

# Evolution of the Bacteriologic Features of Persistent Acute Otitis Media Compared With Acute Otitis Media

## A 15-Year Study

Natalie Loundon, MD; Gilles Roger, MD; Hoang Vu Thien, MD; Pierre Bégue, MD; Erea N. Garabédian, MD

**Objectives:** To define the epidemiologic features of persistent acute otitis media (PAOM) and modifications of these features during the past 15 years and to investigate for possible differences in bacterial resistance between acute otitis media (AOM) and PAOM.

**Design:** Retrospective patient series.

**Setting:** Academic tertiary care center.

**Patients and Methods:** Persistent acute otitis media was defined as AOM lasting longer than 3 weeks despite 1 or several courses of antibiotic therapy, with the persistence of clinical and otoscopic signs of AOM. From 1982 to 1997, 475 children with PAOM were seen in our department. Every patient had 1 or several specimens of aspirations or swabs of spontaneous otorrhea (or both). Microbiologic characteristics of the isolated strains (including antibiotic susceptibility) were analyzed. Four successive series of specimens were analyzed—group 1: from October 1, 1982, to June 30, 1986 (136 patients); group 2: from January 1, 1987, to December 31, 1989 (165 patients); group 3: from January 1, 1992, to April 30, 1993 (73 patients); and group 4: from January 1, 1994, to January 31, 1997 (101 patients). During the same study periods, the bacteriologic results of patients with AOM in the same geographic region were recorded.

**Main Outcome Measures:** A longitudinal comparison between the groups of patients with PAOM and a cross-comparison within each group between patients with PAOM and those with AOM.

**Results:** Obtaining repeated and multiple specimens from patients with PAOM led to a progressive decrease in the

rate of sterile specimens, from 35.3% (group 1, 48 patients) to 14.9% (group 4, 15 patients) ( $P < .01$ ). During this period, the prevalence of *Streptococcus pneumoniae* increased in patients with positive culture results, from 18.2% (group 1, 16 of 88 patients) to 44.2% (group 4, 38 of 86 patients) ( $P < .001$ ). These strains rapidly and dramatically became resistant to penicillin (amoxicillin) (0% through 1989, 76.2% [16 of 21 patients] in 1993, and 97.4% [37 of 38 patients] in 1996) ( $P = .01$ ). The overall prevalence of *Haemophilus influenzae* remained stable (between 31.4% [27 of 86 patients] and 45.4% [40 of 88 patients]), but the proportion of  $\beta$ -lactamase-producing strains increased from 30.0% (group 1, 12 patients) to 55.6% (group 4, 15 patients) ( $P = .04$ ). The prevalences of *Pseudomonas aeruginosa* and *Staphylococcus aureus* did not vary significantly (from 23.1% [group 2, 30 patients] to 10.7% [group 3, 6 patients] and from 10.2% [group 1, 9 patients] to 4.6% [group 4, 4 patients], respectively). Comparing data from patients with PAOM with those with AOM revealed that the increased resistance of *H influenzae* and, in particular, of *S pneumoniae* was more rapid and more marked in patients with PAOM than in those with AOM (highest rate of resistance in AOM: 36.0% [271 of 753 specimens] and 50.6% [398 of 787 specimens] for *H influenzae* and *S pneumoniae*, respectively;  $P < .001$  for *S pneumoniae*).

**Conclusions:** The increase in bacterial resistance frequently encountered during otitis media is even more marked in patients with PAOM. The identification of the organism is essential when the otitis does not resolve, especially in patients with PAOM. Obtaining repeated specimens helps to decrease the rate of sterile cultures.

*Arch Otolaryngol Head Neck Surg.* 1999;125:1134-1140

From the Departments of Pediatric ENT (Drs Loundon, Roger, and Garabédian), Microbiology (Dr Vu Thien), and Infectious Diseases (Dr Bégue), Hôpital d'Enfants Armand Trousseau, Paris, France.

**A**CUTE OTITIS media is one of the main reasons for pediatric consultation. In the past several years, a worrying increase in the number of patients having therapeutic failure has been reported,<sup>1,2</sup> with an increased frequency of recurrent and long-lasting otitis. Bacterial ecological features have also

undergone modifications, with a rapidly growing emergence of *Streptococcus pneumoniae* strains with decreased sensitivity, or resistance, to penicillin and an increase in the proportion of  $\beta$ -lactamase-producing *Haemophilus influenzae*. An empirical approach is, therefore, brought into question, and it is essential to identify strains responsible for a treatment failure

## PATIENTS AND METHODS

Between 1982 and 1997, we performed a retrospective study of patients with PAOM observed by the Department of Pediatric ENT at the Armand Trousseau Hospital, Paris, France. Specimens were taken by different physicians and were not part of a specific trial protocol. The management of such patients, however, has always been performed in a uniform and systematic manner by all of the physicians in the department. Persistent acute otitis media was defined as an episode of acute otitis evolving for longer than 3 weeks despite 1 or several antibiotic treatments. In all the children, antibiotic therapy had failed at the time of their consultation in the department, thus justifying performing a paracentesis systematically to make a microbiological diagnosis. Clinically, otitis was diagnosed in the presence of otalgia, fever, alteration in the child's general state, or digestive disorders (diarrhea and vomiting) and confirmed otoscopically by a rounded tympanic membrane with retrotympanic effusion or recent otorrhea.

From October 1982 to January 1997, 475 children with PAOM were seen in our department. Children with transtympanic drains, chronic otorrhea, or tympanic perforation were excluded. Every patient had 1 aspiration after paracentesis, swab specimens of spontaneous otorrhea at the time of their first consultation, or both. Bilateral specimens were counted as 1 specimen per child. A therapeutic window of 24 to 48 hours was used, given that there were no complications related to the otitis and the patient's general state was satisfactory. If the findings of the direct examination were normal or the culture at 48 hours was negative for pathogens, a second specimen was taken. Swab specimens accounted for 20.2% of specimens in group 1 (27 patients) and 0% in the other groups.

Microaspiration tubes were used to collect specimens, and the tip was cut directly into a sterile container after the discharge was aspirated. The external acoustic meatus was not disinfected, but in patients with otorrhea, a superficial aspiration was performed before taking a more selective specimen near the tympanic membrane. The tube was delivered to the microbiology laboratory within 1 hour of taking the specimen. The specimen was cultured after direct examination. The pus contained in the aspiration tubes was seeded in 0.5 mL of nutrient broth and then cultured on blood and chocolate agar at 36°C in a carbon dioxide-enriched atmosphere. Microbiological characteristics and antibiotic susceptibility (by the gel diffusion test) of the isolated strains were analyzed. The microbiological techniques remained identical between 1982 and 1997.

Four successive series of specimens were analyzed: from October 1, 1982, to June 30, 1986 (136 patients: group 1), from January 1, 1987, to December 31, 1989 (165 patients: group 2), from January 1, 1992, to April 30, 1993 (73 patients: group 3), and from January 1, 1994, to January 31, 1997 (101 patients: group 4).

During the same study periods, the bacteriologic results of patients with AOM in the same geographic area were recorded.<sup>3-7</sup> The patients with AOM had been seen previously by their local practitioners, and a paracentesis was performed because of severe otalgia, fever, or both. None of these children had received any prior treatment. The data on these patients were obtained from published articles. These data were collected in the context of studies of bacteriologic evolution in AOM without an established therapeutic protocol. The results were analyzed for each time period, and intergroup analysis was performed using the  $\chi^2$  test.

Data are expressed as mean  $\pm$  SD.

or a protracted clinical course. Antibiotic therapy can be appropriately altered on the basis of specific epidemiologic and clinical data.

The aim of this study was to evaluate the changes in the epidemiologic features of persistent acute otitis media (PAOM) in the past 15 years and to compare these features with those of acute otitis media (AOM), in particular in patients with bacterial resistance.

## RESULTS

In total, 475 children had a specimen taken between 1982 and 1997. The age of the children included in the study ranged from 3 months to 6 years ( $13.5 \pm 8$  months). The male-to-female ratio was 1:2. The mean number of specimens per child, either unilateral or bilateral, was significantly lower in group 1 ( $1.1 \pm 0.2$ ) than in group 4 ( $1.3 \pm 0.3$ ) ( $P < .001$ ). Treatment was withheld for 24 to 48 hours in 25 (18.4%) of the 136 patients in group 1, which progressively increased to 60 (59.4%) of 101 patients in group 4 ( $P < .001$ ).

The bacteriologic results found in the patients with PAOM are shown in **Table 1**. The rate of sterile specimens decreased between 1982 and 1997 from 35.3% (48 of 136 patients) to 14.9% (15 of 101 patients) ( $P < .01$ ).

During this period, among cultures with positive results, the prevalence of *S pneumoniae* increased from 18.2% (16 of 88 patients, group 1) to 44.2% (38 of 86 patients, group 4) ( $P < .001$ ). These strains became increasingly resistant to penicillin: 0% through 1989, 76.2% (16/21) through 1993, and 97.4% (37/38) through 1996 ( $P = .01$ ).

The overall prevalence of *H influenzae* among patients with positive culture results did not differ significantly: between 45.4% (group 1:  $n = 40$ ) and 31.4% (group 4:  $n = 27$ ) ( $P > .05$ ). The rate of  $\beta$ -lactamase-producing strains increased from 30.0% (group 1:  $n = 12$ ) to 55.6% (group 4:  $n = 15$ ) ( $P = .04$ ).

Among patients with positive culture results, the prevalence of *Pseudomonas aeruginosa* did not vary significantly, from 17.0% (group 1:  $n = 15$ ) to 15.1% (group 4:  $n = 13$ ), with a minimum rate of 10.7% (group 3:  $n = 6$ ) and a maximum of 23.1% (group 2:  $n = 30$ ). Also, the prevalence of *Staphylococcus aureus* did not vary significantly, ranging from 10.2% (group 1) to 4.6% (group 4).

The analysis of organisms observed in AOM during the same periods and in the same region is detailed in **Table 2**. The groups consisted of children aged between 6 months and 5 years ( $24.4 \pm 17.1$  months).

**Table 1. Bacteriologic Results From Ear Specimens in Patients With Persistent Acute Otitis Media, 1982 to 1997\***

Results	Patient Group/Study Period			
	1/Oct 1982-Jun 1986 (n = 136)	2/Jan 1987-Dec 1989 (n = 165)	3/Jan 1992-Apr 1993 (n = 73)	4/Jan 1994-Jan 1997 (n = 101)
<i>Streptococcus pneumoniae</i>	16 (18.2)	27 (20.8)	21 (37.5)	38 (44.2)
PRP	0	0	16 (76.2)	37 (97.4)
<i>Haemophilus influenzae</i>	40 (45.4)	48 (36.9)	22 (39.3)	27 (31.4)
β-Lactamase-producing strains	12 (30.0)	13 (27.1)	12 (54.5)	15 (55.6)
<i>Pseudomonas aeruginosa</i>	15 (17.0)	30 (23.1)	6 (10.7)	13 (15.1)
<i>Staphylococcus aureus</i>	9 (10.2)	9 (6.9)	5 (8.9)	4 (4.6)
<i>Moraxella catarrhalis</i>	0	3 (2.3)	0	0
<i>Streptococcus pyogenes</i>	3 (3.4)	3 (2.3)	0	0
Miscellaneous	5 (5.7)	10 (7.7)	2 (3.6)	4 (4.6)
<b>Total Pathogens</b>	<b>88 (64.7)</b>	<b>130 (78.8)</b>	<b>56 (76.7)</b>	<b>86 (85.1)</b>
Sterile	48 (35.3)	35 (21.2)	17 (23.3)	15 (14.9)

\*Values are number (percentage). PRP indicates penicillin-resistant pneumococci.

**Table 2. Bacteriologic Results From Patients With Acute Otitis Media in the Paris, France, Region, 1982 to 1997, by Study Period\***

Results	Study Period			
	Narcy et al <sup>3</sup> (1982) (n = 461)	Gehanno et al <sup>4</sup> (1987-1989) (n = 422)	Berche et al <sup>5</sup> (1993) (n = 359)	Levy et al <sup>6</sup> and Berche et al <sup>7</sup> (1994-1997)† (n = 2445)
<i>Streptococcus pneumoniae</i>	69 (22.3)	81 (17.6)	86 (28.4)	787 (32.2)
PRP	0	6 (7.4)	43 (50.0)	398 (50.5)
<i>Haemophilus influenzae</i>	50 (25.5)	143 (46.6)	130 (42.9)	753 (30.8)
β-lactamase-producing strains	9 (18.0)	27 (18.9)	46 (35.4)	271 (36.0)
<i>Pseudomonas aeruginosa</i>	18 (5.8)	20 (6.5)	9 (3.7)	24 (1.0)
<i>Staphylococcus aureus</i>	65 (21.0)	28 (9.1)	12 (4.9)	74 (3.0)
<i>Moraxella catarrhalis</i>	0	12 (3.9)	24 (9.8)	599 (24.5)
<i>Streptococcus pyogenes</i>	37 (12.0)	7 (2.3)	6 (2.4)	49 (2.0)
Miscellaneous	40 (12.9)	43 (14.0)	19 (7.8)	159 (6.5)
<b>Total Pathogens</b>	<b>309 (67.0)</b>	<b>307 (72.7)</b>	<b>245 (68.2)</b>	<b>2445 (100.0)</b>
Sterile	152 (33.0)	115 (27.3)	114 (31.8)	0

\*Values are numbers (percentages). PRP indicates penicillin-resistant pneumococci.

†Studies were performed of nasopharyngeal specimens. No study of ear specimens was available for that period in the region.

No child had received any treatment during the 5 days immediately before specimens were taken. During the last period (1994-1997), in the absence of available bacteriologic data from aspirated auricular material in the Paris region, we have compared our results with those of 2 successive studies<sup>6,7</sup> carried out on nasopharyngeal specimens in children with AOM. A good epidemiologic correlation between these specimens, at least for *S pneumoniae* and *H influenzae*, has already been established.<sup>8</sup>

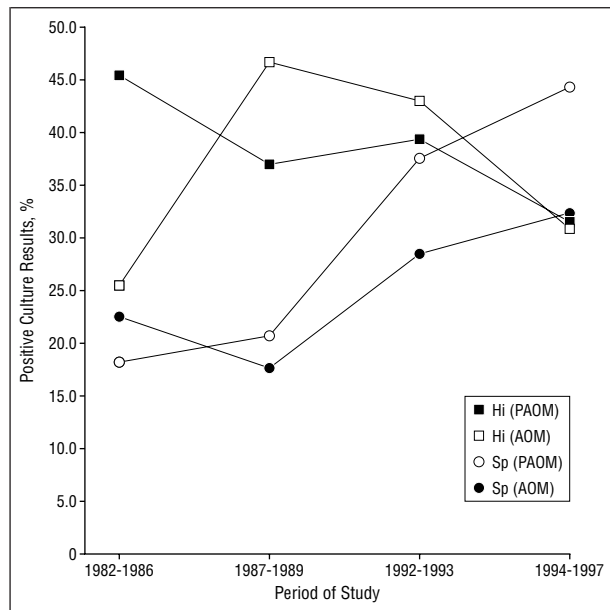
**Figure 1** illustrates the variation of the 2 main pathogens by comparing their respective role in patients having PAOM with those having AOM during the period studied. This comparison was performed among patients with cultures positive for pathogens so as not to modify the results due to the high proportion of sterile specimens in certain groups.

**Figure 2** shows the proportion of resistant strains of *H influenzae* in patients with PAOM compared with those with AOM. When the data for patients with PAOM are compared with those with AOM, the increased resistance of *H influenzae* and, in particular, *S*

*pneumoniae*, is clearly more rapid and more marked in patients with PAOM (12 [30.0%] of 40 patients in 1982-1986 vs 15 [55.6%] of 27 patients in 1994-1997;  $P = .04$ ) as opposed to those with AOM (9 [18.0%] of 50 patients in 1982-1986 vs 271 [36.0%] of 753 patients in 1994-1997;  $P = .02$ ).

## COMMENT

In this retrospective series, we studied the evolution of the bacterial epidemiologic features and the resistance to antibiotics in patients with PAOM. The length of the study allows the evolution of the bacterial ecologic features to be observed and to be compared with those of AOM. We decided to compare PAOM and AOM among groups of patients in the same geographic area. Indeed, studies<sup>5-7</sup> have shown marked regional differences in AOM. In this study, the bacteriologic data have been compared for 2 different modes of care: hospital (public) and private practice. The hospital management of AOM is not routine practice and is usually reserved for difficult or special cases. Thus, a hospital-based group for compari-



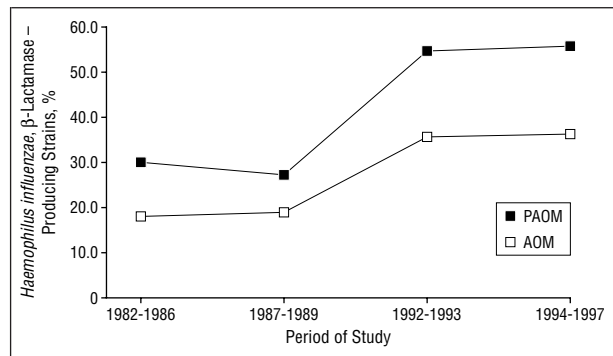
**Figure 1.** Prevalence of cultures positive for *Haemophilus influenzae* (Hi) and *Streptococcus pneumoniae* (Sp) from patients with persistent acute otitis media (PAOM) and acute otitis media (AOM), by period of study.

son could have altered the classic epidemiologic characteristics of this disease. On the other hand, PAOM is managed in a hospital more often because, in patients with this disorder, standard therapies have failed. In this study, we analyzed the variations in the epidemiologic evolution of these 2 disorders in 15 years.

All the children included in the study as having PAOM had previously had at least 2 successive courses of antibiotics for the same infectious episode. Thus, our patients with PAOM differ slightly in the duration of disease and early treatment failure compared with other series in the literature.<sup>9,10</sup> Given that all the children with PAOM in our study had an infectious episode lasting longer than 3 weeks, it is possible that the bacteriologic results obtained were greatly influenced by the preceding antibiotic treatment. These children were also younger than those in the AOM series that was used for comparison. The young age of patients with PAOM may have influenced the microbiologic results. No published study has been done of the bacteriologic features of AOM in the Paris region limited to this age range.

### STERILE SPECIMENS

The percentage of specimens from children with PAOM that were sterile in our study decreased from 35.3% to 14.9% in 15 years. This change occurred at the same time that a therapeutic window for children taking antibiotics was used more systematically, with the obtaining of a second specimen after 48 hours if the initial culture was negative for pathogens. In addition, the bacteriologic study was performed using the aspiration tube rather than swab specimens in almost all patients. For the group, a swab was taken in some patients (20.2% in group 1 and 0% in the other groups). The use of swabs for sampling increases the risk of obtaining a sterile specimen. The dis-



**Figure 2.** Proportion of beta-lactamase-producing strains of *Haemophilus influenzae* among patients with persistent acute otitis media (PAOM) and acute otitis media (AOM), by period of study.

continuation of the use of swab specimens represents an improvement in the sampling technique.

In the large published series<sup>9-11</sup> of antibiotic treatment failures in AOM, 30% to 60% of bacteriologic specimens were sterile. In these studies, no information was given on whether treatment was temporarily withheld. It is probable that these patients had already commenced an initial antibiotic treatment when bacteriologic specimens were taken. Repeated sampling—when results of direct examination or the culture were negative—from the same child before starting treatment allowed an organism to be identified more often in our study. To maximize the value of microbiologic testing, it is best to take an initial specimen at the first consultation and to repeat this, after a therapeutic window, if the specimen is sterile. The temporary withholding of treatment is justified on the basis of the difference between the in vivo and in vitro activity of antibiotics: a low residual level of antibiotic in the specimen may be inadequate to sterilize the source of infection but may inhibit bacterial growth in vitro.<sup>12,13</sup>

In addition, the large number of specimens with sterile bacteriologic results in unresponsive otitis may be related to an associated viral infection. Chonmaitree et al<sup>14</sup> reported a 46% rate of viral infections in patients with AOM (24% of which were isolated viral infections). Fifty-one percent of patients with coinfection had a prolonged clinical course of their otitis media, which was much greater than the rate for patients with bacterial (35%) or viral (19%) infections alone. Pichichero and Pichichero<sup>9</sup> have proposed that viral infection may explain both the unresponsiveness of PAOM to antibiotic therapy and the prolonged clinical course. We are not aware, however, of any study that has specifically investigated the role of viruses in PAOM.

The 2 organisms most commonly detected in this study of PAOM were *S pneumoniae* and *H influenzae*. These 2 bacteria also predominate in patients with AOM, although their distribution and, in particular, their level of resistance are different.

### Pneumococci

The percentage of *S pneumoniae* organisms in patients with PAOM increased from 18.2% to 44.2% in 15 years. In parallel, we observed a particularly rapid emergence of re-

sistance to penicillin, going from 0% to nearly 100% in 5 years. A similar bacteriologic evolution has been documented for AOM. In 1989, Teele et al<sup>15</sup> described the bacteriologic features of 43 children with AOM unresponsive to 36 hours or more of antibiotic treatment. Among the 31 children who were treated with amoxicillin, 40% of specimens were positive for pneumococci, of which 24% involved an organism sensitive to the initial treatment. Thus, at that time, only 20% of the patients with otitis in whom treatment failed had bacteria resistant to the prescribed antibiotics. This conclusion was made during an era when *S pneumoniae* had not yet developed resistance to penicillin.

In 1985, Harrison et al<sup>11</sup> compared the bacteriologic data with the preceding treatment. In patients with AOM unresponsive to treatment, 19.5% of the bacteriologic specimens grew *S pneumoniae*, and this was not significantly different from the result in patients with AOM. There were no cases of otitis due to penicillin-resistant pneumococci (PRP). In patients with unresponsive AOM, 62.4% of the isolated organisms were sensitive to the antibiotics given. Between 1992 and 1994, Block et al<sup>16</sup> studied 246 patients and found *S pneumoniae* in 56% of patients with otitis who had early treatment failure. The proportion of PRP organisms was 31%, which was almost double the highest incidence of PRP organisms reported<sup>12</sup> in patients with AOM in the United States during the same period.

Pichichero and Pichichero<sup>9</sup> investigated the organisms involved in AOM unresponsive to antibiotics in 137 children from 1989 to 1992. All these patients had been given 1 or 2 preceding courses of antibiotics. The duration of the clinical episode (from 10-20 days) was longer than in the study by Block et al.<sup>16</sup> They found a PRP frequency of 18%, but 49% of specimens were sterile, and furthermore, PRP was not systematically screened for until 1992. Once again, this PRP rate of 18% was double that detected in patients with AOM without prior antibiotic treatment.

The resistance rates vary among countries and between regions. This is why we have specifically compared our data with those of other studies performed in France during the same period. In the Paris region, the rate of isolation of PRP increased from 7.4% in 1987 to 50.0% in 1993.<sup>5</sup> Thus, PRP is endemic in this region; it would be particularly useful to identify which subgroups of the population are predominantly subject to PRP.

In 1994, Cohen et al<sup>10</sup> studied 293 patients in the Paris region with treatment-resistant otitis. Almost 50% of bacteriologic specimens were sterile. In the remaining patients, *S pneumoniae* was identified in 55.1% of patients, and 86.4% of the organisms were PRP. This rate is similar to the rate we observed during the same period in patients with PAOM. Thus, once again, we find that the role of *S pneumoniae* and, in particular, PRP is greater in patients with unresponsive otitis and PAOM than in those with AOM. Furthermore, the resistance profile of PRP has evolved toward resistant strains (penicillin minimal inhibitory concentration, >1 mg/L) as opposed to strains that merely show decreased sensitivity. The proportion of resistant strains among PRP

identified in patients with AOM in France<sup>17</sup> has increased from 10.5% in 1988 to 57.5% in 1993. In the Paris region, this progression has been even more marked: from 14% in 1990<sup>4</sup> to 74.4% in 1993 and 47% in 1995.<sup>7</sup> In patients with PAOM, the rate was elevated from the start, as shown by groups 3 and 4 in our study, in whom the proportion was 81.2% and 89.1%, respectively, and no PRP strains had been isolated until 1989. These high percentages are even greater than those (77.3%) reported by Cohen et al.<sup>10</sup> These findings suggest a progression in the rate of resistance among PRP principally according to their geographic distribution and the type of otitis: AOM unresponsive to treatment and PAOM. This clearly can have therapeutic consequences because it has been shown<sup>18</sup> that the bacteriologic evolution and treatment failures with the use of cefuroxime axetil for PRP-related otitis are due to the high level of resistance of the PRP. The empirical treatment of otitis must take into account the clinical situation of the child. In our experience, oral drugs considered to have moderate activity against resistant strains of PRP—the combination of amoxicillin and clavulanate potassium, cefuroxime, and cefpodoxime proxetil—may be effective, even in patients with a penicillin minimal inhibitory concentration of 2 mg/L or more (ie, in patients with AOM from whom the PRP organisms are isolated after paracentesis is performed for pyrexia or persistent pain).<sup>19</sup> Therefore, the context in which the otitis occurs and, in particular, the clinical course appear to be more important than the minimal inhibitory concentration with respect to outcome. In patients with otitis unresponsive to treatment or who have PAOM, it is usually necessary to use drugs with high activity against PRP.

### *H influenzae*

In our studies of PAOM, the percentage of cases due to *H influenzae* has remained stable, from 20% to 30% during the 15 years. This percentage is lower than that seen in AOM. In France, *H influenzae* has always been the predominant organism identified in patients with otitis. The frequency of  $\beta$ -lactamase-producing strains in patients with PAOM, however, has increased from 30.0% to 55.6%. The study by Cohen et al<sup>10</sup> in the Paris region on the failure of the treatment of otitis found *H influenzae* in 22.2% of patients. Only about one third of these organisms were resistant to the initial antibiotic treatment, although the proportion of  $\beta$ -lactamase-producing strains was not detailed. A similar evolution between 1987 and 1993 of the failure of treatment of otitis has been reported<sup>10,20,21</sup> in the United States: the rate of  $\beta$ -lactamase-producing strains increased, from 1 (5.6%) of 18 patients among 18 of 37 (48.6%) with *H influenzae*<sup>20</sup> to 2 (25%) of 8 patients among 8 (53.3%) of 15 with *H influenzae*,<sup>21</sup> and to 21 (32%) of 65 patients among 65 (41.1%) of 158 with *H influenzae*.<sup>10</sup> Harrison et al<sup>11</sup> found that 55 (32.5%) of 169 of organisms were  $\beta$ -lactamase-producing strains in patients with otitis for whom treatment failed, whereas only 11 (8.9%) of 123 of organisms were these resistant strains in patients with AOM. They suggested that this difference was due to in vivo selection because most chil-

dren in whom treatment had failed had taken amoxicillin. Recently, a similar development has been noted in patients with AOM, although the proportions are not as great. This phenomenon had already been noted in 1993,<sup>22</sup> with 25% of strains being  $\beta$ -lactamase producers in patients with AOM, 43.7% in patients with recurrent otitis, and 54.5% in patients with PAOM.

### OTHER BACTERIA

In this study, we have found the frequency of *P aeruginosa* and *S aureus* to be clearly greater in patients with PAOM than in patients with AOM. This may be because 34.4% of *P aeruginosa* and 22% of *S aureus* were detected in bacterial specimens from patients with spontaneous otorrhea, leading to the possibility of contamination of these organisms from the external acoustic meatus. Nevertheless, other authors<sup>2,5,11</sup> have reported a significant incidence of staphylococci: 0% to 5% of patients with AOM and 3% to 5% of patients in whom treatment failed. The prior disinfection of the external acoustic meatus did not modify the isolation rate of these 2 organisms.<sup>4</sup>

*Pseudomonas aeruginosa* is rarely considered to be a pathogen. The studies of patients with AOM performed in the Paris region, however, have consistently found a prevalence of *P aeruginosa* of between 3.7% and 5.8% (Table 2).

The prevalence of *P aeruginosa* varies from 4.5% in patients with AOM to 11% in patients with PAOM.<sup>22</sup> Furthermore, in patients with PAOM, the identification of *P aeruginosa* was more frequently associated with the need for a mastoidectomy, despite appropriate antibiotic treatment (29.5% vs 10% for *S pneumoniae* and 15.1% for *H influenzae*).<sup>23</sup>

These organisms are usually identified in infants (aged between 6 and 12 months), as found in our study population. Because these children had received several antibiotics, 2 hypotheses can be proposed: either the bacteria were not eradicated by conventional treatment or the antibiotics modified the rhinopharyngeal flora in susceptible infants. That all the strains of *S aureus* were sensitive to methicillin does not support the first hypothesis. The bacterial ecosystem is different in the United States. Thus, *Moraxella catarrhalis* is the third most frequently encountered pathogen in the United States after *S pneumoniae* and *H influenzae*.<sup>9,11,16</sup> This organism is much less frequently encountered in France and was virtually never detected in patients with PAOM in this study.

The global increase in the prevalence of resistant organisms identified during otitis may be due to the frequent use of antibiotics in children younger than 2 years. Young age is correlated with a greater failure rate in patients with AOM independently of the emergence of antibiotic-resistant strains.<sup>20</sup> The average age of our population of children with PAOM was even lower than that in several studies of AOM. Several factors may explain the greater treatment failure rate in younger children: the anatomy of the eustachian tube, immaturity of the immune system, viral infections, and frequent recontamination (due to communal activity—eg, day

care centers). These failures themselves lead to the frequent use of antibiotics, further increasing the selective pressures.

In patients with PAOM, even though the same at-risk population is concerned, with the same risks of day care center attendance and the same antibiotic treatments, the rate of the development of resistance is greater than in patients with AOM. This rise in resistance may be directly linked to prior antibiotic treatment. In the absence of bacteriologic studies at the start of PAOM, however, it is impossible to differentiate between the presence of a resistant organism from the start or the modification of the bacterial flora during an infectious episode due to the antibiotics administered.

The risk of complications with PAOM, mainly subacute mastoiditis but also meningitis and septicemia, demands that every effort should be made to prevent the development of PAOM and that therapeutic strategies adapted to the bacterial ecosystem of the patient need to be defined, particularly in susceptible young children.

### CONCLUSIONS

The relentless increase in bacterial resistance that was encountered in patients with AOM was also observed, but more marked, in patients with PAOM. The role of PRP in PAOM was also found to be more prominent. A continuous and worrying rise in the level of resistance was observed. Identification of the organism is essential when otitis does not resolve and especially so in patients with PAOM. In this context, the identification of the organism may require obtaining a second specimen after 24 to 48 hours without antibiotics.

Accepted for publication May 20, 1999.

Presented at the 13th annual meeting of the American Society of Pediatric Otolaryngologists, Palm Beach, Fla, May 12, 1998.

Corresponding author: Natalie Loundon, MD, Department of ENT, Hôpital d'Enfants Armand Trousseau, 26 Ave du Dr A. Netter, 75571 Paris, Cedex 12, France (e-mail: orl.trousseau@trs.ap-hop-paris.fr).

### REFERENCES

1. Poole MD. Otitis media complications and treatment failures: implications of pneumococcal resistance. *Pediatr Infect Dis J*. 1995;14(suppl):S23-S26.
2. Neu H. Otitis media: antibiotic resistance of causative pathogens and treatment alternatives. *Pediatr Infect Dis J*. 1995;14(suppl):S51-S56.
3. Nancy P, Arronio C, Margo JN, et al. Etude bactériologique de l'otite moyenne aigue [Bacteriological study in acute otitis media]. *Ann Otolaryngol Chir Cervicofac*. 1982;99:383-389.
4. Gehanno P, Boucot I, Simonet M, Bingen E, Lambert-Zechovsky N, Berche P. Epidémiologie bactérienne de l'otite moyenne aigue chez l'enfant en région parisienne de 1987 à 1991: à propos de 1232 cas. *Lett Infectiol*. 1991;6:408-414.
5. Berche P, Gehanno P, Duval F, Lenoir G. Epidémiologie bactérienne des otites moyennes aigues de l'enfant en France en 1993. *Lett Infectiol*. 1994;9(suppl 18):11-22.
6. Levy D, Gehanno P, Olivier C, et al. Epidémiologie de la flore nasopharyngée au cours des otites moyennes aigues de l'enfant en 1997. *Med Mal Infect*. 1998;28:8-22.
7. Berche P, Gehanno P, Olivier C, Nguyen L, Boucot I. Epidémiologie de la flore

- nasopharyngée au cours des otites moyennes aiguës de l'enfant. *Med Mal Infect.* 1996;26:5-19.
8. Gehanno P, Lenoir G, Barry B, Bons J, Boucot I, Berche P. Evaluation of nasopharyngeal cultures for bacteriologic assessment of acute otitis media in children. *Pediatr Infect Dis J.* 1996;15:329-332.
  9. Pichichero ME, Pichichero CL. Persistent acute otitis media, I: causative pathogens. *Pediatr Infect Dis J.* 1995;14:178-183.
  10. Cohen R, de la Rocque F, Boucherat M, Doit C, Bingen E, Geslin P. Treatment failure in otitis media: an analysis. *J Chemother.* 1994;6(suppl 4):17-22.
  11. Harrison CJ, Marks MI, Welch DF. Microbiology of recently treated acute otitis media compared with previously untreated acute otitis media. *Pediatr Infect Dis J.* 1985;4:641-646.
  12. Gehanno P, Cohen R, Barry B. Otite moyenne aigue: une antibiothérapie est-elle nécessaire? laquelle en première intention? pour quelle durée? *Med Mal Infect.* 1997;27:397-407.
  13. Bégue P, Quinet B, Denoyelle F, Garabedian EN. Etude pharmacocinétique des antibiotiques dans l'otite [Pharmacokinetic study of antibiotics in otitis]. *Ann Otolaryngol Chir Cervicofac.* 1993;110:393-398.
  14. Chonmaitree T, Owen MJ, Patel JA, Hedgpeth D, Horlick D, Howie VM. Effect of viral respiratory tract infection on outcome of acute otitis media. *J Pediatr.* 1992;120:856-862.
  15. Teele DW, Klein JO, Rosner B. Epidemiology of otitis media during the first seven years of life in children in greater Boston: a prospective, cohort study. *J Infect Dis.* 1989;160:83-94.
  16. Block SL, Harrison CJ, Hedrick JA, et al. Penicillin-resistant *Streptococcus pneumoniae* in acute otitis media: risk factors, susceptibility patterns and antimicrobial management. *Pediatr Infect Dis J.* 1995;14:751-759.
  17. Geslin P, Fremaux A, Sissia G. Evolution de la résistance aux bêta-lactamines des pneumocoques isolés d'otites moyennes aiguës de l'enfant en France depuis 1987: Bilan du Centre national de référence. *Lett Infectiol.* 1994;9(suppl 18):4-10.
  18. Gehanno P, Lenoir G, Berche P. In vivo correlates for *Streptococcus pneumoniae* penicillin resistance in acute otitis media. *Antimicrob Agents Chemother.* 1995;39:271-272.
  19. Roger G, Carles P, Pangon B, et al. Management of acute otitis media caused by resistant pneumococci in infants. *Pediatr Infect Dis J.* 1998;17:631-638.
  20. Carlin SA, Marchant CD, Shurin PA, Johnson CE, Murdell-Panek D, Barenkamp SJ. Early recurrences of otitis media: reinfection or relapse? [published correction appears in *J Pediatr.* 1987;110:668]. *J Pediatr.* 1987;110:20-25.
  21. Del Beccaro MA, Mendelman PM, Inglis AF, et al. Bacteriology of acute otitis media: a new perspective. *J Pediatr.* 1992;120:81-84.
  22. Garabedian EN, Bellity A, Tashjian G, Ghiassi B, Vu Thien H, Begue P. Etat de la résistance du pneumocoque à la pénicilline G dans le cadre de l'épidémiologie bactérienne actuelle de l'otite moyenne aigue de l'enfant. *Med Mal Infect.* 1994;24:674-680.
  23. Denoyelle F, Garabedian EN, Roelly P, Tashjian G. Protracted acute otitis media and subacute mastoiditis: a prospective study of 165 cases. In: Lim DJ, Bluestone CD, Klein SO, Nelson JD, Ogra PL, eds. *Recent Advances in Otitis Media.* Ft Lauderdale, Fla: Decker Periodicals; 1991:264-267.

#### ARCHIVES Web Forum

Discuss key clinical issues with your colleagues in the ARCHIVES' new World Wide Web forum. These moderated online discussions are based on selections from the ARCHIVES' Clinical Challenges in Otolaryngology series. For more details, see the ARCHIVES' Web site at <http://www.ama-assn.org/oto>.