# EVALUATION OF TICKBORNE ENCEPHALITIS CASE CLASSIFICATION IN POLAND

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Central European tickborne encephalitis (TBE) is a viral disease of the central nervous system. Despite a surveillance system for TBE existing in Poland since 1970, there are no standardised case definitions and different diagnostic tests are used in various regions. The purpose of this study was to summarise four years of surveillance data using standardised case definitions. From 1999 to 2002, 607 cases of TBE were reported to Poland's national surveillance system: 386 (63.6%) were males, 331 (54.5%) lived in rural areas, and 186 (30.6%) were between 30 and 50 years old. Of 606 diagnosed cases, 453 (74.7%) had aseptic meningitis, 109 (18.0%) had meningoencephalitis, and 44 (7.3%) had meningoencephalomyelitis. Of the 607 reported cases, 602 (99.2%) could be classified: 153 (25.4%) as confirmed, 343 (57.0%) as probable, and 106 (17.6%) as possible cases. There was a significant difference in classified cases by gender: 28.6% of male cases were classified as confirmed, compared with 19.7% of female cases ($\chi 2$= 10.48, p=0.0053). There was a significant difference in case classification by clinical diagnosis: 32.4% of cases with meningoencephalitis were classified as confirmed cases, compared with 24.7% of cases with aseptic meningitis ($\chi 2$=11.79, p=0.019). There were also significant differences in the distribution by case definition group across geographical regions. For appropriate monitoring of TBE, a uniform and valid case definition should be used in European countries. With only 25% of reported cases meeting the definition for confirmed cases, there is a need for more complete follow-up and standardised testing of suspect cases.

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## Introduction

Central European tickborne encephalitis (TBE) is a viral disease of the central nervous system [1,2]. This infection due to the central European subtype of TBE virus usually progresses biphasically (viraemic phase, then neurological phase). Often, the infection is asymptomatic or influenza-like,. It develops to the second phase only a third of cases. Patients are hospitalised mainly during the neurological phase.

Symptomatic syndromes of TBE include aseptic meningitis, meningoencephalitis, and meningoencephalomyelitis. To confirm the diagnosis of TBE, serological testing and demonstration of specific IgM in the acute phase, or a significant rise in antibody titre is required. All serological IgG tests show cross-reaction with other flaviviruses [3]. In Poland only enzyme-linked immunosorbent assay (ELISA) tests are used. Diagnostic procedures to confirm TBE infection based on available tests were Published by the National Institute of Hygiene [4]. Because of the lack of a commonly accepted case definition, regional health providers use different diagnostic protocols to confirm the diagnosis of TBE.

In Poland, serologic surveys of more then 20 000 foresters and 17 000 blood donors were done in the 1960s and 1970s [5]. Antibodies against the TBE virus were found in 0.5-6.5% of population in different regions and in 7.0-27.0% of foresters. Serologic data has enabled the identification of regions with particularly high infection rates.

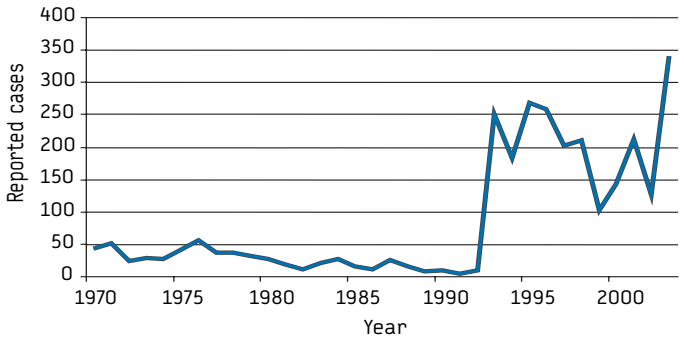
Reporting of TBE cases is mandatory in all central European countries. Thus, cases have been reported in Austria, Byelorussia, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Italy, Latvia, Lithuania, Norway, Poland, Russia, Romania, Slovenia, Slovakia, Sweden and Switzerland [6,7]. The largest number of cases are reported from countries in central Europe. Increasing reports from areas that were previously disease-free (Norway, northern Russia, the Netherlands) have been attributed to global warming and increases in rodent and tick populations [8].

Most of the previous descriptive TBE studies were of hospitalised TBE patients with a neurological presentation [9,10]. Asymptomatic or forms with few symptoms are probably not diagnosed and/or taken into account during consultation. There is a notion of tick bite in 56% to 90% of cases [2]. Patients had often been involved in professional forest activity (56%) or occasional forest activity (48%) [8]. There were also several prospective follow-up studies gathering information about long-term prognosis and possible risk factors [11,12]. The primary weakness of these follow-up studies was the lack of control groups needed to assess risk factors.

TBE surveillance in Poland is integrated into the ongoing communicable disease reporting system. Reporting of TBE cases as a separate syndrome began in 1970, but no uniform case definition was used. Typically, after a medical provider reports a clinically suspected case of TBE-related encephalitis, an epidemiologist from the District Health Department completes the standardised TBE surveillance report. The forms are sent to the National Institute of Hygiene (NIH) in Warsaw, where they are processed. The incidence information is Published in bi-weekly surveillance reports sent to all local health departments and subscribed healthcare providers. Annual reports on tickborne encephalitis are prepared in the Department of Epidemiology of the National Institute of Hygiene. The annual number of reported cases changed dramatically with the introduction of new serologic tests and a countrywide educational campaign in 1993 [FIGURE 1]. Between 1970-1992, only 5 to 50 cases were reported each year. From 1993, 100-350 cases have been reported annually. More than 80% of cases were reported from two northeastern provinces of Poland: Podlaskie and Warminsko-mazurskie. These two provinces are mostly rural and have more tourist traffic, compared with country average. Their forestation rate is similar to country average.

FIGURE 1

**Reported cases of tickborne encephalitis in Poland, 1970-2001**

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The aim of the study was to assess the usefulness of the newly introduced case definitions for differentiation of confirmed, probable and possible cases within the Polish communicable disease reporting system. A descriptive analysis of data was performed, with a comparison of cases by case definition groups.

## Methods

The TBE reports from the years 1999-2002 were analysed using a new case definition, developed by a working group at national level [Table 1]. These case definitions will be implemented in 2005. The forms for years 1999-2002 were used in this study because there were administration reforms in 1998, which affect geographical comparisons of data before and after 1998. Based on data obtained, TBE cases were classified as confirmed, probable and possible cases. Newly defined case groupings were compared by year, season of onset, gender, age group, residential area type, occupation, clinical course and geographic location. Geographic comparisons were performed only for provinces where more than 10 cases were reported during the period 1999-2002.

**Table 1**

**Tickborne encephalitis case definitions, Poland, 1999-2002**

| | |
|---|---|
| **Possible case** | a. clinically compatible disease (febrile illness with diverse neurological symptoms of aseptic meningitis or encephalitis), AND<br>b. onset of illness during a period of increased tick activity (between April and November). |
| **Probable case** | Possible case AND<br>a. visit of ill person to endemic area during previous 6 weeks, OR<br>b. detection of specific IgM antibodies in serum, with no history of vaccination against any flaviviral disease during previous 3 months |
| **Confirmed case** | Possible case AND<br>a. detection of specific IgM or IgG antibodies in cerebro-spinal fluid, OR<br>b. fourfold or greater rise in serum antibody titre, with no history of vaccination against any flaviviral disease during previous 3 months, OR<br>c. viral isolation from tissue, blood, or cerebrospinal fluid (CSF). |

Source: Working group for communicable disease surveillance case definitions, Warsaw, Poland

Data was analysed using SAS software (version 8.2, SAS Institute, Carey, NC, USA). All variables were categorised. Cases were compared using case definition groups with the chi-square test. A logistic model was used to detect factors predicting the probability of being classified as a confirmed case.

## Results

From 1999 to 2002, 607 cases of TBE were reported to Poland's national surveillance system. A total of 386 (63.6%) patients were males and 221 (36.4%) were females. Three hundred thirty one (54.5%) cases lived in rural areas and 276 (45.5%) in urban areas. There were no large differences in the number of cases by age group. By occupation, the largest groups were unemployed (108 cases; 17.8%), retired (106 cases; 17.5%), students (95 cases; 15.7%) and farmers (74 cases; 12.2%). All patients with TBE were hospitalised. The most common signs and symptoms in TBE cases were fever (581 cases, 95.7%), headache (580 cases, 95.6%), meningeal symptoms (479 cases, 78.9%), vomiting (385 cases, 63.4%), muscle pain (151 cases, 24.9%), and respiratory infection (105 cases, 17.3%).

More severe signs and symptoms were less common, including loss of consciousness (85 cases, 14.0%), cerebellar symptoms (38 cases, 6.3%), pyramidal symptoms (22 cases, 3.6%), limb paresis (22 cases, 3.6%), and cranial nerve palsy (12 cases, 2.0%). Based on these clinical signs and symptoms, 606 (99.8% of cases) could be classified into one of three clinical syndromes [Table 2]. Three patients died, giving a four year case fatality rate of 0.5%.

**Table 2**

**Number of tickborne encephalitis cases by clinical syndrome, Poland, 1999-2002**

| Clinical syndrome | 1999 | 2000 | 2001 | 2002 | Total |
|---|---|---|---|---|---|
| Aseptic meningitis | 71 (70.3%) | 130 (75.1%) | 155 (75.2%) | 97 (77.0%) | 453 (74.7%) |
| Meningo-encephalitis | 24 (23.8%) | 29 (16.8%) | 34 (16.5%) | 22 (17.5%) | 109 (18.0%) |
| Meningo-encephalo-myelitis | 6 (6.0%) | 14 (8.1%) | 17 (8.2%) | 7 (5.6%) | 44 (7.3%) |
| Total | 101 (100%) | 173 (100%) | 206 (100%) | 126 (100%) | 606 (100%) |

Of the 607 cases reported, 602 (99.2%) could be classified as a possible, probable, or confirmed case [Table 3]. Four cases could not be classified because their symptoms started after the tick activity season. One person didn't meet the clinical compatibility requirement and had been diagnosed exclusively on serologic results. 153 patients (25.4%) were confirmed TBE cases, 343 (57.0%) were probable cases and 106 (17.6%) were possible cases.

**Table 3**

**Number of tickborne encephalitis cases by case classification, Poland, 1999-2002**

| | | |
|---|---|---|
| **Possible cases** | **106** | **17.6%** |
| a. Clinically compatible | 106 | 100% |
| b. Onset during tick activity season | 106 | 100% |
| **Probable cases** | **343** | **57.0%** |
| a. Visit to endemic area | NA* | - |
| b. Specific IgM in serum | 343 | 100% |
| **Confirmed cases** | **153** | **25.4%** |
| a. Specific IgM or IgG in CSF | 142 | 92.8% |
| b. 4-fold rise in antibody Ig titre | 17 | 11.1% |
| c. viral isolation from tissue | NA** | - |

* NA = not available, data not reported in the forms.
** NA = not available, test not performed in 1999-2002.

There was a significant difference in case classification by gender with 28.6% of male cases classified as confirmed, compared with 19.7% of female cases ( 2=10.48, p=0.0053) [Figure 2]. There was a significant difference in case classification by clinical diagnosis: 32.4% of cases with meningoencephalitis were classified as confirmed cases, compared with 24.7% of cases with aseptic meningitis (X2=11.79, p=0.019) [Figure 3]. The comparison of case classification by province showed highly significant differences by region (X2=94.36, p<0.0001) [Figure 4]. The comparison of case classification for other demographic factors, such as year of onset, season of onset, age, occupation, type of residence (urban/rural), revealed no significant differences.

**Figure 2**

**TBE case classification by gender, Poland, 1999-2002**

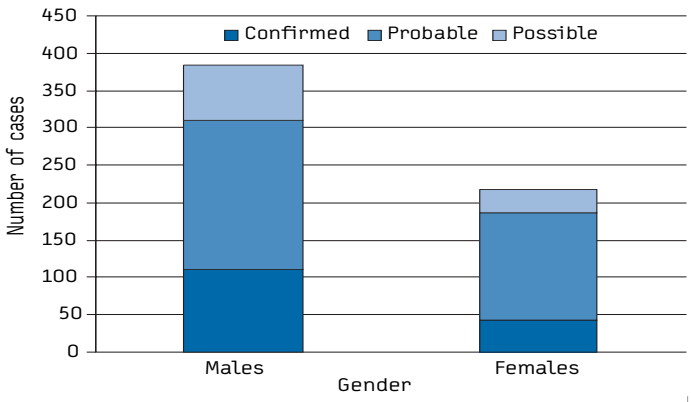


**FIGURE 3**

**TBE case classification by clinical diagnosis, Poland, 1999-2002**

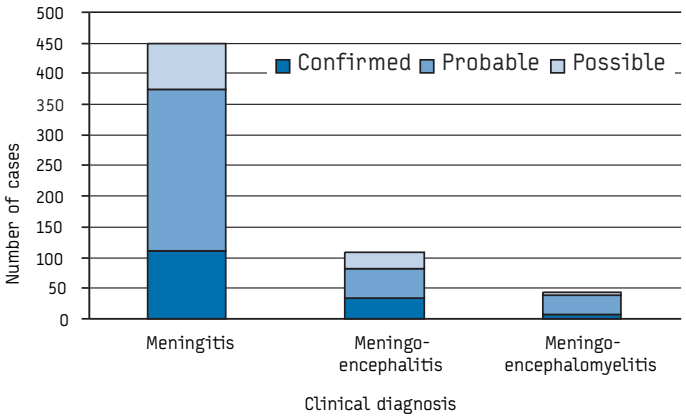
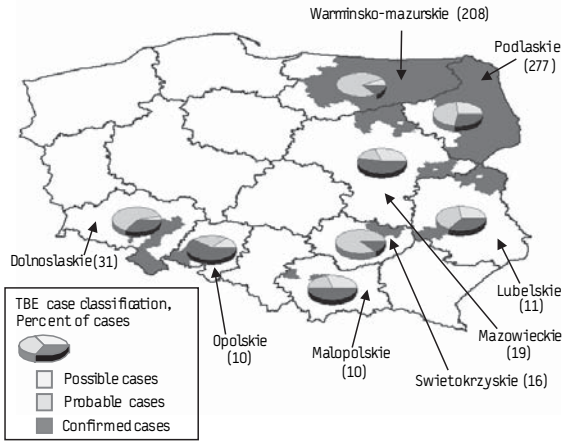



**FIGURE 4**

**Geographic distribution of TBE classification, Poland, 1999-2002**




Notes

The names of provinces are accompanied by number of cases reported from 1999 through 2002

Districts with at least one case reported during > 1 year

The probability of being classified as a confirmed case was modelled. Controlling for geographic location, males were more likely to be classified as confirmed cases, compared to females (OR=1.92, 95% CI: 1.21–3.11). Compared with other provinces, patients living in Warminsko-mazurskie (OR=3.99, 95% CI: 1.65–10.76) and Podlaskie province (OR=1.68, 95% CI: 1.04–2.69) were more likely to be classified as a probable or possible case. Geographical differences in case classification were directly linked to important differences in diagnostic tests used to confirm TBE. The serum IgM test was used extensively in Warminsko-mazurskie (81.3% of cases were classified as probable) and in Podlaskie (45.1% of cases were classified as probable). IgM and IgG tests of cerebrospinal fluid were used to confirm a higher proportion of cases in Opolskie (58.8%), Mazowieckie (52.6%), and Malopolskie (50.0%) provinces.

## Discussion

TBE is an emerging disease spreading from central Europe to western and northern Europe, possibly because of climate change. The disease is endemic in the northeast of Poland with approximately 200 cases a year reported countrywide. For appropriate monitoring of TBE trends, a uniform and valid case definition should be used in European countries. This need is illustrated by the observation that only 25% of cases reported in Poland in 1999-2002 had sufficient diagnostic tests to meet the criteria of a confirmed TBE case. The fact that male TBE cases were more likely to receive a confirmatory diagnosis, needs to be further investigated. The higher incidence of TBE among males may reflect more rigorous investigation. Interview, follow-up and diagnostic procedures were not uniform across various regions of Poland.

Local health departments used different surveillance forms and hospital laboratories used different ELISA tests, resulting in reporting differences. Some endemic northeastern regions of Poland, particularly Warminsko-mazurskie province, were less likely to perform confirmatory diagnostic testing of the cerebrospinal fluid and were more likely to rely on serologic results. The introduction of a new case definition will help to standardise procedures and encourage proper diagnostic methods. Finally, a more accurate surveillance system is crucial to better focus preventive campaigns including immunisation.

The case report form needs to be modified to collect missing information (e.g. residing or visiting an endemic area). Forms of infection that are not symptomatic and which are typically not hospitalised should be included as probable illnesses, based on epidemiological or serological evidence. Also, the case report should include the presence of tick bite and risk factors related to exposure (i.e. forest activities). The present criteria for suspect cases are insufficient to differentiate TBE from other illnesses involving meningitis. Additionally, since a viral isolation test was never used to confirm TBE over a 4 year period, the usefulness of this diagnostic test should be reviewed. The implementation of the new case definition needs to be linked to better education about the appropriate diagnosis of the disease and the need for standard, uniform diagnostic protocols. There is a need to modify diagnostic procedures in clinical settings. Carrying out lumbar puncture should be more systematic for diagnosis confirmation and for the elimination of potential differential diagnosis (herpetic meningoencephalitis, neuroborreliosis, etc.). Moreover, an effort to carry out a second serologic examination seems necessary, especially in cases with no neurological symptoms that are not hospitalised.

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# Surveillance of aseptic central nervous system infections in Poland: is it meeting its objectives?

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**In Poland, a surveillance system capturing generic information on both diagnosed and undiagnosed aseptic central nervous system infections (ACI) has been in operation since 1966. This study evaluates to what extent the ACI surveillance is able to meet its objectives to monitor ACI trends and to detect signals of public health importance such as enteroviral outbreaks, tick-borne encephalitis (TBE) endemic foci, poliovirus appearance or emergence of new neurotropic viruses. Between 2004 and 2008, aetiology was established for 17% of ACI cases. Of the 1,994 reported ACI cases, 232 (11.6%) were diagnosed with TBE virus, 46 (2.3%) with enterovirus, 35 (1.8%) with herpesvirus, and 32 (1.6%) had other viral causes such as Epstein Barr virus or adenovirus. The system's performance varied between the provinces, with the frequency of suspected ACI cases referred for viral aetiology investigation in 2008 ranging from 1.98 to 285.4 samples per million inhabitants. The sensitivity of physicians' reporting, estimated as the proportion of hospitalised ACI cases reported to the surveillance system, was 48% nationally, with vast regional differences (range 30–91%). To conclude, the ACI surveillance system in Poland does currently not meet its objectives, due to limited availability of aetiological diagnosis and microbiological confirmation and to regional differences in reporting sensitivity.**

## Background

Viruses are a common cause of central nervous system (CNS) infections in humans. There is increasing evidence that new neurotropic viruses, mostly of zoonotic origin, emerge regularly [1-5]. Many of these viruses can lead to outbreaks, thus increasing their public health importance [3,4,6,7]. Concrete data on the burden of different neurotropic infections are however limited [8].

In relation to neuroinvasive pathogens, all countries should have efficiently operating surveillance systems for aseptic central nervous system infections (ACI) in place that are able to identify potential threats and raise timely alarms, especially if international spread is involved. *Enterovirus* surveillance systems implemented in several countries have proved to be efficient alternatives to the acute flaccid surveillance and play an important role in the Global Polio Eradication Initiative [8,9].

In Poland, a surveillance system aimed at the collection of generic information for all diagnosed and undiagnosed ACI cases was implemented in 1966. There is no official document in which operational objectives of the system are defined. For the purposes of this paper, we summarise the objectives of the system as follows, taking into consideration current national public health priorities: (i) monitoring overall ACI trends in order to detect outbreaks caused by neurotropic viruses (most commonly coxsackieviruses and echoviruses belonging to the *Enterovirus* family); (ii) identification and monitoring of tick-borne encephalitis (TBE) endemic areas in order to develop evidence-based TBE vaccination recommendations; (iii) monitoring *Enterovirus* strains and referring them for identification of polioviruses as part of the Global Polio Eradication Initiative; (iv) detection of signals indicating the possibility of emergence of neurotropic viruses not yet seen in Poland.

To achieve these objectives efficiently, the ideal surveillance system should perform well at both national and sub-national level, sensitively detect potential public health threats, and ensure regional availability of neuroinvasive virus diagnostics to enable timely and efficient interventions in situations such as enteroviral outbreaks, newly identified TBE foci or poliovirus spread.

The aim of the present study was to evaluate the ACI surveillance system in Poland according to selected performance indicators, with special focus on regional differences in its performance.

## Material and methods

The Polish ACI surveillance system is based on notifications from physicians. Physicians are required by law to notify suspected cases, i.e. those with signs of aseptic meningitis, encephalitis and/or myelitis, to the district sanitary-epidemiological stations (SES). Diagnosed ACI cases for which the viral aetiological agent has been identified, as well as cases classified as ACI of unknown aetiology or viral, unspecified ACI are reported to surveillance. Reports on incident ACI cases are aggregated and forwarded every two weeks to the provincial SES, where, in turn, they are aggregated and sent to the Department of Epidemiology at the National Institute of Public Health (PZH). Currently, each case is assigned to one of nine reporting categories based on the WHO International Classification of Diseases (ICD) (Table 1). Standardised case definitions are used for reporting of TBE and West Nile virus (WNV) infections. In case of TBE, a local case definition was developed [10], and for WNV the EU 2008 case definition was adopted [11].

In each of the 16 Polish provinces, laboratories in the public and private sector offer diagnostics for the most common ACI aetiological agents. Currently, the majority of laboratories receive payment for performing these tests, which are covered by the referring organisation. Only in some public health laboratories is testing of stool and cerebrospinal fluid for enteroviruses performed free of charge.

In the present paper we have summarised data on reported ACI cases, based on annual surveillance reports from 2004 to 2008 [12].To assess the availability of diagnostic testing for viral ACI aetiology we used the results from a survey on the availability of diagnostics for CNS infections conducted in the period from March to December 2009 and covering all Polish provinces. The respondents were 318 epidemiologists working in district SES. Each epidemiologist provided information from hospitals under their responsibility. From each hospital, information on the possibility to hospitalise ACI cases was requested, as well as on the availability of laboratory diagnostics for viral pathogens in the hospital or a subcontracted laboratory. We supplemented the above survey with information on the number of samples tested for viral pathogens in 2008, obtained from an ad hoc survey of laboratories that were identified as offering ACI viral diagnostics in the main survey. We estimated the number of cases referred for diagnosis of ACI viral pathogens in each province. Because of the increasing role of magnetic resonance imaging (MRI) in the diagnosis of herpes simplex encephalitis based on characteristic cerebral lesions [13], we also assessed the availability of MRI in Polish hospitals in the national hospitals registry [14]. All the above information on the availability of ACI diagnostics was collected for the year 2008. We assessed the differences between the 16 provinces by computing measures of location and dispersion (sum, mean, standard deviation, range, median and interquartile range). We compared the frequency of referral for diagnosis of viral aetiology with ACI incidence in each province through scatter plots and computation of Spearman correlation coefficients.

To assess the sensitivity of ACI surveillance during the studied period 2004 to 2008, we compared aggregated data on ACI cases reported as part of routine surveillance with hospital discharge data that are collected annually from approximately 90% of Polish hospitals by the Department-Centre of Monitoring and Analyses of Population Health at PZH. In both systems ICD-10 codes are used to classify diagnosed diseases and syndromes, and for the present assessment we used five-digit codes used in the surveillance system (Table 1). Primary and up to five secondary causes

**Table 1**

List of diseases and syndromes reported in the Polish surveillance system for aseptic central nervous system infections

| ACI syndrome | ICD-9 codes (1972-1996) | ICD-10 codes (1997-2008) |
|---|---|---|
| Viral encephalitis: tick-borne | 063 | A84 |
| West Nile fever | - | A92.3 |
| Viral encephalitis: herpesvirus | 054.3 | B00.4 |
| Viral encephalitis: other virus, specified | 062; 064; 323.1 | A81.1; A83; A85; B02.0 |
| Viral encephalitis: unspecified | 049.9 | A86 |
| Encephalitis: other and unspecified | 323.8; 323.9 | G04.8-9 |
| Viral meningitis: enterovirus | 047 | A87.0 |
| Viral meningitis: herpesvirus | 054.7 | B00.3 |
| Viral meningitis: other specified and unspecified | 049.0; 049.1; 053.0 | A87.1-9; B02.1 |
| Meningitis: other and unspecified | 322 | G03 |

ACI: aseptic central nervous system infection.

of hospitalisation included in the discharge records were extracted from the database and assigned to the patient's province of residence. To account for the diverse proportion of hospitals reporting monthly in particular Polish provinces, we weighted the annual number of hospitalised cases by province, with an underreporting factor constructed in the following way:

$$weight_{(province,year)} = \frac{\sum_{H_{(prov,year)}} B*12}{\sum_{H_{(prov,year)}} B*M}$$

where B is the number of hospital beds, M the number of reporting months summed for hospitals in a given province in a given year, and H all registered hospitals in a given province in a given year.

We evaluated the sensitivity of statutory notifications by calculating the proportion of hospitalised cases that were reported to surveillance. We computed 95% confidence intervals (CI) of obtained sensitivity estimates using the formula for binomial proportions. For data analysis we used STATA version 10 [15].

## Results

### Incidence of aseptic central nervous system infections

In the period 2004 to 2008, aetiology was established for 17% of reported ACI cases in Poland. From the annual average of 1,951 ACI cases reported, 238 (12.2%) were diagnosed as TBE, 46 (2.4%) as enteroviral, 35 (1.8%) as herpes simplex ACI, and 32 (1.6%) as another viral cause such as Epstein Barr virus, adenovirus or other. It was presumed that the viral aetiology of an ACI with unknown cause was based on the general examination of cerebrospinal fluid, and MRI results.

The reported incidence of ACI differed considerably between Polish provinces in the period 2004 to 2008 (Figure 1). An almost 10-fold difference was seen between provinces, with the lowest recorded in Lubuskie and the highest in Podlaskie (20.2 versus 191.4 per million inhabitants, $p<10^{-4}$). This difference could be partly explained by the high TBE incidence in Podlaskie province, however after omitting confirmed TBE cases, the difference in incidence between the two provinces was still almost five-fold (20.2 versus 96.9 per million inhabitants, $p<10^{-4}$).

### Availability of diagnostics for aseptic central nervous system infections in hospitals

According to the survey on the availability of ACI diagnostics, 185 of the 863 hospitals functioning in Poland in 2008 admitted ACI cases (301 wards). ACI cases were admitted predominantly to infectious disease and neurologic units, with occasional admissions to paediatric, internal medicine or intensive care units. Regional differences in the availability of ACI diagnostics were observed. The frequency of suspected ACI cases referred for viral aetiology investigation ranged from 1.98 to 285.4 samples per million inhabitants in the different provinces. Table 2 summarises the descriptive statistics for regional differences in diagnostic performance for ACI.

Serological diagnosis of TBE was available in four laboratories in Poland, which offered ELISA testing for IgM and IgG antibodies against TBE virus. During 2008, these laboratories processed serum or cerebrospinal fluid samples from 908 patients, of which 211 were found positive. Most of the tests were requested for suspected ACI cases living in high-risk areas for TBE, with 60.1% samples referred from three provinces where TBE incidence exceeded 5 per million inhabitants, and 91% samples referred from seven provinces where the TBE incidence was over 1 per million inhabitants (Figure 1). For enteroviral infections, serological diagnosis and isolation from stool samples were available in the 16 public health laboratories located in province capitals; PCR testing for these viruses was not available in Poland during the survey period. Of 568 samples referred for detection of antibodies against

**Table 2**

Selected indicators of the performance of diagnostics for aseptic central nervous system infections, Poland, 2004–2008

| | | Sum | Mean | SD | Range | Median | IQR |
|---|---|---|---|---|---|---|---|
| Units hospitalising ACI | Total | 301 | 19 | 16 | 5–71 | 13 | 11–22 |
| | Per million inhabitants | - | 7.5 | 3.3 | 3.5–5.2 | 6.3 | 5.0–9.6 |
| Samples tested for TBE | Total | 908 | 57 | 86 | 0–241 | 16 | 5–57 |
| | Per million inhabitants | - | 34.6 | 61.4 | 0–202.3 | 5.5 | 1.5–39.3 |
| Samples tested for enteroviruses | Total | 568 | 36 | 37 | 0–118 | 26 | 10–53 |
| | Per million inhabitants | - | 16.9 | 17.5 | 0–52.3 | 11.7 | 3.6–25.5 |
| Samples tested for other viruses | Total | 718[a] | 45 | 46 | 2–141 | 27 | 10–66 |
| | Per million inhabitants | - | 20.1 | 22.9 | 2.0–82.3 | 10.9 | 4.6–27.9 |

ACI: aseptic central nervous system infection; IQR: interquartile range; SD: standard deviation; TBE: tick-borne encephalitis.

[a] of which seven were tested for herpes simplex virus as well as for other viruses, adding up to 725 tests.

enteroviruses in 2008, 57 were determined as positive. For confirmation of herpesviral CNS infections, MRI testing was available in 100 hospitals throughout the country, and PCR diagnosis, currently the reference diagnostic method to confirm herpes simplex virus infection, was offered by four laboratories (both paid for by the referring hospitals). According to our survey, 568 patients were tested for antibodies against herpes simplex virus, and 113 were found positive. Other aetiological agents of viral ACI, including adenovirus, Epstein-Barr virus, cytomegalovirus, mumps, varicella-zoster or measles viruses were investigated in 157 cases, of which 45 were found positive.

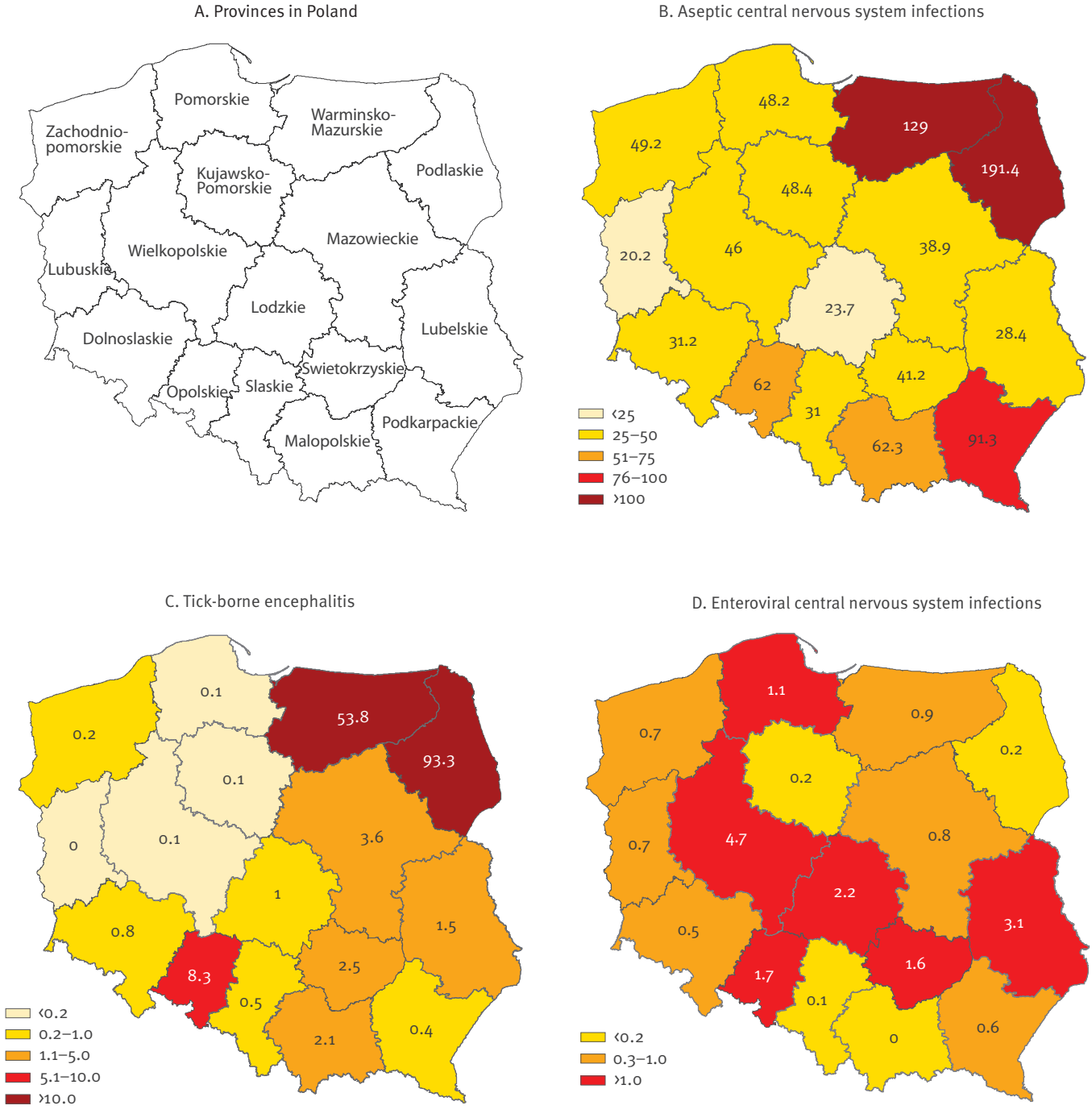
## Sensitivity of reporting of aseptic central nervous system infections

The assessment of ACI reporting sensitivity is summarised in Table 3. From a total of 20,377 ACI cases recorded in Polish hospitals between 2004 and 2008, 9,754 (47.9%) cases were reported to the national surveillance. Important differences in the surveillance sensitivity were observed by year, reporting syndrome, and province.

When the province-specific frequency of referral for viral aetiology diagnosis was compared with ACI incidence, we noted a statistically significant moderate

**Figure 1**

Average incidences of aseptic central nervous system infections per 1,000,000 inhabitants by province, Poland, 2004–2008



correlation with the incidence of reported ACI ($r_s$=0.62, p=0.011) but no correlation with the incidence of hospitalised ACI ($r_s$=0.43, p=0.0097). Plotting the regional frequency of referral for viral testing against the ACI incidence revealed that the same three provinces with known TBE endemic foci were clear outliers, both for hospitalised and reported ACI cases (Figure 2).

Figure 2. Frequency of referral for diagnosis of the viral aetiology of aseptic central nervous system infections in 16 provinces, Poland, 2004–2008

## Discussion

In the present study we analysed the performance of the ACI surveillance system in Poland according to selected indicators. Combining data from different sources, we observed important regional differences in the system's performance. Aetiological diagnosis, a key factor in three of the four surveillance aims, was not uniformly available in all Polish provinces. Moreover, regional differences were observed in the physicians' approach towards reporting of ACI cases with specified or unspecified viral cause.

**Table 3**

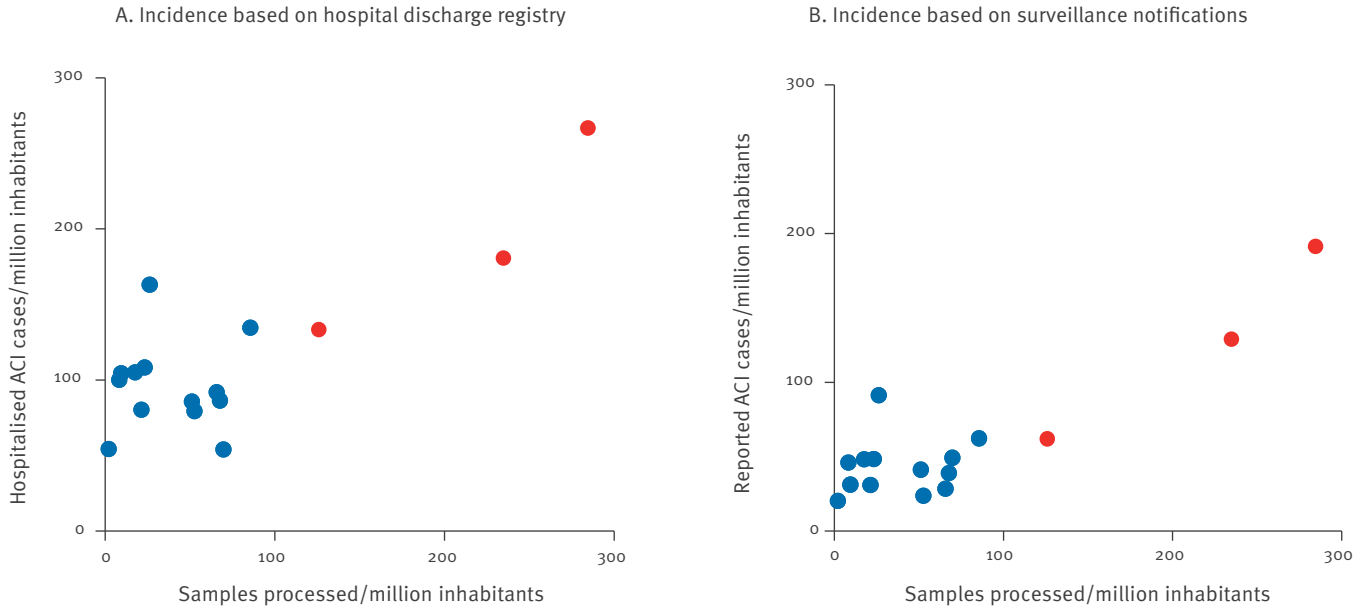
Sensitivity of surveillance for aseptic central nervous system infections by reported syndrome, disease severity and province, Poland, 2004–2008 (n=20,377 hospitalised cases)

| | Hospitalised cases | Reported cases | Proportion reported | 95% CI |
|---|---|---|---|---|
| Reported syndrome | | | | |
| Viral ACI, specified | 2,496 | 1,354 | 54.2 | 52.23–56.17 |
| Viral ACI, unspecified | 9,055 | 6,258 | 69.1 | 68.12–70.03 |
| ACI other, unspecified | 8,826 | 2,142 | 24.3 | 23.37–25.17 |
| Reported disease severity | | | | |
| Meningitis | 16,190 | 6,894 | 42.6 | 41.82–43.35 |
| Encephalitis | 4,187 | 2,860 | 68.3 | 66.87–69.71 |
| Province | | | | |
| with lowest sensitivity | 1,019 | 304 | 29.8 | 27.04–32.75 |
| with highest sensitivity | 457 | 417 | 91.2 | 88.27–93.67 |

ACI: aseptic central nervous system infection; CI: confidence interval.

**Figure 2**

Frequency of referral for diagnosis of the viral aetiology of aseptic central nervous system infections in 16 provinces, Poland, 2004–2008




ACI: aseptic central nervous system infection.
Red dots indicate provinces with tick-borne encephalitis incidence exceeding five cases per million inhabitants during 2004–2008.

Poor availability of aetiological diagnosis in Polish hospitals is an important limitation of the ACI surveillance system. Most Polish provinces are not able to reach any of the four stated surveillance objectives. Firstly, the public health system is probably not detecting the majority of enteroviral outbreaks, as only sporadic cases are diagnosed with enterovirus aetiology and the potential outbreak cases can remain undetected in the mass of undiagnosed cases. Secondly, the ACI surveillance system could be an efficient tool for detecting the location of TBE foci and monitoring its changes, if unspecified ACI cases were referred for testing in all provinces. In provinces not known for high TBE incidence, most locally acquired and imported TBE cases are not diagnosed and remain recorded in the surveillance system as ACI cases of unknown aetiology. Thirdly, it is highly unlikely that cases of polio would be differentiated from cases of aseptic meningitis, particularly if poliovirus is imported from endemic areas in Africa or Asia. Meningitis cases are rarely referred for enterovirus detection, and only as few as two strains and 18 samples for poliovirus isolation from ACI cases throughout the country were sent in 2008 to the National Polio Laboratory at the PZH (personal communication, Magdalena Wieczorek, July 2011). Finally, there is very little chance to detect the emergence of yet unknown viruses causing aseptic meningitis or encephalitis, because suspected ACI cases are rarely tested for viral aetiology. Valid monitoring of neurotropic viruses would require application of standard diagnostic protocols in Polish hospitals, and the possibility of cost-free referral of at least 10% of undiagnosed samples to regional or national reference laboratories.

We can hypothesise that Polish physicians may consider it an unnecessary cost to investigate the viral aetiology since no aetiological treatment is available for most viral ACI except herpes simplex CNS infections. Currently, the National Health Fund, which covers hospitalisation costs, offers the same refund for hospitalisation of ACI cases irrespective of whether the aetiology is confirmed or not. Sparse evidence from European studies indicates that diagnosis of viral pathogens as a cause of CNS infections is also rarely performed in other European countries [8,16].

The regional differences in surveillance sensitivity across Polish provinces (mean 48%, range 30-91%) may be related to different levels of activity of local public health offices, and willingness of physicians to collaborate with the public health system. According to crude data, the highest reported ACI incidence, and some of the highest estimates of surveillance sensitivity were seen in provinces in which TBE diagnostics were widely available (data not shown). Sensitivity of reporting was lower for cases with milder symptoms (meningitis without signs of brain involvement), and for cases classified as 'other' and 'unspecified ACI', comprising all cases which could not be determined as either viral or bacterial.

Although national surveillance systems are the responsibility of the national authorities, there is increasing recognition of the need to collect supranational disease estimates and estimate the international disease burden, to better plan public health resources and detect public health threats. Because increasing international traffic facilitates the spread of infectious diseases, public health research should focus more on the setup and performance of national public health surveillance systems in order to better understand the meaning of numbers provided by the countries. If for example a new food- or waterborne viral strain appeared in a European setting, causing, among others, symptoms of meningitis, one would want to be sure of its timely detection, using standardised laboratory methods, in each country in which it appeared, before it spreads so far as to prevent efficient interventions.

The estimates presented here have several limitations. For the survey of ACI diagnostic availability, the SES did not approach hospitals that had not reported cases in a number of years, assuming that these did not hospitalise ACI cases but referred them elsewhere. Because not all hospitals comply with the procedures of reporting to the local SES, this could have led to underestimation of ACI-hospitalising units. The ad hoc survey of ACI diagnostic testing performance was limited to the major diagnostic laboratories. We could therefore have missed samples referred for testing to other laboratories, for example in the private sector. Since the number of positive samples estimated by our survey matched closely the number of reported cases with established aetiology, we think that our estimates correctly reflect the diagnosis of ACI cases of probable viral aetiology in Poland. Also, the estimation of the physicians' notification sensitivity may be biased, as we compared two different data sources. The weighting factor did not take into account the type of unit in reporting hospitals. If hospitals that were not reporting discharge codes had fewer infectious disease or neurological departments than reporting hospitals, the weighted number of recorded ACI cases could have been overestimated. On the other hand, the majority of units that do not report to the hospital registry are university hospitals which have a higher frequency of admitted ACI cases compared to general hospitals. This would therefore lead to an underascertainment of hospitalised ACI cases.

To conclude, the Polish ACI surveillance system is not meeting most of its objectives, mainly because ACI aetiological diagnosis is not readily available to hospital physicians and because physicians' reporting is inconsistent. More research is necessary to understand the reasons for the poor compliance of physicians with mandatory reporting and for the regional differences in the performance of ACI surveillance. Furthermore, complete evaluation of the ACI surveillance system would be beneficial, using the criteria listed in the guidelines published by the United States Centers for Disease Control and Prevention [17]. Like

other communicable disease surveillance systems in Poland, the ACI surveillance was implemented several decades ago, at a time when highly centralised surveillance systems were operating uniformly in all countries of the Warsaw Pact. Similar to other systems, ACI surveillance has never been evaluated, nor have its goals been stated. Polish society has gone through important changes during the past three decades and it is therefore important to understand whether the communicable disease surveillance objectives defined for the system more than 40 years ago are still valid.

## Recommendations

Based on the results of the present evaluation we recommend the following:

1. Allocation of resources to improved diagnosis of ACI through, i.e. offering diagnosis for selected neurotropic viruses of public health importance in public health laboratories free of charge, or at least at reduced price;
2. Implementation of uniform diagnostic protocols in hospitals, including differential diagnosis of most common causes for ACI and their virological investigation;
3. Creation of a network of hospitals, from which cases would be referred for extended epidemiological and virological investigation of ACI cases in reference laboratories.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