of unnecessary catheters could prevent most episodes of CR-BSI. Total parenteral nutrition was given to 40% of the patients in the present study through multi-lumen catheters. This practice is not recommended by the UK Department of Health [17], but the most recent USA guidelines for the prevention of IVC infection did not consider that specific situation [10].

In conclusion, this study shows clear room for improvement in decisions concerning the choice, indications, duration and care of IVCs, and offers baseline data for the current situation in Europe.

## ACKNOWLEDGEMENTS

The authors are indebted to the 109 colleagues from 21 countries who provided the data reported in this study. The work was supported in part by 'Red Española de Investigación en Patología Infecciosa' (REIPI-C03/14). Some of the results were presented previously at the 42nd International Congress on Antimicrobial Agents and Chemotherapy, San Diego, USA, 2002.

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# RESEARCH NOTE

## Outbreak in France of *Neisseria meningitidis* B:15:P1.12 belonging to sequence type 1403

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## ABSTRACT

This report describes a meningococcal outbreak in France caused by *Neisseria meningitidis* B:15:P1.12 of sequence type 1403, which affected eight young patients, between November 2000 and February 2002. Epidemiological typing confirmed that a single strain was responsible. Favourable outcome, sequelae or death resulted in similar proportions as in other cases of meningococcal disease in France during the same period, but purpura was observed in all eight cases. The patients were aged between 14 and 28 years, whereas the median age of patients affected by other meningococcal strains during this period in the same area was 60.4 years.



**Keywords** France, meningitis, *Neisseria meningitidis*, outbreak

**Original Submission:** 29 October 2003; **Revised Submission:** 26 March 2004; **Accepted:** 30 March 2004

*Clin Microbiol Infect* 2004; 10: 845–848
10.1111/j.1469-0691.2004.00935.x


*Neisseria meningitidis* is an exclusively human pathogen, responsible for bacteraemia and meningitis [1]. However, 10–30% of young adults carry this organism asymptomatically in the nasopharynx [2], where it can either exist transiently or invade the bloodstream, thus causing meningococcal disease [3]. Epidemic and sporadic cases of meningococcal disease occur worldwide. Epidemics are caused by the spread of particular clones (e.g., serogroup A in Asia and Africa in recent years), while sporadic cases are caused by genetically heterogeneous strains, such as those belonging to serogroups B, C, Y and W135, which account for most infections in Europe and North America [4]. In France, the incidence of meningococcal disease has increased since 1995 (364 invasive cases in 1995 vs. 678 in 2002) [5–7]. Serogroup B, which was responsible for more than two-thirds of invasive cases in 1997, remains the serogroup isolated most frequently, accounting for *c.* 54% of cases in 2001, while 38% of cases were caused by serogroup C [6].

The Indre-et-Loire department of France has a mixed urban and rural population, with *c.* 550 000 inhabitants. All patients suffering from severe infectious diseases, or less severe but rare infections, are hospitalised at the Tours University Hospital. On average, between four and six cases of meningococcal disease are reported each year in Indre-et-Loire. However, between November 2000 and February 2002, 13 cases of meningococcal disease, either meningitis or meningococcaemia, were recorded (Fig. 1). Eight of the 13 cases were caused by *N. meningitidis* B:15:P1.12 (Table 1). The isolates, which were typed by restriction fragment length polymorphism analysis of the *pilA*, *pilD*, *crgA*, *regF* and *iga* genes, all had the same restriction patterns [8] and belonged to the same sequence type (ST-1403) according to multilocus sequence typing [9]. Pulsed-field gel electrophoresis following macrorestriction with *Spe*I endonuclease confirmed their clonal nature. *N. meningitidis* B:15:P1.12 strains have been isolated previously in France, but this is the first time that they have been isolated in Indre-et-Loire or neighbouring regions.

The first case of *N. meningitidis* B:15:P1.12 was diagnosed in November 2000, with five more cases diagnosed in a 3-week period during January and February 2001, and two further cases in January and February 2002. All eight patients had cutaneous lesions, with purpura fulminans or petechial purpura. Seven of these patients had classical early signs of an influenza-like syndrome with fever, followed by vomiting, headache, neck stiffness and photophobia. Other neurological signs were noted for five patients (Table 1). The outcome of the illness following treatment with β-lactams and gentamicin was favourable for all patients except patient no. 5. Minor neurological

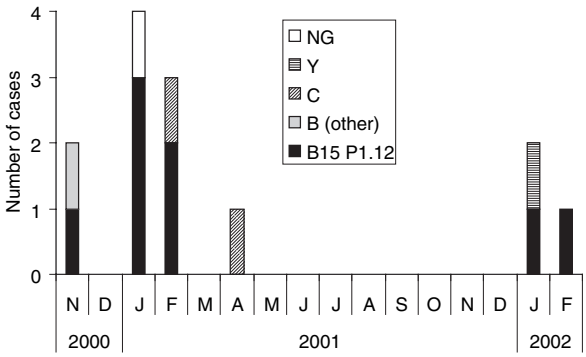


**Fig. 1.** Occurrence of 13 cases of meningococcal disease caused by *Neisseria meningitidis* (eight involving the *N. meningitidis* B:15:P1.12 strain) in Indre-et-Loire between November 2000 and February 2002 (NG, non-groupable).

**Table 1.** Epidemiological and clinical data for 13 cases of invasive meningococcal disease that occurred in Indre-et-Loire between November 2000 and February 2002

| Date | Case no. | Age (years) | Sex | Serotype | Purpura | Neurological signs | Other signs | Outcome/sequelae |
|---|---|---|---|---|---|---|---|---|
| 04/11/00 | – | 73 | F | B:NT:P1.5 | Not known | – | – | Favourable |
| 08/11/00 | 1 | 20 | M | B:15:P1.12 | Ecchymotic | Hyperesthaesia | Epistaxis | Favourable |
| 06/01/01 | 2 | 24 | M | B:15:P1.12 | Petechial | – | – | Favourable |
| 20/01/01 | 3 | 28 | M | B:15:P1.12 | Yes | Occular paralysis | – | Diplopia |
| 28/01/01 | 4 | 22 | M | B:15:P1.12 | Petechial | Convulsions | Disorientation | Diplopia/vertigo |
| 29/01/01 | – | 60 | F | NG | No | No | Pneumonia | Favourable |
| 01/02/01 | 5 | 14 | F | B:15:P1.12 | Petechial | – | Acute respiratory disease syndrome | Death |
| 03/02/01 | 6 | 19 | M | B:15:P1.12 | Extensive | Facial paralysis | Necrosis of the toes | Favourable |
| 03/02/01 | – | 81 | F | C:NT:P1.2,5 | Not known | – | – | Favourable |
| 30/04/01 | – | 52 | F | C:2a:NST | Not known | – | Shock | Favourable |
| 24/01/02 | 7 | 22 | F | B:15:P1.12 | Petechial | – | – | Favourable |
| 30/01/02 | – | 36 | F | Y:15:P1.12 | No | – | – | Favourable |
| 22/02/02 | 8 | 25 | M | B:15:P1.12 | Yes | Amaurosis/disorientation | Shock/cerebral abscess | Favourable |

The eight cases caused by the *N. meningitidis* B:15:P1.12 are numbered in chronological order of their appearance. NG, non-groupable; NT, non-typeable; NST, non-subtypeable.

sequelae were also noted for two patients (no major sequelae were noted). Case no. 5 was different from the others, as neither an influenza-like syndrome, fever, neck stiffness nor photophobia was observed. The patient died before being hospitalised. An autopsy was performed as the haemorrhagic skin lesions were atypical, and this revealed major pleural, pericardial and peritoneal haemorrhages. Cerebrospinal fluid and blood cultures were positive for *N. meningitidis* in all cases, except case no. 5, where the strain was isolated following culture of a meningeal biopsy. The patients were aged between 14 and 28 years; six were male and two were female. Epidemiological investigations revealed that all eight patients lived in the same area, and that case no. 5 was the friend of the brother of case no. 6.

The outcomes of these eight cases were similar in proportion to those of cases of meningococcal disease recorded in other parts of France, where the outcome is favourable in 81% of cases (75% in the present study), major sequelae occur in 5% of cases (0% in the present study, where there was an absence of major neurological sequelae), and death occurs in 15% of cases (12.5% in the present study) [6,7]. Nevertheless, several major observations can be made. First, all of the patients involved in the present outbreak had purpura (petechial, fulminans or extensive), whereas purpura occurs in only 23% of serogroup B cases according to the French epidemiological data [6,7]. Second, this unusual strain spread very rapidly among the population, causing five cases within a 3-week period following the first case. None of the patients had any underlying immune deficiency that might have predisposed them to invasive meningococcal disease, and none had received immunosuppressive therapy. No other cases were reported in 2001 after the short outbreak, and only two cases were reported in 2002 after an interval of about a year. In addition, the outbreak was limited to a small geographical area and did not spread to neighbouring regions. This was surprising because the features described above suggest that the *N. meningitidis* B:15:P1.12 strain is epidemic in character. As new clones appear constantly, this is consistent with the macroevolution of hyper-virulent lineages that emerge at intervals within the population, and then slowly diversify as their initially uniform genomes become increasingly diverse because of highly localised recombination events [10]. No other cases have been described since the eighth case, highlighting the unpredictable changes in meningococcal epidemiology [11,12]. Third, the median age of the patients infected was 21.7 years (the youngest patient in the cohort died); no cases concerned children, neonates or individuals aged >28 years. In contrast, the median age of the five patients infected with other *N. meningitidis* strains during the same period in the same area was 60.4 years (none of these patients died).

Although there has been an increase in the use of preventive antibiotic treatment for people who have come into contact with a patient, data

for France in 2001 indicated that while 88% of family members received antibiotic prophylaxis, only 58% of colleagues, friends or other people in close contact with primary cases were given antibiotics [6]. The outbreak reported in the present study highlights the importance of very early prophylaxis to prevent secondary cases among a family or close contacts. In the present study, at least one patient (who died) was in close contact with the brother of another patient.

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# RESEARCH NOTE

## Identification of *Neisseria meningitidis* sequence type 66 in Poland


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## ABSTRACT

Investigation of two cases of invasive meningococcal disease within a single family revealed the presence of isolates of *Neisseria meningitidis* phenotype C:2b:P1.2,P1.5 belonging to sequence type (ST) 66. The ST66 clone is a single-locus variant of the widely distributed ST8 complex, which has been observed previously in Spain, Belgium, Australia and New Zealand. This hypervariable meningococcal lineage has been responsible for local epidemics worldwide. This is the first report of ST66 meningococcal isolates of this phenotype from Poland.



**Keywords** Epidemiology, meningitis, *Neisseria meningitidis*, typing

**Original Submission:** 8 October 2003; **Revised Submission:** 8 December 2003; **Accepted:** 29 February 2004

*Clin Microbiol Infect* 2004; 10: 848–850
10.1111/j.1469-0691.2004.00941.x


*Neisseria meningitidis* is responsible for various kinds of infections, of which septicaemia and meningitis are the most severe, but the organism can also be carried in the nasopharynx of healthy individuals. Meningococcal infections usually occur sporadically, but local or large-scale out-


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