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PEDIATRIC INFECTIOUS DISEASES (I BROOK, SECTION EDITOR)

Challenges in the Management of Acute Mastoiditis in Children

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Abstract Acute mastoiditis (AM) is a rare but serious complication of otitis media. Recent studies consolidated the role of *Streptococcus pyogenes* as the second most important etiologic agent of AM and suggested an increased involvement of a relatively new pathogen (*Fusobacterium necrophorum*). The recently accumulated evidence on AM epidemiology in children is conflicting and not convincing in demonstrating clear trends during the last years. While a significant decrease was recorded in the incidence of pneumococcal invasive disease and complicated AOM following the introduction of the pneumococcal conjugate vaccines, data on the efficacy of these vaccines in the prevention of AM are limited and did not show any remarkable changes in the dynamics of disease caused by *Streptococcus pneumoniae.* The clinical findings in AM may differ according to the causative pathogen and different patient age subgroups. Together with computerized tomography, magnetic resonance imaging became frequently used, particularly in the diagnosis of AM complications. Simple mastoidectomy remains the most reliable and effective surgical intervention for the treatment of subperiosteal abscesses.

Keywords Mastoiditis · Acute otitis media · *Streptococcus pneumoniae* · Complications · Mastoidectomy · Antibiotic treatment · Pneumococcal conjugate vaccines

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Introduction

Acute mastoiditis (AM) is the most common severe complication associated with acute otitis media (AOM). Its most common pathogens are *Streptococcus pneumoniae*, *Streptococcus pyogenes,* non-typeable *Haemophilus influenzae*, and *Moraxella catarrhalis*. The diagnosis of AM is based on the presence of otitis media on otoscopy, associated with local inflammatory signs over the mastoid bone and systemic and laboratory signs of infection. Radiologic investigations may be critical in refractory to therapy cases and in those situations where the complications of mastoiditis which are suspected. The first line of treatment for AM without any complication includes myringotomy and intravenous antibiotics administration. If intracranial and extracranial complications develop, surgical intervention is required.

The present review will try to summarize the latest developments in the epidemiology, microbiology, management, and prevention of AM in children, with particular emphasis on the developments occurring in these fields since 2010. The role of the pneumococcal conjugate vaccines (PCVs) in the prevention of AM and their impact on the microbiology and management of this challenging pediatric infection will be discussed in detail.

Epidemiology

A decrease in the incidence of AM was noted during the second half of the 20th century, attributed to the introduction of the routine use of antibiotics in the treatment of AOM. With the introduction of antibiotics, AM complicates <1 % of AOM infections, and its occurrence rate decreased to around 1.2–6.1 cases/100,000 children in the developed world [1–6]. The intracranial complications of mastoiditis may reach 5–15 % [7, 8]. However, during the last years, changes were reported

in the disease epidemiology and natural history with a possible increasing incidence and also with changing etiologic pathogens reported more frequently [5, 9–11, 12•, 13, 14, 15•]. During this period, routine treatment of AOM with antibiotics was questioned due to the emergence of increasing numbers of bacterial strains resistant to antibiotics, high rates of spontaneous clinical resolution of AOM and the very low rates of its complications [4, 16–18]. Guidelines advocating for the concept of watchful waiting and delayed treatment of antibiotics in AOM were introduced in many countries over the world in 2004 [16]. However, concern has been expressed that these recommendations could lead to a higher rate of complications associated with AOM, primarily AM. The nonsusceptibility of AOM pathogens to antibiotics and the masking of the signs and symptoms of disease by previous antibiotic therapy, with a delay in treatment, are among the possible hypotheses raised on the causes of the increasing incidence of AM. In a retrospective cohort study in the UK, the risk of AM after otitis media was 1.8/10.000 episodes after antibiotic treatment compared with 3.8/10.000 episodes without previous antibiotics [19]. The authors calculated that general practitioners would need to treat with antibiotics 4831 otitis media episodes in order to prevent one child from developing mastoiditis. Practically, if antibiotics were not anymore prescribed for otitis media, an extra 2555 cases of mastoiditis would be recorded, but there would be 738,775 fewer antibiotics prescriptions/year in the UK [17].

As a matter of fact, the published reports on the incidence of AM in recent years are contradictory. Some reports claim an increase in the number of cases of AM while others do not, despite the fact that the use of antibiotics for the treatment of AOM has generally decreased. Many of these studies are difficult to compare, and the analyzed data were not presented as population-based information, meaning that the real incidence of the disease could not be calculated. In Israel, two recent one-center studies have observed an increasing incidence of AM, including the time period after publication of the AOM treatment guidelines [12•, 13]. The incidence of AM reported in southern Israel in a tertiary care medical center continued to increase during the last two decades (from 6.1/100,000 during 1990–2001 to 11.5/100, 000 during 2002–2012) [15•]. A recent study reported a significant increase during 2002–2013 in the number of AM cases in all Italian pediatric wards but only among children >4 years of age [14].

On the other hand, five studies published since 2010 in Norway, France, Sweden, and Denmark [20–22, 23•] did not report any significant increase in the incidence of AM during the last years. Complete Norwegian data on children aged 0–16 years hospitalized for AM during 1999–2005 showed stable hospitalization rates, ranging from 4.9 to 6.3/100,000, with no increase during the study period [20]. Quesnel et al. [21] reported on 188 children aged 3 months–15 years admitted with AM during 2001–2008 in Paris and found a stable yearly number of cases, ranging between 26 and 38 cases/year. Gorphe et al. [22] described retrospectively 36 cases of AM admitted between 1999 and 2009 in Rouen, France, and reported only a trend toward increased incidence over the time period analyzed. Groth et al. [23•] analyzed the records of 577 patients aged 0–16 years with mastoiditis in Sweden during 1993–2007 and found no increase in the number of cases following the introduction of new guidelines for the management of AOM in 2000. The study found that AM was most common in children <2 years of age, and the proportion of AM increased after 2000 in patients aged 2–23 months (the age group where antibiotics were still recommended in the treatment of all cases of AOM) [23•]. The same group from Sweden reported a 5 % recurrence rate among 798 cases diagnosed with AM [24]. A mean incidence of 4.8/100,000 cases without any evidence of increase in AM was reported among all (214) children aged 0–15 years admitted during 1998–2007 to hospitals in eastern Denmark, a country where a conservative management approach is used in the treatment of AOM [25•]. Furthermore, the penicillin resistance of the *S. pneumoniae* isolates was low (6 %) and the complications were rare.

In summary, the recently accumulated evidence is conflicting and not convincing in demonstrating clear trends in the dynamics of AM in children during the last years. Nevertheless, it is worthwhile to mention that the data presented in this section on the epidemiology of AM did not discuss the impact of the vaccination with the pneumococcal conjugate vaccines on the incidence of the disease. This topic will be discussed in detail in a late section of the present review.

Microbiology

The most common pathogen of AM is *S. pneumoniae* followed by *S. pyogenes* [5–7, 9, 10, 12•, 13, 15•, 18, 21, 22, 25•]. The two other frequently reported pathogens are non-typeable *H. influenzae* and *M. catarrhalis*. The high isolation rates of *S. pyogenes* in AM (around 25 % of all pathogens) are in contrast with its isolation rates among the etiologic agents of AOM, where it represents no more than 4–5 % of all cases [5, 12•, 15•, 26]. The relative risk for development of AM was calculated to be 11.1/1000 among patients with AOM caused by *S. pyogenes*, compared with 2.2 and 0.3/1000 patients only in AM caused by *S. pneumoniae and* non-typeable *H. influenzae* [26]. *S. pyogenes* caused significantly more spontaneous perforations of the tympanic membrane in AOM patients in comparison with the other AOM etiologic agents [26].

Recovery of *Pseudomonas aeruginosa* and *Staphylococcus aureus* has also been reported in AM, particularly in non-acute disease and as part of a polymicrobial infection [4, 7, 9, 12•, 14, 22, 27, 28], although these pathogens may

be considered contaminants in those cases of AM developing shortly after the diagnosis of AOM is made. *P. aeruginosa* was mainly detected in older children, with a clear correlation with the presence of previous tympanostomy tube [27]. Two recent studies suggested that the incidence of *Fusobacterium necrophorum* mastoiditis has increased in the last two decades [29, 30].

Clinical Findings

AM diagnosis is based, in general, on the diagnosis of AOM on otoscopy, the presence of local inflammatory signs over the mastoid (post auricular tenderness, erythema or swelling, protruding auricle, presence of a palpable or fluctuating post auricular mass) and systemic signs (fever, irritability) [8, 28, 31•]. Over diagnosis is common and many patients diagnosed as AM may have, in fact, external otitis or otorrhea with transmyringeal drainage [31•]. Kordeluk et al. [15•] reported that the commonest clinical finding of AM was post auricular swelling (93.8 %), followed by post auricular sensitivity (90.6 %), protrusion of auricle (85.9 %), and post auricular erythema (85.7 %). Otorrhea was found in 32 % and fever and restlessness were uncommon. Leukocytosis >15,000 cells/mm^3 was found in 60 % of patients. About 30 % of AM cases occurred in children treated with antibiotics for AOM prior to AM diagnosis. The main duration of symptoms before diagnosis was 3.56 days [15•]. Amir et al. [12•], in a retrospective study over a period of 25 years, reported fever as the most common symptom (81 %), followed by auricular displacement and post auricular swelling. Subperiosteal abscess was detected in all children. The duration of symptoms prior to diagnosis was relatively short (median 1–4 days). The study suggested that the clinical diagnosis of AOM may be missed due to the rapid progression of the infection from the middle ear to mastoid [12•]. In Denmark [25•], 100 % of the reported patients with AM presented with protrusion of pinna, 95 % with retro auricular swelling and redness; 32 % of them developed subperiosteal abscess.

The clinical findings in AM may differ according to the causative pathogen. Laulajainen-Hongisto et al. [32•] reported that S. *pneumoniae*, especially strains with reduced susceptibility to common antibiotics, may cause severe symptoms and lead to need for mastoidectomy more often than other pathogen; however, this pathogen caused less otorrhea than other pathogens. *S. pyogenes* was found to cause less otalgia and less post auricular symptoms in relation to other pathogens. The majority of children with AM caused by *P. aeruginosa* had tympanostomy tubes. All patients with *P. aeruginosa* had otorrhea, but the clinical picture of AM was milder [32•]. A subperiosteal abscess was diagnosed in all cases of mastoiditis caused by *F. necrophorum*, requiring treatment with cortical mastoidectomy and tympanostomy tube insertion [30]. The clinical symptoms in AM caused by this pathogen were age dependent, with the younger children presenting with less otorrhea and more retro auricular symptoms than the older patients.

Groth et al. [33] compared the characteristics of AM in different age groups and found that the disease was the most common in children <2 years of age. The patients with AM in this age group showed more rapid progress of symptoms and more distinct diagnostic signs, had less antibiotic treatments and a shorter duration of symptoms before admission, were hospitalized for fewer days, and had a lower frequency of complications and mastoidectomies compared with older children. Patients <2 years of age had more distinct clinical signs of mastoiditis, higher fever, C-reactive protein values, and white blood cell counts compared with older ones. Finally, *S. pneumoniae* was recovered more frequently in the younger age group, while the older patients had more *S. pyogenes* and *P. aeruginosa* or negative cultures [33]. AM was reported extremely rare in infants <6 months of age [34]. These patients were reported to have frequently an upper respiratory infection preceding the AM episode and also a very short period of time from the first ear symptoms till hospitalization with AM. *S. pneumoniae* was the most frequently isolated pathogen and surgery was necessary in the majority of the infants [34].

Imaging in Diagnosis of AM and Complications

The infection may spread from the middle ear cleft via bone erosion, thrombophlebitis, periphlebitis, and via the anatomical pathways [35•]. The role of radiology becomes extremely important in diagnosing the complications of mastoiditis which can be serious and life threatening. Luntz et al. [36] found intracranial complications (sigmoid sinus thrombosis, perisinus empyema, subdural abscess, and epidural abscess) in 10/71 (14.1 %) patients hospitalized with AM. However, no differences were found in the most clinical characteristics or presenting signs and symptoms between patients with and those without intracranial complications [36].

In clinical practice, contrast-enhanced computerized tomography (CT) is the first-line imaging technique to be used [37•]. The CT examination is more easily available, and the time of the examination is shorter than in magnetic resonance imaging (MRI) scans. Furthermore, most MRI examinations in children require general anesthesia [37•, 38•]. Clinical otologists are more familiar with CT images which may serve as their preoperative map [35•, 36]. The main disadvantage of the CT scans resides in the possible ionizing radiation of brain, which might have a long-term effect on cognitive functions and has also a cancerigenic potential [39]. Today, CT imaging in children with AM is recommended in patients with neurological signs or a deteriorated general status on admission, patients failing to improve or worsening under conservative treatment, and patients suspected for an intracranial complication [40•].

In the last years more and more studies discussed the role of MRI imaging in the diagnosis of AM and its complications. In comparison with CT, MRI imaging is better in differentiation among soft tissue pathologies [37•]. In the context of AM, MRI is superior to CT in the detection of labyrinth involvement and intracranial infections [35•, 37•]. Saat et al. [37•] assessed the imaging features caused by AM on MRI and their relevance and reported that the most common complications in MRI were temporal abscess (23 %), subperiosteal abscess (19 %), and labyrinth involvement (16 %). Children had significantly higher prevalence (compared with adult patients) of total opacification of the tympanic membrane and mastoid air cells, more intense intramastoid enhancement, more bone erosion, subperiosteal abscesses, and perimastoid meningeal enhancement [37•]. Platzek et al. [38•] assessed the MRI performance in 23 patients with suspected AM, when fluid accumulation, increased contrast enhancement of the mastoid and restricted diffusion in the mastoid were considered signs of mastoiditis on MRI, and the presence of two of these three criteria was required for diagnosis. The authors reported a 100, 66, and 86 % sensitivity, specificity, and accuracy of the examination for the diagnosis of AM. Sensitivity and accuracy of MRI in diagnosing subperiosteal abscess was 100 %. However, destruction of small bony structure (like mastoid septum) cannot be evaluated on MRI, whereas on CT, it is an important sign of mastoiditis [35•].

Treatment

Initial assessment of children with AM includes history and physical examination with particular attention to clinical sings (otalgia, fever, post auricular swelling, protrusion of auricle, post auricular sensitivity, erythema, purulent ear discharge, restlessness) and a high index of suspicion for intra and extra cranial complications.

The treatment of AM begins, in general, with more conservative measures as intravenous antibiotics with myringotomy with or without pressure equalization tube placement without mastoidectomy [40•, 41, 42•, 43]. Psarommatis et al. [42•] recommended a treatment algorithm for AM based on a review of 155 cases. One hundred twelve children with non-complicated AM were treated with intravenous antibiotics and myringotomy with or without pressure equalization tube placement. Seventy-eight (69.6 %) of these children were completely cured following this treatment, whereas 34 (30.4 %) underwent simple mastoidectomy because of poor response after 48 h of conservative treatment. The 43 children with AM and intracranial and extracranial complication (subperiosteal abscess) were treated with simple mastoidectomy, myringotomy, and intravenous antibiotics [23•]. Groth et al. compared the course of the disease and treatment between younger (0–23 months) and older (2–16 years) children and reported that the need for simple mastoidectomy was significant higher among the older patients [33]. The management of AM with subperiosteal abscess was evaluated in 34 children who underwent surgery within 24 h of admission. Thirteen of them underwent simple mastoidectomy with myringotomy and 21 myringotomy with abscess drainage, either by incision or needle aspiration. Nine (43 %) children from the abscess drainage group required simple mastoidectomy due to lack of improvement or worsening of the symptoms. The authors concluded that simple mastoidectomy remains the most reliable and effective operation for the treatment of subperiosteal abscesses [43].

The treatment of AM occurring in children with cochlear implants was recently determined in a systematic review of all publications (12) addressing this topic during 2000–2013 [44]. The mean duration from implantation to the development of mastoiditis was 17.2 months. Of a total of 43 patients, subperiosteal abscess was present in 14.3 %. The patients were treated with intravenous antibiotics only (three studies) and antibiotics + surgery in the additional nine studies (surgery reported in 27.3–100 % of the patients). Device explantation was required in only one patient [44].

Acute Mastoiditis in the Pneumococcal Conjugate Vaccines Era

S. pneumoniae is the most frequent pathogen of AM. In order to prevent pneumococcal disease, including AOM, vaccination with pneumococcal conjugate vaccines (PCVs) was introduced during the last 10–15 years in many countries all over the world. Following the introduction of the 7-valent pneumococcal conjugate vaccine (PCV7) in the national pediatric immunization programs all over the world since 2000, a significant decrease was recorded in the incidence of pneumococcal invasive disease and also in the number of cases of complicated AOM (therapeutic failures, recurrent AOM cases, and cases requiring surgical intervention with insertion of tympanostomy tubes) [45–51]. In parallel, in a short period of time following the PCV7 introduction, an increase was reported in colonization and disease rates with non-PCV7 serotypes (phenomenon known as serotype switching or replacement), particularly serotype 19A, accompanied by an increase in the resistance of these serotypes to beta-lactam antibiotics [48–56]. Therefore, new vaccines, covering more pneumococcal serotypes (PCV10 and PCV13) were developed and introduced since 2010 in the USA, Europe, and many additional countries [57–59]. Recently, the effect of the sequential introduction of 7-valent/13-valent PCV was reported on 6122 AOM episodes (diagnosed by tympanocentesis and culture of the middle ear fluid) in southern Israel [60•]. Compared with the pre-PCV period (2004–2009), AOM caused by PCV7 plus serotype 6A and the five

additional PCV13 serotypes (1, 3, 5, 7F and 19A) decreased by 96 and 85 %, respectively, in a two-step pattern: in the PCV7 period (July 2009–November 2010), only disease caused by PCV7+6A serotypes was decreased and in the PC13 period (December 2010–June 2013), the five additional vaccine type AOM rates decrease, along with an additional PCV7+6A-AOM reduction. Overall, 77 and 60 % reductions of all-pneumococcal and all-cause AOM incidences, respectively, were observed [60•].

Data on the efficacy of PCV7 and particularly of PCV13 in the prevention of AM are limited. Roddy et al. revised retrospectively the hospitalization charts of 122 patients aged 0–19 years diagnosed with acute and chronic mastoiditis during 1995–2005 (68 pre-PCV7 and 54 post-PCV7) and did not find a significant decrease in the number of cases of pneumococcal AM in the post-PCV7 period [61]. Fourty-eight patients received antibiotics in the 4 weeks before presentation and 38 % at presentation. Ceftriaxone nonsusceptibility reached 30 % in the post-PCV *S. pneumoniae* isolates compared with 7 % in the pre-PCV7 isolates. Mastoidectomy was required in 46 % of the patients. In Texas, an increase was reported in the number of pneumococcal mastoiditis cases in the post-PCV7 period, and this increase was related to a significant increase in cases caused by serotype 19A [62]. Multidrug resistance, subperiosteal abscesses, and the need for mastoidectomy characterized the disease caused by serotype 19A isolates. Choi et al. analyzed 96 children with AM during 1996–2009 and showed a 53 % increase in the number of AM cases following the PCV7 introduction, without a parallel significant increase in the number of *S. pneumoniae* cases [63•]. Increased nonsusceptibility of *S. pneumoniae* to penicillin and ceftriaxone was seen in the post-PCV7 group. In New South Wales, Australia, in a retrospective review of 84 children with AM during 2000–2010, pneumococcal AM appeared to fall when PCV7 vaccination was introduced, with a concomitant reduction in overall mastoiditis and intracranial complications [64•]. However, hospitalization rates rapidly returned to pre-vaccination levels, as well as the number of cases with pneumococcal AM. Among 21 cases of AM diagnosed in Athens, Greece, in the period following the introduction of PCV7 (2010–2011), *S. pneumoniae* was isolated in 17 (81 %) and serotype 19A was the predominant one (11 cases, 65 %)-[65•]. Serotype 19A was involved in 66.6 % of the cases complicated with subperiosteal abscess, and all these patients required mastoidectomy. In Denver, CO, the annual incidence of AM in children <2 years of age was 11.0/100,000 in 2001, decreased to 4.6 and 4.3/100,000 in 2002 and 2003, respectively, and increased again to 12.0/100,000 in 2008 [66•]. The number of penicillin-nonsusceptible *S. pneumoniae* isolates increased from 0 (1999–2004) to 38 % (2005–2008).

Information of the effect of PCV13 introduction on AM is scarce, and the short period of time elapsed since the introduction of this vaccine does not allow firm and definitive conclusions on its impact on the dynamics of the disease. Ruck et al. described in 2012 a case of AM caused by serotype 19A multiresistant to antibiotics occurring in a healthy 7-month-old female infant who received three previous PCV13 doses [67]. Kaplan et al. [68] reported in 2013 a 42 % decrease in the rates of pneumococcal invasive infections in children following the introduction of PCV13 and of 57 % in disease caused by vaccine serotypes (comparing the period 2010–2012 with 2007–2009). The number of cases of AM declined from 31 and 27 during 2007 and 2009, respectively, to 13 and 4, respectively, during 2010 and 2011. A high overall incidence of AM (11.5/100/000) was reported among children aged 0–18 years in southern Israel during 2005–2012, without any major changes in the post-vaccine period (2010–2012) compared with the pre-vaccine period (2005–2009) [15•]. A higher (25.6 cases/100,000) AM incidence was reported in Jewish children compared with Bedouin children (4.1/100,000). A significant decrease of 38 % in the rates of the disease was demonstrated during the post-vaccine period among the Jewish children. The pathogen distribution did not change during 2009–2012 compared with the pre-vaccination period, and *S. pneumoniae* remained the main etiologic agent of the disease (28.8 % of all cases and 46 % of all pathogens isolated). The most frequently isolated serotypes were 19A, 3, 19F, and 15A. All PCV13 serotypes were isolated in patients diagnosed during the year 2009 and not vaccinated with PCV13. In fact, serotype 19A was not anymore isolated during 2010–2012 following the introduction of PCV13. Overall, 53.3 % of *S. pneumoniae* isolates were susceptible to penicillin, without any remarkable changes in the dynamics of *S. pneumoniae* susceptibility to penicillin and ceftriaxone during the study years [15•]. Tamir [69] analyzed 58 AM episodes during 2008–2013 in a tertiary medical center in Israel and found fewer negative middle ear fluid cultures and a lower rate of patients previously treated with antibiotics during 2012–2013 compared with 2008–2011. The authors found that any prior PCV13 immunized patient with AM had a significantly lower proportion of *S. pneumoniae* middle ear fluid cultures, compared with unimmunized or PCV7-immunized children [69].

Table 1 summarizes the available and relevant information published during the period 2000–2014 in the English language medical literature and dealing with the impact of PCVs on the epidemiology and microbiology of AM [15•, 61, 62, 63•, 64•, 65•, 66•, 67–69]. Of the 10 studies published, 7 reported data only on PCV7-immunized patients, and 3 on the PCV7/PCV13 sequential impact. Different design, lack of population-based data in the majority of the studies, lack of serotyping of *S. pneumoniae* isolates, and the short period of time available for the analysis of PCV13 impact make a proper comparison between these studies very difficult. However, 2/6 studies analyzing the post-PCV7 period showed an increase in the number of AM cases [62, 63•], one did not find any difference between the pre- to the post-PCV7 period [61] and two reported on an initial decrease followed by a rapid increase in AM in the post-PCV7 period [64•, 66•]. The two studies reporting on *S. pneumoniae*-causing AM reported the

Table 1 Acute mastoiditis (AM) in the era of pneumococcal conjugate vaccines (PCVs): literature summary

Reference	Country	Study years	No. patients (episodes)	Year of PCV7/13 introduction	AM incidence[a] (overall)	AM incidence[a] before/after PCV	SP-AM incidence[a] before/after PCV	Dominant SP serotypes before/after PCVs	Comments
Roddy [61]	USA	1995–2005	122	2000/2010	NA	NA	NA	NA	No differences between pre-PCV7 (56 % of cases) vs. post-PCV7 (44 %); acute and chronic mastoiditis cases presented together; AM caused by antibiotic-resistant SP increased post-PCV7
Ongkasuwan [62]	USA	1995–2007	41	2000/2010	NA	NA	NA	Multiresistant 19A	Increase in the number of SP-AM in 2006–2007
Choi [63•]	USA	1996–2009	96	2000/2010	NA	NA	NA	NA	53 % Increase in AM cases post-PCV7; increase post-PCV7 of SP nonsusceptibility to penicillin and ceftriaxone
Daniel [64•]	Australia	2000–2010	84	2005/2011	NA	NA	NA	NA	AM, SP-AM and complicated AM fell when PCV7 was introduced and subsequently returned to pre-vaccination levels
Giannakopoulos [65•]	Greece	2010–2011	21	2006/2011	NA	NA	NA	NA/19A	19A—the predominant pathogen
Halgrimson [66•]	USA	1999–2008	242 (106 <2 years of age)	2000/2010	8.0 (<2 years) 1.3 (2–18 years)	<2 Years: 10 (1999)[b]; 11.0 (2001)[b]; 4.6 (2002)[b]; 4.5 (2003)[b]; 12.0 (2008)[b]	NA	NA	Annual incidence stable for 2–18 years old; decrease in <2 years for 2002–3 and increase again in 2008; increase in nonsusceptible SP from 0 (1999–2004) to 38 % (2005–2008)
Ruck [67]	USA		1	2000/2010	NA	NA	NA	Multiresistant 19A	Case report; patient previously immunized with 3 PCV13 doses
Kaplan [68]	USA	2007–2011	90	2000/2010	NA	NA	NA	NA	Some decrease form 31, 15, and 27 AM cases in 2007–8–9 to 13 and 4 cases in 2010–11
Kordeluk [15•]	Israel	2009–2012	61 (65)	2009/2010	11.1 2.58 (SP)	10.2/11.1	3.07	14, 19F, 6B/3,19A	Sequential PCV7/PCV13 data from 2009
Tamir [69]	Israel	2008–2013	57 (58)	2009–2010	NA	NA	NA	NA	Proportion of SP (+)–AM decreased in PCV7 and PCV13-immunized children

SP Streptococcus pneumoniae, *NA* not available

[a] Calculated as no. cases/100,000 population

[b] The respective years for the respective incidences

multiresistant 19A serotype as the most frequently isolated pneumococcal serotype before and after the introduction of PCV7. The only population-based study completed in a population immunized sequentially with PCV7 and PCV13 during 2009–2012 [15•] did not find any significant decrease in the AM and SP-AM incidence, but the serotype 19A was not isolated anymore in PCV13 immunized children. Two additional studies including the post-PCV13 period showed some decrease in the number of cases of *S. pneumoniae*-AM [68, 69].

Conclusions

AM is the most serious complication of AOM and the evidence presented on the dynamics of its incidence during the last 10–15 years is conflicting. While *S. pneumoniae* remains its major etiologic agent, *S. pyogenes* emerged during this period as the second most common pathogen of AM, despite being a relatively uncommon agent in the etiology of AOM. AM occurs frequently in patients without previous AOM history and also in patients previously treated with antibiotics for AOM. Magnetic resonance imaging should be considered as an excellent tool in the diagnosis of complications of AM. Surgical intervention (in particular simple mastoidectomy) may be necessary in around half of the cases of AM. Despite the remarkable success in reducing the rates of pneumococcal AOM, PCV7, and PCV13 did not reduce the incidence of AM and of pneumococcal AM. Because the experience with PCV13 is still limited, the next years should provide more conclusive and definitive information on the dynamics of AM during the post-PCV13 period.

Compliance with Ethics Guidelines

Conflict of Interest Sofia Kordeluk, Eugene Leibovitz, and Mordechai Kraus have no relevant disclosures.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by the author.

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