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**Nationales Referenzzentrum
für Meningokokken und *H. influenzae***

Data from the NRZMHi for *H. influenzae* in 2023

1. Introduction

The tasks of the National Reference Laboratory for Meningococci and *Haemophilus influenzae* (NRZMHi) assigned by the Robert Koch Institute for the surveillance of **invasive *Haemophilus influenzae* disease** include serotyping of clinical isolates from blood or cerebrospinal fluid (CSF) and the detection of antibiotic resistance against β-lactam antibiotics. In 2023, all in all 1471 submissions were analyzed including submissions from 1333 patients with invasive infections. The NRZMHi could confirm the diagnosis *Haemophilus influenzae* in 1310 cases where disease isolates were available. In three cases, *H. influenzae* was detected and serotyped by PCR from submitted DNA or native material. In three cases *H. parainfluenzae* and in one case *H. haemolyticus* from blood was detected. Furthermore, thirteen *H. influenzae* isolates derived from primarily sterile sites other than blood or CSF. These cases do not meet the criteria of the reference definition for a notifiable invasive infection.

In 1276 invasive cases, *H. influenzae* was detected from blood, in 37 invasive cases from cerebrospinal fluid (CSF) only. Additionally, there was one invasive case where *H. influenzae* was isolated from both, blood and cerebrospinal fluid (CSF). Detection of *H. influenzae* from these materials must be notified according to the German Infection Protection Act (IfSG).

As in previous years, the majority of blood or CSF isolates was uncapsulated, also known as non-typable *H. influenzae* (NTHi, 1146 isolates, 87 %), followed by Hif as the most frequent capsular serotype (90 cases; 7 %). In 2023 Hie showed the third highest frequency among the serotypes (28 cases; 2,1 %), followed by Hia (25 cases, 1,9 %). Hib was found in 24 cases (1,8 %). Neither Hic, nor Hid were isolated.

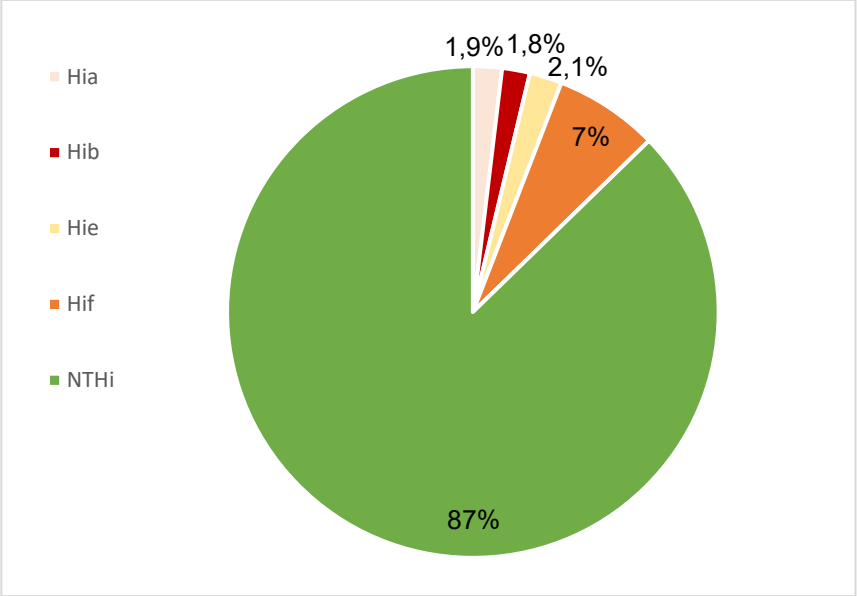
Among the analyzed cases, the age group most affected was > 40 years (1164 cases; 89 % of all cases). In addition, a significant percentage of cases (63 cases; 4,6 %) was found in children aged <5 years, 3,6 % (47 cases) of which was <1 year.

The NRZMHi analyzed the frequency of ampicillin resistance using gradient agar diffusion tests. In three of the total of 1313 cases, no viable isolate was available for testing. 327 isolates (25 %) were ampicillin resistant (MIC > 1 µg/ml), of which 214 (16 % of all tested isolates) showed β-lactamase production. The NRZMHi has tested all isolates for cefotaxime susceptibility. Resistance to cefotaxime was found in 19 isolates (1,5 %).

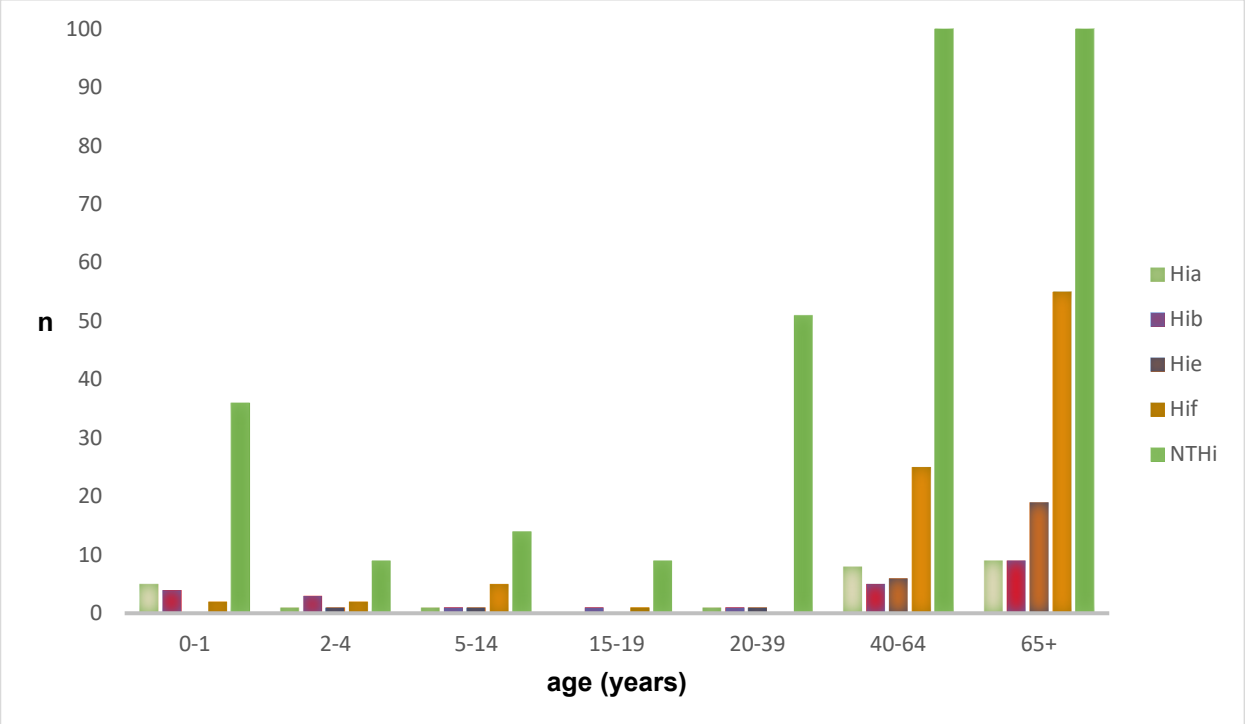
In 2023, the statutory notification system registered 1729 invasive *H. influenzae* infections. Since the NRZMHi transmits all laboratory results to the local health authorities in charge, the coverage of the laboratory surveillance can be estimated based on these data. Thus, a coverage of 76 % can be assumed for 2023.
In 2023, the number of cases of invasive *H. influenzae* infections continued to rise compared to the years in the COVID-19 pandemic from 2020-2022 and has already far exceeded the pre-pandemic level. The proportion of unencapsulated strains increased compared to 2022,

mainly due to an increased number of cases in the > 40 age group. Among the encapsulated strains, the proportion of Hie increased, but in percentage terms the number of cases remained roughly the same at 2% compared to 2022. The increased proportion of Hia, which now exceeds that of Hib, is striking. The rate of resistance to amipicillin has also increased. Resistance to cefotaxime has decreased from 2% to 1.5%. Resistance to cefotaxime is typically infrequent and sporadic. [1, 2]

2. Serotype distribution of *H. influenzae* isolates from blood or CSF in 2022



3. Age distribution of patients with *H. influenzae* detected in blood or CSF

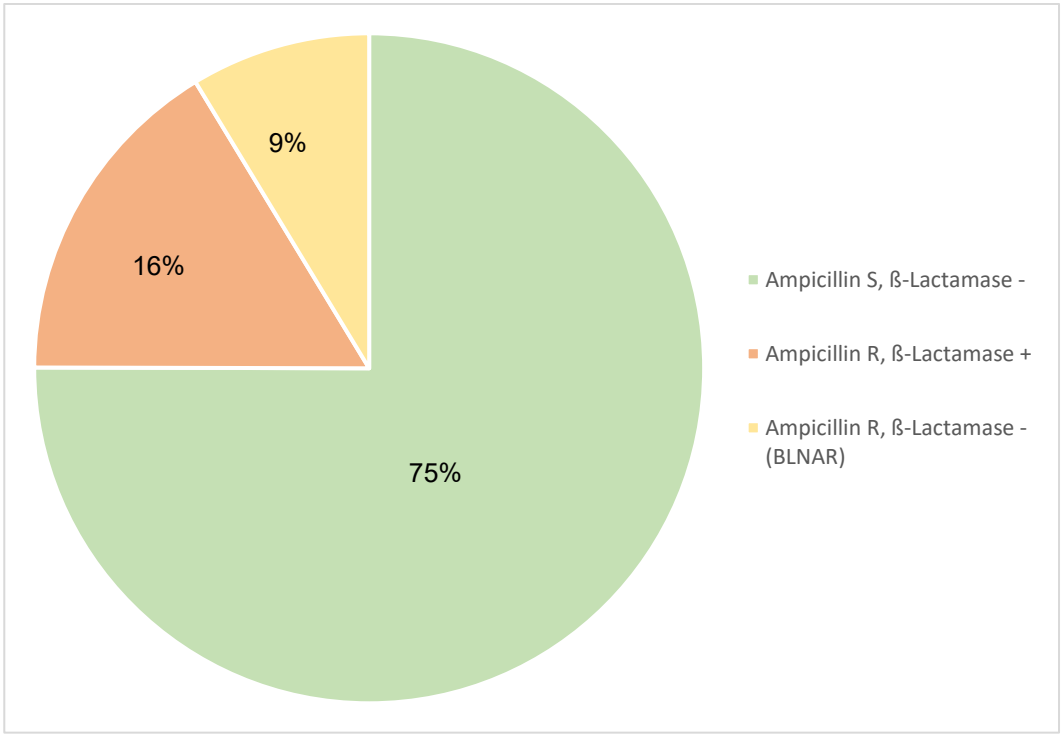


4. Serotype distribution in Federal States

	BW	BY	BE	BB	HB	HH	HE	MV	NI	NW	RP	SL	SN	ST	SH	TH	n.n.	Summe
Hia	**5**	0	**3**	**3**	0	0	**1**	0	**2**	**5**	**1**	0	**3**	**2**	0	0	0	25
Hib	**3**	**1**	**2**	0	0	**2**	**1**	0	**6**	**7**	0	**1**	**1**	0	0	0	0	24
Hic	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hid	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hie	**3**	**2**	**3**	**1**	**2**	**1**	**1**	0	**3**	**6**	**3**	**2**	0	0	**1**	0	0	28
Hif	**14**	**1**	**2**	**2**	0	**4**	**14**	0	**6**	**15**	**4**	**1**	**5**	**1**	**3**	0	0	90
NTHi	**155**	**185**	**63**	**58**	**11**	**30**	**60**	**21**	**99**	**239**	**42**	**15**	**81**	**18**	**33**	**27**	**9**	1149
Total	180	207	73	64	13	37	77	21	116	272	50	19	90	21	37	27	9	1316

BW: Baden-Württemberg, BY: Bayern, BE: Berlin, BB: Brandenburg, HB: Bremen, HH: Hamburg, HE: Hessen, MV: Mecklenburg-Vorpommern, NI: Niedersachsen, NW: Nordrhein-Westfalen, RP: Rheinland-Pfalz, SL: Saarland, SN: Sachsen, ST: Sachsen-Anhalt, SH: Schleswig-Holstein, TH: Thüringen

5. Ampicillin resistance in isolates *H. influenzae* from blood or CSF



6. References

1. Tonnessen, R., et al., *Molecular epidemiology and antibiotic resistance profiles of invasive Haemophilus influenzae from Norway 2017-2021.* Front Microbiol, 2022. **13**: p. 973257.
2. Nurnberg, S., et al., *Cefotaxime resistance in invasive Haemophilus influenzae isolates in Germany 2016-19: prevalence, epidemiology and relevance of PBP3 substitutions.* J Antimicrob Chemother, 2021. **76**(4): p. 920-929.