Outbreaks of Invasive *Kingella kingae* Infections in Closed Communities

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Objectives To describe the results of the epidemiologic investigation of outbreaks of invasive *Kingella kingae* infections among attendees at daycare facilities located in 4 closed communities in Israel.

Study design The preschool-aged population of communities with clusters of *Kingella* cases had oropharyngeal cultures performed. *K kingae* isolates from infected patients and healthy contacts were genotyped by pulsed field gel electrophoresis to determine the spread of outbreak strains.

Results The affected closed communities (3 military bases and 1 "kibbutz" commune) were characterized by tight social and family networks and intensive mingling. The outbreaks affected 9 of 51 attendees (attack rate: 17.6%) age 8-19 months (median: 12 months), within a 21-day period. Cases included skeletal system infections (n = 8) and bacteremia (n = 1); *K kingae* isolates were confirmed by the use of blood culture vials and selective media. Clinical presentation was mild and acute-phase reactants were usually normal or only moderately elevated. Thirty out of 55 (54.5%) asymptomatic children carried the outbreak strains. Analysis of the 3 clusters in which the entire preschool-aged population was cultured revealed that 31 of 71 (43.7%) children younger than 24 months of age were colonized with *K kingae* organisms compared with 8 of 105 (7.6%) older children ($P < .001$).

Conclusions Clusters of invasive *K kingae* infections characterized by sudden onset, high attack rate, and wide dissemination of the outbreak strain can occur in daycare facilities and closed communities. Because the mild clinical presentation of invasive *K kingae* infections and the fastidious nature of the organism, a high index of suspicion and use of sensitive detection methods are recommended. *(J Pediatr 2016;169:135-9)*.

Because of use of improved detection methods, invasive *Kingella kingae* infections are being reported increasingly in young children living in Western countries.[1] The organism is carried as part of the oropharyngeal microbiota,[1-3] and the colonized mucosal surface is the portal of entry of the bacterium in the bloodstream from which it can seed in remote sites.[2,3] Colonization of the oropharynx also may serve as the source of transmission of the organism from child to child.[4,5] Age 6-29 months and daycare attendance have been shown to represent independent risk factors for *K kingae* carriage,[6] transmission,[4] and disease,[1,7] and clusters of invasive infections have been reported among young attendees at out-of-home care facilities.[8-13]

In 2014, 3 separate outbreaks of invasive *K kingae* infections were detected in Israeli daycare facilities located in closed communities, and a previous cluster occurred in 2005.[9] These events were investigated by obtaining oropharyngeal cultures from the preschool age population of the settlements and by genotyping of recovered isolates to study the dissemination of the outbreak strains.

Methods

Cases of invasive *K kingae* infections were classified as confirmed, highly presumptive, or presumptive according to the criteria summarized in **Table I**. Compatible clinical picture refers to the typical spectrum of invasive *K kingae* disease (ie, bacteremia, skeletal system infections, and endocarditis).

Although presumptive cases were not confirmed bacteriologically, the annual incidence of osteomyelitis or septic arthritis in Western countries is <10 per 100 000 children for each infection.[14,15] Therefore, occurrence of >1 case of skeletal system infection among children attending the same daycare center within a short period, should raise the suspicion of a common etiology. To make the criteria for inclusion in the "presumptive case" category more stringent, its definition required a compatible clinical picture (bone, joint, or intervertebral disc infection), detection within a 1-month period of another case (either "confirmed," "highly presumptive," or "presumptive"), and no other etiology identified. Outbreak was defined as occurrence of >1 case of invasive *K kingae* infection (either "confirmed," "highly presumptive," or "presumptive") in a daycare center within a 1-month period.

After obtaining informed consent from their parents, the preschool-aged population of the affected communities had surveillance cultures performed.

PFGE Pulsed field gel electrophoresis

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Table I. Definitions of proven, highly presumptive, and presumptive cases of invasive *K kingae* infections

Case categories	Compatible clinical picture*	Positive *K kingae* culture		Positive *K kingae* PCR assay		Need for another case*
		Normally sterile body fluid	Pharynx	Normally sterile body fluid	Pharynx	
Proven	+	+				
	+	–†		+		
Highly presumptive	+	–†	+			
	+	–†			+	
Presumptive	+	–†				+

PCR, polymerase chain reaction.
*Bacteremia, septic arthritis, osteomyelitis, spondylodiscitis, tenosynovitis, or endocarditis.
†No other pathogen isolated.

Oropharyngeal specimens were obtained using rayon-tipped swabs and processed within 2 hours, as previously described.[2,6,9] Inoculated swabs were streaked onto a selective vancomycin-containing medium designed to facilitate *K kingae* detection,[16] and agar plates were incubated aerobically at 35°C in a 5% CO_2-enriched atmosphere and examined for 2 consecutive days. *K kingae* was identified on the bases of the typical morphologic and biochemical characteristics of the species and confirmed by the API NH kit, (bioMérieux, Marcy-l'Etoile, France) and/or matrix-assisted laser desorption ionization-time of flight mass spectrometry.[17]

Bacterial cells were harvested and chromosomal DNA was prepared as previously described.[2,4,5] After restriction with *Eag*I (New England Biolabs, Inc, Ipswich, Massachusetts), DNA fragments were separated in a CHEF DRII pulsed field gel electrophoresis (PFGE) system (Bio-Rad Laboratories, Hercules, California).

To estimate the genetic relatedness among strains, restriction patterns were interpreted according to the criteria proposed by Tenover et al.[18] Isolates characterized by similar (indistinguishable and closely related) PFGE profiles were considered to belong to the same clone.

Proportions were compared using the χ^2 test. A P value of <.05 was considered statistically significant for all calculations.

Results

Overall, 3 clusters of disease occurred among the civilian population living in military bases A, B, and C, and 1 was detected in a kibbutz (rural commune). The cluster of *K kingae* osteomyelitis that occurred in military base A has been described in detail in an earlier publication.[9]

The 4 closed communities are located in remote areas of the country and are characterized by relative isolation from people outside the community and intensive social mingling among members. The preschool age populations attend day-care facilities located at a close range and segregated according to age. Children spend 9 hours per day in the facilities, 6 days a week, and participate in shared recreational activities in the afternoon hours and weekends. In addition, the day-care population is connected by multiple family ties, and siblings attend the same or neighboring facilities.

Two outbreaks of disease occurred in March, and one each in May and September. Two out of the 4 clusters were preceded by outbreaks of presumed viral diseases: a nonspecific upper respiratory infection in military base A, and hand-foot-and-mouth disease in military base C.

A total of 6 male and 3 female children, all younger than 24 months, were involved in the outbreaks. Skeletal system infections were the most common clinical presentation, followed by bacteremia with no focal infection (**Table II**). Among children with osteomyelitis, the radius was involved in 2 and the ulnar bone in 1.[9] Septic arthritis affected the ankle, wrist, or the sacroiliac joint (1 case each), and a lumbar intervertebral disk was involved in the child with spondylodiscitis. Clinical features were characterized by paucity of systemic and local signs of inflammation: only 1 of 7 patients from whom the information was available were febrile at presentation, in 5 out of 7 children, the

Table II. Case categories and clinical presentation of children involved in clusters of invasive *K kingae* infections in closed communities

Day-care center location		Cases features							
		Proven (n)	Highly presumptive (n)	Presumptive (n)	Age range (mo)	Osteomyelitis (n)	Arthritis (n)	Spondylodiscitis (n)	Bacteremia (n)
2005	Military base A	1	0	2	8-12	3	0	0	0
2014	Military base B	0	0	2	11-14	0	1	0	0
2014	Military base C	0	2	0	17-19	0	1	1	0
2014	Kibbutz	1	1	0	8-16	0	1	0	1
Total		2	3	4	8-19	3	4	1	1