

Nocardiosis in persons with human immunodeficiency virus infection, transplant recipients, and large, geographically defined populations

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To quantify the risk of nocardiosis in various populations, I systematically reviewed articles published between 1966 and 2004. The incidence of nocardiosis in 3 large, geographically defined populations ranged from 0.35 to 0.4 cases per 10^5 persons · year. In contrast, the incidence of nocardiosis among people with human immunodeficiency virus (HIV) infection or acquired immunodeficiency syndrome (AIDS) in 1 study was 53 nocardiosis cases per 10^5 persons · year, approximately 140 times greater than that in the geographically defined populations. The frequency of nocardiosis cases in 4 populations of HIV-infected people averaged 608 cases per 10^5 persons. The incidence of nocardiosis in bone marrow-transplant recipients at 1 hospital was 128 cases per 10^5 persons · year, an incidence approximately 340 times greater than that in the geographically defined populations and in the same range as in HIV-infected people. The frequency of nocardiosis in 21 series of cases in recipients of a variety of transplanted organs averaged 1122 cases per 10^5 persons. These estimated incidence rates are imprecise because they were not collected through prospective surveillance systems, but the estimates for the 3 groups were internally consistent and provide useful information for clinicians. (J Lab Clin Med 2005;145:156–62)

Abbreviations: AIDS = acquired immunodeficiency syndrome; ASD = Adult and Adolescent Spectrum of HIV Disease Study; CMI = cell-mediated immunity; HAART = highly active anti-retroviral therapy; HIV = human immunodeficiency virus; IDSA = Infectious Disease Society of America

Nocardiosis is an uncommon, potentially severe disease caused by *Nocardia asteroides* or one of several other *Nocardia* species. Nocardiosis is more common in persons with HIV infection and other conditions involving diminished CMI,^{1–3} and these conditions have become more

common. Population-based surveillance systems for nocardiosis do not exist, and most clinicians are only vaguely aware of the risk of nocardiosis in healthy people and in individuals with specific underlying conditions.

To provide information to assist clinicians in the diagnosis of nocardiosis, I conducted a systematic analysis of reports of nocardiosis in defined populations. Reports of cases in defined populations of patients with HIV infection or AIDS, transplant recipients, and large, geographically defined populations in disparate locations have been published. Incidence figures from these reports are similar within these populations and biologically and clinically plausible. Although these incidence estimates are imprecise, they provide a substantially better estimate of risk than anything available in the literature.

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Table I. Estimated incidence of nocardiosis

Reference (location)	Incidence	
	Cases/person-years	Cases/10 ⁵ · year
Large geographically defined population		
1972–74, USA ⁶	See text	0.35
1983–88, Queensland, Australia ⁷	See text	0.40
1987–90, France ⁸	See text	0.37
HIV-infected persons, 1990–98, USA ^{4,*}	31/58,750	53
Allogeneic bone marrow recipients, 1969–95, Seattle, Wash ¹²	18/14,101	128

*Dworkin MS, personal communication, 1999.

METHODS

I searched the medical literature for studies in any language that enumerated cases of nocardiosis in defined populations during specified periods. I used the National Library of Medicine (MEDLINE) electronic database, 1966–2004; and the Institute for Scientific Information Expanded Science Citation Index, 1975–2004 (Thomson ISI, Philadelphia, Pa.). My search terms included “*Nocardia*,” “*Nocardia asteroides*,” and “*Nocardia* infections.” I included all studies in which nocardiosis cases were enumerated for quantified populations within a defined period. Populations included case series in which patients received most of their care at the institution(s) at which the study was conducted. I included studies that reported nocardiosis cases of any kind and excluded those that limited cases to a certain organ system (eg, only cases involving the lung or central nervous system). Instances in which *Nocardia* was isolated from a patient without signs or symptoms of disease attributable to *Nocardia* were excluded. Information from the ASD⁴ was supplemented with additional details about cases of nocardiosis (Dworkin MS, personal communication, 1999).

Incidence is expressed as an annualized rate when person-years of observation has been reported or could be determined independently. In other studies, person-years of observation could not be determined, and so the frequency of nocardiosis is expressed as the ratio of number of reported cases divided by the number of patients monitored at some time during the study period. I calculated weighted averages by dividing the sum of numerators in a set of studies by the sum of denominators in the same set of studies. In case series such as the ones included in this analysis, most patients are monitored for periods ranging from a few months to a few years. For the sake of consistency, all rates and frequencies are expressed as cases per 10⁵ people.

RESULTS

Thirty studies met the criteria for this analysis. All but 1⁵ were retrospective. The populations of these studies fell into 3 distinct groups: people with HIV infection, recipients of transplanted organs, and large, geographically defined populations.

Cases of nocardiosis in large, defined populations

were quantified in 3 studies.^{6–8} A survey of members of the IDSA was conducted in 1975 to identify all cases that occurred between July 1, 1972, and June 30, 1974.⁶ Identifying information for the 198 cases reported by IDSA members was compared with information accompanying isolates received by the Centers for Disease Control and Prevention reference laboratory during the same period. Isolates were sent to the reference laboratory in only 7.6% of the cases reported by IDSA members. From this referral percentage and the total number of isolates received, the authors estimated that between 500 and 1000 cases occurred annually in the United States. From a midpoint estimate of 750 cases and the estimated 1973 US population of 212 million,⁹ I calculated an incidence of 0.35 cases per 10⁵ persons (Table I).

Data from 2 other studies supported similar estimates. In the first, a reference laboratory in Queensland, Australia, received 72 *Nocardia* isolates from 1983 to 1988.⁷ On the basis of the 1991 population of Queensland, 2.98 million,¹⁰ I estimated that the annual incidence was 0.4 cases per 10⁵ persons year. In the second study, a reference laboratory in France received 63 *Nocardia* isolates from 1987 to 1990.⁸ These investigators used the referral percentage from the previously cited US study⁶ to estimate that approximately 200 cases occur each year in France. I used the 1990 population of France, 53.9 million,¹¹ to estimate that the incidence in that country was 0.37 cases per 10⁵ persons · year.

Twenty-one case series of nocardiosis in transplant recipients met inclusion criteria. In 1 report, the number of person-years of observation was known for 1 transplant center, and the annualized incidence of nocardiosis in the recipients of bone-marrow transplants at this center was 128 cases per 10⁵ persons · year,¹² approximately 340 times greater than that in large, geographically defined populations (Table I). The frequency of cases at this same center was 18 cases in 5507 recipi-

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