Mycobacterium avium complex

Fact Sheet No 1: Issue No 1 May 2007

This series of fact sheets summarises current knowledge on organisms which are known or potential pathogens, and which may have the possibility of a waterborne route of infection.

Synopsis

Mycobacterium avium is an opportunist human pathogen, which can cause tuberculosis-like symptoms, and develop into disseminated disease in the immunocompromised patient. *M. avium* can be transmitted through inhalation or by ingestion of contaminated water, food, soil or other materials. Disease caused by *M. avium* is uncommon, but rising in developed countries due to disseminated disease in patients with advanced AIDS. However, advances in AIDS therapies are beginning to reverse this trend. The organisms are found in a wide range of environments including soil, natural water and treated water distribution systems with the numbers present dependant upon chemical and physical conditions. *M. avium* is removed with varying efficiencies by standard drinking water treatment processes and shows resistance to chlorination.

M. avium is not usually recovered in the routine water labaroratory by standard analytical procedures due to the slow growth rate, and competition from other organisms. Specific methods have been developed for isolation and enumeration including decontamination methods or the use of selective media.

Genera, species and types

The genus *Mycobacterium* contains both pathogenic and non-pathogenic organisms, the most well known being *Mycobacterium tuberculosis* which is the causative agent of tuberculosis (TB) in humans. Avian tuberculosis was first described in 1890 and the organism responsible found to be a distinct species in 1891, which was later named *M. avium*. *M. avium* strains are divisible into a number of serotypes by agglutination serology and thin layer chromatography. More recently molecular methods including pulsed field gel electrophoresis (PFGE) and analysis of IS1245 have been employed for the typing of *M. avium*.

Synonyms

Mycobacterium avium Complex (MAC) is commonly used to describe a number of closely related bacteria, these have been grouped according to the similarities in culture characteristics and genetic relatedness. The close relationship between *M.intracellulare* and *M. avium* led to the introduction of the term *M. avium-intracellulare* (MAI) which arose after debate as to the uniqueness of these organisms. The term MAIS (*Mycobacterium avium-intracellulare-scrofulaceum*) may be seen in clinical settings, and refers to *Mycobacterium scrofulaceum* along with *M. avium-intracellulare*. Novel genetic techniques are able to distinguish between some or all of these species and clinically the terms are often used synonomously. *M. avium* subspecies paratuberculosis, is different from *M. avium* and is sometimes termed MAP. In this fact sheet the terms *M. avium* and MAC will be used.

Definition

M. avium are gram positive short cocco-bacilli, usually about 1 x 0.5μm in size, which may vary dependant upon growth conditions. Along with all members of the mycobacteriaceae they are characterised by their complex cell envelope containing mycolic acids which gives rise to the acid fast staining properties. Cultures of *M. avium* are differentiated from other slow growing mycobacteria by culture characteristics and drug sensitivity patterns. All strains have the ability to hydrolyse Tween 80 and *in vitro* are resistant to ciprofloxacin, streptomycin, isoniazid, and rifampicin. Cultures may be non-pigmented (non-chromogenic) or produce pigment irrespective of the light conditions (scotochromogenic).

Cultural characteristics

Growth covers a broad temperature range with all cultures growing at 25^{o}C the majority at 37^{o}C and many grow at 45^{o}C. The cultures are slow growing, 14-21 days, producing discrete grey, lemon yellow or occasionally bright yellow colonies about 1mm in diameter. *M. avium* grows well on solid media containing egg such as Lowenstein-Jensen media, and in liquid media without egg such as Middlebrook 7H9 medium.

Mycobacterium avium complex

Fact Sheet No 1: Issue No 1 May 2007

Standards and Guidelines.
Currently there are no national or international standards for *Mycobacterium avium* complex in drinking water. A water borne route has not been recognised and, as a consequence, Mycobacterium avium complex is not considered to be a pathogen in terms of the EC Directive For drinking waters.

Detection methods
M. avium is categorised as a Hazard group 3 organism and must be handled at containment level 3.

M. avium can be detected in sputum, blood and lymph node aspirates by first decontaminating where necessary with NaOH and inoculating onto Lowenstein-Jensen slopes supplemented with pyruvate and into liquid culture systems e.g. MBBacT system, an automated method of detection using modified Middlebrook media, 7H9. Identification is confirmed by macroscopic or microscopic appearance, biochemical analysis, thin layer chromatography or DNA hybridisation and molecular DNA methods.

Methods for the detection of MAC in water need to be sensitive and specific, as the target organisms will be easily out-competed by faster competitor growth rates. The standard method likely to be adopted includes concentration by membrane filtration followed by disinfection to exclude competitors from the growth medium. Inoculation of rapid automated liquid culture systems such as MBBacT is used to enhance the rate of growth.

Health Effects
Human infections due to MAC include three principal syndromes: In children, inflammation of the lymph nodes in the head and neck region (cervical adenitis), primary and secondary lung infections in adults and widespread (disseminated) infection in immunocompromised patients e.g., advanced AIDS, hairy-cell leukaemia, and inherited immune system deficiencies.

In cervical adenitis the disease usually presents in children of 1-5 years of age and is rarely seen in children over 12 years of age. The affected lymph glands are enlarged but usually painless and non-tender with little variation in size. There is rarely an accompanying illness but patients can experience lethargy and loss of appetite. Lung infections in adults can occur in otherwise healthy patients (primary MAC infection) or more often patients with an underlying or pre-existing lung disease (secondary infection). Patients usually present with infection of either one or both of the mid lung fields, and a characteristic pattern of <5mm nodules and bronchiectasis on a chest CT scan. The disease can follow spa use and be referred to as “hot tub lung”. Disseminated MAC presents with fever, weight loss, malaise and sometimes abdominal pain and diarrhoea. Enlarged liver and spleen or lymph nodes may be apparent on physical examination.

M avium subspecies *paratuberculosis* causes John’s disease, a chronic enteritis in cattle. The organism is also suspected of involvement in an inflammatory condition of the bowel in humans (Crohn’s Disease), but the evidence is inconclusive. This is covered in a separate factsheet.

Epidemiology
The oral infectious dose in humans is probably around 10^7 organisms although it is lower for the immunocompromised. Exposure to MAC is common and in healthy populations infection is rare. Where infection does occur in otherwise healthy individuals it is almost always localised in areas such as lungs or lymph nodes.

In children, organisms of the *M. avium* complex are amongst the commonest non-tuberculous mycobacteria isolated from infected cervical nodes. Reports from south east England in 1995, showed that 82% of isolates from infected cervical nodes were MAC and reports from elsewhere in England indicate similar frequencies. The number of children presenting with non-tuberculous mycobacterial adenitis appears to be increasing although this may be due to an increased awareness of the condition by clinicians. Historically, non-tuberculous mycobacterial lung infections appeared in older

patients with predisposing lung conditions such as silicosis and pneumoconiosis due to occupational long term exposure to dusts. In recent years the number of cases of pulmonary MAC in immunocompetent patients has become overwhelmed by the high frequencies of MAC infections in AIDS patients. Disseminated MAC infection occurs almost exclusively in the severely immunocompromised patient, for example, studies in the USA of HIV positive individuals show that 20% of patients with a CD4 count of less than 50 mm^{-3} will develop disseminated MAC each year. Disseminated MAC infections are more prevalent in developed countries, but epidemiological studies have shown that advanced stage AIDS patients with a lifelong exposure to soil and water appear to have a reduced risk of disseminated MAC possibly reflecting a level of acquired immunity, the exact reasons remain unclear.

Routes of transmission

The source of MAC infection appears to be the environment as there is no evidence to date of person to person transmission. Despite extensive investigation the precise mode of transmission of MAC remains undetermined. Infection is thought to occur from colonisation of the gastrointestinal or respiratory tract. This suggests exposure occurs by inhalation or ingestion and there appears to be growing evidence to indicate treated and untreated water as a primary source of infection.

Recently a number of US studies have indicated a close relationship between isolates recovered from hospital water and clinical isolates from patients in the advanced stages of AIDS. A study in Boston and New Hampshire recovered MAC in 17-25 % of distribution samples. Concentrations of MAC ranged from 0.2 100cfu/ml. It is now recognised that Hospital water systems often harbour MAC and may be a source of nosocomial infections. Over the past two decades many institutions have lowered the temperatures of hot water systems and during this same interval disease due to MAC among patients in Northeast USA with and without AIDS has increased 5-10 fold. In home water systems retention times are much lower and hot water temperatures are higher so there is less opportunity for MAC to become established.

A cross sectional study in Florida suggested that soil exposure was an important risk factor in MAC infection (Reed et al, 2006).

In a recent study isolates were recovered from reservoir outlets, inlets to 15 hospitals and hot and cold outlets within the hospital and randomly selected homes in the district. Mac was isolated from all the samples taken in the hospital, 22% of samples from homes, and 38 % of samples from reservoirs. MAC can cause respiratory infection following spa pool and swimming pool use, and as with Legionella can survive for prolonged periods in biofilm.

Reservoirs and Environmental occurrence

M. avium is ubiquitous in the environment. Organisms have been isolated from food, plants, soil, peat, house dust, natural waters, drinking water, surface water, groundwater, domestic hot water and drinking water, animals, fish and birds including poultry along with other sources. *M. avium* will grow in water to which no additional nutrients have been added. Water low in dissolved oxygen and high in organic matter and zinc supports higher numbers of MAC organisms. Single strains of *M. avium* can persist as long as 41 months in water distribution systems. *M. avium* can be isolated in large numbers from peat rich forests in Europe, Canada and the United States.

Water treatment

Water treatment processes, particularly coagulation and sand filtration, appear to reduce numbers of MAC organisms. However, removal is likely to be incomplete and re-growth or extended survival and accumulation may occur within distribution systems, either within the mains water network, or in the water systems of buildings.

Most *Mycobacterium* species survive challenge by 1mg $litre^{-1}$ free chlorine. One study of a water treatment plant showed that mycobacterial numbers were not reduced by chlorination. However, distribution data suggests that chloramines used as a post treatment disinfectant may select for *M.*

avium. High temperatures can kill off *M. avium*, although water must be held at 70^{o}C for 5-60 min to produce a 90% kill of rate. In another study 60^{0}C for 4 min was found to give a 90% reduction in MAC

Assessment of risks in drinking water
Currently it is impossible to identify the exact source of most mycobacterial infections. It has been postulated that inhalation of aerosols or ingestion of water containing MAC organisms could be prime route of infection. However, this evidence is not definitive and there is no unequivocal evidence concerning the risks from drinking water.

What's new
The WHO published a book entitled “Pathogenic Mycobacteria in Water” in 2004. This book covers the biology, ecology, disease, epidemiology and control of MAC infections (Pedley et al, 2004). It identifies four outbreaks of MAC, none of which are related to drinking water.

Date revised
May 2007

Briefing note
M. avium is a bacterium that can cause serious disease in humans. The organism is responsible for a range of illnesses in humans, from lymph node inflammation in children, to tuberculosis-like symptoms in adults and serious disseminated disease in the immunocompromised. *M. avium* infection can affect 20-40% of advanced AIDS patients.

Infection by *M. avium* is thought to occur by the inhalation of aerosols or the ingestion of organisms, rather than from person to person. *M. avium* can be isolated throughout the environment but reports are indicate that water as one of the main sources of infection. Infections and outbreaks have occurred with contaminated spa pools *M. avium* organisms show resistance to chlorination, the number of organisms found in any one distribution system will reflect differences in the pre-treatment steps used to process environmental samples, in isolation media or in water quality.

M. avium will not be detected by the standard procedures used in water microbiology laboratories for routine contamination testing. Methods for the detection of *M. avium* need to be sensitive since the numbers may be low, and specific to allow for the long incubation time. *M. avium* are identified by culture characteristics and drug sensitivity patterns.

Bibliography
Aronson T, Holtzman A, Glover N, Boian M, Froman S, Berlin OGW, Hill H, Stelma Jr G. Comparison of large restriction fragments of *Mycobacterium avium* isolates recovered from AIDS and non-AIDS patients with those of isolates from potable water. J. Clin. Micro. 1999. **37**(4), 1008-1012.

Bodmer T, Miltner E, Bermudez LE. *Mycobacterium avium* resists exposure to the acidic conditions of the stomach. 2000. Fems Micro. Lett. **182**(1), 45-49.

Falkinham JO, III. Epidemiology of infection by nontuberculous mycobacteria. Clin. Micro. Rev. 1996. **9**(2), 177-215.

Grange JM, Yates MD and Boughton E. The avian tubercle bacillus and its relatives. J. Appl. Bacteriol. 1990. **68**, 411-431.

LeChevalier MW, Abbaszadegan M, Camper AK, Hurst CJ, Izaguirre G, Marshall MM, Naumovitz D, Payment P, Rice EW, Rose J, Schaub S, Slifko TR, Smith DB, Smith HV, Sterling CR, Stewart M. Committee report: Emerging pathogens-bacteria. J. Amer. Water Works Assoc. 1999. **91**(9),101-109.

Pedley S, Bartram J, Rees G, Dufor A, Cotruvo JA. Pathogenic Mycobacteria in Water. A guide to Public Health Consequences, Monitoring and Management. 2004. WHO/IWA.

Mycobacterium avium complex

Fact Sheet No 1: Issue No 1 May 2007

Rusin PA, Rose JB, Haas CN, Gerba CP. Risk assessment of opportunist bacterial pathogens in drinking water. 1997. Res. Environ. Contam. Toxicol. **152**. 57-83.

Telles MAS, Yates MD, Curcio M, Ueki SYM, Palaci M, Hadad DJ, Drobniewski FA, Pozniak AL. Molecular epidemiology of Mycobacterium complex isolated from patients with and without AIDS in Brazil and England. 1999. Epidemiol. Infect. **122**. 435-440.

Von Reyn CF, Maslow JN, Barber TW, Falkinham JO 3rd, Arbeit RD. Persistant colonisation of potable water as a source.

What is Mycobacterium avium complex?
Mycobacterium avium is an opportunistic bacterial human pathogen, which can cause tuberculosis-like symptoms, and can develop into disseminated disease in the immunocompromised patient*?*

Can it be transmitted by water?
MAC organisms have frequently been isolated from mains water and water systems in buildings. It is capable of tolerating relatively high levels of disinfection and can survive for long periods in distribution systems. It must therefore be concluded that water has the potential to transmit this organism.

Where does it come from?
Strains of M avium complex have frequently been isolated from marine waters, rivers, streams, ponds and springs though there is some evidence to suggest that soil rather than water is the primary source.

Is it removed by treatment?
Water treatment has some effect, but frequent isolation from distribution systems suggests removal is not complete.

Does it survive in the distribution system?
Yes MAC organisms have been shown to tolerate the residual chlorine concentrations found in distribution systems and to survive for protracted periods in this environment

Is the water fit to drink?
Yes, unless you are severely immunocompromised in which case all water should be boiled before being used for consumption, food preparation e.g. washing of vegetables, ice making and cleaning teeth.

Why boil the water, What do you mean boil?
Boiling will kill any bacteria that are present in the water and prevent you from becoming ill. You should ensure that the water comes to the boil to ensure that all the bacteria are killed. Cover the water and allow it to cool before use.

Is bottled water OK?
Again bottled water is OK to drink unless you are severely immunocompromised, in which case you should boil the water as described above.

Is the water safe for pets and livestock?
Yes, cats and dogs appear to be resistant to the disease, *M. avium* can cause tuberculosis in most types of bird although how susceptible a bird is will vary from species to species. Tuberculosis is rare in sheep, goats and horses, can affect cattle, and is more frequent in pigs.

Can the water be used for washing?
Clothes can be laundered as usual. Baths and showers can be used, immunocompromised people should avoid showering as infection has been linked to the use of institutional showers, such as those found in hospitals.

Irrigation
The water is suitable for irrigation.