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# Chapter 4

## Community-acquired *Haemophilus influenzae* meningitis in adults

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## Abstract

*Haemophilus influenzae* is an uncommon cause of bacterial meningitis in adults. This report describes a prospective evaluation of 16 episodes of community-acquired *H. influenzae* meningitis in a nationwide study on bacterial meningitis. Predisposing conditions were present in eight (50%) of the 16 episodes; the most common predisposing conditions were otitis or sinusitis (five episodes; 31%) and remote neurosurgery or head trauma (three episodes; 19%). One (6%) episode was fatal and hearing loss occurred in four (25%) episodes. It was concluded that *H. influenzae* meningitis in adults is a disease with a rather benign clinical course and a relatively good prognosis compared with pneumococcal meningitis.

## Introduction

*Haemophilus influenzae* meningitis occurs sporadically in adults and has been described in small retrospective case series as a disease following remote head trauma or neurosurgery, or in patients with predisposing conditions.<sup>1-5</sup> A recent report described a prospective nationwide cohort study in The Netherlands that involved 696 adults with community-acquired bacterial meningitis.<sup>6</sup> The present report describes the clinical features, complications and outcome for adults in the cohort with *H. influenzae* meningitis.

## Methods

The methods used have been described previously.<sup>6</sup> In brief, eligible patients were aged >16 years, had bacterial meningitis confirmed by culture of cerebrospinal fluid (CSF), and were listed in the database of The Netherlands Reference Laboratory for Bacterial Meningitis between October 1998 and April 2002. The treating physician was contacted and informed consent was obtained from participating patients or their legal representatives. The study was also approved by the local ethics committee. Patients with hospital acquired meningitis (defined as meningitis that occurred during hospitalisation or within 1 week of discharge), neurosurgical devices and/or a history of recent (within 1 month) head trauma or neurosurgery were excluded. Patients with an altered immune status caused by use of immunosuppressive drugs, splenectomy, diabetes mellitus or alcoholism were considered to be immunocompromised. Predisposing factors for developing bacterial meningitis were defined as otitis, sinusitis, pneumonia, an immunocompromised state, remote neurosurgery and remote head trauma (occurring <1 month before the onset of meningitis). Patients underwent a neurological examination at discharge, and outcome was graded with the Glasgow outcome scale. Complaints of hearing loss were confirmed by an audiogram examination.

## Results

All patients with bacterial meningitis and CSF cultures positive for *H. influenzae* were included in this study. In total, 16 episodes of community-acquired *H. influenzae* meningitis were identified in 15 patients (Table 1). The calculated annual incidence was 0.04 cases / 100 000 adults. Predisposing conditions were present in eight (50%) of 16 episodes. The most common predisposing conditions were otitis or sinusitis (five episodes; 31%) and remote neurosurgery or head trauma (three episodes; 19%). A previous episode of meningitis had occurred for three (19%) of the 16 episodes. The clinical severity upon presentation was relatively mild, with only one (6%) episode having a change in mental status (defined as a Glasgow Coma Score <14); none of the patients had focal cerebral

**Table 1.** Clinical, laboratory and radiological characteristics upon admission for 16 episodes of community-acquired *Haemophilus influenzae* meningitis.<sup>a</sup>

Characteristic	Frequency (%)	Characteristic	Frequency (%)
Mean age (SD)	47 (9)	Focal neurologic deficits	
Male gender	9/16 (56%)	Focal cerebral deficits <sup>c</sup>	0
Predisposing factors		Cranial nerve palsies	1/16 (6%)
Immunocompromised state	1/16 (6%)	Laboratory examination <sup>d</sup>	
Pneumonia	1/16 (6%)	Indices of CSF inflammations	
Otitis or sinusitis	5/16 (31%)	Opening pressure mm of water	360 (300-480)
Remote neurosurgery <sup>b</sup>	3/16 (19%)	White cell count per mm <sup>3</sup>	3337 (115-38784)
Remote head trauma	1/16 (6%)	<100/mm <sup>3</sup>	0
CSF leak	1/16 (6%)	100-999/mm <sup>3</sup>	1/16 (6%)
Recurrent meningitis	3/16 (19%)	>999/mm <sup>3</sup>	15/16 (94%)
Pretreated with antimicrobial agents	1/16 (6%)	Protein g/L	2.58 (1.3-3.8)
Duration of symptoms <24 hours	4/15 (27%)	CSF/serum glucose ratio	0.07 (0.0-0.28)
Seizures	0	CSF Gram's stain	
Symptoms upon presentation		Negative	9/15 (60%)
Headache	16/16 (100%)	Gram-negative bacilli	5/15 (33%)
Nausea	15/16 (94%)	Gram-negative cocci	1/15 (7%)
Neck stiffness	12/16 (75%)	Blood culture	
Temperature ≥38° C	11/14 (79%)	<i>H. influenzae</i>	6/11 (56%)
Glasgow Coma Scale score upon presentation		Negative	5/11 (44%)
Median (SD)	15 (0.8)	Radiological evaluation	
<14 (indicating altered mental status)	1/16 (6%)	Computer tomography (CT) brain scan	9/16 (63%)
<8 (indicating coma)	0	Abnormal CT brain scan	3 <sup>e</sup> /9 (33%)
Triad of fever, neck stiffness, and change in mental status	1/16 (6%)	CT before lumbar puncture	6/9 (67%)

<sup>a</sup> Continuous data are denoted as the median value (range) unless otherwise stated. <sup>b</sup> Two acoustic neurinomas, one trauma. <sup>c</sup> Aphasia, monoparesis or hemiparesis. <sup>d</sup> CSF pressure was measured in three episodes; CSF white cell count was determined in 16 episodes; CSF protein concentration was determined in 13 episodes; CSF/serum glucose ratio was determined in 12 episodes. <sup>e</sup> Post-operative defects; sinusitis; combination of a sub-arachnoid cyst and pneumatocephalus. CSF denotes cerebrospinal fluid.

deficits upon admission. All patients underwent a lumbar puncture. At least one individual CSF finding predictive of bacterial meningitis (glucose <1.9 mmol/L, CSF serum glucose ratio <0.23, protein concentration >2.20 g/L, white cell count >2000 cells/mm<sup>3</sup> or CSF neutrophil count >1180 cells/mm<sup>3</sup>)<sup>7</sup> was observed in 15 (94%) of the 16 episodes. Complications developed in a relatively low proportion of patients (Table 2). One (6%) patient died after developing hemiparesis, impaired consciousness and septic shock, but all other patients had a good recovery. Hearing impairment was found at discharge in four (27%) of 15 episodes, and memory deficits were reported in one (7%) episode.

Serotyping of *H. influenzae* was performed on 15 isolates and revealed one each of serotypes b, e and f, together with 12 non-typeable isolates. In one episode, the *H. influenzae* isolate was b-lactamase-positive; this isolate was of type b and caused the only fatal case in this case series. All cases received adequate microbiological cover by the initial therapy

**Table 2.** Therapy, complications during admission and outcome of cases of adult *H. influenzae* meningitis

Characteristic	Frequency (%)
Therapy	
Penicillin or amoxicillin	7/16 (44%)
Third-generation cephalosporin	4/16 (25%)
Combination	3/16 (19%)
Other	2/16 (13%)
Complications	
Cardiorespiratory failure	1/16 (6%)
Mechanical ventilation	1/16 (6%)
Seizures	1/16 (6%)
Impaired consciousness	4/16 (25%)
Hemiparesis	1/16 (6%)
Hearing impairment	4/16 (25%)
Scores on the Glasgow Outcome Scale	
1 (death)	1/16 (6%)
2 (vegetative state)	0/16
3 (severe disability)	0/16
4 (moderate disability)	0/16
5 (mild or no disability)	15/16 (94%)
Sequelae at discharge	
Hemiparesis	0/15
Hearing impairment	4/15 (27%)

administered. Adjunctive steroids were given to one patient after clinical deterioration. One patient was included in the European Dexamethasone Study and was randomised to the placebo group.<sup>8</sup>

## Discussion

Overall, these findings indicate that *H. influenzae* meningitis in adults is a relatively benign disease, especially in comparison with pneumococcal meningitis.<sup>6</sup> Only one patient presented with a change in mental status, although previous reports have described impaired consciousness in a greater proportion (16-67%) of patients with *H. influenzae* meningitis.<sup>4,5,9</sup> The benign character of this disease was also reflected in the low mortality rate (6%). Predisposing factors were present in 50% of the episodes, which corresponds with a previous description of predisposing conditions in 55% of 119 adults with *H. influenzae* meningitis.<sup>4</sup> The high percentage of patients with anatomical defects and ear or sinus infections as an underlying cause of *H. influenzae* meningitis justifies consultation with an otolaryngologist for this patient group.

Most (80%) *H. influenzae* isolates in this series were non-typeable, which corresponds with epidemiological trends observed after the introduction of Hib vaccination.<sup>10-12</sup> The single serotype b strain was b-lactamase-positive and caused sepsis and death, despite adequate antibiotic therapy. The most important mechanism of antibiotic resistance in *H.*

*influenzae* involves b-lactamase production, and occurs in 4-31% of all *H. influenzae* isolates worldwide.<sup>13,14</sup> Empirical therapy for *H. influenzae* should include a third-generation cephalosporin until susceptibility testing has been performed.<sup>2,14</sup>

The most common sequela was hearing loss, at 25%. This is an exceptionally high rate and is much higher than that described for children with *H. influenzae* meningitis.<sup>15,16</sup> A meta-analysis of children with *H. influenzae* meningitis found that adjunctive dexamethasone treatment was associated with a decline in the rate of hearing impairment.<sup>17</sup> In adults with bacterial meningitis, adjunctive dexamethasone therapy has now been established clearly to be beneficial.<sup>2,8,18,19</sup> Since this study was performed before routine use of dexamethasone in adults with bacterial meningitis, only one patient received treatment with dexamethasone, which was prompted by clinical deterioration.

This study has several limitations. First, only patients with a positive CSF culture were included.<sup>1,6</sup> However, the clinical presentation in patients with positive and negative CSF cultures was similar to that in previous studies.<sup>1,20</sup> In patients found to have space-occupying lesions following computed tomography scan, or with coagulation disorders or severe septic shock, lumbar puncture might not be performed or might be postponed, which can result in negative CSF cultures.<sup>6</sup> Therefore, these patient groups were probably only partly represented in the study.

## Conclusion

*H. influenzae* meningitis in adults is a disease with a rather benign clinical course and a relatively good prognosis, especially when compared with pneumococcal meningitis. Many adults with *H. influenzae* meningitis have predisposing conditions, and the need to consult an otolaryngologist concerning these patients is emphasised.

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