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Review Article

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Summary — *Mycobacterium avium* causes tuberculosis in chickens and other fowls but can also infect an extensive range of different animal species. The authors reviewed the available literature on this organism to show the importance of *M avium* infection.

***Mycobacterium avium* / tuberculosis / bird / domestic mammal / wild mammal**

Résumé — **Infections à *Mycobacterium avium* chez l'animal.** *Mycobacterium avium* est à l'origine de la tuberculose chez la poule et chez d'autres oiseaux. Elle peut également infecter un éventail très vaste d'espèces animales. Les auteurs font la revue de la littérature sur cet organisme pour démontrer l'importance de l'infection à *M avium*.

***Mycobacterium avium* / tuberculose / oiseau / mammifère domestique / mammifère sauvage**

INTRODUCTION

Mycobacterium avium is an ubiquitous opportunist pathogenic bacillus frequently found in humans and animals (Feldmann, 1938; Haffar, 1994; Zorawski, 1995). In animals, this mycobacteria is responsible for infections in a very large range of species, particularly in swine. Moreover, *M avium* is the agent of poultry tuberculosis. In the environment, domestic and wild birds can become infected by ingesting food and/or soil contaminated with *M avium* excreted in large quantities in the feces of

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sick birds. In other animals, the infection is also caused by ingestion of poultry or contaminated soils (Inderlied et al, 1993)

In the laboratory, *M avium* is the most frequently isolated *Mycobacterium* after *M bovis*. We isolated *M avium* mainly from pigs and birds but also from cattle, goats, dogs, cats, horses and wild animals (table I).

This paper is divided into three sections. The first part describes the disease in birds, the second part describes the disease in domestic animals (cattle, swine, goats and sheep, horses, cats and dogs, farmed deer) and the last part deals with non-domestic mammals (wild animals)

DISEASE IN BIRDS

Tuberculosis in chickens and captive and wild birds is considered to be a contagious disease. The disease caused by *M avium* serovars 1, 2 or 3 is characterized by its chronic nature, its persistence in a flock or aviary once established, and its tendency to induce wasting and finally death. The disease occurs in domestic and wild birds in many countries. *M avium* has been reported in a wide variety of fowl, game birds, waterfowl and birds of prey (Thoen et al, 1984; Brown et al, 1992; Shane et al, 1993; Singbeil et al, 1993; Thorel and Moutou, 1994; Cvetnic et al, 1994; Van der Heyden and Kornelsen, 1994; Haffar, 1994; Hoop et al, 1994; Reed and Johnson, 1994, Snyder et al, 1994; Morita et al, 1994a; Hejlicek and Treml, 1995a; Stanz et al, 1995; Tully et al, 1995).

A major problem in the elimination of the disease is related to the ability of the organism to survive in the soil.

Clinical signs: few symptoms of the disease are commonly observed in chickens and birds. An infected bird appears in poor physical condition during the advanced stages of the disease. The feathers may develop a dull and ruffled appearance and the comb and wattles become anemic. On palpation of the abdomen of the emaciated

Table I. *Mycobacterium avium* isolated from animals during a 6-year period (1990–1995).

Animal species	*Number of* M avium *isolates*[a] *in France*	*Number of* M avium *isolates*[b] *in South Africa*
Cattle	26	4
Pig	45	389
Fowl	20	2
Other birds	10	3[d]
Wild animals	8[c]	3[e]
Farmed crocodiles	–	3
Laboratory animals	2	–
Cat	1	–
Dog	–	3
Total	110	407

[a] Isolates made from tissues submitted to Centre national d'études vétérinaires et alimentaires (Cneva) à Maisons-Alfort, France. [b] Isolates made from tissues submitted to the Tuberculosis Laboratory, Onderstepoort Veterinary Institute, Onderstepoort South Africa. [c] *M avium* was isolated from one kangaroo, six red deers and one roe deer. [d] *M avium* was isolated from one greeflying falcon, one parrot and one farmed ostrich. [e] *M avium* was isolated from one warthog and one buffalo from Kruger park, and one gorilla from National Zoological Gardens, Pretoria, South Africa.

birds, the liver may be hypertrophied and nodular masses may be detected along the intestine. Affected birds die within 2 months or may survive for 6 months depending on the extent of disease.

On necropsy, macroscopic lesions are most often seen in the liver, spleen, intestine and bone marrow. Disease is characterized by greyish white nodules of varying sizes in the organs. The liver and spleen are generally enlarged.

Histopathologic examination of a spleen with lesions usually reveals granulomas characterized by a central area of necrosis and an outer zone of epithelioid cells. Multinucleated giant cells are located around the periphery of the central areas of necrosis. Lesions in the liver can contain a central area of necrosis surrounded by an accumulation of epithelioid cells. Numerous acid-fast bacilli are often found in lesions after staining by the Ziehl Neelsen method. Microscopic examination of intestine sections may reveal typical granulomas characterized by central areas of caseous necrosis. In some instances, however, such as in early stages of infection, the lesions may appear as diffuse accumulations of lymphocytes and epithelioid cells.

A presomptive diagnosis of tuberculosis in fowls can usually be made on the basis of gross lesions present at necropsy (spleen and liver) and the finding of acid-fast bacilli in lesion smears. To confirm a diagnosis, it is essential to isolate and identify the organisms using bacteriological and serological procedures.

A tuberculin skin test on the wattles provides a satisfactory method for determining whether or not tuberculosis is present in a flock of chickens.

A rapid whole blood agglutination test has been reported to have a reliability comparable to that of the tuberculin skin test (Pavlas et al, 1993; Cromie et al, 1993).

Avian tuberculosis has been reported in free flying birds and is common in exotic birds maintained in captivity. In the unnatural environment of captivity the incidence of the disease frequently equals or exceeds that found in domestic species of fowl.

DISEASE IN DOMESTIC MAMMALS

Swine

M avium complex serovars 1, 2 and 3 are the acid-fast organisms most frequently isolated from granulomatous lesions in swine. However, numerous other strains of *M avium* complex serovars 4 to 23 have also been isolated from swine. Their importance as pathogens in the animals is considered less significant. One exception is the occurrence of *M avium* serovar 8 infections in large confined swine herds (Thorel, 1980; Knudsen, 1992; Leinemann, 1993; Leinemann et al, 1993; Morita et al, 1994 b, c).

Epizootics of infection have been observed in many countries of the world. Epidemiological studies on mycobacterial lymphadenitis indicate that the environment may represent a possible source of infection. Because swine are not routinely tested for tuberculin, the only sources of information on the prevalence of the disease are data obtained from meat inspection records. (Thoen et al, 1984; Carpenter and Hird, 1986; Gardner and Hird, 1989; Alfredsen and Skjerve, 1993; Szazados, 1993; Margolis et al, 1994; Sigurdardottir et al, 1994).

Tuberculosis lesions in swine usually involve the lymph nodes of the head and neck or the mesenteric nodes. The disease may be localized or may involve a number of lymph nodes along the intestinal tract. Some cases involving lesions exclusively located in bronchial lymph nodes have also been observed (Di Guardo et al, 1991).

On necropsy, the lesions due to *M avium* complex are not easily enucleated. Diffuse granulomas with large areas of caseation may be present; however, usually there is little or no evidence of mineralization.

Microscopically, the changes induced in the swine lymph node by *M avium* are characterized by central areas of caseous necrosis bordered by epithelioid and giant cells that form focal granulomas. Many appropriately stained acid-fast bacilli can usually be observed in the lesions. Generalized tuberculosis is not commonly seen in swine. Only about 1% of the cases provide evidence that the disease has extended beyond the regional lymph nodes to other tissues.

No consistent differences are observed in lesions from which the different serotypes of *M avium* complex are isolated.

A clinical diagnosis of tuberculosis in swine is based on the use of tuberculin skin tests using avian PPD tuberculin, but generally tuberculosis in swine is observed at the slaughter-house. Serological procedures have been developed, such as enzyme-linked-immunosorbant assay, for detecting circulating antibodies in the sera of infected swine. Diagnosis of *M avium* complex infection requires isolation and identification of the acid-fast organism.

Cattle

The susceptibility of cattle to *M avium* is well established. Serovars 1 and 2 are the strains of *M avium* most commonly isolated from slaughtered animals.

The importance of these infections is magnified as the incidence of bovine tuberculosis is reduced to low levels because these organisms can cause non-specific tuberculin reactions in cattle (Thorel, 1978; He et al, 1994; Tkatschenko and Schewziw, 1994; Hejlicek and Treml, 1995b; Bastawrows et al, 1995).

The lesions are limited to the lymph nodes of the digestive tract (retropharyngial and mesenteric lymph nodes) and the pulmonary lymph nodes (tracheobronchial and mediastinal). Some other localizations are also observed in the liver, spleen, kidney, lung and peritoneum and sometimes in the mammary glands and genitals causing mammitis and abortion. However, cases of generalized disease have been reported.

The histopathologic changes observed in the lymph nodes are characterized by disintegration and necrosis with giant cells of a Langhans type and numerous acid-fast bacilli.

On necropsy, the lymph node lesions due to *M avium* complex are difficult to distinguish from those caused by *M bovis*. The pathogenicity of *M avium* has been studied in calves inoculated with *M avium* serotype 2 and 8. The lesions initially observed were caseocalcareous granulomas that became encapsulated and non-progressive, and which were confined to the inoculation sites and their regional lymph nodes. In the same study, calves inoculated with similar doses of *M bovis* showed disseminated progressive lesions without encapsulation (Mc Gavin et al, 1977).

The way to distinguish between *M bovis* and *M avium* is to culture the lesions found at slaughter, or in a field situation to use the comparative cervical tuberculin test (Badger, 1988).

Deer

Deer are susceptible to tuberculosis caused by *Mycobacterium* spp (Griffin, 1988; Arora, 1993; De Lisle et al, 1995).

Deer tuberculosis is similar to that found in cattle and is mostly caused by *M avium* or *M bovis*. Members of *M avium* complex have been cultured from deer but were only associated with clinical disease in a few cases (De Lisle and Havill, 1985). Isolates

come from animals reacting to the skin test and from lesions detected at meat inspection. One red deer had lesions in the submaxillary and prescapulary lymph nodes, another had lesions in the retropharyngeal lymph nodes and one roe deer had lesions in the mesenteric lymph nodes and Ziehl-Neelsen's method of staining revealed numerous acid-fast bacilli. One deer had generalized tuberculosis with caseous adenitis.

The histological findings were necrosis and granulomatous lymphadenitis, rich in epithelioid cells, a few giant cells and numerous acid-fast bacilli.

Infection of animals with *M avium* may produce caseocalcified lesions within the lymph nodes that are microscopically indistinguishable from *M bovis* lesions. Avian tuberculosis in deer usually produces lesions in the intestinal wall and in the mesenteric lymph nodes. Lesions may be caseous or granulomatous. A haematogenous spread to the liver and lungs may occur to produce miliary lesions and a terminal septicemia.

Deer tuberculosis may be a serious problem from a zoonotic point of view especially in zoos (Sood et al, 1989; Thorel and Moutou, 1994).

Mycobacteriosis has been reported in roe-deer due to *M silvaticum*. This isolate resembled *M avium* because of it pathogenicity for chickens. Some strains of *M avium* also require mycobactin for their initial growth.

Sheep and goats

Although the disease is rare in sheep and goats, intestinal lesions and generalized disease due to *M avium*, have been reported. The animals with generalized disease showed evidence of progressive anemia, loss of condition, increasing anorexia and fever (Anderson and King, 1993).

Tuberculin testing can be performed in sheep and goats using avian and mammalian PPD tuberculin injected in the cervical region (Thoen et al, 1984).

Horses

Tuberculosis due to *M avium* is not a common disease in the horse. The limited information available on the clinical and pathological aspects of *M avium* infection as a naturally acquired disease emphasized the need for more definitive studies.

Infections with *Mycobacterium* spp have been implicated as being the causative agents of granulomatous enteritis and colitis in a number of equine cases. Microscopically, granulomas found in the intestine of horses appeared very similar to lesions observed in the intestines of other species. However, a case of generalized avian tuberculosis in a horse has been reported in Norway (Gunnes et al, 1995).

In another report, chronic weight loss and hypoproteinemia were the major clinical abnormalities in three horses. Gross pathologic lesions were characterized by chronic enterocolitis with mesenteric lymphadenopathy in two horses and hepatic granulomas in the third horse (Buergelt et al, 1988).

A spontaneous abortion by a mare at 160 days of gestation has been reported. Postmortem examination of the fetal membranes and fetal carcass revealed no gross abnormalities. Histological examination of the fetal tissues revealed numerous, discrete, non-caseating granulomas in the small intestine, splenic lymph node, lung, liver, amnio and allantochorion. They were most prominent in the small intestine, consisting of large submucosal aggregates of epithelioid macrophages and multinucleate inflammatory giant cells. Ziehl-Nielsen staining revealed many acid-fast bacilli within the phagocytes of these granulomas. The mare was then euthanasized for postmortem examination. The absence of significant

gross or histologic inflammatory lesions in the uterus was unexpected, given the disseminated fetal infection and widespread involvement of the maternal gastrointestinal tract (Cline et al, 1991).

Avian tuberculosis dermatitis in a yearling colt with progressive weight loss has been reported. This animal had a chronic granulomatous enterocolitis with associated granulomatous mesenteric lymphadenitis, splenitis, peritonitis, pneumonia and diffuse dermatitis (Flores et al, 1991).

Cats and dogs

Only limited information is available on *M avium* complex infections in cats and dogs.

Disseminated tuberculosis in cats caused by members of the *M avium* complex has been observed (Stewart et al, 1993; Jordan et al, 1994; Perkins et al, 1995; Van Dongen et al, 1996). Such cases are very rare and are more likely to occur in immunocompromised animals. It is highly likely that immunosuppression caused by infection with viruses such as the feline immunodeficiency virus predisposes cats to infection with mycobacteria (De Lisle, 1992).

Dogs can develop generalized fatal infections caused by members of the *M avium* complex (Zeiss et al, 1994; Miller et al, 1995). In New Zealand, one case of generalized *M avium* complex infection in a dog has been diagnosed. This occurred in a 16-month-old Maltese terrier that had enlarged spleen and lymph nodes. Multiple lesions were also present in its intestinal tract and liver. A feature of this case was the very large numbers of acid-fast bacilli present in the lesions (De Lisle, 1992).

Based on the tissues affected, the disease has been categorized as having pulmonary, gastrointestinal, cutaneous and disseminated forms.

Granulomatous myelitis due to *M avium* in a dog has been also described. This case was unusual in that the lesion was limited to a focal area of the spinal cord with large numbers of macrophages containing numerous intracellular organisms (Kim et al, 1994).

The tuberculosis lesions in carnivores differ from those in other species. Caseous necrosis and multinucleated giant cells, which are typical of tuberculosis, are not common in dogs and cats with *M tuberculosis* and *M bovis* infections.

NON-DOMESTIC MAMMALS

Naturally acquired infections with *M avium* complex are reported to be rare in non-human primates and exotic hoofed animals. *M avium* was isolated from several species of macaques, from mink, from freeliving hedgehogs, and from kangaroos.

In certain exotic species, lesions due to *M avium* are most often observed in the lymph nodes associated with the intestinal tract. However, generalized disease does occur (Thoen, 1989).

Mycobacterial osteomyelitis was detected in three marsupials. *M avium* serotype 15 was isolated from the ischium and liver. A case of chronic lameness in the hock joints of a bettong (*Bettongia penicillata*) was observed. The tail and the digits of the forelimb were also involved. *M intracellulare* has been rarely found in marsupials but some authors reported that it caused a proliferative pneumonitis and caseous lesions of the mesenteric lymph nodes, spleen and liver in the opossum (Mann et al, 1982; Richardson and Read, 1986; Burns et al, 1994).

M intracellulare serotype 10 was detected in rhesus monkeys (*Maccaca mulatta*). One animal with advanced disease was characterized by weight loss, anemia, weakness, prostration, disseminated granulomas in the lungs, spleen, liver, kidneys, lymph nodes, salivary glands and intestine (Fleischman

et al,1982). *M avium* serotype 2 was detected in three rhesus monkeys and one cynomolgus (*M fascicularis*). The monkeys had macroscopic or microscopic lesions consisting of united macro- or microgranulomas with central necrosis, involving the lung or mesenteric lymph nodes (Goodwin et al, 1988). Atypical mycobacterial disease due to *M avium intracellulare* serotypes was the most frequent single disease agent recognized (Holmberg et al, 1985).

CONCLUSION

The animal reservoir for *M avium* complex is very large. Mycobacterial infections including tuberculosis in mammals and birds, in captivity and under farming conditions, may pose a serious health problem to the in-contact animals and humans concerned. *M avium intracellulare*, an ubiquitous environmental pathogen, was rarely responsible for disseminated disease before the epidemic of acquired immune deficiency syndrome (AIDS) (Thoen, 1994; Falkinham, 1996).

M avium causes tuberculosis in chickens and other fowls but may also infect an extensive range of other animals species. Most *M avium* infections are found in swine. In animals other than birds, the lesions are mostly restricted to the lymph nodes close to the alimentary tract.

The serotypes of *M avium* and their distribution are very similar in pigs and humans, and it has been suggested that humans can be infected by eating pork. However, many investigations have been performed but no support for this hypothesis has been found. Currently, it is generally accepted that both humans and animals become infected from the same environmental source. Although infection occurs in humans and animals there is no evidence that cross-infection occurs (Inderlied et al, 1993).

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