PEER REVIEWED FEATURE 2 CPD POINTS

Key points

- Diagnosis of acute otitis media (AOM) can be challenging in infants and children because of factors such as poor compliance with examination and inconclusive signs.
- A reddened tympanic membrane alone is not sufficient for diagnosis; a cloudy, bulging membrane with reduced mobility on pneumatic otoscopy combined with a typical clinical history is pathognomonic of AOM.
- Antibiotic treatment is recommended for children with AOM aged 6 months or younger, those aged over 6 months with otorrhoea or severe symptoms, those aged between 6 and 24 months with bilateral AOM and those whose follow up is uncertain or difficult.
- Observation and follow up after 24 to 48 hours is an option for some children aged over 6 months who meet specific criteria.
- Specialist referral is warranted for persisting or recurrent disease, complications or concerns about speech and language.

Acute otitis media in young children Diagnosis and management

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Acute otitis media is one of the most common reasons children are prescribed antibiotics. However, it is notoriously difficult to diagnose with certainty in infants and young children and management, especially when to use antibiotics, has been controversial. Updated guidelines may help resolve these problems.

here is little doubt that acute otitis media (AOM) is one of the most common inflammatory diseases in childhood. It is a major cause of morbidity in children and one of the most common reasons children are prescribed antibiotics. However, diagnosis of AOM can be difficult as symptoms and signs are not necessarily definitive and physical examination can be challenging in this age group. In addition, management of AOM has been widely debated, with numerous different treatment guidelines in the published literature.¹⁻⁴ The use of these guidelines is further complicated by confusion between the categories of otitis media. Overdiagnosis of AOM is believed to be common, leading to the inappropriate use of antibiotics, which promotes antibiotic resistance and unnecessarily increases the risk of side effects.

DEFINITIONS OF OTITIS MEDIA

Otitis media is a collective of infective or inflammatory disorders of the middle ear. It has been described as a continuum, ranging from AOM and recurrent AOM through to otitis media with effusion and chronic suppurative otitis media, and can have a significant impact on hearing.^{5,6} The categories of otitis media are defined in Box 1.⁶

EPIDEMIOLOGY

Two-thirds of children will have an episode of AOM by their third birthday, and around half will have three or more episodes. The incidence of AOM is highest in the first two years of life.⁷ There is a peak in incidence in babies aged under 1 year, with a further peak around age 5 years.⁶ In the community, AOM is one of the most common reasons for children under 5 years of

Dr Wood is a Registrar in Otolaryngology and Professor Vijayasekaran is an Otolaryngologist and Clinical Associate Professor in the Department of Otolaryngology, Head and Neck Surgery, Princess Margaret Hospital For Children, University of Western Australia, Perth, WA. age both to present to a doctor and to be prescribed antibiotics.⁸ The burden to the community is significant, with a recent survey showing that more than 50% of parents with children diagnosed with AOM have to take time off work.⁸

It has been well documented that certain populations have a much higher incidence of AOM and otitis media with effusion. Australian Aboriginal children have the highest published prevalence of AOM in the world, with a study of around 700 children showing that nearly 91% had some form of otitis media. Of these, nearly a third were classified as having AOM.9 This study was conducted in 29 remote communities before the introduction of the seven-valent pneumococcal conjugate vaccine, which has reduced the incidence of AOM.¹⁰ Nevertheless, the incidence of ear disease in the Australian Aboriginal population, and in indigenous communities worldwide, remains much higher than in the general population.

AETIOLOGY

The pathogenesis of AOM is multifactorial, involving a complex interaction between microbial agents, host immune response, cell biology of the middle ear and nasopharynx and environmental factors.¹¹ The bacteria *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Moraxella catarrhalis* are those most commonly implicated in upper respiratory tract infections and most frequently isolated from middle ear effusions in AOM (Table 1).^{12,13}

Viruses also appear to have a role. AOM is typically preceded by a viral infection of the upper respiratory tract, most commonly due to respiratory syncytial virus; other common causes include influenza viruses, parainfluenza viruses, rhinoviruses and adenoviruses. A role for viruses in the pathogenesis of AOM is further supported by the results of a randomised controlled trial of the early use of oseltamivir in influenza. The incidence of AOM development during the influenza illness was decreased by 85% in children who commenced oseltamivir within 12 hours of the onset of influenza symptoms.¹⁴

There is further evidence of a virus–bacterial interaction in AOM. The presence of the respiratory viruses rhinovirus and adenovirus in the



nasopharynx in asymptomatic children has been associated with the detection of M. catarrhalis.15 Further studies in an Australian Indigenous population suggested that a virus-bacterial interaction led to more severe symptoms.¹⁶ In addition, studies in animal models found an increased load of H. influenzae in the nasopharynx after nasopharyngeal inoculation with respiratory syncytial virus. Infection of the airway has been proposed to downregulate expression of β-defensin, an antimicrobial peptide implicated in the resistance of epithelial surfaces to microbial colonisation.17 In addition, Sendai virus co-infection with S. pneumoniae and M. catarrhalis was noted to increase the incidence and duration of AOM and bacterial load.18

FACTORS INFLUENCING AOM INCIDENCE Age and other biological factors

The most important risk factor for AOM is young age, with the highest incidence of the condition in the first two years of life.⁷ This may be partly explained by the anatomy of the Eustachian tube, which is shorter, more horizontal

1. CATEGORIES OF OTITIS MEDIA*

Acute otitis media (AOM): Infection of the middle ear with acute onset, middle ear effusion and signs of inflammation

Recurrent AOM: At least three episodes of AOM in six months, or four episodes in 12 months

Otitis media with effusion: A middle ear effusion without signs of acute infection or inflammation ('glue ear')

Chronic suppurative otitis media: Continuing inflammation in the middle ear leading to otorrhoea and perforation of the tympanic membrane

 * Adapted from Birman C. Med Today 2005; 6(8): 14-22. 6

and more compliant at this age than in older children and adults. Other factors that may play a role include the limited immunological response to antigens in this age group, cessation of breastfeeding and increased exposure to environmental pathogens.¹⁹ The role of the latter is supported by the second peak of incidence, which occurs at around 4 to 5 years of age, when children typically begin to attend preschool.⁵

Children with recurrent AOM are slightly more likely to be male and to have ceased breastfeeding before the age of six months.²⁰ Recurrent AOM is also increased in patients with immune deficiencies and in those with craniofacial disorders (including cleft palate) and Down syndrome, possibly because of Eustachian tube dysfunction.²¹

Genetic factors may also have a role in susceptibility to otitis media.^{21,22} Twin and triplet studies have shown a substantial heritable component to the clinical spectrum of otitis media.²³

Pneumococcal immunisation

The use of the seven-valent pneumococcal vaccine has reportedly reduced the risk of AOM by up to 34%, but little information has been published as yet on the further

TABLE 1. BACTERIA ISOLATED FROM CHILDREN WITH ACUTE OTITIS MEDIA*

Bacterium	% of cases
Haemophilus influenzae	57%
Streptococcus pneumoniae	31%
Moraxella catarrhalis	5–10%
Group A streptococci	2%
Staphylococcus aureus	1%
Pseudomonas aeruginosa	1%

* Modified from Qureishi A, et al. Infect Drug Resist 2014; 7: 15-24¹² and Coker TR, et al. JAMA 2010; 304: 2161-2169.¹³

impact of the 13-valent vaccine.¹⁰ There is, however, evidence that pneumococcal vaccination may allow nonvaccine serotypes of *S. pneumoniae* to increase in prevalence in Australia, as they did in the USA.²⁴ Nevertheless, there has been a reduction in the incidence of pneumococcal diseases overall and otitis media has become a milder condition since the introduction of the pneumococcal vaccine together with the *H. influenzae* vaccine.^{25,26} Furthermore, studies show that *H. influenzae* is now the most commonly isolated organism in the middle ear of children with recurrent AOM.²⁷

Environmental factors

It is well documented that children attending daycare are significantly more likely to develop AOM. A study of more than 600 children found that those who attended daycare had more than twice the odds of having an ear infection in the preceding week.²⁰ Interestingly, the same study failed to demonstrate an increased incidence of AOM in children with increased measures of overcrowding. Nevertheless, low socioeconomic status and overcrowding are often documented as risk factors for AOM.⁵ Overcrowding facilitates the transmission of upper respiratory tract infections, the most frequent risk factor for AOM.⁵

In addition, a multivariate analysis of factors related to otitis media showed that maternal smoking increases the infant's risk of otitis media more than ninefold, and paternal smoking more than sixfold.²⁰

Seasonal variation

There is some evidence that the incidence of AOM may be highest in autumn and winter, and lowest in summer.²⁸ It is also suggested that children born in autumn may be more susceptible to recurrent AOM as they are exposed to winter pathogens during their most vulnerable months.

Indigenous status

As discussed above, the rate of AOM and chronic suppurative otitis media is significantly higher in the Australian Aboriginal population than in the general population.

DIAGNOSIS

Recent guidelines from the American Academy of Pediatrics emphasise the importance of accurate diagnosis of AOM for clinical decision-making and also for providing the framework for high quality research.² Overdiagnosis leads to overtreatment, with the risks of antibacterial resistance and medication side effects such as skin rash and diarrhoea. Underdiagnosis may delay adequate treatment and potentially increase the risk of complications.

However, diagnosis of AOM may be difficult as there are no definitive symptoms and no 'gold standard' for diagnosis. Signs can cover a spectrum as the disease progresses. An erythematous tympanic membrane together with otalgia have been regarded as indicating AOM, but only 40% of children with these features actually have AOM.⁵ In addition, otoscopy is recognised as one of the most technically difficult tasks to perform in young children.

A recent systematic review recommended three main criteria that need to be met for a diagnosis of AOM:

• acute symptoms of infection

practice can be more complicated.

• evidence of middle ear inflammation, such as tympanic membrane erythema

 presence of middle ear effusion.¹³ Requirements of Australian guidelines are similar.²⁹ This approach provides a simple framework for diagnosis, but clinical

Symptoms of AOM

Typical symptoms associated with AOM and their sensitivity and specificity for diagnosis are shown in Table 2.^{5,30} A systematic review found that otalgia had the highest predictive value for diagnosis of AOM but was present in only 50 to 60% of cases.³¹ Not only may specific ear symptoms be absent but they may also fail to be recognised by parents, particularly in very young children.³²

Evidence suggests that symptoms such as restless sleep, ear rubbing, fever, and nonspecific respiratory or gastrointestinal tract symptoms are not able to differentiate children with and without AOM. For example, a questionnaire survey of 469 parents who suspected their child had AOM based on symptoms found that fewer than half actually had AOM, based on strict otoscopic criteria.³³ The time course of symptoms is important, with AOM typically having a short history.

Otoscopy

Similarly, diagnosing AOM based on otoscopic signs can be difficult in children. Otoscopy requires patience, a compliant child and a parent confident enough to adequately restrain their child if required.³⁴ Furthermore, in nearly 80% of children under the age of 12 months, the tympanic membranes are either partially or totally obscured by wax, hindering accurate diagnosis.³⁵

Otoscopy can be more fruitful if the

TABLE 2. SYMPTOMS OF ACUTE OTITIS MEDIA AND SENSITIVITY AND SPECIFICITY FOR DIAGNOSIS*

Symptoms	Sensitivity (%)	Specificity (%)
Common symptoms		
Otalgia	54	82
Pulling/tugging of ear	42	87
Fever	40	48
Irritability	55	69
Other symptoms		
Otorrhoea	-	-
Vomiting	11	89
Anorexia	36	66
Diarrhoea	-	-
Lethargy	-	-

* Adapted from Coates HL. Med Today 2001; 2(11): 42-52⁵ and Pichichero ME. Pediatr Clin N Am 2013; 60: 391-407.³⁰

child is positioned on the parent's lap, with one of the parent's arms restraining the child's shoulder and the other arm holding the child's head against the parent's chest. If wax is present, it can be removed in a compliant child with a wax curette or with the help of topical preparations.

Distinguishing AOM from other forms of otitis media

AOM is differentiated from otitis media with effusion and chronic suppurative otitis media based on history and examination findings.¹² Differentiating AOM from otitis media with effusion enables unnecessary antibiotic treatment to be avoided. Typically, as AOM is a purulent middle ear process, signs and symptoms consistent with acute inflammation should be present.

The American Academy of Pediatrics guidelines state that AOM should be diagnosed in:

- children with moderate to severe bulging of the tympanic membrane and new-onset otorrhoea in the absence of otitis externa
- children with mild bulging of the tympanic membrane and recent-onset

otalgia or intense erythema of the tympanic membrane (Figure 1a).²

A recent systematic review confirmed that otoscopic findings of middle ear inflammation, effusion and a bulging tympanic membrane are positive predictors of AOM.13 The presence of a 'cloudy' bulging tympanic membrane with impaired mobility on pneumatic otoscopy (discussed below) is considered the best predictor of AOM.² A bulging tympanic membrane is also highly correlated with the finding of a bacterial pathogen on tympanocentesis: middle ear fluid from children with a bulging tympanic membrane alone yielded a positive bacterial culture in 75% of cases, increasing to 80% if the tympanic membrane was discoloured to yellow.36 The absence of middle ear fluid excludes AOM.

In the presence of the above symptoms and signs, the diagnosis of AOM is almost unequivocal, but in their absence, the diagnosis can be difficult to make with any certainty. The addition of pneumatic otoscopy to assess the mobility of the tympanic membrane increases the accuracy of AOM diagnosis, with a sensitivity of over 90% and specificity of nearly 80%.³² In this



Figures 1a and b. Otoscopic view in patients with (a, left) acute otitis media, showing a reddened bulging tympanic membrane, and (b, right) otitis media with effusion, showing a fluid level.

technique, positive and negative pressure is applied to the tympanic membrane in the presence of a well-formed seal between the speculum and the external auditory meatus. Mobility of the tympanic membrane is typically decreased or absent in the presence of a middle ear effusion. This test cannot differentiate AOM from otitis media with effusion (Figure 1b), but its use together with clinical history and other examination results can help diagnosis.

Nevertheless, a study using video otoendoscopic images found that the ability of different doctor groups to differentiate AOM from otitis media with effusion varied. A correct diagnosis was made by otolaryngologists 70% of the time, by paediatricians 50%, and by GPs 45%.³⁷ In addition, there is evidence AOM may be overdiagnosed clinically in more than 30% of children.³²

In summary, diagnosis of AOM should be based on clinical history and careful evaluation of the tympanic membrane, using adequate illumination in the presence of a clear ear canal. The best predictor of AOM is a cloudy, bulging tympanic membrane. Although there is evidence that a distinctly red, haemorrhagic tympanic membrane may indicate AOM, only 40% of children with this sign have AOM.³² The addition of pneumatic otoscopy increases the accuracy of AOM diagnosis, but lack of access to adequate equipment and lack of education and skills may hinder the use of this technique.

MANAGEMENT

Controversy about management

The rapid increase in antibiotic resistance and major contribution of AOM to antibiotic prescription in children has prompted concern about the accuracy of AOM diagnosis and inappropriate prescribing of antibiotics. Treatment of AOM also remains controversial, with different national guidelines around the world.1-4 Typically, AOM follows a relatively benign course in the absence of antibiotic treatment, with symptomatic relief with analgesia and antipyretics alone. A recent meta-analysis showed that nearly 80% of children had spontaneous relief within two to 14 days.12 However, in children younger than 2 years the corresponding percentage is estimated at around 30%.

Because of the high rates of spontaneous resolution of AOM, the use of antimicrobials has been questioned, with a recent Cochrane review finding only a modest reduction in symptoms with use of antimicrobials.38 However, closer analysis of the studies included in this review identified issues with both the populations and diagnosis of AOM. Children with severe symptoms were specifically excluded but are the group most likely to require antibiotics. Secondly, in a number of the studies only a minority of children had a bulging tympanic membrane, a clinical sign previously discussed as being important in the diagnosis of AOM.

Antibiotic treatment

Who should be treated with antibiotics? Currently, guidelines appear to be unanimous in recommending antibiotic treatment for children aged 6 months or younger with AOM.^{2,29} The American Academy of Pediatrics updated their guidelines in 2013, recommending that antibiotics should also be given to children older than 6 months with evidence of AOM if:^{2,10}

- they have otorrhoea or
- they have severe symptoms or
- they are aged between 6 months and 2 years and have bilateral AOM or
- follow up is uncertain or difficult (Table 3).

The role of observation, with follow up after 24 to 48 hours, for the management of AOM is limited to: 2,10

- children older than 2 years who do not have otorrhoea or severe symptoms
- children aged between 6 months and 2 years who do not have otorrhoea or severe symptoms and have only unilateral AOM.

Australian guidelines recommend that in the absence of systemic features such as fever, antibiotic therapy be delayed in children over the age of 6 months.²⁹ Review is recommended after 24 hours in children aged between 6 months and 2 years and after 48 hours in childen older than 2 years, with antibiotics typically prescribed if there has been no improvement.

Reportedly, for every 100 healthy children with AOM, 80 will improve within three days without antibiotic therapy, compared with 92 if treated with amoxycillin.³⁸ Of those 100 children treated with the antibiotic, reportedly 10 would develop a rash and 10 would develop diarrhoea.³⁹ Consequently, the prescription of antibiotics is not without risk.

The fear of developing a complication of AOM, such as mastoiditis, is thought to prompt the prescription of antibiotics; however, 4800 children must be treated to prevent one case of mastoiditis. Additionally, the recommended follow up after 24 to 48 hours would identify patients who are not improving. Therefore, with adequate assessment

Age of child	AOM with otorrhoea		AOM without otorrhoea		AOM with severe symptoms	
	Unilateral	Bilateral	Unilateral	Bilateral	Unilateral	Bilateral
0 to 6 months	Antibiotics	Antibiotics	Antibiotics	Antibiotics	Antibiotics	Antibiotics
6 months to 2 years	Antibiotics	Antibiotics	Antibiotics or observation	Antibiotics	Antibiotics	Antibiotics
Over 2 years	Antibiotics	Antibiotics	Antibiotics or observation	Antibiotics or observation	Antibiotics	Antibiotics

TABLE 3. AMERICAN ACADEMY OF PEDIATRICS TREATMENT RECOMMENDATIONS FOR ACUTE OTITIS MEDIA (2013)*

ABBREVIATION: AOM = acute otitis media. * Adapted from Lieberthal AS, et al. Pediatrics 2013; 131: e964-e999² and Dickson G. Prim Care 2014; 41: 11-18.¹⁰

and follow up such cases should be rarer. It is important to note that these guidelines are not appropriate for Australian Aboriginal and Torres Strait Islander people, who should commence antibiotic treatment in all cases.⁴⁰

What antibiotics should be used?

Bacterial resistance is a significant concern and an increasing clinical problem in AOM. Although some strains of H. influenzae and M. catarrhalis are resistant to amoxycillin through their production of beta-lactamase, this can typically be overcome by including a beta-lactamase inhibitor such as clavulanic acid in the treatment regimen. The prevalence of antibiotic-resistant S. pneumoniae and beta-lactamase producing H. influenzae is influenced by patient age, recent exposure to antibiotics, attendance at daycare and pneumococcal immunisation. A study reported penicillin resistance in nearly half of all nasopharyngeal isolates of these two bacteria.12

First-line antibiotics for AOM include:

- amoxycillin (50 to 60 mg/kg per day in two or three doses), unless the child has received this antibiotic in the previous month
- cefuroxime (30 mg/kg per day in two divided doses) as an alternative
- in the case of penicillin allergy, erythromycin (30 to 50 mg/kg per day in three divided doses) or clarithromycin (15 mg/kg per day in two divided doses). For treatment failure, second-line anti-

biotics include:

amoxycillin plus clavulanic acid

(22.5 + 3.2 mg/kg three times per day)

- clindamycin (30 to 40 mg/kg per day in three doses)
- a third-generation cephalosporin, such as ceftriaxone 50 mg/kg per day intramuscularly or intravenously, particularly if amoxycillin has been used in the previous 30 days.² Adults are nearly 20 times less likely to develop AOM than children; their management should follow similar principles to those used in children.

Analgesia

Analgesia is an important part of AOM management, and under-reported in the literature. Paracetamol or NSAIDs can be used for pain relief. This may be required for up to seven days despite antibiotic treatment. Other oral medications (such as antihistamines) and decongestants have little evidence to support their use but a five to eight times increase in the risk of side effects.¹⁰

SPECIALIST REFERRAL When to refer

Although most episodes of AOM resolve, it is important to recognise when to refer children to an otolaryngologist. Even after an uncomplicated episode of AOM, there is a possibility of developing recurrent AOM or a persisting middle ear effusion. Such an effusion is recognised in 63% of children after AOM at two weeks, 40% at one month, and 26% at three months.⁶ After three months, the likelihood of this effusion resolving is reduced. Consequently, referral to an otolaryngologist is recommended for children who have recurrent episodes of AOM or persisting effusion.¹⁰ Earlier referral is recommended for children with speech and language delay, cognitive delay or craniofacial abnormalities affecting middle ear and Eustachian tube function. Emergent referral is recommended in patients who have suspected complications such as mastoiditis, facial paralysis, labyrinthitis, meningitis or brain abcess.⁵ In addition, children with a chronically discharging ear should be referred for further management and examination for suspected cholesteatoma.⁶

Further management options

Options for further management by an otolaryngologist include a formal assessment of hearing and insertion of ventilation (tympanostomy) tubes, either alone or in conjunction with adenoidectomy. A Cochrane review noted that the number of patients free from acute otitis media in the included studies was higher in those with ventilation tubes.⁴¹ There is also significant evidence of short-term improvement in quality of life with the insertion of ventilation tubes. Their role in preventing recurrent AOM is still debated, particularly given the difficulty surrounding inclusion criteria for randomised controlled trials.42 Consequently, the American Academy of Otolaryngology Head and Neck Surgery clinical practice guidelines currently recommend ventilation tubes in children who have recurrent AOM and an effusion at the time of assessment.42

A recent meta-analysis found a benefit for adenoidectomy in children under 2 years of age with recurrent AOM and in those older than 4 years of age with otitis media with effusion.⁴³ The role of adenoidectomy together with the insertion of ventilation tubes has been controversial, with some studies noting benefits in only some subgroups.²⁸ A 2014 meta-analysis suggested that children with otitis media with effusion who also underwent adenoidectomy had a greater chance of clinical improvement.⁴³

CONCLUSION

Although AOM typically presents with a set of distinct diagnostic features, diagnosis can be challenging in infants and young children because of poor compliance with examination, anatomical features and inconclusive signs. A reddened tympanic membrane alone is not sufficient for a diagnosis of AOM, but a cloudy, bulging membrane with pneumatic otoscopic features consistent with effusion on the background of a typical clinical history is pathognomonic of the disease. Nevertheless, overdiagnosis is common, with evidence that nearly a third of all AOM diagnoses are in fact otitis media with effusion.³⁰ This leads to the inappropriate use of antibiotics, with the accompanying problem of increased bacterial resistance. The rate of spontaneous resolution in AOM is high, but a careful examination is required for diagnosis, along with adequate symptomatic support. Further management should be decided in conjunction with the parent, particularly if observation is chosen as initial management. MT

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A list of references is included in the website version (www.medicinetoday.com.au) and the iPad app version of this article.

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