



# Isolated Nocardiosis, an Unrecognized Primary Immunodeficiency?

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Nocardiosis is an infectious disease caused by the gram-positive bacterium *Nocardia* spp. Although it is commonly accepted that exposure to *Nocardia* is almost universal, only a small fraction of exposed individuals develop the disease, while the vast majority remain healthy. Nocardiosis has been described as an “opportunistic” disease of immunocompromised patients, suggesting that exposure to the pathogen is necessary, but a host predisposition is also required. Interestingly, increasing numbers of nocardiosis cases in individuals without any detected risk factors, i.e., without overt immunodeficiency, are being reported. Furthermore, a growing body of evidence have shown that selective susceptibility to a specific pathogen can be caused by a primary immunodeficiency (PID). This raises the question of whether an undiagnosed PID may cause nocardiosis affecting otherwise healthy individuals. This review summarizes the specific clinical and microbiological characteristics of patients with isolated nocardiosis published during the past 30 years. Furthermore, it gives an overview of the known human immune mechanisms to fend off *Nocardia* spp. obtained from the study of PIDs and patients under immunomodulatory therapies.

**Keywords:** *Nocardia*, nocardiosis, infection, primary immunodeficiencies, immune response, isolated nocardiosis, PID

## INTRODUCTION

In 1888, while investigating a disease in cattle called “*francine du boeuf*,” the veterinarian Edmond Nocard identified a gram-positive, acid-fast agent as causative of this disease (1). A year after, Trevisan named this genus *Nocardia* in honor of Nocard (2). Shortly thereafter, Eppinger isolated from the brain abscess of a 52-year-old patient, an organism that produced star-shaped colonies when grown in agar. Although he called it *Cladothrix asteroides*, it was later found to be *Nocardia asteroides*. This finding made *Nocardia* be the first human pathogenic aerobic actinomycete described in the literature (3, 4). Since then and until the advent of antibiotics, over 30 cases of nocardiosis were described published, all but three with fatal outcome or very severe sequelae (5). After the generalization of antibiotic therapy, recovery rates improved to 54%, and an increased number of patients were every year (6). At this point, reports started to associate nocardiosis with underlying conditions. The first of such reports was published in 1954 in a patient with nocardiosis during Hodgkin’s lymphoma (7). Many reports followed showing cases of nocardiosis in patients with alveolar proteinosis (8), prolonged steroid usage (9, 10),