Rhinoceros' Rhinorrhea: Cause of an Outbreak of Infection Due to Airborne *Mycobacterium bovis* in Zookeepers

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Seven of 24 zookeepers exposed to a Southern white rhinoceros infected with *Mycobacterium bovis* were presumably infected via aerosols generated in the cleaning of the barn for the rhinoceros. All demonstrated conversion by the intermediate-strength purified-protein-derivative skin test, but none had clinical illness. In certain occupational settings like zoos and abattoirs, exposure to *M. bovis* may be an occupational hazard, and routine periodic tuberculin screening should be performed.

Mycobacterium bovis, once a common cause of human infection, is now a pathogen that is rarely considered in the differential diagnosis of mycobacterial diseases in humans. In fact, a computer search of the literature from 1965 to 1991 and cross-referencing yielded only 15 articles on human infection with *M. bovis* other than the attenuated form of *M. bovis* (bacillus of Calmette and Guérin [BCG]) [1–15]. In the older medical literature, there are reports that the usual mode of transmission was via ingestion of infected milk, which would typically produce cervical lymphadenitis, intraabdominal disease, or cutaneous lesions sometimes with regional reactive lymphadenopathy. Diseases of bones, joints, meninges, lungs, and other organs have also been recognized [16]. There has been some controversy in the past over the importance of aerosol transmission of this organism [17]. We report an airborne outbreak of *M. bovis* that infected seven of 24 zookeepers (29%) exposed to a Southern white rhinoceros (*Ceratotherium simum simum*) that died of severe *M. bovis* pneumonia. These zookeepers all exhibited conversion to ≥10 mm induration in the intermediate-strength purified-protein-derivative (IPPD) skin test over a 6-month period of exposure to the sick rhinoceros. None were clinically ill, but all received preventive therapy with isoniazid.

Outbreak Report

Wooley, a male white rhinoceros ~32 years of age, had been captured in the wild of Africa. In 1974, the animal was sent on breeding loan from the New York Zoological Park (New York) to the Audubon Park Zoo (New Orleans) where he remained until his death in June 1991. He and his three barn mates, two female and one male white rhinoceroses, had been tested for tuberculosis in the past and showed some skin-test reactivity; however, the significance and interpretation of skin-test reactions in this species are unclear [18, 19]. In March 1991, the animal exhibited signs of illness including stranguria, diarrhea, coughing, and a copious clear nasal discharge. Cultures of the discharge yielded *Streptococcus*, *Klebsiella*, and *Neisseria* species. Culture for mycobacteria was not done. The rhinoceros was treated with tetracycline for 1 week without response and then with trimethoprim-sulfamethoxazole. On 17 May, the animal appeared lethargic and had a worsening cough. Sputum culture yielded *Pseudomonas* and *Acinetobacter* species. He was treated with amikacin (10 g im b.i.d.) and ceftiofur sodium from 24 May 1991 until 6 June 1991. The animal appeared to be wasting, with an estimated weight loss of 1,200 lb. On 10 June, the rhinoceros was sedated for bronchoscopy but died several hours after the procedure. Necropsy showed evidence of severe bilateral granulomatous pneumonia.

The animal was dismembered and buried. Fourteen persons were involved in the necropsy and burial. Necropsy cultures from pulmonary granulomas and thoracic lymph nodes yielded *M. bovis*. The cultures were studied at the United States Department of Agriculture National Veterinary Services Laboratory in Ames. Iowa, and at Ochsner Medical Institutions' laboratories in New Orleans. The organism was identified as *M. bovis* on the basis of the following characteristics and test results: growth rate on subculture at 30 days; nonpigmentation; pH 7 68°C catalase test, negative; semiquantitative catalase <45 mm; niacin, negative; nitrate reduction, negative; 4-day and 7-day pyrazinamidase test, negative; tellurite reduction, negative; Tween-80 hydrolysis, negative; and urease, positive. The organism was positive for *Mycobacterium tuberculosis* complex by DNA probe (Genprobe. San Diego. CA). It was susceptible to isoniazid, 0.2 μg/mL; streptomycin, 2 μg/mL; ethambutol, 5 μg/mL; and rifampin, 1 μg/mL.

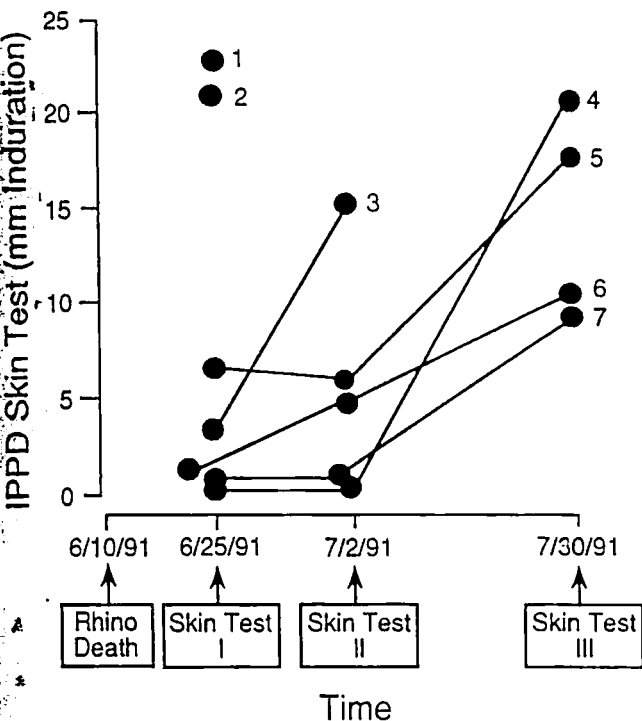The Audubon Park Zoo identified 24 animal handlers who may have had contact with the animal. One of these 24

Figure 1. Results of reactivity to serial intermediate-strength purified-protein-derivative (IPPD) skin tests of exposed zookeepers who demonstrated any induration ≥10 mm

persons had a history of positive tuberculin reactivity dating from childhood; the other 23 had been tuberculin-negative in January 1991 (by Tine Test PPD; Lederle Laboratories, Wayne, NJ) in the zoo's annual tuberculosis skin-testing program. These 23 zookeepers were tested by the Mantoux method with 5 units of IPPD. Serial skin testing of the persons most likely to have been exposed to infection was done 25 June 1991, 2 July 1991, and 30 July 1991. The second skin test was performed 1 week after the first for detecting the possibility of the booster phenomenon, since these zoo employees had received annual skin tests as part of their employment [20]. A third skin test was performed 50 days after the necropsy and burial of the rhinoceros for detecting persons who might have been infected late and who had not converted at the time of the initial skin testing. Any person who developed skin-test reactivity of ≥10 mm induration was considered positive and was not tested further.

Skin-test results for the seven zookeepers who demonstrated any reactivity of ≥10 mm induration are shown in figure 1. Seven of the 23 persons had skin-test reactions of ≥10 mm induration for one of the skin tests performed. Zookeepers 1–6 were exposed to the animal during periods when the barn was being hosed down. There were reportedly large amounts of mucus, urine, and feces on the cement floor of the barn. Hosing the contaminated floor in a closed environment provided an ideal means of aerosol transmission of infection, which was believed to be the probable means of infection of these zookeepers. Zookeeper 7 did not recall having been in the barn during cleaning but was present at the necropsy and had periodically walked through the barn before the rhinoceros died. Zookeeper 3 could be considered to represent either the booster phenomenon or true infection from the rhinoceros [20].

All seven of the animal handlers who were identified as skin-test converters and the employee who had a history of a positive IPPD skin test were evaluated with physical examination, chest radiography (posteroanterior and lateral views), determinations of complete blood count and erythrocyte sedimentation rate, and urinalysis. All test results were normal. All skin-test converters received preventive therapy with isoniazid, 300 mg daily for 9 months. One of these persons was intolerant of the drug, and therapy was discontinued. None of the skin-test converters identified any other potential exposures to tuberculosis.

Until the recognition of *M. bovis* infection in this rhinoceros, no other cases of *M. bovis* infection had been identified from the animal collection at the Audubon Park Zoo. Two rhinoceroses living in the same barn as the infected animal and one other that died during the previous year had shown no evidence of *M. bovis* infection. Cultures of tracheal lavage specimens and transthoracic lung aspirates from the two barn mates of the dead animal were negative for mycobacteria by smear and cultures. Since no other animals or humans were recognized as having active *M. bovis* infection, the source of the organism infecting the index case rhinoceros is unknown. However, the disease is believed to be reactivation of an infection acquired in the wild.

Discussion

This outbreak provides an example of the potential for aerosol transmission of *M. bovis* from animals to humans. On the basis of a review of the literature, there seems to be an evolution in the concept of the relative virulence and clinical picture of disease relative to the route of transmission of *M. bovis* from animals to humans [17]. Dr. Robert Koch reported in the *New York Herald* on 27 July 1901 that *M. bovis* was not transmissible to humans: "Professor Koch's New Discovery—Bovine Tuberculosis Not Transmissible to Man, and Very General Fear Unfounded—No Harm to Use Milk or Meat—Diet from Infected Cattle Can Be Consumed with Impunity" (cited by Hughes [21]). Koch later retracted his statements. Ravenel in 1902 was the first person to prove conclusively that *M. bovis* could cause disease and death in humans [22]. Raw stated in 1937 [23] that bovine tuberculosis could cause practically every kind of disease in humans.

The frequency with which *M. bovis* was reported to cause extrapulmonary disease was probably related to the route of infection rather than the affinity of *M. bovis* for specific tissues. Ingestion of contaminated milk may produce cervical

lymphadenitis or intraabdominal disease. Inoculation of the skin produces cutaneous infection and regional lymphadenitis [17].

Cases of pulmonary tuberculosis caused by *M. bovis* that are indistinguishable from those caused by *M. tuberculosis* have been reported in abattoir workers in Australia [4]. In the abattoir workers tested in this report, 57% were IPPD positive. The authors concluded that their detection of five cases of pulmonary *M. bovis* infection and one documented episode of transmission to a family member of one of the abattoir workers strongly suggested that inhalation was the main route of infection. Another paper from Australia reported isolated pulmonary *M. bovis* infection in 67 patients, most of whom had work-related or domestic exposure to cattle [5]. The authors also suggested that the respiratory tract is an important route for infection with *M. bovis.*

There is evidence that *M. bovis* transmission may also be a problem in the elk industry [6]. In a study of PPD skin-test reactivity in elk farmers, veterinarians, laboratory workers, and tanners involved in contact with *M. bovis*–infected elk herds in Canada, high frequencies of positive results of IPPD skin tests were found. The index case prompting this investigation involved a veterinarian who attended to an *M. bovis*–infected elk and developed a positive response to the IPPD skin test and for whom a sputum culture became positive for *M. bovis*, despite the absence of clinical illness or abnormal findings on a chest radiograph.

M. bovis can infect domestic pets (cats, dogs), cattle, buffalo, horses, camels, bison, swine, elk, donkeys, deer, antelope, monkeys, rabbits, guinea pigs, mice, and large zoo mammals like rhinoceroses and elephants [17–19]. Although the risk of transmission to humans is low, certain settings like abattoirs, zoos, or animal health care facilities may provide opportunities for efficient transmission of *M. bovis* to humans. Annual programs for tuberculosis skin testing seem appropriate for these types of institutions. Specific policies for monitoring the transmission of mycobacterial diseases should be developed if there is any evidence of active mycobacterial diseases caused by *M. bovis* or *M. tuberculosis* in animals or humans. Wearing respirators with filters capable of filtering airborne mycobacteria may be appropriate for protecting workers who might be exposed in certain work settings.

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