The Relationship Between In-Home Water Service and the Risk of Respiratory Tract, Skin, and Gastrointestinal Tract Infections Among Rural Alaska Natives

Thomas W. Hennessy, MD, MPH, Troy Ritter, REHS, MPH, Robert C. Holman, MS, Dana L. Bruden, MS, Krista L. Yorita, MPH, Lisa Bulkow, MS, James E. Cheek, MD, MPH, Rosalyn J. Singleton, MD, MPH, and Jeff Smith, MS, RS

Objectives. We investigated the relationship between the presence of in-home piped water and wastewater services and hospitalization rates for respiratory tract, skin, and gastrointestinal tract infections in rural Alaska.

Methods. We determined in-home water service and hospitalizations for selected infectious diseases among Alaska Natives by region during 2000 to 2004. Within 1 region, infant respiratory hospitalizations and skin infections for all ages were compared by village-level water services.

Results. Regions with a lower proportion of home water service had significantly higher hospitalization rates for pneumonia and influenza (rate ratio [RR]=2.5), skin or soft tissue infection (RR=1.9), and respiratory syncytial virus (RR=3.4 among those younger than 5 years) than did higher-service regions. Within 1 region, infants from villages with less than 10% of homes served had higher hospitalization rates for pneumonia (RR=1.3) and respiratory syncytial virus (RR=1.2) than did infants from villages with more than 80% served. Outpatient *Staphylococcus aureus* infections (RR=5.1, all ages) and skin infection hospitalizations (RR=2.7, all ages) were higher in low-service than in high-service villages.

Conclusions. Higher respiratory and skin infection rates were associated with a lack of in-home water service. This disparity should be addressed through sanitation infrastructure improvements. (*Am J Public Health.* 2008;98:2072–2078. doi:10.2105/AJPH.2007.115618)

Modern sanitation services (potable drinking water and safe wastewater disposal) are a cornerstone of public health progress and have contributed to decreased infectious disease morbidity and mortality. In 1950, 64.5% of US homes had complete sanitation services (a flush toilet, shower or bath, and kitchen sink).[1] This increased to 93.1% by 1970 and to 99.4% by 2000.[2,3]

In 2000, 93.7% of Alaskan homes had complete sanitation, which ranked Alaska last among US states.[3] In rural Alaska, where the vast majority of people are Alaska Natives, a much higher proportion lack basic sanitation facilities. Providing in-home sanitation services is difficult in remote villages where small, isolated populations live in a harsh, cold climate. Although many rural village homes lack in-home water service, nearly all villages have access to safe drinking water.[4] Significant gains in health status indicators have occurred among rural Alaska Natives; however, the ongoing disparity in sanitation services remains unsolved in most of rural Alaska. Furthermore, there is a disparity in infectious disease hospitalizations among Alaska Natives compared with the general US population.[5] To our knowledge, there are no evaluations of the health effects of a lack of modern sanitation services for rural Alaskans.

Alaska village residents who live without pressurized in-home water service typically obtain water from a community-based water point and bring it home in 5-gallon (19-L) plastic containers. As of 2000, one third of rural Alaska residents obtained water this way.[4] Although water is available in centralized locations, some families must travel long distances or cross rivers to obtain safe water. This distribution method makes it difficult to obtain adequate amounts of water needed for basic consumption and hygiene practices.[6] Alaska homes lacking pressurized in-home water service also lack flush toilets. Residents use outhouses or in-home waste containers commonly known as "honeybuckets" that require manual removal to a centralized waste disposal site or lagoon. Sanitation infrastructure is provided to rural Alaskans by state- and federally funded programs that have provided service first where the greatest number of homes could be served at the lowest cost.

Although it has long been recognized that access to modern sanitation services can reduce morbidity and mortality from gastrointestinal illnesses, recent data have established the important role of adequate water supplies for preventing respiratory diseases.[7–9] The value of adequate supplies of safe water has been attributed to the prevention of both waterborne diseases, in which the pathogen can be ingested from contaminated water, and water-washed disease, in which hygienic practices such as handwashing and bathing play a role.[10] We sought to describe the relationship between in-home water and wastewater service and the risks of waterborne and water-washed infectious diseases in rural Alaska. We used existing sanitation service data for rural Alaska along with hospital discharge records, a respiratory disease surveillance system, and a skin infection outbreak investigation to explore whether improved sanitation service was associated with improved health status among rural Alaska Native people.

METHODS

Population

The approximately 120 000 Alaska Natives are descendants of the indigenous population and represent 19% of Alaskans. Approximately 60% of Alaska Natives live in rural or remote villages. Of the approximately 170 rural villages, most have fewer than 300 residents, and the vast majority are Alaska Natives. Most villages are not accessible by road; travel between villages is mainly by airplane, snowmobile, or boat. Health care services are administered by regional Alaska Native–managed tribal health organizations, with some statewide facilities and services shared and coadministered, such as the referral medical center in Anchorage.

Sanitation Services

The Rural Alaska Housing Sanitation Inventory documented water and wastewater service in rural villages from July 2001 through April 2004. Each home was evaluated, and a statewide database was created. We defined "served" homes as having pressurized, in-home water service including piped water service from a municipal system or on-site well and septic tank or drain field systems, or "closed haul" systems in which water is delivered to storage tanks and distributed throughout the home via internally pressurized plumbing. For the latter, wastewater from flush toilets is held in a storage tank and periodically evacuated by a pump truck. We used data from 6 predominantly rural regions that were defined according to the boundaries of the tribal health care organizations. We defined "high-service" regions as those in which 80% or more of homes had service and "low-service" as those in which less than 80% were served.

Water service data for 1 region (region A) were used in a village-level analysis. Because water improvements are ongoing, we excluded from analysis villages in which more than 50% of homes had new water service from 1999 through 2004 (5 villages with 2740 persons, or 11.6% of the region's population). We categorized the remaining 47 villages into tertiles according to the proportion of homes served. We analyzed region A's largest town separately because it has near-complete water service and a population approximately 5 times larger than that of the next-largest village. Household size and income data were obtained from the 2000 US Census.[11]

Regional Disease Rates

Hospital discharge data for the fiscal years 2000 to 2004 for Alaska Natives in Alaska were obtained from the Indian Health Service's (IHS's) Direct and Contract Health Service inpatient data set.[12] These data include patient discharge records from IHS-operated, tribally operated, and community hospitals that were contracted with IHS or with tribes to provide health care services to eligible persons.[13] We selected hospitalizations for the 6 predominantly rural regions and urban Anchorage. Three regions were excluded because of small hospital discharge numbers.

Hospital discharges were selected for infectious gastroenteritis, pneumonia or influenza, skin or soft tissue infection, and methicillin-resistant *Staphylococcus aureus* (MRSA) infections for all ages, and respiratory syncytial virus (RSV) for children younger than 5 years. A record was selected if 1 of these diseases was listed among the first 6 discharge diagnoses according to the *International Classification of Diseases, 9th Revision, Clinical Modification* (*ICD-9-CM*).[14]

The definitions of infectious gastroenteritis included diarrhea of determined etiology (bacterial: 001–005, 008.0–008.5, excluding 003.2; parasitic: 006–007, excluding 006.3–006.6; and viral: 008.6–008.8) and diarrhea of undetermined etiology (presumed infectious: 009.0–009.3). Pneumonia and influenza were identified with codes 480 to 487. Skin and soft tissue infections were identified with codes 680 to 682, 684, 686.8, and 686.9. Hospitalizations for MRSA were selected by code V09.0 (infection with microorganisms resistant to penicillins) among codes 038.11 (*S aureus* septicemia), 482.41 (other bacterial pneumonia caused by *S aureus*), and 041.11 (*S aureus* bacterial infection in conditions classified elsewhere and of unspecified site). Infection with RSV was defined as codes 480.1, 079.6, and 466.11. Because patient identifiers were not available, repeated hospitalizations could not be excluded.

Hospitalization rates were calculated per 10 000 persons per year for region of residence. The IHS fiscal year 2002 user population estimates (released March 2002) were used as the denominator. The user population included all Alaska Natives who had received IHS-funded health care at least once over the previous 3 years.[12] We calculated age group–specific rates, categorizing age as younger than 1 year, 1 to 4 years, 5 to 19 years, 20 to 44 years, 45 to 64 years, and 65 years or older. Rate ratios with 95% confidence intervals (CIs) were calculated with Poisson regression analysis.[15] Age adjustment with the direct method for the user population of Alaska did not substantially change the rates and is not reported.

Disease Rates Within Region A

We conducted ongoing surveillance of hospitalizations for acute lower respiratory tract infections (LRTIs) among children for region A and selected 1999 to 2004 to examine rates by village.[16,17] We abstracted clinical and laboratory information from the computerized medical records for children younger than 1 year hospitalized at the regional hospital, or in Anchorage or who received contracted medical care at a nontribal hospital. We obtained for each hospitalization the birth dates, admission and discharge rates, *ICD-9-CM* diagnosis codes and narrative, and RSV test result. We merged duplicate hospitalization data on patients transferred to another hospital. A child was classified as having pneumonia if the discharge diagnoses included 1 of *ICD-9-CM* codes 480.1, 485, 486, or 507. Infection with RSV was defined as a hospitalized child younger than 1 year with acute LRTI and a nasopharyngeal aspirate positive for RSV by culture or a rapid identification method (enzyme immunoassay or direct fluorescent antibody). The majority of RSV testing was performed with Directogen (Bectin Dickenson, Cockeysville, MD). Comparable data for all Alaska Natives and for the US general population were obtained from published sources.[17,18]

Skin infection hospitalization data were obtained from an outbreak investigation in region A.[19] We included hospitalizations for skin infections from July 1, 1999, through June 30, 2000, and used *ICD-9-CM* codes (680.0–682.9) to include carbuncle, furuncle, and cellulitis. The regional hospital laboratory was used to identify all confirmed *S aureus* cultures from skin infections for the same period. The MRSA infections were defined by a minimum inhibitory concentration of oxacillin at 2 μg/mL or greater. Clinical samples obtained at village-based clinics must be transported to the regional hospital for culture and confirmation, introducing a potential diagnostic access bias. To avoid overestimating infection rates in the 10 villages closest to the regional hospital, whose residents might seek care directly at the hospital-based clinics and hence be diagnosed more often, we excluded

TABLE 1—In-Home Water and Wastewater Service to Homes, by Region: Alaska, 2000

Region	American Indian/Alaska Native Population,[a] No.	Communities Surveyed, No.	Homes Surveyed, No.	Homes With Water Service, No. (%)	Homes With Wastewater Service, No. (%)
High service					
F	5409	25	1555	1387 (89)	1349 (87)
E	12370	26	2834	2499 (88)	2403 (85)
D	4518	4	368	368 (100)	368 (100)
Low service					
C	6867	10	834	626 (75)	627 (75)
B	7274	14	1376	782 (57)	751 (55)
A	20714	49	5513	3360 (61)	3328 (60)
Total	57152	128	12480	9022 (73)	8826 (71)

[a]Data from the 2000 US Census.[11]

from analysis persons from these villages. Population denominators were obtained from the 2000 Census.[11]

The χ^2 test for trend was used to compare hospitalization rates for villages with differing levels of water service. We adjusted for a potential confounder (number of persons per household) with the Cochran–Mantel Haenszel test comparing high-service to low-service villages.

RESULTS

Rural In-Home Water Service

We obtained water service data from 128 villages and a total of 12 480 homes in the 6 regions. Overall, 73% of homes had in-home water service (range by region: 57% to 100%). Wastewater service was present in 71% of homes; the percentages by region were similar to the proportion of homes with water service by region (Table 1). The high-service regions had 91% of homes with in-home water service compared with 61% of homes in the low-service regions.

Regional Hospitalization Rates and Water Service

Hospitalization rates by region for the 5 infectious disease categories varied by water service level (Table 2). The RSV hospitalization rate for children younger than 5 years was higher in the low-service regions than in the high-service regions (rate ratio [RR]=3.4; 95% CI=3.0, 3.8). For all ages, rates for pneumonia and influenza (RR=2.5; 95% CI=2.4, 2.7), skin or soft tissue infection (RR=1.9; 95% CI=1.8, 2.1), and MRSA infection (RR=4.5; 95% CI=3.6, 5.7) hospitalizations were also higher for low-service regions.

Hospitalization rates for infectious diarrhea did not differ between high- and low-service regions (RR=0.94; 95% CI=0.78, 1.2). Diarrhea of undetermined etiology as the only diarrhea-coded diagnosis was reported for only 4.2% of the diarrhea hospitalizations, and the removal of this diagnosis did not affect the overall rate comparison.

Higher pneumonia and influenza hospitalization rates seen among the low-service regions were seen in each age group; however, the overall excess rate was greatest among the very young and the elderly (Table 3). The hospitalization rate among children younger than 1 year was 5 times higher in low-service regions than in the high-service regions. For children aged 1 to 4 years and persons 65 years or older, the rates were at least 2 times higher in the low-service regions than in the high-service regions.

Water Service in Region A

In region A, 61% of homes had water service, but service was not uniformly distributed throughout the region (Table 4). Water service was available in less than 10% of homes for 20 villages (30% of population), in 10% to 79% for 13 villages (20% of population), and in 80% or more for 14 villages (27% of population). The largest town, with 23% of the region's population, had 99.5% of homes with water service. With the exclusion of the largest town, the other groups of villages were similar in persons per household and mean household income. Villages with less than 10% of homes served had a slightly lower median population than those with a greater proportion of homes served. The population ranges overlapped for all 3 groups, and the largest difference in median village population between groups was 181 persons.

Hospitalization Rates and Water Service in Region A

Among the regions, the highest hospitalization rates for each of the diagnoses were among persons in region A (Table 2). In particular, pneumonia and influenza hospitalization rates among the region's infants (2550 per 10 000) were more than 2 times higher than the rates for any other region (Table 3). On average, more than 25% of the birth cohort was hospitalized with this diagnosis yearly.

Hospitalization rates for infants with LRTI, pneumonia, and RSV were highest among infants in villages with the lowest level of in-home water service compared with those in other villages (Table 4). Also, we noted a trend of lower hospitalization rates for infants from villages with increasing proportions of homes served by in-home water service (Figure 1). This trend was highly significant for hospitalizations because of LRTI ($P=.002$) and LRTI with pneumonia ($P=.007$) and was present, but not statistically significant, for RSV infections and RSV pneumonia.

Relative hospitalization rates of infants from the lowest-service compared with those from the highest-service villages were as follows: LRTI (RR=1.2; 95% CI=1.1, 1.4), pneumonia (RR=1.3; 95% CI=1.1, 1.5), and RSV (RR=1.2; 95% CI=1.0, 1.6). These rate ratios were similar after adjustment for the number of household members. Compared with the overall US infant population, infants in the lowest-service villages had a 5-times-higher rate of both LRTI and RSV hospitalizations and an 11-times-higher hospitalization rate for pneumonia.

Region A had the highest rate of hospitalization for skin and soft tissue infections and for MRSA infections (Table 2). Within this region, we observed a significant trend of

TABLE 2—Hospitalization Rates per 100 000 for Specific Infections and the Proportion With In-Home Water Service, by Region: Alaska, 2000–2004

Region	Water-Served Homes, %	Infectious Diarrhea, Hospitalization Rate (No.)	RSV,[a] Hospitalization Rate (No.)	Pneumonia or Influenz,[a,b] Hospitalization Rate (No.)	Skin or Soft Tissue Infection,[b] Hospitalization Rate (No.)	MRSA Infection, Hospitalization Rate (No.)
Urban Anchorage	100	7.14 (106)	78.5 (130)	63.24 (939)	50.71 (753)	5.25 (78)
High-service region						
F	89	5.80 (16)	148.29 (39)	85.93 (237)	47.86 (132)	2.90 (8)
E	88	9.73 (70)	29.76 (15)	42.12 (303)	26.0 (187)	1.25 (9)
D	100	6.43 (14)	214.69 (57)	98.26 (214)	41.32 (90)	1.38 (3)
Total high-service regions	91	7.64 (206)	90.1 (241)	62.8 (1693)	43.07 (1162)	3.63 (98)
Low-service region						
C	75	5.78 (20)	136.42 (59)	100.87 (349)	34.10 (118)	0.58 (2)
B	57	4.06 (16)	129.48 (56)	90.82 (358)	39.07 (154)	1.27 (5)
A	61	8.72 (96)	314.48 (481)	199.82 (2200)	113.62 (1251)	26.70 (294)
Total low-service regions	61	7.17 (132)	248.90 (596)	157.89 (2907)	82.72 (1523)	16.34 (301)
Rate ratio[c] (95% CI)		0.94 (0.78, 1.17)	2.81 (2.42, 3.26)	2.54 (2.39, 2.70)	1.93 (1.79, 2.08)	4.51 (3.59, 5.66)

Note. RSV = respiratory syncytial virus; MRSA = methicillin-resistant *Staphylococcus aureus;* CI = confidence interval. Number is the total number of hospitalizations for that disease.
[a]Respiratory syncytial virus, for hospitalizations among children younger than 5 years.
[b]Three pneumonia- or influenza-associated hospitalizations and 8 skin- or soft tissue-infection hospitalizations did not have community of residence available.
[c]High- vs low-service regions.

TABLE 3—Age-Specific Hospitalization Rates for Pneumonia and Influenza and Proportion With In-Home Water Service, by Region and In-Home Water Service Level: Alaska, 2000–2004

Service Unit	Age <1 Year, Hospitalization Rate (No.)	Age 1–4 Years, Hospitalization Rate (No.)	Age 5–19 Years, Hospitalization Rate (No.)	Age 20–44 Years, Hospitalization Rate (No.)	Age 45–64 Years, Hospitalization Rate (No.)	Age ≥65 Years, Hospitalization Rate (No.)
Urban Anchorage	246.69 (81)	76.11 (100)	13.57 (60)	31.8 (179)	112.4 (286)	384.11 (233)
High-service region						
F	989.47 (47)	143.85 (31)	15.22 (14)	19.16 (17)	97.21 (47)	397.06 (81)
E	333.33 (20)	51.80 (23)	8.03 (18)	15.46 (40)	64.02 (83)	211.37 (119)
D	750.00 (42)	190.93 (40)	9.39 (7)	27.30 (19)	102.19 (35)	552.53 (71)
Total high-service regions	386.30 (190)	88.87 (194)	11.89 (99)	26.0 (255)	96.65 (451)	335.53 (504)
Low-service region						
C	988.64 (87)	194.48 (67)	17.88 (23)	32.32 (35)	73.83 (33)	492.89 (104)
B	1435.48 (89)	124.16 (46)	20.38 (26)	27.50 (37)	89.07 (55)	399.24 (105)
A	2549.75 (756)	317.11 (391)	22.83 (90)	34.4 (117)	139.88 (205)	954.58 (641)
Total low-service regions	2087.35 (932)	258.73 (504)	21.4 (139)	32.4 (189)	115.81 (293)	742.03 (850)
Rate ratio[a] (95% CI)	6.57 (5.58, 7.72)	2.96 (2.51, 3.50)	1.80 (1.39, 2.33)	1.25 (1.03, 1.51)	1.20 (1.04, 1.39)	2.31 (2.06, 2.59)

Note. CI = confidence interval. Number is the total number of hospitalizations for that disease.
[a]High- vs low-service regions.

increased disease rates associated with lower levels of in-home water service for infections caused by *S aureus*, MRSA, and hospitalizations for skin infections (*P*<.001 for each; Table 4). The risk of skin infections was substantially higher among persons from villages with the least water service than for those villages with the highest water service for each of *S aureus* infections (RR=5.1; 95% CI=3.0, 8.7), MRSA infections (RR=7.1; 95% CI=3.6, 14.0), and skin infection hospitalizations (RR=2.7; 95% CI=1.8, 4.1; *P*<.001 for each comparison).

DISCUSSION

This is the first study to associate the absence of in-home water service with an increased risk of lower respiratory tract and skin infections among Alaska Natives. Using aggregated data from regions across Alaska, we found that hospitalization rates for pneumonia and influenza, skin and soft tissue infections, MRSA infections, and childhood RSV were 2 to 4 times higher in regions with a low proportion of homes with water service than in regions with a high proportion of homes with

TABLE 4—Village Demographic Characteristics and Annualized Rates of Respiratory Disease Hospitalizations (Children Younger Than 1 Year) and Soft Tissue Infections (All Ages), by Percentage With In-Home Water Service for Region A: Alaska, 1999–2004, and 1999–2000

Characteristic	Percentage of Community With In-Home Water Service: <10	10–79	≥80	100	P: For Trend[a]	≥80% vs 100%
Population (% of total)	6956 (30)	4743 (20)	6415 (27)	5459 (23)		
Number of villages	20	13	14	1[b]		
Median village population (range)	312 (49–1042)	370 (96–651)	493 (202–832)	5459	.31	Not tested
Average no. persons per home[c]	4.7	4.2	4.2	4.2	.09	Not tested
Average household income, $ per year	30 633	28 393	31 160	57 321	.87	Not tested
Infections, hospitalization rate (no.[d])						
All LRTI	351 (338)	304 (121)	282 (218)	227 (141)	.002	.02
Pneumonia LRTI	238 (229)	201 (80)	185 (143)	130 (81)	.007	.006
RSV-positive	140 (135)	118 (47)	113 (87)	93 (58)	.08	.24
Pneumonia RSV	78 (75)	63 (25)	63 (49)	51 (32)	.23	.34
Staphylococcus aureus infection, any	13.8 (55)	10.8 (43)	2.7 (17)	8.4 (46)	<.001	<.002
MRSA infection, any	11.3 (45)	7.3 (29)	1.6 (10)	5.5 (30)	<.001	.01
Hospitalized for skin infection	12.8 (89)	9.6 (45)	4.8 (30)	5.5 (30)	<.001	.61

Notes. LRTI = lower respiratory tract infection; RSV = respiratory syncytial virus; MRSA = methicillin-resistant *Staphylococcus aureus*.
[a]Trend among villages excluding largest town in region.
[b]Largest town in region.
[c]Averages are weighted by village population size.
[d]Number is the total number of hospitalizations for that disease.

water service. Although suggestive, this relation was not entirely consistent and was influenced greatly by high hospitalization rates within region A. However, within region A, we undertook a closer look at disease rates by village-level water service and found that villages with the lowest level of water service (less than 10% of homes served) had the highest hospitalization rates for respiratory infections among infants and for skin and soft tissue infections among persons of all ages. The hospitalization rates demonstrated a typical dose–response group relation in which lower rates were related to progressively higher levels of in-home water service.

Because of the study design, these data fall short of establishing a causal relation between water service and infectious disease risks. However, the strength of the association, the dose–response group relation within region A, and the biological plausibility all support the conclusion that pressurized, in-home water service is an important determinant of health status and contributes to reducing transmission of these communicable diseases.

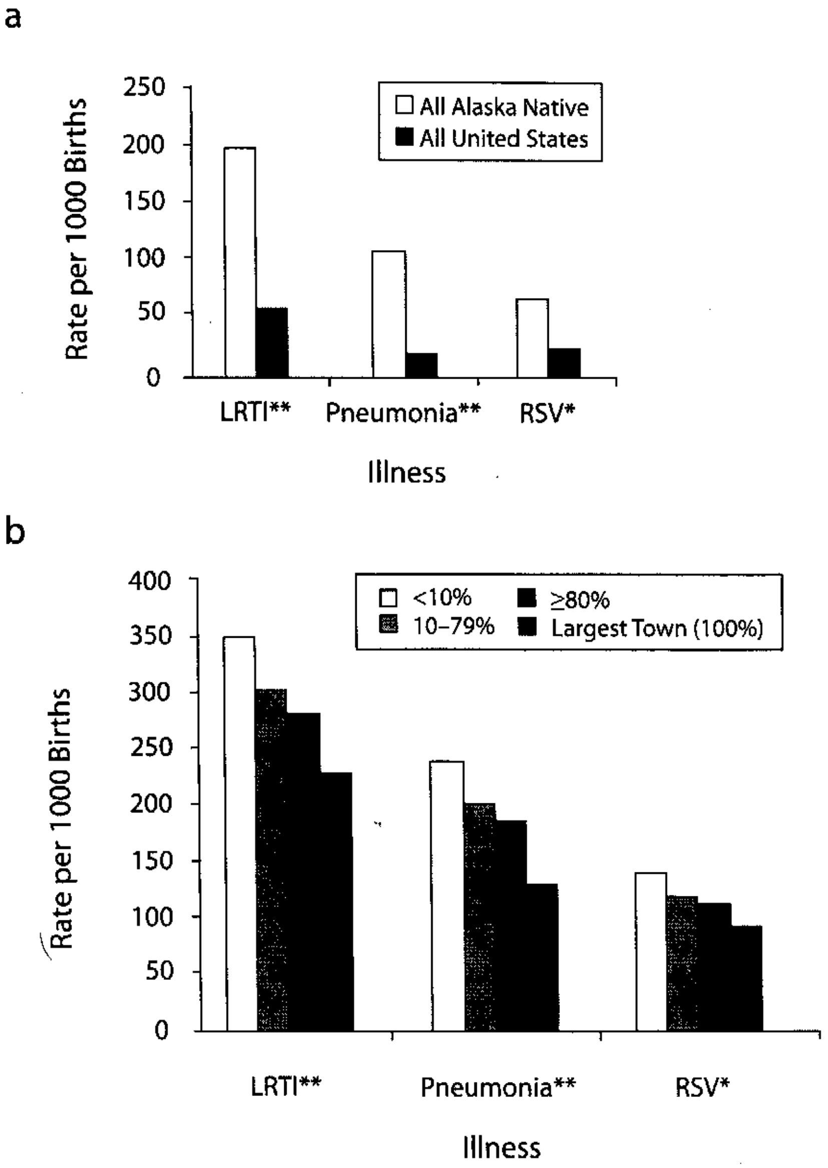
The infectious diarrheal hospitalization rate among Alaska Natives was similar to that among the general US population and did not differ significantly by water service.[20,21] This may seem unexpected because high diarrheal disease rates are seen in other populations that lack in-home water and wastewater service. However, gastrointestinal disease morbidity and mortality among American Indian and Alaska Native populations has been declining since the 1950s.[13,20] The current low rates are likely because of the availability of safe drinking water in nearly all villages (even those with no in-home water service); the relatively cold source water, which does not support propagation of waterborne bacterial pathogens; and the population's overall good nutritional status.

The diarrheal hospitalization rates were in stark contrast to the disparities noted for respiratory and skin infection rates in lower–water service villages. Particularly disturbing was the 5-times higher rate of LRTI hospitalizations and 11-times higher rate of pneumonia hospitalizations among infants in low-service villages in region A compared with the general US population.[17,18] Because infant pneumonias in region A have been identified as a precursor to chronic respiratory diseases such as bronchiectasis and chronic productive cough, many of these children will likely have ongoing health problems because of these infections.[22,23]

Because respiratory and skin infections are not typically contracted through water, the higher rates in low-water-service villages may appear paradoxical. This is best explained by the important role water plays in preventing respiratory and skin infections through handwashing and other personal hygienic measures.[24] It is known that the availability of pressurized, in-home water service increases both water consumption and hygiene practices.[6,25] Thus, the availability of potable water appears to have stabilized waterborne disease rates in Alaska, but it is the water-washed diseases that remain health threats for villages lacking in-home water service. Our findings are consistent with other studies that have shown an association between handwashing and respiratory infectious diseases.[7–9]

Limitations

Some limitations should be considered when one interprets these data. Because of the study design, we cannot be certain that



Note. Comparison rates for all Alaska Natives and all United States from references 17 and 18.
[a]Region A's largest town had water service in almost all homes and was analyzed separately.
*P=.08 for trend, region A; **P<.05 for trend, region A.

FIGURE 1—Hospitalization rate among infants for lower respiratory tract infections (LRTI), pneumonia, and respiratory syncytial virus (RSV) in region A compared with all Alaska Native and US infants, by percentage of village homes with water service: Alaska, 1999–2004.

these associations arose from a cause-and-effect relationship. Water service may be a marker for other factors related to these health outcomes. When comparing regions, we could not control for factors such as income, village size, and crowding that might have confounded the associations. However, within region A, these characteristics were either similar across villages or were accounted for. The sanitation survey preceded some of the illness data; thus, some relevant water service improvements may not have been included. This could have led to overestimation of water service differences. In the region A analysis we accounted for this by removing villages that had received water service improvements over the study period. Finally, our study did not include data on outpatient respiratory or gastroenteric infections, personal hygiene practices, water quality, water quantity, or the different water delivery systems in use.

Conclusions and Recommendations

In 1954, Public Law 83-568 established the US Public Health Service Indian health program (later named the Indian Health Service) as responsible for improving the health of Alaska Native people. At that time, infectious diseases caused 46% of all Alaska Native deaths. Providing potable water and safe wastewater disposal services for Alaska Native communities was a primary objective.[26]

The IHS, along with the State of Alaska, US Environmental Protection Agency (EPA), US Department of Agriculture Rural Development Program, and Alaska's Tribal Health Organizations, has worked to increase the proportion of rural Alaska homes with modern sanitation service from less than 10% in 1950 to 84% in 2006 (W. Griffith, Village Safe Water Program, written communication, April 2006).

Sanitation improvements have been credited with contributing to the dramatic improvements in Alaska Natives' health.[4] However, substantial progress must be made to bring sanitation service in rural Alaska up to the modern standard enjoyed by 99.4% of the US population. The EPA has established the goal of providing modern sanitation services for 94% of rural Alaskan homes by 2011 (D. Wagner, Alaska EPA Drinking Water Program, written communication, April 2006). Even if this can be achieved, it will leave many rural Alaskans with substandard water and sanitation facilities.

Our study indicated that in-home water service is an important determinant of health in rural Alaska communities. Lower levels of water services were associated with a higher burden of hospitalizations for pneumonia and influenza, skin infections, and LRTIs. This finding was suggested by data in region-to-region analyses and is strongly supported by the village comparisons within region A.

These health disparities were borne disproportionately by Alaska Native infants, children, and elderly who resided in low-water-service villages. Of particular concern was that up to one fourth of region A infants were hospitalized annually for respiratory infections.

Further prospective studies could assess the relative contributions of hygienic practices, the volume of water used, and the water distribution system while accounting for potential confounding factors and the economic benefits of in-home water service for prevention of infectious diseases. Although those data would be helpful, we believe that the long-recognized value of in-home service along with the data from our study are convincing enough that programs should proceed with adequate support toward a goal of providing modern water and sanitation service to each home in rural Alaska villages. ■

About the Authors

Thomas W. Hennessy, Dana L. Bruden, Lisa Bulkow, and Rosalyn J. Singleton are with the Arctic Investigations Program, Centers for Disease Control and Prevention, Anchorage, AK. Troy Ritter and Jeff Smith are with the Division of Environmental Health and Engineering, Alaska Native Tribal Health Consortium, Anchorage. Robert C. Holman and Krista L. Yorita are with the Division of Viral and Rickettsial Diseases, Centers for Disease Control and Prevention, Atlanta, GA. James E. Cheek is with the National Epidemiology Program, Indian Health Service, Albuquerque, NM.

Requests for reprints should be sent to Thomas Hennessy, 4055 Tudor Centre Dr, Anchorage, AK 99508 (e-mail: thennessy@cdc.gov).

This article was accepted September 12, 2007.

Note. The findings and conclusions in this article are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Contributors

T.W. Hennessy originated the study, supervised its conduct, conducted analyses, and was the principal writer. T.Ritter originated the study, analyzed water use data, and wrote sections of the article. R.C. Holman conducted analyses related to water use and regional hospitalization rates and assisted with writing. D.L. Bruden conducted analyses related to water use and disease rates within region A and assisted with writing. K.L.Yorita was involved in data preparation and analysis for water use and regional hospitalization rates and assisted with writing. L.Bulkow provided population data and oversaw the statistical analyses. J.E. Cheek originated the study. R.J. Singleton provided and analyzed data on respiratory hospitalization, assisted with writing, and participated in interpretation of the data. J.Smith was involved in the design and oversaw the water use data acquisition and analysis.

Acknowledgments

We acknowledge Ryan DeLuche, Sue Ehrhart, and Edna Paisano of the Indian Health Service for their technical assistance; the staff who collected the Rural Alaska Housing Sanitation Inventory data; and the staff at the hospitals and clinics in the Alaska Native Health Services.

Human Participant Protection

Institutional review board approval for this study was obtained from the Centers for Disease Control and Prevention and the Alaska Area institutional review board of the Indian Health Service for the respiratory hospitalization data in region A. The hospital discharge administrative and disease outbreak data were determined to be exempt from review because they lacked patient identifiers and were obtained in a public health response to a disease outbreak, respectively.

References

1. US Census Bureau. *Census of Housing, 1950.* Available at: http://www.census.gov/hhes/www/housing/census/historic/plumbing.html. Accessed January 27, 2008.

2. US Census Bureau. *Census of Housing, 1970.* Available at: http://www.census.gov/hhes/www/housing/census/historic/plumbing.html. Accessed January 27, 2008.

3. US Census Bureau. *US Summary, 2000.* Available at: http://www.census.gov/prod/2002pubs/c2kprof00-us.pdf. Accessed January 27, 2008.

4. *Sanitation 2000: Water and Wastewater in Rural Alaska.* Anchorage: Alaska Dept of Environmental Conservation, Village Safe Water Program; 2000.

5. Holman RC, Curns AT, Kaufman SF, Cheek JE, Pinner RW, Schonberger LB. Trends in infectious disease hospitalizations among American Indians and Alaska Natives. *Am J Public Health.* 2001;91:425–431.

6. Howard G, Bartram J. *Domestic Water Quantity, Service Level and Health.* Geneva, Switzerland: World Health Organization; 2003:17–19. Available at: http://www.who.int/water_sanitation_health/diseases/WSH03.02.pdf. Accessed January 28, 2008.

7. Luby SP, Agboatwalla M, Feikin DR, et al. Effect of handwashing on child health: a randomised controlled trial. *Lancet.* 2005;366:225–233.

8. Ryan MA, Christian RS, Wohlrabe J. Handwashing and respiratory illness among young adults in military training. *Am J Prev Med.* 2001;21:79–83.

9. Fung IC, Cairncross S. Effectiveness of handwashing in preventing SARS: a review. *Trop Med Int Health.* 2006;11:1749–1758.

10. White GF, Bradley DJ, White AU. *Drawers of Water: Domestic Water Use in East Africa.* Chicago, IL: University of Chicago Press; 1972.

11. Alaska Department of Labor and Workforce Development. *Census and Geographic Information Network, Research and Analysis Section.* Available at: http://almis.labor.state.ak.us/?PAGEID=67&SUBID=114. Accessed October 24, 2005.

12. *Inpatient/CHS Inpatient Data Fiscal Years 2000–2004. National Patient Information Reporting System.* Albuquerque, NM: Indian Health Service; 2005.

13. *Trends in Indian Health–2000–2001.* Rockville, MD: Indian Health Service; 2004.

14. *International Classification of Diseases, Ninth Revision, Clinical Modification.* 6th ed [CD-ROM]. Washington, DC: US Dept of Health and Human Services; 2005.

15. Kleinbaum DG, Kupper LL, Muller KE, Nizam A. *Applied Regression Analysis and Other Multivariable Methods.* Pacific Grove, CA: Duxbury Press; 1998.

16. Singleton RJ, Bruden D, Bulkow LR, Varney G, Butler JC. Decline in respiratory syncytial virus hospitalizations in a region with high hospitalization rates and prolonged season. *Pediatr Infect Dis J.* 2006;25:1116–1122.

17. Peck AJ, Holman RC, Curns AT, et al. Lower respiratory tract infections among American Indian and Alaska Native children and the general population of U.S. children. *Pediatr Infect Dis J.* 2005;24:342–351.

18. Holman RC, Curns AT, Cheek JE, et al. Respiratory syncytial virus hospitalizations among American Indian and Alaska Native infants and the general United States infant population. *Pediatrics.* 2004;114:437–444.

19. Baggett HC, Hennessy TW, Leman R, et al. An outbreak of community-onset methicillin-resistant *Staphylococcus aureus* skin infections in southwestern Alaska. *Infect Control Hosp Epidemiol.* 2003;24:397–402.

20. Holman RC, Parashar UD, Clarke MJ, Kaufman SF, Glass RI. Trends in diarrhea-associated hospitalizations among American Indian and Alaska Native children, 1980–1995. *Pediatrics.* 1999;103:E11.

21. Mounts AW, Holman RC, Clarke MJ, Bresee JS, Glass RI. Trends in hospitalizations associated with gastroenteritis among adults in the United States, 1979–1995. *Epidemiol Infect.* 1999;123:1–8.

22. Redding G, Singleton R, Lewis T, et al. Early radiographic and clinical features associated with bronchiectasis in children. *Pediatr Pulmonol.* 2004;37:297–304.

23. Singleton RJ, Redding GJ, Lewis TC, et al. Sequelae of severe respiratory syncytial virus infection in infancy and early childhood among Alaska Native children. *Pediatrics.* 2003;112:285–290.

24. Cairncross S, Valdmanis V. Water supply, sanitation and hygiene promotion. In: Jamison DT, Breman JG, Measham AR, et al., eds. *Disease Control Priorities in Developing Countries.* 2nd ed. New York, NY: Oxford University Press; 2006:771–792.

25. Curtis V, Kanki B, Mertens T, et al. Potties, pits and pipes: explaining hygiene behavior in Burkina Faso. *Soc Sci Med.* 1995;41:383–393.

26. Alaska Dept of Health and Social Services. *Health Status in Alaska.* Available at: http://www.hss.state.ak.us/dph/targets/PDFs/history2000.pdf. Accessed December 26, 2006.

Lack of Piped Water and Sewage Services is Associated with Pediatric Lower Respiratory Tract Infection in Alaska

BRADFORD D. GESSNER, MD, MPH

Objectives To determine the association between the high incidence of lower respiratory tract infection (LRI) documented among young Alaskan children and the absence of modern water service (in-home piped water/septic system or water delivered by closed haul truck) found commonly in rural Alaskan communities.

Study design A community-level analysis was performed of all 108 Alaskan communities with at least 15 children <2 years of age enrolled in Medicaid during 1998-2003. Community LRI incidence rates were determined from a Medicaid database with standard LRI billing codes. Potentially confounding community-level demographic variables were obtained, as was availability of water service.

Results During linear regression analysis, the percentage of households with modern water service in a community predicted community-level outpatient (beta = −0.53; $P < .001$) and inpatient (beta = −0.15; $P = .088$) LRI incidence rates when controlling for the degree of household crowding, unemployment, adult education, tobacco cigarette use, wood stove use, and poverty. Modest improvements in water service delivery were not shown to be associated with changes in LRI burden.

Conclusions Lack of modern water service in Alaska is associated with high pediatric LRI incidence. These communities should receive modern water service, but this intervention alone may not dramatically reduce LRI burden. *(J Pediatr 2008;152:666-70)*

Alaska Native people in Southwest Alaska have among the highest lower respiratory infection incidence rates ever reported, mainly because of bronchiolitis.[1-3] Reasons for this increase in risk are not well described. One possibility is that lack of clean water and wastewater disposal systems contribute to risk by making handwashing more difficult and thus less likely. Many small, rural, primarily Alaska Native communities lack any piped water and wastewater disposal services, and entire regions have service rates that remain below national standards. This evaluation examined the effect of modern water service on pediatric lower respiratory tract infection (LRI) incidence rates by community among Medicaid-enrolled Alaskan children age <2 years.

METHODS

Healthcare in Alaska

During the study period, health care services in Alaska were delivered through a variety of private, public, nonprofit, Native Corporation, and Indian Health Service entities. Alaska Native people constituted the state's largest racial minority and predominant rural residents and usually received services through Native Corporation and Indian Health Service facilities. Care in most small villages was provided at clinics staffed by Community Health Aides, with support provided by physicians based at regional centers. For Medicaid-enrolled persons, all in-state facilities billed Medicaid regardless of where a specific individual obtained care. During 1999-2000, approximately 94% of Alaska Native infants were enrolled in Medicaid at some point during their first 2 years of life versus 46% of non-Native infants.

Data Sources

The Alaska Division of Medical Assistance provided a master file that consisted of data for all persons younger than 2 years of age and enrolled in Medicaid from October

ICD-9	International Classification of Diseases, 9th Revision	LRI	Lower respiratory tract infection

From the Maternal-Child Health Epidemiology Unit, Alaska Division of Public Health, Anchorage, AK.

Supported in part by project H18 MC-00004-14 from the Maternal and Child Health Bureau (Title V, Social Security Act), Health Resources and Services Administration, Department of Health and Human Services.

Submitted for publication Jun 23, 2007; last revision received Oct 3, 2007; accepted Oct 25, 2007.

Reprint requests: Bradford D. Gessner, MD, MPH, Maternal-Child Health Epidemiology Unit, Alaska Division of Public Health, P.O. Box 240249, 3601 C Street, Suite 576, Anchorage, AK 99524. E-mail: Brad_Gessner@health.state.ak.us.

0022-3476/$ - see front matter

10.1016/j.jpeds.2007.10.049

1, 1998, through June 30, 2003.[4] The master file was then linked to an outcomes data file containing all provider, inpatient facility, and outpatient clinic approved billing claims for International Classification of Diseases, 9th Revision (ICD-9) codes 466 (acute bronchitis and bronchiolitis), 480-487.1 (pneumonia and influenza with pneumonia), 490 (bronchitis not specified as acute or chronic), and 510-511 (empyema and pleurisy). LRI was defined as an approved billing for any of these codes. Of the total number of LRI inpatient events, 63% (928 of 1475) were due to acute bronchiolitis (ICD-9 code, 466.1) or pneumonia caused by respiratory syncytial virus (ICD-9 code 480.1), as were 50% (5186 of 10,401) of outpatient LRI events. The master Medicaid enrollment file was linked to a birth certificate database to allow evaluation of birth-related risk factors.

To determine community-level outpatient and inpatient LRI incidence rates, all children born from October 1, 1998, through June 30, 2001, were followed up through the Medicaid database from birth through 2 years of age. Incidence rates were then calculated for each community by summing the number of events and dividing by the sum of the number of days of follow-up (not all children were enrolled continuously during a given year). Rates were calculated only for communities that had at least 15 children enrolled in Medicaid during the study period to eliminate instances where small numbers of events dramatically altered community-level values. A file was created with 1 record for each community, and that included outpatient and inpatient LRI incidence rates. This file then was linked to a file of community-level census variables provided by the Alaska Department of Labor.

Based on input from the US Centers for Disease Control and Prevention, Arctic Investigations Program, the current evaluation tested the hypothesis that the presence of modern water services in a community predicts respiratory tract infection risk. For each Alaskan community, the Alaska Department of Environmental Conservation provided data from a survey conducted during 1999, 2001, 2002, 2003, and 2005 on the proportion of households with modern water service. Modern water service included piped water delivery and septic removal from a municipal source, on-site well and septic tank with a drain field, or water delivery and septic tank evacuation by covered haul vehicles. For most communities, this proportion did not change during 1999 to 2005, and thus 2005 data were used. Twenty of the final 108 communities included in analysis experienced increases of at least 10% in the proportion of houses with modern water service during 2001 or 2002. For these communities, LRI incidences rates were calculated for the period up to the year that water service coverage changed.

Analysis

Linear regression models were created that allowed an evaluation of the independent effect of community water service on LRI incidence when controlling for potential confounding variables. Census variables entered into the model included the proportion of residents that were Alaska Native people, the average number of children younger than age 3 years per household, the proportion of residents below the federal poverty line, the proportion of adults age 16 years and older and in the labor force that were employed, the proportion of adults age 25 years and older with less than 12 years of formal education, and the proportion of households using wood fuel for heat. Additionally, the cumulative years of Medicaid enrollment among children in the community were added from the Medicaid database, and the proportion of mothers in the community that used tobacco cigarettes prenatally was entered from the birth certificate database. Because of issues with multicollinearity, regression models did not include the average number of persons per household. Potential confounding variables were removed from the models in a stepwise fashion on the basis of a P value $<.05$. All analyses were performed with SPSS version 13.0 statistical software (SPSS Inc., Chicago, Ill).

RESULTS

Descriptive Analysis

There were 263 Alaskan communities with at least 1 child age <2 years enrolled in Medicaid during the study period, of which 117 had at least 15 children enrolled during the study period. Of these, 108 had information on water service, and these communities formed the basis for all subsequent evaluations.

Among the 108 evaluated communities, the mean outpatient LRI incidence rate was 56 per 100 child-years of follow-up (median, 42; standard deviation, 41; range, 0 to 153), and the mean inpatient LRI incidence rate was 11 per 100 child-years (median, 7.0; standard deviation, 11; range, 0 to 50). The mean percentage of homes that had modern water service was 69% (median, 89%; standard deviation, 38%; range, 0 to 100%).

Communities with a low percentage of houses with modern water service were not distributed randomly in the state. Twenty-one communities had less than 20% of homes connected to modern water service, and 6 had 20% to 39% of homes connected. These 27 communities were located in just 5 of Alaska's 24 census areas, all in the Western and Northern regions. These 27 communities also were more likely to have a higher mean percentage of residents who were Alaska Native people (94% vs 54%; $P < .001$) and living in poverty (26% vs 17%; $P < .001$) and a higher mean percentage of adults with less than a twelfth-grade education (33% vs 19%; $P <$ 001). They did not have a higher mean percentage of maternal prenatal tobacco use (29% vs 31%; $P = .72$).

Higher inpatient and outpatient LRI incidence rates also tended to occur in communities with high proportions of Alaska Native people, more poverty, and a less educated population (Table). Inpatient and outpatient LRI incidence rates decreased as modern water service increased (Figure). Of the 27 communities with <40% of homes connected to modern water service, the mean inpatient LRI incidence was

Table. Community characteristics and community level incidence of inpatient and outpatient LRI among Medicaid-enrolled children age <2 years; Alaska, 1998–2003

	Inpatient LRI incidence ≥15 per 100 child-years			Outpatient LRI incidence ≥90 per 100 child-years		
Community characteristic	**Yes (n = 32)**	**No (n = 76)**	***P* value**	**Yes (n = 30)**	**No (n = 78)**	**Risk ratio (95% confidence interval)**
Mean percent Alaska Native	93%	52%	<.001	93%	53%	<.001
Mean percent living in poverty	25%	16%	<.001	26%	16%	<.001
Mean percent of persons 25 years or older with <12 years of education	34%	18%	<.001	34%	19%	<.001
Mean percent of mothers reporting prenatal tobacco use	19%	35%	<.001	17%	35%	<.001

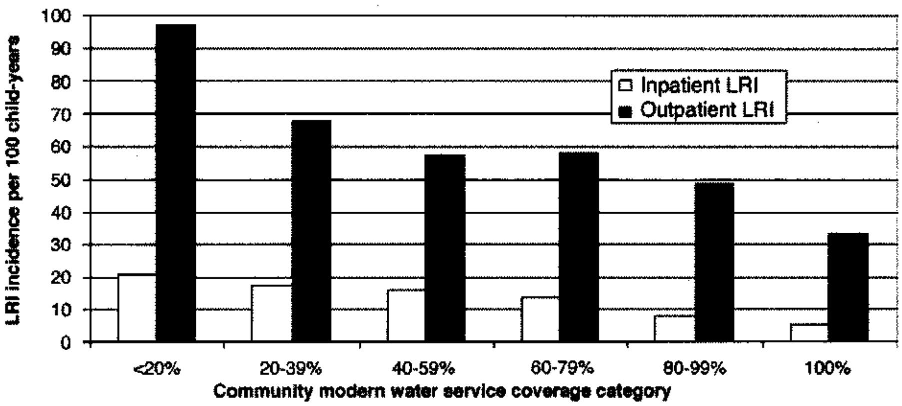


Figure. Incidence of community-level inpatient and outpatient LRI in children younger than 2 years of age by percentage of households in community with modern water service; Alaska, 1998-2003.

20 per 100 child-years compared with 8.5 per 100 child-years for the remaining 81 communities ($P < .001$); the analogous values for mean outpatient LRI incidence were 91 and 45 per 100 child-years, respectively ($P < .001$).

Multivariate Analysis of Risk Factors

During linear regression analysis, predictor variables that remained in the final model for community-level outpatient LRI incidence rate included the proportion of households with modern water service ($\beta = -0.53$; $P < .001$), the proportion of adults with less than 12 years of education ($\beta = 0.46$; $P < .001$), and the proportion of mothers of study subjects who used prenatal tobacco ($\beta = -0.74$; $P < .001$). The final model contained an interaction term created as the product of the water and tobacco use variables ($P = .002$). No interaction was noted between the other independent variables in the model. The r^2 for the final model was 0.60.

Predictor variables that remained in the final model for community-level inpatient LRI incidence rate were identical and included the proportion of households with modern water service ($\beta = -0.15$; $P = .088$), the proportion of adults with less than 12 years of education ($\beta = 0.57$; $P < .001$), and the proportion of mothers of study subjects who used prenatal tobacco ($\beta = -0.36$; $P < .001$). No interaction between variables was noted, and thus no interaction terms were entered. The r^2 for the final model was 0.54.

Changes in Modern Water Service and LRI Incidence

During 1999 versus 2002, the mean outpatient LRI incidence rates across all 108 villages were 46 versus 34 per 100 child-years, and inpatient LRI incidence rates were 15 versus 4 per 100 child-years. Of communities with increases in modern water service of at least 10%, 85% were located in 5 Western and Northern Alaska census areas. For the 54 study communities in these 5 census areas, univariate regression analysis showed that the percentage improvement from 1999 to 2002 in the number of homes with modern water service did not predict changes in outpatient ($\beta = 0.10$; $P = .47$) or inpatient ($\beta = 0.22$; $P = .12$) LRI incidence rates over the same time period.

DISCUSSION

This study found a strong association between modern water services in a community and outpatient LRI incidence rates among children <2 years of age; a weaker association existed for inpatient LRI incidence. Children living in communities with the lowest levels of modern water service had LRI incidence rates 3- to 4-fold higher than those found in communities with the highest levels of modern water services. Many of the communities had LRI incidence rates substantially higher than the 6.3 and 20.7 per 100 per year reported for U.S. children age younger than 5 years.[5] This high burden of disease is compounded by the frequent long-term chronic respiratory problems experienced by children who have had severe LRI during early childhood.[6,7] Although specific LRI disease syndromes were not evaluated in this study, a recent evaluation of risk factors for avian influenza A (H5N1) infection in Vietnam found an association between infection and lack of an indoor water source.[8] This raises the possibility that lack of modern water services puts Alaskan populations at increased risk of contributing to pandemic influenza spread.

The mechanism by which in-home water could decrease respiratory infection risk remains unknown, but the most likely explanation is that it increases the ease and thus the frequency of handwashing. Two recent reviews found that handwashing decreases the risk of respiratory tract infection; however, both evaluations noted the paucity of rigorous studies.[9,10] A more recent and methodologically sound randomized trial in Pakistan noted a protective effect of handwashing, with households that received plain soap and handwashing promotion reporting a 50% lower incidence of pneumonia compared with control subjects.[11] The stronger association with outpatient than inpatient LRI incidence in this study supports this hypothesis. Lack of handwashing is likely to increase the risk of acquiring an infection and presenting to an outpatient clinic, and factors such as maternal education, health care access, and background level of health may contribute more to determining whether an LRI, once acquired, results in hospitalization.

The State of Alaska's Department of Environmental Conservation, Indian Health Service, U.S. Environmental Protection Agency, and Alaska's Tribal Health Organizations have successfully increased the mean proportion of households in Alaskan communities with modern water service to 69%. Much work remains to be done, however. In 27 of the 108 evaluated communities, less than 40% of households had access to modern water services.

Equally important as the continued low level of modern water service availability in many Alaskan communities is the distribution of these communities. Mirroring what was found for communities with high LRI burden, communities with poor access to modern water service were located mainly in the rural Western and Northern parts of the state, had predominantly Alaska Native residents, and had more impoverished and less educated populations. In addition to modern water services, these same communities have had inadequate investment in schools, transportation infrastructure, and job creation. Not unexpectedly, these communities have high rates of many diseases, both infectious[12-14] and noninfectious.[15,16]

No relationship was identified between modest changes over time in modern water service delivery and LRI incidence, emphasizing the lack of a simple relationship between these factors. Changes in LRI incidence over time may have been effected by temporal changes in the geographic distribution of yearly influenza and respiratory syncytial virus epidemics, changes in risk factors such as day care attendance and breast feeding, and changes in diagnostic and reporting biases, all factors not available for this analysis. In addition to this limitation, differences in reported outpatient LRI rates may reflect interobserver variability in the diagnosis of lower respiratory tract disease, and differences in inpatient LRI rates may reflect differences in access to hospital care.

Finally, this analysis could not control for all potential confounding variables or even all available variables because of issues of multicollinearity. Consequently, the identified association between LRI incidence and modern water service availability may not be causal. The strong and consistent association between inpatient or outpatient LRI incidence and adult education levels and maternal prenatal tobacco use underline the multifactorial nature of LRI risk. Although seemingly paradoxical, the inverse association between prenatal tobacco use and LRI risk likely reflects the practice among tobacco-using Western and Northern Alaska Native women of switching from tobacco cigarettes to chewing tobacco during pregnancy.[17] Maternal use of chewing tobacco may cause high infant tobacco exposure either inadvertently through the practice of pre-chewing food or directly by giving tobacco to the infant as a pacifier,[17] with subsequent increased LRI risk, particularly with bacterial organisms.[18]

All citizens in the United States have a basic right to clean water and sewage, but this has not yet occurred. This study found that a lack of modern water service in Alaska predicted increased LRI risk among young children. A similar association might exist for other small, rural U.S. communities as well as other communities worldwide. Even though modern water service availability may decrease LRI burden, available data did not allow estimation of the expected long-term degree of improvement.

The author acknowledges Phillip Mitchell of the Alaska Bureau of Vital Statistics and Ingrid Zaruba of the Alaska Department of Labor for provision of data.

REFERENCES

1. Holman RC, Curns AT, Cheek JE, Bresee JS, Singleton RJ, Carver K, et al. Respiratory syncytial virus hospitalizations among American Indian and Alaska Native infants and the general United States infant population. Pediatrics 2004;114:437-44.
2. Karron RA, Singleton RJ, Bulkow L, Parkinson A, Kruse D, DeSmet I, et al. Severe respiratory syncytial virus disease in Alaska native children. RSV Alaska Study Group. J Infect Dis 1999;180:41-9.
3. Bulkow LR, Singleton RJ, Karron RA, Harrison LH; Alaska RSV Study Group. Risk factors for severe respiratory syncytial virus infection among Alaska native children. Pediatrics 2002;109:210-6.
4. Gessner BD, Neeno T. Trends in asthma prevalence, hospitalization risk, and inhaled corticosteroid use among Alaska Native and nonnative Medicaid recipients less than 20 years of age. Ann All Asth Immunol 2005;94:372-9.
5. Peck AJ, Holman RC, Curns AT, Lingappa JR, Cheek JE, Singleton RJ, et al. Lower respiratory tract infections among American Indian and Alaska Native children and the general population of U.S. Children. Pediatr Infect Dis J 2005;24:342-51.
6. Redding G, Singleton R, Lewis T, Martinez P, Butler J, Stamey D, et al. Early radiographic and clinical features associated with bronchiectasis in children. Pediatr Pulmonol 2004;37:1-8.

7. Singleton RJ, Redding GJ, Lewis TC, Martinez P, Bulkow L, Morray B, et al. Sequelae of severe respiratory syncytial virus infection in infancy and early childhood among Alaska Native children. Pediatrics 2003;112:285-90.
8. Dinh PN, Long HT, Tien NT, et al. Risk factors for human infection with avian influenza A H5N1, Vietnam, 2004. Emerg Infect Dis 2006;12:1841-7.
9. Fung IC, Cairncross S. Effectiveness of handwashing in preventing SARS: a review. Trop Med Int Health 2006;11:1749-58.
10. Rabie T, Curtis V. Handwashing and risk of respiratory infections: a quantitative systematic review. Trop Med Int Health 2006;11:258-67.
11. Luby SP, Agboatwalla M, Feikin DR, Painter J, Billhimer W, Altaf A, et al. Effect of handwashing on child health: a randomized controlled trial. Lancet 2005; 366:225-33.
12. Davidson M, Parkinson AJ, Bulkow LR, Fitzgerald MA, Peters HV, Parks DF. The epidemiology of invasive pneumococcal disease in Alaska, 1986-1990—ethnic differences and opportunities for prevention. J Infect Dis 1994;170:368-76.
13. Ward JI, Lum MK, Hall DB, Silimperi DR, Bender TR. Invasive *Haemophilus influenzae* type b disease in Alaska: background epidemiology for a vaccine efficacy trial. J Infect Dis 1986;153:17-26.
14. Harpaz R, McMahon BJ, Margolis HS, Shapiro CN, Havron D, Carpenter G, et al. Elimination of new chronic hepatitis B virus infections: results of the Alaska immunization program. J Infect Dis 2000;181:413-8.
15. Gessner BD. Temporal trends and geographic patterns of teen suicide in Alaska, 1979-93. Suicide Life Threat Behav 1997;27:264-73.
16. Egeland GM, Perham-Hester KA, Gessner BD, Ingle D, Berner J, Middaugh JP. Fetal alcohol syndrome in Alaska, 1977-92. Am J Pub Health 1998;88:781-6.
17. Renner CC, Patten CA, Enoch C, Petraitis J, Offord KP, Angstman S, et al. Focus groups of Y-K Delta Alaska Natives: attitudes toward tobacco use and tobacco dependence interventions. Prev Med 2004;38:421-31.
18. Fainstein V, Musher DM. Bacterial adherence to pharyngeal cells in smokers, nonsmokers, and chronic bronchitics. Infect Immun 1979;26:178-82.

Invasive Pneumococcal Disease in Alaskan Children

Impact of the Seven-Valent Pneumococcal Conjugate Vaccine and the Role of Water Supply

Jay D. Wenger, MD, Tammy Zulz, MPH,* Dana Bruden, MS,* Rosalyn Singleton, MD, MPH,* Michael G. Bruce, MD, MPH,* Lisa Bulkow, MS,* Debbie Parks, BS,* Karen Rudolph, PhD,* Debby Hurlburt, RN,* Troy Ritter, REHS, MPH,† Joseph Klejka, MD,‡ and Thomas Hennessy, MD, MPH**

Background: Alaska Native (AN) children, especially those in the Yukon-Kuskokwim region (YK-AN children), suffer some of the highest rates of invasive pneumococcal disease (IPD) in the world. Rates of IPD declined after statewide introduction of the 7-valent pneumococcal conjugate vaccine (PCV7) in 2001, but increased in subsequent years.

Methods: Population-based laboratory surveillance data (1986–2007) for invasive *Streptococcus pneumoniae* infection in Alaskan children <5 years old were used to evaluate the association of IPD rates and serotype distribution with immunization, socioeconomic status, and in-home water service.

Results: Introduction of PCV7 vaccine resulted in elimination of IPD caused by vaccine serotypes, but was followed by increasing rates of IPD caused by nonvaccine serotypes. Among YK-AN children IPD rates dropped by 60%, but then rose due to non-PCV7 serotypes to levels 5- to 10-fold higher than rates in non-YK-AN children and non-AN children. IPD rates in YK-AN children were twice as high in villages where <10% of houses had in-home piped water compared with villages where more than 80% of houses had in-home piped water (390 cases/100,000 vs. 146 cases/100,000, $P = 0.008$).

Conclusions: High IPD rates in Alaska are associated with lack of in-home piped water (controlling for household crowding and per capita income). The effect of in-home piped water is most likely mediated through reduced water supply leading to limitations on handwashing.

Key Words: invasive pneumococcal disease, water, pneumococcal conjugate vaccine, *Streptococcus pneumoniae*

(*Pediatr Infect Dis J* 2010;29: 000–000)

Nearly 50% of Alaskans live in the Anchorage metropolitan area, but one-third of the remaining population lives in small rural communities of 50 to 1000 persons dispersed throughout the remainder of the state. Alaska Native (AN) people comprise approximately 20% of the population and are the predominant inhabitants of small communities in the northern and western regions of the state.[1] These communities are not connected by a highway system, and many do not have piped water systems.

High rates of serious pneumococcal disease were recognized several decades ago in Alaska.[2] Rates of invasive pneumococcal disease (IPD) in AN children in the Yukon-Kuskokwim region in western Alaska (YK-AN children) are among the highest in the world.[3] Subsequent evaluations confirmed high rates of disease in other AN children, and identified a significant disparity in rates between AN children and non-AN children. For example, the rate of culture-positive pneumonia in AN children <2 years old was 10-fold higher than that of non-AN children <2 years old.[4]

Underlying diseases (eg, immunosuppressive disorders, congenital abnormalities, chronic lung disease, or prematurity) as well as behavioral risk factors (eg, day care attendance, household crowding, and lack of breast-feeding[5–7]) contribute to increased risk of IPD in children.[4,5,8–10] However, no combination of these previously identified risk factors explained a health disparity of the magnitude observed in Alaska, which was consigned to "... unexplored social, ... and environmental factors."[4] Two recent studies from Alaska demonstrated that lack of in-home piped water (ie, hauling of water to and waste from the home) was associated with higher rates of hospitalization for respiratory diseases.[11,12]

Introduction of 7-valent pneumococcal conjugate vaccine (PCV7) in early 2001 raised hopes of addressing IPD in Alaska populations, despite underlying causes. IPD caused by serotypes present in the vaccine decreased rapidly, narrowing the disparity between AN children and non-AN children but IPD rates caused by nonvaccine serotypes increased subsequently, specifically in AN children less than 5 years old.[13]

We evaluated IPD surveillance data from Alaska through 2007 to further characterize the impact of PCV7 vaccine introduction, and to evaluate potential associations between socioeconomic indicators, water supply, and IPD in the postvaccine era.

METHODS

Invasive Disease Surveillance

Since 1986, cases of IPD (defined as isolation of *S. pneumoniae* from a normally sterile site in an Alaska resident) are reported from clinical laboratories throughout Alaska to the CDC's Arctic Investigations Program (AIP) in Anchorage. Isolates are sent to AIP where identification, serotyping, and antimicrobial susceptibility testing are performed using standard methods. Annually, participating laboratories compare their records with a list of isolates received by AIP and report any missing cases.

Data on cases are collected from clinical laboratories, medical records, or the patient's clinician, and include demographic information, clinical syndrome and outcome. We report data on cases of IPD in children aged <5 years in Alaska identified between January 1, 1986 and December 31, 2007. We studied 3 specific time periods to assess impact of PCV7 and characterize disease in the conjugate vaccine era. Time periods were defined as:

- Period 1, prevaccine introduction (1996–2000).

Accepted for publication August 24, 2009.
From the *Arctic Investigations Program, National Center for Preparedness, Detection and Control of Infectious Diseases, Centers for Disease Control and Prevention, Anchorage, Alaska; †Division of Environmental Health and Engineering, Alaska Native Tribal Health Consortium, Anchorage, Alaska; and ‡Yukon-Kuskokwim Health Corporation, Bethel, Alaska.
Address for correspondence: Jay D. Wenger, MD, Arctic Investigations Program, Centers for Disease Control and Prevention, 4055 Tudor Centre Dr, Anchorage, AK 99508. E-mail: jdw2@cdc.gov.

ISSN: 0891-3668/10/2903-0001
DOI: 10.1097/INF.0b013e3181bdbed5

- Period 2, early vaccine period (2001–2004), during which rates in both AN children and non-AN children dropped below the lowest rates in period 1.
- Period 3, late vaccine period (2005–2007) during which rates in both AN children and non-AN children rose above period 2 nadirs.

Socioeconomic Factors and Water Supply Data

The Rural Alaska Housing Sanitation Inventory documented in-home water service in rural areas of Alaska between 2001 and 2004. We obtained data on factors potentially associated with IPD (household size, income data, percent of homes heated with wood, and water service in villages/cities not in the inventory) at the village level from the 2000 US Census.[1] In-home water service was defined as pressurized water service within the household, either from a centralized piped water service system or a closed haul system. In a closed haul system, water is delivered to an external holding tank and distributed throughout the household in pressurized pipes. We calculated the percent of households with water service by AN health care system regions. In YK, we categorized villages (N = 55) into low service (<10% of households served), midlevel service (10%–<80% of households served), and high service (≥80% of households served).

Vaccination Coverage

We obtained the coverage rate with 3 doses of PCV7 in 19- to 35-month-old children in the United States population overall, and for Alaskan children by race from the National Immunization Survey public use files for July 3, 2003 through June 3, 2007.[14] We obtained coverage data for AN children by region from computerized health records for AN children.

Statistical Analysis

Vaccine coverage is presented with the 95% confidence interval for a binomial proportion. Statistical analyses and comparisons of rates and proportions between study periods were evaluated using the χ^2 test (Mantel-Haenszel). *P*-values are exact where appropriate and 2-sided. All statistical analyses were conducted using SAS 9.2 (SAS Institute, Cary, NC), EpiInfo 3.5 (Centers for Disease Control, Atlanta, GA).

We used a multivariate analysis of variance model (MANOVA) to test if 3 potential risk factors (household size, per capita income, and water service level) jointly differed between YK and other regions. The unit of analysis was village/city. The city of Anchorage was presented separately for IPD rates and socioeconomic factors. It was not included in the MANOVA as it was the only unit of analysis in the region. We tested IPD rates among YK villages with different levels of water service by use of a trend test for Poisson rates.[15] We adjusted and tested for confounding of socioeconomic factors by the use of Poisson regression.

RESULTS

Vaccination Coverage

Among AN children, coverage with 3 doses of PCV7 in 19- to 35-month olds rose from 93% (95% CI: ±6.3%, July 2003–June 2004) to 98% (±3.6%, July 2006–June 2007).[14] Vaccine coverage in Alaska white nonhispanic children rose from 65% (±9%) to 90% (±5%) while coverage with 3 doses of PCV7 vaccine in the United States population rose from 71% (±1%) to 89% (±1%)[14] during the same time periods. Among YK-AN children, coverage rose from 95% to 98% during the same time periods (AN health system data).

Overall IPD Rates in Alaskan Children

IPD rates in Alaskan children <5 years of age are shown in Figure 1. IPD in all Alaskan children declined from 97 cases/100,000 per year in the prevaccine period (period 1) to 41/100,000 in period 2 ($P < 0.002$), and then rose to 63/100,000 in period 3 ($P < 0.002$, period 2 vs. period 3). Rates of disease in AN children were 2- to 5-fold higher than in non-AN children during period 1. IPD rate disparities disappeared in 2001, when PCV7 was introduced, but re-emerged later, with rates in AN children 3 to 5 times higher than those in non-AN children ($P < 0.001$).

IPD Rates by Ethnicity, Setting, and Vaccine Type Status

Table 1 shows rates of IPD, IPD caused by vaccine serotypes, and nonvaccine serotypes. Among AN children, rates of vaccine type disease were highest in YK. YK-AN children also had the highest rates of nonvaccine type disease before introduction of PCV7. Vaccine-type disease disappeared in all population groups. IPD due to nonvaccine serotypes increased in both AN children and non-AN children in recent years. Following an initial postintroduction decline in YK, rates of nonvaccine type IPD increased more than 3-fold ($P < 0.0001$, period 3 vs. period 2, Table 1). In all other population groups (except urban AN children) nonvaccine type IPD in period 3 also increased significantly ($P < 0.02$ for comparisons of period 1 vs. period 3).

Serotype Distribution

Serotypes causing at least 90% of IPD in Alaskan children during each period are shaded in Table 2. In period 1, 11 serotypes caused 92% (201/219) of all IPD. In period 2, the most common 18 serotypes (causing 93% (71/76) of all IPD) included 8 of the 11 major serotypes in period 1 plus an additional 10 serotypes present previously, but which had not caused substantial amounts of disease. In period 3, three non-PCV7 serotypes (19A, 7F, and 6A), each among the 11 most common causes of IPD in period 1, caused 56% of all IPD. An additional 22% of all disease in period 3 was caused by serotypes that emerged as significant contributors to IPD in period 2. Serotypes included in the 13-valent pneumococcal conjugate vaccine under development caused 67% of IPD in period 3.

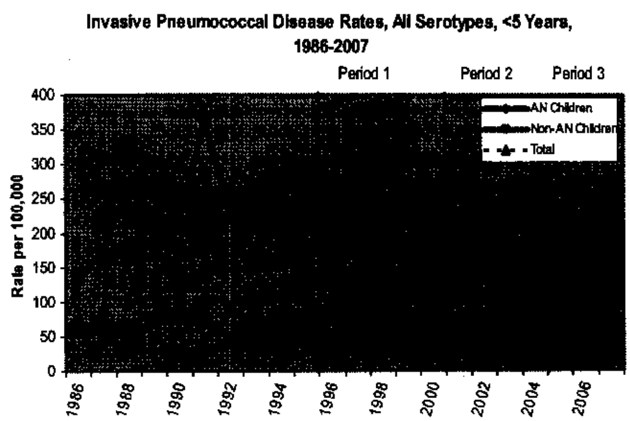


FIGURE 1. Invasive pneumococcal disease (IPD) in Alaskan children less than 5 years of age, 1986 to 2007, cases/100,000 children/y. Total rate (lines with triangles), rate in non-Alaskan Native children (lines with boxes) and rate in Alaskan Native children (lines with diamonds).

TABLE 1. Rates of Invasive Pneumococcal Disease (IPD) by Race, Geographic Location and Time Period, Alaskan Children <5 Year of Age

	Period 1, 1996–2000	Period 2, 2001–2004	Period 3 2005–2007	P Period 1 vs. 2	P Period 2 vs. 3
Rate of total IPD (cases of IPD/100,000 children <5)					
All	97 (242)*	41 (83)	63 (101)	<0.001	0.003
Alaska native–all	227 (135)	77 (42)	142 (62)	<0.001	0.002
YK	547 (81)	148 (18)	426 (40)	<0.001	<0.001
Other rural	87 (25)	59 (16)	87 (18)	0.2	0.3
Urban	182 (29)	53 (8)	30 (4)	0.001	0.3
Alaska non-native–all	56 (107)	27 (41)	32 (37)	<0.001	0.5
Rural	34 (18)	26 (11)	24 (8)	0.5	0.9
Urban	65 (89)	28 (30)	34 (29)	<0.001	0.4
Rate of IPD caused by serotypes in PCV7 (cases of PCV 7 serotype IPD/100,000 children <5)†					
Alaska native					
YK	344 (51)	8 (1)	0	<0.001	0.4
Other rural	70 (20)	11 (3)	10 (2)	<0.001	0.9
Urban	133 (18)	0	0	<0.001	—
Alaska non-native					
Rural	28 (15)	7 (3)	0	0.02	0.1
Urban	49 (67)	11 (12)	0	<0.001	<0.002
Rates of IPD caused by serotypes not in PCV7 (cases of non PCV 7 serotype IPD/100,000 children <5)†					
Alaska native					
YK	142 (21)	124 (15)	405 (38)‡	0.7	<0.001
Other rural	14 (4)	47 (13)	77 (16)‡	<0.02	0.2
Urban	38 (6)	47 (7)	30 (4)	0.7	0.5
Alaska non-native					
Rural	5.7 (3)	19 (8)	24 (8)‡	0.06	0.6
Urban	10 (14)	13 (14)	34 (29)‡	0.5	0.002

*Number of cases in parentheses.
†Serotype specific rates represent cases in which serotype information is available.
‡Rate in period 3 significantly greater than rate in period 1, $P < 0.02$.

Clinical Presentation

The proportion of AN children IPD case-patients with pneumonia rose from 62% (period 1) to 71% (period 3, $P > 0.05$). A higher proportion of YK case-patients had pneumonia (80%) than AN children from outside of YK (54%, $P < 0.01$). The proportion of non-AN children case-patients with pneumonia rose from 17% in period 1 to 30% in period 3 ($P = 0.05$). AN children case-patients were more likely to have pneumonia than non-AN children in each time period ($P < 0.01$), while non-YK AN children did not differ significantly from non-AN children. Seven to 15% of case-patients had meningitis, with no significant difference by race or time period. The case fatality rate ranged from 1.7% to 2.5%, with no significant difference by race or time period.

Underlying Diseases

Information on underlying diseases was available for at least 94% of patients in periods 2 and 3, but only 39% of patients from period 1. Among those with information, 12%, 18%, and 38% reported underlying diseases in periods 1, 2, and 3, respectively ($P < 0.01$ for period 1 or 2 compared with period 3). During periods 2 and 3,YK-AN children were more likely to report an underlying illness (22% and 49% for period 2 and period 3, respectively) than non-YK-AN children (21% and 43%, respectively), or non-AN children (10% and 19%, respectively) though the differences between population groups within a time period are not statistically significant.

Asthma was a common underlying disease reported for YK-AN children (11% and 24% of YK-AN children in periods 2 and 3, respectively). In contrast, 8% and 4% of non-YK-AN children cases reported these diseases in period 2 and 3, respectively, and 2% and 8% of non-AN children cases reported asthma during the same time periods. The only other commonly reported underlying disease, congenital anomalies or abnormalities, was reported in 5% to 13% of each group in period 2 and 15% to 17% of each group in period 3. Thus, the increase in proportion of children with an underlying disease is likely attributable to both (1) a general increase in reporting underlying disease and (2) an increasing proportion of all cases occurring in YK-AN children (22% of cases in period 2 and 41% of cases in period 3), in whom asthma was more commonly reported in all periods.

Geographic Variation in IPD Rates and Socioeconomic Risk Factors for IPD

IPD rates in the postvaccine era (periods 2 and 3 combined) varied widely among geographic regions in Alaska (Table 3). YK had significantly higher rates of IPD (267 cases/100,000 children <5) than the 3 next highest regions (67, 94, and 80/100,000, $P < 0.0001$), which in turn had higher rates of IPD than other regions (all <45/100,000, $P = 0.004$). YK had the lowest average annual per person family income and the highest number of average persons per household (Table 3). YK also had the smallest proportion of houses with piped, in-home water service (61%). YK differed significantly in water service level, household size, and per capita income from the other regions (MANOVA, $P < 0.01$).

Within YK communities identified as having low water service the rate of IPD was 391/100,000 children <5 years old; communities with midlevel water service had a rate of 263/100,000 and communities with high water service had a rate of 147/100,000 (P-for trend = 0.008, Table 4). The association between IPD rate and water service remained statistically significant when stratified by income per person, median family income, median household size, and proportion of houses heated with wood ($P < 0.02$ for each comparison, data not shown).

DISCUSSION

IPD decreased in Alaska immediately after introduction of PCV7, but increased in subsequent years, especially in YK-AN

TABLE 2. Most Common *S. pneumoniae* Serotypes Causing Invasive Pneumococcal Disease (IPD) in Alaskan Children <5-Year-Old by Time Period

Serotype	Period 1: 1996-2000 Cases, (%)	Period 2: 2001-2004 Cases, (%)	Period 3:2005-2007 Cases, (%)
14* (PCV7)			-
6B* (PCV7)			-
19F* (PCV7)			-
18C* (PCV7)			-
9V* (PCV7)		1 (1)	1 (1)
23F* (PCV7)			1 (1)
19A*			
4* (PCV7)		-	-
6A*			
1*		-	-
7F*			
38	†		1 (1)
33F	3 (1)		
15C*	1 (0.5)		1 (1)
22F	3 (1)		
10A	†		
15B	1 (0.5)		1 (1)
12F	†		
3*	†		
8	†		-
22A	1 (0.5)		1 (1)
23B	†	1 (1)	
15A	1 (0.5)	-	
16F	†	-	
35F	1 (0.5)	-	
9N	2 (1)	-	
17F	§	1(1)	1 (1)
% of IPD (top 3 serotypes)	58%	41%¶	58%¶
% of IPD (top 5 serotypes)	71%	51%¶	71%¶
% of IPD (top 10 serotypes)	92%	73%¶	86%¶
% of IPD (PCV7 serotypes)	80%	26%¶	2%¶
% of IPD (6 additional serotypes in PCV13)	13%	35%¶	65%¶
% of IPD (PCV13 serotypes)	92%	61%¶	67%¶

*In 13-valent pneumococcal conjugate vaccine.
†Isolated from IPD in Alaskan children <5 yr of age in 86–95.
‡No IPD, but present in carriage specimens from period 1 IPD.
§Isolated from Alaskan adults during period 1.
¶P value <0.05 when compared with previous period.
‖Shading shows rank-ordered serotypes included in cumulative frequency of ≥90%.

children. By 2007, IPD rates in YK-AN children were again 5 to 10 times higher than in other populations in Alaska. We characterized potential contributors to this persistent increased risk, and identified a significant association of IPD with lack of in-home water supply.

Among Alaska regions, YK has the lowest per capita income, the largest households and the lowest proportion of villages with a piped water supply. Within YK, lack of piped water was significantly associated with risk of IPD (controlling separately for per capita income, household crowding, and wood heating in the home). The most likely explanation for such an effect is that reduced availability of water decreases handwashing, leading to increased transmission of respiratory pathogens. A randomized trial of handwashing in Pakistan showed 50% lower rates of lower respiratory tract infection in the hand-washing group.[16] Reduction in risk of respiratory disease was associated with handwashing in a military population,[17] for SARS transmission,[18] and for respiratory infections in general.[19] For IPD, the implications of increased person-to-person transmission of respiratory pathogens may be 2-fold–(1) enhanced spread of pneumococcal colonization and (2) increased transmission of other respiratory viruses that could facilitate development of IPD among persons colonized with pneumococci. The impact of water supply on IPD appears to be unrelated to water purity or contamination. Neither study identifying water supply as a risk factor for increased rates of hospitalization for skin and respiratory infection in Alaska found an associated increase in diarrheal diseases.[11,12]

TABLE 3. Water Supply, Socioeconomic Data and Invasive Pneumococcal Disease (IPD) Rates (2001–2007) by Region Within Alaska

Region	Total Population Size	Population (<5 Years of Age)	% of Population Alaska Native	No. Villages	Overall Rate of IPD <5 Years of Age (Cases)	Proportion of Households With Water Service	Socioeconomic Factors: Median Persons/Household	Socioeconomic Factors: Per Capita Income ($1000)	Socioeconomic Factors: Median Family Income ($1000)
YK	23,415	3024	88%	50	267 (59)	61%	4.7	6.5	33.2
A	7965	900	86%	13	94 (6)	86%	4.4	14.7	58.1
B	9196	1045	79%	17	80 (6)	72%	3.8	9.8	40.9
C	7445	675	73%	26	67 (3)	89%	3.4	17.0	57.4
D	6346	685	71%	7	44 (2)	100%	3.9	17.4	68.2
E	259,889	21,069	10%	1	37 (57)	100%	3.2	20.0	63.7
F	143,494	9693	12%	124	37 (27)	95%	3.3	17.8	56.9
G	96,228	7970	14%	66	29 (16)	92%	3.1	14.9	46.8
H	72,954	4743	22%	43	25 (8)	95%	3.1	19.8	62.4

TABLE 4. Rates of Invasive Pneumococcal Disease (IPD) in Children <5 yr of Age in YK, 2001–2007 by Water Service Level and Socioeconomic Factors

Socioeconomic Factor	Socioeconomic Level	IPD Rate (Cases/100,000 per Year)	Univariate P
Water service	<10%*	390.9	0.008
	10%–80%*	262.9	
	80%+*	146.7	
Income per person	<$6000 per year	286.3	0.71
	≥$6000	256.6	
Median family income	<$32,000 per year	302.6	0.33
	≥$32,000	232.4	
Household size	≥5 persons	345.0	0.06
	<5 persons	199.2	

*Of homes served with running water.

The retrospective, observational nature of our study limits our ability to conclusively define the role of water supply in IPD in Alaska. It is possible that the elevated risk we identified represents the impact of other factors associated with water supply. Data from other sources provides some information on the potential role of other putative risk factors. Several studies suggest a slightly higher prevalence of underlying illnesses associated with risk of IPD[6,7,10,20] among AN children, including major birth defect anomalies,[21] low birth weight,[22] and anemia.[23] In period 3, 49% of YK-AN children and 43% of non YK-AN children with IPD reported an underlying disease. While increased rates of children with underlying disease may contribute to increased overall IPD rates, even if all cases reporting underlying disease are removed from the analysis, rates of disease in YK-AN children was still 4-fold greater than the rate in non- YK-AN children. Thus, while presence of underlying diseases increases risk for IPD, they do not explain the increase in rates observed in YK-AN children.

Behavioral risk factors associated with IPD in children include day care attendance, household crowding, lack of breast-feeding, and possibly indoor air pollution, the most likely correlate of which in Alaska is use of wood for heating.[5–7,20,24] Some data is available to address their potential contribution to increased rates of disease in YK-AN children. There are 8 licensed day care facilities in the Southwest region of Alaska, which includes YK. In contrast, there are 5 times more daycare facilities per unit population elsewhere in Alaska.[25] Thus, licensed day care attendance is unlikely to be a major contributor to increased risk of IPD in YK-AN children. Most (76%) women in Southwest Alaska are breast-feeding their babies at 4 weeks postpartum, well within the range of all regions in Alaska (70%–86%), therefore, differential breast-feeding rates do not appear to contribute to the disparity in risk.[26] Finally, according to US Census data, the proportion of homes heated with wood was low in YKD, did not differ significantly among water service categories (range among water service categories, 8.9%–10.5%) and thus did not contribute to the increased risk attributed to lack of in-home water supply. We addressed household crowding and income level directly in the analysis (Results section, and Table 4) and demonstrated that the association of IPD with water supply was independent of these risk factors. Additional study is needed to confirm this association since it is possible that other unidentified covariates may contribute to the apparently increased risk associated with lack of in-home water use. A prospective evaluation of the impact of provision of in-home piped water on infectious diseases in AN people is now underway.

The interaction of several factors led to multiple levels of risk in Alaska (Table 1). In all groups, from YK-AN children (highest risk) to non-AN rural children (lowest risk), introduction of PCV7 was accompanied by rapid disappearance of vaccine-type IPD. In 4 of 5 population groups, disappearance of PCV7 strains was followed by statistically significant increases in rates of disease caused by nonvaccine strains. As a result, the net impact of PCV7 in Alaskan children (where 80% of baseline disease was caused by vaccine type strains) was a 30% decline in IPD. This finding contrasts with the experience in the general US population, where overall disease rates in children <5 years of age fell from 99 to 23 cases/100,000 between 1998 to 1999 and 2004 (a 77% decrease) and rates of nonvaccine type IPD rose minimally.[27] Rates of IPD in White Mountain Apache children less than 2 years old in Arizona decreased from 470 to 120/100,000 after PCV7 introduction, with no increase in nonvaccine type IPD.[28] In Spain and France, countries with substantially lower PCV7 coverage rates, a modest overall reduction in rates of vaccine type IPD (21% and 40% decrease in children <2, respectively), was associated with a marked increase in nonvaccine type IPD rates (85% and 530%, respectively).[29,30] However, both studies noted an overall increase in IPD rates in the postvaccine era, and the impact of concurrent changes in surveillance methodology was unclear.[31] While long-term follow-up from a vaccine efficacy trial in South Africa suggests an increase in nonvaccine serotype IPD, data from other developing countries with population-wide use of PCV7 is not yet available.[32]

Several factors may contribute to the differences observed in nonvaccine serotype IPD in the postvaccine era. High rates of IPD in AN children are propelled by intense transmission of the pathogen and possibly viral cofactors, by household crowding, lack of piped water supply, and other unidentified factors. IPD after PCV7 introduction is likely a function of (1) level and duration of coverage with PCV7, (2) underlying transmission characteristics operating in the population of concern, (3) host characteristics, and (4) invasiveness of existent serotypes.[33] The complex interplay between these and other factors is illustrated by varying patterns of replacement noted in Alaska, the rest of the United States, and western Europe.

Our findings on incidence and serotype distribution are limited by the small population size leading to small numbers of cases and increased variability of the point estimates. Long-term surveillance is important to confirm the trends we identified. It is also possible that variations in surveillance sensitivity exist. However, increased sensitivity would only lead to even more elevated rates of IPD, emphasizing the importance of addressing key risk factors. In addition, the association of IPD with water supply was noted not only across regions (where some variation in surveillance capacity is possible), but also within the highest risk region (where surveillance is uniform), suggesting it is not a surveillance artifact. While IPD rates were available each year, data on crowding and income were projected from the 2000 census, and though changes in these parameters could have occurred over the course of the study, it is unlikely that these parameters changed substantially. Finally, the association between water service and IPD rates was demonstrated at the village level, and may not represent the strength of the association at the individual or household level.

High rates of IPD in Alaska are associated with lack of in-home piped water, an effect most likely mediated through limitations on handwashing. The pattern of emergence of serotypes after vaccine introduction highlights the potential of broader spectrum pneumococcal vaccines and the importance of continued surveillance, especially in developing countries where environmental conditions predispose to high risk of IPD. While development of vaccines with broader coverage will undoubtedly reduce IPD burden, addressing infrastructure disparities such as in-home water supply may be a key component for controlling IPD in Alaska and other areas where such risk factors for IPD exist.

ACKNOWLEDGMENTS

The authors thank the clinicians and microbiology laboratory personnel of the hospitals participating in state wide surveillance for IPD in Alaska, as well as serotyping personnel at the AIP laboratory (Marcella Harker-Jones, Julie Morris, and Alisa Reasonover for serotyping the pneumococcal isolates, and Kim Boyd-Hummel for summarizing clinical information on cases. Note: The findings and conclusions in this article are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

REFERENCES

1. State of Alaska Department of Labor and Workforce Development. Population estimates, 2008. Available at: http://almis.labor.state.ak.us/?PAGEID=67&SUBID=115.
2. Gilsdorf J. Bacterial meningitis in southwestern Alaska. *Am J Epidemiol.* 1977;106:388–391.
3. Davidson M, Shraer C, Parkinson A, et al. Invasive pneumococcal disease in an Alaska Native Population, 1980 through 1986. *JAMA.* 1989;261:715–718.
4. Davidson M, Parkinson A, Bulkow LR, et al. The epidemiology of invasive pneumococcal disease in Alaska, 1986–1990–ethnic differences and opportunities for prevention. *J Infect Dis.* 1994;170:368–376.
5. Gessner BD, Ussery XT, Parkinson AJ, et al. Risk-factors for invasive disease caused by Streptococcus pneumoniae among Alaska Native children younger than 2 years of age. *Pediatr Infect Dis J.* 1995;14:123–128.
6. Levine OS, Farley M, Harrison LH, et al. Risk factors for invasive pneumococcal disease in children: a population-based case-control study in North America. *Pediatrics.* 1999;103:E28.
7. Hjuler T, Wohlfahrt J, Simonsen J, et al. Perinatal and crowding-related risk factors for invasive pneumococcal disease in infants and young children: a population-based case-control study. *Clin Infect Dis.* 2007;44:1051–1056.
8. Burman LA, Norrby R, Trollfors B. Invasive pneumococcal infections-incidence, predisposing factors, and prognosis. *Rev Infect Dis.* 1985;7:133–142.
9. Kaplan SL, Mason EO, Wald ER, et al. Six year multicenter surveillance of invasive pneumococcal infections in children. *Pediatr Infect Dis J.* 2002;21:141–147.
10. Hjuler T, Wohlfahrt J, Kaltoft MS, et al. Risks of invasive pneumococcal disease in children with underlying chronic diseases. *Pediatrics.* 2008;122:E26–E32.
11. Gessner BD. Lack of piped water and sewage services is associated with pediatric lower respiratory tract infection in Alaska. *J Pediatr.* 2008;152:666–670.
12. Hennessy TW, Ritter T, Holman R, et al. The relationship between in-home water service and the risk of respiratory tract, skin and gastrointestinal tract infections among rural Alaska Natives. *Am J Public Health.* 2008;98:2072–2078.
13. Singleton RJ, Hennessy TW, Bulkow LR, et al. Invasive pneumococcal disease caused by nonvaccine serotypes among Alaska Native children with high levels of 7-valent pneumococcal conjugate vaccine coverage. *JAMA.* 2007;297:1784–1792.
14. Centers for Disease Control and Prevention, 2008. Available at: http://www.cdc.gov/nip/coverage/NIS.
15. Neter J, Kutner M, Nachtsheim C, et al. *Applied Linear Statistical Models.* Boston, MA: WCB-McGraw Hill; 1996.
16. Luby SP, Agboatwalla M, Feikin DR, et al. Effect of handwashing on child health: a randomized controlled trial. *Lancet.* 2005;366:225–233.
17. Ryan MA, Christian RS, Wohlrabe J. Handwashing and respiratory illness among young adults in military training. *Am J Prev Med.* 2001;21:79–83.
18. Fung IC, Cairncross S. Effectiveness of handwashing in preventing SARS: a review. *Trop Med Int Health.* 2006;11:1749–1758.
19. Rabie T, Curtis V. Handwashing and risk of respiratory infections: a quantitative systematic review. *Trop Med Int Health.* 2006;11:258–267.
20. Haddad MB, Porucznik CA, Joyce KE, et al. Risk factors for pediatric invasive pneumococcal disease in the intermountain West, 1996–2002. *Ann Epidemiol.* 2008;18:139–146.
21. Schoellhorn K, Beery A. *Alaska Maternal and Child Health Data Book 2005: Birth Defects Surveillance Edition.* Anchorage, AK: Alaska Department of Health and Social Services; 2006.
22. Alaska Native Epidemiology Center. *Regional Health Profile for Yukon-Kuskokwim Health Corporation.* Anchorage, AK: Alaska Native Epidemiology Center; 2007.
23. DiGirolamo AM, Perry GS, Gold BD, et al. Helicobacter pylori, anemia, and iron deficiency-relationships explored among Alaska Native children. *Pediatr Infect Dis J.* 2007;26:927–934.
24. Dherani M, Pope D, Mascarenhas M, et al. Indoor air pollution from unprocessed solid fuel use and pneumonia risk in children aged under five years: a systematic review and meta-analysis. *Bull World Health Organ.* 2008;86:390–398.
25. Division of Public Assistance. *2007 Child Care Market Rate Survey.* Alaska Department of Health and Social Services; 2007.
26. Perham-Hester K, Wiens HN, Schoellhorn J. *Alaska Maternal and Child Health Data Book, 2004:PRAMS Edition.* Anchorage, AK: Alaska Department of Health and Social Services; 2005.
27. Centers for Disease Control and Prevention. Invasive pneumococcal disease in children 5 years after conjugate vaccine introduction-eight states, 1998–2005. *MMWR.* 2008;57:144–148.
28. Lacapa R, Bliss SJ, Larzelere-Hinton F, et al. Changing epidemiology of invasive pneumococcal disease among White Mountain Apache persons in the era of the pneumococcal conjugate vaccine. *Clin Infect Dis.* 2008;47:476–484.
29. Lepoutre A, Varon E, Georges S, et al. Impact of infant pneumococcal vaccination on invasive pneumococcal diseases in France, 2001–2006. *Euro Surveill.* 2008;13.
30. Munoz-Almagro C, Jordan I, Gene A, et al. Emergence of invasive pneumococcal disease caused by nonvaccine serotypes in the era of 7-valent conjugate vaccine. *Clin Infect Dis.* 2008;46:174–182.
31. Moore MR, Whitney CG. Emergence of nonvaccine serotypes following introduction of pneumococcal conjugate vaccine: cause and effect? *Clin Infect Dis.* 2008;46:183–185.
32. Madhi SA, Adrian P, Kuwanda L, et al. Long-term immunogenicity and efficacy of a 9-valent conjugate pneumococcal vaccine in human immunodeficient virus infected and non-infected children in the absence of a booster dose of vaccine. *Vaccine.* 2007;25:2451–2457.
33. Hanage WP. Serotype replacement in invasive pneumococcal disease: where do we go from here? *J Infect Dis.* 2007;196:1282–1284.