

Association of an Important *Neisseria* Species, *Neisseria elongata* subsp. *nitroreducens*, with Bacteremia, Endocarditis, and Osteomyelitis

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We retrospectively analyzed epidemiologic information associated with 22 cultures of *Neisseria elongata* subsp. *nitroreducens* (formerly CDC group M-6) submitted to the Microbial Diseases Laboratory, California Department of Health Services, Berkeley, over a 16-year period. The most common illnesses noted with this bacterium were endocarditis, bacteremia, and osteomyelitis. Risk factors associated with *N. elongata* subsp. *nitroreducens* infections included dental manipulations and/or a previous history of endocarditis, valve damage, or rheumatic heart disease.

The genus *Neisseria* is presently composed of 10 distinct species, only two of which are primary pathogens of humans (4). The preeminent pathogen of this group is *N. gonorrhoeae*, one of the leading causes of sexually transmitted disease in the United States and responsible for thousands of cases of acute urethritis in males and endocervical infections in females on an annual basis. The other major pathogen of this genus is *N. meningitidis*, a common cause of meningitis and invasive disease in children under 2 years of age, in military recruits, and in persons with severe deficiencies in the latter components (C5 to C9) of the complement pathway. The other eight neisserial species have only sporadically been associated with human illness and are generally regarded as saprophytic microorganisms under most circumstances.

In late 1990, the Centers for Disease Control (CDC) reported on the analysis of 95 strains that had previously been assigned to CDC group M-6 (3). On the basis of biochemical and DNA studies, these strains were found to belong to the genus *Neisseria* and the species *N. elongata*. Since these strains, however, were capable of reducing nitrates, a trait not associated with the other two subspecies of this taxonomic unit, they were placed into a third subspecies designated *N. elongata* subsp. *nitroreducens* subsp. nov. Of paramount interest concerning this subspecies was the fact that 27% of the strains received at the CDC originated from blood and were mostly associated with cases of bacterial endocarditis (3). This association is in stark contrast to that of the other two subspecies, which have only been infrequently isolated and rarely recovered from clinical material. On the basis of this report, we have retrospectively reviewed information concerning the cultures of *N. elongata* subsp. *nitroreducens* submitted to the Microbial Diseases Laboratory, California Department of Health Services, Berkeley, over a 16-year period and have found an even more striking association of this subspecies with human infection and disease. The Microbial Diseases Laboratory serves as the State of California's reference laboratory for the identification of bacterial, mycobacterial,

parasitic, and fungal agents involved in human disease. From 1974 to 1990, the Microbial Diseases Laboratory received for identification 22 cultures that were subsequently identified as CDC group M-6 by established biochemical criteria (1). Some of these strains were additionally forwarded to the CDC for culture confirmation. When available, clinical and medical histories on each patient from whom *N. elongata* subsp. *nitroreducens* was isolated were obtained either from submittal forms or from follow-up consultations with relevant medical personnel. Case 3 in this study has been reported by the CDC as case 1 in a recent epidemiologic survey (3). A report on case 4 has also been published (5).

Of the 22 strains of *N. elongata* subsp. *nitroreducens* received over a 16-year period, 12 (55%) originated from blood, 4 (18%) were recovered from wounds, four (18%) were recovered from respiratory secretions, and 1 each (9%) was recovered from peritoneal fluid and peritoneal dialysis fluid. The relevant medical and epidemiologic information on the 12 bacteremic patients is listed in Table 1.

All 12 patients with *N. elongata* subsp. *nitroreducens* sepsis presented with monomicrobial bacteremias; in 10 of 11 patients for whom data were available, multiple isolates of the organism were obtained from blood (range, two to six). Of the 12 bacteremic strains, 9 (75%) were associated with the clinical diagnosis of endocarditis. Antecedent events thought to play a potential role in the development of *N. elongata* subsp. *nitroreducens* bacteremia included various dental procedures (four patients) and heart catheterization (one patient). In 58% of the bacteremia cases, a precipitating event could not be identified or information was unavailable. Another striking feature of *N. elongata* subsp. *nitroreducens* sepsis in these individuals was a previous history of rheumatic heart disease, endocarditis, or valve damage. Four patients had had episodes of bacterial endocarditis due to streptococci (patients 4, 5, and 9) or *Cardiobacterium hominis* (patient 12) and four individuals (patients 1, 2, 4, and 5) had had rheumatic heart disease. For patients 3, 4, and 8, valve replacement was required in addition to antimicrobial chemotherapy. In only one instance (patient 3) were we unable to identify a precipitating event or a potential under-

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TABLE 1. Salient features of *N. elongata* subsp. *nitroreducens* infections

Patient	Age (yr)/sex ^a	Clinical diagnosis	Underlying disease(s)	Date of onset (mo/yr)	Precipitating event	Laboratory findings ^b	
						Source	No. of times isolated
1	69/F	Endocarditis	Rheumatic fever, valve disease	7/1974	Dental work (2 mo prior to illness)	Blood	4
2	46/F	Septicemia	Rheumatic heart disease	8/1975	Unknown	Blood	1
3	25/M	Endocarditis	Unknown	9/1979	Unknown	Blood	6
4	57/M	Endocarditis	Previous SBE, ^c rheumatic fever, valve disease	3/1982	Catheterization	Blood	5
5	60/F	Endocarditis	Rheumatic heart disease, previous SBE	1/1984	Unknown	Blood	?
6	42/F	Endocarditis	Unknown	3/1984	Flulike illness	Blood	5
7	?/M	Endocarditis	Unknown	5/1986	Dental work (4 days prior to illness)	Blood	2
8	37/M	Endocarditis	Unknown	3/1987	Dental work (date unknown)	Blood	3
9	53/M	Endocarditis	Previous SBE, valve replacement	4/1987	Flulike illness (2 wk prior to illness)	Blood	3
10	66/M	Septicemia	Arthritis	10/1988	Dental work (date unknown)	Blood	4
11	29/M	Septicemia	Unknown	8/1989	Unknown	Blood	3
12	34/M	Endocarditis	Previous SBE, valve replacement	8/1990	Unknown	Blood	4

^a F, female; M, male.

^b All strains were isolated in pure cultures.

^c SBE, subacute bacterial endocarditis.

lying risk factor associated with *N. elongata* subsp. *nitroreducens* endocarditis or bacteremia.

In three of the four patients with *N. elongata* subsp. *nitroreducens* wound-associated infections, the bacterium was thought to be clinically significant; in one instance, another potential pathogen (*Staphylococcus aureus*) was simultaneously isolated. Two wound infections appeared to be simple cases of bacterial cellulitis in which trauma to the leg and wrist introduced the infecting organism. Two other cases involved more fulminant infections which apparently led to the tentative diagnosis of osteomyelitis. One of the individuals had sustained an open fracture to the leg which continuously drained for several years and led to osteomyelitis; *N. elongata* subsp. *nitroreducens* was recovered from the right thigh. The other patient had undergone over an 11-month period multiple tooth extractions in which the sockets had failed to heal; subsequently, she underwent debridement of the right maxilla and mandible for probable osteomyelitis. *N. elongata* subsp. *nitroreducens* was recovered from the right maxillary tissue along with normal oropharyngeal flora.

Of the remaining six strains, those recovered from respiratory secretions were not thought to be clinically significant and were recovered from individuals with metastatic processes or apparently noninfectious processes of the upper respiratory tract. In the two cases of peritonitis, not enough medical information was available to address the significance of the strains recovered from peritoneal or peritoneal dialysis fluids.

The results of this survey and the previously published survey by the CDC (3) suggest that *N. elongata* subsp. *nitroreducens* is an important pathogen of the genus *Neisseria* and is responsible in humans for significant infections, such as endocarditis, septicemia, and osteomyelitis. Individuals at risk for developing such infections appear to be those undergoing dental manipulations or persons with preexisting

heart damage, including endocarditis and rheumatic heart disease. In the only three known publications on CDC group M-6 prior to these two studies, two cases of endocarditis were linked to valve disease (6) and heart catheterization (5), and a case of osteomyelitis was preceded by dental surgery on a tooth abscess by 6 months (2). These collective findings suggest common predisposing factors for developing serious *N. elongata* subsp. *nitroreducens* infections. Because of the nature of this survey, the outcome for only three patients (patients 1, 3, and 4) were known; all recovered after successful chemotherapy and surgery (valve replacement in two instances). Although susceptibility studies on a large collection of these strains have not as yet been published, these strains appear uniformly susceptible to most agents, including ampicillin.

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