■ SPECIAL ARTICLE

National Consensus on Acute Otitis Media

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ETIOLOGY AND EPIDEMIOLOGY OF ACUTE OTITIS MEDIA

Acute otitis media (AOM) is one of the most common infectious diseases in children. Two out of every 3 children are estimated to have suffered at least 1 episode during the first year of life and more than 90% by the time they are 5 years of age[1]; between 10%-20% of all patients suffer frequent episodes of AOM.[2] The most common pathogens involved in AOM are *Streptococcus pneumoniae* (30% of cases), *Haemophilus influenzae* (20%-25%), and *Moraxella catarrhalis* (10%-15%),[3] although in Spain *Moraxella catarrhalis* is rarely the cause.[4] Other less frequent pathogens are *Streptococcus pyogenes* (3%-5%), *Staphylococcus aureus* (1%-3%), and, more rarely, anaerobic Gram negative bacilli such as *Escherichia coli* or *Pseudomonas aeruginosa*. Viral etiology in AOM is a highly debated issue. It is universally accepted that viral respiratory tract infection fosters AOM; however, there is no consensus among the authors in acknowledging these agents as an exclusive cause, even less so when it has been impossible to prove replication inside the cavity of the middle ear.[5]

In recent years, the increase in bacterial resistance has become a problem, especially in the case of pneumococcus, which has had an important impact on how this condition is treated. At present, more than 50% of the *S pneumoniae* strains have lost sensitivity to penicillin, and one third of all isolates are resistant to this micro-organism.[6]

This is particularly evident in children and even more so in upper respiratory infections, where strains that have lost sensitivity to penicillin may account for up to 70% of the cases.[7] Nevertheless, recent data in Spain indicate a decrease in this resistance,[8] perhaps related to a more rational use of antibiotic therapy and the administration of the conjugate pneumococcal vaccine (7-v CPV); nevertheless, this hypothesis is pending confirmation in the coming years.

Another, more recent change is the modification of bacterial colonization of the respiratory tract in countries with a high rate of implantation of the heptavalent pneumococcal vaccine.[9] The pneumococcal strains included in the vaccine have decreased significantly as causal agents of AOM, while new strains not included in the vaccine have replaced the former ones, but with the peculiarity that they are more sensitive to antibiotics.[10]

This change has been accompanied by an increase of *H influenzae* in children with AOM vaccinated with the 7-v CPV, the epidemiological and therapeutic scope of which remains unknown.[11]

DIAGNOSIS OF ACUTE OTITIS MEDIA

Although in recent years considerable progress has been made in what is known about AOM and its diagnosis, the diagnosis of this illness remains pending: "Although there is general agreement that antibiotics are indicated in the treatment of AOM, no such agreement exists when making a diagnosis."[12] However, recent studies have begun to shed some light on the subject and have revealed that the diagnosis of AOM must include consideration of the most specific signs and symptoms, such as earache, acute otorrhea, or otoscopy, with unequivocal data of inflammation, and eliminating other more non-specific ones, such as fever, rhinitis, vomiting, and insignificant otoscopy.[3-15] The problem is that pain is difficult to evaluate in young children, precisely those in whom AOM is most serious and most common. There are no studies dealing with the characteristics of earache in babies, and it is generally indicated with the imprecise term "irritability" or "sleeplessness." However, although we do not have scientific studies in this regard, sudden awakening and inconsolable crying after several hours of deep sleep, or unjustified, prolonged daytime irritability is highly characteristic of earache in children,[16] albeit these data have not been sufficiently underscored in medical literature.

An important guideline has recently been published regarding the attitude to be adopted in AOM that, to a large

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extent, sets the foundation for common policies, albeit it leaves some important aspects unresolved.[17]

If AOM is a local inflammation, it is logical for its diagnosis to require the classical signs of pain, oedema (in this case exudate), and reddening. Therefore, the new diagnostic criteria proposed by the American guideline are: *a)* acute onset; *b)* presence of exudate in the middle cavity of the ear, demonstrated by bulging of the tympanum, pathological pneumatoscopic findings, or otorrhea; and *c)* inflammatory signs and symptoms, such as earache or evident reddening of the tympanum. However, if we put this magnificent proposal under well-reasoned criticism, we find that, if strictly applied, it fails to include all possible cases of AOM; hence, it does not provide a diagnostic guarantee, since when translated to the real world, it gives rise to 2 different diagnostic situations.

1. In one, the 3 criteria are met and one can speak of *confirmed AOM*, as occurs in the case of acute otorrhea (recent + exudate + inflammation) or in acute earache with demonstrated transtympanic exudate (recent + exudate + inflammation).

Table 1. Diagnostic Criteria for Acute Otitis Media

Confirmed acute otitis media
Otorrhea with onset in the last 24-48 h, or
Earache appearing in the preceding 24-48 h plus tympanic bulging, with or without bright red appearance
Probable acute otitis media*
Without earache. Evidence of exudate in the middle ear, with bright reddening of the tympanic membrane + recent cold
Without otoscopy. Frank earache in the older child or sudden, unexplained crying, particularly at night and after several hours in the bed in infants + recent cold

*This diagnosis should be highly restricted and individualized, and assessed in the presence of risk factors.

Table 2. Factors for Poor Prognosis

Onset of AOM within the first 6 months of life
Recurrent AOM (rule out persistent AOM)*
First degree relatives with otic complications due to inflammatory illness

*Persistent acute otitis media (AOM): early relapse (within the first week) following treatment. Should be considered to be the same episode.

2. In the other situation, not all the criteria are satisfied, albeit there is a high possibility of the patient presenting AOM: a) earache in which it is impossible to confirm the presence of exudate in the middle ear (presence of cerumen that cannot be removed, a complicated external auditory canal, otoscopic findings that are difficult to interpret), and b) otoscopic confirmation of exudate in the middle ear, but without earache. In the absence of pain or otorrhea, there is no complete guarantee that the exudate is due to AOM and not to secretory otitis media, since pain is the only thing that differentiates it.[18] Nor does earache offer absolute sensitivity for AOM[14] and, furthermore, as pointed out, it can be difficult to recognize in the very young child.[16]

To get around this difficulty and offer the paediatrician an acceptable solution, we propose that the second situation be called *probable AOM* and that confirmed AOM be considered when it is accompanied by a recent cold in the upper airways, given the strong association between both processes (Table 1). In any case, careful consideration must be given to a diagnosis of probable AOM and paediatricians must assess their own expertise and the risks of a wrong diagnosis. We are also of the opinion that when there is a doubtful diagnosis (probable AOM), paediatricians must take into account the presence of factors for poor prognosis (Table 2), since these factors are causes of recurrent AOM, deafness, and more surgical interventions.[1,9,20] We propose that probable AOM should be considered confirmed in the presence of these prognostic factors for a poor course of illness. The most important differential diagnosis of AOM is presented in Table 3.

CLINICAL FORMS OF ACUTE OTITIS MEDIA

Recurrent Acute Otitis Media

Recurrent AOM is defined as the presentation of AOM with a minimal frequency of one episode every 2 months plus at least a 6-month history of evolution; that is, a minimum of 3 episodes over the preceding 6 months.[21]

However, this clinical form includes 2 very distinct situations: patients who present sustained effusion (chronic secretory otitis media) between episodes of AOM and patients with a normal otoscopy between episodes of AOM. In the first case, the episodes of AOM can be considered exacerbations of a continuum, known by some authors as

Table 3. Differential Diagnosis of Acute Otitis Media*

	Differential Diagnosis	*Differential Clinical Picture*
AOM with otorrhea	Otitis externa	Pain and/or hypersensitivity of the pinna
AOM with earache	Secretory otitis media, rhinitis, and acute tube obstruction	Evident bulging and/or reddening of the ear drum
AOM with irritability or unexplained crying in small children	Pain of other origin: unseen trauma, intestinal invagination, tourniquet syndrome, other	Pathological findings on otoscopy

*AOM indicates acute otitis media.

otic disease,[22] and in the second as recurrent AOM, in the strict sense of the term. Nevertheless, recurrent AOM diagnosis and follow-up in both situations should not differ and tympanostomy tube implantation should only be considered in the case of chronic secretory otitis media; it should be pointed out that medical treatments for this condition achieve scant results, if any.[23]

Among the possible risk factors for recurrent AOM, the following are worth mentioning: low socioeconomic level, cold months, attending a day-care centre, being male, family history of recurrent AOM, use of artificial milk, smoking in the home, and early onset of the first episode.[20,24]

Persistent Acute Otitis Media or True Relapse

There is no universally accepted definition for persistent acute otitis media or true relapse and in the medical literature it is often confused with recurrent AOM and with treatment failure.[25]

From a microbiological perspective, true relapse or persistence is considered to be when the causal micro-organism is the same in the first and second episodes while recurrence is when the micro-organisms are different. Nevertheless, this definition is not of much use in routine daily practice.

However, recent studies are of some help in finding that true relapse due to *H influenzae* occurs in the first 2 weeks, whereas when *S pneumoniae* is the causative agent, relapse can take place at any time, although it also tends to present in the first 15 days.[26] Therefore, we believe that any other episode during the first month following treatment, even more so in the first 15 days, should be considered to be the same one and be treated as such and, in this case, not count as a new AOM during the follow-up of recurrent AOM.

Acute Otitis Media in an Ear With a Previous Perforation

This is defined as the presence of acute suppuration in patients diagnosed or treated for chronic otitis media, with alterations in the integrity of the tympanic membrane. This type of patient includes individuals with chronic perforation of the eardrum in tympanostomy tube users. In these cases, *P aeruginosa*, enterobacteria, and *S aureus* are commonly detected in the purulent exudate.

COMPLICATIONS OF ACUTE OTITIS MEDIA

One quarter (25%) of all patients with AOM or chronic otitis media present complications prior to the introduction of antibiotics.[27] Two per cent develop suppurative, intracranial complications, with fatal outcome in 75% of cases. However, despite the widespread use of antibiotics for the treatment of the AOM in the last 50 years, there are still sequelae and complications that can even be life-threatening. In recent years, there have been more publications addressing the growing incidence of intratemporal and intracranial complications of AOM.[28,29]

The most common complication is acute mastoiditis, particularly common in infants and young children. Other complications are facial paralysis, due to compression and oedema of the facial nerve; laberynthitis, owing to the spread of the infection from the middle ear or from the mastoid cells, and meningitis, either as a result of direct spread or bacteraemia. The incidence of mastoiditis has decreased following the introduction of antibiotic therapy, despite the fact that in recent years there has been an increase,[30] even in Spain.[31] Nowadays, other complications are rare.

The diagnosis of mastoiditis is largely based on clinical criteria. It debuts with pain, swelling, and erythema in the mastoid area, generally associated with anteversion of the external ear. There may be otorrhea. The presence of fluctuation in the area behind the ear should lead the clinician to suspect the presence of a subperiosteal abscess. In doubtful cases or in those in which the presence of subperiosteal abscesses is suspected, a computerized tomography should be performed. In case of doubt, intravenous treatment is recommended before carrying out the computerized tomography, assessing the subsequent course of the illness.[32]

THE ROLE OF THE ENT SPECIALIST IN ACUTE OTITIS MEDIA

In the Diagnosis

The ENT specialist plays a key role in the diagnosis of AOM[33] (Table 4). The difficulties of conventional otoscopy, in some cases due to problems of interpretation and in others, to cerumen in the external auditory canal, can be overcome by the ENT specialist by using aspiration cannulae or specific pincers, and otoscopic microscopy. This is particularly important in the case of probable AOM, when there is a need for diagnostic confirmation.

In the Course of the Illness

The poor course of AOM or when complications are suspected may require consultation with the ENT specialist to assess the need for imaging studies or surgical intervention.

In Treatment

The most specific action carried out by the ENT specialist in the diagnostic process is tympanocentesis or

Table 4. Situations That May Require Participation of the ENT Specialist in Otoscopic Diagnosis*

Patients with a narrow or anfractuous canal
Patients with EAC blocked with secretions, debris, or wax
Patients in whom otoscopy is difficult
Patients with doubtful interpretation of otoscopy: presence of inflammatory versus seromucous content

*EAC indicates external auditory canal.

Table 5. Indications for Tympanocentesis*

Samples taken from the middle ear for microbiological culture
Patients properly treated who fail to present clinical response
AOM in neonates
AOM in immunodepressed individuals
Treatment for pain fails to respond to the usual analgesics

*AOM indicates acute otitis media.

myringotomy.[34] The indication for this technique is presented in Table 5. It is advisable that it be performed with sedation and in some cases, with general anaesthesia, evaluating the placement of a tympanostomy tube. Some indications for this technique in uncomplicated AOM are presented below:

– Take other samples for culture without requiring a new myringotomy.
– Monitor the course of the AOM, by looking for the presence of exudate through the tube.
– Use topical treatments if indicated by the microbiology.
– Prevent relapses of the illness.

TREATMENT

Symptomatic

The treatment of choice in all cases is analgesia and in most cases ibuprofen or paracetamol suffices.[17] If there is no response, tympanocentesis should be considered.

Antibiotic Therapy

Antibiotic treatment for AOM should be the sum of good knowledge of the antibiotics available, the patient's characteristics, and of the disease process. Hence, for proper choice of antibiotic therapy it is essential that the activity and drug properties of the antibiotics must be understood, as well as bearing in mind the characteristics of the illness. AOM is an illness that entails a spontaneous cure rate of 80%-90%.[35] However, this spontaneous cure rate is not the same for all the different causal pathogens, and is around 80% in the case of *M catarrhalis*, 50% in *H influenzae*, and 16% in *S pneumoniae*.[36] This high spontaneous cure rate hinders the study of the illness and limits outcomes in many scientific trials dealing with antibiotic therapy[37]; in addition to disguising alleged clinical efficacy. Some meta-analyses of antibiotic effectiveness in AOM have found that 14-17 patients need to be treated for 1 of them to benefit from treatment, with the uniqueness that at present we do not know which patient will be favoured.[38,39] However, we do know that the spontaneous cure rate of the illness is lower in children under the age of 2 years[35] and that response to antibiotic therapy is better in patients with severe AOM (high fever or severe earache).[40] Likewise, we know that infants with AOM and patients with a positive family history are more prone to presenting repeated AOM and have more surgery.[41,42] For all these reasons, small children with AOM, patients of any age with severe AOM, and those with a family history of ear sequelae due to AOM are those who benefit most from antibiotic therapy.

Many different antibiotics can be used in AOM. However, the choice of antibiotic therapy must be guided by pharmacodynamic criteria and activity against the causal pathogens. Previous and recent studies have demonstrated a correlation between bacteriological eradication and clinical cure. A classical study found a clinical response rate of 93% in patients in whom the pathogenic strains had been eradicated from the middle ear in comparison with 63% in those in whom the causal bacteria had not been eradicated.[43] These results have been confirmed in another more recent study.[44] Antibiotics with a powerful eradicating capacity must therefore be used.

The administration of high dose amoxicillin oral (80-90 mg/kg/day) achieves concentrations in the middle ear that are capable of eradicating sensitive, intermediate and even penicillin-resistant pneumococci.[45-47] As a result, the empirical use of amoxicillin at high doses has high rates of eradication of pneumococcus. However, amoxicillin alone might fail to eradicate betalactamase-producing *H influenzae*, where high doses of amoxicillin are insufficient.[47] *H influenzae* causes approximately 20% of the cases of AOM and has 20%-25% amoxicillin-resistant strains, which means that approximately 1 of every 8 or 9 cases of AOM may be caused by amoxicillin-resistant strains,[48] with the consequent risk of failure. Only oral amoxicillin-clavulanic acid and cephalosporins (especially cefuroxime axetil, cefpodoxime proxetil, and cefnidir) present good activity against betalactamase-producing *H influenzae* and *M catarrhalis*, albeit with discreet activity against pneumococci that are not sensitive to penicillin.[49,50] Nevertheless, amoxicillin at high doses, associated with clavulanic acid at a ratio of 8:1, presents adequate activity against all the strains indicated; consequently, this is the antibiotic of choice in cases in which the entire spectrum must be covered. Macrolides present scant activity on the extracellular pathogens present in the middle ear and, furthermore, in Spain, approximately between 30% and 50% of pneumococci are resistant to them[7,8]; hence, their use in AOM should be limited to those situations in which there is no other alternative, such as in patients who present severe anaphylactic reaction to betalactames. Ceftriaxone should not be used for AOM treatment outside hospital settings (its use is not authorized in these circumstances) except for exceptional situations, with a precise indication from a hospital and under strict control by a specialist. Eardrops containing antibiotics are never indicated in the usual forms of AOM. Their use may be contemplated in exacerbations of chronic otitis media with perforation and in tympanostomy tube carriers.

Our proposal is presented in Table 6. The antibiotic of choice is amoxicillin, at a dosage of 80-90 mg/kg/day, divided into 3 doses. High dose amoxicillin associated with clavulanic acid, at a ratio of 8:1, is a second choice antibiotic. Its precise indication has not been scientifically defined, although it may be indicated in patients with high fever or severe earache, as well as in patients in whom initial

treatment with amoxicillin has failed.[17] The guidelines of the American Academy of Pediatrics and the American Academy of Family Physicians also consider high dose amoxicillin with clavulanic acid should be the treatment of choice in AOM caused by ampicillin-resistant *H influenzae* or *Moraxella catarrhalis*.[17] Nevertheless, in daily clinical practice, it is impossible to know if this is the case, unless, of course, there has been previous treatment failure with amoxicillin.

However, given that AOM in infants, particularly less than 6 months of age and in children with a family history of sequelae due to AOM, presents a high risk of repetition, we propose high dose amoxicillin associated with clavulanic acid as the first treatment choice in these cases (Table 6).

Optimal treatment duration is a matter of debate. In the comparison of 5 days of antibiotic therapy versus 7-10 days, the longer treatment regime was somewhat more efficacious at the end of the treatment period, but at 20-30 days, both were similar in terms of outcome, such that 44 children would have to be treated for 7-10 days, instead of 5 days, in order for one to benefit.[51]

Therefore, treatment duration should factor in the child's age, prior history of recurrent AOM and the presence or absence of previous treatment failure. Treatment duration of 10 days is advised for young children in severe and recurrent AOM.[17] If there is early relapse (persistent AOM), the same antibiotic therapy is to be repeated, but for longer the second time around.

TREATMENT OF COMPLICATIONS

Acute Mastoiditis

Significant controversy surrounds the treatment of acute mastoiditis, which is based on intravenous antibiotic therapy. The antibiotics of choice are amoxicillin with clavulanic acid, 100-150 mg/kg/day or cephotaxim, 100-150 mg/kg/day. This antibiotic therapy should be modified in the event that there is microbiological information available from the exudate of the middle ear or from the mastoid exudate. However, early myringotomy is more arguable, as some authors advise it in all cases of acute mastoiditis,[30] whereas others believe that it should be postponed depending on the response to antibiotic therapy. Mastoidectomy is indicated at 2-5 days if there is no response to antimicrobial treatment or in the event that complications arise.[52] In the past, mastoidectomy was standard in almost all patients with complications, although in recent years it has been a less common practice and today, more conservative treatments are used.

Nowadays, initial treatment with intravenous antibiotic therapy with or without myringotomy is recommended. If there is a subperiosteal abscess, simple drainage is performed.[53] Mastoidectomy is carried out if, after simple drainage, the patient fails to evolve favourably within 48 h, when there is facial paralysis or if there are intracranial complications. This consensus recommends the treatment displayed in Figure.

Table 6. Antibiotic Treatment of Acute Otitis Media

Child with an evident diagnosis and mild or moderate involvement Amoxicillin, 80-90 mg/kg/day, distributed every 8 h for 5-7 days If clinical failure after 48-72 h of treatment: change to amoxicillin-clavulanic acid (8:1), 80 mg of amoxicillin/kg/day, in divided doses every 8 h, for 5-10 days In children over the age of 2 years, without factors indicative of poor prognosis, one alternative to antibiotic therapy is analgesic treatment with re-evaluation after 48 hundred
Children with evident diagnosis and severely affected (fever ≥39ºC or severe earache) or under the age of 6 months
Amoxicillin-clavulanic acid (8:1), 80 mg of amoxicillin/kg/day, distributed every 8 h for 7-10 days If clinical failure after 48-72 h of treatment: tympanocentesis should be performed and treatment according to Gram's staining, culture and antibiogram
Children with "possible" AOM
Be sure to establish a sure diagnosis If mild or moderate: wait and see If intense: assess initiating treatment with amoxicillin associated with clavulanic acid or not, according to the child's age and history
Failure of previous treatment (lack of clinical response)
If initial treatment with amoxicillin: administer amoxicillin-clavulanic acid (8:1), 80 mg/kg/day, for 10 days If initial treatment with amoxicillin-clavulanic acid: administer ceftriaxone, i.m., 50 mg/kg/day, for 3 days If treatment with ceftriaxone: tympanocentesis and treatment, depending on Gram's staining, culture and antibiogram
Children allergic to penicillin
If non-anaphylactic reaction: cefpodoxime proxetil or cefuroxime axetil, for 10 days. If anaphylactic reaction (type 1): azithromycin (or clarithromycin). Bear in mind the possible suitability of performing tympanocentesis if there is significant involvement or if clinical failure

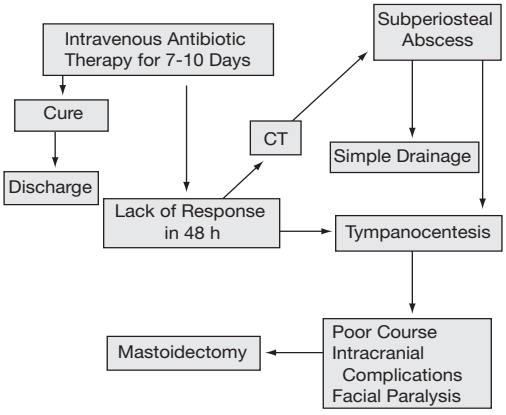

Figure. Treatment algorithm for acute mastoiditis.

Mastoiditis Without Subperiosteal Abscess

Start treatment with antibiotic therapy with intravenous amoxicillin-clavulanic acid or intravenous cephotaxim/ceftriaxone. If no positive response is seen within 48 h, tympanocentesis should be performed.

If the infection presents an unfavourable course or if a subperiosteal abscess should develop, proceed with a simple drainage. Mastoidectomy may not be mandatory and is only indicated in those cases that evolve poorly after the previously described treatments or if facial paralysis, or intracranial complications develop.

Facial Paralysis Without Acute Mastoiditis

If this second complication arises, tympanocentesis should be performed and antibiotic therapy started.

Acute Labyrinthitis

Treatment consists of antibiotic therapy, as in AOM, without the need for surgical measures.

Intracranial Complications

A multidisciplinary team comprising a neurosurgeon, a paediatrician, and an ENT specialist is required and hence it falls beyond the scope of this consensus document.

PROPHYLAXIS

There are 3 major lines of prophylaxis: antibiotics, vaccines, and surgery.

Antibiotic prevention is indicated for recurrent AOM (see above) and is achieved with amoxicillin, 20 mg/kg/day, in a single dose, during the winter months.

However, prophylaxis decreases 0.1-0.2 episodes of AOM per month in children under the age of 2 years,[54] while at the same time it fosters bacterial resistances, owing to selection for intermediate and resistant strains. Hence, its use is highly controversial.

The pneumococcal vaccines has a prevention rate of 6%-7% in cases of AOM and is somewhat higher in recurrent AOM.[9,55] Another good alternative for prevention against AOM is the use of flu vaccines,[56] particularly if the intranasal mode of delivery becomes regularized,[57] although these data require more comprehensive information than is currently available.

The surgical alternative consists of inserting tympanostomy tubes. The function of these tubes is to substitute the Eustachian tube and facilitate ventilation and the positive pressure within the cavity of the middle ear. Exclusive adenoidectomy is not indicated in recurrent AOM, although it may be contemplated after an imaging study and in the event that tubes are to be inserted.[58]

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