Invasive pneumococcal disease in Greenland

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ABSTRACT
Introduction. The purpose of the present study was to evaluate the incidence and outcome of pneumococcal infections in Greenland with special reference to serotypes. Study Design. Retrospective study of invasive pneumococcal infections in Greenland in the period 1996-2002. Methods. Cases were defined as patients with positive cultures of *Streptococcus pneumoniae* from blood and/or CSF received at the microbiological laboratory of Dronning Ingrids Hospital in Nuuk. Cultures were sent to Statens Serum Institut in Copenhagen for serotyping. Medical charts were reviewed. Results. Fifty-one cases were identified. Incidence among Inuit was 54 and among non-Inuit 17 per 100,000 per year. Twenty-one patients were in the age group 35-49 years and 20 in the age group 50-64 years. Twenty patients had meningitis (incidence 6 per 100,000). Seventeen patients died (33%). Most common serotypes were 1 (6 cases) and 12F (8 cases). Mortality rate was significantly higher among patients with 12F than among others (p<0.01). No patients with serotype 1 died. Conclusion. Like in Canada and Alaska, the incidence of invasive pneumococcal disease, especially meningitis, is high among the Inuit in Greenland. Young and middle-aged adults were most frequently affected. Serotype seems to be an important determinant of the outcome of invasive pneumococcal disease.

Keywords: *Streptococcus pneumoniae*, Greenland, Inuit, meningitis, serotype, pneumonia.

INTRODUCTION
*Streptococcus pneumoniae* remains a leading cause of serious infections (1). It has been shown that the natives of Alaska and Canada have higher incidence rates than non-Inuit (2,3). In Alaska, age-adjusted incidence was 74 per 100,000 for natives (Inuit, Indians and Aleuts) and 16 for non-natives. The overall case-fatality rates were identical (3). The general opinion is that the picture is the same in Greenland. This has, however, not previously been investigated.

Greenland is a huge country with a small population of 56,000 citizens living in small towns and settlements scattered along the coastline. Each town has its own medical centre. The only microbiological laboratory is situated in the capital Nuuk with 13,570 inhabitants (10,000 Inuit)(4). Blood samples and cerebrospinal fluid (CSF) have to be sent from the coast hospitals to Nuuk for cultivation. Therefore, diagnostic procedures as well as adequate treatment may be difficult in several areas of Greenland.

The aim of the present study was to evaluate incidence and outcome of invasive pneumococcal infections in Greenland with special reference to serotypes and thereby evaluate the need for preventive measures.

MATERIALS AND METHODS
Cases were defined as patients with positive cultures of *Streptococcus pneumoniae* from isolates of blood or CSF received at the laboratory in Nuuk.

All cultures were sent to Statens Serum Institute in Copenhagen for serotyping.

The patients were identified retrospectively by
going through the laboratory files in Nuuk of the past seven years, from January 1996 to January 2003. Subsequently, medical charts were reviewed for underlying conditions, clinical observations and outcome of the infection. Pneumonia was defined by radiographic pulmonary infiltrates and/or obvious clinical symptoms of an acute pulmonary infection. Meningitis was defined by isolate of *S. pneumoniae* from CSF. If medical charts were not available, patients were registered as dead of the actual pneumococcal infection if they had died within two days after the date of the culture.

Patients were categorized as Inuit if they were born in Greenland. Proportions were compared using Fisher’s exact test. P<0.05 was considered significant.

**RESULTS**

A total of 51 cases were identified. Twenty patients had *Streptococcus pneumoniae* isolated from the cerebrospinal fluid (CSF), and 37 had positive culture from the blood. Out of these, 6 patients had positive cultures of isolates from both blood and CSF at the same time. One patient had two recurrent infections and one had three. Since the patients recovered fully between the episodes and they all had different serotypes (although in one case serotyping was not possible for the second episode), each episode was registered as a case. Relatively few isolates were sent from the coast centres to Nuuk as shown in Table I. Since data from 1996 and 1997 were scarce, the calculated incidence rate is based on the data from Nuuk in the years 1998-2002.

Thirty patients were identified in that period, 44.4 per 100,000 per year. The annual incidence rate was 54 per 100,000 for Inuit, 17 per 100,000 for non-Inuit. More males than females were infected (28:23).

There was a concentration of cases among the young and middle-aged (Figure 1).

In the period 98-02 we found 20 cases in Nuuk among Inuit older than 35 years, giving an annual incidence rate of 96 per 100,000 in this group.

For 16 cultures serotyping was not possible since the culture did not survive the transportation to Copenhagen. The most common serotypes were 1 and 12F. All patients with serotype 1 and six out of eight with serotype 12F were from Nuuk.

| Table I. Cases of Invasive Pneumococcal Disease in Nuuk and Coast hospitals by diagnosis and outcome in the period 1996-2002. |
|-----------------------------------------------------------------------------------------------------------------|
| **Nuuk** | **Coast hospitals** | **Recovered** | **Complications** | **Dead** | **Total** | **Recovered** | **Complications** | **Dead** | **Total** |
| Meningitis | 0 | 3 | 4 | 7 | 5 | 4 | 4 | 13 |
| Pneumonia | 13 | 3 | 5 | 21 | 1 | 0 | 0 | 1 |
| Septicaemia* | 4 | 1 | 1 | 6 | 0 | 0 | 3 | 3 |
| Total | 17 | 7 | 10 | 34 | 6 | 4 | 7 | 17 |

*Septicaemia: Bacteraemia without signs of focal infection. Three patients whose clinical or radiological data were not available are included.*
Twenty patients had meningitis, 22 had clinical and/or radiological signs of pneumonia and nine patients had *S. pneumoniae* isolated from the blood, but no identified focus of infection (Table III).

Seven cases of meningitis were registered in Nuuk and 13 in the coast hospitals. Seventeen of the 20 cases of meningitis occurred in the period 98-02, giving a total annual incidence of 6 per 100,000 for the whole of Greenland.

All patients received treatment with relevant antibiotics in sufficient doses (data available on 40 patients). Treatment was initiated immediately after hospitalization.

Total case fatality was 33%. Eight patients with meningitis died (40%) and seven had complications (35%). One third of the patients were alcoholics. Mortality among alcoholics was 60% and among non-alcoholics 40% (NS). There was no difference in mortality between patients with or without predisposing medical conditions (27% and 33% respectively).

Patients with serotype 12F had a significantly higher mortality rate than patients with other serotypes (p<0.01, serotype 1 excluded). One of the two survivors from 12F had severe complications (impaired memory and a left-sided hemiparesis) and the other patient died six weeks after another pneumococcal infection, in which case serotyping was unfortunately not possible. There was no clustering and only two patients were known alcoholics (data on five out of eight).

No patients with serotype 1 died and they all had clinically mild infections with pneumonia that resolved quickly.

**DISCUSSION**

This is a small study based on 51 cases. Strong efforts were made to retrieve medical charts of all the patients from the coast as well, but for five patients this was not possible. Even when successful, data on all parameters were not always available as indicated under Results.

Furthermore, the clinical practice for taking blood and CSF for culture differs between Nuuk and the coast hospitals. Samples from the coast hospitals have to be transported over vast distances to the laboratory and the transport may take several days. Blood sampling for culture is therefore more seldom performed in the Coast. Accordingly, relatively few positive blood cultures were found on the coast, whereas the incidence of positive CSF cultures was almost proportionate to the size of the population.

Reliable incidence rates for invasive pneumococcal disease (IPD)
could only be calculated on the basis of the
Nuuk population.

There was a 3-fold higher incidence rate
among the Inuit (54 per 100,000 per year) than
among other populations. This is consistent with
other studies showing a clear racial difference in
susceptibility to pneumococcal infections (1,3).

The proportion of patients with predisposing
medical conditions was comparable to the find-
ings in other studies. One third were alcoholics,
indicating alcohol abuse to be an important risk
factor as seen elsewhere (5,6).

More males than females were infected, as
seen in other studies as well (7).

As mentioned above, the proportion of menin-
gitis registered among patients from the coast
was high, probably because of differences in cli-
nical practice. This might explain the higher
mortality among patients from the coast. Consi-
dering only meningitis, mortality was apparent-
ly lower on the coast than in Nuuk (Table I). This,
however, was not significant.

12F was the most common infecting serotype
(23% of typeable cases). In addition, 12F had a
significantly higher case fatality rate than other
serotypes. Earlier studies have shown that type
3 is more virulent than others, confirming that
there is a notable difference in virulence be-
tween serotypes (8).

Furthermore, it has been shown that 12F is
more invasive than other serotypes, being found
more frequently among CSF isolates (9).

This might be part of the explanation why the
incidence of meningitis caused by S. pneunoni-
ae is six times higher than in other parts of the
world, where incidence rates seem to be very
stable around 1 per 100,000 (6,10-13).

Also case fatality of meningitis was twice as
high as seen elsewhere (14,15).

The high frequency and poor outcome of
pneumococcal infections with serotype 12F
seems to be part of the reason for the relatively
high total mortality of invasive pneumococcal
disease in Greenland (33 %).

Most cases of serotype 12F and all cases of
type 1 were from Nuuk, which is consistent with
the assumption that the relatively more mild and
fatal cases were diagnosed and cultured here.

Few patients were older than 65 years. This
can be explained by the low average age in
Greenland. It is possible that the incidence and
fatality rates will increase as the population
may get older in the future.

In Denmark and other countries a 23-valent
vaccine against S. pneumoniae is offered to
people above the age of 65 years because of the
increased risk in this age group. The incidence
among Greenland Inuit older than 35 years is
comparable to that seen among the elderly in
Denmark (9). As indicated by serotyping, the
coverage rate by the 23-valent vaccine should
be 94 %.

All patients received adequate antibiotic
treatment and where possible, relevant treatment
in intensive care units. Therefore the most obvi-
ous way of improving the strategy concerning
invasive pneumococcal disease may be vacci-
nation of the Inuit population above the age of
35. Measures should also be taken to improve
living standards in general and to treat alco-
holism in particular.

CONCLUSIONS
Invasive pneumococcal infections are frequent
and have serious outcome for patients in Green-
land. The Inuit seem to be at higher risk, as seen
elsewhere. This study indicates that the serotype
distribution in a given population is an important
factor in determining clinical presentation and
outcome of IPD, infections with serotype 12F
being especially frequent and especially deleter-
ious for Inuit in Greenland. Cost-benefit analy-
sis of a general vaccination programme should
be carried out.

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REFERENCES

1. Robinson KA, Baughman W, Rothrock G et al. Active Bacterial Core Surveillance (ABCS)/Emerging Infections Program Network. Epidemiology of invasive Streptococcus pneumoniae infections in the United States, 1995-1998: Opportunities for prevention in the conjugate vaccine era. JAMA 2001;285(13):1729-1735.

2. Vaudry W, Talling D. Invasive pneumococcal infection in first nations children in northern Alberta. Can Commun Dis Rep 2002;28(20):165-172.

3. Davidson M, Parkinson AJ, Bulkow LR, Fitzgerald MA, Peters HV, Parks DJ. The epidemiology of invasive pneumococcal disease in Alaska, 1986-1990--ethnic differences and opportunities for prevention. J Infect Dis. 1994;170(2):368-376.

4. Greenlands statistic. http://www.statgreen.gl/ [Accessed August 2003]

5. Örtqvist Å, Kalin M, Julander I, Mufson MA. Deaths in Bacteremic Pneumococcal Pneumonia. A Comparison of Two Populations – Huntington, WV, and Stockholm, Sweden. Chest 1993;103(3):710-716.

6. Dahl MS, Trollfors B, Claesson BA, Brandberg LL, Rosengren A. Invasive pneumococcal infections in Southwestern Sweden: a second follow-up period of 15 years. Scand J Infect Dis. 2001;33(9):667-672.

7. Torres JM, Cardenas O, Vasquez A, Schlossberg D. Streptococcus pneumoniae bacteremia in a community hospital. Chest 1999;113(2):387-390.

8. Austrian R. The enduring pneumococcus: unfinished business and opportunities for the future. Microb Drug Resist 1997;3(2):111-115.

9. Konradsen HB, Kaltoft MS. Invasive pneumococcal infections in Denmark from 1995 to 1999: epidemiology, serotypes, and resistance. Clin Diagn Lab Immunol 2002;9(2):358-365.

10. Urwin G, Yuan MF, Feldman RA. Prospective study of bacterial meningitis in north East Thames region, 1991-3, during introduction of Haemophilus influenza vaccine. BMJ 1994;309:1412-1414

11. Schuchat A, Robinson K, Wenger JD et al. Bacterial meningitis in the United States in 1995. Active Surveillance Team. N Engl J Med 1997;337(14):970-976.

12. Domínguez A, Salleras L, Cardenosa N et al. The epidemiology of invasive Streptococcus pneumoniae disease in Catalonia (Spain). A hospital-based study. Vaccine 2002;20(23-24):2989-94.

13. Sankilampi U, Herva E, Haikala R, Liimatainen O, Renkonen OV, Leinonen M. Epidemiology of invasive Streptococcus pneumoniae infections in adults in Finland. Epidemiol Infect 1997;118(1):7-15

14. Tang LM, Chen ST, Hsu WC, Lyu RK. Acute bacterial meningitis in adults: a hospital-based epidemiological study. QJM 1999;92(12):719-25.

15. Schuchat A, Robinson K, Wenger JD et al. Bacterial meningitis in the United States in 1995. Active Surveillance Team. N Engl J Med 1997;337(14):970-976.

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