charles S Haworth

e) Whole-genome sequencing to identify transmission of *Mycobacterium abscessus* between patients with cystic fibrosis: a retrospective cohort study: *Lancet* 2013; 381: 1551–60 R Andres Floto

f) Molecular Characterization of *Mycobacterium massiliense* and

Mycobacterium bolletii in Isolates Collected from Outbreaks of Infections after Laparoscopic Surgeries and Cosmetic Procedures_ J CLIN MICRO, March 2008, p. 850–855 Vol. 46, No. 3 Cristina Viana-Niero,1 Karla Vale´ria Batista Lima,2 Maria Luiza Lopes,

g) Phenotypic and molecular characterization of quinolone resistance in Mycobacterium abscessus subsp. bolletii recovered from postsurgical infections.J Med Microbiol. 2012 Jan;61(Pt 1):115-25.de Moura VC[1], da Silva MG, Gomes KM, Coelho FS, Sampaio JL, Mello FC, Lourenço MC, Amorim Ede L, Duarte RS.

h) Respiratory Outbreak of Mycobacterium abscessus Subspecies massiliense in a Lung Transplant and Cystic Fibrosis Center

To the Editor: AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE VOL 185 2012 Moira L. Aitken, M.D.

NTM Identification section 4.6

States "Refer to individual SMIs for organism identification. Organisms may be further identified if this is clinically or epidemiologically indicated"

Comments: As stated within ref **41**

" For some NTM isolates, especially rapidly growing mycobacterial (RGM) isolates (*M. fortuitum*, *M abscessus*, and *M. chelonae*), other identification techniques may be necessary including extended antibiotic *in vitro* susceptibility testing, DNA sequencing or polymerase chain reaction (PCR) restriction endonuclease assay (PRA)."

"Because of differences in antimicrobial susceptibility that determine treatment options, species-level identification of the NTM is becoming increasingly clinically important. Several factors increase the likelihood of clinical significance of NTM isolates, including the recovery from multiple specimens or sites, recovery of the organism in large quantities (AFB smear–positive specimens), or recovery of an NTM isolate from a normally sterile site such as blood. For initial clinical mycobacterial isolates, however, it is sometimes difficult to determine the clinical significance of the isolate without species identification. Therefore, identification of most mycobacterial isolates to the species level and not merely as groups, such as "*M. chelonae/abscessus* group" is strongly recommended. If, after consultation between the clinician and the laboratorian and in the event that a specific laboratory does not have the necessary technology for species identification of an NTM isolate, the isolate could be sent to a reference laboratory for further analysis."

Comments:

Why does this SMI document refer to MALDI-TOF for identification of *Mycobacterium* spp that has not been fully validated yet does not discuss the standard HAIN assay that is currently in use for the identification of NTM, or its limitations(see ref i below and ref 111)? With reference to NTM in particular the abscessus complex HAIN is unable to separate the members of the complex and is known to mis identify some strains as *M chelonae*. In addition there is no recommendation to refer these isolates to a specialist reference laboratory that uses molecular identification methods e.g Colindale deploys sequencing of housekeeping genes *rpoB*, *hsp65*, *sodA*, nor does it recommend strain typing of the *M abscessus* complex. Whilst this document quotes there is no evidence of person to person spread of NTM, without typing how do you know? Colindale are working toward WGS but currently strain type *M abscessus* complex using VNTR sequence cluster analysis.

This is an important point especially with respect to CF isolates as without proper identification and strain typing we will not be able to monitor *M abscessus* complex effectively. See refs d, e, f, g and h

i) Comparison of two methods for identification of Mycobacterium abscessus and Mycobacterium chelonae by K.M. Sands, A. Nicholson, C. Rennison, A. Barrett, S. Bourke, A. Robb, K. Gould, J.G. Magee Journal of Cystic Fibrosis (Vol.11) Volume 11, Supplement 1 , Page S85, June 2012 http://www.cysticfibrosisjournal.com/article/S1569-1993%2812%2960284-7/abstract?source=aemf

Rapid Growing species

States “M. abscessus more so than the other non-tuberculous mycobacterium are an increasing problem for the cystic fibrosis patient group [49]. Testing should be considered in patients who show deteriorating lung function but where no clear pathogen has been identified [50-52]”

Comments: The CF trust recommends annual screening of CF sputum for NTM, we would query why.