## Surveillance reports

## EPIDEMIOLOGY OF MENINGOCOCCAL MENINGITIS AND CHANGES IN THE SURVEILLANCE SYSTEM IN POLAND, 1970-2006

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The objective of this study was to describe the general features of meningococcal meningitis epidemiology in 1970-2006 in Poland, in the context of changes made in surveillance system methods. Because of limited availability of case-based data, a more detailed analysis was performed only for the period 1994-2006 with special focus on case-fatality and diagnostic certainty. The reported annual number of meningococcal meningitis cases reached its peak of 416 (incidence 1.2 per 100,000) in 1981, after which it decreased to 76 cases in 2003 (incidence 0.2), and then increased to 151 cases in 2006 (incidence 0.4 per 100,000). The observed decrease was consistent with the decline in the number of live births and the drop in mortality from meningococcal disease observed using an independent reporting of death certificates. In 1994-2006, 1,677 cases of meningococcal meningitis were registered, with annual incidence varying between 0.2 and 0.5 per 100,000 inhabitants. Median age of patients was 4 years and 73% of cases were under 18 years of age. The majority of cases were caused by group B meningococci, but a trend towards increasing proportion of serogroup C has been identified. Meningococcal meningitis only was reported in 79% of cases, and meningitis with concomitant septicaemia in 21%. The overall case fatality was 3.7% - 4.5% in cases of meningitis only, and 7.1% in cases of meningitis with septicaemia. Based on the case definition introduced in 2005, 88.1% of the cases would be classified as confirmed and 4.8% as probable, whereas 7.1% would not fulfil the criteria of the case definition. Although diagnostic certainty of reported cases has improved in recent years, it is still problematic. Further efforts are needed to increase the proportion of serogrouped cases and assess the burden of meningococcal disease in Poland.

## Introduction

The most common manifestations of the invasive meningococcal disease in Europe include meningitis (50-55% of all cases), septicaemia (5-20%), and meningitis accompanied by septicaemia (20-30%) [1]. Meningococcal meningitis occurs particularly often among infants and young children. It may cause serious neurological defects and is often lethal, if treatment is delayed. Meningococcal disease can be confirmed by microbiological examination (Gram stain of samples from cerebrospinal liquid or blood culture). Meningococcal infection can be usually successfully treated, if antibiotics are administered early after the onset of illness [1-3]. Appropriate epidemiological investigation of meningococcal disease clusters is also important, including contact tracing and providing chemoprophylaxis for the household and other close contacts. When chemoprophylaxis is administered within 24 h from the contact it may decrease secondary case rates by almost 90% [3]. In recent years several countries in Europe introduced group C conjugate vaccine in their immunisation schedule [4,5].

Trends observed while monitoring only meningococcal meningitis correlate well with the total burden of meningococcal disease, and in some countries with clinician-based surveillance systems surveillance of meningococcal disease has been restricted to meningitis cases only [6]. In Poland the surveillance of meningococcal invasive disease, initiated in 1970, was limited to meningitis cases until 2005 [7].

Meningococcal vaccine is not included in the Polish mandatory and free-of-charge immunisation programme. However, since 2003, vaccination against group C meningococci is recommended for children above 2 years of age and for patients who have undergone splenectomy. The list of recommended vaccines is published by the Poland's Chief Medical Officer and is used to advise parents, but the full cost of the vaccine has to be covered by them alone. The official estimates indicate a very poor vaccine uptake, ranging from 834 persons vaccinated in 2003 to 1,851 vaccinated in 2005 (data for 2006 is not available yet).

The primary aim of this study was to describe the general features of meningococcal meningitis epidemiology in 1970-2006, in the context of changing surveillance system. The secondary aim was the description of clinical outcomes and diagnostic procedures used to confirm meningococcal meningitis in 1994-2006.

## **Methods**

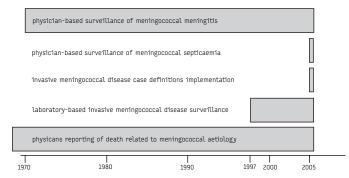
The Polish epidemiological surveillance system is still paperbased, but has been considerably modified in recent years. Physicians are obliged by law to report all newly diagnosed cases of meningococcal meningitis (since 2005 invasive meningococcal disease) to the local sanitary-epidemiological stations (SES). Typically, public health officers carry out epidemiological investigation of cases and their closest contacts and complete the standardized surveillance reports. Data on cases are collected at local SES and forwarded biweekly to the National Institute of Hygiene which publishes regular surveillance reports on its website (http://www. pzh.gov.pl/epimeld). Additionally, every three months completed surveillance reports containing demographic, clinical and laboratory data on each case are sent through regional SES to the National Institute of Hygiene. Annual reports on meningococcal disease are prepared at the Department of Epidemiology of the National Institute of Hygiene [7]. Independently of mandatory reporting of communicable diseases to SES, physicians are required to fill in death certificates, including the primary and secondary causes of death, and submit them to the Central Statistical Office. Data from death certificates, including information on meningococcal disease coded using the International Classification of Diseases, are available at least since 1968, when ICD-8 and ICD-9 classifications

were used (036 - Meningococcal infection), followed by ICD-10 used since 1999 (A39 - Meningococcal disease).

Changes in surveillance of meningococcal disease since the beginning of its reporting in 1970 are schematically presented on Figure 1. The case definition for meningococcal disease was implemented in 2005. Before 2005, cases were ascertained based on clinical diagnosis and potential laboratory confirmation. In 1997, the National Reference Laboratory (NRL) for Meningococci started a separate, sentinel-type laboratory system requiring hospitals to send strains isolated from meningococcal disease cases to the NRL for further analysis (Figure 1). Data from the two systems are not collated at the national level. Therefore, the information on laboratory tests performed and serogroup used in this study was obtained exclusively from epidemiological surveillance forms.

#### FIGURE 1

## Surveillance of meningococcal disease in Poland, 1970-2006



The present study is based on aggregated data for 1970-1993 and case-based data for 1994-2006. Individual level information from the period 1970-1993 is not available. Surveillance forms for the period 1994-1998 did not include information on exposures and epidemiological links. Therefore, part of the analysis is limited to years 1999-2006.

In order to assess trends in diagnostic certainty of cases reported to the Polish surveillance system, data for 1994-2004 were retrospectively described using the case classification used currently in Poland, being a slightly modified translation of the case definition recommended by the European Centre for Disease Prevention and Control (ECDC). Because the case definition was not used before 2005, all cases of meningococcal meningitis have been included to calculate the incidence. Population data and data on disease-specific mortality were obtained from the Central Statistical Office (http://www.stat.gov.pl).

Case definition of meningococcal disease used in Poland since 2005

## **Clinical description:**

Clinical picture compatible with meningococcal disease, e.g. meningitis and/or meningococcemia that may progress rapidly to purpura fulminans, shock and death. Other manifestations are possible.

## Laboratory criteria for diagnosis:

► Isolation of *Neisseria meningitidis* from a normally sterile site (e.g. blood or cerebrospinal fluid (CSF) or, less commonly, joint, pleural or pericardial fluid)

▶ Detection of *N. meningitidis* nucleic acid from normally sterile site

Demonstration of Gram-negative diplococci from normally sterile site by microscopy For probable case:

Single high titre of meningococcal antibody in convalescent serum

## **Case classification**

Possible: N.A.

Probable: A clinical picture compatible with invasive eningococcal disease without any laboratory confirmation, or with *N. meningitidis* identification from a non-sterile site, or with high levels of meningococcal antibody in convalescent serum.

Confirmed: A clinically compatible case that is laboratoryconfirmed.

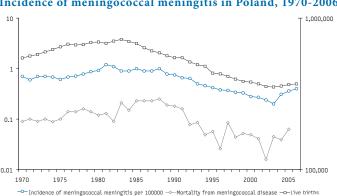
Note that asymptomatic carriers should not be reported

## Results

## Incidence of meningococcal meningitis

Incidence of meningococcal meningitis during 1970-2006 ranged between 0.2 and 1.2 per 100,000 (Figure 2). In this period, the reported number of meningococcal meningitis cases decreased from the maximum of 416 (incidence 1.2 per 100,000) in 1981 to the minimum of 76 cases in 2003 (incidence 0.2) and then increased to 151 cases in 2006 (incidence 0.4 per 100,000). The observed decrease in meningococcal meningitis incidence was consistent with the decline in number of live births in Poland. The decrease in mortality from meningococcal disease in the period 1985-2006, as shown by death certificate data, provides an independent confirmation of meningococcal disease burden decrease in Poland (Figure 2). The number of deaths attributed to meningococcal infection decreased from 96 in 1986 (mortality 0.25 per 100,000) to 6 in 2002 (mortality 0.02). Since 2003, an increase in meningococcal meningitis incidence has been observed, with parallel increase in meningococcal disease mortality.





#### Incidence of meningococcal meningitis in Poland, 1970-2006

### Demographic data

During 1994-2006, 1,676 cases of meningococcal meningitis were registered, of which 966 (58%) were males (mean annual incidence 0.40), and 710 (42%) were females (mean annual incidence 0.28).

Mean age of patients was 14.4 years; median age was 4.0 years. Out of 1,677 reported cases 73% of patients were under 18 years of age. Age-group specific incidence of meningococcal meningitis during the years 1994-2006 is presented in Figure 3. A decreasing trend was observed in age group 0-4, ranging from 4.5 per 100,000 in 1994 to 1.8 in 2002. The highest incidence was seen in infants, ranging from 13.2 per 100,000 in 1994 to 5.4 in 2003. An increase in meningococcal meningitis incidence in age groups 5-14 and 15-24 was detected, ranging from 0.2 in 2003 to 0.7 in 2006 in the age group 5-14, and from 0.3 in 2003 to 0.7 in 2006 in the age group 15-24. Out of the total of 433 adult patients with known occupation, 233 (54%) were students, 115 (27%) were retired or unemployed, 53 (12%) were physical workers, and 18 (4%) were office workers. There were 9 cases of meningitis registered among recruits. The incidence of meningococcal disease displayed seasonal variations with an autumn increase starting in October and highest levels in winter months with the peak in January.

#### Serogroup distribution

Between 1994 and 2006, meningococcal strains from 624 cases (37%) were serogrouped. The number of cases according to serogroups during this period is shown in Figure 4. Among serogrouped strains, 415 (67%) were group B strains and 176 (28%) were group C. Additionally, there were 28 strains (4%) established as serogroup A, but these results were not confirmed by the national reference laboratory and were merged into the group labelled "other", along with two cases reported as I, two as Y, and one reported as serogroup D. The proportion of cases with serogroup C of *N. meningitidis* increased gradually reaching the highest value (51% of serogrouped strains) in 2006. Serogroup B was most common in children under 10 years of age (75%) and adults over 50 years old (83.3%), and the median age of group B cases was 2.0 years. Serogroup C was more common in teenagers and young adults aged between 10 and 24 years (median age of group C cases: 12.5 years).

#### Clinical manifestation

During 1994-2006, meningococcal meningitis only was diagnosed in 1,325 cases (79%) and meningitis with septicaemia in 351 cases (21%). There were 75 fatal cases (4.5%), with median age at death being 31.8 years. Table 1 shows case-fatality ratios (CFR) specific to clinical manifestation, stratified by age, gender and serogroup.

#### Case classification

Out of 1,676 cases, 1,477 (88.1%) met criteria for confirmed cases (Table 2). Cerebrospinal fluid culture was performed in the majority of cases, showing positive results in 1,142 cases (77.3% of the confirmed cases). The number of microbiological examinations per patient increased from 1.1 in 1994 to 2.3 in 2006. Of the 80 cases (4.8% of all cases) classified as probable, 21 were diagnosed as meningococcal infection based exclusively on clinical presentation (Waterhouse-Fridriechsen syndrome or petechial/purpuric skin lesions), 59 had also positive antigen test for *N. meningitidis*. The remaining 119 reported cases (7.1%)

had neither microbiological nor clinical compatibility required for case confirmation.

#### Discussion

Since 1981 the incidence of meningococcal meningitis in Poland had been decreasing, but an increase was noted in 2004, 2005 and 2006. However, the incidence rates are still rather low compared to other European countries [1,9-11]. The systematic decrease of meningococcal meningitis incidence during preceding two decades could be explained by decreasing birth rate and decreasing incidence of meningococcal infections in infants possibly related to improvement of living conditions and healthcare services in Poland. The unexpected increase in meningococcal meningitis incidence in 2004-2006 may be related to a real increase in meningococcal disease activity in Poland but can also be simply a result of its improved surveillance. However, the fact that this increase occurred mainly in the teenage age group and was accompanied by a systematic increase in proportion of serogroup C observed in epidemiological surveillance and increasing number of cases of ST11 and ST8 clonal complex reported by the reference laboratory indicates that the epidemiological situation in Poland is changing [12-13]. The increasing proportion of serogroup C meningococci strains isolated from cases in neighbouring countries in previous decades, was accompanied by an increase in disease incidence among adolescents and young adults [1,9,11].

The case fatality rates (CFR) based on Polish surveillance data parallel the epidemiological situation of meningococcal disease in developed countries in the pre-vaccination stage. As in other European studies, case fatality was highest in people over 50 years of age, and in those with concomitant septicaemia [1,14,15]. Unlike in published studies, group B meningococci were associated with higher CFR, compared to group C strains. This can be however related to the low proportion of serogrouped strains during the studied period, and to the higher proportion of group B meningococci diagnosed in adults over 50 years of age, where the case fatality is highest.

In order to assess the possible distortion of these results due to the fact that only data on meningococcal meningitis was available for the entire period of study, a sub-analysis was performed using data on the entire spectrum of invasive meningococcal disease available for 2005-2006 (n = 440). In this analysis the CFR was still found higher among serogroup B, compared to serogroup C cases (12.8% vs. 10.8%). Age-specific case-fatality ratio was highest in group B cases aged 10-14 years (1/4, 25%), 5-9 years (2/14, 14.3%) and 0-4 years (9/64, 14.1%). In group C cases, CFR was highest in adults aged over 25 years (4/11, 36%) and teenagers aged 15-19 years (2/12, 16.7%). A recent emergence of outbreaks caused by serogroup C strains has caused serious media concerns and improvement of surveillance sensitivity, as well as microbiological confirmation of individual cases, with increasing proportion of serogrouped strains.

As the level of underascertainment of meningococcal disease in Poland is not known, further enhancement of laboratory and epidemiological surveillance is needed. Some improvements have already been introduced in 2005, namely the extension of surveillance of meningococcal disease to include all its manifestations and the implementation of case definition. Proper attention must be paid to contact tracing and appropriate administering of chemoprophylaxis in order to prevent the occurrence of clusters of the disease.

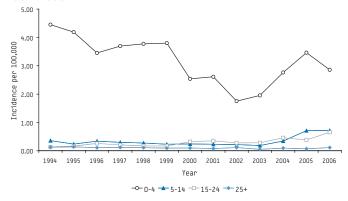
## TABLE 1

# Number of meningococcal neuroinfections, deaths and case fatality according to clinical manifestation, gender and serogroup distribution in Poland, 1994 - 2006

	Clinical syndrome										
		Meni	ngitis		Meningitis with septicemia						
	Cases	deaths	case fatality (%)	95% CI	Cases	deaths	case fatality (%)	95% CI			
Total	1325	50	3.7	2.7 - 4.8	351	25	7.1	4.4 - 9.8			
				Age groups (yea	rs)						
0	355	4	1.1	0.0 - 2.2	99	8	8.1	2.7 - 13			
1	148	3	2.0	0.0 - 4.3	56	4	7.1	0.4 - 13			
2	71	0	-	-	34	4	11.8	0.9 - 22.			
3	54	0	-	-	23	3	13.0	0.0 - 26			
4	22	0	-	-	18	0	-	-			
5-9	90	2	2.2	0.0 - 5.3	34	0	-	-			
10-14	85	1	1.2	0.0 - 3.5	21	1	4.8	0.0 - 13			
15-19	144	2	1.4	0.0 - 3.3	35	1	2.9	0.0 - 8.			
20-24	56	1	1.8	0.0 - 5.3	7	0	-	-			
25-49	162	13	8.0	3,8 - 12.2	14	3	21.4	0.0 - 42			
50-64	91	14	15.4	8.0 - 22.8	6	1	16.7	0.0 - 46			
65+	47	10	21.3	9.6 - 33.0	4	0	-	-			
				Gender							
Males	775	33	4.3	2.8 - 5.7	191	16	8.4	4.4 - 12.			
Females	550	17	3.1	1.6 - 4.5	160	9	5.6	2.1 - 9.			
				Serogroup							
В	313	12	3.8	1.7 - 6.0	102	6	5.9	1.3 - 10.			
С	126	4	3.2	0.1 - 6.2	50	2	4.0	0.0 - 9.			
Other	41	2	4.9	0.0 - 11.5	6	0	-	-			

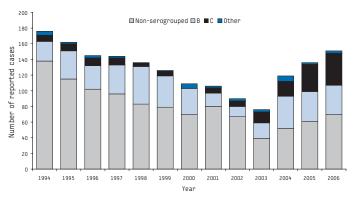






## FIGURE 4

Cases of meningococcal meningitis by serogroup, Poland, 1994-2006



#### TABLE 2

Number of cases of meningococcal neuroinfections by case classification and year, Poland, 1994-2006

Year							
	Demonstration of gram-negative diplococci	negative meningitidis from meningitidis from meningitidis DNA Total		Total	Probable cases	Discarded cases	
1994	44 (30.8%)	94 (65.7%)	6 (4.2%)	0 (0.0%)	143	2	31
1995	48 (34.3%)	113 (80.7%)	8 (5.7%)	0 (0.0%)	140	1	21
1996	62 (44.3%)	115 (82.1%)	19 (13.6%)	0 (0.0%)	140	0	5
1997	48 (36.6%)	100 (76.3%)	19 (14.5%)	0 (0.0%)	131	0	13
1998	32 (26.0%)	106 (86.2%)	23 (18.7%)	0 (0.0%)	123	0	13
1999	47 (41.2%)	92 (80.7%)	16 (14.0%)	0 (0.0%)	114	9	3
2000	23 (24.0%)	79 (81.4%)	21 (21.9%)	0 (0.0%)	97	10	2
2001	34 (34.7%)	74 (75.5%)	21 (21.4%)	0 (0.0%)	98	6	2
2002	26 (32.9%)	64 (81.0%)	10 (12.7%)	0 (0.0%)	79	7	4
2003	20 (30.3%)	50 (75.8%)	18 (27.3%)	0 (0.0%)	66	7	3
2004	32 (33.0%)	71 (73.2%)	32 (33.0%)	0 (0.0%)	97	18	4
2005	34 (27.6%)	97 (78.9%)	35 (28.5%)	9 (7.3%)	123	12	1
2006	25 (19.8%)	87 (69.0%)	48 (38.1%)	9 (7.1%)	126	8	17
Total	475 (32.2%)	1142 (77.3%)	276 (18.7%)	18 (1.2%)	1477	80	119

Detailed and more complete data on serogroups are needed in view of developing evidence-based vaccination recommendations for general public.

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