NETHERLANDS REFERENCE LABORATORY FOR BACTERIAL MENINGITIS

# BACTERIAL MENINGITIS IN THE NETHERLANDS

## ANNUAL REPORT 2015


**AMC**
**Academic Medical Center**
**University of Amsterdam**

**RIVM**
**National Institute of Public Health**
**and**
**Environmental Protection**

**BACTERIAL MENINGITIS IN THE NETHERLANDS**

**ANNUAL REPORT 2015**

**NETHERLANDS REFERENCE LABORATORY FOR BACTERIAL MENINGITIS**

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*Netherlands Reference Laboratory for Bacterial Meningitis (AMC/RIVM)*
*Bacterial meningitis in the Netherlands; annual report 2015*
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# 1 INTRODUCTION

This is the **44th** Annual Report of the Netherlands Reference Laboratory for Bacterial Meningitis of the Academic Medical Center (AMC) and the National Institute of Public Health and the Environment (RIVM). The Reference Laboratory is located within the Department of Medical Microbiology of the AMC in Amsterdam. Nearly all clinical microbiology laboratories of the Netherlands collaborate by submitting bacterial isolates and/or cerebrospinal fluid samples from patients with meningitis and we are most grateful to our colleagues for their cooperation.

The Reference Laboratory started collecting isolates of *Neisseria meningitidis* in 1959 and of other bacteria causing meningitis in 1975.

In the archives of the Reference Laboratory data from approximately 69.160 isolates are now available for studies on the epidemiology of bacterial meningitis and on the pathogenicity and antibiotic susceptibility of isolates.

The objectives of the Reference Laboratory are:
- to perform surveillance of bacterial meningitis;
- to describe the epidemiology of bacterial meningitis in the Netherlands;
- to provide keys for the development of potential vaccine components;
- to provide data about antibiotic susceptibility of isolates.

The information is presented in tables and figures and shortly discussed in the text.

We would appreciate receiving your opinion and suggestions on this report.

Amsterdam, September, 2016

dr. A. van der Ende PhD, biochemist
drs. M. Kolader, medical microbiologist

# 2 ISOLATES, CSF SPECIMENS AND SERA RECEIVE

The Netherlands Reference Laboratory for Bacterial Meningitis collects isolates from cerebrospinal fluid (CSF) and blood from patients with proven meningitis (CSF and possibly blood culture positive) or with bacteraemia and suspected meningitis (blood culture positive only). Unless otherwise indicated, every isolate from CSF, from CSF and blood, and from blood represents a patient with meningitis, a patient with meningitis and bacteraemia, and a bacteraemia patient, respectively. Incidences have been calculated by dividing the number of isolates collected over one year (in a certain patient's age group) by the number of inhabitants over one year (in that age group) multiplied by 100,000. Population figures were obtained from Statistics Netherlands (Centraal Bureau voor de Statistiek, http://www.cbs.nl) using StatLine. By estimation, the Reference Laboratory receives about 90% of the isolates of Dutch meningitis patients, hence incidences presented in this report are likely to be underestimated.

In 2015, the Reference Laboratory received isolates from CSF and / or blood from 1404 patients, and 23 specimens of CSF and/or serum wich were positive in PCR (or crypt. agglutination.) (table 2.1/table 11.1). Of these patients, 309 were confirmed cases of bacterial meningitis.

Table 2.1

| | Number of specimens |
|---|---|
| **Isolate (CSF and/or blood)** | 1404 |
| **CSF samples (without isolate)** | 142 |
| **Sera (and other fluid, without isolate)** | 8 |
| **Total** | **1554** |

In 2015, 51 (52) clinical microbiology laboratories submitted isolates to the Reference Laboratory.

Table 2.2 shows the 1404 isolates according to species and to laboratory where cases were diagnosed.

Table 2.2 Number of isolates from CSF and/or blood received in 2015, according to laboratory

| Location | Laboratory | Nm | Hi | Sp | Ec | Sag | Lm | Spy | Sau | Cns | Cn | Ot | nv | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Alkmaar** | MCA lab. Med. Microbiologie | 3 | 2 | 3 | - | - | 1 | - | - | - | 1 | - | - | **10** |
| **Amersfoort** | Meander Medisch Centrum | 1 | 5 | 3 | 3 | 1 | - | - | - | - | - | 1 | - | **14** |
| **Amsterdam** | Academisch Medisch Centrum | - | 2 | 33 | 3 | 3 | - | 1 | 4 | - | 1 | 20 | - | **67** |
| | Academisch ziekenhuis VU | 3 | - | - | - | - | - | - | - | - | - | - | - | **3** |
| | Onze Lieve Vrouwe Gasthuis | 6 | 2 | 9 | - | 5 | 1 | 1 | 1 | - | - | - | - | **25** |
| **Apeldoorn** | Gelre Ziekenhuizen | 1 | 2 | 10 | - | 1 | 1 | - | - | - | - | 1 | - | **16** |
| **Arnhem** | Rijnstate | 1 | 4 | 45 | - | 1 | 4 | - | - | - | - | 1 | - | **56** |
| **Breda** | Amphia Ziekenhuis | - | 4 | 4 | - | 3 | - | 1 | - | - | 1 | - | - | **13** |
| **Capelle ad IJssel** | IJsselland Ziekenhuis | - | - | 1 | - | - | - | - | - | - | - | - | - | **1** |
| **Delft** | Reinier de Graaf groep | 1 | 4 | 3 | - | 2 | - | - | - | - | - | - | - | **10** |
| **Den Bosch** | Regionaal laboratorium Den Bosch | 3 | 5 | 3 | 1 | 1 | 1 | - | 1 | - | - | - | - | **15** |
| **Den Haag** | Haga Ziekenhuis, loc. Leyenburg | - | 4 | 11 | - | 6 | 1 | 2 | - | - | - | - | - | **24** |
| | MA Haaglanden, loc Westeinde | - | - | 3 | - | 1 | 1 | - | - | | | - | | **5** |
| **Deventer** | Deventer Ziekenhuis | - | 2 | 1 | - | 4 | - | - | - | - | - | - | - | **7** |
| **Doetinchem** | Slingeland Ziekenhuis | - | 1 | 4 | - | - | - | - | - | - | - | - | - | **5** |
| **Dordrecht** | RLM Dordrecht / Gorinchem | 1 | 4 | 59 | 1 | 5 | 1 | 1 | - | - | - | - | - | **72** |
| **Ede** | Gelderse Vallei | 3 | 10 | 4 | 2 | 1 | 2* | 1 | - | - | - | 1 | - | **24** |
| **Gouda** | Groene Hart Ziekenhuis | 3 | 1 | 4 | - | - | - | - | - | - | - | - | - | **8** |
| **Groningen** | Certe, Lab. v. Infectieziekten | 8 | 17 | 9 | - | - | 2 | - | 1 | - | 1 | - | - | **38** |
| | UMCG | - | 6 | 4 | 1 | - | - | - | - | - | - | - | - | **11** |
| **Haarlem** | St. Streeklab voor de Volksgezondheid | 2 | 4 | 67 | - | 1 | 5 | 1 | - | - | - | 3 | - | **83** |
| **Harderwijk** | St. Jansdal Ziekenhuis | 1 | 4 | 3 | - | - | - | - | 1 | - | - | - | - | **9** |
| **Hengelo** | LabMicTa | 8 | 16 | 124 | - | 7 | 3 | 1 | - | - | - | - | - | **159** |
| **Hilversum** | Centraal Bact. Ser. Lab. | 2 | 2 | 2 | - | - | - | - | - | - | - | - | - | **6** |
| **Hoorn** | Westfries gasthuis | - | 5 | 5 | 1 | - | 1 | - | - | - | 1 | 1 | - | **14** |
| **Leeuwarden** | Izore, centrum infectieziekten Friesland | 5 | 11 | 103 | - | - | 1 | - | 1 | - | - | 6 | - | **127** |
| **Leiden** | Alrijne ziekenhuis | 3 | 4 | 2 | - | - | - | - | - | - | - | - | - | **9** |
| | LUMC, KML, Lab.voor Bacteriologie | 1 | 5 | 7 | 2 | 1 | - | - | - | - | 2 | - | - | **18** |
| **Maastricht** | Acad. Ziekenhuis Maastricht | 1 | - | 1 | - | - | - | - | - | - | - | - | - | **2** |
| **Nieuwegein** | St. Antonius Ziekenhuis | - | 7 | 81 | - | - | 5 | - | 2 | - | - | - | - | **95** |
| **Nijmegen** | Canisius Wilhelmina Ziekenhuis | 1 | 1 | 1 | - | 1 | - | - | - | - | - | - | - | **4** |
| | UMC St. Radboud | 2 | 6 | 9 | 2 | 4 | 2 | - | - | - | - | 1 | 1 | **27** |
| **Roermond** | St. Laurentius Ziekenhuis | - | 2 | - | - | - | - | - | - | - | - | | - | **2** |
| **Roosendaal** | St. Fransiscus Ziekenhuis | 3 | - | 2 | - | - | - | - | - | - | - | - | - | **5** |

| Location | Laboratory | Nm | Hi | Sp | Ec | Sag | Lm | Spy | Sau | Cns | Cn | Ot | nv | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Rotterdam** | Erasmus MC Med. Microbiologie | 1 | 4 | 10 | 3 | 1 | 1 | 2 | 3 | - | - | - | - | **25** |
| | Ikazia Ziekenhuis | - | 2 | 3 | - | 1 | 1 | - | - | - | - | - | - | **7** |
| | Maasstad Ziekenhuis | 3 | 1 | 3 | - | 2 | - | - | - | - | - | - | - | **9** |
| | St.Franciscus Gasthuis | - | - | 5 | - | 1 | 1 | 1 | - | - | - | - | - | **8** |
| **Schiedam** | Vlietland ziekenhuis | - | 2 | 4 | - | - | 1 | 1 | - | - | - | - | - | **8** |
| **Sittard** | Zuyderland Medisch Centrum | 1 | 8 | 49 | 2 | 1 | 4 | 1 | 2 | 2 | 1 | 2 | - | **73** |
| **Terneuzen** | Zorgsaam Zeeuws-Vlaanderen | - | - | - | - | - | 1 | - | - | - | - | 1 | - | **2** |
| **Tilburg** | Streeklab. Tilburg | 1 | 5 | 69 | - | 2 | 2 | - | - | - | 1 | - | - | **80** |
| **Utrecht** | Diakonessenhuis | 2 | 4 | 4 | - | - | 2 | - | - | - | - | - | - | **12** |
| | UMC Med. Microbiologie | 1 | 6 | 10 | 7 | - | - | - | - | - | - | - | - | **24** |
| **Veldhoven** | PAMM, Lab. Med. Microbiologie | 1 | 9 | 107 | - | 6 | 2 | 2 | - | - | - | - | - | **127** |
| **Vredenburg** | Medical Microbology, Curacao | - | - | 4 | - | - | - | - | - | - | - | - | - | **4** |
| **Venlo** | Vie Curie medisch centrum | - | - | 3 | - | - | - | - | - | - | - | 1 | - | **4** |
| **Vlissingen** | Lab. Voor Med. Microbiologie & Imm. | - | 2 | 2 | - | 1 | - | - | - | - | - | - | - | **5** |
| **Weert** | St. Jans gasthuis | 1 | - | 1 | - | - | - | - | - | - | - | - | - | **2** |
| **Woerden** | Zuwe Hofpoort Ziekenhuis | 3 | - | 1 | - | - | - | - | - | - | - | - | - | **4** |
| **Zaandam** | CoMicro ZMC | 3 | 4 | - | - | 1 | - | - | - | - | - | - | - | **8** |
| **Zwolle** | Isala Klinieken LMMI | 4 | 6 | 6 | - | 1 | - | - | - | - | - | 1 | - | **18** |
| **Total** | | 84 | 195 | 901 | 28 | 65 | 47 | 16 | 16 | 2 | 9 | 40 | 1 | **1404** |

# **Nm:** *N. meningitidis*; **Hi:** *H. influenzae*; **Sp:** *S. pneumoniae*; **Ec:** *E. coli*; **Sag:** *S. agalactiae*; **Lm:** *L. monocytogenes*; **Spy:** *S.pyogenes*; **Sau:** *S. aureus*; **Cns:** Coagulase negative staphylococcus; **Cn:** *C. neoformans;* **ot:** other bacteria; **nv:** non-viable

The distribution of the isolates received in the 5 year period 2011 through 2015 is presented in table 2.3. The number of total isolates increased from 1243 in 2014 to 1404 in 2015. The number of cases of meningococcal disease was higher compared to the number of cases in 2014 (2015: 84; 2014: 73; 2013: 111; 2012: 81). Since June 2006, children born after the first of April 2006 are vaccinated with a conjugated polysaccharide vaccine against *Streptococcus pneumoniae*. The number of *S. pneumoniae* isolates from CSF decreased from more than 200 yearly before 2007 to 147 in 2015. The number of *Listeria monocytogenes* was high in 2005 (81), most likely due to an intensified surveillance performed by the RIVM. In 2014, the number of *L. monocytogenes* isolates was 47. The number of *Haemophilus influenzae* isolates increased, mainly due to a higher number of *H. influenzae* isolates from blood.

Table 2.3 Number of isolates from CSF and/or blood received in the years 2011 – 2015

| Species | 2011 | | | 2012 | | | 2013 | | | 2014 | | | 2015 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | CSF | Blood | Total | CSF | Blood | Total | CSF | Blood | Total | CSF | Blood | Total | CSF | Blood | Total |
| ***N. meningitidis*** | 37 | 53 | 90 | 41 | 40 | 81 | 39 | 72 | 111 | 31 | 42 | 73 | 33 | 51 | 84 |
| ***H. influenzae*** | 13 | 126 | 139 | 16 | 124 | 140 | 16 | 144 | 160 | 21 | 140 | 161 | 22 | 173 | 195 |
| ***S. pneumoniae*** | 163 | 753 | 916 | 138 | 731 | 869 | 138 | 768 | 906 | 142 | 627 | 769 | 147 | 754 | 901 |
| ***E. coli*** | 8 | 7 | 15 | 5 | 8 | 13 | 8 | 18 | 26 | 8 | 24 | 32 | 8 | 20 | 28 |
| ***S. agalactiae*** | 19 | 44 | 63 | 23 | 57 | 80 | 20 | 52 | 72 | 23 | 48 | 71 | 19 | 46 | 65 |
| ***L. monocytogenes*** | 8 | 53 | 61 | 9 | 50 | 59 | 6 | 46 | 52 | 19 | 51 | 70 | 8 | 39 | 47 |
| ***S. pyogenes*** | 4 | 10 | 14 | 3 | 9 | 12 | 9 | 22 | 31 | 2 | 6 | 8 | 3 | 13 | 16 |
| ***S. aureus*** | 4 | 0 | 4 | 7 | 1 | 8 | 5 | 18 | 23 | 13 | 10 | 23 | 8 | 8 | 16 |
| **Coag.neg.Staph.** | 0 | 0 | 0 | 6 | 0 | 6 | 6 | 0 | 6 | 2 | 0 | 2 | 2 | 0 | 2 |
| ***C. neoformans*** | 5 | 2 | 7 | 9 | 1 | 10 | 6 | 2 | 8 | 4 | 3 | 7 | 7 | 2 | 9 |
| **others** | 14 | 6 | 20 | 17 | 8 | 25 | 14 | 6 | 20 | 22 | 4 | 26 | 30 | 10 | 40 |
| **non viable** | 0 | 2 | 2 | 0 | 1 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 0 | 1 | 1 |
| **Total** | **275** | **1056** | **1331** | **274** | **1030** | **1304** | **267** | **1149** | **1416** | **287** | **956** | **1243** | **287** | **1117** | **1404** |

CSF: CSF or CSF and blood
blood: blood only

The incidence of isolation of the different bacterial species from CSF and/or blood over the years 2011 to 2015 is shown in table 2.4. The incidence of *H. influenzae* infection was 50% lower than in the years before vaccination was introduced (2.1 in 1992; 1.15 in 2014). The incidence *of H. influenzae* infection increased from 2010 until now, mainly caused by an increase in the number of cases of bacteraemia due to unencapsulated *H. influenzae*.

Table 2.4 Number of isolates from CSF and/or blood per 100,000 inhabitants, 2011 - 2015

| Species | 2011 | 2012 | 2013 | 2014 | 2015 |
|---|---|---|---|---|---|
| ***N. meningitidis*** | 0.54 | 0.48 | 0.66 | 0.43 | 0.50 |
| ***H. influenzae*** | 0.83 | 0.84 | 0.95 | 0.96 | 1.15 |
| ***S. pneumoniae*** | 5.50 | 5.19 | 5.40 | 4.57 | 5.33 |
| ***E. coli*** | 0.09 | 0.08 | 0.15 | 0.19 | 0.17 |
| ***S. agalactiae*** | 0.38 | 0.48 | 0.43 | 0.42 | 0.38 |
| ***L. monocytogenes*** | 0.37 | 0.35 | 0.31 | 0.42 | 0.28 |
| ***S. pyogenes*** | 0.08 | 0.07 | 0.18 | 0.05 | 0.09 |
| ***S. aureus*** | 0.02 | 0.05 | 0.14 | 0.14 | 0.09 |
| ***Coag. neg. Staph.*** | 0.00 | 0.04 | 0.04 | 0.01 | 0.01 |
| ***C. neoformans*** | 0.04 | 0.06 | 0.05 | 0.04 | 0.05 |
| ***others*** | 0.12 | 0.15 | 0.12 | 0.15 | 0.24 |
| ***non viable*** | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 |
| ***Total*** | **7.99** | **7.79** | **8.44** | **7.39** | **8.31** |

Table 2.5 Total number of isolates from CSF and/or blood received in 2015, according to bacterial species and specimen source

| Species | | CSF or CSF and blood | Blood only | Total | % |
|---|---|---|---|---|---|
| ***Neisseria meningitidis*** | | 33[1] | 51 | 84 | |
| ***Haemophilus influenzae*** | | 22 | 173 | 195 | |
| ***Streptococcus pneumoniae*** | | 147 | 754[2,3,4] | 901 | |
| ***Escherichia coli*** | | 8 | 20[5] | 28 | |
| ***Streptococcus agalactiae*** | | 19 | 46 | 65 | |
| ***Listeria monocytogenes*** | | 8 | 39 | 47 | |
| ***Streptococcus pyogenes*** | | 3 | 13 | 16 | |
| ***Staphylococcus aureus*** | | 8 | 8 | 16 | |
| **Coagulase-negative staphylococcus** | | 2 [6,7] | - | 2 | |
| ***Cryptococcus neoformans*** | | 7 | 2 | 9 | |
| **Others total** | | 30 | 10 | 40 | |
| **Others** | *Pseudomonas aeruginosa* | *3*[8] | *0* | *3* | |
| | *Pseudomonas stutzeri* | *1* | *0* | *1* | |
| | *Cryptococcus deuterogattii* | *1* | *0* | *1* | |
| | *Serratia marcescens* | *3* | *0* | *3* | |
| | *Serratia odorifera* | *1* | *0* | *1* | |
| | *Acinetobacter johnsonii* | *1* | *0* | *1* | |
| | *Campylobacter fetus* | *1* | *0* | *1* | |
| | *Klebsiella oxytoca* | *1* | *0* | *1* | |
| | *Moraxella osloensis* | *1* | *1* | *2* | |
| | *Neisseria cinerea* | *0* | *1* | *1* | |
| | *Neisseria polysaccharea* | *0* | *1* | *1* | |
| | *Streptococcus anginosus* | *1* | *0* | *1* | |
| | *Streptococcus constellatus* | *1* | *0* | *1* | |
| | *Streptococcus cristatus* | *1* | *0* | *1* | |
| | *Streptococcus gallolyticus ssp gallolyticus* | *0* | *2* | *2* | |
| | *Streptococcus gallolyticus ssp pasteurianus* | *0* | *1* | *1* | |
| | *Streptococcus infantis* | *1* | *0* | *1* | |
| | *Streptococcus intermedius* | *1* | *0* | *1* | |
| | *Streptococcus lutetiensis* | *0* | *1* | *1* | |
| | *Streptococcus mitis* | *1* | *0* | *1* | |
| | *Streptococcus oligofermentans* | *1* | *0* | *1* | |
| | *Streptococcus oralis* | *2* | *0* | *2* | |
| | *Streptococcus parasanguinis* | *0* | *1* | *1* | |
| | *Streptococcus salivarius* | *2* | *0* | *2* | |
| | *Streptococcus sanguinis* | *1* | *0* | *1* | |
| | *Streptococcus suis* | *1* | *0* | *1* | |
| | *Haemophilus parainfluenzae* | *0* | *2* | *2* | |
| | *Enterococcus faecalis* | *1* | *0* | *1* | |
| | *Enterococcus faecium* | *3* | *0* | *3* | |
| **Non viable** | | 0 | 1 [9] | 1 | **0.1** |
| **Total %** | | **287** | **1117** | **1404** | **100.0** |

1 In three patient we received a blood isolate and a CSF sample. *CSF was positive with CtrA PCR, therefore those patients were counted as CSF*

2 In two patients *Streptococcus pneumoniae* and *Haemophilus influenza* were islated from the blood.

3 In one patient *Streptococcus pneumoniae* and *Streptococcus agalatiae* were islated from the blood.

4 In one patient *Streptococcus pneumoniae* was isolated from blood, more than one month later the same isolate was isolated from CSF and blood.

5 In one patient *Escherichia coli* and *Streptococcus agalatiae* were islated from the blood.

6 From 2 Coagulase-negative staphylococcus one was *Staphylococcus epidermidis* and the other a *Staphylococcus haemoliticus*

7 In one patient *Staphylococcus haemoliticus* and an *Enterococcus faecalis* were isolated from CSF

8 In one patient *Pseudomonas aeruginosa* and *Serratia marcescens* were isolated from CSF

9 Non viable, in one patient a Listeria monocytogenes was isolated from the blood. The isolate was non viable.

Table 2.5 shows the distribution of isolates according to the specimen from which they were cultured. The predominant species were *N. meningitidis, H. influenzae* and *S. pneumoniae*. Patients with two different isolates were counted twice. Example, patients mentioned in footnote nr 2 were counted once for *S. pneumoniae* and once for *H. influenzae*.

# 3 BACTERIAL MENINGITIS - general data

In 2015, the Reference Laboratory received CSF isolates from 281 patients. Furthermore, 22 culture-negative CSF samples appeared to be positive by antigen detection or PCR (Table 11.1). Of these CSF samples, 8 were positive for *N. meningitidis* an, 14 for *S. pneumoniae.* Including these cases, the total number of patients with confirmed meningitis amounted to 303. The proportion of meningococcal and pneumococcal meningitis among these patients was 14% and 50%, respectively (Figure 3.1). Of 8 meningococcal and 14 pneumococcal meningitis cases identified by a PCR positive CSF, 3 had a meningococcial isolate from the blood and also 3 a pneumococcal isolate from the blood, respectively. In the next chapters, these 6 patients were added to the group with a CSF isolate.

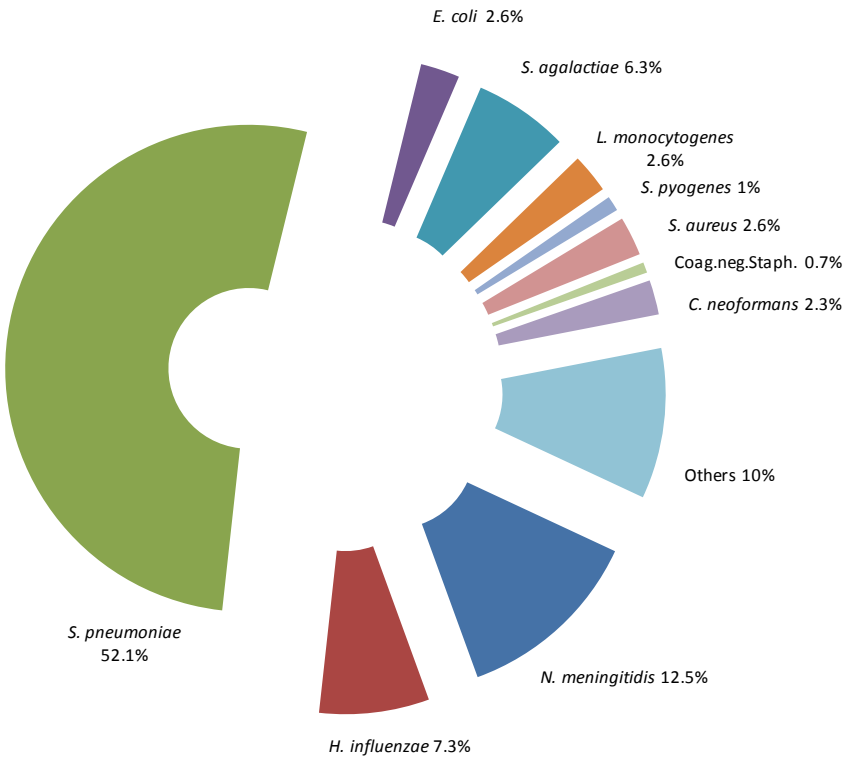


**Figure 3.1** *Proportional distribution of CSF isolates and CSF positive samples, 2015*

Figure 3.2 shows the annual total number of bacterial isolates from CSF during the period 2006-2015. The 10 years trend line indicates a decrease over the last decade. The incidence per 100,000 inhabitants also shows a decreasing trend and varied between 2.8 and 1.6 during the period 2006-2015 (Figure 3.2).
Data concerning *N. meningitidis, H. influenzae* and *S. pneumoniae* during the same period are presented in figure 3.3. Since the introduction of vaccination against *H. influenzae* type b in 1993, the incidence of *Haemophilus* meningitis decreased to 0.12 per 100,000 and remained at this low level. The number of cases of meningococcal meningitis (with an isolate) decreased from 480 cases (incidence of 3.1) in 1993 to 33 cases (incidence of 0.20) in 2015, mainly due to a decline in the number of cases of serogroup B and C meningitis. Nationwide vaccination against serogroup C meningococci was started in 2002. The year 2003 was the first year, since two decades, in which *N. meningitidis* was not the main cause

of bacterial meningitis in the Netherlands. Pneumococcal meningitis was slowly increasing since 1991 as the annual incidence rose from 1.0 to 1.6 per 100,000 inhabitants in 2004, but had decreased to 0.87 in 2015 due to vaccination against pneumococci introduced in June 2006 in the National Immunisation Programme.

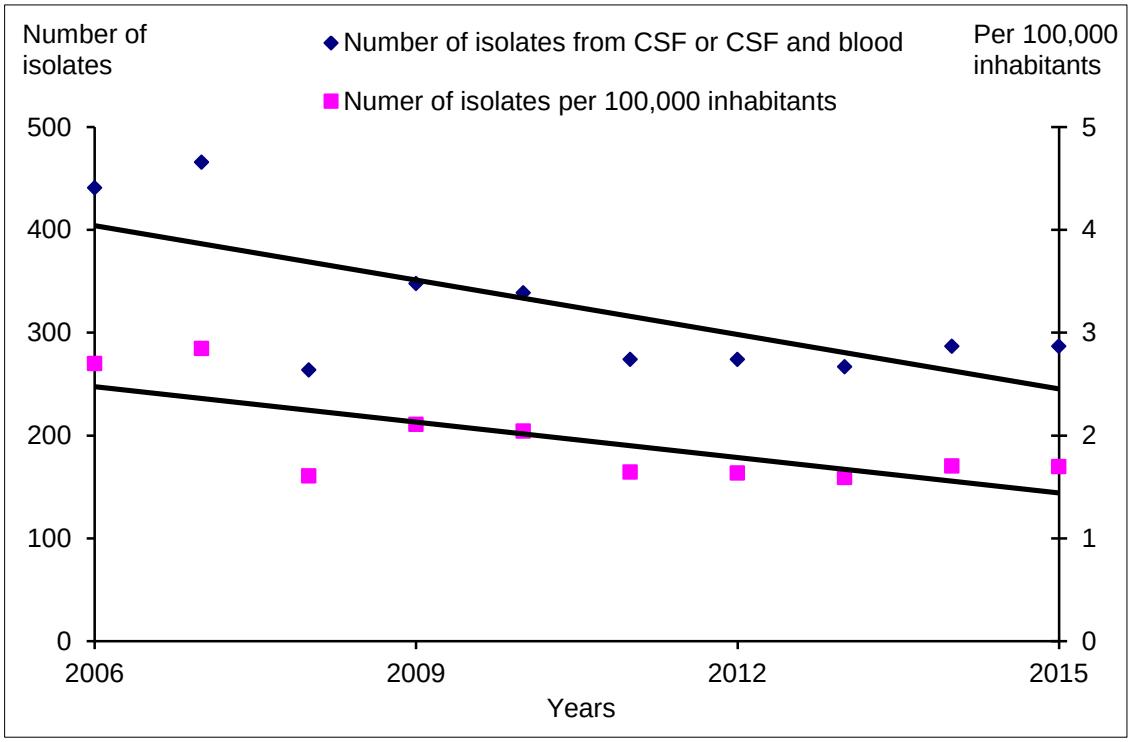


**Figure 3.2** *Isolates from CSF, 2006-2015*

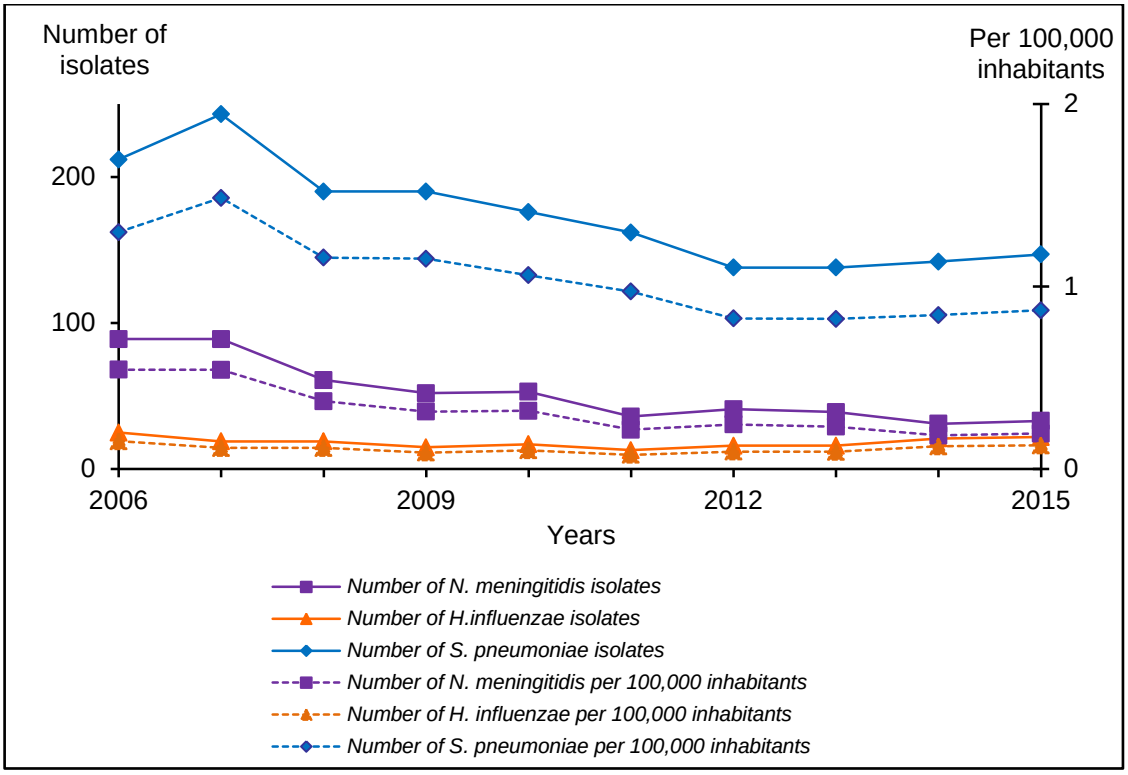


**Figure 3.3** *Meningococcal, Haemophilus and pneumococcal meningitis, 2006-2015*

Table 3.1 shows the frequency of isolation of the different bacterial species from CSF by annual quarter. As in previous years, most strains were received during the first quarter of the year.

Table 3.1 Isolates from CSF by annual quarter, 2015

| | ANNUAL QUARTER | | | | | |
|---|---|---|---|---|---|---|
| **SPECIES** | **First** | **Second** | **Third** | **Fourth** | **Total** | **%** |
| ***N. meningitidis*** | 7 | 7 | 3 | 16 | **33** | *11.5* |
| ***H. influenzae*** | 6 | 6 | 4 | 6 | **22** | *7.7* |
| ***S. pneumoniae*** | 51 | 41 | 21 | 34 | **147** | *51.2* |
| ***E. coli*** | 2 | 4 | 1 | 1 | **8** | *2.8* |
| ***S. agalactiae*** | 5 | 6 | 4 | 4 | **19** | *6.6* |
| ***L. monocytogenes*** | 2 | 1 | 2 | 3 | **8** | *2.8* |
| ***S. pyogenes*** | 1 | 2 | 0 | 0 | **3** | *1.0* |
| ***S. aureus*** | 2 | 1 | 3 | 2 | **8** | *2.8* |
| **Coag.neg.Staph.** | 0 | 1 | 1 | 0 | **2** | *0.7* |
| ***C. neoformans*** | 1 | 2 | 2 | 2 | **7** | *2.4* |
| **Others** | 3 | 8 | 10 | 9 | **30** | *10.5* |
| **non viable** | 0 | 0 | 0 | 0 | **0** | *0.0* |
| **Total** | **80** | **79** | **51** | **77** | **287** | ***100.0*** |
| ***%*** | ***27.9*** | ***27.5*** | ***17.8*** | ***26.8*** | ***100.0*** | |

Tables 3.2 and 3.3 show the distribution of the bacterial species isolated from CSF according to the age of the patient and the age-specific incidence per 100,000, respectively. *Streptococcus agalactiae* is still the predominant species isolated in neonates (younger than 1 month), and represented 52% of the isolates in this age group, whereas in the age group 1-11 months the predominant species were *S. pneumoniae* and *N. meningitidis* (together 760%). Since the introduction of the vaccine against *H.influenzae* type b, the number of cases of *H.influenzae* meningitis in the age group 0-4 year has strongly decreased (1992: 231; 2004: 17 and 2015: 7).

Table 3.2 Isolates from CSF grouped according to patients' age, 2015

| | AGE ( MONTHS) | | | AGE (YEARS) | | | | | | | | | TOTAL | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Group** | **0** | **1-11** | **12-59** | **0-4** | **5-9** | **10-14** | **15-19** | **20-29** | **30-39** | **40-49** | **50-64** | **65-79** | **≥80** | **Total** | **%** |
| ***N. meningitidis*** | 0 | 7 | 4 | 11 | 4 | 2 | 6 | 3 | 0 | 0 | 4 | 3 | 0 | **33** | ***11.5*** |
| ***H. influenzae*** | 0 | 3 | 4 | 7 | 2 | 0 | 0 | 0 | 2 | 4 | 6 | 1 | 0 | **22** | ***7.7*** |
| ***S. pneumoniae*** | 3 | 15 | 6 | 24 | 3 | 4 | 0 | 0 | 9 | 15 | 42 | 40 | 10 | **147** | ***51.2*** |
| ***E. coli*** | 5 | 0 | 0 | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | **8** | ***2.8*** |
| ***S. agalactiae*** | 12 | 3 | 0 | 15 | 0 | 0 | 0 | 0 | 0 | 1 | 2 | 1 | 0 | **19** | ***6.6*** |
| ***L. monocytogenes*** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 2 | 1 | 4 | **8** | ***2.8*** |
| ***S. pyogenes*** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 2 | 0 | 0 | **3** | ***1.0*** |
| ***S. aureus*** | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 0 | 0 | 3 | 0 | 2 | **8** | ***2.8*** |
| **Coag.neg.Staph.** | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | **2** | ***0.7*** |
| ***C. neoformans*** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 1 | 3 | 0 | **7** | ***2.4*** |
| **Others** | 2 | 1 | 0 | 3 | 2 | 0 | 0 | 2 | 5 | 2 | 11 | 5 | 0 | **30** | ***10.5*** |
| **non viable** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **0** | ***0.0*** |
| **Total** | **23** | **29** | **14** | **66** | **11** | **6** | **8** | **8** | **19** | **23** | **74** | **55** | **17** | **287** | *100* |
| ***%*** | ***8.0*** | ***10.1*** | ***4.9*** | ***23.0*** | ***3.8*** | ***2.1*** | ***2.8*** | ***2.8*** | ***6.6*** | ***8.0*** | ***25.8*** | ***19.2*** | ***5.9*** | ***100*** | |

As anticipated from table 3.2, the incidence of bacterial meningitis was highest in the age group of 0 years (table 3.3).

Table 3.3 Age-specific incidence of bacterial meningitis per 100,000 inhabitants grouped according to species, 2015

| SPECIES | AGE (YEARS) | | | | | | | | | | | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | 1-4 | 5-9 | 10-14 | 15-19 | 20-29 | 30-39 | 40-49 | 50-64 | 65-79 | ≥80 | |
| ***N. meningitidis*** | 4.01 | 0.56 | 0.43 | 0.20 | 0.60 | 0.14 | 0.00 | 0.00 | 0.38 | 0.13 | 0.00 | **0.20** |
| ***H. influenzae*** | 1.72 | 0.56 | 0.22 | 0.00 | 0.00 | 0.00 | 0.10 | 0.16 | 0.57 | 0.04 | 0.00 | **0.13** |
| ***S. pneumoniae*** | 10.30 | 0.84 | 0.32 | 0.40 | 0.00 | 0.00 | 0.45 | 0.61 | 4.01 | 1.76 | 1.36 | **0.87** |
| ***E. coli*** | 2.86 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.10 | 0.04 | 0.14 | **0.05** |
| ***S. agalactiae*** | 8.59 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.04 | 0.19 | 0.04 | 0.00 | **0.11** |
| ***L. monocytogenes*** | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.05 | 0.00 | 0.00 | 0.19 | 0.04 | 0.54 | **0.05** |
| ***S. pyogenes*** | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.04 | 0.19 | 0.00 | 0.00 | **0.02** |
| ***S. aureus*** | 0.57 | 0.00 | 0.00 | 0.00 | 0.10 | 0.05 | 0.00 | 0.00 | 0.29 | 0.00 | 0.27 | **0.05** |
| **Coag.neg.Staph.** | 0.00 | 0.00 | 0.00 | 0.00 | 0.10 | 0.05 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | **0.01** |
| ***C. neoformans*** | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.15 | 0.00 | 0.10 | 0.13 | 0.00 | **0.04** |
| **Others** | 1.72 | 0.00 | 0.22 | 0.00 | 0.00 | 0.09 | 0.25 | 0.08 | 1.05 | 0.22 | 0.00 | **0.18** |
| **non viable** | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | **0.00** |
| **Total** | **29.77** | **1.96** | **1.18** | **0.59** | **0.80** | **0.38** | **0.94** | **0.93** | **7.07** | **2.42** | **2.31** | **1.70** |

Table 3.4 shows the frequency of the isolates per species from CSF according to gender of the patients. For most species the Male/Female ratio varied between 1.0 and 1.7. The M/F ratio among patients infected with *S. aureus* or an isolate from the group "Other" were 2.0 and 3.3 respectivily. The overall M/F ratio was 1.2.

Table 3.4 Isolates from CSF according to patients' gender, 2015

| SPECIES | M | F | M/F – ratio | Sex not known | Total | % |
|---|---|---|---|---|---|---|
| ***N. meningitidis*** | 18 | 15 | **1.2** | 0 | **33** | *11.5* |
| ***H. influenzae*** | 11 | 11 | **1.0** | 0 | **22** | *7.7* |
| ***S. pneumoniae*** | 73 | 73 | **1.0** | 1 | **147** | *51.2* |
| ***E. coli*** | 5 | 3 | **1.7** | 0 | **8** | *2.8* |
| ***S. agalactiae*** | 12 | 7 | **1.7** | 0 | **19** | *6.6* |
| ***L. monocytogenes*** | 3 | 5 | **0.6** | 0 | **8** | *2.8* |
| ***S. pyogenes*** | 2 | 1 | **2.0** | 0 | **3** | *1.0* |
| ***S. aureus*** | 3 | 5 | **0.6** | 0 | **8** | *2.8* |
| **Coag.neg.Staph.** | 1 | 1 | **1.0** | 0 | **2** | *0.7* |
| ***C. neoformans*** | 3 | 4 | **0.8** | 0 | **7** | *2.4* |
| **Others** | 23 | 7 | **3.3** | 0 | **30** | *10.5* |
| **non viable** | 0 | 0 | **0.0** | 0 | **0** | *0.0* |
| **Total** | **157** | **129** | **1.2** | **1** | **287** | ***100.0*** |
| **%** | ***54.7*** | ***45.0*** | | ***0.3*** | ***100.0*** | |

# 4 NEISSERIA MENINGITIDIS

## 4.1 General features

In 2015, the Reference Laboratory received 84 *Neisseria meningitidis* isolates, of which 33 were isolated from CSF (or CSF and blood) (32 in 2014) and 51 from blood only (42 in 2014). This means that 61% of cases of meningococcal disease concerned patients with a positive blood culture only, either because no meningitis was present or because no CSF specimen was obtained. The distribution of isolates according to month of receipt shows the highest number of isolates in the fourth quarter, while in previous years the highest number of isolates was received in the first quarter of the year (figure 4.1).

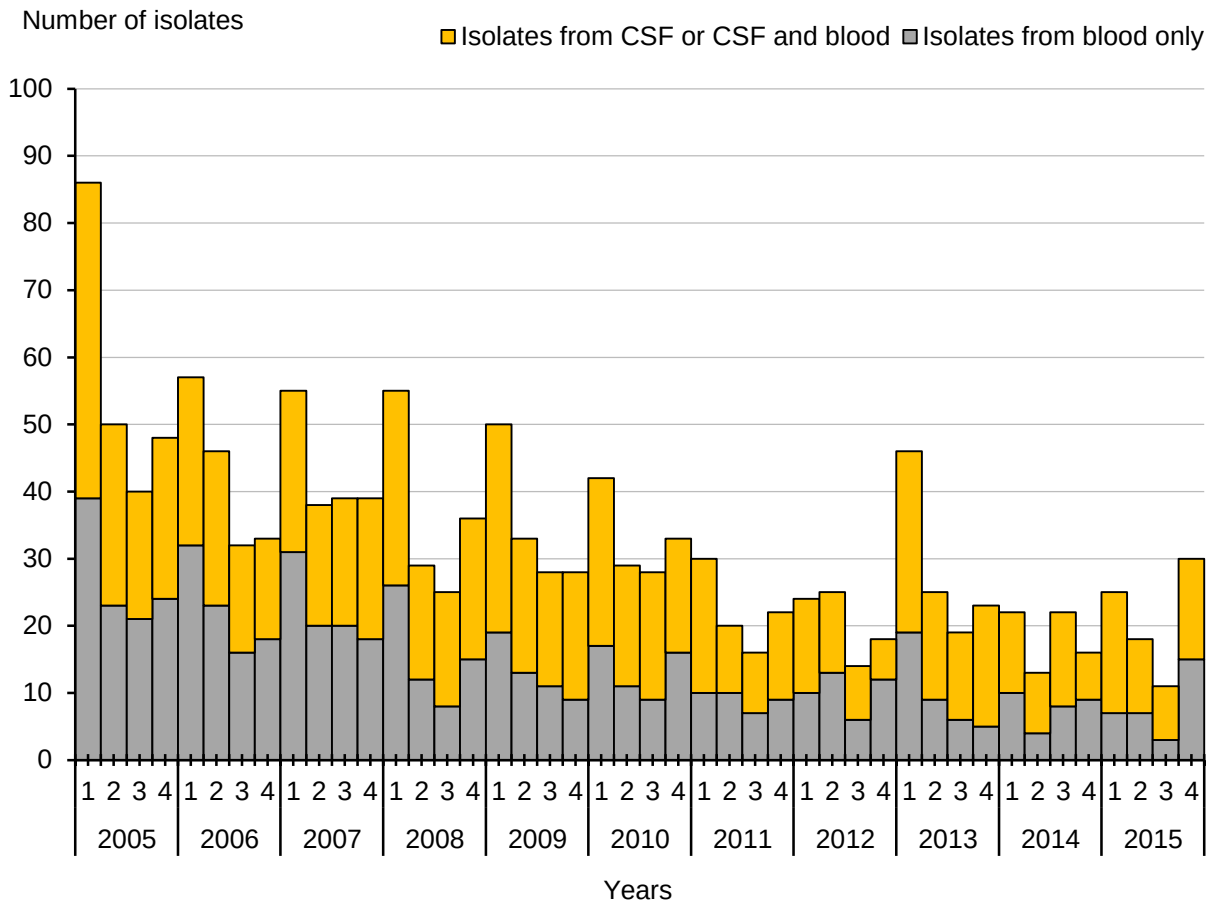


**Figure 4.1** *Seasonal distribution of meningococcal disease, 2005-2015*

## *4.2 Antibiotic susceptibility*

Ninty-five percent of all isolates (80/84) were susceptible to penicillin (MIC ≤ 0.064 µg/ml; CSF isolates 100%, isolates from blood only 93%). This is higher than in previous years. (86% in 2014;79% in 2013; 65% in 2012; 70% in 2011). This increased proportion of penicillin-susceptible isolates is mainly due to a reduction of the number of intermediate susceptible isolates (table 4.1, 4.2 and 4.3). In general, mutations in *penA* encoding a penicillin binding protein confers the meningococcus to reduced penicillin susceptibility. Nucleotide sequence analyses of *penA*, confirmed the decrease of the number of reduced penicillin susceptible meningococcal isolates. All isolates were susceptible to rifampicin.

Table 4.1 Susceptibility of N. meningitidis CSF and/or blood isolates to penicillin, 2015

| | Penicillin* | | | | | |
|---|---|---|---|---|---|---|
| | MIC ≤ 0.064 sensitive | 0.064< MIC≤0.25 | 0.25< MIC≤1.0 | MIC >1.0 | Total | % |
| **CSF or CSF and blood** | 32 | 1 | 0 | 0 | **33** | **39** |
| **Blood only** | 48 | 3 | 0 | 0 | **51** | **61** |
| **Total** | **80** | **4** | **0** | **0** | **84** | **100** |
| **%** | **95** | **5** | **0** | **0** | **100** | |

* MIC values in µg/ml

Table 4.2 Susceptibility of *N. meningitidis* isolated from CSF or CSF and blood to penicillin, 2009-2015

| | Penicillin* | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | MIC ≤ 0.064 sensitive | | 0.064< MIC≤0.25 | | 0.25< MIC≤1.0 | | MIC >1.0 | | Total |
| | n | % | N | % | n | % | n | % | |
| **2009** | 51 | **98.1** | 1 | **1.9** | 0 | **0.0** | 0 | **0.0** | **52** |
| **2010** | 43 | **81.1** | 10 | **18.9** | 0 | **0.0** | 0 | **0.0** | **53** |
| **2011** | 29 | **78.4** | 8 | **21.6** | 0 | **0.0** | 0 | **0.0** | **37** |
| **2012** | 24 | **58.5** | 16 | **39.0** | 1 | **2.4** | 0 | **0.0** | **41** |
| **2013** | 35 | **89.7** | 3 | **7.7** | 1 | **2.6** | 0 | **0.0** | **39** |
| **2014** | 26 | **83.9** | 5 | **16.1** | 0 | **0.0** | 0 | **0.0** | **31** |
| **2015** | 32 | **97.0** | 1 | **3.0** | 0 | **0.0** | 0 | **0.0** | **33** |

* MIC values in µg/ml

Table 4.3 Susceptibility of *N. meningitidis* isolated from blood only to penicillin, 2009-2015

| | Penicillin* | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | MIC ≤ 0.064 sensitive | | 0.064< MIC≤0.25 | | 0.25< MIC≤1.0 | | MIC >1.0 | | Total |
| | n | % | n | % | n | % | n | % | |
| **2009** | 77 | **88.5** | 10 | **11.5** | 0 | **0.0** | 0 | **0.0** | 87 |
| **2010** | 67 | **84.8** | 12 | **15.2** | 0 | **0.0** | 0 | **0.0** | 79 |
| **2011** | 34 | **64.2** | 19 | **35.9** | 0 | **0.0** | 0 | **0.0** | 53 |
| **2012** | 27 | **67.5** | 13 | **32.5** | 0 | **0.0** | 0 | **0.0** | 40 |
| **2013** | 53 | **73.6** | 18 | **25.0** | 1 | **1.4** | 0 | **0.0** | 72 |
| **2014** | 37 | **88.1** | 5 | **11.9** | 0 | **0.0** | 0 | **0.0** | 42 |
| **2015** | 48 | **94.1** | 3 | **5.9** | 0 | **0.0** | 0 | **0.0** | 51 |

* MIC values in µg/ml

### *4.3 Serogroups*

Serogroup B accounted for 74% (2014: 73% 2013: 75%) of all isolates. Group C and Y are responsible for 8% each and group W for about 10% (table 4.4). The proportion of serogroups C, Y and W isolates is gradually increasing since 2008, partly due to a decrease in the number of serogroup B isolates and to a small increase in the number of serogroups C, Y and W isolates. The serogroup distribution observed during the whole collection period 1959 - 2015 (figure 4.2) shows that in 2014 the number of group B isolates (53 cases) was the lowest since 1976. In 2015, the number of group B isolates (62) was slightly higher than the previous year. The proportion of group C isolates was 24% in 1991, decreased to about 10% in 1994 and was since then increasing, with a sharp rise from 19% (105 cases) in 2000 to 40% (276 cases) in 2001 (figure 4.2 and figure 4.2.1). In June 2002, vaccination against serogroup C was included in the National Immunisation Programme. Since then, the number of serogroup C isolates received by the Reference Laboratory rapidly decreased to only a few isolates per year; in 2015 there was a slight increase from 3 group C isolates in 2014 to 7 in 2015 (figure 4.3).

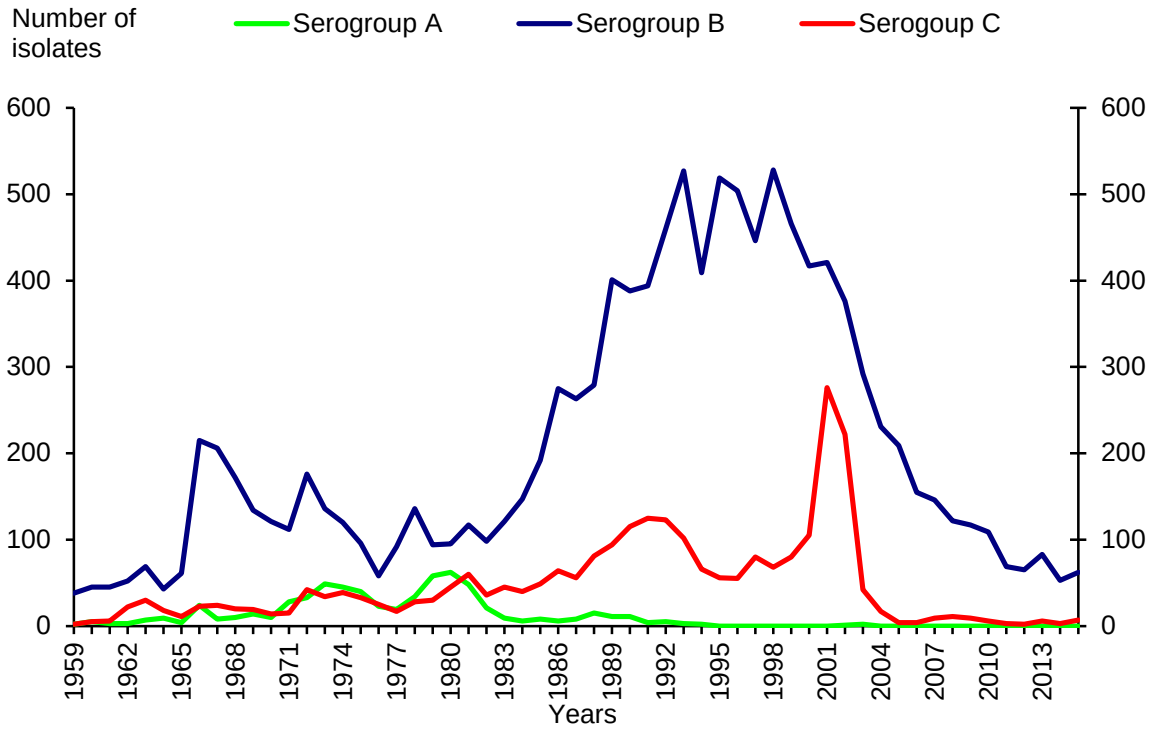


**Figure 4.2**. *Distribution of meningococcal serogroups A, B and C, 1959-2015*

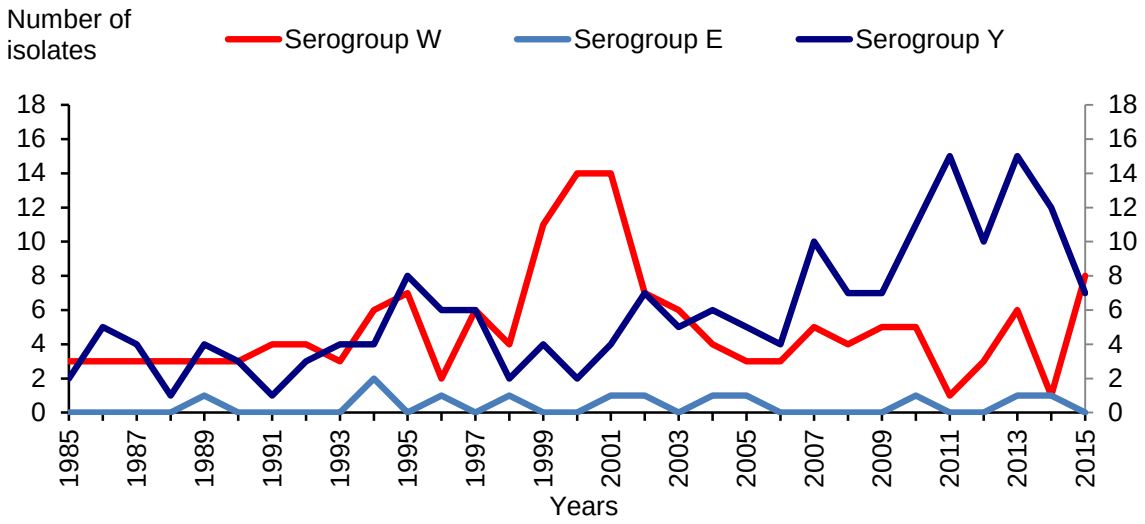


**Figure 4.2.1**. *Distribution of meningococcal serogroups Y, W and E, 1985-2015*

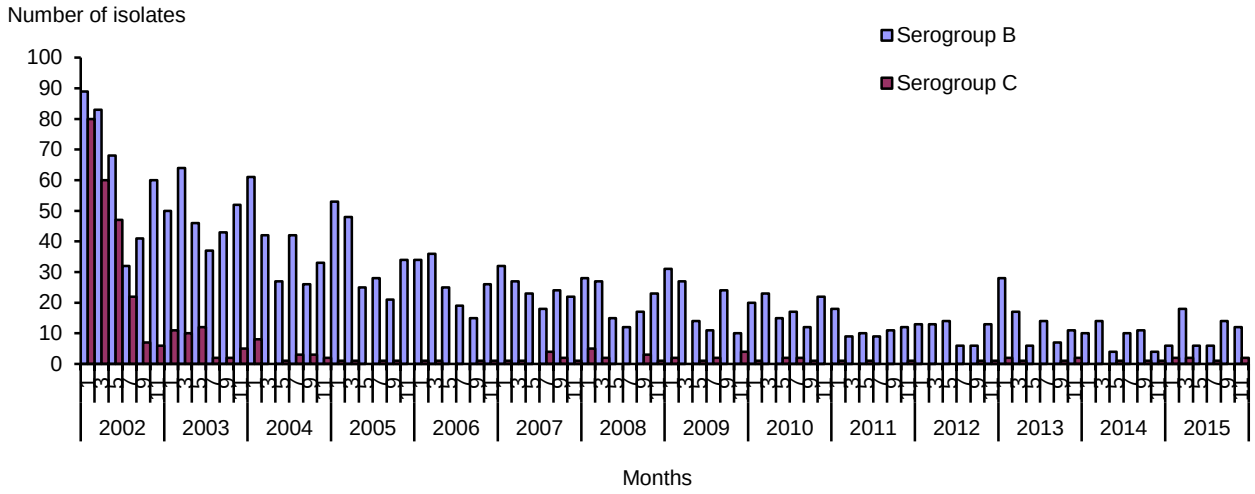


**Figure 4.3** *Bimonthly distribution of meningococcal serogroups B and C, 2002-2015*

## *4.4 Serogroup and age*

The age distribution of patients with meningitis and/or meningococcemia shows that 27% (23 of 84) of the patients was younger than 5 years (table 4.4, figure 4.4). Among patients from whom meningococci were isolated from blood only, 25% was younger than 5 years, while almost 35% was older than 65 years of age (table 4.7). Fifty percent of cases due to serogroup C, Y and W was older than 65 years of age.
Of the 8 serogroup W isolates, 5 were received in the last quarter of 2015.

Table 4.4 Serogroups of *N. meningitidis* (all isolates: from CSF and /or blood, absolute numbers) by patient age, 2015

| | AGE ( MONTHS) | | | AGE (YEARS) | | | | | | | | TOTAL | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Group | 0 | 1-11 | 12-59 | 0-4 | 5-9 | 10-14 | 15-19 | 20-24 | 25-29 | 30-49 | 50-64 | ≥65 | T | % |
| **B** | 0 | 9 | 11 | 20 | 5 | 2 | 11 | 6 | 1 | 0 | 7 | 10 | **62** | ***73.9*** |
| **C** | 0 | 2 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 3 | **7** | ***8.3*** |
| **Y** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 6 | **7** | ***8.3*** |
| **W** | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 3 | 2 | **8** | ***9.5*** |
| **Total** | **0** | **12** | **11** | **23** | **5** | **2** | **11** | **8** | **2** | **2** | **10** | **21** | **84** | ***100.0*** |
| ***%*** | ***0.0*** | ***14.3*** | ***13.1*** | ***27.4*** | ***5.9*** | ***2.4*** | ***13.1*** | ***9.5*** | ***2.4*** | ***2.4*** | ***11.9*** | ***25.0*** | ***100.0*** | |

Table 4.5 Serogroups of *N. meningitidis* (isolates from CSF, or CSF* and blood; absolute numbers) by patient age, 2015

| | AGE ( MONTHS) | | | AGE (YEARS) | | | | | | | | TOTAL | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Group | 0 | 1-11 | 12-59 | 0-4 | 5-9 | 10-14 | 15-19 | 20-24 | 25-29 | 30-49 | 50-64 | ≥65 | T | % |
| **B** | 0 | 5 | 4 | 9 | 4 | 2 | 6 | 3 | 0 | 0 | 4 | 3 | **31** | ***94.0*** |
| **C** | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **1** | ***3.0*** |
| **Y** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **0** | ***0.0*** |
| **W** | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **1** | ***3.0*** |
| **Total** | **0** | **7** | **4** | **11** | **4** | **2** | **6** | **3** | **0** | **0** | **4** | **3** | **33** | ***100.0*** |
| ***%*** | ***0.0*** | ***21.2*** | ***12.1*** | ***33.3*** | ***12.1*** | ***6.1*** | ***18.2*** | ***9.1*** | ***0.0*** | ***0.0*** | ***12.1*** | ***9.1*** | ***100*** | |

* From 3 patients with a meningococci isolated from blood, CSF was culture-negative but PCR positive for meningococcal DNA. 2 cases were in age group 5-9 years and one in older than 65 years

Table 4.6 Age distribution of meningitis (incidence per 100,000 inhabitants) by different serogroups of *N. meningitidis* (isolates from CSF, or CSF and blood), 2015

| | AGE (YEARS) | | | | | | | | | | TOTAL |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Group | 0 | 1-4 | 5-9 | 10-14 | 15-19 | 20-24 | 25-29 | 30-49 | 50-64 | ≥65 | T |
| **B** | 2.86 | 0.56 | 0.43 | 0.20 | 0.60 | 0.28 | 0.00 | 0.00 | 0.12 | 0.10 | **0.18** |
| **C** | 0.57 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | **0.01** |
| **Y** | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | **0.00** |
| **W** | 0.57 | 0.14 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | **0.01** |
| **Total** | **4.01** | **0.56** | **0.43** | **0.20** | **0.60** | **0.28** | **0.00** | **0.00** | **0.12** | **0.10** | **0.20** |

Table 4.7 Serogroups of *N. meningitidis* (isolates from blood only, absolute numbers) by patient age, 2015

| | AGE ( MONTHS) | | | AGE (YEARS) | | | | | | | | TOTAL | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Group | 0 | 1-11 | 12-59 | 0-4 | 5-9 | 10-14 | 15-19 | 20-24 | 25-29 | 30-49 | 50-64 | ≥65 | T | % |
| **B** | 0 | 4 | 7 | 11 | 1 | 0 | 5 | 3 | 1 | 0 | 3 | 7 | **31** | ***60.8*** |
| **C** | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 3 | **6** | ***11.8*** |
| **Y** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 6 | **7** | ***13.7*** |
| **W** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 3 | 2 | **7** | ***13.7*** |
| **Total** | **0** | **5** | **7** | **12** | **1** | **0** | **5** | **5** | **2** | **2** | **6** | **18** | **51** | ***100.0*** |
| ***%*** | ***0.0*** | ***9.8*** | ***13.7*** | ***23.5*** | ***2.0*** | ***0.0*** | ***9.8*** | ***9.8*** | ***3.9*** | ***3.9*** | ***11.8*** | ***35.3*** | ***100.0*** | |

Table 4.8 Age distribution of meningococcemia (incidence per 100,000 inhabitants) by different serogroups of *N. meningitidis* (isolates from blood only), 2015

| | AGE (YEARS) | | | | | | | | | | TOTAL |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Group | 0 | 1-4 | 5-9 | 10-14 | 15-19 | 20-24 | 25-29 | 30-49 | 50-64 | ≥65 | T |
| **B** | 2.29 | 0.98 | 0.11 | 0.00 | 0.50 | 0.28 | 0.10 | 0.00 | 0.09 | 0.23 | **0.18** |
| **C** | 0.57 | 0.00 | 0.00 | 0.00 | 0.00 | 0.09 | 0.00 | 0.02 | 0.00 | 0.10 | **0.04** |
| **Y** | 0.00 | 0.00 | 0.00 | 0.00 | 0.10 | 0.00 | 0.00 | 0.02 | 0.00 | 0.20 | **0.04** |
| **W** | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.09 | 0.10 | 0.00 | 0.09 | 0.07 | **0.04** |
| **Total** | **2.86** | **0.98** | **0.11** | **0.00** | **0.50** | **0.47** | **0.19** | **0.04** | **0.17** | **0.60** | **0.30** |

## *4.5 Group B meningococci*

Figure 4.4 shows the age distribution of group B meningococcal disease. The age-specific incidences per 100,000 inhabitants in the age groups younger than 5 years and 15 - 19 years were 2.25 and 1.10 respectively. The age-specific incidences per 100,000 inhabitants in the age groups >19 years was less than 0.5 except for the age group 90-95 years (incidence of 1.04).

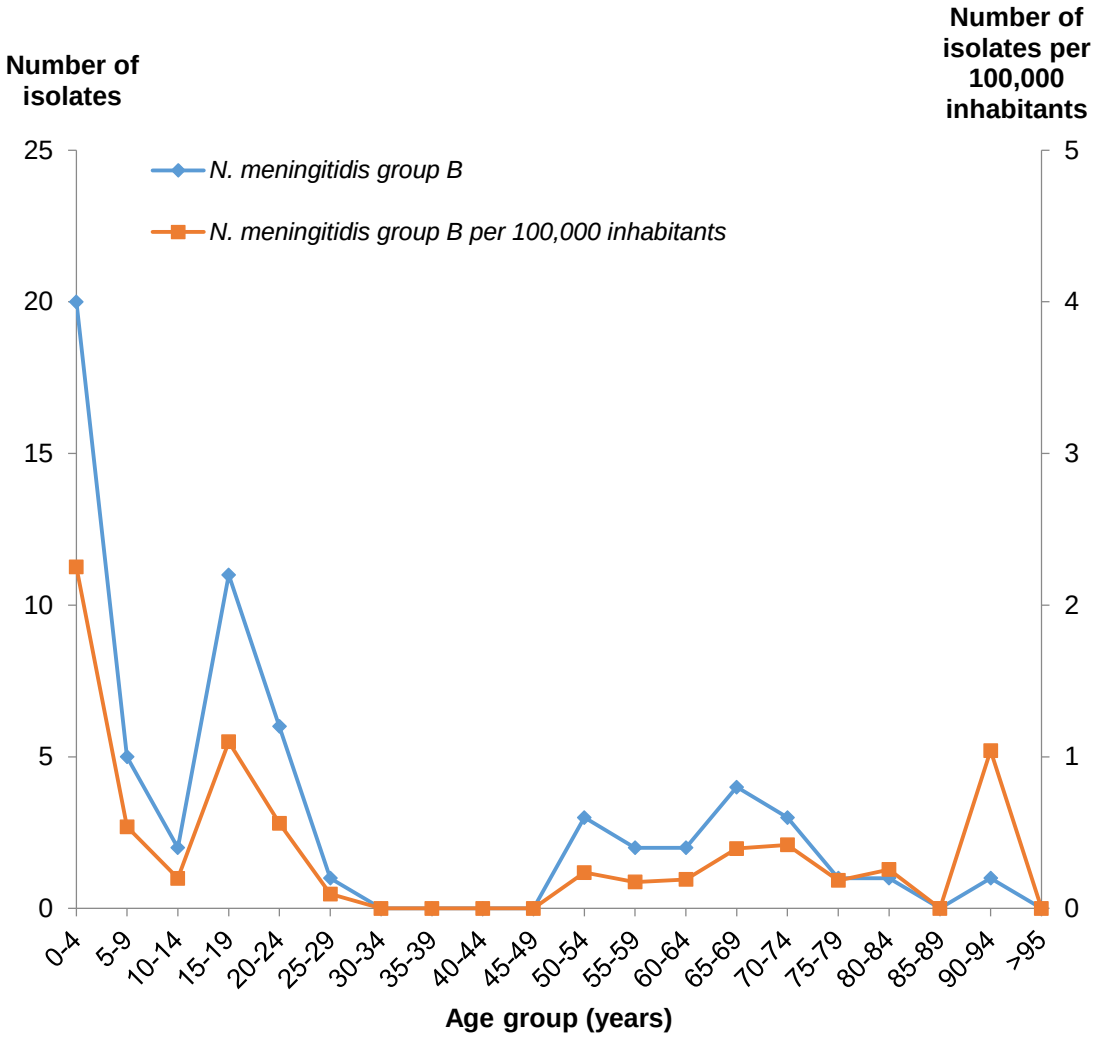


**Figure 4.4** *Age distribution of serogroup B meningococcal disease in 2015*

## *4.6 Distribution of PorA genosubtypes among serogroup B and C meningococci*

The monoclonal antibodies used for (sub)typing of meningococci are no longer available. Therefore, from January 1, 2005 on, typing of meningococcal isolates using monoclonal antibodies is not performed anymore by the Reference Laboratory. Instead, epitopes of PorA and FetA are determined by sequencing of their DNA coding regions.

The epitopes of PorA that react with the monoclonal antibodies of the subtyping scheme are encoded by the variable regions VR1 and VR2 of *porA*, encoding the outer membrane protein PorA. Since 2000 we routinely sequence the DNA regions which encode VR1 and VR2 of PorA of all meningococcal isolates. The DNA sequences are translated into putative amino acid sequences, which are then compared with the PorA epitopes present in the database available on the website: http://neisseria.org/nm/typing/pora/.

In 2015, 32 different VR1/VR2 combinations were encountered among serogroup B meningococci (2012: 31; 2013: 39; 2014: 28). The proportion of the dominant PorA genosubtype P1.7-2,4 decreased from 40% of all serogroup B isolates in 2000 to 11% in 2015 (figure 4.5, figure 4.7; table 4.9).

The seven serogroup C isolates had only one VR1/VR2 combination, P1.5,2. Of the 8 serogroup W isolates, 6 had P1.5,2, two had P1.18-1,3 and one had P1.7-50,1-10.

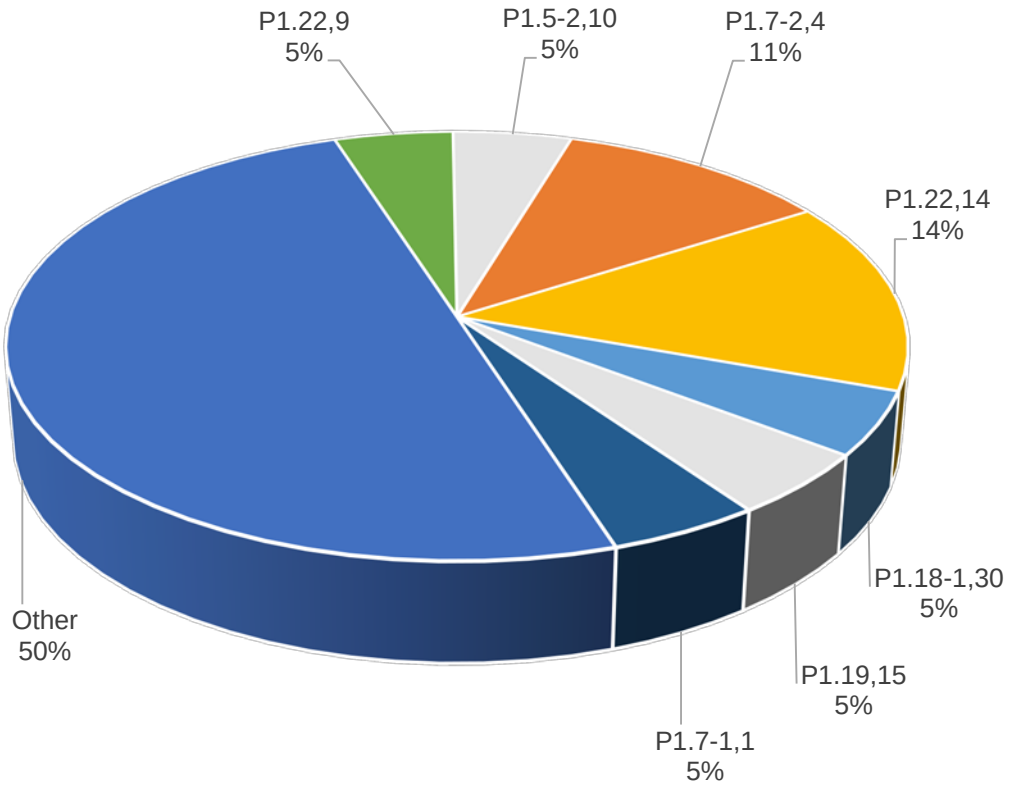


**Figure 4.5** *Distribution of group B meningococcal PorA types, 2015*

Table 4.9 *N. meningitidis* serogroup B isolates according to PorA genosubtype, 2011-2015

| | VR1,VR2 combination | YEAR | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 2011 | | 2012 | | 2013 | | 2014 | | 2015 | |
| | | No. | % | No. | % | No. | % | No. | % | No. | % |
| Vaccine types* | 1.5-1, 2-2 | 0 | **0** | 0 | **0** | 0 | **0** | 0 | **0** | 0 | **0** |
| | 1.5-1, other | 1 | **1.4** | 3 | **4.6** | 1 | **1.2** | 1 | **1.9** | 1 | **1.6** |
| | 1.5-2,10 | 2 | **2.9** | 4 | **6.2** | 7 | **8.4** | 4 | **7.5** | 3 | **4.8** |
| | 1.5-2, other | 3 | **4.4** | 0 | **0** | 0 | **0** | 1 | **1.9** | 2 | **3.2** |
| | 1.7,16 | 1 | **1.4** | 0 | **0** | 1 | **1.2** | 0 | **0** | 1 | **1.6** |
| | 1.7, other | 4 | **5.8** | 1 | **1.5** | 5 | **6.0** | 1 | **1.9** | 2 | **3.2** |
| | 1.7-1, 1 | 2 | **2.9** | 2 | **3.1** | 0 | **0** | 1 | **1.9** | 3 | **4.8** |
| | 1.7-1, other | 0 | **0** | 0 | **0** | 0 | **0** | 1 | **1.9** | 0 | **0** |
| | 1.7-2,4 | 10 | **14.5** | 6 | **9.2** | 7 | **8.4** | 8 | **15.0** | 7 | **11.3** |
| | 1.7-2, other | 4 | **5.8** | 8 | **12.3** | 13 | **15.7** | 3 | **5.7** | 5 | **8.2** |
| | 1.12-1, other | 1 | **1.4** | 1 | **1.5** | 1 | **1.2** | 1 | **1.9** | 2 | **3.2** |
| | 1.18-1,3 | 2 | **2.9** | 1 | **1.5** | 3 | **3.6** | 0 | **0** | 1 | **1.6** |
| | 1.18-1, other | 2 | **2.9** | 5 | **7.7** | 3 | **3.6** | 9 | **17.0** | 5 | **8.2** |
| | 1.19,15-1 | 1 | **1.4** | 0 | **0** | 3 | **3.6** | 2 | **3.7** | 2 | **3.2** |
| | 1.19, other | 2 | **2.9** | 4 | **6.2** | 3 | **3.6** | 3 | **5.7** | 3 | **4.8** |
| | 1.22,14 | 14 | **20.3** | 12 | **18.5** | 9 | **10.9** | 9 | **17.0** | 9 | **14.6** |
| | 1.22,other | 5 | **7.3** | 8 | **12.3** | 6 | **7.3** | 3 | **5.7** | 3 | **4.8** |
| | Other, 14 | 2 | **2.9** | 0 | **0** | 2 | **2.4** | 1 | **1.9** | 1 | **1.6** |
| | Other, 16 | 3 | **4.4** | 2 | **3.1** | 3 | **3.6** | 1 | **1.9** | 2 | **3.2** |
| | **Subtotal vaccine types** | 59 | **85.5** | 57 | **87.7** | 67 | **80.7** | 49 | **92.5** | 52 | **83.9** |
| NVT** | Other **Non Vaccine Type** | 10 | **14.5** | 8 | **12.3** | 16 | **19.3** | 4 | **7.5** | 10 | **16.1** |
| | Total | 69 | **100.0** | 65 | **100.0** | 83 | **100.0** | 53 | **100.0** | 62 | **100.0** |

*based on a nonavalent PorA vaccine, NonaMen; serosubtypes P1.7,16; P1.5-1,2-2; P1.19,15-1; P1.5-2,10; P1.12-1,13; P1.7-2,4; P1.22,14; P1.7-1,1 and P1.18-1,3,6

**Non vaccine type

## *4.7 Distribution of FetA genosubtypes among serogroup B and C meningococci*

In addition to sequencing of PorA epitopes, meningococcal isolates are also characterized by sequencing of an epitope of FetA. This outer membrane protein is involved in iron uptake by meningococci and is considered as a potential vaccine component. Therefore, the variability of this protein has been investigated intensively. The most variable part of the protein, called VR, has been used to establish a typing scheme. Analogous to PorA typing, the VR part of *fetA* is sequenced and translated to a putative aminoacid sequence. So far, about 270 VR sequences comparising 6 classes, are identified, available at
http://neisseria.org/perl/agdbnet/agdbnet.pl?file=fetavr.xml
As an example of a type designation: F5-2, in which the first digit indicates the class and the second digit the variant of this class.

In 2015, 18 different FetA variants were observed among serogroup B meningococci. The dominant types were F5-1 and F1-5, accounting for 16% each of group B meningococci (figure 4.6 and 4.7; table 4.10). In previous years the dominant type was F1-5 wich was strongly linked with PorA VR1/VR2 P1.7-2,4 and together to the MLST clonal complex ST41/44. In 2015, Fet A type F1-5 of 10 isolates was linked with 5 different PorA types. FetA type F1-5 was 5 times linked with PorA VR1/VR2 P1.7-2,4 and 7 times with P1.7-2 (7 in 2014; 5 in 2013; 4 in 2012; 8 in 2011; 20 in 2010).

The seven serogroup C meningococci had FetA type F3-3.

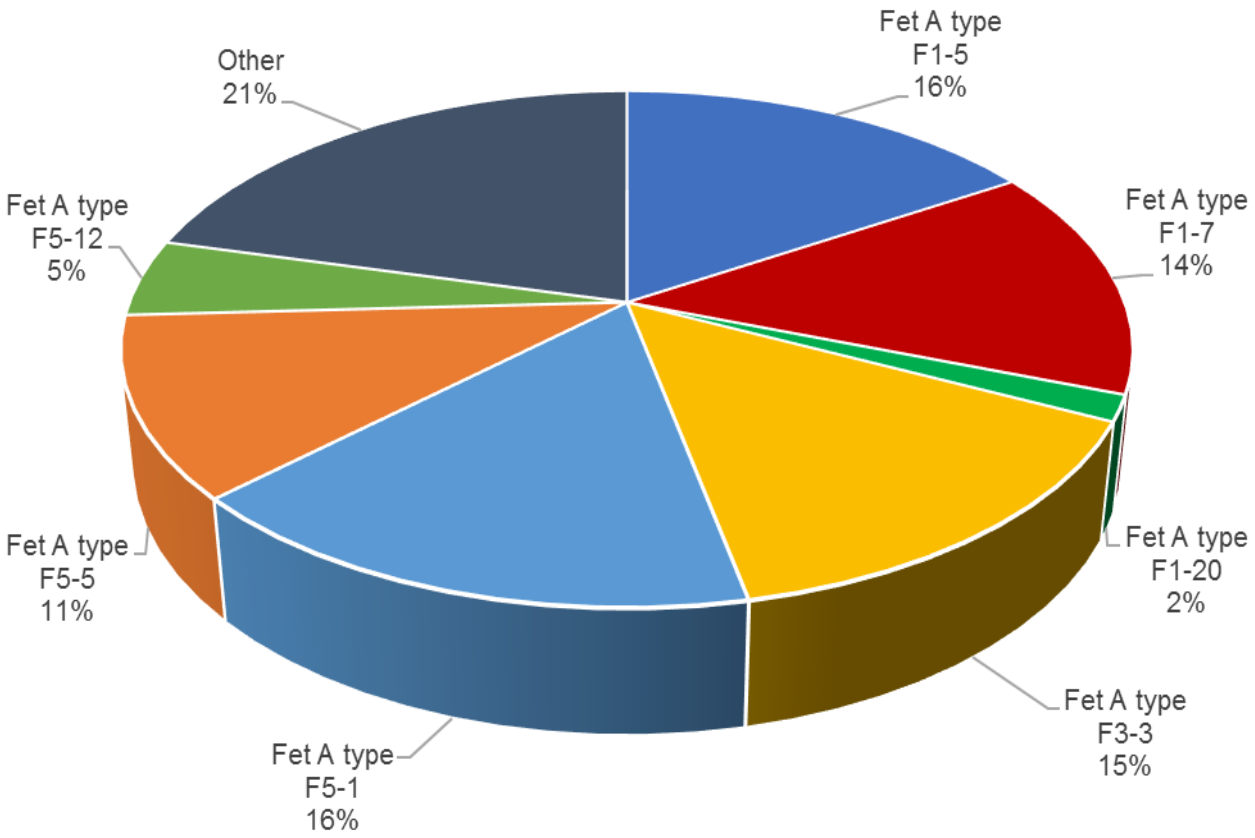


**Figure 4.6** *Distribution of group B meningococcal FetA genosubtypes, 2015*

Table 4.10 *N. meningitidis* serogroup B isolates according to FetA genosubtype, 2011-2015

| FetA type | YEARS | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 2011 | | 2012 | | 2013 | | 2014 | | 2015 | |
| | No. | % | No. | % | No. | % | No. | % | No. | % |
| **F1-5** | 17 | 24.6 | 23 | 35.4 | 17 | 20.5 | 8 | 15.1 | 10 | 16.1 |
| **F1-7** | 4 | 5.8 | 2 | 3.1 | 6 | 7.2 | 5 | 9.4 | 9 | 14.5 |
| **F1-15** | 1 | 1.5 | 1 | 1.5 | 1 | 1.2 | 1 | 1.9 | 1 | 1.6 |
| **F3-3** | 6 | 8.7 | 4 | 6.2 | 6 | 7.2 | 10 | 18.9 | 9 | 14.5 |
| **F3-7** | 2 | 2.9 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| **F3-9** | 3 | 4.3 | 3 | 4.6 | 2 | 2.4 | 1 | 1.9 | 0 | 0.0 |
| **F4-1** | 0 | 0.0 | 2 | 3.1 | 2 | 2.4 | 1 | 1.9 | 2 | 3.2 |
| **F5-1** | 8 | 11.6 | 7 | 10.8 | 14 | 16.9 | 14 | 26.4 | 10 | 16.2 |
| **F5-2** | 2 | 2.9 | 0 | 0.0 | 2 | 2.4 | 0 | 0.0 | 2 | 3.2 |
| **F5-5** | 10 | 14.5 | 11 | 16.9 | 8 | 9.7 | 4 | 7.5 | 7 | 11.3 |
| **F5-8** | 0 | 0.0 | 1 | 1.5 | 0 | 0.0 | 1 | 1.9 | 1 | 1.6 |
| **F5-12** | 2 | 2.9 | 2 | 3.1 | 0 | 0.0 | 1 | 1.9 | 3 | 4.8 |
| **Other** | 14 | 20.3 | 9 | 13.8 | 25 | 30.1 | 7 | 13.2 | 8 | 13.0 |
| **Total** | **69** | **100.0** | **65** | **100.0** | **83** | **100.0** | **53** | **100.0** | **62** | **100.0** |

In 2015, 32 different VR1/VR2 combinations and 18 different FetA variants were encountered among serogroup B meningococci. Among the dominant FetA type F5-1, accounting for 16% of group B meningococci, 3 were of P1.5-2,10:F5-1 and 3 were of type P1.19,15:F5-1 (4.8% each of group B meningococci). Frequently found combinations are P1.22,14:F5-5 (9.8%) and P1.7-2,4:F1-5 (8.1%) (Figure 4.7).

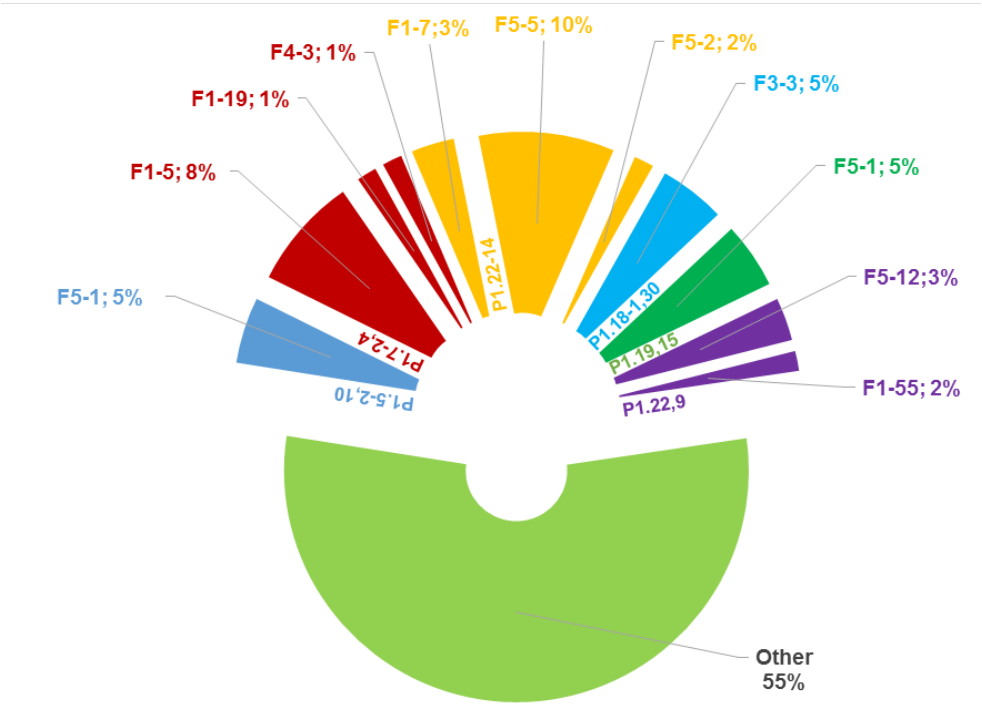


**Figure 4.7** *Distribution of group B meningococcal PorA and FetA geno(sub)types, 2015*

# 5 *HAEMOPHILUS INFLUENZAE*

## *5.1 General features*

In total, 195 *Haemophilus influenzae* isolates were submitted to the Reference Laboratory. This number is higher than in previous years (table 2.3, figure 3.3, figure 5.1). Twenty-two strains were isolated from CSF (or CSF and blood) (2014: 21; 2013: 16; 2012: 16; 2011: 13), and 173 from blood only. Thirty-four (17%) of the isolates were *H. influenzae* type b (table 5.1). From 1999 to 2004, the number of *H. influenzae* type b isolates received by the Reference Laboratory increased, but decreased after 2004. (table 5.4). The higher number of *H. influenzae* type b isolates was mainly due to an increase of *H. influenzae* type b cases among elderly people.

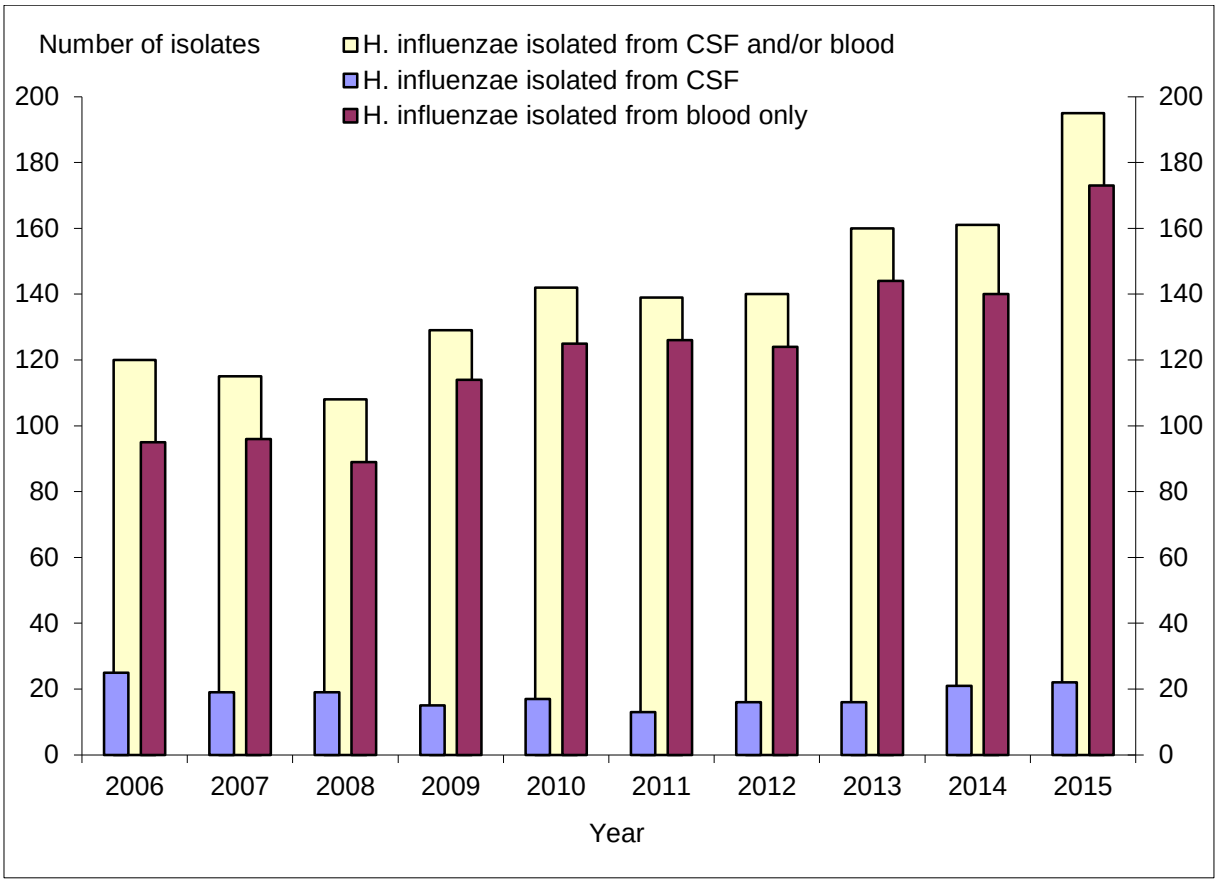


**Figure 5.1** *Distribution of H. influenzae, 2006-2015*

## *5.2 Antibiotic susceptibility*

The proportion of ß-lactamase producing invasive *H. influenzae* isolates (CSF and/or blood) was decreasing since 2004 and reached a remarkable low value of less than 1% in 2008. 2010 shows the highest value (14.8%) in 25 years. During the history of the Reference Laboratory the proportion has always fluctuated. The reason for this fluctuation is unknown.

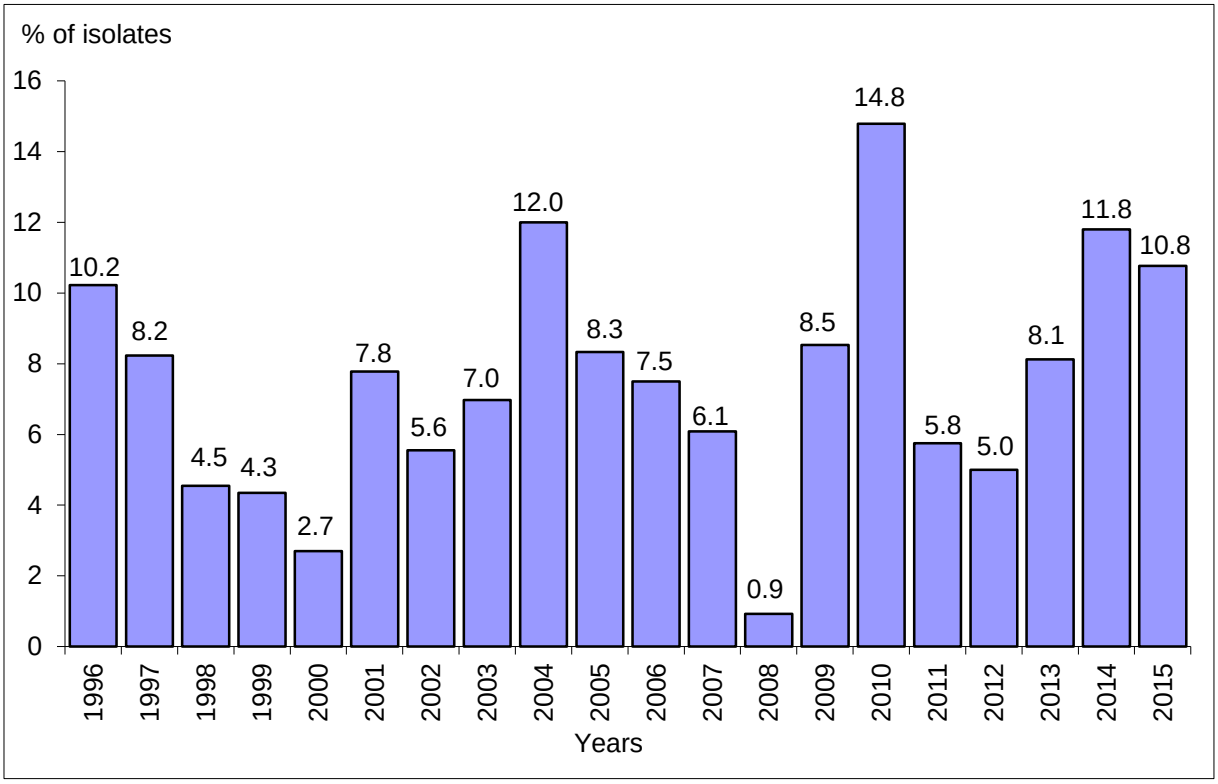


**Figure 5.2** *Percentage β-lactamase producing H. influenzae, 1996-2015*

## *5.3 Serotype and age*

Eight cases of *H. influenzae* type b invasive disease were observed among children younger than 2 years of age (6 in 2014; 9 in 2013; 3 in 2012) (figure 5.3). Of 195 *H. influenzae* isolates, 132 were non-typeable; 22 isolated from CSF (or CSF and blood) and 118 isolated from blood only (table 5.1, 5.2 and 5.3). Non-typable strains were isolated more frequently than type b isolates (table 5.1).

Table 5.1 Total number of *H.influenzae isolates* from CSF and/or blood, according to serotype and age, 2015

| TYPE | AGE ( MONTHS) | | | AGE (YEARS) | | | | | TOTAL | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | 1-11 | 12-59 | 0-4 | 5-9 | 10-19 | 20-49 | ≥50 | T | % |
| **a** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | **1** | ***0.5*** |
| **b** | 0 | 3 | 10 | 13 | 1 | 0 | 5 | 15 | **34** | ***17.4*** |
| **e** | 0 | 2 | 0 | 2 | 0 | 0 | 2 | 4 | **8** | ***4.1*** |
| **f** | 0 | 2 | 0 | 2 | 0 | 0 | 1 | 17 | **20** | ***10.3*** |
| **n.t.*** | 3 | 5 | 4 | 12 | 3 | 1 | 20 | 96 | **132** | ***67.7*** |
| **Total** | **3** | **12** | **14** | **29** | **4** | **1** | **28** | **133** | **195** | ***100*** |
| ***%*** | ***1.5*** | ***6.2*** | ***7.2*** | ***14.9*** | ***2.0*** | ***0.5*** | ***14.4*** | ***68.2*** | ***100*** | |

* non-typable

Table 5.2 *H.influenzae* isolates from CSF (or CSF and blood), according to serotype and age, 2015

| TYPE | AGE ( MONTHS) | | | AGE (YEARS) | | | | | TOTAL | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | 1-11 | 12-59 | 0-4 | 5-9 | 10-19 | 20-49 | ≥50 | T | % |
| **a** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **0** | ***0.0*** |
| **b** | 0 | 2 | 3 | 5 | 1 | 0 | 0 | 0 | **6** | ***27.3*** |
| **e** | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | **1** | ***4.5*** |
| **f** | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | **1** | ***4.5*** |
| **n.t.*** | 0 | 0 | 1 | 1 | 1 | 0 | 5 | 7 | **14** | ***63.7*** |
| **Total** | 0 | **3** | **4** | **7** | **2** | **0** | **6** | **7** | **22** | ***100.0*** |
| ***%*** | ***0.0*** | ***13.6*** | ***18.2*** | ***31.8*** | ***9.1*** | ***0.0*** | ***27.3*** | ***31.8*** | ***100.0*** | |

* non-typable

Table 5.3 *H. influenzae* isolates from blood only, according to serotype and age, 2015

| TYPE | AGE ( MONTHS) | | | AGE (YEARS) | | | | | TOTAL | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | 1-11 | 12-59 | 0-4 | 5-9 | 10-19 | 20-49 | ≥50 | T | % |
| **a** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | **1** | ***0.6*** |
| **b** | 0 | 1 | 7 | 8 | 0 | 0 | 5 | 15 | **28** | ***16.2*** |
| **e** | 0 | 2 | 0 | 2 | 0 | 0 | 1 | 4 | **7** | ***4.0*** |
| **f** | 0 | 1 | 0 | 1 | 0 | 0 | 1 | 17 | **19** | ***26.0*** |
| **n.t.*** | 3 | 5 | 3 | 11 | 2 | 1 | 15 | 89 | **118** | ***68.2*** |
| **Total** | **3** | **9** | **10** | **22** | **2** | **1** | **22** | **126** | **173** | ***100.0*** |
| ***%*** | ***1.7*** | ***5.2*** | ***5.8*** | ***12.7*** | ***1.2*** | ***0.6*** | ***12.7*** | ***72.8*** | ***100.0*** | |

* non-typable

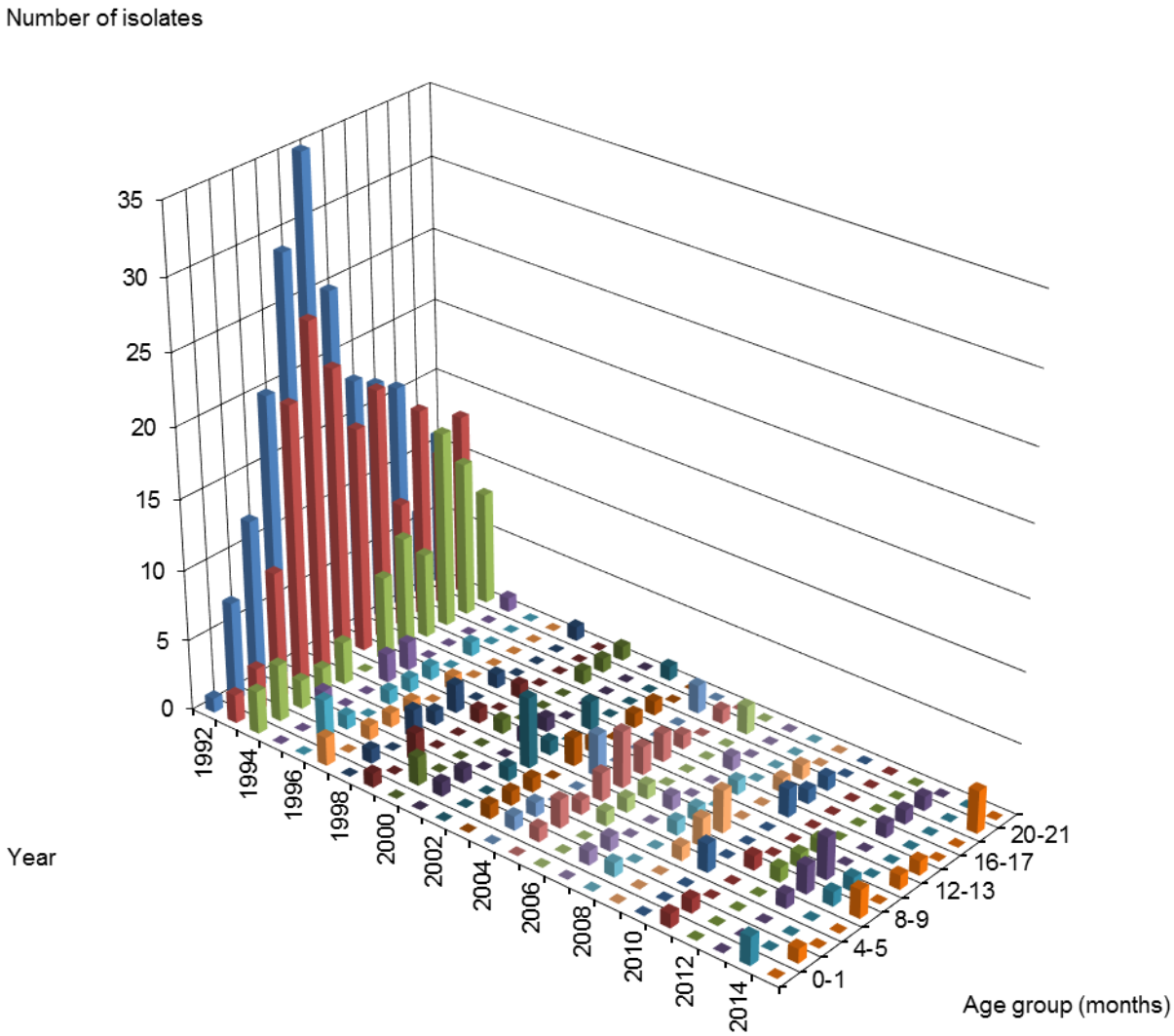


**Figure 5.3** *Age distribution of H. influenzae type b invasive disease in the first two years of life, 1992-2015*

## *5.4 Distribution of non-typable H. influenzae*

The proportion of non-typable isolates increased from 6% in 1992 to about 70% from 1997 onwards (table 5.4). In 2015 the proportion of non-typable isolates was 67.7%.

Table 5.4 *H. influenzae* isolates from CSF and/or blood received from 1992 to 2015 according to year and serotype.

| | SEROTYPE | | | | | | TOTAL | | CSF (or CSF and blood) | Blood Only |
|---|---|---|---|---|---|---|---|---|---|---|
| YEAR | a | b | d | e | f | n.t.* | Total | % n.t.* | | |
| **1992** | - | 294 | - | - | 1 | 20 | 315 | **6.3** | 241 | **74** |
| **1993** | - | 244 | 1 | 1 | 3 | 28 | 277 | **10.1** | 204 | **73** |
| **1994** | - | 148 | - | - | 2 | 26 | 176 | **14.8** | 112 | **64** |
| **1995** | - | 60 | - | - | - | 36 | 96 | **37.5** | 50 | **46** |
| **1996** | - | 30 | - | - | 6 | 52 | 88 | **59.1** | 28 | **60** |
| **1997** | - | 19 | - | 1 | 6 | 59 | 85 | **69.4** | 22 | **63** |
| **1998** | - | 19 | 1 | - | 5 | 63 | 88 | **71.6** | 31 | **57** |
| **1999** | - | 12 | - | 1 | 1 | 55 | 69 | **79.7** | 23 | **46** |
| **2000** | 4 | 15 | 1 | 2 | 4 | 48 | 74 | **64.9** | 24 | **50** |
| **2001** | - | 17 | - | 2 | 8 | 63 | 90 | **70.0** | 19 | **71** |
| **2002** | - | 31 | - | 1 | 13 | 63 | 108 | **58.3** | 28 | **79** |
| **2003** | - | 31 | - | - | 8 | 90 | 129 | **69.8** | 27 | **102** |
| **2004** | - | 48 | - | 2 | 4 | 71 | 125 | **56.8** | 32 | **93** |
| **2005** | 1 | 41 | - | 2 | 10 | 78 | 132 | **59.1** | 37 | **95** |
| **2006** | - | 24 | - | 4 | 7 | 85 | 120 | **70.8** | 25 | **95** |
| **2007** | - | 24 | - | 2 | 2 | 87 | 115 | **75.7** | 19 | **97** |
| **2008** | - | 25 | - | - | 11 | 72 | 108 | **66.7** | 19 | **89** |
| **2009** | - | 32 | 1 | 3 | 9 | 84 | 129 | **65.1** | 15 | **114** |
| **2010** | 1 | 37 | - | 3 | 5 | 96 | 142 | **67.6** | 17 | **125** |
| **2011** | - | 22 | - | 8 | 11 | 98 | 139 | **70.5** | 13 | **126** |
| **2012** | 1 | 28 | - | 2 | 8 | 101 | 140 | **72.1** | 16 | **124** |
| **2013** | - | 29 | - | 3 | 13 | 115 | 160 | **71.9** | 16 | **144** |
| **2014** | 2 | 30 | 1 | 3 | 8 | 117 | 161 | **72.7** | 21 | **140** |
| **2015** | 1 | 34 | - | 8 | 20 | 132 | 195 | **67.7** | 22 | **173** |

* non-typable

In 2015, the number of *H. influenzae* type f and non-typeable *H. influenzae* increased compared to the previous year (2014: 8 and 117, respectively; 2015: 20 and 132, respectively) (Table 5.4) The absolute number of non-typable isolates from CSF remained stable during the period 1992 to 2006, but decreased somewhat from then on as shown in figure 5.4. In 2014 15 non-typable isolates from CSF were received; 2.5 times more than in 2013. The number of non-typable *H. influenzae* isolates from blood increased during the period 1992 to 2015 from 15 to 118 (figure 5.4).

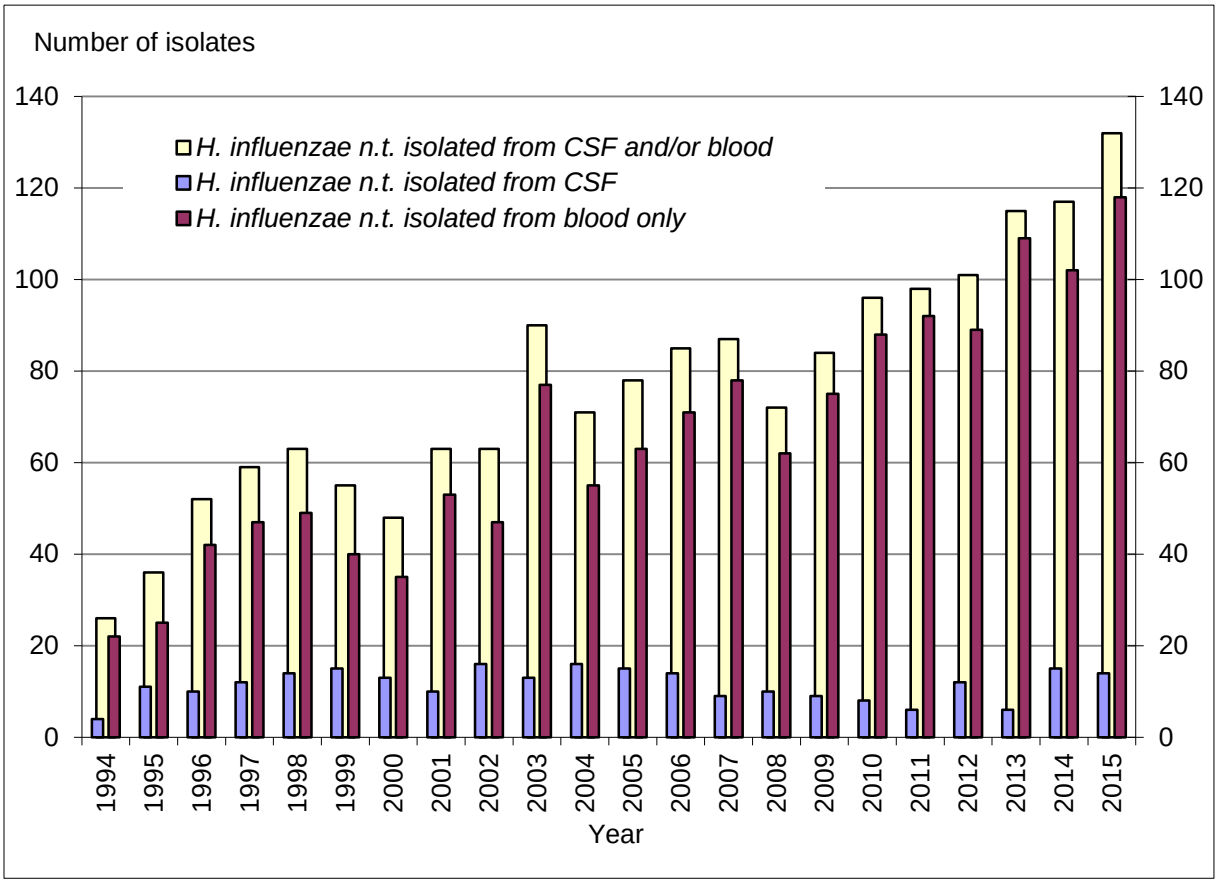


**Figure 5.4** *Non-typable H. influenzae isolates from CSF and/or blood received from 1994-2015*

Table 5.5 Non-typable *H. influenzae* isolates from CSF and/or blood received from 2006 to 2015 according to year and biotype.

| | Biotype | | | | | | | Total |
|---|---|---|---|---|---|---|---|---|
| **2006** | 11 | 44 | 25 | 3 | 2 | - | - | **85** |
| **2007** | 12 | 47 | 19 | 1 | 7 | 1 | - | **87** |
| **2008** | 16 | 29 | 18 | 3 | 5 | 1 | - | **72** |
| **2009** | 28 | 30 | 12 | 10 | 3 | 1 | - | **84** |
| **2010** | 20 | 49 | 19 | 2 | 6 | - | - | **96** |
| **2011** | 27 | 41 | 24 | 3 | 2 | 1 | - | **98** |
| **2012** | 25 | 49 | 17 | 2 | 6 | 1 | 1 | **101** |
| **2013** | 25 | 44 | 30 | 7 | 7 | 2 | - | **115** |
| **2014** | 16 | 56 | 32 | 1 | 9 | 3 | - | **117** |
| **2015** | 22 | 55 | 45 | 1 | 8 | - | 1 | **132** |

*non-typable

Among non-serotypable *H. influenzae* isolates biotype II was the predominant biotype during the last ten years. The number of Biotype III isolates was higher than in previous years (Table 5.5).

# 6 *STREPTOCOCCUS PNEUMONIAE*

## *6.1 General features*

The Reference Laboratory received 901 *S. pneumoniae* isolates. Of these, 147 were isolated from CSF or from CSF and blood (table 2.3; figure 6.1). The incidence of pneumococcal meningitis gradually rose from 1.0 in 1990 to 1.6 in 2004; due to vaccination with the hepta-valent polyscaccharide conjugate vaccine it slightly decreased to 1.0 in 2015. A steep increase in the number of pneumococcal blood isolates had occurred between 1994 (312 isolates) and 2003 (1471 isolates). This increase can be explained by the increasing use of automated blood culture devices by the contributing laboratories and by a real increase in the number of cases of pneumococcal bacteremia due to pneumonia among patients of the increasing cohort of the elderly (figure 6.1) and by a more complete submission of isolates by the laboratories.
The number of isolates from blood sent to the Reference Laboratory decreased from 1471 in 2003 to 759 in 2015. This was due to a change in policy: from 2003 onwards, we asked only nine sentinel laboratories, evenly distributed over the country, to submit pneumococcal blood isolates. Thus, the numbers of *S. pneumoniae* from blood only are incomplete.

This policy has been changed to monitor the effect of the introduction of the 7-valent conjugate pneumococcal polysaccharide vaccine by June 1st, 2006. In April 2011 the 10-valent vaccine was introduced for all newborns born March 1, 2011. From 2006 onwards, all laboratories are requested to send all invasive pneumococcal isolates from patients in the age group 0-4 year, while from patients older than 4 year only isolates from CSF are requested. Again, from nine sentinel laboratories we ask all invasive pneumococcal isolates from all patients.

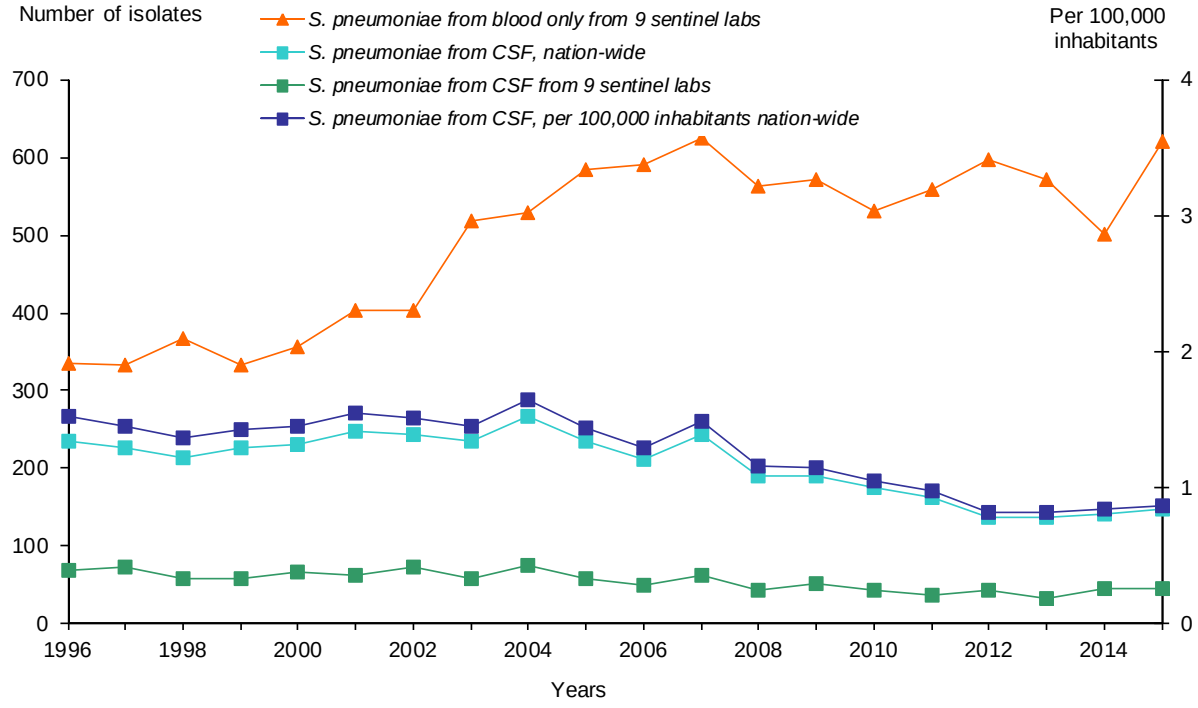


**Figure 6.1** *Distribution of S. pneumoniae isolates, 1996-2015*

## *6.2 Antibiotic susceptibility*

Among 147 isolates from CSF (or CSF and blood) and 754 isolates from the blood only, 21 isolates from the blood (2.3%) were intermediately susceptible to penicillin (0.06< MIC≤2.0 mg/L, table 6.1). Four (0.5%) strains isolated from CSF were resistant to penicillin (MIC > 0.06 mg/L).

Table 6.1 Susceptibility of *S. pneumoniae* isolates to penicillin, 2015

| | Penicillin* | | | | |
|---|---|---|---|---|---|
| | S | I | R | Total | % |
| MIC for CSF | MIC ≤ 0.06 | | MIC > 0.06 | | |
| **CSF or CSF and blood** | 143 | 0 | 4 | **147** | ***16.3*** |
| MIC for blood | MIC ≤ 0.06 | 0.06< MIC ≤ 2.0 | MIC >2.0 | | |
| **Blood only** | 733 | 21 | 0 | **754** | ***83.7*** |
| **Total** | **876** | **21** | **4** | **901** | ***100.0*** |
| *%* | ***97.2*** | ***2.3*** | ***0.5*** | ***100.0*** | |

* MIC values in µg/ml according to EUCAST guidelines

Figure 6.2 shows the distribution of *S. pneumoniae* isolates according to the patients' age. The incidence of pneumococcal meningitis is highest among patients in the age group 60 – 64 year (Table 6.4).

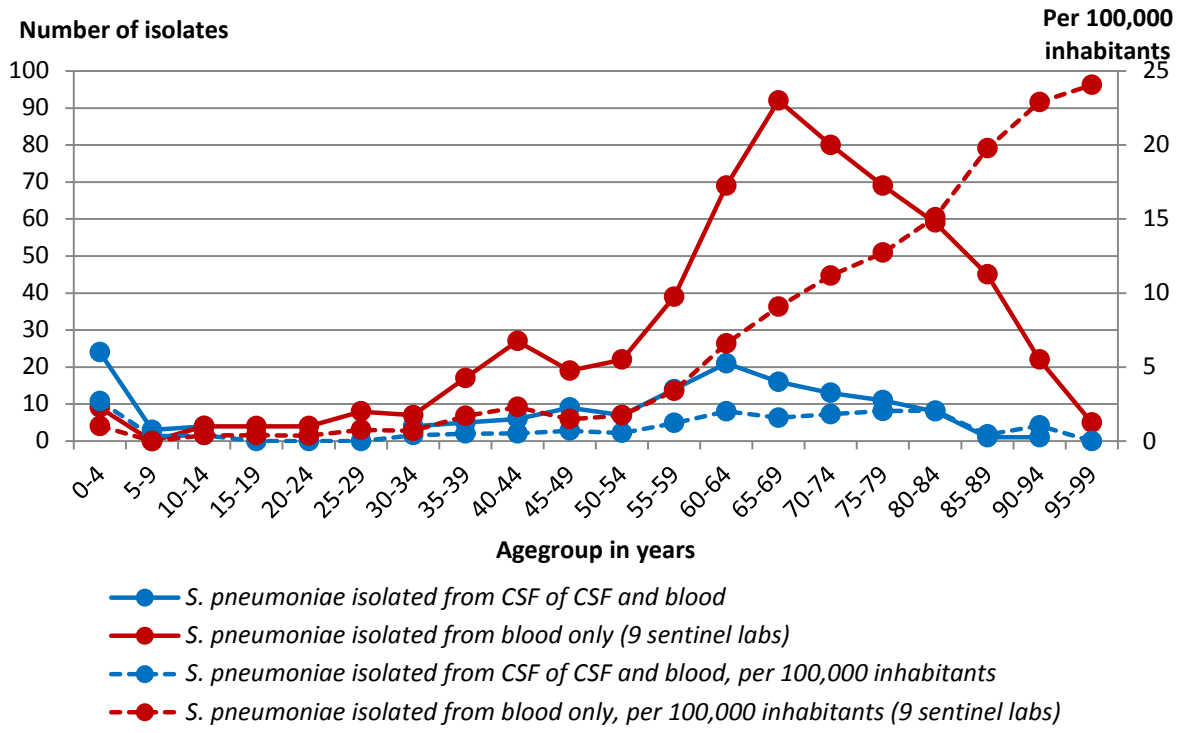


**Figure 6.2** *Distribution of S. pneumoniae isolates received in 2015 according to age*

## *6.3 Distribution according to serotype*

The relationship between age and major types of all isolates (received from the 9 sentinel laboratories) is shown in table 6.2. For isolates from CSF (or CSF and blood), the distribution of serotypes by age of the patient is presented in table 6.3, while the incidence of *S. pneumoniae* meningitis per serotype per 100,000 inhabitants is shown in table 6.4. The distribution of serotypes by age of the patient for pneumococcal isolates from blood only is shown in table 6.5. As aforementioned, incidences of *S. pneumoniae* from blood only are incomplete. Effect of the 10-valent vaccine can been seen in table 6.6 and table 6.7, showing a reduction of the number of isolates with vaccine types. However, the overall number of invasive pneumococcal disease isolates increased due to an increase of the number of isolates with non-vaccine types.

Table 6.6 shows the distribution of CSF isolates according to serotype over the last 10 years. Table 6.7 shows the distribution of blood only isolates from the 9 selected laboratories according to serotype over the last 10 years. After the introduction of the 7-valent polysaccharide conjugate vaccine in the National Immunisation Programme the number of isolates with a vaccine type decreased dramatically. However, the effect was abrogated by an increase of the number of isolates with non-vaccine types (Table 6.6 and 6.7).

Table 6.2 *S. pneumoniae* isolates from CSF and/or blood (from the 9 sentinel laboratories), by serotype and age of patients, 2015

| | AGE ( MONTHS) | | | AGE (YEARS) | | | | | | | | | | TOTAL | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| TYPE | 0 | 1-11 | 12-59 | 0-4 | 5-9 | 10-14 | 15-19 | 20-29 | 30-39 | 40-49 | 50-64 | 65-79 | ≥80 | T | % |
| **1** | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 2 | 4 | 12 | 7 | 12 | 2 | **42** | ***6.3*** |
| **3** | 1 | 1 | 0 | 2 | 0 | 0 | 0 | 0 | 1 | 3 | 8 | 18 | 7 | **39** | ***5.9*** |
| **4** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 5 | 0 | **6** | ***0.9*** |
| **6** | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 0 | 2 | 2 | 5 | 10 | 8 | **29** | ***4.3*** |
| **7** | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 3 | 2 | 6 | 13 | 20 | 12 | **59** | ***8.9*** |
| **8** | 1 | 1 | 0 | 2 | 0 | 1 | 0 | 3 | 5 | 8 | 33 | 71 | 21 | **144** | ***21.6*** |
| **9** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 10 | 10 | 11 | **32** | ***4.8*** |
| **10** | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 2 | 4 | 6 | 3 | **18** | ***2.7*** |
| **12** | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 3 | 4 | 7 | 8 | 6 | **30** | ***4.5*** |
| **14** | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 5 | **7** | ***1.0*** |
| **18** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 2 | **5** | ***0.7*** |
| **19** | 0 | 1 | 2 | 3 | 0 | 0 | 0 | 0 | 3 | 6 | 22 | 37 | 22 | **93** | ***13.9*** |
| **22** | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 3 | 15 | 20 | 6 | **46** | ***6.9*** |
| **23** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 4 | 6 | 4 | **17** | ***2.6*** |
| **Others** | 0 | 2 | 2 | 4 | 1 | 0 | 0 | 3 | 4 | 5 | 15 | 42 | 26 | **99** | ***15.0*** |
| **Total** | **2** | **8** | **5** | **15** | **1** | **5** | **4** | **13** | **26** | **56** | **145** | **267** | **135** | **667** | ***100.0*** |
| *%* | ***0.3*** | ***1.2*** | ***0.7*** | ***2.2*** | ***0.2*** | ***0.7*** | ***0.6*** | ***2.0*** | ***3.9*** | ***8.4*** | ***21.7*** | ***40.0*** | ***20.3*** | ***100.0*** | |

Table 6.3 *S. pneumoniae* isolates from CSF (or CSF and blood)* nation-wide, by serotype and age of patients, 2015

| | AGE ( MONTHS) | | | AGE (YEARS) | | | | | | | | | TOTAL | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| TYPE | 0 | 1-11 | 12-59 | 0-4 | 5-9 | 10-14 | 15-19 | 20-29 | 30-39 | 40-49 | 50-64 | 65-79 | ≥80 | T | % |
| **1** | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **1** | ***0.7*** |
| **3** | 0 | 1 | 1 | 2 | 2 | 0 | 0 | 0 | 2 | 1 | 5 | 4 | 0 | **16** | ***10.9*** |
| **4** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **0** | ***0.0*** |
| **6** | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 2 | 1 | 1 | **7** | ***4.8*** |
| **7** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 2 | 1 | 2 | **7** | ***4.8*** |
| **8** | 2 | 2 | 0 | 4 | 0 | 0 | 0 | 0 | 1 | 3 | 7 | 7 | 2 | **24** | ***16.3*** |
| **9** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 5 | 0 | **6** | ***4.1*** |
| **10** | 0 | 2 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 1 | 2 | 1 | 0 | **6** | ***4.1*** |
| **12** | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 5 | 2 | 0 | **9** | ***6.1*** |
| **14** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | **1** | ***0.7*** |
| **18** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | **1** | ***0.7*** |
| **19** | 1 | 2 | 1 | 4 | 0 | 0 | 0 | 0 | 2 | 2 | 2 | 2 | 0 | **12** | ***8.1*** |
| **22** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 5 | 5 | 2 | **12** | ***8.1*** |
| **23** | 0 | 1 | 1 | 2 | 0 | 2 | 0 | 0 | 2 | 1 | 3 | 6 | 1 | **17** | ***11.6*** |
| **Others** | 0 | 6 | 2 | 8 | 1 | 0 | 0 | 0 | 1 | 4 | 7 | 5 | 2 | **28** | ***19.0*** |
| **Total** | **3** | **15** | **6** | **24** | **3** | **4** | **0** | **0** | **9** | **15** | **42** | **40** | **10** | **147** | ***100.0*** |
| *%* | ***2.0*** | ***10.2*** | ***4.1*** | ***16.3*** | ***2.0*** | ***2.7*** | ***0.0*** | ***0.0*** | ***6.1*** | ***10.2*** | ***28.6*** | ***27.3*** | ***6.8*** | ***100.0*** | |

* From 4 patients with a pneumococcus isolated from blood, CSF was culture-negative but PCR was positive for pneumococcal DNA. Cases were in age groups 50-64 years (1), 65-79 years (1) and ≥80 (2)

Table 6.4 Age-specific incidence of pneumococcal meningitis nation-wide (isolates from CSF or CSF and blood) per 100,000 inhabitants according to type, 2015

| | AGE (YEARS) | | | | | | | | | | | TOTAL |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| TYPE | 0 | 1-4 | 5-9 | 10-14 | 15-19 | 20-29 | 30-39 | 40-49 | 50-64 | 65-79 | ≥80 | |
| **1** | 0 | 0 | 0 | 0.10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.01 |
| **3** | 0.57 | 0.14 | 0.22 | 0 | 0 | 0 | 0.10 | 0.04 | 0.14 | 0.18 | 0 | 0.09 |
| **4** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| **6** | 0.57 | 0 | 0 | 0.10 | 0 | 0 | 0 | 0.04 | 0.06 | 0.04 | 0.14 | 0.04 |
| **7** | 0 | 0 | 0 | 0 | 0 | 0 | 0.05 | 0.04 | 0.06 | 0.04 | 0.27 | 0.04 |
| **8** | 2.29 | 0 | 0 | 0 | 0 | 0 | 0.05 | 0.12 | 0.20 | 0.31 | 0.27 | 0.14 |
| **9** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.03 | 0.22 | 0 | 0.04 |
| **10** | 1.14 | 0 | 0 | 0 | 0 | 0 | 0 | 0.04 | 0.06 | 0.04 | 0 | 0.04 |
| **12** | 0 | 0.14 | 0 | 0 | 0 | 0 | 0 | 0.04 | 0.14 | 0.09 | 0 | 0.05 |
| **14** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.04 | 0 | 0.01 |
| **18** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.03 | 0 | 0 | 0.01 |
| **19** | 1.72 | 0.14 | 0 | 0 | 0 | 0 | 0.10 | 0.08 | 0.06 | 0.09 | 0 | 0.07 |
| **22** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.14 | 0.22 | 0.27 | 0.07 |
| **23** | 0.57 | 0.14 | 0 | 0.20 | 0 | 0 | 0.10 | 0.04 | 0.09 | 0.26 | 0.14 | 0.10 |
| **Others** | 3.43 | 0.28 | 0.11 | 0 | 0 | 0 | 0.05 | 0.16 | 0.20 | 0.22 | 0.27 | 0.17 |
| **Total** | **10.30** | **0.84** | **0.32** | **0.40** | **0** | **0** | **0.45** | **0.61** | **1.21** | **1.76** | **1.36** | **0.87** |

Table 6.5 All *S. pneumoniae* isolates from blood only (from the 9 sentinel laboratories), by serotype of patients, 2015

| | AGE ( MONTHS) | | | AGE (YEARS) | | | | | | | | | | TOTAL | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| TYPE | 0 | 1-11 | 12-59 | 0-4 | 5-9 | 10-14 | 15-19 | 20-29 | 30-39 | 40-49 | 50-64 | 65-79 | ≥80 | T | % |
| **1** | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 2 | 4 | 12 | 7 | 12 | 2 | **41** | ***6.6*** |
| **3** | 1 | 1 | 0 | 2 | 0 | 0 | 0 | 0 | 1 | 3 | 8 | 14 | 7 | **35** | ***5.6*** |
| **4** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 5 | 0 | **6** | ***1.0*** |
| **6** | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 0 | 2 | 1 | 4 | 10 | 8 | **27** | ***4.4*** |
| **7** | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 3 | 2 | 6 | 12 | 20 | 10 | **56** | ***9.0*** |
| **8** | 1 | 0 | 0 | 1 | 0 | 1 | 0 | 3 | 4 | 7 | 32 | 68 | 20 | **136** | ***21.9*** |
| **9** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 10 | 9 | 11 | **31** | ***5.0*** |
| **10** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 2 | 3 | 5 | 3 | **15** | ***2.4*** |
| **12** | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 3 | 4 | 7 | 8 | 6 | **30** | ***4.8*** |
| **14** | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 5 | **7** | ***1.1*** |
| **18** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 2 | **4** | ***0.6*** |
| **19** | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 3 | 4 | 20 | 36 | 22 | **86** | ***13.9*** |
| **22** | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 3 | 15 | 18 | 6 | **44** | ***7.1*** |
| **23** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 3 | 3 | 4 | **13** | ***2.1*** |
| **Others** | 0 | 1 | 1 | 2 | 0 | 0 | 0 | 3 | 3 | 2 | 14 | 40 | 26 | **90** | ***14.5*** |
| **Total** | **2** | **4** | **3** | **9** | **0** | **4** | **4** | **13** | **24** | **49** | **136** | **250** | **132** | **621** | ***100.0*** |
| *%* | ***0.3*** | ***0.6*** | ***0.6*** | ***1.5*** | ***0.0*** | ***0.6*** | ***0.6*** | ***2.1*** | ***3.9*** | ***7.9*** | ***21.9*** | ***40.3*** | ***21.2*** | ***100.0*** | |

Table 6.6 Distribution of pneumococcal CSF isolates according to serotype nation-wide, 2006-2015

| | | TYPE | Year 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 23-valent vaccine | 10-valent vaccine | 7-valent vaccine | 4 | 12 | 5 | 8 | 4 | 3 | 2 | 4 | 2 | 2 | - |
| | | | 6B | 21 | 12 | 11 | 3 | - | 2 | - | - | - | 1 |
| | | | 9V | 6 | 10 | 7 | 2 | 2 | - | 3 | 1 | 1 | - |
| | | | 14 | 28 | 18 | 8 | 3 | 5 | 2 | 1 | - | - | 1 |
| | | | 18C | 19 | 17 | 8 | 6 | 5 | 5 | 2 | 2 | - | 1 |
| | | | 19F | 15 | 11 | 7 | 10 | 2 | 6 | 4 | 2 | 4 | 2 |
| | | | 23F | 16 | 22 | 17 | 5 | 4 | 2 | 1 | - | - | 1 |
| | | | **Subtotal** 7-valent vaccine | *117* | *95* | *66* | *33* | *21* | *19* | *15* | *7* | *7* | *6* |
| | | | 1 | 1 | 8 | 8 | 8 | 3 | 1 | 1 | 3 | 4 | 1 |
| | | | 5 | 1 | - | - | - | 2 | - | 3 | - | - | - |
| | | | 7F | 18 | 36 | 25 | 25 | 20 | 28 | 16 | 15 | 8 | 7 |
| | | | **Subtotal** 10-valent vaccine | *137* | *139* | *99* | *66* | *46* | *48* | *35* | *25* | *19* | *14* |
| | | | 2 | - | - | - | - | - | - | - | - | - | - |
| | | | 3 | 20 | 16 | 17 | 24 | 20 | 7 | 13 | 16 | 13 | 16 |
| | | | 8 | 10 | 21 | 9 | 10 | 10 | 17 | 9 | 16 | 23 | 24 |
| | | | 9N | 2 | 4 | 1 | 3 | 6 | 7 | 4 | 2 | 6 | 6 |
| | | | 10A | 7 | 8 | 7 | 10 | 9 | 7 | 9 | 7 | 12 | 5 |
| | | | 11A | 3 | 4 | 2 | 8 | 1 | 5 | 1 | 1 | 3 | 2 |
| | | | 12F | 1 | 4 | 2 | 2 | 3 | 7 | 10 | 9 | 8 | 9 |
| | | | 15B | - | 1 | 4 | 8 | 2 | 3 | 1 | - | - | - |
| | | | 17F | - | 1 | - | - | 4 | 3 | 1 | 1 | 1 | - |
| | | | 19A | 2 | 9 | 8 | 6 | 20 | 16 | 6 | 9 | 7 | 10 |
| | | | 20 | 1 | - | 1 | - | 1 | - | - | 1 | 1 | 1 |
| | | | 22F | 9 | 2 | 10 | 13 | 14 | 16 | 11 | 8 | 8 | 11 |
| | | | 33F | 3 | 5 | 6 | 6 | 7 | 5 | 6 | 3 | 2 | 4 |
| | | | **Subtotal** 23-valent vaccine | *195* | *214* | *166* | *156* | *143* | *141* | *106* | *98* | *103* | *102* |
| | | | 6A | 5 | 5 | 4 | 6 | 5 | 1 | 1 | 1 | 3 | - |
| | | | 6C | 1 | 2 | - | - | 3 | 4 | 2 | 6 | 3 | 6 |
| | | | 7B | - | - | - | - | - | - | - | 1 | - | - |
| | | | 10F | - | - | - | - | - | - | - | - | - | - |
| | | | 10B | - | - | - | - | - | - | 1 | - | 1 | 1 |
| | | | 12A | - | - | - | - | - | - | - | - | - | - |
| | | | 13 | - | - | - | 1 | - | - | - | - | - | - |
| | | | 15A | - | 1 | 1 | - | 1 | 1 | 1 | 4 | 6 | 7 |
| | | | 15C | 1 | 1 | 3 | 1 | 2 | - | 3 | - | - | 1 |
| | | | 16F | 2 | 2 | 2 | - | 5 | 4 | - | 5 | 2 | 1 |
| | | | 17A | - | - | - | 1 | - | - | - | - | - | - |
| | | | 18F | - | - | - | - | - | - | - | - | - | - |
| | | | 18A | - | - | - | - | - | - | - | - | - | - |
| | | | 18B | 1 | 1 | 1 | - | - | - | 1 | - | - | - |
| | | | 21 | - | 1 | - | - | - | 1 | - | - | - | - |
| | | | 22A | - | 1 | - | 1 | 1 | - | - | - | - | 1 |
| | | | 23A | - | 3 | 1 | 3 | 3 | 2 | 4 | 4 | 4 | 5 |
| | | | 23B | 2 | 2 | 3 | 7 | 5 | 2 | 5 | 7 | 8 | 11 |
| | | | 24F | - | 3 | 2 | 6 | 1 | 1 | 4 | 4 | 7 | 7 |
| | | | 24B | - | - | - | - | - | - | 2 | - | - | - |
| | | | 25 | - | - | 1 | - | - | - | - | - | - | - |
| | | | 27 | - | 1 | 2 | - | - | - | 1 | - | 2 | 1 |
| | | | 28F | - | - | - | - | - | - | - | 1 | - | - |
| | | | 28A | - | - | - | - | - | 1 | - | - | - | - |
| | | | 29 | - | - | - | - | - | - | 1 | - | - | - |
| | | | 31 | 2 | 2 | - | 1 | 1 | - | 1 | - | 1 | - |
| | | | 33A | - | - | - | - | - | - | - | - | - | - |
| | | | 34 | - | 1 | 1 | 1 | - | 1 | - | - | - | 1 |
| | | | 35F | 1 | 2 | 2 | 2 | 4 | 1 | - | 2 | 1 | 2 |
| | | | 35B | 1 | 1 | - | - | 1 | - | 1 | 3 | 1 | 1 |
| | | | 37 | - | - | - | 1 | - | 1 | 2 | 1 | - | - |
| | | | 38 | 1 | - | 1 | 3 | 1 | - | 2 | 1 | - | - |
| | | | Rough (n.t.) | - | - | - | - | - | - | - | - | - | - |
| | | | Total | 212 | 243 | 190 | 190 | 176 | 163 | 138 | 138 | 142 | 147 |

Table 6.7 Distribution of *S. pneumoniae* from blood only (from the 9 sentinel laboratories), according to serotype, 2006-2015

| | | TYPE | 2006 | 2007 | 2008 | 2009 | 2010 | Year 2011 | 2012 | 2013 | 2014 | 2015 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 23-valent vaccine | 10-valent vaccine | 7-valent | 4 | 52 | 54 | 30 | 26 | 17 | 27 | 11 | 13 | 6 | 6 |
| | | | 6B | 21 | 26 | 25 | 12 | 8 | 3 | 3 | 3 | 3 | 4 |
| | | | 9V | 65 | 53 | 42 | 26 | 21 | 5 | 2 | 4 | 1 | 5 |
| | | | 14 | 86 | 84 | 54 | 34 | 22 | 19 | 12 | 8 | 2 | 7 |
| | | | 18C | 12 | 13 | 15 | 15 | 7 | 8 | 4 | 8 | 2 | 2 |
| | | | 19F | 19 | 11 | 9 | 10 | 5 | 9 | 3 | 5 | 7 | 8 |
| | | | 23F | 29 | 39 | 13 | 12 | 13 | 5 | 3 | 1 | 2 | 1 |
| | | | **Subtotal** 7-valent vaccine | *284* | *280* | *188* | *135* | *93* | *85* | *38* | *42* | *23* | *33* |
| | | | 1 | 25 | 75 | 64 | 65 | 53 | 40 | 50 | 40 | 41 | 41 |
| | | | 5 | - | 3 | 2 | 6 | 7 | 11 | 8 | 9 | 2 | 1 |
| | | | 7F | 75 | 55 | 65 | 86 | 72 | 91 | 92 | 75 | 53 | 56 |
| | | | **Subtotal** 10-valent vaccine | *384* | *413* | *319* | *292* | *225* | *227* | *188* | *166* | *119* | *131* |
| | | | 2 | - | - | - | - | - | - | - | - | - | - |
| | | | 3 | 32 | 30 | 31 | 34 | 30 | 36 | 45 | 40 | 31 | 35 |
| | | | 8 | 42 | 47 | 46 | 52 | 60 | 59 | 88 | 108 | 93 | 136 |
| | | | 9N | 19 | 13 | 19 | 18 | 19 | 17 | 20 | 19 | 21 | 26 |
| | | | 10A | 6 | 4 | 7 | 9 | 9 | 14 | 8 | 6 | 16 | 15 |
| | | | 11A | 6 | 16 | 3 | 12 | 12 | 9 | 14 | 16 | 8 | 6 |
| | | | 12F | 9 | 5 | 6 | 5 | 13 | 19 | 25 | 22 | 28 | 30 |
| | | | 15B | 5 | 1 | 4 | 6 | 7 | 4 | 1 | 7 | 7 | 2 |
| | | | 17F | 1 | 3 | 1 | 7 | 4 | 8 | 7 | 4 | 8 | 6 |
| | | | 19A | 21 | 25 | 33 | 30 | 57 | 63 | 78 | 61 | 44 | 78 |
| | | | 20 | 2 | 3 | 3 | 3 | 3 | 4 | - | 1 | 4 | 2 |
| | | | 22F | 19 | 18 | 24 | 24 | 29 | 37 | 41 | 45 | 34 | 43 |
| | | | 33F | 10 | 6 | 10 | 11 | 10 | 15 | 22 | 12 | 12 | 19 |
| | | | **Subtotal** 23-valent vaccine | *556* | *584* | *506* | *503* | *478* | *503* | *537* | *507* | *425* | 529 |
| | | | 6A | 7 | 10 | 18 | 11 | 9 | 2 | 6 | 2 | - | 2 |
| | | | 6C | - | 2 | 1 | 7 | 9 | 7 | 10 | 10 | 7 | 21 |
| | | | 7C | 2 | 1 | - | - | - | - | - | - | - | - |
| | | | 9A | - | - | - | - | - | - | 1 | - | 1 | - |
| | | | 10F | - | - | 1 | - | - | - | - | - | 1 | - |
| | | | 10B | - | - | - | - | - | - | - | 1 | - | - |
| | | | 11B | - | 1 | - | - | - | - | - | - | - | - |
| | | | 12A | - | - | - | - | - | - | - | - | - | - |
| | | | 13 | - | - | - | - | - | 1 | - | - | - | - |
| | | | 15F | - | - | - | - | - | - | - | 1 | - | - |
| | | | 15A | - | 1 | 1 | 1 | - | 2 | 7 | 13 | 14 | 18 |
| | | | 15C | - | 1 | 2 | 2 | 1 | 2 | 1 | 4 | 4 | 3 |
| | | | 16F | 6 | 6 | 9 | 8 | 10 | 7 | 6 | 7 | 5 | 2 |
| | | | 17A | - | - | - | - | - | 2 | - | - | - | - |
| | | | 18F | - | - | - | - | - | - | - | - | - | 2 |
| | | | 18A | - | 1 | - | 1 | 1 | 1 | - | - | - | - |
| | | | 18B | - | 1 | - | - | - | - | 1 | 1 | - | - |
| | | | 21 | - | - | - | - | - | - | - | 2 | 1 | - |
| | | | 22A | 3 | 2 | 1 | - | 1 | 1 | - | 1 | - | 1 |
| | | | 23A | 2 | 6 | 3 | 9 | 7 | 2 | 6 | 6 | 7 | 7 |
| | | | 23B | 1 | 1 | 3 | 6 | 3 | 9 | 3 | 6 | 15 | 5 |
| | | | 24F | 1 | 1 | 7 | - | 2 | 3 | 2 | 4 | 4 | 7 |
| | | | 25F | 1 | - | 1 | - | - | - | - | - | - | 1 |
| | | | 27 | - | - | 1 | 1 | - | 1 | - | 1 | - | 1 |
| | | | 28A | - | - | - | - | - | - | - | - | - | - |
| | | | 29 | - | - | - | - | - | - | 1 | - | - | - |
| | | | 31 | 1 | 1 | 3 | 1 | 4 | 2 | 6 | 2 | 2 | 4 |
| | | | 33A | - | - | - | - | - | - | 1 | - | - | - |
| | | | 34 | 1 | 1 | - | 1 | 1 | - | 1 | 2 | 1 | - |
| | | | 35F | 2 | 1 | 2 | 4 | 5 | 6 | 5 | 6 | 7 | 7 |
| | | | 35A | - | - | - | - | - | - | 1 | - | - | - |
| | | | 35B | 3 | - | - | 4 | - | 3 | 1 | 7 | 6 | 8 |
| | | | 37 | - | 1 | - | - | 1 | - | - | - | 1 | 1 |
| | | | 38 | 3 | 2 | 3 | 5 | - | 3 | - | 1 | 2 | 2 |
| | | | 40 | - | - | - | - | - | - | - | 1 | - | - |
| | | | Rough (n.t.) | 2 | - | - | - | - | 2 | - | - | - | - |
| | | | Total | 591 | 624 | 562 | 564 | 532 | 559 | 596 | 585 | 503 | 621 |

Table 6.8 Distribution of *S. pneumoniae* isolates from CSF (or CSF and blood) nation-wide, by serotype and age of patients, 2015.

| | | TYPE | AGE ( YEARS) 0-4 | 5-9 | 10-14 | 15-19 | 20-29 | 30-39 | 40-49 | 50-64 | 65-79 | ≥80 | Total | % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 23-valent vaccine | 10-valent vaccine | 7-valent vaccine 4 | - | - | - | - | - | - | - | - | - | - | - | - |
| | | 6B | - | - | 1 | - | - | - | - | - | - | - | 1 | ***0.7*** |
| | | 9V | - | - | - | - | - | - | - | - | - | - | - | - |
| | | 14 | - | - | - | - | - | - | - | - | 1 | - | 1 | ***0.7*** |
| | | 18C | - | - | - | - | - | - | - | 1 | - | - | 1 | ***0.7*** |
| | | 19F | - | - | - | - | - | - | 1 | - | 1 | - | 2 | ***1.3*** |
| | | 23F | - | - | - | - | - | 1 | - | - | - | - | 1 | ***0.7*** |
| | | ***Subtotal* 7-valent vaccine** | *-* | *-* | *1* | *-* | *-* | *1* | *1* | *1* | *2* | *-* | *6* | ***4.1*** |
| | | 1 | - | - | 1 | - | - | - | - | - | - | - | 1 | ***0.7*** |
| | | 5 | - | - | - | - | - | - | - | - | - | - | - | - |
| | | 7F | - | - | - | - | - | 1 | 1 | 2 | 1 | 2 | 7 | ***4.8*** |
| | | ***Subtotal* 10-valent vaccine** | *-* | *-* | *2* | *-* | *-* | *2* | *2* | *3* | *3* | *2* | *14* | ***9.6*** |
| | | 2 | - | - | - | - | - | - | - | - | - | - | - | - |
| | | 3 | 2 | 2 | - | - | - | 2 | 1 | 5 | 4 | - | 16 | ***10.9*** |
| | | 8 | 4 | - | - | - | - | 1 | 3 | 7 | 7 | 2 | 24 | ***16.3*** |
| | | 9N | - | - | - | - | - | - | - | 1 | 5 | - | 6 | ***4.1*** |
| | | 10A | 1 | - | - | - | - | - | 1 | 2 | 1 | - | 5 | ***3.4*** |
| | | 11A | - | - | - | - | - | - | 1 | 1 | - | - | 2 | ***1.3*** |
| | | 12F | 1 | - | - | - | - | - | 1 | 5 | 2 | - | 9 | ***6.1*** |
| | | 15B | - | - | - | - | - | - | - | - | - | - | - | - |
| | | 17F | - | - | - | - | - | - | - | - | - | - | - | - |
| | | 19A | 4 | - | - | - | - | 2 | 1 | 2 | 1 | - | 10 | ***6.8*** |
| | | 20 | - | - | - | - | - | - | 1 | - | - | - | 1 | ***0.7*** |
| | | 22F | - | - | - | - | - | - | - | 4 | 5 | 2 | 11 | ***7.5*** |
| | | 33F | 2 | - | - | - | - | - | - | - | 2 | - | 4 | ***2.7*** |
| | | ***Subtotal* 23-valent vaccine** | *14* | *2* | *2* | *-* | *-* | *7* | *11* | *30* | *30* | *6* | *102* | ***69.4*** |
| | | Other | 10 | 1 | 2 | - | - | 2 | 4 | 12 | 10 | 4 | 45 | ***30.6*** |
| | | Total | 24 | 3 | 4 | - | - | 9 | 15 | 42 | 40 | 10 | 147 | ***100.0*** |

# 7 *ESCHERICHIA COLI*

The Reference Laboratory received 28 *Escherichia coli* strains, 8 isolated from CSF (or CSF and blood) and 20 from blood only (table 7.1, 7.2 and 7.3). Eighty-two percent of the cases of *E. coli* meningitis occurred in the first month of life.

Interestingly, the types O non typable and O11 are prevalent among non-K1 isolates, while the types O non typable (4), O1 (3), O2 (2), O6 (2), O14, O18, O25 (4), O45, O46, O75, O83, O117 (2), O166 and O175 are found among K1 isolates.

Table 7.1 Serotypes of *E. coli* isolates from CSF and/or blood, by age of patients, 2015

| TYPE | AGE ( MONTHS) | | | AGE (YEARS) | | | | | TOTAL | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | 1-11 | 12-59 | 0-4 | 5-9 | 10-19 | 20-49 | ≥50 | T | % |
| **Non K1** | 2 | - | - | 2 | - | - | - | 1 | **3** | ***11*** |
| **K1** | 21 | 2 | - | 23 | - | - | - | 2 | **25** | ***89*** |
| **Total** | **23** | **2** | **-** | **25** | **-** | **-** | **-** | **3** | **28** | ***100*** |
| **%** | ***82*** | ***7*** | ***0*** | ***89*** | ***0*** | ***0*** | ***0*** | ***11*** | ***100*** | |

Table 7.2 Serotypes of *E. coli* isolates from CSF (or CSF and blood), by age of patients, 2015

| TYPE | AGE ( MONTHS) | | | AGE (YEARS) | | | | | TOTAL | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | 1-11 | 12-59 | 0-4 | 5-9 | 10-19 | 20-49 | ≥50 | T | % |
| **Non K1** | - | - | - | - | - | - | - | 1 | **1** | ***13*** |
| **K1** | 5 | - | - | 5 | - | - | - | 2 | **7** | ***87*** |
| **Total** | **5** | **-** | **-** | **5** | **-** | **-** | **-** | **3** | **8** | ***100*** |
| **%** | ***63*** | ***0*** | ***0*** | ***63*** | ***0*** | ***0*** | ***0*** | ***37*** | ***100*** | |

Table 7.3 Serotypes of *E. coli* isolates from blood only by age of patients, 2015

| TYPE | AGE ( MONTHS) | | | AGE (YEARS) | | | | | TOTAL | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | 1-11 | 12-59 | 0-4 | 5-9 | 10-19 | 20-49 | ≥50 | T | % |
| **Non K1** | 2 | - | - | 2 | - | - | - | - | **2** | ***11*** |
| **K1** | 16 | 2 | - | 18 | - | - | - | - | **18** | ***89*** |
| **Total** | **18** | **2** | **-** | **20** | **-** | **-** | **-** | **-** | **20** | ***100*** |
| **%** | ***89*** | ***11*** | ***0*** | ***100*** | ***0*** | ***0*** | ***0*** | ***0*** | ***100*** | |

Since 2012 all isolates were tested for the H – type. Almost 50% of all K1 isolates were of type H4 and H7 (table 7.4)

Table 7.4 H-type versus K-type of *E. coli* isolates from CSF and/or blood, 2015

| TYPE | K1 | Non K1 | Total |
|---|---|---|---|
| **H1** | 1 | 0 | **1** |
| **H4** | 6 | 0 | **6** |
| **H5** | 1 | 2 | **3** |
| **H6** | 2 | 0 | **2** |
| **H7** | 6 | 0 | **6** |
| **H11** | 1 | 0 | **1** |
| **H15** | 1 | 0 | **1** |
| **H18** | 2 | 0 | **2** |
| **H31** | 2 | 0 | **2** |
| **H33** | 1 | 0 | **1** |
| **H-** | 2 | 1 | **3** |
| **Total** | **25** | **3** | **28** |
| **%** | ***89*** | ***11*** | ***100*** |

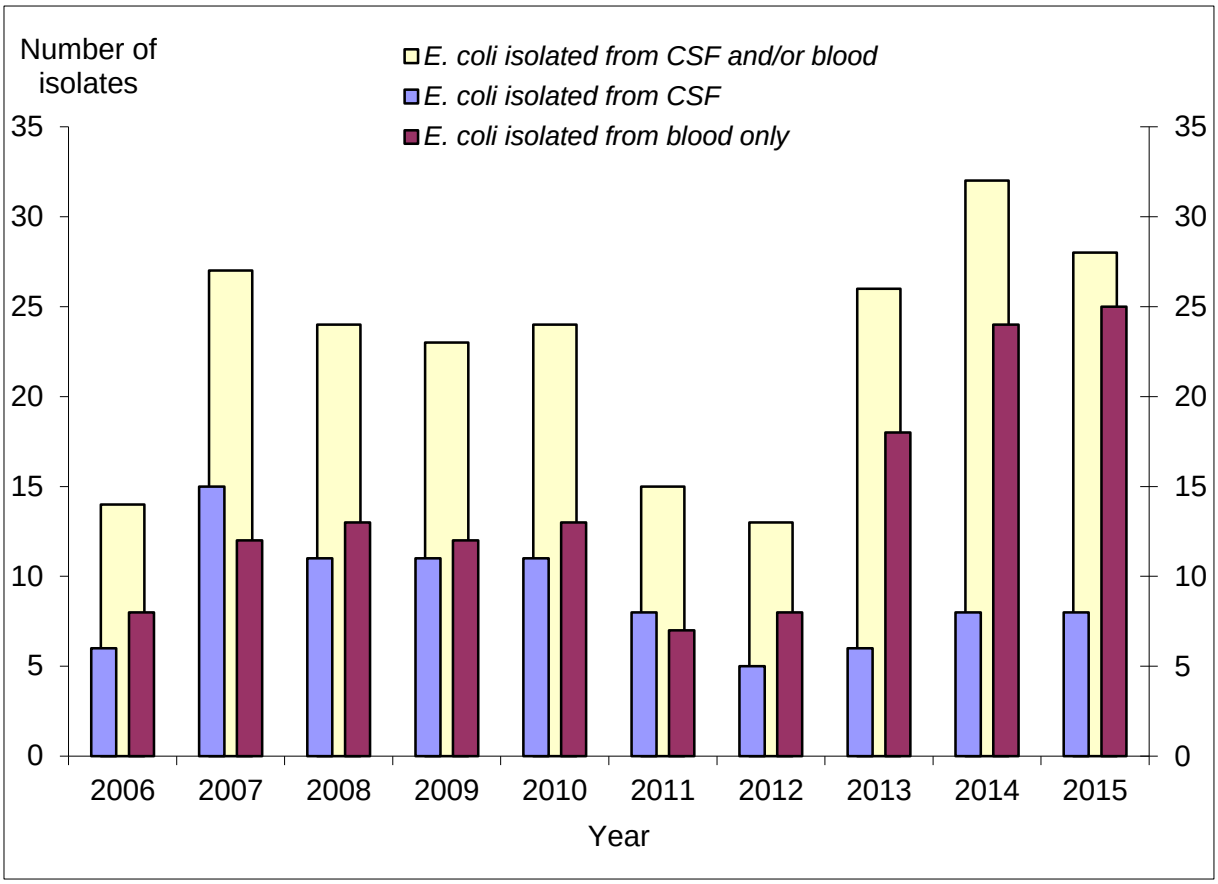


**Figure 7.1** *Distribution of E. coli, 2006-2015*

# 8 *STREPTOCOCCUS AGALACTIAE* – (group B)

In 2015 the Reference Laboratory received 65 *Streptococcus agalactiae* isolates, lower than that in the previous years (2015: 65; 2014: 71; 2013: 72; 2012: 80, figure 8.1). Nine-teen *S. agalactiae* isolates were from CSF (or CSF and blood) and 46 from blood only (table 8.1, 8.2 and 8.3). Eighty percent of the cases occurred in the first month of life. Serotype III was the most prevalent (table 8.1). In addition, the absolute number as well as the proportion of serotype Ia isolates increased (2014: 6 (8.5%); 2015: 16 (25%).

Table 8.1 Serotypes of *S. agalactiae* isolates from CSF and/or blood, by age of patients, 2015

| TYPE | AGE ( MONTHS) | | | AGE (YEARS) | | | | | TOTAL | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | 1-11 | 12-59 | 0-4 | 5-9 | 10-19 | 20-49 | ≥50 | Total | % |
| **Ia** | 12 | 2 | 0 | 14 | 0 | 0 | 0 | 2 | **16** | ***25*** |
| **Ib** | 5 | 0 | 0 | 5 | 0 | 0 | 1 | 0 | **6** | ***9*** |
| **II** | 5 | 0 | 0 | 5 | 0 | 0 | 0 | 0 | **5** | ***8*** |
| **III** | 29 | 5 | 0 | 34 | 0 | 0 | 0 | 2 | **36** | ***55*** |
| **IV** | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | **2** | ***3*** |
| **Total** | **52** | **7** | **0** | **59** | **0** | **0** | **2** | **4** | **65** | ***100*** |
| **%** | ***80*** | ***11*** | ***0*** | ***91*** | ***0*** | ***0*** | ***3*** | ***6*** | ***100*** | |

Table 8.2 Serotypes of *S. agalactiae* isolates from CSF (or CSF and blood), by age of patients, 2015

| TYPE | AGE ( MONTHS) | | | AGE (YEARS) | | | | | TOTAL | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | 1-11 | 12-59 | 0-4 | 5-9 | 10-19 | 20-49 | ≥50 | Total | % |
| **Ia** | 2 | 1 | 0 | 3 | 0 | 0 | 0 | 2 | **5** | ***26*** |
| **Ib** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **0** | ***0*** |
| **II** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **0** | ***0*** |
| **III** | 10 | 2 | 0 | 12 | 0 | 0 | 0 | 1 | **13** | ***69*** |
| **IV** | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | **1** | ***5*** |
| **Total** | **12** | **3** | **0** | **15** | **0** | **0** | **1** | **3** | **19** | ***100*** |
| **%** | ***63*** | ***16*** | ***0*** | ***79*** | ***0*** | ***0*** | ***5*** | ***16*** | ***100*** | |

Table 8.3 Serotypes of *S. agalactiae* isolates from blood only, by age of patients, 2015

| TYPE | AGE ( MONTHS) | | | AGE (YEARS) | | | | | TOTAL | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | 1-11 | 12-59 | 0-4 | 5-9 | 10-19 | 20-49 | ≥50 | Total | % |
| **Ia** | 10 | 1 | 0 | 11 | 0 | 0 | 0 | 0 | **11** | ***24*** |
| **Ib** | 5 | 0 | 0 | 5 | 0 | 0 | 1 | 0 | **6** | ***13*** |
| **II** | 5 | 0 | 0 | 5 | 0 | 0 | 0 | 0 | **5** | ***11*** |
| **III** | 19 | 3 | 0 | 22 | 0 | 0 | 0 | 1 | **23** | ***50*** |
| **IV** | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | **1** | ***2*** |
| **Total** | **40** | **4** | **0** | **48** | **0** | **0** | **1** | **1** | **46** | ***100*** |
| **%** | ***87*** | ***9*** | ***0*** | ***96*** | ***0*** | ***0*** | ***2*** | ***2*** | ***100*** | |

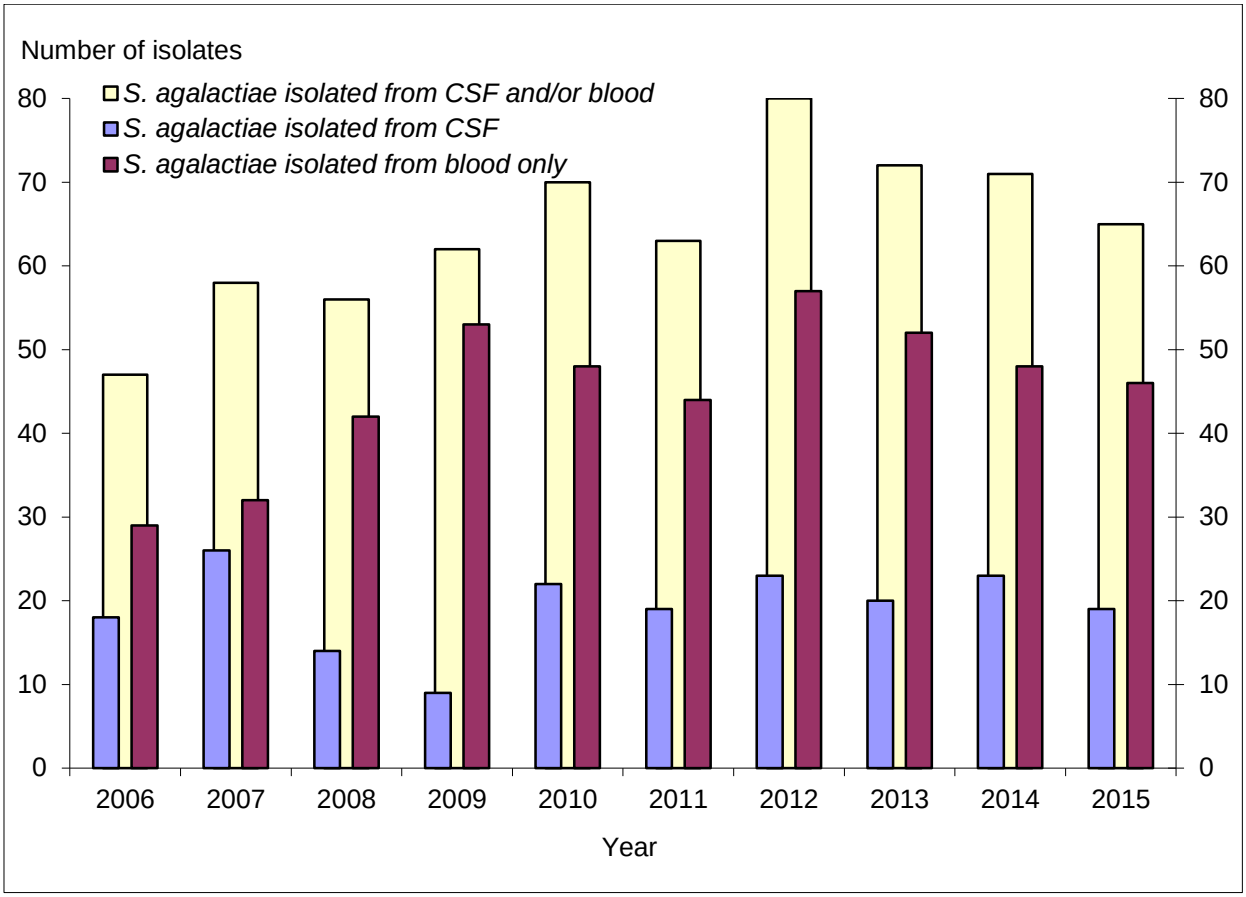


**Figure 8.1** *Distribution of S. agalactiae, 2006-2015*

# 9 *LISTERIA MONOCYTOGENES*

Fourty-Seven strains of *Listeria monocytogenes* were submitted to the Reference Laboratory. Eight isolates were from CSF (or CSF and blood) and 39 from blood only (figure 9.1). (2014: 19 CSF and 51 blood only; 2013: 6 CSF and 46 blood only). Most cases (88%) occurred among persons older than 50 years. In 2015 (as in previous years) serotypes 1/2a and 4b were most prevalent (table 9.1).

Table 9.1 *L. monocytogenes* isolates from CSF/blood, by type and age of patients, 2015

| TYPE | AGE ( MONTHS) | | | AGE (YEARS) | | | | | TOTAL | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | 1-11 | 12-59 | 0-4 | 5-9 | 10-19 | 20-49 | ≥50 | T | % |
| **1/2a** | 1 | 0 | 0 | 1 | 0 | 1 | 2 | 17 | **21** | ***45*** |
| **1/2b** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 6 | **6** | ***13*** |
| **1/2c** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | **1** | ***2*** |
| **3c** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | **1** | ***2*** |
| **4b** | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 16 | **18** | ***38*** |
| **Total** | **2** | **0** | **0** | **2** | **0** | **1** | **3** | **41** | **47** | ***100*** |
| **%** | ***4*** | ***0*** | ***0*** | ***4*** | ***0*** | ***2*** | ***6*** | ***88*** | ***100*** | |

Table 9.2 *L. monocytogenes* isolates from CSF (or CSF and blood), by type and age, 2015

| TYPE | AGE ( MONTHS) | | | AGE (YEARS) | | | | | TOTAL | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | 1-11 | 12-59 | 0-4 | 5-9 | 10-19 | 20-49 | ≥50 | T | % |
| **1/2a** | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 2 | ***25*** |
| **1/2b** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **0** | ***0*** |
| **1/2c** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **0** | ***0*** |
| **3c** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **0** | ***0*** |
| **4b** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 6 | **6** | ***75*** |
| **Total** | **0** | **0** | **0** | **0** | **0** | **1** | **0** | **7** | **8** | ***100*** |
| **%** | ***0*** | ***0*** | ***0*** | ***0*** | ***0*** | ***12*** | ***0*** | ***88*** | ***100*** | |

Table 9.3 *L. monocytogenes* isolates from blood only, by serotype and age, 2015

| TYPE | AGE ( MONTHS) | | | AGE (YEARS) | | | | | TOTAL | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | 1-11 | 12-59 | 0-4 | 5-9 | 10-19 | 20-49 | ≥50 | T | % |
| **1/2a** | 1 | 0 | 0 | 1 | 0 | 1 | 1 | 16 | **19** | ***49*** |
| **1/2b** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 6 | **6** | ***15*** |
| **1/2c** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | **1** | ***3*** |
| **3c** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | **1** | ***3*** |
| **4b** | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 10 | **12** | ***30*** |
| **Total** | **2** | **0** | **0** | **2** | **0** | **1** | **2** | **34** | **39** | ***100*** |
| **%** | ***5*** | ***0*** | ***0*** | ***5*** | ***0*** | ***3*** | ***5*** | ***87*** | ***100*** | |

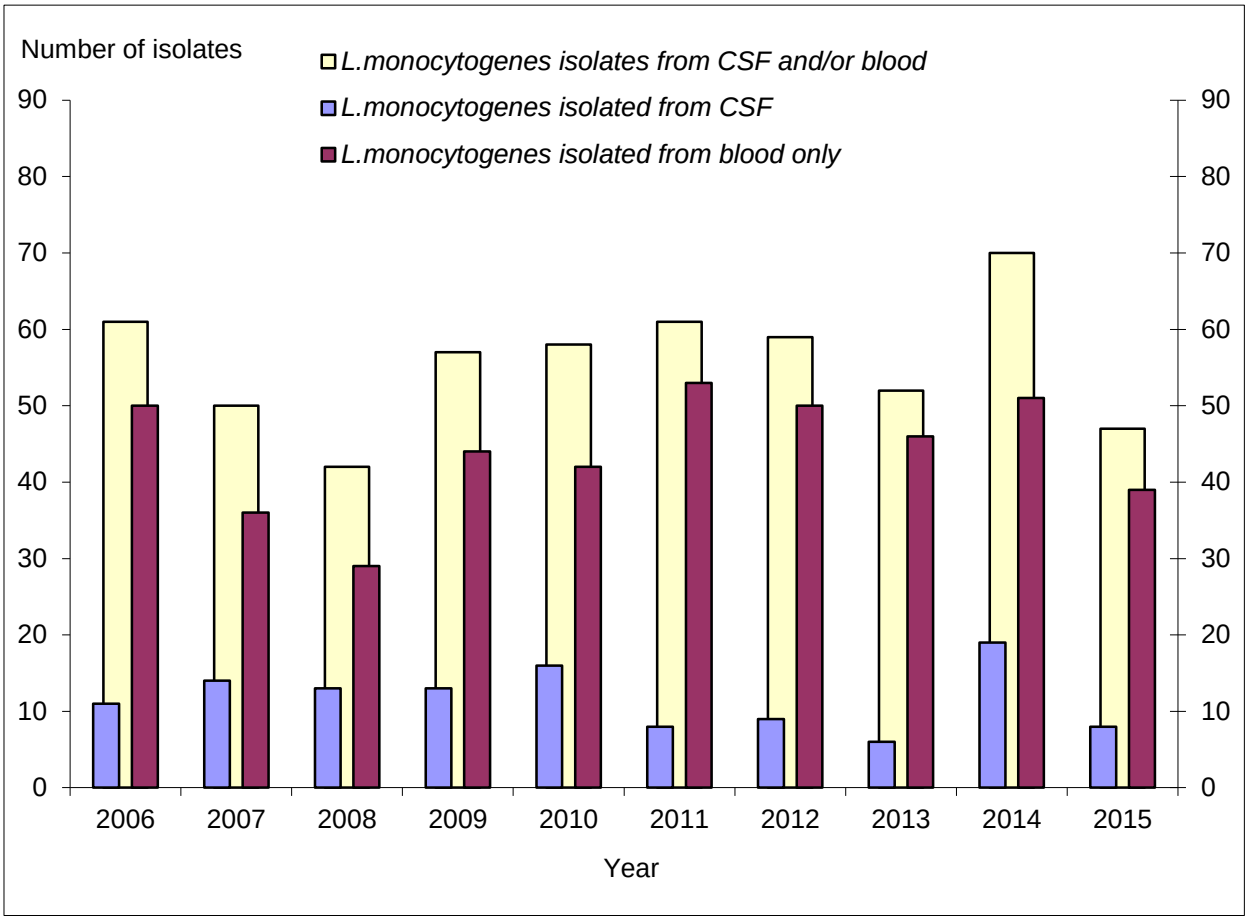


**Figure 9.1** *Distribution of L. monocytogenes, 2006-2015*

# 10 *STREPTOCOCCUS PYOGENES*

Fifteen *Streptococcus pyogenes* isolates were submitted to the Reference Laboratory, 3 isolated from CSF (or CSF and blood) and 13 from blood only.

Table 10.1 *S. pyogenes* isolates from CSF and/or blood received in 2015 according to source of isolation and age

| TYPE | AGE ( MONTHS) | | | AGE (YEARS) | | | | | TOTAL | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | 1-11 | 12-59 | 0-4 | 5-9 | 10-19 | 20-49 | ≥50 | T | % |
| **CSF** | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 2 | **3** | ***19*** |
| **Blood** | 0 | 1 | 5 | 6 | 1 | 1 | 1 | 4 | **13** | ***81*** |
| **Total** | **0** | **1** | **5** | **6** | **1** | **1** | **2** | **6** | **16** | ***100*** |
| **%** | ***0*** | ***6.25*** | ***31.25*** | ***37.5*** | ***6.25*** | ***6.25*** | ***12.5*** | ***37.5*** | ***100*** | |

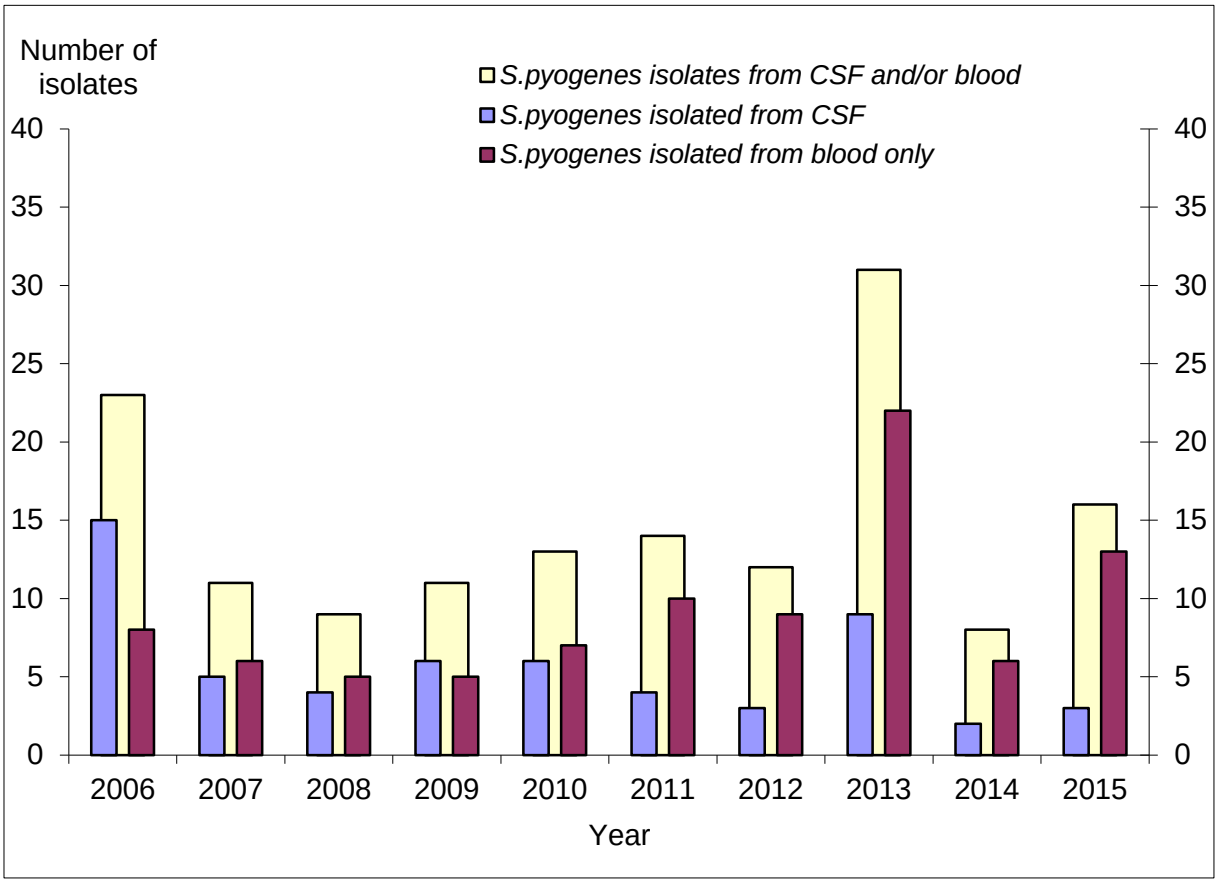


**Figure 10.1** *Distribution of S. pyogenes, 2006-2015*

# 11 ANTIGEN AND DNA DETECTION

The Reference Laboratory received 150 culture-negative specimens of CSF, serum or other body fluids for antigen or DNA detection. Polyclonal antibodies were used in latex-agglutination. PCR was performed with primers and probes specific for *N. meningitidis* (targeted on the *ctrA* gene) and for *S. pneumoniae* (targeted on the *pia* gene). When CSF was positive in the meningococcal PCR, it was then subjected to serogroup-specific PCR.

Of 150 specimens, 23 (15 %) were positive by agglutination or PCR. Eight (6 CSF and 2 DNA samples isolated from a skinbiopsy) were positive for *N. meningitidis* and 15 (14 CSFand 1 serum) were positive for *S. pneumoniae*.

Thus, in 2015, PCR-positive, culture-negative CSF samples accounted for 20 % of cases of meningococcal meningitis registered in the database of the Reference Laboratory. For *S. pneumoniae*, this percentage was 9%.

Table 11.1 CSF and serum samples, tested for antigens or DNA, 2015

| Antigen of | CSF (or DNA from CSF) | SERA | Other | TOTAL |
|---|---|---|---|---|
| ***C. neoformans*** | 0 | 1 | 0 | **1** |
| ***H. influenza type b*** | 0 | 0 | 0 | **0** |
| **DNA of** | | | | |
| ***N. meningitidis*** | 1 | 0 | 0 | **1** |
| ***N. meningitidis group B*** | 6 | 0 | 0 | **6** |
| ***N. meningitidis group C*** | 1 | 0 | 0 | **1** |
| ***S. pneumoniae*** | 14 | 1 | 0 | 15 |
| **Sub Total** | **22*** | **1** | **0** | **23** |
| **Antigen and PCR negative** | 120 | 4 | 3 | **127** |
| **Total** | **142** | **5** | **3** | **150** |

* From 3 patients with a *S. pneumoniae* isolated from blood, the CSF was culture-negative but PCR-positive for pneumococcal DNA.
From 3 patients with a *N. meningitidis* isolated from blood, the CSF was culture-negative but PCR-positive for meningococcal group B DNA.

# 12 VACCINATION PROSPECTS

## *12.1 N. meningitidis*

In the Netherlands, vaccination against serogroup C meningococcal disease has been introduced in June, 2002. All children born on or after June 1st, 2001 are vaccinated at the age of 14 months as part of the regular National Immunisation Programme. In addition, between June, 2002 and October, 2002 children and adolescents from 14 months to 19 years have been vaccinated. In 2015, 7 cases of meningococcal disease (8.31% of all cases, table 4.4) were due to serogroup C meningococci (2014: 4.1%; 2013: 5.4%; 2012: 2.5%; 2011: 3.3%; 2010: 4.5%; 2009: 6.5%; 2002: 36%). Five patients were not vaccinated because of age (2 and 8 months and 68, 71 and 76 years of age. From 2 patients who should have been vaccinated, the vaccine status is unknown. This indicates that the vaccination programme is successful. (figure 12.1)

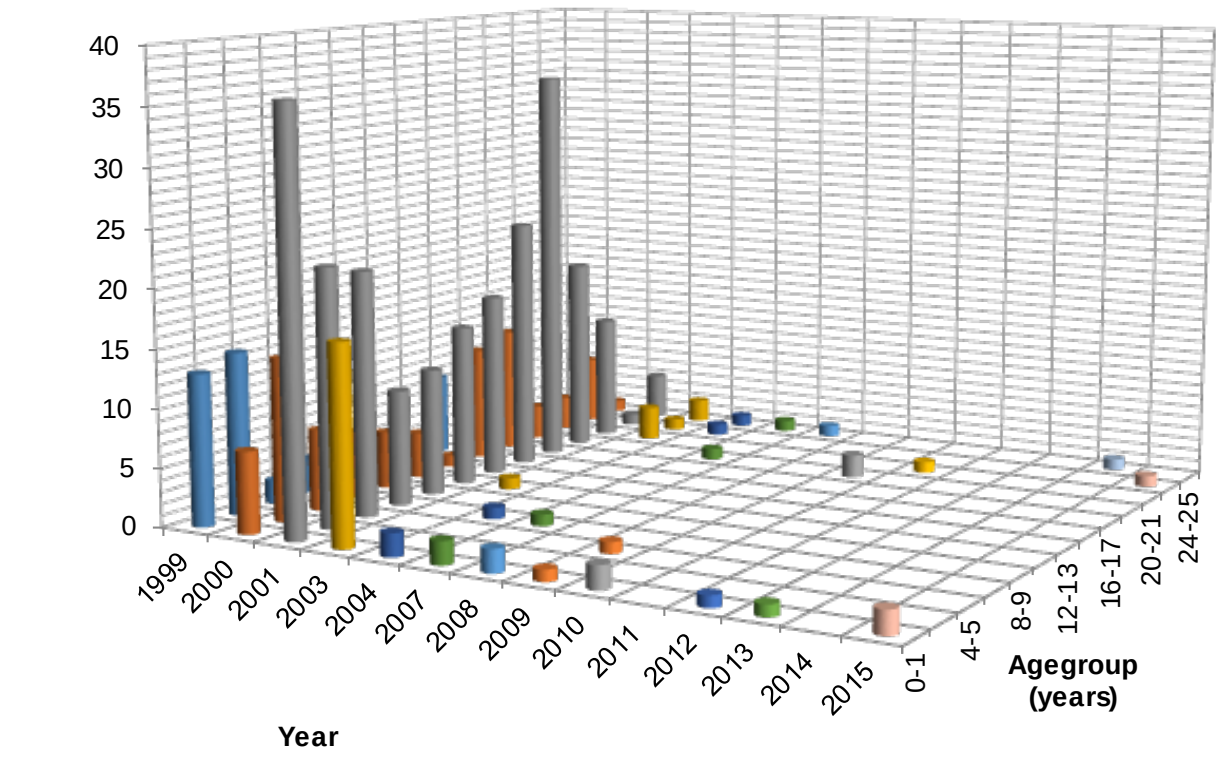


**Figure 12.1** *Age distribution of N.meningitidis serogroup C invasive disease in the first 24 years of life, 1999-2015.*

A PorA-based protein vaccine composed of nine different genosubtypes (P1.7,16; P1.5-1,2-2; P1.19,15-1; P1.5-2,10; P1.12-1,13; P1.7-2,4; P1.22,14; P1.7-1,1 and P1.18-1,3,6), if available, would have prevented 53 cases (86%; table 4.9) of serogroup B meningococcal disease and 62 (74%) of all 84 cases of meningococcal disease.

## *12.2 H. influenzae*

The existing *H. influenzae* vaccine consists of the type b polysaccharide conjugated to a protein, tetanus toxoid. Since July 1993, children born after the first of April 1993 are vaccinated with the PRP-T vaccine, at first at the age of 3, 4, 5, and 11 months, and since 1999 at the age of 2, 3, 4 and 11 months. The effect of vaccination on the frequency of *H. influenzae* meningitis cases is shown in figure 12.2. The number of *H. influenzae* meningitis cases gradually decreased since the introduction of the vaccine, while the number of meningitis cases caused by *H. influenzae* non-type b did not alter. In 2014, the number of invasive isolates of *H. influenzae* type b, received from patients that should have been vaccinated (<22 years of age) increased from 12 to 14 in 2015 (2014: 12; 2013: 14; 2012: 11; 2011: 7) (figure 12.2 and 12.3). Of those 14 patients, Five had received all doses, one received three doses and one received only one doses of the vaccine. Seven patients were not vaccinated.

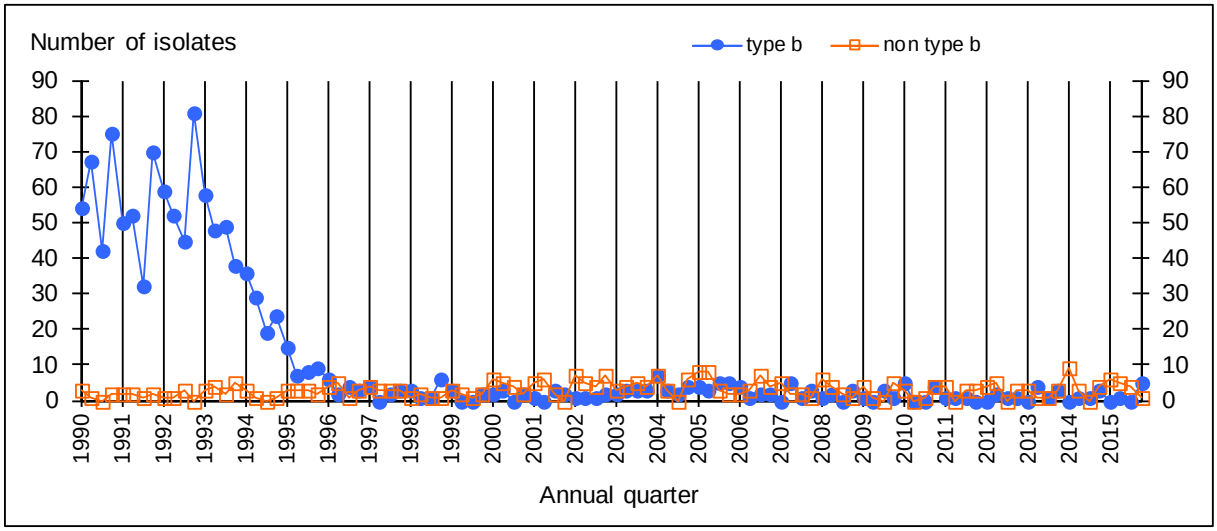


**Figure 12.2** *The distribution of H. influenzae type b and non-type b meningitis cases according to annual quarter, 1990 –2015*

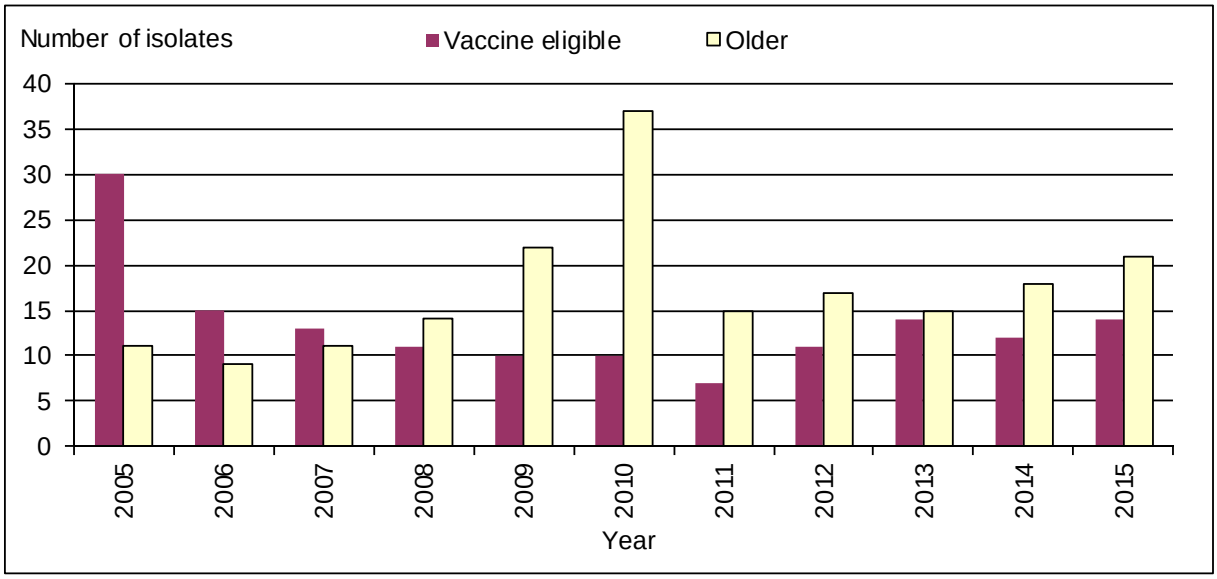


**Figure 12.3** *The distribution of H. influenzae type b cases (CSF or blood) among patients eligible for vaccination and among older patients, 2005 –2015*

## *12.3 S. pneumoniae*

The pneumococcal conjugated polysaccharide vaccine contains 7 serotype-specific polysaccharides linked to inactive diphtheria toxin (7-valent polysaccharide conjugate vaccine. PCV7). Since July 2006, children born after the first of April 2006 are vaccinated with this vaccine at age of 2, 3, 4 and 11 months. In April 2011 the 10-valent vaccine (PCV10) was introduced for all newborns born since March 1, 2011. In 2015, four percent of the CSF isolates were of a serotype covered by this hepta-valent conjugate polysaccharide vaccine, while 9.5% of the isolates were covered by the 10-valent vaccine (table 6.6). In 2015 the proportion of CSF isolates with a PVC7 serotype was lower than that in previous years (2015: 4%; 2014: 5%; 2013: 5%; 2012:11% ; 2011:12%; 2010: 12%; 2009: 18%; 2008: 35%; 2007: 42%; 2006: 56%; 2005: 46%; 2004: 53%; 2003: 52%), as a result of the vaccination. There were 6 patients with invasive pneumococcal disease due to pneumonococci with a vaccine (PVC7) serotype (6B, 14, 18C, 19F and 23F) and 8 patients with invasive pneumococcal disease due to pneumonococci with a vaccine (PVC10-7) serotype (1 and 7 times 7F). Those 14 patients were not vaccinated because of age. The beneficial effect of vaccination is partly abrogated by an increase of the number of cases due to non-vaccine types (figure 12.4).

The pneumococcal non-conjugated polysaccharide vaccine contains 23 serotype-specific polysaccharides. Sixty percent of the CSF isolates were of a serotype which is represented in this vaccine (table 6.6) (2014: 73%; 2013: 71%; 2012: 77%; 2011: 87%; 2010: 84%; 2009: 85%; 2008: 89%; 2007: 90%).

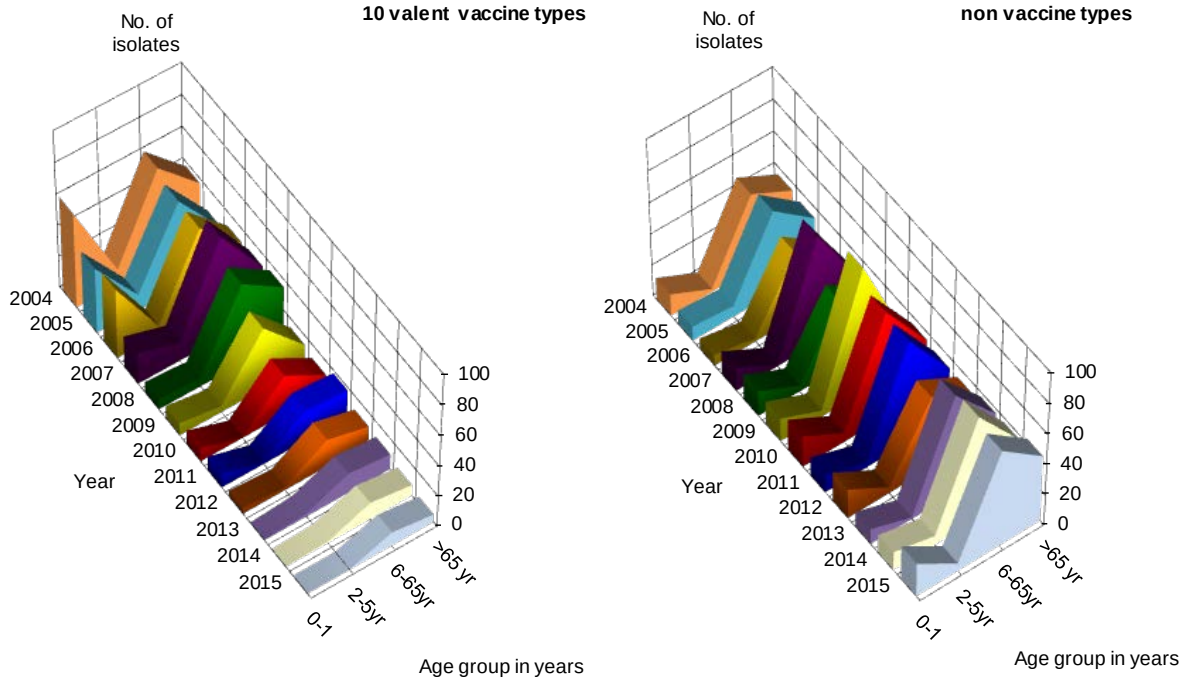


**Figure 12.4** *The age distribution of S.pneumoniae invasive disease due to pneumococci of serotypes included in the hepta-valent conjugated polysaccharide vaccine, 2004-2015. Left: vaccine types. Right: types not included in this 10 valent vaccine*

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