Epidemiology of selected mycobacteria that infect humans and other animals

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Summary
This paper provides a summary of salient clinical and epidemiological features of selected mycobacterial diseases that are common to humans and other animals. Clinical and diagnostic issues are discussed and related to estimates of the incidence and prevalence of these diseases among humans. Source of infection, route of transmission and control measures are also presented. The mycobacteria discussed in this paper are Mycobacterium bovis, M. ulcerans, M. leprae and M. avium complex, although this is by no means a complete list of the mycobacteria common to humans and other animals. Certain generalities can be made regarding these species of mycobacteria and their occurrence in humans and other animals; firstly, current understanding of the epidemiology and control of many of the resultant diseases is incomplete; secondly, environmental sources other than animal reservoirs may play a role in transmission (with M. leprae perhaps being the exception); and thirdly, the incidence and prevalence of these diseases in many countries of the world are unclear, principally because of the complexity of diagnosis and lack of reporting systems.

Keywords

Mycobacterium bovis
Aetiology, human disease and diagnosis
Mycobacterium bovis is a member of the M. tuberculosis complex of mycobacteria, a group of mycobacterial species that includes M. tuberculosis, M. bovis, M. africanum and M. microti. A smooth colony variant of M. tuberculosis, named M. canetti, has been proposed as an additional member of this complex. The above-mentioned species are slowly growing, non-photochromogenic acid-fast bacilli (84). Infection of humans with any one of these four mycobacteria can result in the disease termed 'tuberculosis', and regardless of the species responsible, the resulting disease is indistinguishable clinically, radiologically and pathologically (108). However, prior to bovine tuberculosis control programmes, and in areas of the world in which milk is still the primary vector for M. bovis, this species was and is more commonly associated with primary tuberculosis outside the lung (extra-pulmonary disease) (65, 99). Prior to the control of bovine tuberculosis and the implementation of pasteurisation programmes in Northern Europe, the majority of cases of M. bovis infection among humans were extra-pulmonary, with the following organ systems being affected in decreasing order of frequency: lymph nodes, skin, skeletal, genito-urinary and central nervous system (meningitis) (57, 66, 124).

Following exposure, development of disease in humans depends on the ability of the mycobacterium to establish infection and grow within host cells. Some evidence suggests that M. bovis does not establish itself in humans as readily as M. tuberculosis (57). Following infection, M. bovis is phagocytosed by macrophages, and is carried to lymph nodes, parenchyma of the lung and other sites. In macrophages, bacilli resist being killed by blocking maturation and fusion of phagosomal compartments, and limiting their differentiation into active vacuoles (7, 58, 59, 60), and natural resistance to the oxidative burst (89, 137, 139). Thus, the bacilli are able to multiply, destroy phagocytes and escape into intracellular
spaces. This, in turn, stimulates the accumulation of other phagocytes, creating the typical histopathological lesion of tuberculosis—the granuloma. These granulomas can continue to expand with new phagocytic cell infiltration, giant cell formation and fibrosis. Eventually, macroscopic lesions known as tubercles are formed (139). The resulting disease is known as tuberculosis. The incubation period can last from weeks to decades.

Although the diagnosis of tuberculosis can be performed using radiology and microscopic examination of smears of sputum (or other secretions or tissues) using acid-fast or other stains, the identification of the specific aetiological agent (as M. bovis or another mycobacterium) depends on the ability to culture the organism and identify any mycobacteria that are isolated (25, 108). Both culture and identification of these mycobacterial species are complicated, potentially dangerous, and require expertise that is common in the developed world, but extremely rare in the developing world. Since identification of the infecting species has minimal effect on management of the tuberculosis patient, there is little incentive from health care providers to identify the mycobacterial species associated with tuberculosis. In the United States of America (USA), the current molecular probe diagnostic assay, which is routinely used for confirmation of suspected tuberculosis cases, does not distinguish among the species of the M. tuberculosis complex.

Incidence, prevalence and groups at risk

As identification of the species of infecting mycobacteria among tuberculosis cases is not routine in most of the world, and because no specific serological or skin test exists, the precise incidence and prevalence of human disease caused by M. bovis are unknown. However, the burden of M. bovis infections among humans can be estimated from existing data of tuberculosis incidence and data regarding the proportion of tuberculosis due to M. bovis in various parts of the world (52, 85). In Europe and North America, 0.5% to 1.0% of human tuberculosis cases are estimated to be a result of M. bovis infection (69, 121, 123, 150). This represents a considerable reduction since the 1960s and the intensification of bovine tuberculosis control programmes, before this time, the proportion of cases due to M. bovis was between 5% and 20% (62). In countries in which bovine tuberculosis is still common and pasteurisation of milk rare, an estimated 10% to 15% of human cases of tuberculosis are caused by M. bovis, an annual incidence world-wide of between 90,000 and 1,350,000 cases of M. bovis-associated tuberculosis can be estimated. The prevalence of bovine tuberculosis in the world has been recently reviewed (31).

Sub-populations at risk for M. bovis infection include any population consuming unpasteurised contaminated milk, abattoir workers, veterinarians, hunters and HIV-infected or other potentially immunologically-compromised populations (36, 37, 62, 64, 88, 119). Given that both HIV and M. bovis transmission are high in Africa, with 90% of the population of Africa living in areas where neither pasteurisation nor bovine tuberculosis programmes occur and up to one in ten adults being infected with HIV, the association between these two diseases is of particular concern for much of this continent (88).

Source of infection, route of transmission and infectious dose for human disease

Mycobacterium bovis causes tuberculosis in a broad range of mammalian hosts including cattle and other ruminants, felids, canids, lagomorphs, porcids, camelids, cervids and primates including humans (12, 15, 16, 20, 24, 26, 29, 30, 43, 56, 100, 102, 123, 136). Infection in livestock and wild animals is discussed in more detail in the papers by Cousins, de Lisle et al. and Skinner et al. in this issue of the Review (32, 44, 127). Maintenance of M. bovis is believed to be primarily related to ruminants, although other species of animals have been demonstrated to maintain infection from generation to generation (20, 102). Unpasteurised contaminated milk (133) and other secretions or tissues from any of these species (but primarily from cattle) can serve as the source of infection for humans (62). Although M. bovis may survive in soil, on fomites and in faeces for days to months, depending on local environmental conditions and sunlight, this is not considered an important source of infection for humans (but may be for cattle) (6, 47, 90).

Mycobacterium bovis can enter human hosts through ingestion, inhalation or direct contact with mucous membranes or broken skin. Milk is still regarded as the principal vehicle for transmission to humans in countries where bovine tuberculosis is not controlled. Infection in livestock and wild animals is more often associated with scrofula, abdominal tuberculosis and other extra-pulmonary forms of the disease (124). Among cattle, M. bovis is spread primarily by the respiratory route, and humans can also be infected by this route (34, 88, 119, 126). Although considered uncommon, contact of contaminated animal products with broken skin can lead to cutaneous tuberculosis, also known as butcher's or prosector's wart (63). Whatever the route, the infectious dose for humans is unknown, but estimated to be in the region of tens to hundreds of organisms by the respiratory route and millions by the gastrointestinal route (108). Based on animal models and outbreak investigations, the infectious dose is known to
be influenced by species of host (potentially higher for humans than cattle), other host factors (e.g. immune status), route of infection (higher for ingestion) and strain of bacteria (108).

Human-to-human infection has been reported (67, 143), but is considered unlikely (62). One report of human-to-human transmission was among HIV-infected individuals in a hospital setting (67), suggesting that the HIV epidemic might increase the potential for human-to-human spread of M. bovis.

Control
As this disease is primarily transmitted from cattle to humans in milk, control of human infection can be achieved by pasteurisation and control of bovine tuberculosis. Testing of cattle with an intradermal tuberculosis test (or by inspection at slaughter), combined with removal or quarantine of infected herds and pasteurisation of milk, has proven very effective in reducing the incidence of M. bovis infection in humans (26, 102, 108). Elimination is complicated by the several wildlife reservoirs of M. bovis present in most countries of the world (43, 56, 122). However, practical elimination of human infection can be achieved with a control programme targeting only domestic animals. Such control programmes may appear simple, but require the following elements:

a) political commitment to control the disease
b) public agreement regarding the benefit
c) adequate public funding for a potentially very expensive disease control programme
d) an extensive public or private veterinary infrastructure
e) organised meat inspection for identification and tracing of infected herds
f) availability and maintenance of skin test antigen for identification of infected animals
g) a centralised dairy industry that employs pasteurisation or public education regarding the risks of unpasteurised dairy products.

Without these requirements, as seen in much of the developing world, M. bovis will continue to be a common public health problem.

Mycobacterium ulcerans

Aetiology, human disease and diagnosis
Mycobacterium ulcerans is a slow-growing acid-fast bacillus that causes a cutaneous infection known as Buruli ulcer, now considered the third most common mycobacterial infection in immunocompetent humans (8, 115). In common with M. haemophilum and M. marinum, M. ulcerans prefers low temperatures (32°C), which may restrict spread to the body surfaces (45). Unusual among mycobacteria, M. ulcerans produces one or more polyketide toxins strongly implicated in disease (45, 86). The disease is believed to begin with the entrance of the organism into the dermis or subcutis, where following a latent period of undetermined length, the bacteria proliferate and secrete toxin (74, 80). The toxin appears to cause preferential necrosis of adipocytes, without provoking a local inflammatory response. At this stage, a pre-ulcerative lesion may become clinically apparent in the form of a painless, palpable subcutaneous nodule. Alternatively, active disease can first manifest as a raised papule, a diffuse, non-pitting oedema or a well-defined, elevated, indurated plaque (8). Histopathological examination at the pre-ulcerative stage reveals abundant acid-fast bacilli in the centre of a region of fat necrosis. Without treatment, a pre-ulcerative lesion may progress to an ulcer over the course of several weeks to months (107, 125). Progressive penetration of the mycobacterial toxin through the panniculus, in combination with destruction of blood vessels, causes extensive necrosis within the dermis. Damage to the epidermis results, leading to an ulcer with deeply undermined edges, often reaching the fascia, but not affecting the muscle (74, 80, 142). In the ulcerative stage, microcolonies of acid-fast bacilli are observed in the necrotic base of the ulcer or in the necrotic fat at the ulcer margin, which can extend quite far underneath the damaged skin. Healing starts with the formation of granulation tissue at the base of the ulcer, and may be linked to the initiation of a cell-mediated immune response (138). Healed ulcers are often marked by a characteristic depressed stellate scar. Serious sequelae include contraction deformities, ankylosis and, less frequently, osteomyelitis and amputation (142). The existence of disseminated disease arising from recurrent M. ulcerans infection is controversial (80, 113). The incubation period for active disease is unknown, but estimates range between one to four weeks and three to four months (5, 125).

Currently available diagnostic methods for Buruli ulcer are time-consuming and labour-intensive. Culture of M. ulcerans from clinical specimens is expensive, difficult and insufficiently sensitive (142). Ziehl-Neelsen staining for acid-fast bacilli is the simplest method to confirm M. ulcerans infection, but commonly yields false-negative results (142). Histopathological examination of lesions is considered to be a time-tested, sensitive and reliable technique, but requires significant expertise (27, 74). Recently, polymerase chain reaction (PCR) has been used to detect the M. ulcerans-specific insertion sequence, IS2404, in clinical specimens (68). The sensitivity of this repetitive sequence PCR technique compares favourably with histology (68). Other PCR techniques (such as amplified fragment length polymorphism [AFLP]) and 16S ribosomal ribonucleic acid (rRNA) sequencing hold great promise for fingerprinting strains to characterise transmission patterns within particular regions (8, 68, 111, 112). However, the areas in which Buruli ulcer is highly endemic are developing countries where PCR technology is restricted to specialised reference laboratories and therefore is impractical for routine diagnosis. As a result,
diagnosis based on clinical criteria prevails in those areas in which *M. ulcerans* infection is most common.

**Incidence, prevalence and groups at risk**

Buruli ulcer occurs in tropical countries, with prominent foci in West Africa (3, 38, 97, 101, 104), Central Africa (9, 42, 128) and the Western Pacific (23, 72, 118). Cases have also been reported from Asia and the Americas (8, 51, 140). The true incidence and prevalence of the disease world-wide is unknown, due to inadequate surveillance data at national and international levels. Moreover, the routine lack of case confirmation, and the likely under-reporting from passive surveillance systems, renders an estimation of the global burden of Buruli ulcer difficult.

Incidence and prevalence have been reported in a few locations under special circumstances. In Uganda, cases of Buruli ulcer were observed for the first time in a group of 2,500 refugees from Rwanda that had been moved to a camp near the Nile River in 1964. This cohort was monitored intensively until 1970, when the population moved away from the endemic area (5). The highest annual rate recorded was 7/100 people in the ten- to fifteen-year-old age group in 1966 and 1967 (5).

In endemic villages of the Amanse West District of Ghana, prevalence has been reported to range from 4% to 24% (8). In the course of conducting a case-control study in the Daloa Region of Côte d’Ivoire, overall prevalence of past or present Buruli ulcer was estimated to be between 1.3% and 1.6%, reaching 16% in certain villages (8). Populations at risk appear to be those in tropical climates, exposed to stagnant, slow-moving water sources. In almost all of the case series analysed, the sexes are equally represented, but children between the ages of two and fifteen years are disproportionately affected. The reasons are unknown, but some aspect of behaviour among children is presumed to place them at higher risk. In Africa, the majority of those afflicted are poor rural farmers who live adjacent to swampy environments; farming near the Lobo River was found to be a risk factor in a case-control investigation. However, the disease does not discriminate by race or socio-economic status; in Australia, Buruli ulcer appeared in a relatively wealthy white community near an irrigated golf course (120).

**Source of infection, route of transmission and infectious dose for human disease**

Despite the long-standing inability to culture *M. ulcerans* from environmental specimens (11, 134), the organism is clearly associated with swampy, riverine environments with stagnant, slow-moving bodies of water. Another key feature of outbreak settings is environmental change, for example the damming of a stream to create an artificial lake on a university campus in Nigeria (107), flooding in Uganda (73), irrigation of a golf course with water from a swamp created by damming in Phillip Island in Australia (120). A suggested mode of transmission is through predaceous insects of the genera *Naucoris* and *Diplonychus* that feed on other water-filtering organisms, and could passively concentrate *M. ulcerans*, subsequently transmitting the organism to humans via bites (114, 134). Koalas, rats and possums have been shown to be naturally infected in endemic areas of Australia (14, 75, 98), and armadillos can be infected experimentally (147).

The route of infection is unknown. The organism is postulated to enter at sites of trauma to the skin (94). No confirmatory evidence exists for human-to-human transmission (10), although prolonged skin-to-skin contact leading to ulcer has been suggested (8). Animal models for *M. ulcerans* infection exist, including mice, guinea-pigs and armadillos, but it is difficult to extrapolate these data to humans. Inoculation of $10^2-10^4$ colony-forming units (CFU) is sufficient to induce swelling in the mouse footpad model (40), but the infectious dose for humans is not known.

**Control**

Due to a fundamental lack of understanding of the mechanism of disease transmission, prevention strategies have not been developed. Vaccination with bacillus Calmette-Guérin (BCG) has been suggested to have a moderate, short-lived protective effect against Buruli ulcer (4, 130). Currently, control methods in endemic countries are limited to early diagnosis and surgical treatment. Surgical intervention at the pre-ulcerative stage of disease can prevent the development of the ulcerative disease. However, well-controlled clinical trials have not been published. Education of the population at risk may be an important strategy to reduce the marginal increased morbidity and mortality that results from delayed treatment.

**Mycobacterium leprae**

**Aetiology, human disease and diagnosis**

*Mycobacterium leprae* is a slowly growing, acid-fast bacillus which causes leprosy. *Mycobacterium leprae* grows best between 27°C and 30°C, thus restricting the disease to cooler areas of the human body. Attempts to culture *M. leprae* on artificial media have proved unsuccessful, but fortunately, the use of animal models such as the armadillo, nude mouse and the mouse footpad has allowed therapeutic, pathological and immunological studies to be undertaken (82). Much of the pathogenesis of *M. leprae* infection remains unknown (2).

Among persons who develop disease, the incubation period can last between five and twenty years (154). Many patients may develop single lesions that self heal (intermediate leprosy). Without treatment and in the absence of self-healing, the disease progresses to the paucibacillary or multibacillary stage (54). The World Health Organization (WHO) defines paucibacillary leprosy as five or fewer skin lesions with no acid-fast bacilli on skin smears, and multibacillary leprosy as six or more lesions with positive acid-fast bacilli (154).
Diagnosis is based on clinical suspicion of anaesthetic or hypoanaesthetic cutaneous lesions as well as palpation of peripheral nerves for enlargement and/or tenderness with sensory and motor evaluation, followed by confirmation via biopsy of the skin lesion (82). The Ziehl-Neelsen staining technique can be employed to examine nasal excretions for acid-fast bacilli in individuals with lepromatous or borderline leprosy, whereas the Fite-Faraco stain is recommended for histopathological preparations (28). The development of additional diagnostic assays such as measurement of phenolic glycolipid-I (PGL-I) antibodies, deoxyribonucleic acid (DNA) specific probes, and DNA amplification of M. leprae may allow for a more rapid, specific diagnostic test for leprosy. These techniques may be used to complement clinical and histopathological diagnosis in patients when definitive diagnosis is hampered by a lack of bacilli (17, 83, 151). The latter techniques are not widely available in the developing world.

Incidence, prevalence and groups at risk

The true incidence of leprosy is unknown (55, 131). The WHO uses prevalence as an indicator for world-wide leprosy by using case detection rates (CDR; i.e. all new cases registered annually at health care facilities). This figure is inherently flawed as an indicator of incidence for several reasons. Many factors prevent infected people from seeking treatment (e.g. the long incubation period, the stigma of diagnosis of leprosy and the inaccessibility of health services), therefore many 'new cases' are not new but represent a hidden 'backlog'. In addition, duplicate registering, relapse cases, and identification of cases that self-heal may inflate the number of new cases registered (144).

At the beginning of the year 2000, 738,284 new cases were registered (12.3/100,000), 753,263 cases were in treatment (1.25/100,000) and 10,759,213 people were cured with multi-drug therapy (MDT). South-East Asia accounted for 84.2% of new cases, followed by 7.5% in Africa. In 1999, the following thirty-two countries reported a leprosy prevalence exceeding 1/100,000: Bangladesh, Benin, Brazil, Burkina Faso, Cambodia, Chad, Colombia, Congo, Democratic Republic of the Congo, Côte d’Ivoire, Egypt, Ethiopia, Guinea, India, Indonesia, Madagascar, Mali, Mexico, Mozambique, Myanmar, Nepal, Niger, Nigeria, Pakistan, Philippines, Senegal, Sudan, Thailand, Venezuela, Vietnam, Yemen and Zambia. Eleven countries accounted for 672,596 registered cases: India, Brazil, Myanmar, Indonesia, Nepal, Madagascar, Ethiopia, Mozambique, Democratic Republic of the Congo, Tanzania and Guinea. During the 1990s, the registered prevalence decreased dramatically, but currently shows signs of levelling off (154).

Source of infection, route of transmission and infectious dose for human disease

The principal reservoir of M. leprae is humans. Mycobacterium leprae is transmitted through frequent close contact with untreated, infected persons by droplets from the nose and mouth, whereas dissemination through skin lesions seems to be of lesser importance (1). Mycobacterium leprae is not thought to be extremely pathogenic, since most infections do not result in disease. Polymerase chain reaction studies on nasal carriage suggest that infected individuals have a period of transient nasal excretion, lending evidence to temporary carriage or subclinical infection, and further indicating the poor ability of M. leprae to cause disease (33, 70, 141). The infectious dose of M. leprae for humans is unknown.

Infection and disease also occurs naturally in wild animals. Natural M. leprae infections have been documented in the nine-banded armadillo (Dasypus novemcinctus), the sooty mangabey monkey (Cercocebus atys), and in chimpanzees (46, 95, 96, 129). Aerosol transmission and maternal milk are probable routes of transmission among armadillos (148). No concrete evidence has been uncovered to suggest that any of these animals serve as the reservoir of human infection.

Control

Current efforts to control leprosy are dependent upon early detection of infection, adequate treatment using MDT with rifampicin, clofazimine and dapsone, and examination of contacts of the index case. Public education to reduce the stigma associated with leprosy as well as effective treatment is essential for the control of the disease. Multi-drug therapy is recommended for twelve months for multibacillary patients and six months for paucibacillary patients. Many countries employing the MDT according to WHO guidelines have been successful in achieving a significant reduction in the prevalence and number of new cases detected. The WHO target prevalence level is 1/10,000. Prevalence is used as a tool to measure the success of the elimination strategy rather than incidence, due to the long incubation period before disease development and the lack of tools to measure infection and disease status. Thus, new cases will continue to occur despite implementation of MDT, because of the long incubation period. Expansion of MDT to poorly served areas in endemic countries will further reduce the increase as new cases appear. Contact examination will remain an important aspect of control in addition to patient follow-up to maintain compliance with MDT (154).

Mycobacterium avium complex

Aetiology, human disease and diagnosis

The M. avium complex (MAC) of mycobacteria addressed in this section includes both M. avium and M. intracellulare. These are slowly growing, non-photochromogenic, acid-fast bacilli that were first isolated from birds in the 19th Century (149). The first case of human disease due to M. avium was reported in 1943, in a middle-aged man with underlying lung disease (53). Following an incubation period suspected to be weeks to months, infection of humans with these mycobacteria can lead to three basic forms of disease: pulmonary disease, lymphadenitis and disseminated disease. However, any organ system may be affected. Disease due to
MAC can occur among healthy or, more commonly, among immunologically compromised populations. The disease is characterised, on pathological examination, by granuloma and tubercle formation. The pulmonary form of MAC infection has been observed primarily in white males from forty-five to sixty-five years old, with underlying lung disease (49, 50, 146). The symptoms of this form of MAC infection are non-specific, with fever, weight loss, non-productive cough, dyspnoea, sweats, fatigue and haemoptysis. Cavitational lesions, diffuse interstitial infiltrates and nodular lesions have all been described following radiographical examinations of the chest (22, 116). Mycobacterium avium complex is a common cause of granulomatous lymphadenitis in children of one to five years of age. This form of MAC infection is characterised by painless unilateral enlargement of cervical, sub-maxillary, sub-mandibular or pre-auricular lymph nodes (13, 61). Disseminated disease rarely occurs in individuals not affected by acquired immune deficiency syndrome (AIDS) (77). Prior to the availability of antiviral therapy for HIV infection, disseminated MAC infection was the most frequent bacterial complication of AIDS, constituting 45% or more of AIDS-defining infection in the USA, Japan and Europe (76). Among AIDS patients, disseminated MAC infection is characterised by weight loss, fever, anemia, sweats, diarrhoea and anorexia (although none of these are pathognomonic signs) (76, 156). A CD4 cell count of less than 100 is an important predisposing risk factor (79). Disseminated MAC infection usually involves widespread involvement of the reticuloendothelial system, with resulting hepato-splenomegaly and lymphadenopathy (117).

The diagnosis of disease caused by MAC requires isolation of the organism and compatible clinical and pathological features. Respiratory tract colonisation can occur and must be distinguished from disease (21, 132). The microscopic appearance of M. tuberculosis and MAC bacteria are identical, and culture and identification by biochemical analysis or DNA probes are required to distinguish these species. Culture from a normally sterile tissue source, such as blood, is highly correlated with disseminated MAC (71, 135). Culture and identification of MAC require expertise that is common in the developed world, but extremely rare in the developing world.

Incidence, prevalence and groups at risk

The true incidence and prevalence of MAC infection world-wide are unknown. Prior to improved combination therapy for HIV infection, between 25% and 50% of AIDS patients in the USA were infected with MAC (76, 105), and proportions were similar in other parts of the developed world (39, 78, 110). Since the introduction of potent anti-retroviral therapies, these proportions have been considerably reduced in the developed world. In one study conducted between 1994 and 1997, the period when these new anti-HIV therapies were being introduced, the rates of MAC disease decreased from 22 to 4 cases per 100 AIDS patient person years (109). Available data suggest that, even before the introduction of improved anti-retroviral therapies, the incidence of MAC infections among AIDS patients in the developing world was low (103, 106). As stated, the primary risk groups are immuno-compromised populations in the developed world, and possibly patients with chronic lung disease.

Source of infection, route of transmission and infectious dose for human disease

Mycobacterium avium complex is ubiquitous in the environment, and has been isolated from water, soil, food, dust and domestic and wild animals (81, 152, 153, 155). Mycobacterium avium infection is an important disease of poultry and swine, and the pathogen is commonly excreted in the faeces of birds, but not swine (92). However, no particular source has been identified as being more likely for human infection, and the mode of transmission and route of infection are unknown. Hospital water systems appeared to be the source of infection in one cluster of five AIDS patients affected by MAC (145). Ingestion has been postulated as the route of infection for AIDS patients (19, 35). Results of skin test surveys of relatives and housemates of case-patients suggest that human-to-human transmission of M. avium did not occur (48). The infectious dose for humans is unknown.

Control

Control strategies for interrupting transmission are not possible without knowledge of sources of infection and routes of transmission. In addition, due to the ubiquitous presence of M. avium, strategies aimed at controlling particular sources are not likely to be successful. Control strategies among AIDS patients have been limited to reducing the likelihood of developing disease through the use of chemoprophylaxis (18). Chemoprophylaxis with clarithromycin or azithromycin has been demonstrated to reduce the likelihood of developing MAC disease among AIDS patients (18). Furthermore, improved anti-retroviral therapy also contributes to controlling the incidence and prevalence of this disease (109). Morbidity and mortality can also be reduced through early use of combined therapy with at least clarithromycin and ethambutol (91).
Épidémiologie de quelques maladies dues à des mycobactéries communes à l’homme et aux animaux

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Résumé
Les auteurs présentent un résumé des principales caractéristiques cliniques et épidémiologiques de quelques maladies dues à des mycobactéries communes à l’homme et aux animaux. Ils traitent ce sujet sous l’angle de la clinique et du diagnostic ainsi que de la relation avec les estimations relatives à l’incidence et à la prévalence de ces maladies chez l’homme. Ils passent également en revue les sources d’infection, les modes de transmission et les mesures de prophylaxie. Les mycobactéries objet de cet article sont Mycobacterium bovis, M. ulcerans, M. leprae et le complexe M. avium, sachant que cette liste des mycobactéries communes à l’homme et aux animaux n’est en aucun cas exhaustive. Ces espèces de mycobactéries et leur présence chez l’homme et les animaux appellent plusieurs remarques à caractère général ; tout d’abord, la connaissance de l’épidémiologie et de la prophylaxie de nombre de maladies qui en résultent est, pour le moment, incomplète ; ensuite, des sources d’infection présentes dans l’environnement, autres que les animaux réservoirs, peuvent jouer un rôle dans la transmission (à l’exception, peut-être, de M. leprae) ; et, enfin, on ne connaît pas encore avec précision l’incidence et la prévalence de ces maladies dans nombre de pays, essentiellement en raison de la complexité du diagnostic et de l’absence de systèmes de notification.

Mots-clés
se conoce con precisión el nivel de incidencia y prevalencia de esas enfermedades en muchos países del mundo, debido principalmente a la complejidad de su diagnóstico y a la falta de sistemas de notificación.

**Palabras clave**

**References**


