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Clinical practice guidelines for the diagnosis and management of otitis media with effusion (OME) in children in Japan – 2022 update ☆

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ABSTRACT

This is an update of the 2015 Guidelines developed by the Japan Otological Society and Oto-Rhino-Laryngeal Society of Japan defining otitis media with effusion (OME) in children (younger than 12 years old) and describing the disease rate, diagnosis, and method of examination. Recommended therapies that received consensus from the guideline committee were updated in consideration of current therapies used in Japan and based on available evidence.

Method: Regarding the treatment of OME in children, we developed Clinical Questions (CQs) and retrieved documents on each theme, including the definition, disease state, method of diagnosis, and medical treatment. In the previous guidelines, no retrieval expression was used to designate a period of time for literature retrieval. Conversely, a literature search of publications from March 2014 to May 2019 has been added to the JOS 2015 Guidelines. For publication of the CQs, we developed and assigned strengths to recommendations based on the collected evidence.

Results: OME in children was classified into one group lacking the risk of developing chronic or intractable disease and another group at higher risk (e.g., children with Down syndrome, cleft palate), and recommendations for clinical management, including follow-up, is provided. Information regarding management of children with unilateral OME and intractable cases complicated by adhesive otitis media is also provided.

Abbreviations: Guidelines of OME, - 2022 update.

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Conclusion: In clinical management of OME in children, the Japanese Clinical Practice Guidelines recommends management not only of complications of OME itself, such as effusion in the middle ear and pathologic changes in the tympanic membrane, but also pathologic changes in surrounding organs associated with infectious or inflammatory diseases.

Chapter 1. Action statement and issues updated in the present Guidelines

1.1. Summary of action statement

Based on public comments presented after publication of the 2015 JOS (Japan Otological Society) Guidelines, the update committee made revised plans, as follows. The committee also revised its plans reflecting discussions following committee reports presented during the annual meetings of the JOS in 2020 and 2021.

(1) Supplemental figures have been added to introductory remarks regarding the pathology, diagnosis, and medical treatment of otitis media with effusion (OME) in children.
(2) In the Introduction (**1.4.:** representing Chapter 1-Section 4), international OME guidelines were reviewed in Section 1.5).
(3) Terminology related to the topic has been added in the section defining OME in children (**1.18**).
(4) Regarding the method for evaluating the quality of evidence and strength of recommendations, the committee referred to a proposal described in the Medical Information Network Distribution Service Japan (MINDS) Handbook for Clinical Practice Guideline Development 2014 and 2020 and the method recommended by the American Academy of Pediatrics (AAP). Again, the method recommended by the AAP was applied to evaluate recommendations, with reference to methods recommended in the MINDS Handbook and Guidelines of Recommendations Assessment, Development, and Evaluation (GRADE).
(5) In the 2015 JOS Guidelines, adenoidectomy was not recommended as an initial procedure for treating OME in children in the absence of clear indications with regard to upper airway lesions. The committee revised recommendations on this issue according to recent meta-analyses and categorized the recommendations for patients under or above 4 years of age. In the latter group, adenoidectomy combined with tympanostomy (TS) tube insertion is expected to reduce the recurrence rate of OME. Therefore, the combination of adenoidectomy and TS tube insertion may be considered (**3.CQ9**).
(6) In the 2015 JOS OME Guidelines (Clinical Question [CQ]-9), myringotomy alone was not recommended for the treatment of OME in children. Based on recent evidence, however, the recommendation was revised as follows (**3.CQ5**):
(7) Myringotomy is recommended for the diagnosis and determination of treatment protocol for OME in children. It is effective for short-term prognosis, but it is not recommended for the purpose of long-term treatment.
(8) In terms of indications for TS tube insertion attributed to hearing difficulties, children with moderate or severe hearing loss (≥40 dB) and those with hearing loss of 25-39 dB were graded with recommendations A and B, respectively. Conversely, the present guidelines have simplified and updated the recommendation for patients presenting with hearing difficulties, and hearing loss (≥30 dB) in the ear on the better-hearing side is documented (**3.CQ6**).
(9) The committee added a new CQ focusing on unilateral OME, titled "Is the tympanostomy tube effective for unilateral OME?" (**3.CQ10**). Moreover, the Supplemental CQ titled "How do I take care of children with complicated adhesive otitis media?" was also added.
(10) In **Chapter 4**, which focuses on the management of OME in children with Down syndrome (DS) or cleft palate, commentary was updated with reference to recent evidence, and the practical guidelines were clarified.
(11) Supplemental notes referring to future prospects for improving diagnostic techniques have been added in the final **Chapter 5**.

1.2. Guideline composers

All authors of this article represent the constituent members of the Clinical Practice Guideline Development Committee for OME in children. The Japan Otological Society and the Pediatric Otorhinolaryngology Society of Japan composed this committee. The inaugural meeting of the committee was held on February 28, 2013, at which time the guideline-making process was begun. After publication of the 2015 JOS Guidelines, plans for revising the Guidelines were initiated at the 12th meeting held on May 18, 2017. Thereafter, the draft edition of the present Guidelines was evaluated by external reviewers, including otolaryngologists and experts in guideline development, and the Committee considered their remarks at the 26th meeting, held on October 15, 2021.

The academic board of the Oto-Rhino-Laryngological Society of Japan offered comments for revisions, and these is-

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sues were investigated at the 27th meeting, held on February 1, 2022. The descriptions and recommendations of the final version of the Guidelines were approved on February 25, 2022.

The committee requested that an incorporated nonprofit organization, the Japan Medical Library Association, retrieve documents for preparing the first edition of the Guidelines.

1.3. Financial backers and sponsors

Production of the Guideline was funded by JOS operating expenses. The JOS does not receive support from any specific organizations or companies. A list of organizations and companies that posed non-personal financial conflicts of interest (COIs) to members of the Clinical Practice Guideline Subcommittee during production of the Guideline is provided (attachment). Members of the Subcommittee with a COI were excluded from drafting the portion of the Guideline affected by the COI. To avoid undue influence of COIs of certain Guideline Committee members, all Guideline Committee members confirmed and approved the descriptions and recommendations contained in the final Guideline.

1.4. Background and history

1.4.1. Pathoetiology of OME

In the present Guidelines, OME is defined as "otitis media with middle-ear effusion (MEE) without tympanic membrane (TM) perforation, which causes hearing loss but lacks signs of acute inflammation of the ear, such as otalgia and fever" (refer to Section 1.18). OME is a ME disease that affects 90% of preschool children at least once [1], and it is the most frequent cause of pediatric hearing loss. More than 50% of children experience OME before the age of 1 year, and >60% of children experience OME by the age of 2 years [2]. While most cases resolve spontaneously within 3 months, 30–40% of cases involve recurrent OME, and 5–10% of children have episodes lasting 1 year or longer [1,3,4]. As OME sometimes causes sequelae, long-term medical management is required (refer to Section 1.19).

OME in adults differs from that in children with regard to its etiological background, such as Eustachian tube (ET) dysfunction and nasopharyngeal tumors in adults; thus, OME in adults is outside the scope of the present Guidelines. The present Guideline provides recommendations for the treatment of OME in children younger than 12 years of age.

As many as 50% of children develop OME with a cold or after acute otitis media (AOM) [5]. Common cold, inflammation in the nose and/or paranasal sinuses, and AOM, which is characterized by ME infection with acute onset of symptoms and signs, may cause MEE. Particularly in cases involving tubal dysfunction and poor development of mastoid cells, MEE can sometimes progress to OME (Fig. 1). Guidance is required regarding the timing and criteria for diagnosing OME in cases involving MEE after AOM or previously unnoticed MEE that is diagnosed by chance.

The primary symptoms of OME in children include hearing loss and aural fullness, whereas fever and otalgia are rarely observed. Although some cases resolve spontaneously, the absence of acute symptoms of inflammation can result in the condition being overlooked for a long time. If OME is left untreated for a long period, affected children are at risk of hearing loss that can delay language development and interfere with learning, as well as the risk of pathological changes in the TM and ME, such as adhesive otitis media (refer to Sections 1.19. and 3.11. **Supplemental CQ**). Surgical intervention (TS tube insertion is the first-line treatment) is the preferred initial procedure, and although it is useful for improving hearing loss, it may also cause persistent perforation of the TM and tympanosclerosis (refer to Section 1.19., 3.CQ6–8).

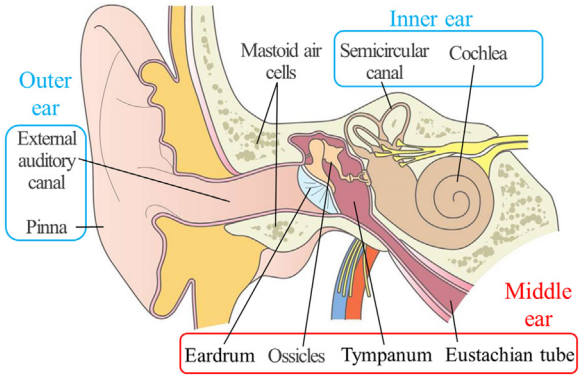

Fig. 1. Schematic illustration of the middle ear. The middle ear is the part of the ear consisting of the tympanic membrane (eardrum), tympanic cavity, ossicles, and Eustachian tube, which connects the middle ear with the nasal cavity (nasopharynx). The ossicles transmit the vibrations of the tympanic membrane to the inner ear. The mastoid cells and mastoid antrum are hollow spaces around the tympanic cavity that function in the ventilation and protection of the middle ear as well as Eustachian tube.

1.4.2. Historical development of the OME guidelines

Existing overseas guidelines for diagnosing and managing OME include the USA 2004 Clinical Practice Guideline [6], the UK 2008 National Institute for Health and Care Excellence (NICE) Guidelines for OME in children under 12 years [7], and the Korean 2012 Clinical Practice Guidelines [8], as well as other similar guidelines published in the other countries (Table 1). Treatment guidelines for TS tube insertion in children have also been developed in the United States [9].

The main objective of the US and European guidelines is to establish when children with OME should be referred to an ear, nose, and throat (ENT) specialist for TS tube insertion. In contrast, in Japan, otolaryngologists are generally responsible for the primary care of children with OME as well as for surgery; OME is diagnosed and treated in conjunction with related inflammatory lesions of surrounding organs. In other words, clinical management of OME in children usually involves treatment not only of direct OME-related conditions such as MEE and pathological changes in the TM but also the patient's overall clinical state, and ENT specialists in Japan treat any related lesions of the surrounding organs. In consideration of the current status of management of OME in Japan, the JOS and the Japan Society for Pediatric Otorhino-

Table 1. Guidelines in various countries.

Author	Journal information	Year	Affiliates	Outlines
Bull et al. [7]	London: RCOG Press. 1-74	2008	National Collaborating Centre for Women's and Children's Health	• Working Group included nurses and patients. • Health economics are also discussed.
Lee et al. [8]	J Korean Med Sci. 27:835-48	2012	Korean Otologic Society	• Guidelines for AOM and OME. • Recommendations are graded.
Rosenfeld et al. [9]	Otolaryngol Head Neck Surg. 149(1):S1-35	2013	American Academy of ORL-HNS	• Guidelines for tympanostomy tubes in children. • 15 systematic reviews or meta-analyses. • 113 RCTs.
Ito et al. [10,11]	Tokyo, Kanehara Publishing, 1-90 [in Japanese]. Auris Nasus Larynx. 44(5):501-8	2015 2017	Japan Otological Society, Japan Society for Pediatric ORL	• The first edition of the present guidelines. • Recommended management not only of OME itself but also pathological abnormalities in surrounding organs.
Heidemann, et al. [12]	Int J Pediatr Otorhinolaryngol. 87: 154-63	2016	Danish Health and Medicines Authority, Danish Society of ORL-HNS	• Working group. • Recommendations were graded according to the GRADE system.
Rosenfeld et al. [13]	Otolaryngol Head Neck Surg.154: S1-41	2016	American Academy of ORL-HNS, American Academy of Pediatrics, American Academy of Family Medicine	• Update of 2004 guidelines. • 4 new practice guidelines. • 20 new systematic reviews. • 49 RCTs.
Blanc et al. [14]	Eur Ann Otorhinolaryngol Head Neck Dis. 135(4): 269-273.	2018	Société Française d'ORL	• Based on extensive review (1996-2016).
Simon et al. [15]	Eur Ann Otorhinolaryngol Head Neck Dis. 135(1S): S33-S39.	2018	International consensus assessment (France, UK, USA, China, South Africa)	• Guidelines specialists from each area of the world recommended the best practices for OME management.

Abbreviations: ORL, otorhinolaryngology; HNS, head and neck surgery; RCT, randomized controlled trial

laryngology developed evidence-based guidelines to support the diagnosis and treatment of OME in children [10,11].

After publication of the 2015 JOS Guidelines, the Danish Guidelines on management of OME [12] were issued, the US guidelines [13] were updated, and French guidelines [14] were also reported. Furthermore, an international consensus report was presented in the panel discussion during the 2017 International Federation of Oto-rhino-laryngological Societies Congress, as guidelines specialists in each area of the world met to recommend the best practices for OME management [15]. The content of the consensus report is broadly consistent with the policies of the 2015 JOS Guidelines.

The committee preparing the 2022 JOS Guidelines changed the criteria regarding judgment of the strength of recommendations according to recent advances in methodology in guidelines development. In the process of selecting the evaluation method, the committee referred to a proposal described in the MINDS Handbook for Clinical Practice Guideline Development 2014 [16] and MINDS Manual for Guideline Development 2017 [17] and ultimately decided to apply the method recommended by the AAP [18]. This method enabled us to easily and comprehensively evaluate the quality of evidence and place a high priority on the balance between benefit and harm for patients when evaluating recommendations. During the process of revising the 2015 JOS Guidelines, the committee changed some CQs and added new figures and a glossary to enhance user understanding (Figs. 1–4).

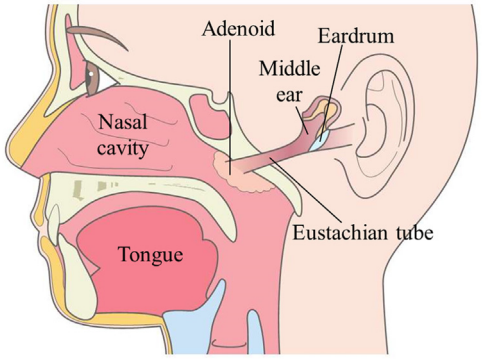

Fig. 2. Positional relationship between the middle ear (Eustachian tube) and the adenoids. The adenoids are located just beside the pharyngeal orifice of the Eustachian tube, and biofilm formation in the adenoids is responsible for the pathogenetic mechanism of hypertrophic adenoids in otitis media with effusion.

1.4.3. Value of OME guidelines

As shown in Fig. 4, findings regarding the TM and MEE in pediatric OME are diverse. The etiology and pathophysiology are complex, and considerable inter-individual differences are

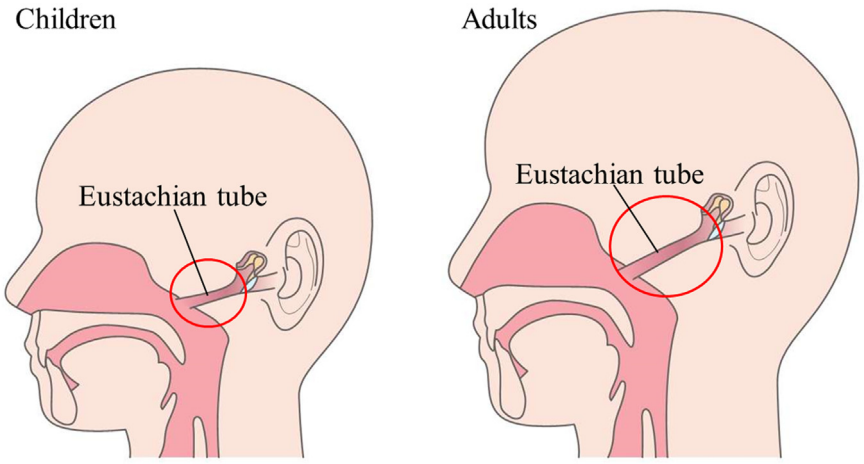

Fig. 3. Differences of the eustachian tube in children and adults. In children, the eustachian tube is immature, shorter and more horizontal than that of adults. Thus, dysfunction of the eustachian tube leads to less ventilation and protection of the middle ear, and therefore, infants are at increased risk of acute otitis media and otitis media with effusion.

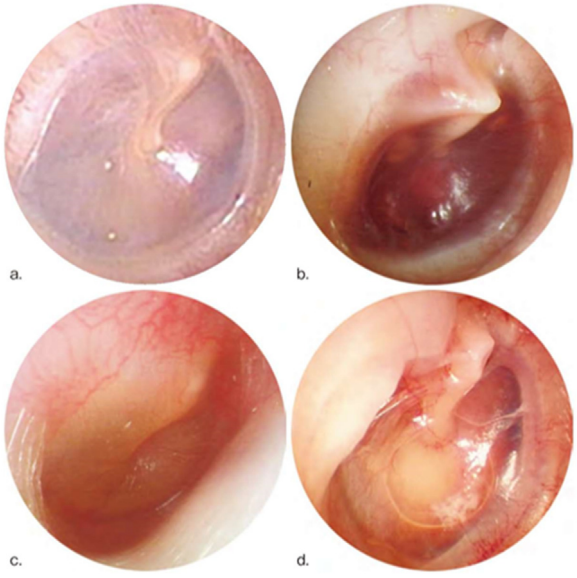

Fig. 4. Eardrum findings of normal ear (a) and ear with otitis media with effusion (b-d). In otitis media with effusion, pathological conditions of the tympanic membrane are observed, such as retraction (b), swelling (c), and thinning (d).

observed in terms of the mechanism of onset, prolongation, and recurrence of OME. In addition, there is no clear indicator to determine to what degree lesions in the surrounding organs affect the pathophysiology of OME in each case. We note that the present Guidelines are based on evidence for pediatric OME in general and do not provide the best recommendations for all individual cases.

These clinical practice guidelines are intended to support clinical practice but are not intended to restrict the clinical judgment of individual clinicians in the management of OME*. Clinicians can decide how to apply the present Guidelines to patients in various clinical settings, based on their knowledge and experience and considering the intentions and preferences of the children and their guardians. A lack of sufficient evidence regarding the efficacy of a treatment does not always directly imply that the treatment is not effective or that clinicians should not provide that treatment to patients. However, it is necessary to closely assess the validity of clinical efficacy and to communicate clearly with patients and their guardians when applying management options that are not included in the Guidelines. It is necessary to emphasize that each recommendation in the Guidelines does not have legal binding force for individual medical practice involving patients with specific medical circumstances [19]. The 2022 JOS Guidelines will be periodically revised to reflect not only the opinions of guideline-users and patients but also the results of external evaluations, as was done with the 2015 JOS Guidelines.

*NOTE: Guideline hierarchy:

Regulations > Directives > Recommendations > Guidelines

1.5. Objective and aim of production

The 2022 JOS Guidelines were produced to describe diagnostic and testing methods for childhood OME (below the age of 12 years* [refer to note 2]) and represent the evidence-based consensus of the members of the Subcommittee of Clinical Practice. The aim is that the present Guidelines be used to assist clinical decision-making in the care of children with OME and that the recommendations will prove beneficial in the diagnosis and treatment of patients with OME.

*NOTE 2: Pediatric OME often resolves spontaneously in the latter half of childhood (2 years to 11 years). The number of cases of OME is markedly reduced in adolescents (12–16 or 12–18 years). In the present Guidelines, we have used the general criterion of children younger than 12 years of age.

1.6. Users and strategies for public dissemination

The present Guidelines are intended for all clinicians, including otolaryngologists and pediatricians, who engage in medical treatment of pediatric OME. To be widely used in clinical settings, the present Guideline will be published as a

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Table 2. Subjects of the JOS 2022 Guidelines and patients not covered.

Subjects covered	• Children younger than 12 years (of either sex) with a definitive diagnosis of OME • OME with DS and all types of cleft palate • More than 3 weeks after the disappearance of symptoms of acute inflammation Note: Indications for surgical intervention for pediatric OME in children less than 3 years old should be considered carefully.
Not covered	• OME with immunodeficiency • OME with acute inflammation

booklet and on the websites of the JOS and MINDS. In the previous 2015 JOS Guideline [10,11], the Committee published an article introducing important content. Additionally, a leaflet targeting patients and their families was published in 2016. The Committee will update the leaflet in the near future.

Users themselves must determine whether the interventions noted in the Guideline are difficult to apply in consideration of their specialty area and experience. Because the present Guidelines includes surgical interventions generally performed by otolaryngologists, clinicians should be prepared to refer to specialists in case they cannot offer the recommended management options themselves, even when necessary.

For health care workers other than physicians (e.g., nurses, laboratory technicians, speech therapists), the present guidelines are useful for learning more about pediatric OME.

1.7. Subjects

The subjects covered by as well as patients that are not covered are listed in Table 2. The subjects of the present guidelines are children younger than 12 years of age (of either sex) with a definitive diagnosis of OME, including children with DS and all types of cleft palate. In cases of post-AOM, subjects include patients in which more than 3 weeks have passed after the disappearance of symptoms of acute inflammation. In children less than 3 years old, AOM are more often encountered than OME. Again, precise hearing tests are difficult to administer in these children. Therefore, indications for surgical intervention for pediatric OME in children less than 3 years old should be considered carefully. Patients with the following conditions are excluded from the subjects covered by the present guidelines: OME with immunodeficiency or acute inflammation. The clinical management practices outlined in the present guidelines cover the following three areas:

① Clinical management with regard to diagnosis, such as auditory functional tests (refer to Sections 2.1–2.9.)
② Clinical management with regard to follow-up (refer to Section 3.**CQ1**)
③ Clinical management regarding treatment, conservative treatment such as medication or topical treatment, and surgical treatment

Screening tests for OME and prevention management are not covered by the present guidelines.

1.8. Collection of evidence

1.8.1. Document retrieval

To prepare the 1st edition of the Guideline [10,11], the Committee contracted with a specified nonprofit corporation, the Japan Medical Library Association support service, to cooperatively develop the medical guidelines and retrieve documents. PubMed, Ichushi Web (the website of the Japan Medical Abstracts Society), and the Cochrane Library were used. Information was retrieved from February to April 2014 without using any retrieval expression designating period of publication time for retrieval, as that was the first edition of the Guideline.

In preparing the present 2nd edition, a retrieval expression (refer to supplemental file indicating the formula for retrieval) was used to designate the period of publication time since March 2014, corresponding to the retrieval period for the 1st edition. The exceptions included newly developed CQs (**3.CQ5,10. and 3.11.**), where no retrieval expression was used to designate period of time, similar to the 1st edition.

Evidence was retrieved regarding disease definition, cause of disease, disease state, complications, sequelae, methods of diagnosis and examination, treatments with regard to each relevant CQ, and DS and cleft palate. The retrieval expressions used for searching PubMed and Ichushi Web consisted of keywords pertaining to diseases and primary keywords pertaining to each theme. The target age was 0–18 years. The languages of publications were limited to English and Japanese.

Although the Committee made it a fundamental policy not to narrow the search results by research design or form of thesis, depending on the number of retrieved documents and on the contents of the theme, thesis forms were limited to medical guidelines, systematic reviews, and meta-analyses, etc. In the Cochrane Library, systematic reviews and randomized controlled trials (RCTs) were searched using disease-specific keywords.

In addition, for each theme, each member of the Guideline Development Committee hand-searched through documents. Documents were added based on collective decisions by the Guideline Development Committee.

1.8.2. Policy for selecting documents

Based on the title and abstract of retrieved documents, those that apparently deviated from the target theme were excluded, and the contents of the remaining documents were evaluated. For items concerning treatment, when the existence of appropriate systematic reviews or meta-analyses was noted, these were adopted as evidence, adding new RCTs published after the research included in the remaining documents. When

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Table 3. Quality of evidence.

A.	Well-designed RCTs or diagnostic studies on relevant populations. **[Strong evidence]**
B.	RCTs or diagnostic studies with minor limitations; overwhelmingly consistent evidence from observational studies. **[Sufficient (moderate) evidence]**
C.	Observational studies (case control and cohort design). **[Weak evidence]**
D.	Expert opinions, case reports, reasoning from first principles. **[Insufficient (very weak) evidence]**
X.	Exceptional situations in which validating studies could not be performed and there was a clear preponderance of benefit over harm.

neither systematic reviews nor meta-analyses were found, RCTs were adopted as evidence, and when no systematic reviews, meta-analyses, or RCTs were identified, non-RCTs or observational studies (such as cohort/case-control studies) were adopted as evidence. Also with regard to items related to treatment, the Committee made it a rule to adopt results of scientific investigations relating to adverse effects or complications, regardless of the level of evidence. With regard to other items (except treatment), the Committee primarily adopted existing systematic reviews, meta-analyses, and reviews as evidence and secondarily included epidemiologic studies, RCTs, non-RCTs, observational studies, and basic experimental studies.

1.9. Evaluation of evidence

For each theme in the Guidelines, a 2-person subcommittee excluded documents that deviated with regard to the condition of child patients targeted by the Guideline as mentioned in "7. Subjects" or that deviated from the theme. The Subcommittee then extracted primary information from the remaining documents and evaluated the methodological bias of the research and developed the evidence tables. In addition, according to the above-mentioned policy for selecting documents, the Subcommittee selected documents to adopt as evidence. Each document was evaluated not only by the 2-person Subcommittee but also by all members of the Committee.

In the process of preparing the present Guidelines, the Committee referred to a proposal described in the MINDS Handbook for Clinical Practice Guideline Development [20]. Specifically, we applied the method recommended by the AAP [18] according to a previously published guideline regrading AOM [21,22], as shown in Table 3.

First, the quality of evidence was evaluated with regard to the type of study and various factors that could reduce the quality of evidence, as follows.

① Risk of bias (selection bias, performance bias [blinding of participants and personnel], detection bias [blinding of outcome assessors], attrition bias [against intention-treat analysis or incomplete outcome data], selective outcome reporting bias, early stopping bias, and other biases, including COIs).
② Directness (external validity, generalizability, applicability): In the next step, studies were integrated in each group with the same outcome and same study design to determine the quality of the aggregate body of evidence.
③ Consistency (support from multiple studies).
④ Imprecision. In the case of observational studies, factors as documented below were taken into consideration:
  - A large effect of the intervention;
  - A dose-dependent gradient;
  - Plausible confounders that reduced the effects.

Finally, the body of evidence was summarized by evaluating the strength of evidence according to the conducted review related to each topic (Table 3). Moreover, the quality of evidence for recommendations regarding each CQ was rated across outcomes as a summary of evidence.

1.10. Decision criteria for recommendations and degree of recommendation

Specifying recommendations and the degree of recommendation for each CQ is an important role that clinicians expect guidelines to play. However, considerable discussion has focused on what factors should be taken into consideration when adopting recommendations and when determining the degree of recommendation. While developing CQs regarding treatment, the Committee gathered and integrated members' opinions regarding "what outcomes are focused on when deciding recommendations and the degree of recommendation" and extracted the following outcomes.

- Hearing
- Language development
- Quality of life (QOL)
- Influence on school performance and daily activities
- Transition to refractory otitis media with effusion (including adhesive otitis media, etc.)
- Presence of ME effusion
- Adverse events

When deciding recommendations for treatments, the Committee considered suggestions by Fukui and Tango (Procedure for Clinical Practice Guideline Development, version 4.3) in the MINDS Handbook for Clinical Practice Guideline Development 2007, 2014, and 2020 [20,23]. Moreover, the Committee referred to the GRADE concepts [24,25] and took into consideration the following factors for judging recommendations:

- Clinical applicability
- Value of each patient
- Evidence regarding harms and costs

The Committee finally applied the method recommended by the AAP, following the strategies adopted by the Clinical Practice Guidelines for Acute Otitis Media–2018 update

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Table 4. Strength of recommendations [18,21,22].

Strong recommendation	A strong recommendation means the benefits of the recommended approach clearly exceed the harms (or that the harms clearly exceed the benefits in the case of a strong negative recommendation), and that the quality of the supporting evidence is excellent (grade A or B). In some clearly identified circumstances, strong recommendations may be made when high-quality evidence is impossible to obtain (X) and the anticipated benefits strongly outweigh the harms.
Recommendation	A recommendation means the benefits exceed the harms (or that the harms clearly exceed the benefits in the case of a strong negative recommendation), but the quality of evidence is not as strong (grade B or C). In some clearly identified circumstances, strong recommendations may be made when high-quality evidence is impossible to obtain (X) and the anticipated benefits strongly outweigh the harms.
Option	An option means that either the quality of evidence that exists is suspect (grade D) or that well-done studies (A, B, or C) show little clear advantage to one approach over another.
No recommendation	No recommendation means there is both a lack of pertinent evidence (grade D) and unclear balance between benefits and harms.

Table 5. Relationship between evidence quality and benefit-harm balance in determining the strength of a recommendation [21–23].

Evidence Quality		Preponderance of Benefits over Harms	Balance between Benefits and Harms
A.	**Well-designed RCTs or diagnostic studies on relevant populations**	**Strong Recommendation**	**Opinion**
B.	**RCTs or diagnostic studies with minor limitations; overwhelmingly consistent evidence from observational studies**	**Recommendation**	
C.	**Observational studies (case-control and cohort design)**		
D.	**Expert opinions, case reports, reasoning from first principles**	**Opinion**	**No recommendation**
X.	**Exceptional situations in which validating studies cannot be performed and there is a clear preponderance of benefit over harm**	**Recommendation**	

(Tables 4 & 5) [21,22]. Several guidelines that used AAP proposals to evaluate the evidence of quality and strength of the recommendations have been published in recent years [26–29]. The AAP method, as well as the GRADE system, emphasize the balance between benefits and harms to patients when judging the strength of a recommendation as well as the evidence quality. Moreover, strong recommendations are possible in clinical practice when the anticipated benefits strongly outweigh the potential harms, even though the evidence may be poor due to difficulties that prevented performance of a high-quality study.

These features of the AAP method fit members' philosophy well, and the Guideline Committee reached a consensus to use this method.

The above-mentioned recommendations were proposed by the Guideline Committee and reviewed by the board members of Otology Japan and the Oto-Rhino-Laryngological Society of Japan. The Committee finally decided to adopt these recommendations, and the degree of each recommendation was ultimately decided based on discussions referring to the opinions and/or comments by the board members of Otology Japan and the Oto-Rhino-Laryngological Society of Japan. While the Committee attempted to maintain objectivity and transparency in deciding these recommendations and the degree of recommendation, there is no guarantee of completeness.

With regard to revision of the present guidelines, the Committee will continue to improve the system to accept users' opinions and suggestions regarding the recommendations and the degree of each recommendation stated in the present guidelines.

It should be noted that the Committee judged that it is not suitable to simply apply the above-mentioned evidence levels, recommendations, and degrees of recommendation to "Chapter 2: Diagnosis and examinations" and showed neither the evidence level nor recommendations nor the degree of recommendation for the corresponding items. Instead, the meaning and point of each diagnosis and the method of examination and outline regarding the clinical meaning are shown.

1.11. Reviews before the release

Prior to release of the present guidelines, the Committee asked otolaryngologists and pediatricians engaged in the treatment of OME in children and experts in preparing guidelines to carry out an external review of the draft edition of the present guidelines. The external reviewers are listed in Supplementary-Table A. Three reviewers were asked to review the Guideline according to Appraisal of Guidelines for Research & Evaluation II (AGREE II), and the other two reviewers were free to review the Guideline as they saw fit.

1.11.1. Review according to AGREE II

AGREE II is a tool managed by the AGREE Research Foundation and used to review the quality of a guideline from the point of view of how strictly the guideline was developed and how much transparency occurred in the development process (http://www.agreetrust.org). The review table consists of 6 fields, with 23 items and 2 total evaluation items. In the 6 fields/23 items, reviewers evaluate each item according to "Scope and Purpose", "Stakeholder Involvement", "Rigor of Development", "Clarity of Presentation", "Applicability", and "Editorial Independence" and give each item a score from 1

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(Strongly Disagree) to 7 (Strongly Agree). Among all evaluation items, reviewers express the grade of the guideline in a range from 1 (lowest possible quality) to 7 (highest possible quality) and decide whether to recommend use of the guideline. We calculated the results of the AGREE II evaluation carried out by the external reviewers according to a ruled method. Specifically, we summed all points given by all reviewers to each field and calculated the percentage of the total score relative to the highest possible score for the field. The two reviewers' total score in each field was as follows: Field 1 (Scope and Purpose) = 100%, Field 2 (Stakeholder Involvement) = 65.1%, Field 3 (Rigor of Development) = 81%, Field 4 (Clarity of Presentation) = 76.2%, Field 5 (Applicability) = 61.9%, and Field 6 (Editorial Independence) = 88.1%. Finally, all three reviewers offered a recommendation of high-quality guideline.

1.11.2. Review in free style

Another two external reviewers were asked to review the draft edition of the Guideline without designating the review method. They reviewed the accuracy of medical statements, the validity of the interpretation of evidence, and the validity of the developed recommendations primarily from the perspectives of otorhinolaryngology and pediatrics.

1.11.3. Issues pointed out by the external reviewers, and solutions

The Committee gathered issues pointed out by the five external reviewers and discussed how to deal with them (Supplementary-Table B). The Committee developed the final edition of the Guideline to reflect the results of these discussions.

1.12. Planned updates

The Guideline is scheduled to be updated in 3–5 years. After publication of the Guideline, work will begin on the organization of a new Clinical Practice Guideline Subcommittee. Newly published evidence will be systematically assessed and reviews carried out, with a Working Group established to contribute resources for the updated Guideline. Should partial updates to the Guideline be required, these will be published on the societies' websites as appropriate.

1.13. Monitoring and validation

1.13.1. Monitoring

After the publication of this 2022 Guideline, the Committee is planning to administer a questionnaire survey to otolaryngologists, pediatricians, and general physicians. Based on the results, we will aim to spread the use of the present guidelines. As standards for monitoring, the following issues will be considered:

① Penetration and utilization of the present Guidelines
② Utilization compared with the previous version of the Guideline
③ Adherence to each statement
④ The evidence-practice gap of each statement and reasons for the gap

In parallel with those surveys, the Committee will also administer a questionnaire survey to patients and their family members to solicit comments about penetration, user-friendliness, reflection of patients' perspective, and areas for improvement.

1.13.2. Validation

To evaluate quality indicators (QIs) incorporating the present Guideline in clinical settings, several QIs will be administered, as follows:

① Period between initial visit to undergoing insertion of a tympanostomy tube
② Whether or not hearing evaluation and/or tympanogram was conducted, and their measuring methods
③ Whether patient's case was complicated with pathological abnormalities in surrounding organs, such as infections or inflammatory diseases
④ The type, dosage, and administration of drugs used for medical therapy
⑤ The prevalence of remission or recurrence, and the rate of developing adhesive otitis media.

The above-mentioned criteria may be improved or modified according to the future studies. The corresponding data will be surveyed among multi-institutional collaborative studies and/or nationwide studies using a large-scale database, evaluating changes in the quality of medical procedures.

1.14. Recommendations and explanation of reasons

The present Guidelines was formulated for all physicians who treat childhood OME, including otolaryngologists and pediatricians as users, but it is also expected to be useful as a reference in all situations in which clinical judgments are made concerning the diagnosis and treatment of childhood OME by all medical professionals involved in the treatment of this condition in a wide variety of clinical settings. The specific relationships between recommendations and the literature on which they are based are described in each section of the Guideline. It must again be emphasized that the recommendation grades indicated in the present Guidelines do not constitute an alternative to the judgment of an experienced medical practitioner but are only provided to assist his or her decision-making.

1.15. Patients' wishes

In the process of formulating the recommendations in the present Guideline, the wishes of patients or their parents or guardians were considered. The benefits and risks of doing so were also taken into consideration. An important issue to be noted when dealing with individual patients in clinical situations is that applying the recommendations without exception in every case is to miss what is important in light of the spirit of the Guideline as an aid to decision-making

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in actual clinical situations. Again, it must be emphasized that decision-making in actual clinical situations must always be carried out by taking into account the evidence and recommendations contained in the Guideline and elsewhere, the experience and specialist knowledge of the medical practitioner, and the wishes and values of the patient and his or her parents or guardians. Future revisions of the Guideline will consider efforts to reflect the wishes of patients and their parents and guardians to a greater extent.

1.16. Algorithms

The generally recommended algorithms for patients without risk factors for intractable disease are included in Fig. 5 (also, refer to **Chapter 3**).

1.17. Practical consideration

In the present Guideline, medications and instruments are essentially referred to by their generic names rather than brand names. The reasons for this include concerns that it would be unfair to refer only to selected products by name in the Guideline as well as the strong influence of expert opinion. In addition to which all generic products are fully included, and updating this information to include brand names would pose too great a burden on the Clinical Practice Guideline Subcommittee. For this reason, we advise the preparation of clinical paths or manuals that take into account the status of medications used and other specific attributes of individual facilities to enable the smooth acceptance of the recommendations in the Guideline in actual clinical settings.

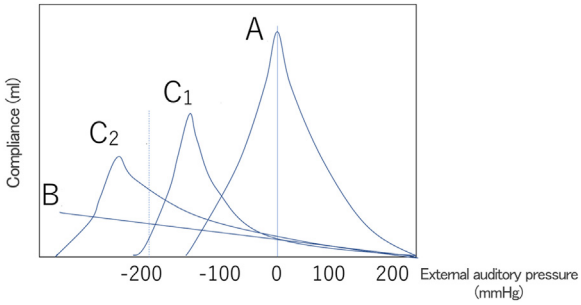

Fig. 5. Tympanogram. Tympanogram of type A in a normal ear, as the pressure in the middle ear cavity is equal to the pressure in the external auditory canal, and the mobility of the eardrum and ossicles is normal. In otitis media with effusion, however, the pressure in the middle ear becomes negative, and the tympanogram shows no peak (type B) or a negatively shifted peak (type C). On the boundary of 200 mm, the type C tympanogram is subdivided into type C1, in which the peak is located on the positive-pressure side, and type C2, in which the peak is located on the negative-pressure side.
*: At 25-30 dB, TS tube insertion may be performed, but indications should be considered more carefully (refer to 3.CQ6). **: Pathological changes in the tympanic membrane that require TS tube insertion are as follows: severe retraction in the pars tensa or flaccida of the tympanic membrane, destruction of the ossicles, and adhesive retraction of the tympanic membrane (refer to Table 6).

1.18. Definition of OME in children (Table 6)

In the present Guidelines, OME is defined as follows: Otitis media with ME effusion without TM perforation, which causes hearing loss. In addition, OME lacks signs of acute

Table 6. Definitions of terms.

Otitis media with effusion (OME)	This is a condition in which there is fluid in the ME without acute inflammation: "otitis media without perforation of the tympanic membrane (TM), resulting in fluid in the ME cavity and causing hearing loss, but without acute inflammatory symptoms, i.e., otalgia or fever" (refer to Sections 1.4. and 1.19). The term OME can also be translated as serous/secretory otitis media in English.
Acute otitis media (AOM)	An acute infection of the ME accompanied by otalgia, fever, and otorrhea (refer to Section 1.4).
Middle-ear effusion/fluid	Fluid collection in the ME behind the TM for some reason, such as inflammation. It may also be present in acute otitis media and may persist for weeks or months after the symptoms have resolved (refer to Section 1.19).
Pathological changes in the TM	Pathological conditions affecting the TM, such as severe retraction of the TM at the pars flaccida or tensa, destruction of the ossicles, thinning of the TM (phimosis), tympanosclerosis, or severe retraction in the TM that causes it to adhere to the promontory (refer to Sections 1.20. and 3.11).
TM atelectasis	A pathological change in the TM, particularly involving thinning and adhesion to the walls of the tympanic chamber, called atelectatic TM (refer to Sections 1.20 and 3.11).
Adhesive otitis media	This is a condition in which the TM becomes immobile due to adhesion to the promontory or the ossicles, which is often associated with the presence of prolonged otitis media and functional or organic disturbance of the ET (refer to Sections 1.20 and 3.11).
Conductive hearing loss	Caused by a disturbance in the process of sound transmission, often due to a disorder of the external auditory canal or ME, such as cerumen or OME.
Sensorineural hearing loss	Caused by a disturbance in the process of perceiving sound, often due to a disorder of the inner ear, such as age-related hearing loss.
Adenoids	Also known as pharyngeal tonsils, these are part of the same tonsillar tissue as the palatine tonsils. They are located in the nasopharynx near the nasopharyngeal orifice of the ET (behind the nasal cavity). The adenoids are thought to be the site of bacterial infection and are involved in the development of OME (refer to Sections 2.7 and 3. CQ9).
Nasal and paranasal sinuses	A general term for the nasal cavity and the paranasal sinuses (which include the maxillary, ethmoid, sphenoid, and frontal sinuses) (refer to Sections 2.7. and 3. **CQ2–4**).
Pneumatic otoscope	Similar to tympanometry, an otoscope is used to observe the movement of the TM while changing the pressure in the external auditory canal (refer to Section 2.3).
Tympanometry	A device that pressurizes and decompresses the sealed external auditory canal to check the TM's mobility and the ME's condition. The results are called a tympanogram (Fig. 5, Section 2.5).

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inflammation of the ear, such as otalgia and fever. In the US Guideline, "Clinical Practice Guideline: Otitis Media with Effusion" [6], OME is defined as fluid in the ME without signs or symptoms of acute ear infection.

OME is classified into three stages: (1) acute phase: within 3 weeks after onset, (2) subacute phase: between 4 weeks and 3 months, (3) chronic phase: more than 3 months after onset [30]. The differential diagnosis between AOM and OME is very important. In the Guideline "The Management of Acute Otitis Media in Children" in Japan, AOM is defined as follows: AOM is an acute inflammation of the ME, accompanied by otalgia, fever, and otorrhea [21,22]. It is sometimes difficult to diagnose OME and AOM via otoscopic findings, particularly in young children. Therefore, symptoms such as fever, crying at night, and emotional upset are critical signs to diagnose AOM.

Persistent ME effusion is frequently found in children after resolution of acute inflammation in AOM. In a meta-analysis of 7 articles regarding the natural course of AOM, MEE was found in 41% at 4 weeks and 25% at 12 weeks after onset of AOM [31]. In addition, in cases involving administration of antibiotics, MEE was found in 45% at 4–6 weeks and 21% at 3 months after onset [5]. Therefore, persistent MEE after AOM in the subacute and chronic phases is also included in the category of OME.

A summary of terms related to the present Guidelines is provided in Table 6.

1.19. Pathogenesis of OME in children

The main feature of the pathogenesis of OME in children has long been considered the hydrops *ex vacuo* theory: the production of inflammatory exudate and negative ME pressure due to the stenosis or obstruction of the ET. However, infection is now considered a primary cause of the formation of OME, similar to AOM. The pathogens associated with OME are the same as those in AOM. Immune complexes, endotoxins, viruses (rhinovirus and respiratory syncytial virus), and bacteria (*Streptococcus pneumonia, Haemophilus influenzae*, and *Moraxella catarrhalis*) have been detected in MEEs from patients with OME [32–35]. OME occurs directly after AOM in approximately 50% of children, although OME can also occur in the absence of previous AOM [35].

In the presence of ET dysfunction, the ME pressure becomes gradually negative. As a result, a prolonged pathological state in which both negative pressure and fluid retention coexist in the ME is established. Thus, tubal dysfunction plays an important role in the prolongation of the pathological state of OME [36]. In contrast, ET closing dysfunction, which sounds rather opposite to the pathogenesis of OME, has been detected in some patients with OME, especially in intractable cases [36–43]. These patients obtain temporary relief from the aural symptoms by sniffing, because sniffing closes the patulous ET, but it seems to be related to susceptibility to OME by creating negative ME pressure and/or enabling infection through the ET [36,43].

The risk factors of OME in children are quite varied: cleft palate, craniofacial abnormality, DS, hypertrophy of adenoids, upper respiratory tract infection, and rhinosinusitis. As to the pathogenetic mechanism of hypertrophic adenoids in OME, biofilm formation in the adenoids is responsible more than the mechanical obstruction of the ET [44]. With regard to allergic rhinitis, allergic inflammation of the mucosa is more likely to be related to the pathogenesis of OME than to the mechanical influence of nasal mucosal swelling [45]. The prevalence of allergic rhinitis among children with OME is approximately 5 times greater than that among non-affected children. There is insufficient evidence on gastroesophageal reflux disease in children with OME from previous reports of meta-analyses, but its incidence in children with OME is considered to be higher than in normal children [46]. In addition, the following factors are reportedly related to the intractability of OME in children: immunodeficiency, use of pacifiers [47] and artificial milk [48], poor social environment, numerous opportunities to come in contact with other children [49], and passive smoking exposure.

Considering the high incidence of recurrent AOM with OME in young children under the age of 3 years, we describe several important points in determining the surgical treatment of these patients (refer to **Addendum**). For children between the ages of 3 and 9 years, the focus should be on management to improve hearing loss due to MEE, whereas for children over 10 years of age, the focus should be on the prevention of morbid changes in the TM and intractable otitis media, including adhesive otitis media (refer to Section 3.11).

- ▶ Addendum: Management of OME in younger children (under 3 years old)

As previously mentioned above in "Definition of OME", differential diagnosis from AOM is important in the diagnosis of OME. Differential diagnosis from AOM or from prolonged MEE after AOM is sometimes difficult based only on TM findings as well as the precise evaluation of hearing level in children, especially at younger ages. Moreover, treatment for AOM rather than OME is sometimes necessary in younger children, because young age is a risk factor for recurrent otitis media. Therefore, physicians should be careful in determining the indications for surgery to treat OME in children under the age of 3 years. Surgery should not necessarily be recommended in children of this age with only MEE but instead recommended for those with obvious hearing impairment or severe pathological changes in the TM (refer to Section 3 CQ5–10).

Moreover, a differential diagnosis should address the possibility of causes of hearing loss other than OME when children have more than a moderate degree of hearing loss. Particularly in cases where the coexistence of other diseases such as congenital cholesteatoma or sensorineural hearing loss is suspected, drainage of MEE through surgery should be considered during differential diagnosis.

1.20. Complications and sequelae of OME

The main goals of interventions to treat pediatric OME should focus on preventing hearing impairment attributed to MEE and irreversible changes in the ME. Although OME

persists in only 5% of children, suggesting a high incidence of spontaneous remission, it also carries risks for additional disorders or structural changes in the TM or ME, including atelectatic TM, adhesive otitis media, tympanosclerosis, ossicular fixation, and cholesteatoma [50,51].

In cases of persistent OME, surgical interventions such as TS tube insertion are usually considered. However, even after TS tube insertion, some complications and developmental sequelae should be considered in some patients. Specifically, TM calcification is a common complication, followed by persistent TM perforation and cholesteatoma formation [50,51]. Considering the relatively higher prevalence of spontaneous remission, a benefits-harms assessment (preponderance of harm over benefit) of proposed medical treatment should be mandatory in the management of pediatric OME.

1.20.1. Atrophic TM, atelectatic TM, and adhesive otitis media

(Refer to Fig. 4 and Section 3.11).

Long-term inflammatory sequelae of OME can lead to the disappearance of the organized collagenous layer of the TM, deteriorating its elasticity and stiffness [52,53]. Some chemical mediators of MEE have been found to play roles in these pathological changes [54,55]. Congenital vulnerabilities in the TM have also been reported as pathogenic factors [56].

On the other hand, segmental atrophy of the TM is a common morphologic and functional disorder associated with TS tube insertion. The prevalence of segmental atrophy ranges from 16 to 75% in ears with a history of TS tube insertion, whereas it lies between 3 and 31% in ears without such history [50]. A prospective, randomized clinical trial reported an estimated risk ratio of developing segmental atrophy in operated ears of 17.4 [57].

Segmental atrophy would not manifest as a complication in ears with normal ventilation and/or pressure-regulating functions of the ME. However, segmental atrophy may contribute to more serious complications, including adhesive otitis media and cholesteatoma, specifically in conditions such as late recovery or long-term ET dysfunction. The latter contributes to sniffing habits and may induce formation of a retraction pocket predisposed from the segmental atrophic area, in turn leading to development of adhesive otitis media or acquired cholesteatoma.

Atelectatic TM is defined as a ME condition in which the atrophic TM touches the incudo-stapedial joint and/or the promontrium of the ME (refer to Section 3.11). Regarding low-grade atelectatic TM, surgical intervention is not recommended for the following reasons: (1) low risk (<2%) of developing cholesteatoma, (2) small chance of worsening the patient's hearing, and (3) a good chance of spontaneous remission or at least long-term stability of the disease [58].

Conversely, adhesive otitis media results from long-lasting and/or acute inflammatory ME disease complicated by the disappearance of mucosal layers covering the inner layer of the TM and the medial wall of the tympanum. The TM adheres partially or totally to the medial wall of the tympanum (refer to Fig. 4) [33,53,59]. In describing such a condition, several reports have advocated surgical interventions because of the higher risk of developing acquired cholesteatoma or interrupting the ossicular chain [59,61–63]. Specifically for adhesive otitis media in pediatric patients, the degree of adhesion or retraction is usually milder than in adult patients. Therefore, several reports have recommended tympanoplasty to interfere effectively before deleterious and irreversible adhesive changes have set in [64,65].

1.20.2. Myringosclerosis

Myringosclerosis represents a formation of sclerotic plaques in the TM. While myringosclerosis has been attributed to sub-epithelial hyalinization of the ME mucosa following an inflammatory process, current data indicate that tissue trauma caused by TS tube insertion is possibly a key factor contributing to formation. Indeed, the prevalence of myringosclerosis is much higher in TMs with a history of TS tube insertion than those without such history (39-65% vs. 0-10%) [50]. Sclerotic plaques are also more frequent in ears that have had several tube insertions compared with a single insertion [50].

Despite its frequent occurrence, myringosclerosis rarely develops into sclerotic changes of the ossicle, and the impact on hearing is not significant, as it does not usually exceed 0.5 dB [50]. Observational follow-ups are thus recommended in cases with a mild air-bone gap in hearing tests.

1.20.3. ME cholesteatoma

Formation of cholesteatoma is the most serious sequelae and/or complication of pediatric OME. However, the prevalence of cholesteatoma is reportedly less than 1% [66]. The above-mentioned segmental atrophy and retraction of the TM would presumably contribute to the pathogenesis. Preventing these conditions has been a goal of treatment for OME. However, the role of TS tube insertion in preventing the development of cholesteatoma has yet to be determined. Only a few recent studies have reported the influence of the procedure on the formation of cholesteatoma by comparing the prevalence of cholesteatoma surgery before and after the use of a ventilation tube. These studies concluded that the number of operations declined after the induction of TS tube insertion, but they also reported that other factors might be responsible for the decline in surgery for cholesteatoma [67,68]. Other population-based retrospective large cohort studies showed that the rate of development of cholesteatoma increases 10% for each additional year in age before the first ventilation tube insertion [69]. These results indicate that early prompt surgical intervention, including TS tube insertion, is helpful for preventing cholesteatoma, specifically for cases in which the development of ET dysfunction is difficult to anticipate.

Conversely, cholesteatoma formation following tube insertion has been reported, and this issue is addressed below (refer to Section 3 CQ7, Addendum 2).

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Chapter 2. Diagnosis and examinations

2.1. Is it necessary to ask for a patient's history to diagnosis OME?

It is useful to ask for a background and the history of a patient to understand the risk factors for prolongation and degree of OME and to predict the possibility of refractory disease.

2.1.1. Background

OME is seen mostly in infants. The staging and pathological condition of OME are marked by considerable change and affected by diseases and function of the ME, ET and diseases affecting surrounding organs. It is useful to ask the patient (or patient's parent or guardian) about the presence of disease and function of the ME, ear canal, and surrounding organs, as this will facilitate examination of the etiology and may be useful in the treatment of OME. Also, OME patients may have various long-term risk factors that could provide valuable data for analysis and consideration.

2.1.2. Commentary

The Eustachian tubes (ET) are sites of OME in childhood. Rhinosinusitis and adenoids also affect the pathology of OME and function of the ear tubes. Therefore, medical staff should ask about the presence of rhinosinusitis and adenoids. The purpose of the interview is as follows (Table 7):

(1) Estimate the onset of OME;
(2) Estimate the risk factors of OME;
(3) Estimate intractable risk factors of OME.

It has been reported that the course of otitis media is related to the age of the first AOM episode and the history of AOM. The interview assessing the history of AOM is also important for the management of OME [10,70,71]. However, it is not possible to make a diagnosis of OME only by interview. The questionnaire for a child with OME is shown in Table 7.

2.2. What TM findings aid in the diagnosis of OME?

2.2.1. Background

Although it is sometimes difficult to differentiate between OME and AOM based on TM findings alone, ME effusion without acute inflammatory symptoms (e.g., otalgia and fever) is seen in OME. Detailed observation of the TM is important to definitively diagnose OME [6,23,72,73].

2.2.2. Commentary

In a patient without signs of acute inflammation, a diagnosis of OME is made when the TM findings described below are observed:

① Presence of MEE: MEE sometimes fills the entire ME cavity, and bubbles and effusion lines are sometimes seen.
② Color of MEE: a yellow or brownish-red color of the effusion is observed most often. Blackish-brown MEE can also be observed, although this is seen at a low frequency.
③ Thickness of the TM and buckling: various findings can be observed, such as thinning, thickening, calcification, and partial adhesion of the TM.

The nature of the MEE in this disease varies but is largely classified into 3 types: serous, viscous, and mucopurulent. Retraction, bulging, or opacity of the membrane, diminished or absent light reflex, presence of MEE (e.g., presence of

Table 7. Objectives and details of questionnaire for a child with OME.

Purpose of questionnaire
1) Estimate the onset of OME
2) Estimate the risk factors of OME
3) Estimate intractable risk factors of OME
Questionnaire item
1. Family history (parents and siblings, presence or absence of the following diseases)
1) Ear diseases (long-term morbidity and/or surgical history of OME, chronic otitis media including the ME cholesteatoma)
2) Allergies (allergic rhinitis, including hay fever, bronchial asthma, atopic dermatitis, or food allergies)
3) Chronic rhinosinusitis (including surgical history)
4) Cleft palate (including the soft palate cleft)
5) Adenoids or tonsils surgical history
2. Disease, morbidity and treatment history
1) Allergies (allergic rhinitis, including hay fever, bronchial asthma, atopic dermatitis, or food allergies)
2) Acute otitis media (recurrent or intractable, initial onset, history of treatment)
3) Past treatment for OME
4) Gastroesophageal reflux disease
5) Cleft palate (including the soft palate cleft)
6) Systemic disease (such as chromosomal abnormalities, craniofacial developmental abnormalities, or metabolic abnormalities)
3. Growth and life history
1) Day care (age when first started attending a nursery)
2) Smoking by family members
4. Questionnaire for estimating the onset of OME
1) OME-related diseases (rhinosinusitis, acute otitis media, upper respiratory inflammation, allergic rhinitis, others)
2) Symptoms corresponding to OME (hearing loss, asking to repeat many times, touching one's ear, shaking one's head, cocking one's head to the side to listen more closely, slow development of language, abnormal pronunciation)

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bubbles and gas or a liquid phase), variously colored MEE, etc., can be observed on examination of the TM in cases of OME. Furthermore, diminished or reduced mobility of the TM can be confirmed with a pneumatic otoscope.

In the examination of patients with OME, it is desirable to observe the TM in detail using an operating microscope, otoendoscope, or pneumatic otoscope[#]. In observation of the TM, the positions of the tense and flaccid parts of the TM, and the color, transparency, mobility, and thinning/thickening of the TM are examined. Furthermore, the examiner also looks through the TM to check for MEE behind the TM and to estimate its nature and amount.

[#]"Pneumatic otoscope" as referred to in the text collectively represents a conventional pneumatic otoscope used with an operating microscope, pneumatic magnifying otoscope (magnifying otoscope with a pneumatic attachment), and pneumatic otoendoscope (otoendoscope with a pneumatic attachment).

2.3. Is pneumatic otoscopy useful for observation of the pathological condition of OME?

Diagnosis of OME in children is made when effusion is present in the middle ear cavity in the absence of acute inflammatory findings.

Visual inspection of the TM via pneumatic otoscopy is the first examination performed to diagnose OME in children (check for MEE).

2.3.1. Background

A pneumatic otoscope is used to observe the mobility of the TM by compressing and decompressing the external auditory canal. An otoscope is usually utilized along with a pneumatic device. When an operating microscope is used instead, an otoscope without a magnifying lens is employed.

2.3.2. Commentary

Visual inspection via pneumatic otoscopy is the first examination performed to diagnose OME in children, and this is performed before tympanometry. Use of both examinations improves the diagnostic accuracy. Pneumatic otoscopy can detect abnormal TM findings, enabling the differentiation of OME from AOM [74,75].

A systematic review of 52 articles regarding different diagnostic methods for OME in children (including myringotomy [refer to Section 3 CQ5], pneumatic otoscopy, tympanometry, etc.) revealed the highest diagnostic accuracy for pneumatic otoscopy, with a sensitivity of 93.8% and specificity of 80.5% [76]. Although the diagnosis can be affected by the level of examiner experience, the reported correct diagnosis rate for OME in children aged 1 to 3 years by experienced examiners using pneumatic otoscopy is 70 to 79% [77]. An RCT conducted by Al-Khatib et al., in which 29 pediatric residents watched pneumatic otoscopy and otoendoscopy videos to learn to diagnose OME found that the rate of correct OME diagnosis was significantly higher in the pneumatic otoscopy group (91%) than the otoendoscopy group (78%) ($p = 0.0003$). Pneumatic otoscopy, which allows examination of the mobility of the TM, is a useful tool for the accurate diagnosis of OME [78]. In addition, it has been reported that pneumatic otoscopy is particularly useful for the diagnosis of refractory or persistent OME, because loss of TM mobility is highly correlated with filling of the entire ME cavity with effusion in cases of OME; thus, pneumatic otoscopy could serve as a guide for surgical treatment [79].

2.4. Is pure-tone audiometry useful for diagnosing OME?

Pure-tone audiometry is an examination for diagnosing the severity and type of hearing loss, and it is also performed when confirming hearing loss before and after TS tube insertion, determining surgical indications, and testing for the presence of sensorineural hearing loss.

2.4.1. Background

An age-appropriate audiometric test should be performed before TS tube insertion when OME in children persists and there is obvious hearing loss, as well as when delayed language development is observed.

2.4.2. Commentary

The tympanostomy tube guidelines of the American Academy of Otolaryngology-Head and Neck Surgery recommend performing an age-appropriate audiometric test before TS tube insertion when OME has persisted for ≥3 months [9,13]. An audiometric test is also necessary when delayed language development is seen in children, when there is a learning disorder problem, or when clear hearing loss is suspected. Pure-tone audiometry is performed to measure air and bone conduction [73]. Ungkanont et al. performed pneumatic otoscopy examinations and hearing tests in 63 cases of OME in children and reported an average hearing loss of 31.7 ± 10.3 dB in 92.1% of the examined cohort. Specifically, the threshold had increased 7.2 dB in cases in which the TM was thickened and opacified and 5.1 dB in cases in which the TM had retracted. The authors advised performance of an audiometric test, especially when TM status is poor [80]. In addition, improvements in hearing acuity after treatment should be evaluated by pure-tone audiometry.

► Note

In children ≤4 years of age, conditioned auditory response audiometry (COR) or play audiometry are performed as needed instead of pure-tone audiometry [75,77].

2.5. Is tympanometry useful for diagnosing OME?

After OME in children has been diagnosed by otomicroscopy, otoendoscopy, pneumatic otoscopy, etc., tympanometry may be used to confirm MEE.

2.5.1. Background

Tympanometry measures changes in the compliance of the TM and ME by changing the air pressure in the external

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auditory canal after it has been sealed shut. It is a reliable test to identify the presence of MEE in the tympanic cavity.

2.5.2. Commentary

Type B tympanograms indicate the presence of MEE under conditions in which TM mobility is reduced (Fig. 6). Type C tympanograms are associated with severe negative pressure in the ME and a severely retracted state of the TM [74]. In a systematic review that assessed 52 studies comparing methods of diagnosing OME by myringotomy and otoscopy, tympanometry, etc., the sensitivity of diagnosing OME with type B and type C2 tympanograms was 93.8%, and the specificity was 61.8% [76]. The diagnostic accuracy of tympanometry improves when performed simultaneously with pneumatic otoscopy.

According to a study in which high-resolution computed tomography (CT) and tympanometry were performed in 51 ears affected by OME, MEE was observed by CT in 94% of the ears with type B tympanograms. Ears with type C2 tympanograms were divided into two groups based on the presence/absence of MEE. No MEE was observed with type A or type C1 tympanograms [81].

►Note

Because the external auditory canal cartilage of infants is soft, it is impossible to accurately diagnose MEE using 226-Hz tympanometry [82]. A study in newborn infants using otomicroscopy and 226-Hz and 1000-Hz tympanometry reported that 1000-Hz tympanometry was particularly reliable at and below 9 months of age; thus, 1000-Hz tympanometry was recommended in these patients [83]. In Japan, 226-Hz tympanometry is commonly used, whereas 678-Hz and 1000-Hz tympanometry are also used in newborn infants in Western countries.

In terms of multi-frequency tympanometry (MFT), refer to **Chapter 5**, which addresses future prospects for improving diagnostic techniques.

2.6. Is otoacoustic emission (OAE) useful for the diagnosis of hearing loss with OME?

OAE reflects the functions of the inner ear, especially outer hair cells, and it is therefore a useful tool for evaluating the degree of inner ear damage and hearing loss.

2.6.1. Background

Evaluation of the level of hearing loss is important in determining the treatment strategy for infant OME. It is sometimes difficult to evaluate the precise hearing level in infants and children. Therefore, an objective hearing test such as an auditory brain-stem response (ABR) and/or an auditory steady-state evoked response test is often needed.

2.6.2. Commentary

Evoked OAE, which is induced within the inner ear via sound stimulation, is divided into two types. Transiently evoked otoacoustic emission (TEOAE) is evoked by a click (broad frequency range) or tone burst (brief duration pure tone) stimulus. Distortion product otoacoustic emission (DPOAE) is evoked by a pair of primary tones (f1 and f2)

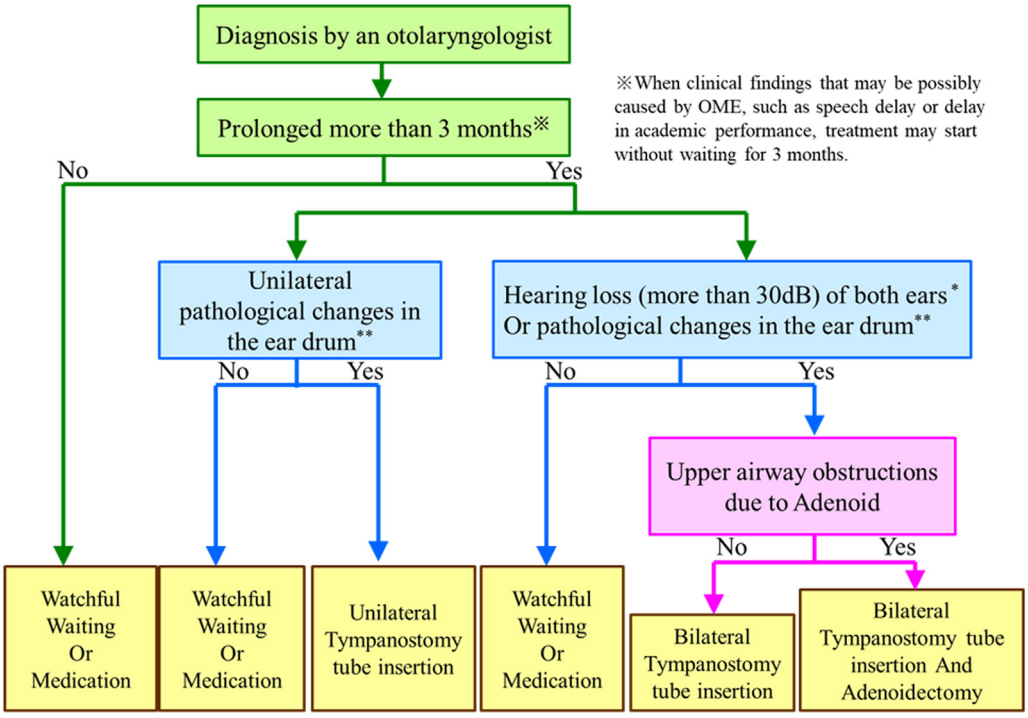

Fig. 6. Treatment algorithm for otitis media with effusion in children. For conservative treatment, please refer to the following: 3.CQ2: Antibiotics, 3.CQ3: Other medication, 3.CQ4: Conservative treatment other than medications. Follow-up should be performed at least once every 3 months until the tympanic cavity is aerated and the eardrum findings and hearing are normalized. Indications for adenoidectomy are described in 3.CQ9. Indications for unilateral otitis media with effusion are described in 3.CQ10.

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with a particular intensity and ratio. OAE is a useful objective hearing test that can be done noninvasively in a short time, even in children. However, there are several disadvantages to OAE. For example, OAE cannot be detected in the case of external auditory canal lesions, earwax plugs, retrocochlear hearing loss, or hypertrophy hypoplasia of the cochlear nerve. It should also be noted that OAE in the low tones is noisy for neonates or infants.

Several reports have described the use of OAE as a screening tool. Yilimaz et al. compared the results of OAE tests in 116 cases, discriminating between those with and without OME in patients ranging from 15 to 25 years in age. They found that OAE could be used to detect irreversible damage to the ME or cochlea caused by otitis media [84]. Another study, which used TEOAE as a screening tool in 116 school children, reported 100% sensitivity in diagnosing hearing loss >30 dB and 90% sensitivity and 64% specificity in diagnosing hearing loss >25 dB [85]. Balatsouras et al. evaluated TEOAE in the diagnosis of OME as compared with tympanometry in 38 children (76 ears) with bilateral otitis media and reported that TEOAE was absent in 51 ears (67%) and diminished in the remaining 25 ears (33%) [86]. Thus, TEOAE was recommended as an objective diagnostic tool for OME when used in conjunction with tympanometry [86,87]. By comparing the results of pure-tone audiometry and TEOAE tests in young children with OME prior to and after TS tube insertion, a high correlation was found between tests; thus, OAE was considered the method of choice for hearing screening [88–90].

►Note

In Japan, OAE is approved only for the evaluation of inner ear function. Its use in OME children is recommended only when inner ear damage is suspected.

2.7. Are findings regarding peripheral organs (paranasal sinuses and epipharynx) helpful in understanding the clinical condition of OME?

To understand diseases that are considered related to OME in children, findings regarding peripheral organs (paranasal sinuses and epipharynx) are helpful. In a clinical setting, the physician asks a subject (or parent/guardian) regarding the patient's nasal symptoms, the extent of mouth breathing, snoring and sleep apnea at nighttime, and seasonal or perennial rhinitis symptoms. This is followed by observation of the patient's nasal cavity, oral cavity, and pharynx. Further tests should only be conducted after considering the balance between reasons for conducting the tests and invasiveness and costs.

2.7.1. Background:

OME in children is often associated with rhinosinusitis, allergic rhinitis, and adenoid hypertrophy. These diseases can directly or indirectly contribute to the clinical condition of OME.

2.7.2. Commentary:

a) Rhinosinusitis

The complication rate of rhinosinusitis associated with OME in children in Japan prior to the 21st century was reportedly 70-80% [91] and 25-60% outside Japan [92–94]. Several factors affect how rhinosinusitis contributes to OME in children. In a bacteriological examination of 32 OME cases in children associated with chronic rhinosinusitis, 69% of bacteria taken from MEEs and aspirates taken from the maxillary sinus matched, suggesting that rhinosinusitis is the infection source via the ET [95]. In pediatric patients with OME, it has been shown that the mucociliary function of the nasal cavity/pharyngeal orifice of the auditory tube is significantly lower than that of healthy subjects, indicating that rhinosinusitis may give additive effects [96,97]. In addition, occlusion of the pharyngeal orifice of the auditory tube due to postnasal discharge and sniffing are also suspected as playing a role [98]. In terms of the efficacy of drugs used for treating rhinosinusitis in children with OME, please refer to Sections 3.2–3.4.

b) Allergic rhinitis

The complication rate of allergic rhinitis associated with OME in children is reportedly 24-89% [99,100]. Some reports indicate an epidemiologic link between OME in children and allergic rhinitis, but other reports do not [45,101,102]. Clinical studies of nasal provocation tests using mites in perennial allergic rhinitis patients showed occlusion of the ET in 55% of ears [103]. Both Th1-type and Th2-type cytokines have been detected in MEEs of OME patients, but IL-4 concentrations are significantly higher in OME patients with allergic rhinitis than OME patients without allergic rhinitis. This indicates that IL-4 concentration affects mucin production in the ME cavity [104].

With respect to atopic factors underlying allergic rhinitis (i.e., patients have been sensitized to inhalant allergens), it has been shown that the numbers of eosinophils, T cells, IL-4–positive cells, and IL-5–positive cells invading the mucosa of the pharyngeal orifice of the auditory tube are significantly higher in atopic patients than non-atopic patients [105]. In allergic rhinitis patients, mucosal edema, mucus production, and ciliary dyskinesia on the ET are thought to be caused by either the allergens themselves inducing inflammation of the mucosa of the ET via IgE or by cytokines and other mediators produced on the nasal mucosa that affect the mucosa of the ET [100]. For a discussion of the efficacy of allergic rhinitis drugs in children with OME, please refer to Section 3.3.

c) Adenoid hypertrophy

Adenoids usually enlarge physiologically in early childhood, and most studies have failed to show any relationship between OME in children and the size of the adenoids [106–109]. However, some recent reports showed a tendency of larger adenoids in pediatric patients with OME than children with healthy ears [110,111]. Most studies have shown that almost the same bacteria and endotoxins are found in MEEs and adenoids [112–116]. However, 16S rRNA phylogenetic

analyses showed that the bacteria detected in MEEs and adenoids are different [117–119]. In children with OME, reports indicate that collapse of the mucosal barrier on the adenoid surface, biofilm formation, a decrease in normal flora on the epipharynx, and other factors may have a relationship with OME [120–122]. No evidence indicating that adenoids compress the ET and inhibit its permeability was found in a comparison of ET function before and after adenoidectomy; therefore, adenoids are thought to affect the clinical condition of OME as the source of infection/inflammation of the epipharynx [123]. For a discussion of adenoidectomy with regard to surgical treatment, please refer to Section 3.9.

Current data indicate that diseases associated with peripheral organs are related to OME in children and can affect the pathogenesis of OME. The clinical condition of OME in children is complex, and there are large individual differences in terms of mechanism of onset, prolongation, relapse, and intractability. Therefore, findings regarding peripheral organs are important for understanding the clinical condition of OME in each case.

2.8. Are language development tests (articulation tests, development tests) useful for determining the pathology of OME?

There is a relationship between a child's language development and hearing loss, cognition, and social development. After a diagnosis of OME in a child, language development tests are performed when delayed language development or an articulation disorder is suspected.

2.8.1. Background

OME in children affects speech and language development, intelligence, attention at school, activity at school, manual skills, and social behavior. However, OME particularly affects the speech and language development in young children up to 47 months of age [124].

2.8.2. Commentary

A meta-analysis examining 11 papers published between 1996 and 2002 did not show any clear associations between OME in preschool children and vocabulary, syntax, or speech development, but the study did find negative correlations between OME and receptive and expressive language. Negative correlations between hearing loss due to OME in infancy and receptive and expressive language have also been reported [125]. Majerus et al. assessed language development at 8 years of age in 20 children with OME that had persisted for at least 3 months by 3 years of age, comparing these children with 20 control children with no history of OME. They reported that verbal short-term memory and new-word learning ability were not affected by OME based on assessment of language skills at 8 years of age [126]. Another study that assessed word recognition thresholds categorized by age in children with and without OME reported an increase in threshold of 4-5 dB in children with unilateral OME and 15 dB in children with bilateral OME. Specifically, OME affected the word recognition threshold in children 31 months and 43 months of age. OME that starts early and persists has a greater impact on word recognition [127]. However, the authors of that study also reported that OME had no clear impact on word recognition and no long-term impact in children 61 months of age who had a type A tympanogram [127]. These reports showed that although OME in children affects language development in infancy, there are no differences in language development by the time the children reach school age.

Language development tests include the Picture-Vocabulary Test-Revised, National Rehabilitation Center for the Disabled's Test for Language-Retarded Children, the TK-style Language Development Diagnostic Test, Kyoto Scale of Psychological Development 2001 Version, Enjoji Scale for Infant Analytical Development Test, the Tsumori-Inage Infant Mental Development Test, and the Denver Developmental Screening Test II. These tests are selected based on patient age and symptoms.

2.9. Is it useful to perform imaging studies to diagnose OME?

The onset and prognosis of OME is related to the development of mastoid cells. Imaging of the temporal bone is thus useful for estimating the development of mastoid cells.

2.9.1. Background

Development of the temporal bone is reportedly related to susceptibility and prognosis of OME. The status of ME ventilation is also related to the development of mastoid cells. The prognosis of OME is related to the degree of mastoid cell development. Imaging of the temporal bone is thus useful for estimating the severity and prognosis of OME.

2.9.2. Commentary

Aoki et al. (1989) reported that a child with good development of mastoid cells was unlikely to suffer from OME but could easily heal even if the child did develop OME [128]. In addition, Ando (1992) and Takahashi (1986) reported that the incidence of inflammatory disease of the ear and the prognosis of ear disease were correlated with the development of mastoid cells [129,130].

Takahashi (1998, 2017) reported that ears with good gas exchange function have significantly better development of mastoid cells [131,132]. Therefore, it is useful to check the development of mastoid cells in imaging studies to assess the pathology of OME and its prognosis in children. Several methods are useful for diagnostic imaging, such as simple X-ray, CT, and magnetic resonance imaging [133]. Considering the influence of exposure on children, radiological imaging techniques such as CT should be limited to the minimum necessary [134]. A patient with hearing loss presumably attributed to a pathogenesis other than OME (i.e., congenital cholesteatoma and ossicular malformation) would be a candidate for CT. In simple X-ray exams, the Shüller position is commonly used to assess the development of mastoid cells.

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Chapter 3. Treatment algorithm and CQs for OME in children

Fig. 6 presents a clinical management algorithm recommended for OME in children without risk of intractability and sequelae. The algorithm was created by integrating evidence obtained from systematic reviews and the expert opinion of the Guideline Committee. The algorithm should therefore be applied in clinical practice in consideration of the unique circumstances of each individual patient. Clinicians should not adhere to the algorithm in treating patients that do not show improvement with the treatments recommended herein or to patients with sequelae such as adhesive otitis media or cholesteatoma formation. These are described separately (**3.11.** Supplemental CQs).

In addition, the treatment of OME in children with DS and cleft palate, who are at high risk for pediatric OME, is described separately in Chapter 4.

3.1. CQ1: How long is the appropriate period to monitor OME?

3.1.1. Recommendation (refer to Fig. 6)

Watchful waiting for 3 months from the date of effusion onset or from the date of diagnosis is recommended for managing a child with OME who is not at risk for pathological changes in the TM.

[Recommendation Strength: **Strong Recommendation**, Evidence quality: **A**]

The clinician has an option to continue close monitoring of patients in which OME is prolonged >3 months, specifically in cases without hearing impairment or any pathological changes (i.e., adhesions or retractions) in the TM.

[Recommendation Strength: **Recommendation**, Evidence quality: **B**]

3.1.2. Background

If a child with OME does not show spontaneous resolution within 3 months after onset, the chances of spontaneous resolution will be lower.

3.1.3. Aggregate evidence quality

- **Benefits for patients:** Potential to avoid undergoing unnecessary medication in cases with presumably spontaneous remission.
- **Risks, harms for children:** Pain, discomfort, and need for physical restraint during the physical examinations, including inspection of TM and earwax removal. Time-consuming medical economic burden for attending hospitals.
- **Benefits–harms assessment:** Benefits exceed harms if patients undergo careful follow-up.
- **Patient preference:** Adequate informed consent is requisite.
- **Exclusions:** None.

3.1.4. Commentary

Although persistent asymptomatic MEE after the resolution of acute inflammatory responses is common, approximately 75 to 95% of the residual OME after an AOM episode resolves spontaneously by 3 months [5,75]. Meta-analyses addressing the spontaneous regression of OME in pediatric patients reported that 25% of newly detected OME in children resolved by 3 months. However, longer spontaneous resolution after 6 to 12 months was observed in only 30%, with only marginal benefits if observed longer [5,6]. Namely, children in whom OME does not show spontaneous resolution in 3 months after onset would not show spontaneous recovery. Based on these results, watchful waiting is recommended for a child with OME at 3 months after onset [6].

Ventilation tube (VT) treatment of OME improves hearing for approximately 6-9 months compared with no VT. The difference decreases gradually with time as hearing improves in the untreated ear, but the long-term effect on hearing status has yet to be determined [51,73,135]. Among children with OME prolonged for more than 3 months, many will not show marked hearing loss of >30 dB or pathological changes in the TM. In terms of the balance between benefits and harms attributed to interventions, the clinician has an option to continue careful monitoring of these patients.

3.2. CQ2: are antibacterial agents effective for treating OME?

3.2.1. Recommendation (Fig. 7)

The use of antibacterial agents for treating OME in children is not recommended. As an exception, macrolide treatment (long-term, low-dose clarithromycin) is a therapeutic option in children with OME associated with rhinosinusitis.

[Recommendation degree: **Recommendation**, Level of evidence: **B**]

In cases without bacterial infection of the surrounding organs, administration of antibacterial agents for OME in children is not recommended because the risks outweigh the benefits.

[Recommendation degree: **Recommendation**, Level of evidence: **B**]

3.2.2. Background

The rate of bacterial detection in MEE from children with OME is high [136]; therefore, antibacterial agents can be effective in the short-term. In addition, antibacterial agents are effective for bacterial infection of the surrounding organs. This includes rhinosinusitis; as this condition is a precipitating factor for OME in children, its treatment can result in OME resolution. However, the use of antibacterial agents may cause adverse effects and increase the risk of development of bacterial resistance.

3.2.3. Aggregate evidence quality

- **Benefits for children:** Appropriately selected antibacterial agents for bacterial infections of peripheral organs may be useful in the treatment of OME in children.
- **Risks and harms for children:** Antibacterial treatment may lead to gastrointestinal symptoms, particularly diarrhea. All antimicrobials can lead to the development of drug resistance in bacteria.

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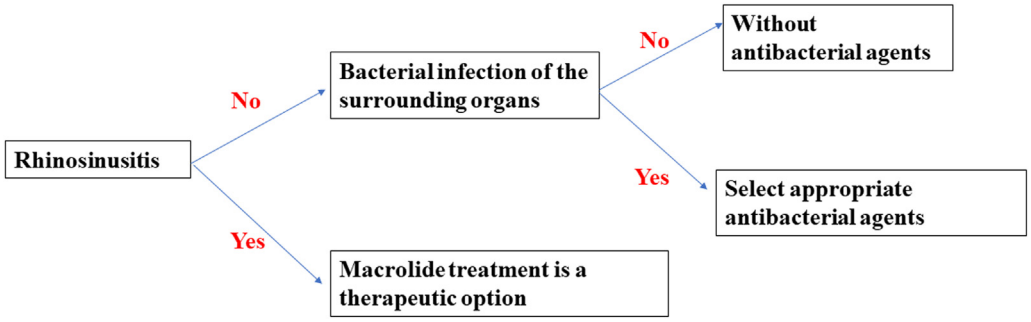

Fig. 7. Treatment algorithm for prescribing antibacterial agents for otitis media with effusion in children.

- **Benefits–harms assessment:** The benefits outweigh the harms if the choice of antibacterial agent is adapted to the type of bacteria causing the infection.
- **Patient preferences:** Patients must be fully informed, and consent must be obtained.
- **Exceptions:** Do not use antibacterial agents to which the patient is allergic.

3.2.4. Commentary

Cure rates of 65.6% and 16.1% were reported for 55 patients (96 ears) treated with a low-dose macrolide (clarithromycin: CAM) and 19 patients (31 ears) treated with usual-dose cephem antibiotics (control group), respectively. The efficacy was significantly higher in the low-dose CAM treatment group, especially in patients with sinusitis [137]. It was also reported that treatment with low-dose CAM (at the usual dose for one cycle) plus an inhaled nasal steroid for 8-12 weeks was effective in 88.7-95.2% of children with OME when treated within 3 months after infection, and this approach provided significant improvement compared with children receiving an inhaled nasal steroid alone (50.9–60.3%) [138]. In addition, administration of low-dose CAM plus an inhaled nasal steroid for 8 weeks was effective in 72.1% of children with OME when treated more than 3 months after infection. However, the number of cases was small (26 cases in this study); thus, further investigation is required. Another study showed that macrolide treatment was only minimally effective in children aged 2 years or younger and in patients with associated adenoid vegetation [137]. Given the decreasing susceptibility of *Streptococcus pneumoniae* and *Haemophilus influenzae* to macrolide antibiotics in Japan, the widespread use of these agents in cases in which they are anticipated to be minimally effective should be avoided.

Antibacterial agents other than low-dose CAM have short-term efficacy (2–8 weeks) for OME in children, but their long-term efficacy is unproven. Given the possibility of adverse effects (such as cutaneous drug eruption, vomiting, and diarrhea), microbial substitution of resident flora in the nasopharynx, increasingly resistant bacteria, and a poor cost-effectiveness ratio, the use of antibacterial agents is not recommended [75].

In an analysis of two systematic reviews, Williamson concluded that the risks of antibacterial agents for OME outweigh the benefits; thus, they should not be recommended [139]. A Cochrane review of 3,027 cases from 23 articles compared the clearance rate of MEE at 2-3 months after treatment between patients treated with or without antibacterial agents and concluded that use of antibacterial agents should not be recommended [140,141].

Antibacterial agents should be used for the treatment of AOM in children with OME in accordance with the "Clinical Practice Guidelines for the Diagnosis and Management of Acute Otitis Media (AOM) in children in Japan – 2018 update [21,22]." The present Guidelines is not intended to prevent reasonable treatment for complicating bacterial infections of other surrounding organs. In children with upper respiratory inflammation or rhinosinusitis, OME often develops, worsens, or becomes prolonged. In such cases, antibacterial agents should be considered, but their widespread use should be avoided.

►Note: Japanese Health Insurance does not allow antibiotic treatment for OME. Our Guideline states that antibiotic treatment is indicated for bacterial infections of the surrounding organs.

3.3. CQ3. Are drug therapies other than antibacterial agents effective for the treatment of OME?

3.3.1. Recommendation

a) **Carbocysteine**

Carbocysteine is recommended as a treatment option.

[Recommendation Strength: **Strong recommendation**, Evidence quality: **A**]

b) **Corticosteroids**

Oral corticosteroids have short- but not long-term efficacy for the treatment of OME in children but are not recommended because the risks outweigh the benefits.

[Recommendation Strength: **Strong negative recommendation**, Evidence quality: **A**]

On the other hand, inhaled nasal corticosteroids are associated with a low risk of adverse events and have recently been shown to be effective.

[Recommendation Strength: **Recommendation**, Evidence quality: **B**]

c) **Antihistamines**

Second-generation antihistamines for treating OME in children should be considered a treatment option in patients with allergic rhinitis. The efficacy of first-generation antihistamines for the treatment of OME in children has not been demonstrated, and they are thus not recommended because the risks outweigh the benefits.

[Recommendation Strength: **Recommendation**, Evidence quality: **B]**

3.3.2. Background

Carbocysteine is the only oral medicine currently approved in Japan for treating OME in children, and it is expected to be effective for inflammatory lesions of the surrounding organs. Rhinosinusitis, allergic rhinitis, and chronically inflamed adenoids are considered precipitating factors for OME in children and have been implicated in its pathophysiology. The present Guidelines are not intended to prevent the treatment of complicating lesions in the surrounding organs.

3.3.3. Aggregate evidence quality

- **Benefits for children:** Improvement of inflammatory lesions in the surrounding organs, which may improve OME. Patients do not receive unnecessary antibacterial treatment. Patients may benefit from a reduction in adverse effects such as gastrointestinal symptoms (mainly diarrhea) and a reduction in the likelihood of drug-resistant bacteria developing.
- **Risks and harms for children:** Adverse effects of individual drugs. Stress for parents and children (e.g., time-consuming, reluctance to take medication), and costs (e.g., drug costs) associated with taking medication.
- **Benefits–harms assessment:** The benefits outweigh the harms if a drug therapy is chosen that has minimal harmful adverse effects and reduces inflammatory lesions in the surrounding organs.
- **Patient preferences:** Patients must be fully informed, and consent must be obtained.
- **Exceptions:** Do not use agents to which the patient is allergic.

3.3.4. Commentary

a) Carbocysteine

Based on a systematic review (meta-analysis of 7 articles) of controlled clinical studies of carbocysteine, Moore et al. reported an improvement rate of 35% with administration of carbocysteine for 1–3 months, compared with 17% improvement in control groups. Adverse effects are unlikely to occur, and therefore, carbocysteine is recommended for treatment of OME in children [142]. It was shown that mucociliary function in the nasal cavity and pharyngeal orifice of the ET was significantly deteriorated in children with OME compared with healthy children, and carbocysteine may be associated with improvement of mucociliary function. Data also showed that carbocysteine is effective for treating adult chronic rhinosinusitis, and the agent is commonly used for this purpose in Japan [143,144].

To summarize, carbocysteine is a treatment option during the follow-up period for children with OME and rhinosinusitis.

b) Corticosteroids and antihistamines

A Cochrane systematic review on the efficacy of drug treatment for OME in children using oral or inhaled nasal steroids or first-generation antihistamines has been published [145]. This review showed that oral corticosteroids in combination with antibacterial agents led to a quicker resolution of MEE (7-28 days) compared with antibacterial agents alone but did not improve auditory acuity. There is no evidence that oral steroids alone or inhaled nasal steroids are effective in resolving MEE and improving auditory acuity. Long-term use of oral steroids may increase the risk of systemic side effects, and therefore, the risks outweigh the benefits, and these agents are thus not recommended for treatment of OME in children, which has other treatment options and does not require immediate care.

In contrast, inhaled nasal steroids have a low risk of adverse events and have recently been shown to be effective in clearing effusions and improving hearing [146–148]. Efficacy in adenoid hyperplasia has also been shown, and inhaled nasal steroids are reportedly effective in allergic rhinitis and adenoid hyperplasia cases rather than in OME itself [149]. In Japan, however, inhaled nasal steroids are not currently covered by health insurance for treating OME in children.

There is no evidence of benefit from treatment with first-generation antihistamines, either alone or in combination with decongestants, in the short- or long-term, for resolution of MEE or improvement of auditory acuity. In addition, 10% of patients receiving antihistamines experience adverse effects. Therefore, they are not recommended because the risks outweigh the benefits [149–152].

Given that allergic rhinitis and allergic reactions may have a negative impact on OME in children, oral second-generation antihistamines or inhaled nasal steroids should be administered to treat allergic rhinitis.

c) Other medications

In terms of Kanpo medicine, there is no established evidence available for OME treatment. However, because the conditions of OME are thought to be caused by water poisoning, diuretic prescriptions are mainly used. Saireito (an herbal medicine) has a diuretic effect and is thus used for treatment of edema. Saireito also has anti-inflammatory and anti-allergic effects, and it is reportedly effective in the treatment of OME [153].

3.4. CQ4: Are conservative therapies effective for the treatment of OME?

3.4.1. Recommendation

a) Local treatment

Although there is insufficient evidence as to whether local treatment of the paranasal sinus or ME inflation procedure on

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an outpatient basis at an ENT department is effective for treatment of OME in children, these treatments may be performed during the monitoring period prior to surgical treatment.

[Recommendation Strength: **Option**, Evidence quality: **C**]

b) Autoinflation

Autoinflation using a balloon more than 3 times a day is recommended as a treatment option.

[Recommendation Strength: **Recommendation**, Evidence quality: **B**]

3.4.2. Background

ME inflation is a treatment procedure for low pressure in the ME due to ET dysfunction. Local treatment of the paranasal sinus can treat rhinosinusitis, which is a precipitating factor for OME in children, and it is thus expected to lead to OME resolution. However, this has not yet been demonstrated.

3.4.3. Aggregate evidence quality

- **Benefits for children:** Improvement of clinical symptoms such as hearing loss and aural fullness.
- **Risks and harms for children:** The procedure may induce AOM during upper respiratory tract infection. Local procedures (other than autoinflation) are associated with social and economic disadvantages of hospital visits. ET ventilation (catheterization) can result in TM perforation and affect the surrounding organs (epistaxis, emphysema, etc.).
- **Benefits–harms assessment:** The benefits outweigh the harms if guidance is given, (e.g., do not perform the procedure during the infection).
- **Patient preferences:** Adequate explanation and consent for the procedure is required.
- **Exceptions:** none.

3.4.4. Commentary

Etiologies of OME in children include ET dysfunction and inflammation of surrounding organs. Low pressure at the tympanum can be resolved by opening the ET, but it recurs after treatment. Therefore, the treatment should be performed frequently to increase its effectiveness. It was shown that self-treatment by opening the ET is not effective at a frequency of 1-2 times per day, but it is effective if done 3 times per day [154–156]. A systematic review found no evidence of the efficacy of tympanograms or pure-tone audiometry alone but significant benefit when they are combined. It is thus reasonable to consider its use during the follow-up period due to its cost and low risk of adverse effects (harm) [157,158]. RCTs have also reported its efficacy [159].

Therefore, opening the ET may be planned both as autoinflation and as an outpatient treatment at an ENT department. It has also been reported that recurrences can be reduced after repeating autoinflation [160], and thus, the treatment may be indicated for recurrences. If performing this treatment at an ENT department can ensure the resolution of low pressure, even in the short-term, this may prevent adhesion of the TM. In addition, observation of the TM before and after such outpatient treatment may help in the evaluation of disease conditions (e.g., by observing whether the TM is adhesive or just in contact). Complications associated with autoinflation with nasal balloon inflation include AOM, injury of the TM, and mucosal damage. It should be suggested that this treatment be avoided in cases of upper respiratory tract infection because AOM occurs frequently in this context.

Recently, the efficacy of balloon Eustachian tuboplasty was reported in adults with ET stenosis. Although it is reportedly effective in children [161], it is not indicated for children in Japan, and there are no reports of long-term outcomes.

3.5. CQ5: Is myringotomy effective for the treatment of OME?

3.5.1. Recommendation

Myringotomy is recommended for the diagnosis and determination of treatment protocol for OME in children. It is effective for short-term prognosis, but it is not recommended for the purpose of long-term treatment.

[Recommendation Strength: **Option**, Evidence quality: **D**]

3.5.2. Background

Myringotomy involves making a small incision or perforation in the TM using a myringotomy knife or laser. While the perforation remains patent, pressure between the ME cavity and the atmosphere is equalized, and the MEE resolves [73]. Fluid can be suctioned from the ME cavity through this perforation, enabling rapid improvement in hearing even in the early stages after OME onset. Therefore, myringotomy can be recommended and performed without hesitation in cases complicated by moderate or severe hearing loss.

3.5.3. Aggregate evidence quality

- **Benefits for children:** Promotes rapid improvement of clinical symptoms, such as hearing impairment and aural fullness.
- **Risks and harms for children:** Bleeding, pain and discomfort, and the need for physical restraint during the procedure, and otorrhea and a risk of persistent perforation after the procedure, etc.
- **Benefit–harms assessment:** Benefits exceed harms in selected patients, based on symptoms and otoscopic findings in short-term prognosis. Harms exceed benefits in repeated myringotomy for long-term treatment.
- **Patient preferences:** Appropriate informed consent is requisite.
- **Exceptions:** Proper skills and equipment are essential; clinicians should not implement this procedure otherwise.

3.5.4. Commentary

Myringotomy can provide immediate improvement in hearing impairment due to OME. In the present Guidelines, TS tube insertion is recommended for children with OME for 3 months or longer duration after onset or detection (refer to Section 3.6). However, for patients with hearing impairment or other symptoms caused by OME that interfere with daily

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life or group life, such as school life, myringotomy should be considered for selection as a treatment method, as it provides immediate effect during conservative treatment.

We reviewed three RCTs examining treatment with a myringotomy knife [162–164]. With regard to important clinical outcomes such as resolution of MEE and hearing improvement, the results of the three studies with myringotomy alone using a myringotomy knife were less effective than those for TS tube insertion. Reflecting similar interpretations of this evidence, myringotomy alone using a myringotomy knife is not recommended as a therapeutic approach in OME treatment guidelines outside Japan [7,16]. Another study [164] divided cases of OME into untreated, myringotomy alone, and TS tube insertion groups and reported that MEE was observed in 64%, 61%, and 17%, respectively, at 1 year. Although it was concluded from these results that myringotomy alone has no therapeutic effect on long-term prognosis, there was no discussion regarding the short-term effects of myringotomy for children with OME.

In myringotomy using a myringotomy knife (incisional myringotomy), the incision usually closes in a few days, whereas in laser-assisted myringotomy, the incision remains open for an average of 2 weeks [165,166]. A systematic review of laser-assisted myringotomy included 3 RCTs [167–169] and 5 case control studies [170]. Yousaf et al. reported that 89.7% and 53% of OME cases treated with laser-assisted tympanostomy had continued hearing improvement after 30 days and 6 months, respectively. Conversely, in cases with TS tube insersion, hearing improvement was observed in 91% and 79.5% of cases after 30 days and 6 months, respectively. Therefore, even for laser-assisted procedures, tympanostomy is considered less effecitive in treating children with OME than TS tube insertion. In addition, they conducted a comparsion between laser-assisted tympanostomy and myringotomy with a myrintotomy knife, and the rates of hearing improvement after 2 weeks, 4 weeks, 2 months, and 6 months were 92%, 92%, 62%, and 54%, respectively, for laser-assisted tympanostomy and 80%, 60%, 36%, and 24%, respectively, for myringotomy knife treatment. According to these results, the authors concluded that laser-assisted tympanostomy is more effetecive than myringostomy using a myringostomy knife [168].

Regarding complications, the perforation rate of laser-assisted tympanostomy over 6 months is reportedly 0.8 to 1.9% [166,169], which is considerably lower than the perforation rate for TS tube insertion (2.2% for short-term tube and 16.6% for long-term tube).

These findings show that myringotomy alone using a myringotomy knife for OME in children is unlikely to have any long-term treatment effects on MEE or hearing and that the therapeutic effect of laser-assited tympanostomy is inferior to that of TS tube insertion but superior to that of knife myringotomy alone. However, it should be noted that laser-assisted tympanosotmy is not covered by national health insurance in Japan at present.

Myringotomy is ineffective for OME in children because the incision closes quickly. However, it may be useful for diagnosis or determining the therapeutic approach. Rapidly ventilating the tympanic cavity may improve hearing; therefore, myringotomy can be effective for diagnosing complications of ME lesions, such as ossicular malformations and congenital cholesteatoma, as well as sensorineural hearing loss. Furthermore, there are cases of OME in children in which the patients and their guardians do not notice the hearing loss. In such cases, myringotomy can enable awareness of hearing improvements within only a few days of surgery. For the patients and their guardians, awareness of hearing loss can provide motivation for subsequently undergoing appropriate follow-up and treatment.

Myringotomy is an effective procedure that can be performed by an otolaryngologist under local anesthesia in an outpatient clinic, and it is useful for diagnosis, determining the therapeutic approach, and providing rapid improvement of hearing loss in children with OME. However, myringotomy is an invasive procedure for pediatric patients, and sufficient explanation should be given to both the patients and their guardians. Furthermore, myringotomy should be performed under a microscope or other magnifying device for safety.

It is recommended that myringotomy be performed in the anterioinferior quadrant of the TM, where there is little impact on the ossicular chain. An aberrant course of the internal carotid artery may, on rare occasions, be observed in the anterioinferior quadrant of the TM [171,172], and a high jugular bulb may be present in the ME [173,174]. These vascular anomalies are usually observed by pulsation of the vessels or visibility of the vessels through the TM. However, it may be difficult to identify these signs because of fluid in the ME or a child's crying and vigorous movement. Therefore, careful attention is required for myringotomy.

3.6. CQ6: What are surgical indications for TS tube insertion?

3.6.1. Recommendation **(refer to** Fig. 6**):**

Clinicians should offer TS tube insertion for children with bilateral OME that has persisted for 3 months or more AND as follows:

1. When pathological changes of the TM such as atelectasis and TM adhesion are observed.

[Recommendation Strength: **Strong Recommendation**, Evidence Quality: **B**]

2. When hearing difficulties with hearing loss (≥30 dB) of the ear on better-hearing side are documented.

[Recommendation Strength: **Recommendation**, Evidence Quality: **B**]

3. When clinical findings that may be caused by OME are revealed, such as impaired academic performance, problems in behavior, vestibular symptoms, hypoactivity, ear discomfort, and decrease in QOL. However, symptoms due to developmental disorders are excluded.

[Recommendation Strength: **Recommendation**, Evidence Quality: **B**]

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3.6.2. Background

Pediatric OME is a disease that can be expected to spontaneously resolve. However, once OME has persisted accompanied by hearing loss in both ears for a long period of time, there is a risk of negative effects on child development. Moreover, serious pathological changes in the TM may cause adhesive otitis media or cholesteatoma.

3.6.3. Aggregate evidence quality

- **Benefits for children:** Decrease in the negative effects on child development associated with hearing loss. Decrease in the frequency of other otitis media (AOM, adhesive otitis media, and cholesteatoma).
- **Risks and harms for children:** Pain, discomfort, and need for physical restraint during the surgical procedure under local anesthesia to the TM. Potential risks of general anesthesia in cases of surgery performed under general anesthesia. Otorrhea while tubes are in place, spontaneous drop of TS tube into the tympanic cavity, and adverse events affecting the TM, including persistent perforations and tympanosclerosis after extrusion or removal of tubes. Medical economic burden such as surgical cost of TS tube insertion and outpatient fee after the insertion. Restrictions on swimming, the need for earplugs, etc.
- **Benefits–harms assessment:** Benefits exceed harms because adverse consequences, including perforation of the TM, can be reduced by choosing short-term TS tubes.
- **Surgical cost:** TS tube insertion (K309).
- **Patient preference:** Adequate informed consent is requisite.
- **Exclusions:** Those with DS and cleft palate are excluded in this CQ; refer to **Chapter 4**.

3.6.4. Commentary

Regarding the effectiveness of TS tube insertion for OME in children, three systematic reviews of RCTs have been reported [51,73,135]. The literature search did not find any new RCTs on TS tube insertion after the most recent RCT by Berkman, which was considered in the present systematic review.

Hellstrom et al. and Browning et al. qualitatively evaluated the results of their studies without conducting a meta-analysis [51,135]. In the RCTs examined in these systematic reviews, the effectiveness of the following three treatments were compared among children with bilateral OME aged 1 to 12 years: TS tube insertion, myringotomy, and/or medication with a policy of performing TS tube insertion if necessary after 2-3 months or longer period of follow-up.

As for complications of TS tube insertion, Kay et al. conducted observational studies of OME in children and integrated the incidence of complications and sequelae in an RCT [175].

In this section, we make recommendations for this CQ by comprehensively evaluating the evidence of the benefits and harms of TS tube insertion for OME in children, focusing on the results of these systematic reviews and meta-analyses.

3.6.1. Benefits of TS tube insertion

The benefits of TS tube insertion are decreasing MEE and negative influences with OME such as hearing loss.

Hearing is the most important outcome of pediatric OME. Browning et al. performed an RCT and meta-analysis in which children with OME were randomly assigned to two groups, TS tube insertion and non-TS tube insertion. They found that the mean hearing levels were 11.9 dB and 4.2 dB better in TS tube insertion group children than in the non–surgically treated children at 3 and 6-9 months after surgery, respectively. However, the difference in mean hearing level between the two groups at 12 and 18 months after surgery was 0.41 dB and 0.02 dB, respectively, and no statistically significant differences were found [135].

In addition, in a meta-analysis of three studies in which random assignment was performed for each ear in bilateral pediatric OME, TS tube insertion was found to improve hearing levels by 10.1 dB and 5.2 dB at 4-6 months and 7-12 months after surgery, respectively. However, the difference between the two groups at 24 months after surgery was only 2.1 dB, revealing no statistically significant difference [135]. Hellström et al. qualitatively integrated eight RCTs and reported that TS tube insertion treatment of OME improved hearing level until 9 months after surgery, but the effect gradually diminished; thus, the long-term effect was unknown [51].

The effect of TS tube insertion on reducing MEE, which is the exact pathophysiology of pediatric OME, has also been examined. Browning et al. estimated the incidence of MEE within 1 or 2 years after TS tube insertion by a meta-analysis of several studies [135]. In each study, the incidence of MEE within 1 year after TS tube insertion in the TS tube insertion group and in the myringotomy/medication group were 17-36% and 48-70%, respectively [165,176,177]. These findings showed that the TS tube insertion group was 32% less likely to have MEE within 1 year than the myringotomy/medication group [135]. Similarly, the proportion of periods during which MEE was observed within 2 years after intervention in the TS tube insertion group and in the myringotomy/medication group were 30-35% and 40-51%, respectively [164,177,178], and TS tube insertion therapy was 13% less likely to involve MEE during the first two postoperative years than myringotomy/medication therapy [135].

Only one RCT has examined the incidence of AOM during the course of OME. The number of incidences of AOM per year per patient within 3 years after TS tube insertion, myringotomy, or non-surgery was 0.18, 0.58, and 0.38, respectively [162].

Three studies (average age of children: 1.6 to 3.3 years) on speech perception and production were analyzed by systematic reviews [135]. Meta-analyses of these RCTs revealed no statistically significant differences in language or speech development at 6-9 months after TS tube insertion [135,176,179,180]. Paradise et al. assessed speech, language, and cognition at the age of 3 years, vocabulary, intelligence, and speech processing ability at the age of 6 years, and speech development, speech processing ability, and understanding of phoneme at the age of 9-11 years in children with bilateral pediatric OME, but no significant differences between

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the early treatment group and late-treatment groups were observed [177,181,182]. Hall et al. tracked children in Maw's RCT for a longer period, and they reported that language development at the age of 4.5 years was better in the TS tube insertion group than in the non-surgery group, with an adjusted odds ratio of 3.45, but there was no statistically significant difference between the two groups in language development test results at the age of 8 years [183].

The effect of TS tube insertion on behavioral development was evaluated in two RCTs. Wilks et al. evaluated pediatric OME using behavioral checklists and found that the proportion of children with behavioral problems was significantly lower in the TS tube insertion group (30%) than the non-TS tube insertion group (47%) at 9 months after surgery, but no difference between the two groups was observed at 18 months [184]. In the other RCT, children with OME were evaluated via a behavioral checklist at the age of 3, 6, and 9-11 years, and again, there was no difference between the TS tube insertion group and non-TS tube insertion group [177,181,182].

The QOL of children with OME was analyzed in Rovers' RCT using the TNO-AZL Infant Quality of Life, a comprehensive QOL scale for children aged 1-4 years. There was no statistically significant difference in QOL in children with OME aged 1 to 2 years at 6 and 12 months after TS tube insertion between the TS tube insertion and non-TS tube insertion groups [185].

3.6.2. Harms of TS tube insertion

The risks and harm associated with TS tube insertion include various complications (otorrhea, granulation formation, tympanosclerosis, pocket and cholesteatoma formation, persistent TM perforation, damage to the ossicular chain and injury to the high jugular bulb, and accidental drop of the TS tube insertion into the tympanic cavity), pain, discomfort, need for physical restraint during the surgical procedure under local anesthesia to the TM, potential risks of general anesthesia, and medical economic burden, such as surgical cost of TS tube insertion and outpatient fees after surgery.

Knutsson et al. conducted an RCT including 800 ears and reported that infection was found more than once in 13.8% (infection occurring more than twice was observed in 3.1%), and infection was less frequent in patients with silicon tubes [186].

Kay et al. conducted systematic reviews of short-term adverse events of TS tube insertion for OME based on 70 observational studies and 64 RCTs [175]. After TS tube insertion, transient otorrhea occurred in 16% of patients within 4 weeks after surgery (26.1% after a longer period), whereas persistent otorrhea lasting for more than 3 months after surgery was observed in 3.8%, recurrent otorrhea in 7.4%, and otorrhea requiring TS tube insertion removal in 4.0% (long-term TS tube insertion was used in 87% of cases).The incidence of adverse events during TS tube insertion, except for otorrhea, were tube occlusion (6.9%), granulations that did not require treatment (4.2%), granulation requiring treatment (gromets and/or granulation removal, 1.8%), early spontaneous extubation (3.9%), and spontaneous drop of the tube into the tympanic cavity (0.5%).

Pathological changes in the TM after tube removal included tympanosclerosis (31.7%), atrophy and retraction (24.6%), and retraction at the pars tensa (3.1%). Persistent perforation of the TM after tube removal was found in 2.2% and 16.6% of short-term and long-term TS tube insertions, respectively. In addition, cholesteatoma was observed in 0.8% of short-term TS tube insertion cases and 1.4% of long-term TS tube insertion cases [175]. For a discussion of the formation of cholesteatoma as a complication of TS tube insertion, refer to Section 3.7.

Kay et al. also estimated the relative risk of tympanic changes after TS tube insertion in a meta-analysis [175]. The relative risk of TM atrophy and retraction was 1.7 (n = 10 studies), and that of sclerosis of the TM was 3.5 (n = 13 studies) for the TS tube insertion group vs. the non-surgical or myringotomy groups. As the lower limit of the 95% confidence interval was close to 1.0 for the outcome of TM atrophy and retraction, it is possible there was no substantial difference. In a survey of 297 ears of 156 patients by Branco et al., tympanosclerosis was observed in 35.7%, and the authors stated that this is more likely to occur in cases with more frequent otitis media (p = .001) and otorrhea (p = .0029) and less likely in cases less than 12 months after TS tube insertion (p=.009) [187].

Two cohort studies observed hearing for more than 10 years after TS tube insertion. One was a birth cohort study, which showed a tendency toward worse hearing of 5-10 dB in patients with a history of TS tube insertion compared with those without a history of TS tube insertion at the age of 18 years [188]. In another cohort study, 224 patients with OME who underwent TS tube insertion on one side at an early age and myringotomy on the other side showed no difference in hearing level between ears [189]. Thus, the long-term effect of TS tube insertion on hearing has not been conclusively shown [135].

3.6.3. Decision regarding recommendations

In determining recommendations for indications of TS tube insertion, not only the above-mentioned benefits and harms of TS tube insertion, but also the characteristics of OME should be considered. The Committee for the present 2022 Guideline recommends watchful waiting for 3 months from the date of effusion onset or diagnosis of OME for managing a child with OME, because the influence of pediatric OME on hearing usually ranges from none to moderate (refer to Section 2.4.), and the disease sometimes spontaneously resolves. However, early TS tube insertion is recommended in cases of bilateral OME persisting for more than 3 months in the following cases: (1) when pathological changes of the TM occur, such as atelectasis and adhesions (refer to Section 1.20); (2) when a hearing loss of ≥30 dB is documented in the better-hearing ear; and (3) in the presence of clinical findings that may be associated with hearing loss due to OME, such as decreased activity in school.

This recommendation is based on the consideration that, despite the possibility of spontaneous resolution of the disease, once OME has persisted in both ears for a long period of time, there is a potential risk for negative effects associated

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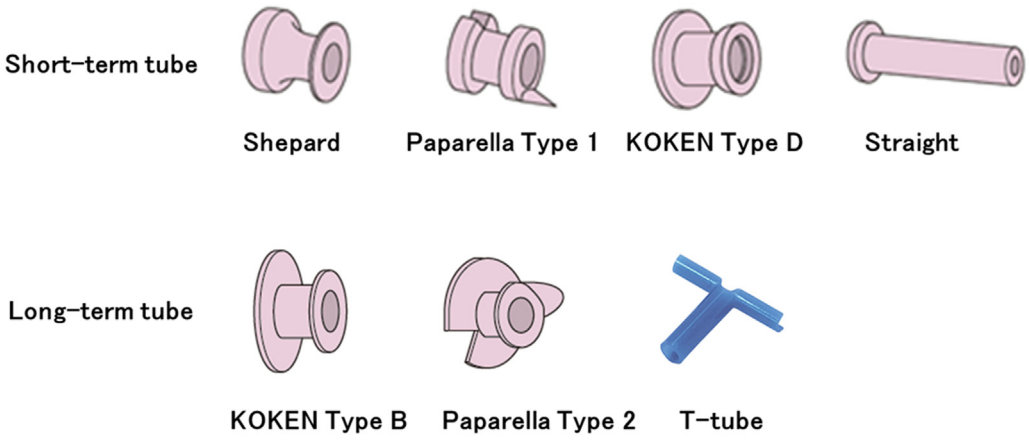

Fig. 8. Types of tympanostomy tubes.

with hearing loss on child development in terms of learning, emotions, and communication ability, etc. Moreover, if an irreversible change in the TM progresses to adhesive otitis media or cholesteatoma occurs (refer to Section 3.11), treatment becomes more difficult, and patients may have permanent and irreversible hearing problems.

On the other hand, early TS tube insertion may also be recommended in cases with a hearing level between 25 and 30 dB bilaterally; in those with risk factors of prolonged OME, such as poor development of mastoid cells; or in those showing a clinical finding that may be associated with hearing loss due to OME, such as slowing of academic progress. However, we do not consider that immediate TS tube insertion on all children with OME is justified. This is because several reports have demonstrated with high evidence levels that hearing improvement resulting from TS tube insertion is expected only during 6 to 9 months after the procedure [135]. Harms such as postoperative complications and sequelae must be considered more carefully. For a discussion of indications of TS tube insertion in unilateral OME, refer to Section 3.10.

Although there is no evidence to provide quantitative criteria for pathological changes in the TM for which TS tube insertion effectively prevents, abnormal TM findings relevant to sequelae include the following (expert opinion good practice point): severe retraction in pars tensor or flaccida of the TM, destruction of the ossicles, and adhesive retraction of the TM [6,9].

In addition, TS tube insertion may be effective in preventing MEE and retraction of the TM and cholesteatoma in cases when patients can overcome sniffing habit. This is described in detail in the section regarding the etiology and pathophysiology of OME [43,192]. In any case, the decision regarding whether to perform TS tube insertion should be shared with parents by comprehensively judging the degree of hearing loss, symptoms other than hearing loss, TM findings, duration of disease, intentions of the patient and their family, medical expenses required for treatment, etc.

► Appendix: Selection of tympanostomy tube.

There are two types of tympanostomy tube: short-term and long-term (Fig. 8). While tubes can remain in the TM for varying lengths of time, the mean duration of short-term tubes is 8-16 months, accompanying many cases of spontaneous extrusion and closure of the TM perforation, and the rate of persistent perforation is approximately 2% [73,175]. Conversely, long-term tubes are intended to remain in the TM for at least 15 months, with spontaneous extubation occurring at a mean of 18-36 months, and many cases eventually require removal [31,73]. Compared with short-term tubes, long-term tubes are often associated with otorrhea and a high rate (17%) of residual perforation [175].

As most RCTs examining the treatment effects of tube insertion have focused on short-term tubes, the evidence suggests that short-term tubes should be the first choice for initial TS tube insertion for OME in children not at risk of becoming refractory. As OME recurs after extubation in 20–50% of cases, in which tube re-insertion is required within 3 years [162,164,193], recovery without sequelae can be achieved with a single short-term tube insertion in 50-80% of cases. Consideration should also be given to long-term tubes in cases showing pathological changes such as atelectatic ear and adhesive otitis media, in which short-term tubes are susceptible to premature extrusion. Even at the first surgery, long-term tympanostomy tube can be considered for children with OME that appears to be refractory [186].

For a discussion of indications of TS tube insertion in cases involving atelectasis or adhesive otitis media, refer to Section 3.11.

3.7. CQ7: How should physicians manage tympanostomy tubes after surgery?

3.7.1. Recommendation

Early postoperative and routine follow-up (up to once every 4-6 months) is recommended to observe the postoperative condition of tympanostomy tubes and to evaluate hearing. Follow-up and evaluation of recurrence of OME and the necessity for additional treatment (including re-insertion) is required after a tympanostomy tube is extubated.

[Recommendation Strength: **Strong Recommendation**, Evidence Quality: **A**]

Table 8. Risk factors for developmental difficulties in children with OME (at-risk children; adapted from **Rosenfeld et al. 2016**).

Permanent hearing loss independent of OME
Suspected or confirmed speech and language delay or disorder
Autism spectrum disorder or other pervasive developmental disorders#)
Syndromes (e.g., Down's) or craniofacial disorders that include cognitive, speech, or language delays
Blindness or uncorrectable visual impairment
Developmental delay

#): A group of complex neurodevelopmental disorders characterized by repetitive and characteristic patterns of behavior and difficulties with social communication and interaction.

3.7.2. Background

After TS tube insertion, it is necessary to confirm the therapeutic effect and cure of OME, as well as manage any complications and sequelae of TS tube insertion.

3.7.3. Aggregate evidence quality

- **Benefits for children:** Decreased negative effects associated with hearing loss on development. Reduced frequency of complications due to TS tube insertion.
- **Risks and harms to children:** Medical, economic, and physical burdens, time constraints for follow-up visits to doctor's office after TS tube insertion.
- **Benefits–harms assessment:** When performing appropriate postoperative management, benefits exceed harms.
- **Patient preference:** Appropriate informed consent is requisite.
- **Exclusions:** None.

3.7.4. Commentary

It is difficult to establish a uniform standard follow-up program after TS tube insertion because the local medical situation and the disease condition in each case can vary. Considering these issues, the Guideline Committee recommends early postoperative and routine follow-up (up to once every 4-6 months) to observe the postoperative condition of the tympanostomy tube and to evaluate hearing. Children and their guardians should be advised to undergo re-examination when problems occur, such as recurrence of OME after natural removal of the TS tube insertion or otorrhea due to infection. After the tympanostomy tube is extubated, further follow-up is necessary to check for recurrence of OME and to assess the necessity for additional treatment (re-TS tube insertion). Within 1-3 months after extubation, the condition of the TM and presence or absence of MEE should be checked, and a final evaluation should be made to ensure that OME is cured with no need for re-insertion 6 to 12 months after extubation.

If a child with OME has another disease causing hearing loss, TS tube insertion may not sufficiently improve hearing (refer to Table 8 in Section 3.10). Therefore, improvement in hearing should be confirmed early after surgery, and another cause of hearing loss should be examined if improvement of hearing loss is poor. During follow-up, in case the tympanostomy tube becomes invisible, hearing loss is suspected, or complications of TS tube insertion are observed, consultation with a more-advanced medical institution should be considered.

Complications of TS tube insertion include obstruction of the tube, recurrent/protracted otorrhea resistant to conservative treatment, granulation formation, enlargement of the perforation, and dropping of the tube into the tympanic cavity [9,141,194].

Complications after removal of a tympanostomy tube include tympanosclerosis, persistent perforation, atrophy or retraction of the TM, and cholesteatoma formation (refer to Appendix 2, Kay et al., 2001). In particular, when TM perforation remains, it may cause hearing loss depending on the size of the perforation, and even small perforations can lead to infection in the tympanic cavity. In cases of TM perforation or pathological changes requiring surgery or cholesteatoma formation, consultation with a higher medical institution may also be required. Refer also to Section 3.6**–8.** for a discussion of complications and sequelae of TS tube insertion.

► Appendix 1: Guidance on bathing and swimming after TS tube insertion.

The use of earplugs when swimming after TS tube insertion is not always recommended. Carbonell et al. analyzed the results of two RCTs and nine cohort studies and reported that use of earplugs during swimming as well as prophylactic use of antibacterial ear drops after swimming did not reduce the risk of AOM [195]. Goldstein et al. performed an RCT in which 201 children with OME who received bilateral TS tube insertion were randomly assigned to with or without earplugs groups during bathing or swimming. They reported that the incidence of otorrhea was significantly reduced in the "with earplugs" group [196]. However, the effectiveness of earplugs is limited, and the frequency of otorrhea is reduced from 56% to 47% by constant wearing of earplugs, indicating that 2.8 years continuous use of earplugs is necessary to prevent even only one episode of otorrhea [9,196].

To avoid excessively restricting the activity of the patient, continual use of earplugs should not be recommended. Patients should be instructed to avoid swimming in lakes and oceans (where the chance of infection is higher), diving deep in swimming pools, or submerging themselves in bathtubs. Conversely, specifically in cases in which these situations cannot be avoided or in cases in which a child has repeated otorrhea or complains of otalgia or otorrhea during swimming, they should be instructed to use earplugs.

► Appendix 2: Cholesteatoma formation as a complication of TS tube insertion.

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Cholesteatoma may arise from the retracted fragile part or edge of the perforation of the TM as a complication of TS tube insertion [50]. On average, the incidence of cholesteatoma after TS tube insertion is approximately 1% and less than 1% in cases attributed to ET dysfunction [50,175]. Golz et al. retrospectively examined 2,829 pediatric OME patients (5,575 ears) who received TS tube insertion and reported that the incidence of cholesteatoma occurring in the ME side of the normal TM or at the margin of the TM perforation was 1.1% (62 ears). The authors commented that the incidence was significantly higher in children in whom TS tube insertion was performed under 5 years of age, as well as in those who received three or more TS tube insertions in the past [197].

In a large cohort study by Spilsbury et al., cholesteatoma developed in 460 of 45,980 children with a history of at least one TS tube insertion. It is reported that the cholesteatoma was diagnosed on average 3.8 years after the last TS tube insertion. In addition, analyses of risk factors for cholesteatoma revealed that the risk of cholesteatoma formation increases with the number of TS tube insertions in children with OME (without cleft palate). For example, children who had four TS tube insertions had 5.6 times greater risk of cholesteatoma than those who had only one TS tube insertion. Children who have received TS tube insertion several times thus need to be followed more carefully. On the other hand, although the incidence of cholesteatoma in children with cleft palate is as high as 4.3%, an increase in the number of TS tube insertions does not lead to an increase in the hazard ratio, and ET dysfunction may be more involved than TS tube insertion in these cases [69].

3.8. CQ8: How long should a tympanostomy tube be inserted?

3.8.1. Recommendation

In cases of OME in children not at risk of becoming refractory, the standard duration of TS tube insertion should be about 2 years. Tube removal should also be considered in patients with otorrhea resistant to conservative treatment or with severe inflammatory changes (granulation) at the tube insertion site.

[Recommendation Strength: **Recommendation**, Evidence Quality: **C**]

3.8.2. Background

For children with OME, a longer period of tube therapy is desirable; however, long-term TS tube insertion also increases the risk of sequelae.

3.8.3. Aggregate evidence quality

- **Benefits for children:** Intentional extubation at the appropriate time reduces the incidence of OME recurrence as well as complications due to TS tube insertion.
- **Risks and harms for children:** In case of recurrence of OME after extubation, risks, harms, and burdens will increase with re-TS tube insertion (refer to Section 3.6).
- **Benefits–harms assessment:** Extubation at the appropriate time reduces adverse events, and thus, benefits exceed harms.
- **Patient preference:** Appropriate informed consent is requisite.
- **Exclusions:** Those with history of multiple TS tube insertion, DS, and cleft palate are excluded in this CQ.

3.8.4. Commentary

Tympanostomy tubes are classified as short-term (8-18 months) or long-term (15 months or longer) [31]. It is known that long-term tubes have a higher incidence of otorrhea and persistent perforation of the TM than short-term tubes [175]. If otorrhea or granulation formation is observed during the follow-up period after TS tube insertion, removal of the tube may be necessary if it is not improved by conservative treatment (refer to Section 3 **CQ6–7** for a discussion of complications due to tube type and frequency of sequelae).

While it has been pointed out that cure of OME is related to the period of tube therapy, the appropriate period necessary for the cure of OME remains unclear. A histopathological study of the temporal bone of children with OME suggested 6 months or more [198], and other studies suggested 12 months or more [199], 13 months or more [200], 12 to 18 months [201], 18 months or more [202,203], 18 to 24 months [204], 19 months or more [205], or 19 to 36 months [206]. As many short-term tympanostomy tubes are spontaneously extubated 10 to 18 months after insertion, it may not be necessary to intentionally remove the tube considering the minimum required period. On the other hand, there are individual differences in the amount of time the tube stays in position, and it may be more important to consider removal of the tube if it stays in position for more than 2 years. If a long-term tube tends to stay in the TM for 2–3 years or even longer, tube removal also should be considered in such cases. It has been reported that the incidence of persistent perforation of the TM, which is a complication of TS tube insertion, is 3% when the tube is removed less than within 3 years after insertion, but the risk increases to 15% when the tube stays in for more than 3 years [207].

3.9. CQ9: Are adenoidectomy and tonsillectomy effective for OME?

3.9.1. Recommendation **(Fig. 9)**

a) Adenoidectomy

If adenoid hyperplasia is present, adenoidectomy is effective in the treatment of OME. However, it is a more invasive procedure and should be performed with the following considerations in mind:

① In the absence of a clear indication for adenoidectomy in upper airway disease, it is not recommended as the initial surgery for OME in patients under 4 years of age.

[Recommendation Strength: **No recommendation**), Evidence Quality: **A**]

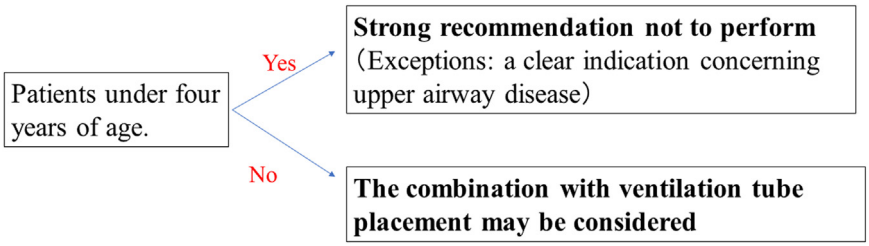

Fig. 9. Treatment algorithm for planning adenoidectomy.

① Adenoidectomy combined with TS tube insertion is expected to reduce the recurrence rate of OME in patients above 4 years of age. The combination of adenoidectomy and TS tube insertion may be considered.

[Recommendation Strength: **Strong recommendation**, Evidence Quality: **A**]

① At the time of reoperation for recurrent cases of ventilation tube dislodgement after the initial surgery, adenoidectomy should be performed if the absence of cleft palate has been confirmed.

[Recommendation Strength: **Recommendation**, Evidence Quality: **B**]

b) Tonsillectomy

Tonsillectomy should not be performed for the treatment of OME in children.

[Recommendation Strength: **There is sufficient evidence of no benefit**), Evidence Quality: **A**]

3.9.2. Background

Adenoids contribute to clinical status in OME in children (refer to Section 2.7), and adenoidectomy is performed as treatment for OME in children in clinical practice.

3.9.3. Aggregate evidence quality

- **Benefits for children:** Prevention of OME recurrence in patients above 4 years old.
- **Risks and harms for children:** Risks associated with the use of general anesthesia, intraoperative bleeding, postoperative pain and bleeding, and hyper-nasal speech.
- **Benefits–harms assessment:** The benefits outweigh the harms in recurrent cases and in children above 4 years of age.
- **Socioeconomic disadvantages:** Hospitalization for several days, surgery under general anesthesia.
- **Surgical cost:** Adenoidectomy (K370).
- **Patient preference:** Adequate explanation and consent are required.
- **Exceptions for patients under 4 years of age:** Consider adenoidectomy in cases of upper airway involvement caused by adenoids (e.g., pharyngotonsillitis, severe nasal obstruction, and obstructive sleep apnea). It is essential to have the necessary skills and equipment to perform the surgery safely.

3.9.4. Commentary

a). Adenoidectomy

Two systematic reviews have been reported investigating the effects of adenoidectomy for OME in children [73,208]. Among them, van den Aardweg et al. also reviewed recurrent AOM in addition to OME. After publication of these reports, the results of the Trial of Alternative Regimens in Glue Ear Treatment (TARGET) study, a large-scale RCT regarding OME, were released [209]. Berkman et al.'s review [73] comprised a qualitative evaluation of the TARGET study and the seven OME studies included in the review by van den Aardweg and colleagues. According to these three studies, this Guideline's recommendations have been developed based on the eight RCTs (patient age range, 2 years 1 month – 14 years).

The effects of adenoidectomy on OME in children were evaluated based mainly on the following outcomes: rate of OME improvement, duration of MEE, and degree of hearing improvement.

A meta-analysis of three RCTs by van den Aardweg et al. revealed that the rates of OEM improvement with adenoidectomy were 22% and 29% at 6 and 12 months, respectively, compared to those of watchful waiting [208]. These results indicate that adenoidectomy for OME in children improves MEE to some degree. However, in three RCTs that compared adenoidectomy and watchful waiting, hearing tests at 6 and 12 months showed no significant difference between the two approaches [163,190,209].

Four RCTs have evaluated the additional benefits of adenoidectomy as an adjunct to TS tube insertion. An RCT by Roydhouse et al. found no significant difference in the mean rates of effusion recurrence between adenoidectomy TS plus tube insertion and TS tube insertion alone at 12 (18% vs. 23%, respectively) or 24 (15% vs. 18%, respectively) months [73,210]. Another study comparing adenoidectomy plus TS tube insertion and TS tube insertion alone found that the proportions of examination days on which MEE was observed over the 2-year follow-up were 26%±21% and 36%±24% (mean ± SD), respectively, showing a significantly better outcome with adenoidectomy combined with TS tube insertion (p=0.0101) [178]. Furthermore, rates of repeated surgery during the 2-year follow-up were significantly lower for adenoidectomy plus TS tube insertion (14%) than for TS tube insertion alone (28%; $p = 0.007$). Casselbrant et al. compared adenoidectomy plus TS tube insertion and TS tube insertion alone and found no significant difference in the proportion

of patients who developed MEE during the 36 months after surgery (20.6% vs. 18.6%) [211].

The TARGET study compared the treatment effects of adenoidectomy plus TS tube insertion and TS tube insertion alone on hearing [191]. No significant difference in hearing TARGET was observed up to 6 months, possibly because of functioning tympanostomy tube. Conversely, at 12-24 months, hearing with combination adenoidectomy was better at 4.2 dB ($p < 0.001$) than with TS tube insertion alone. The TARGET study also investigated the proportion of patients who underwent repeat surgery. Comparison of adenoidectomy plus TS tube insertion and TS tube insertion alone revealed that, with hearing loss of 25 dB as the criterion for repeat surgery, the proportions of repeat surgery did not differ significantly between the approaches at 6 months. However, in the second year after surgery, the chance of repeat surgery was approximately 3 times higher (relative risk, 2.7) with TS tube insertion alone compared with combination adenoidectomy (35% vs. 13%), respectively [191].

Boonacker et al. performed a meta-analysis of 10 RCTs with or without adenoidectomy in cases of OME and recurrent otitis media (1,761 patients under 12 years of age). In patients aged ≥4 years affected by OME, the prevalence of treatment failure at 12 months (i.e., persistent OME) was 51% in the group that underwent adenoidectomy and 70% in the group without adenoidectomy. Moreover, additional surgery was required in 2.2% of patients in the adenoidectomy group and 18.8% of patients in the group without adenoidectomy. On the other hand, in patients under 4 years of age, fluid retention after 12 months was 23.4% in the adenoidectomy group and 9.7% in the other group. There was no significant difference in the effect between the two groups [212].

In a systematic review and meta-analysis by Mikals et al. [213] that included 15 studies, the recurrence rate was 17.2% when adenoidectomy was combined with TS tube insertion and 31.8% when the surgery was limited to TS tube insertion . In patients above 4 years of age, the recurrence rate for the two groups was 16.8% and 35.5%, respectively. There was no apparent benefit for patients under 4 years of age, with recurrence rates of 19.2% vs. 16.8% [213]. According to the international consensus on the management of OME summarized at the International Federation of Otorhinolaryngological Societies Annual Congress in 2017, the indication for TS tube insertion plus adenoidectomy was only for patients above 4 years of age and for those with obstructive disease of the upper airway [15]. In a large prospective study conducted in Taiwan using the National Health Insurance Research Database, the rate of repeated TS tube insertion was 5.1% when adenoidectomy plus TS tube insertion was performed and 9% when TS tube insertion alone was performed ($p = 0.002$). When the age range was divided into subgroups (0-2, 2-4, 4-6, and 6-9 years), the decrease in the recurrence rate with combined adenoidectomy and TS tube insertion was found to be especially pronounced in patients above 4 years of age ($p = 0.02$ at age 4-6 years, $p < 0.001$ at age 6-9 years) [214].

Thus, adenoidectomy combined use with TS tube insertion has additional benefits, particularly with regard to reducing the need for tube re-insertion. However, adenoidectomy is more invasive than TS tube insertion and associated with increased risks of complications of anesthetic, intra- and postoperative hemorrhage (0.2-0.6%), [191,215], and other problems. Therefore, since the harmful effects outweigh the benefits, it is not recommended as an initial procedure. A total of 50-80% of pediatric patients with OME recover with just one TS tube insertion [164,194]; therefore, exposing all patients to the risks of adenoidectomy as an initial procedure should not be recommended.

Specifically, in patients above 4 years of age, performance of adenoidectomy in combination with TS tube insertion should be considered at the time of recurrence, as it is expected to reduce the recurrence rate. In Japan, most adenoidectomies are performed under general anesthesia and require several days of hospitalization. Adequate explanations and consent are required.

In principle, adenoidectomy may be indicated for adenoid vegetation in the case of upper airway lesions (including pharyngotonsillitis, choanal atresia, and obstructive sleep apnea syndrome) caused by the adenoids. Adenoidectomy is not recommended in patients with cleft palate due to the risk of velopharyngeal insufficiency [216]. Preoperative evaluation for concomitant conditions, including submucous cleft palate, should be performed.

b) Tonsillectomy

Many studies have reported a lack of efficacy of tonsillectomy for OME in children. An RCT by Maw et al. included 103 patients aged between 2 and 11 years (mean age: 5.25 years). The healing rate of OME 6 weeks after surgery was 16% for the group that only underwent TS tube insertion, 39% for the group that underwent TS tube insertion plus adenoidectomy, and 59% for the group that underwent TS tube insertion plus adenoidectomy plus tonsillectomy. These rates at 1 year after surgery were as follows: 26%, 72%, and 62%, respectively. Adenoidectomy ($p < 0.001$), adenoidectomy and palatine tonsillectomy ($p < 0.01$), and adenoidectomy and tonsillectomy ($p < 0.01$) were more effective than TS tube insertion alone in curing otitis media. Whereas adenoidectomy and tonsillectomy ($p < 0.01$) were effective, no additive effect from the addition of tonsillectomy compared with adenoidectomy alone was observed [217].

The risk of postoperative hemorrhage of approximately 4% [215] means that tonsillectomy should not be recommended for the treatment of OME in children. Similar recommendations are found in treatment guidelines for OME in children outside Japan [6].

3.10. CQ10: Is the tympanostomy tube effective for unilateral OME?

3.10.1. Recommendation

Similar to the case of bilateral OME (**3.CQ6**), clinicians may consider TS tube insertion for children with unilateral OME complicated with pathological changes of the TM (refer

to Table 6). Conversely, watchful waiting with monitoring of the bilateral hearing level is recommended in cases without such pathological changes.

[Recommendation strength: **Recommendation**, Evidence Quality: **C**]

Exceptions include children who are more susceptible to developing sequelae involving speech and language (at-risk children), and clinicians should offer more proactive management than for otherwise healthy children. Children suffering from unilateral OME should receive personalized medical care with monitoring of hearing on the contralateral side.

[Recommendation strength: **Recommendation**, Evidence Quality: **C**]

3.10.2. Background

Children with unilateral OME would experience less-severe impact on language development than those with bilateral OME. Clinical recommendation should depend on presence or absence of pathological changes in the TM. Specifically, clinicians should follow up patients carefully, avoiding the overlooking of non-evident pathologies, including congenital cholesteatoma.

3.10.3. Aggregate evidence quality

- **Benefits for children:** As long as there is minimal effect on language development, patients can avoid undergoing unnecessary interventions.
- **Risks and harms for children:** Pain, discomfort, and need for physical restraint during the surgical procedure under local anesthesia to the TM. Potential risks of general anesthesia in cases of surgery performed under general anesthesia. Otorrhea while tubes are in place, accidental drop of tympanostomy tube into the tympanic cavity, and adverse events affecting the TM, including persistent perforations and tympanosclerosis after extrusion or removal of tubes. Medical economic burden such as surgical cost of TS tube insertion and outpatient fees after TS tube insertion. Restrictions on swimming, the need for earplugs, etc.
- **Benefits-harms assessment:** Benefits exceed the harms as long as patients undergo watchful waiting and hearing evaluation in a careful and deliberate manner.
- **Surgical cost:** TS tube insertion (K309).
- **Patient preference:** None.
- **Exclusion:** In cases presumably involving cholesteatoma, including congenital cholesteatoma.

3.10.4. Commentary

a) Unilateral OME complicated with pathological changes in the TM

As in the case of bilateral OME, TS tube insertion is a treatment strategy used in the following pathological cases: severe retraction pocket predisposed from the segmental atrophic area and/or atelectatic TM because ME cholesteatoma and adhesive otitis media are serious sequelae of these pathological conditions [218].

b) Unilateral OME without pathological changes in the TM

As long as normal hearing on the contralateral side can be retrained, children would be less adversely affected in their language development. TS tube insertion would not be recommended in such cases with minimal hearing disorder without pathological changes in the TM, and watchful waiting should be recommended. The US Clinical Practice Guideline updated in 2016 recommended regular follow-up to evaluate hearing status on the healthy side and careful examination of the TM to identify any abnormalities, as mentioned above [6,9,13]. Again, the incidence of underlying intractable otologic pathophysiologies should be monitored, such as congenital cholesteatoma and ET dysfunction [219].

Conversely, even in cases of unilateral OME, insertion of a tympanostomy tube to resolve effusion and facilitate better assessment of hearing status may be appropriate on an individual basis for children who are disproportionately affected by MEE. Specifically, clinicians should determine if a child with OME is at increased potential risk and/or showing signs of speech, language, or learning problems due to MEE. Children who are at risk for developmental difficulties would likely be disproportionately affected by hearing problems from OME sequelae as compared with otherwise healthy children. The US Clinical Practice Guideline updated in 2016 defined these children collectively as “At-risk Children”, particularly for speech and language disorders, imbalance, developmental delays, and being less task oriented and less capable of independent classroom work [9,13].

In cases of hearing loss on the contralateral side to the ear with OME, interventions including TS tube insertion would contribute to normalization of language development. Specifically, children with blindness or uncorrectable visual impairment depend on hearing more than their normal-vision counterparts. Even if OME is encountered on the unilateral side, these children are further susceptible to OME sequelae, including difficulties with speech perception in noise, sound localization in the environment, and impairment of activities requiring balance [6,9,13,75].

Children with autism spectrum disorder and other pervasive developmental disorders are also included in the “At Risk Children” category, as shown in Table 8. By evaluating hearing impairment and characteristics associated with poorer QOL attributed to OM [220], clinicians should plan individual treatment strategies, including insertion of a tympanostomy tube. Finally, patients with DS and cleft palate are discussed in **Chapter 4**.

3.11. Supplemental CQ: how are children with OME complicated with adhesive otitis media clinically assessed and managed?

3.11.1. Recommendation

Tympanoplasty can be recommended as an option for patients whose TM exhibits atrophy and adhesions, complicated with otorrhea and/or hearing loss, and cases progressing to cholesteatoma.

[Recommendation strength: **Recommendation**, Evidence Quality: **X**]

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3.11.3. Aggregate evidence quality

- **Benefits for children:** Surgical intervention could relieve otologic symptoms, including hearing loss and otorrhea, and also prevent the lesion from progressing to cholesteatoma.
- **Risks and harms for children:** Risks of general anesthesia, bleeding during or after surgery, postoperative pain, risks and costs associated with general tympanoplasty.
- **Cost of surgical procedures:** Tympanoplasty with intact chain preservation (K319-1) or with reconstruction of ossicular chain (K319-2).
- **Benefits-harms assessment:** Benefits exceed the harms in selected patients, based on symptoms and clinical course, after sufficient evaluation of individual patients.
- **Patient preference:** Appropriate informed consent is requisite.
- **Exclusion:** Skills and equipment are essential; if not, clinicians should not carry out this procedure.

3.11.2. Background

Adhesive otitis media is a condition in which an atrophic or retracted TM is fixed by adhesions to the promontrium and/or may be fixed to other ME structures, including ossicles. These conditions are usually attributed to long-term suffering from otitis media and functional or structural disorders of the ET. Negative ME pressure is induced by clearance of ME fluid, impairment of the ventilation and pressure regulatory system of the ET and ME, and/or habitual sniffing.

Specifically, gas exchange functions of the ME deteriorate in ears with poor mastoid pneumatization or loss of aeration in the ME. The above-mentioned negative ME pressure is thus persistent and may develop to retraction of the TM. To prevent these progressions from atelectatic TM to the adhesive otitis media, insertion of the ventilation tube with induction of aeration of the mastoid is important to keep the pathological condition in the earliest stage and prevent sequelae [132].

In addition to tubal stenosis, many cases involve dysfunction of the ET, including patulous ET and habitual sniffing associated with closing failure of the ET. Clinicians should ask about the patient's habit of sniffing in order to correct ear discomfort due to patulous ET and should evaluate tubal functions as far as possible.

Adhesive otitis media often accompanies hearing loss. However, factors that can predict the progression of hearing loss of this disease have not yet been revealed. Borgstein [221] revised the classification of TM retraction and adhesion by Sade´& Beroco [222] and proposed a new classification for ME atelectasis in children. This system would be useful in that it follows the natural progression of the disease and would therefore be more practical in determining therapeutic strategies at each stage (Fig. 10) [221]. However, consensus has not yet been established in terms of the timing, stage of progression, and management strategies by surgical interventions.

3.11.4. Commentary

3.11.1. Pathogenesis

Among pathological changes of the TM, atelectatic TM refers to a reduction in volume of the ME space, and it is associated with medial displacement of the TM toward the promontory; it can be fixed or mobile. Long-term OME progressively induces atrophic TM, accompanied by loss of tension and elasticity attributed to a loss of the organized collagenous layer that maintains the tension of the intrinsic layers of the TM [222–224]. Long-lasting negative ME pressure also contributes to the progression, and the atrophic TM adheres to the promontrium and/or the incudostapedial complex [224]. Without MEE, patients with atelectatic TM tend to have less-severe hearing loss, but progression to the adhesive otitis media is regarded as a serious change and should be carefully monitored in those patients.

In the atelectatic TM, retraction of the TM can be released by applying positive pressure to the ME cavity. Conversely, in adhesive otitis media, the TM is partially or totally fixed by adhesions to the ME structures. To differentiate these two pathological conditions, it is useful to examine the mobility of the atelectatic TM by applying the Valsalva maneuver, tympanic inflation, and/or pneumatic otoscope (refer to Section 2.3). Some atelectatic TM without MEE or adhesions shows Ad-type tympanograms. Conversely, partial or total adhesion to the ME structures sometimes presents a type with a biphasic peak or type B, respectively.

Among these refractory cases, clinicians may encounter patients whose case is complicated by not only tubal stenosis but also functional disorders of the ET, including patulous ET causing habitual nasal sniffing. By correctly diagnosing the patient's tubal pathophysiology and offering appropriate interventions, clinicians can achieve dramatic curative effects [37–39,41,43,225]. Evaluating tubal functions using tubal function tests is thus recommended in these intractable cases [42,132,226]. Practically, tubal function tests are not applicable to infants. We thus recommend a questionnaire, given the risk of habitual nasal sniffing.

Finally, ME cholesteatoma is the most serious sequela of OME. In ears with OME complicated by severe retracted TM, medialization of the TM sometimes predisposes to focal retraction pockets in the pars flaccida and evolves into acquired cholesteatoma (refer to Section 2.19.). Conversely, adhesive changes affecting the posterosuperior quadrant of the pars tensa progress to pars tensa cholesteatoma [224].

3.11.2. Treatment

In cases complicated by pathological conditions of surrounding organs, such as rhinosinusitis and allergic rhinitis, clinicians should provide therapy to these structures. Again, in cases involving habitual sniffing associated with closing failure of the ET, clinicians should explain its harmful effects and advise patients to refrain from sniffing habitually (refer to Section 2.7., 3.CQ2–4). In refractory patients resistant to conservative treatment, clinicians can offer tympanoplasty

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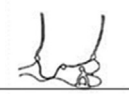
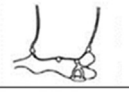
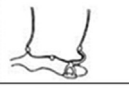
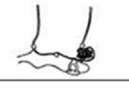
	Description	Stage proposed by Borgstein et al.	Sade´ stage
	Atrophic eardrum, not adherent	1	1 2 3
	Adherent to promontory	2	4
	Adherent to incus and/or stapes	3	2
	Deep retraction pocket towards attic	4	2
	Cholesteatoma in retraction pocket	5	Non classifiable

Fig. 10. Alternative classification by Borgenstein et al. (2007), categorized according to the severity of retraction and/or adhesion of the pars flaccida. Comparison with the Sade system is also shown.

tube insertion. Specifically, in the case of atelectatic TM, clinicians should choose the most suitable tube according to the severity of atelectasis and/or history of ventilation tube insertion (refer to Section 3. CQ6, Fig. 3).

Specifically for cases lacking enough space for ventilation tube insertion, some reports alternatively advocate the subannular tube (SAT) method [227–229]. In this method, after the tympanomeatal flap is elevated, a T-tube is inserted through the bony external auditory canal wall to the ME sub-annularly, leaving the TM intact. Without invasive procedures affecting the TM, this method has an advantage in terms of avoiding postoperative sequelae such as myringosclerosis or persistent perforation (refer to Section 1.20., 3.CQ7). Again, patients whose case is complicated by thinned TM attributed to atelectasis and/or patients who have undergone repeated insertion of a tympanic ventilation tube are reportedly candidates for the SAT method [230]. However, pediatric patients undergoing these procedures need general anesthesia [231].

Several reports have recommended tympanoplasty in patients with adhesive otitis media because of potential risk of progression to cholesteatoma and possible negative effects on the ossicular chain [58,60–63]. Specifically, adhesive otitis media in pediatric patients is usually a less-severe condition than in adolescents, involving a higher prevalence of partial adhesion rather than total adhesion. Several reports have thus advocated earlier surgical interventions to prevent progression toward higher pathological stages of the adhesive TM [64,232–234]. On the other hand, we have not yet reached conclusions whether such earlier surgical interventions could improve long-term prognosis or prevent development of cholesteatoma [58]. In planning for the indications and timing of surgical interventions, radiological imaging, including CT, should be considered to evaluate development and pneumatization of mastoid air cells with favorable gas exchange functions (refer to Section 2.9.) [132,235]. With regard to CT, imaging should be kept to the minimum necessary [134].

Chapter 4. Management of OME in patients with Down Syndrome (DS) or cleft palate

4.1. Management of OME in children with DS

4.1.1. Prevalence of hearing impairment

DS is caused by 21 trisomy, and it is one of the most frequent congenital aberrations (1:700 live births) [236]. There are approximately 2200 DS births per year in Japan according to recent surveillance [237]. This syndrome is characterized by several abnormalities of external and visceral malformations, and results in mental and physical retardation. In the otolaryngological field, anomalies such as hearing loss, stenosis of the external ear canal, and cleft lip and palate are frequently associated with this syndrome.

Various degrees of hearing loss are noted in 39–78% of children with DS. Most of the children show conductive hearing loss caused by OME. The prevalence of sensorineural hearing loss is higher in children with DS than those without DS, and the prevalence increases with age in children with DS. According to the results of a recent newborn hearing screening test in the United States, the rate of “refer” was 26.2% in babies with DS, much higher than those without DS [238]. Approximately half of the children who receive a “pass” in newborn screening tests later show conductive hearing loss associated with OME and undergo TS tube insertion [238]. Iino et al. reported that 54% of children aged 3 months to 13 years showed moderate or severe hearing loss [239]. Kreicher et al. studied hearing acuity in 1,760 ears

of children with DS using pure-tone audiometry and showed mild hearing loss in approximately 30%, whereas moderate or greater loss was observed in <20%. The hearing loss was mostly conductive hearing loss and improved with age. In contrast, the hearing level of children with mixed hearing loss or sensorineural hearing loss tended to deteriorate with age [240].

To summarize, the rate of "refer" in newborn hearing screening tests in babies with DS is approximately 25% and significantly higher than in healthy babies. Half of children with DS will later show mild to moderate hearing loss, and most of them appear to have conductive hearing loss associated with OME.

4.1.2. Prevalence of OME and its clinical course

The most frequent type of hearing loss in young children is conductive deafness caused by OME. The incidence of OME in DS is 40–70% according to several reports [239–241]. Approximately 60% of children with DS show MEE on unilateral or bilateral ears under an operating otomicroscope using a pneumatic otoscope [239]. Morimoto et al. also reported that 43% of children with DS are diagnosed with OME [242]. The prevalence of OME in DS is high in younger-aged children and approximately 60% at the age of 6 years and 38% at the age of 8 years [243]. Clinicians should be careful that in children with DS, the TM looks very dark, suggesting MEE; however, this is sometimes due to the remnant of mesenchymal tissue of the ME [244].

OME gradually tends to resolve with age in healthy children. On the other hand, in children with DS, OME persists for a long period of time despite conservative and surgical treatments. Less than 50% of children aged 2–12 years at the last visit show resolution of MEE, despite medical treatment lasting for more than 1 year. The same poor results were obtained in children with DS aged ≥10 years [239], and 24% of children aged 7–18 years still had OME [245]. These results clearly indicate that OME in DS is refractory otitis media.

The reasons of the high prevalence of OME in children with DS are as follows: (1) frequent upper respiratory infections (90% of children with DS suffer from upper respiratory infections 4 times or more per year); (2) short skull and narrow nasopharynx; (3) poorly pneumatized mastoid; and (4) extremely poor tubal function. Children with DS tend to have infectious diseases because they have immunodeficiencies such as dysfunction of T- and B-lymphocytes and dysfunction of neutrophil chemotaxis. They also have a short ET and tubal dysfunction. The latter may be caused by the collapse of the ET resulting from a decrease in chondrocytes in the cartilaginous portion of the tube. In addition, hypotonia of the tensor veli palatine muscle, which is responsible for opening the ET, causes dysfunction of the tube.

4.1.3. Efficacy of insertion of TS tubes

There have been several reports concerning the efficacy of insertion of TS tubes. Selikowitz et al. reported that in children with DS (6 years and older, mean age: 8.1 years) who received a TS tube, 60% showed improvement in hearing, whereas 91% of healthy children showed improvement in hearing [246]. In that study, it was suggested that late intervention using a TS tube failed to improve hearing. Shott et al. reported a high success rate for hearing improvement. Ninety-three percent of the children with DS were judged to have normal hearing 2 years after TS tube insertion when they received the TS tube at the age of 2 years or younger. The rate of resolution of OME was 3.6 times higher in DS children who received TS tube insertion than in those who did not [247]. On the other hand, DS children with a TS tube who were followed for more than 3 years and assessed at the age of 7 years exhibited a significantly lower resolution rate of OME compared with healthy control children with a TS tube. In addition, sequelae such as atelectasis, adhesion, and otorrhea from the tube were more frequently observed in DS children than controls [248]. A study of OME in 57 children with DS followed for 15 years showed that TS tube insertion was performed in 88.8% of the cases, resulting in improved hearing of normal to mild loss in 83.3%. However, 17% of the cases had persistent TM perforation [249].

A study by Whiteman et al. showed significantly higher verbal expression scores in DS youth treated with a TS tube than in children without TS tube treatment. From these results, it is apparent that long-lasting hearing impairment affects language development in DS children [250].

To summarize, as OME in DS is very refractory and persistent, TS tube insertion is strongly indicated. TS tube insertion should be performed as early as possible to help with speech development. However, if the TS tube is in place for a long period, ME pathologies can appear as sequelae (refer to **3.CQ6–7**). The indications for TS tube insertion in DS children are as the same as for those in healthy children (refer to **3.CQ6**). Regarding hearing acuity, it is sometimes difficult to obtain accurate hearing levels by pediatric audiometry tests such as COR (refer to Section 2.4–5). Repeated pediatric audiometry should be performed by skilled speech therapists, and ABR is sometimes needed to judge the accuracy.

At the time of TS tube insertion, the external ear canal of children with DS is extremely narrow, and it is relatively difficult to obtain patient adherence to treatment in the outpatient setting. Therefore, TS tube insertion is usually done under general anesthesia. Before surgery, it is necessary to check for complications such as congenital heart disease, pulmonary hypertension, gastro-esophageal reflux, laryngeal stenosis, or atlantoaxial subluxation and then consult with pediatricians or anesthesiologists about the operation. Informed consent from caregivers of the children is also necessary to ensure they are aware of potential complications such as otorrhea from the tube, tube re-insertion, and persistent perforation of the TM after extubation. It has been reported that adenoidectomy is not effective for the resolution of OME in children with DS [251].

4.1.4. Use of hearing aids

In the British NICE guidelines (refer to Section 1.4.), wearing a hearing aid is the first-line treatment for OME in children with DS, because early intervention is possible and there are no complications [7,252]. There are no negative outcomes associated with the use of a hearing aid. Therefore, physicians

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should not hesitate to recommend use of a hearing aid for children with DS. However, in children with DS, ingenuity is required to ensure the hearing aid remains in the ear or on the auricle, because the external ear canal is extremely narrow, and the auricle cartilage is very thin and floppy. In addition, some children with DS refuse to wear a hearing aid with an ear mold. It has been reported that only half of DS children can wear hearing aids successfully [253]. Everyday training with hearing aids results in active phonation and speech and increased interest in sounds and people. Yamashita et al. reported that children who failed to wear hearing aids exhibited severe mental retardation. Their caregivers had the following opinions [254]:

"My child does not wear the hearing aid and takes it off immediately."

"The efficacy of hearing aids is uncertain."

"There is a lot of stress for caregivers to force a child to wear a hearing aid against his or her will."

"It is an economic burden to buy a hearing aid."

Recent reports have described the use of bone-anchored hearing aids (BAHAs) in children with DS who were unable to use a hearing aid or undergo TS tube insertion [255]. The children themselves and their caregivers were totally satisfied with BAHAs, although early complications involving the soft tissue were seen in approximately half of the children. BAHAs are thus an option for children with DS with hearing loss. In other reports, use of a sound field amplification system (including an FM device) in school can selectively amplify a teacher's voice (improvement of signal/noise ratio), resulting in better performance and good effects on speech development in children with DS [256]. We anticipate further advances to improve hearing loss in children with DS.

4.1.5. Guidelines for the management of OME in DS

① Babies with DS are strongly recommended to have a newborn hearing screening test to diagnose hearing impairment as early as possible.
② Early diagnosis and intervention are necessary. The main goal of the management of OME is to improve hearing acuity and associated language and speech development.
③ TS tube insertion is one of the treatment options. TS tube insertion is recommended as early as possible to help with speech development. However, if the TS tube remains in place for a long period, ME pathologies can develop as sequelae, such as persistent TM perforation and adhesive otitis media after extubation.
④ Regular follow-up is mandatory. The assessment of otoscopic findings, hearing acuity, and speech development should be done once every 3 or 4 months, with removal of earwax.

4.2. Management of OME in children with cleft palate

The prevalence of OME is very high in children with cleft palate, and many of the cases are intractable. TM status and the extent of hearing loss should be evaluated at approximately 1 year of age. Specifically, when TM status is abnormal or there is definite hearing loss, inserting a TS tube and prescribing a hearing aid should be considered. Because many cases are intractable, long-term follow-up is necessary.

4.2.1. Pathology

The tensor veli palatini muscle and the levator veli palatini muscle are involved in opening the ET, and their orientations are abnormal in children with cleft palate. Moreover, since the cartilage of the auditory tube is fragile and the auditory tube tends to remain open, there is impaired closure. Once the pressure inside the tympanic cavity becomes negative because of sniffling, etc., it is impossible to eliminate the negative pressure when swallowing. The developments of the mastoid air cells are suppressed in children with a cleft palate in comparison with children without cleft palate, and their mastoid air cells are significantly smaller from 1 year of age onward. The mastoid air cells develop as children grow, but even at 5 years of age, their area never catches up with their area in children without a cleft palate. Moreover, even when a TS tube has been inserted, their area is smaller than in children without cleft palate [257]. The ME is ventilated by gas exchange through the mucosa of the mastoid air cells as well as the auditory tube. Not only is middle eaer ventilation in children with cleft palate impaired because of abnormal auditory tube morphology and function, their mastoid air cells are smaller, and gas exchange is also poor. Because these conditions result in greater susceptibility to OME, most of the children have intractable OME. Therefore, long-term follow-up is necessary.

4.2.2. Epidemiology

In a study of the incidence rate of OME, MEE was observed in 456 (71.9%) of 634 ears of Asian children with cleft palate in whom myringotomy was performed at the same time as palatoplasty [258]. Flynn et al. conducted a longitudinal study extending from 1 year to 5 years of age to assess the incidence of OME in children with both unilateral cleft lip and cleft palate and children without cleft palate. OME developed in 74.7% of the children with cleft palate and 19.4% of children without cleft palate, and thus, it developed in significantly more children in the cleft palate group ($p<0.001$). Even at 5 years of age, abnormal TM findings and abnormal tympanometry findings were observed in close to 90% of the children with cleft palate. When followed up for an even longer time, the percentages with abnormal TM findings and hearing loss decreased as the children grew. However, even at 16 years of age, abnormal findings were seen in the ME of 19% of the subjects [259].

In a longitudinal study of 146 cleft palate and cleft lip and palate cases from birth to 15 years of age, more cases of OME were observed in the latter group, and more ventilation tubes were placed. The cumulative incidence of OME increased rapidly until the age of 2 to 4 years and then continued to increase at a lower rate until the age of 8 years and remained unchanged thereafter. At 15 years of age, 73% of patients with cleft palate had a history of OME, and 44% of patients had a history of at least one TS tube insertion. In

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patients with cleft lip and palate, 90% had a history of OME, and 67% had a history of TS tube insertion [260].

On the other hand, Kwinter et al. examined 58 patients under 15 years of age (mean age: 5.8 years) with submucosal cleft palate. Sixteen of these patients presented chromosomal abnormalities, including 7 cases of 22q11.2 deletion syndrome [261]. In their study, 30 patients (51.7%) had OME, 3 had recurrent otitis media, and 31 patients (47%) had a history of at least one bilateral TS tube insertion.

In a report on patients under 7 years of age that compared the incidence of OME in 111 ears from patients with cleft palate, 65 ears from patients with submucosal cleft palate, and 50 ears from patients with congenital nasopharyngeal atresia, the incidence of OME was 69%, 62%, and 28%, respectively. There was a significant difference in the prevalence rate between cases of cleft palate and congenital nasopharyngeal atresia, but no obvious difference was noted between cases of cleft palate and submucosal cleft palate [262].The study concluded that in children with cleft palate, observation of the TM and otorhinolaryngological examinations should be performed from birth and followed for an extended period of time.

4.2.3. Diagnosis

(1) Observation. Observation of the TM with a pneumatic otoscope is useful at diagnosis. Otomicroscopes and otoscopes are also used, but many children with a cleft palate have a narrow external auditory canal. Specifically, flexible electronic scopes are suitable for observation of the TM in children with a narrow external auditory canal.

(2) Tympanometry (refer to Section 2.5). Tympanometry (Fig. 5) is useful for confirming MEE after observation with a pneumatic otoscope. Chen et al. assessed 634 ears of cleft palate patients by tympanometry. Of the 456 ears in which myringotomy revealed a MEE, the tympanogram was type B in 436 ears, type A in 11 cases, and type C in 9 cases [209].

The sensitivity of type B tympanograms was 0.956, and the specificity was 0.596. When assessed according to month of age, the results for specificity were 0.375 in 9-month-old infants and 0.857 in infants 14 months of age and over [209]. Caution is required at diagnosis based on the results of tympanometry in infants up to 9 months of age. Examinations at 678 Hz and 1000 Hz are performed on infants in Western countries [82,263].

(3) Hearing tests. Yang et al. performed tympanometry and recorded TEOAEs and ABRs in 42 children 6 to 24 months of age with cleft palate [264]. The tympanogram was type A in 30 ears, and the TEOAE results were poor in 5 ears (5.9%). The ABR results showed moderate conductive hearing loss in 3 ears and moderate sensorineural hearing loss in 2 ears. The TEOAE results were poor in all of the tympanogram type B and type C cases.

The ABR thresholds were in the 30-95 decibel normal hearing level (dBnHL) range in all of the cases, and the mean threshold was 53.5 ± 13.6 dBnHL. The concordance rate between the TEOAE and ABR results was 80% [264].

Flynn et al. performed inspections with an otomicroscope, tympanometry, and hearing tests in 58 children with cleft palate at 7, 10, 13, and 16 years of age and reported that abnormal TM findings and hearing test results improved as the children aged [265]. However, they reported no improvement with age in the 6000-Hz and 8000-Hz threshold values. They also reported differences according to cleft type: the proportion of children who had abnormal TM findings was smaller among cases with cleft palate alone than among cases accompanied by cleft lip, and cases with bilateral cleft lip and cleft palate had the poorest hearing at high-frequency thresholds [265]. It is desirable to perform regularly scheduled age-appropriate hearing tests, including newborn hearing screening, in children with a cleft palate.

4.2.4. Treatment

(1) Insertion of a TS tube (refer to 3.CQ6).

a) Indication. There is a report of TS tube insertion at the same time as palatoplasty in almost every case [266], and a report of tube insertion in selected cases. Phua et al. conducted a comparative study of a group of 45 patients in which they performed the customary treatment consisting of palatoplasty and routine simultaneous intubation and a select group of 189 patients in which they performed tube insertion when the following indications were fulfilled: “recurrent AOM, a clear 30-dB or more hearing loss, and a parent pointed out hearing loss”. In the latter group, tube insertion according to these indications was performed in 79 (41.8%) of 189 children with cleft palate. There were more cases of postoperative recurrent AOM and abnormal TM findings in the customary group, and they reported that tube insertion should be performed in children with cleft palate who have recurrent otitis media, clear hearing loss, etc., and not as a customary practice [267].

Szabo et al. considered the indications to be: “observation of ME effusion at the time of cheiloplasty, or bilateral conductive hearing loss of 25 dB or more that persists for 3 months or more.” The subsequent analysis showed that tube insertion had been performed at least once by 5 years of age in 98% of the patients and that it had been performed an average of 1.7 times [268]. Kobayashi et al. considered the indications for tube insertion to be “when ME effusion persisting for 3 months or more, severe retraction of the TM, bilateral hearing loss of 30 dB or more, and language development delay are observed.” They performed tube insertion by 5 years of age in 38% of 108 children with cleft palate. Tube insertion was particularly often necessary in cases with poor mastoid air cell development at 1 year of age, and there were also many cases with a poor course from 5 years of age onward [269].

In a systematic review of 18 papers, Ponduri et al. reported that there is insufficient evidence that routinely performing tube insertion early in cleft palate cases has any long-term benefits in terms of auditory, conversational, linguistic, or psychosocial development [270]. Another recent systematic review included 9 studies selected from 488 articles published between 1982 and 2013, and the rate of TS

tube insertion for OME ranged from 38% to 53%, with a tendency to be performed more often in refractory cases. This trend persisted for 1 to 9 years after TS tube insertion. TS tube insertion had a positive effect on language development [271].

These results suggest that TS tube insertion is not necessary for every child with cleft palate. In cleft palate patients, TS tube insertion is often performed at the same time as palatoplasty around the age of 1 year to minimize the number of procedures requiring general anesthesia. Before palatoplasty, it is necessary to check the TM findings and the degree of hearing loss.

b) Duration of tube insertion and complications. Tube insertion is not necessary in every child with a cleft palate. However, some cases require two or more tube insertions, and in some cases, long-term tube insertion is necessary. Ahn et al. reported that during a mean follow-up period of 4.9 years in 213 cases in which they performed tube insertion during palatoplasty, there were 140 cases in which tube insertion was performed once and 73 cases in which tube insertion had been performed 2 or more times [272].

Yamada et al. performed tube insertion at the same time as palatoplasty at 1 year of age and assessed the tube insertion period in the 133 ears whose course they had followed until ≥6 years of age. The mean tube insertion period was 22.3 months in the recurrent cases, 32.6 months in the cases with a favorable course, and 43.9 months in the cases with a persistent TM perforation [273]. Long-term tube insertion for approximately 30 months appears to be necessary in children with cleft palate.

One study reported that by 18 years of age, cholesteatoma was observed in 38 (4.4%) of 869 cases of cleft palate in which tube insertion had been performed one or more times; cholesteatoma developed in 556 (1.0%) of 56,080 cases without a cleft palate during the same period, and development of cholesteatoma was more common among the cleft palate cases ($p < 0.001$) (refer to **3.CQ6, 3-11. Supplemental CQ**) [274]. Regular otoscopic examination is thus necessary even after tube insertion.

(2) Palatoplasty. There have been few reports on the degree to which palatoplasty directly contributes to improving OME. When patients had reached 12 months of age, Klockars et al. compared a group in which soft palate closure and tube insertion had been performed at 3-4 months of age with a group in which tube insertion alone had been performed at 3-4 months of age. They reported that the rates of recurrence of OME after tube extrusion and of tube occlusion were significantly lower in the group in which the soft palate had been closed early [275].

It is also possible that the incidence of postoperative OME may differ depending on the specific palatoplasty technique employed. In a recent systematic review of 7 studies that examined the number of postoperative TS tube insertion for OME, it was found that the Sommerlad and Furlow methods were associated with a lower incidence of OME and TS tube insertion [276].

(3) Hearing aids. TS tube insertion is a common treatment for hearing loss caused by OME. However, complications such as ear discharge and permanent perforation of the TM frequently occur. Therefore, some authors have recommended the use of hearing aids [277,278]. The use of hearing aids is associated with fewer complications than TS tube insertion.

4.2.5. Guidelines for the management of OME in cleft palate

① Early diagnosis of hearing loss using newborn hearing screening tests.
② If the result of a newborn hearing screening test is 'refer', a detailed hearing test should be performed as soon as possible (refer to Section 2.4–6).
③ Prior to palatoplasty at around 1 year of age, observation of the TM and auditory evaluation should be performed to determine the indication for TS tube insertion. (For the degree of hearing loss to be used as a criterion, refer to **3.CQ 6**).
④ Cleft palate may require long-term or multiple TS tube insertions. The risks of infection and permanent perforation of the TM are therefore increased. The use of hearing aids should also be considered in future studies.
⑤ If the TM findings are abnormal, imaging studies should be performed, but attempts should be made to minimize radiation exposure.
⑥ Long-term follow-up is necessary.

Chapter 5. Supplementary note: future prospects for improving diagnostic techniques

5.1. New screening tests for pediatric OME

This chapter introduces promising new diagnostic techniques for ME transmission disorders: MFT, wide-band tympanometry (WBT), and optical coherence tomography (OCT).

Conventional 226-Hz tympanometry is a simple and minimally invasive testing method. It is especially useful for the diagnosis of OME and evaluation of ME transmission disorders. This test is used widely by otolaryngologists as an indispensable test. However, the test has a limitation: due to the anatomical characteristics of the infant ear canal, the reliability of 226-Hz tympanometry in infants is reduced, and utilization of 1000-Hz tympanometry is recommended (refer to Section 2.5). MFT can not only overcome this limitation, it also allows acquisition of a large amount of information. It has been reported that high-frequency tympanograms are superior for evaluation of the ME in newborns [279]. Studies on MFT were started as early as in the 1970s, and the usefulness of the test has been demonstrated. However, marketing of MFT has stalled due to not only the complexity of the device, but also the complexity of the analysis [279,280].

With the recent innovations and advances in computer processing speed, it has become easier to control and analyze MFT data, allowing commercialization of the technique. OCT is an unfamiliar term in the field of otolaryngology; however, it is an indispensable device for retinal diagnosis in the field

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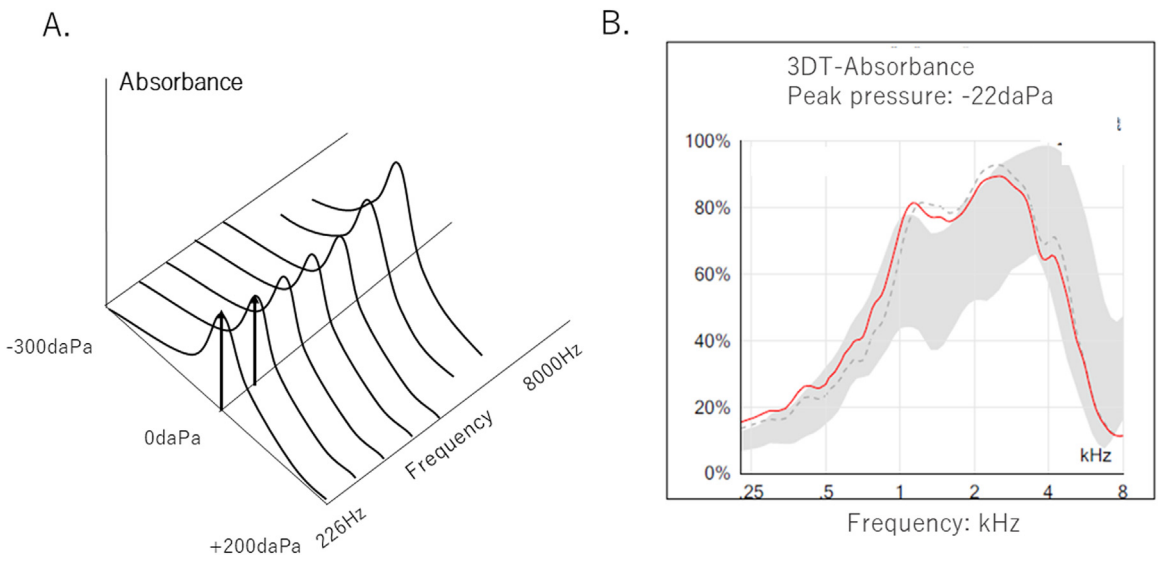

Fig. 11. Wideband tympanometry. A: Absorbance as a 3D pattern diagram in relation to frequency and pressure. B: Example of a wideband tympanogram. Absorbance plotted as a function of frequency. Solid line: absorbance curve at tympanometric peak pressure; Dotted line: absorbance curve at ambient pressure. Shaded regions and fine line: Pediatric normative data (age 3 to 11 years, 10th and 90th percentiles).

of ophthalmology, and it is expected to be applied in the field of otolaryngology in the future.

The clinical usefulness of OCT has been demonstrated in a variety of medical and surgical applications, including in the fields of gastroenterology, dermatology, cardiology, and oncology. OCT is a non-invasive, non-contact modality that uses the light interference properties generated by near-infrared light. OCT can produce three-dimensional tomographic images with high resolution. Therefore, there is no concern about radiation exposure, and it can provide tomographic images of various organs of the human body. A system for imaging cross-sections of the TM and diagnosing otitis media using OCT is currently under development.

5.2. WBT

Tympanometry using a single frequency (226 Hz) is an essential tool for the diagnosis of ME disorders. However, the use of a single frequency makes it difficult to detect subtle changes in the physical mechanism of sound transmission in the ME. WBT, a type of MFT, is used to diagnose ME disorders. WBT sweeps external ear canal pressures and frequencies from low to high (4000-8000 Hz) (Fig. 11). This measurement method allows testing over a wide range of frequencies, and it is affected to a lower degree by the external ear canal space between the probe and the TM. MFT is reportedly useful not only for diagnosing ME disorders and dislocation or fixation of the ossicles but also for the diagnosis of labyrinthine diseases.

Of the types of MFT, WBT has been studied since the 1990s. The test involves repeated use of a click stimulus over a wide frequency range (226 to 8000 Hz) delivered from a probe placed at the external ear canal [281,282]. A microphone in the probe measures the reflected sound energy from the TM (reflected power) after the incident sound energy is sent into the external ear canal. The ratio (absorbance) of the reflected power to the sound energy that finally passes to the ME is then calculated. As the absorbance varies depending on the frequency and the surrounding environment, the features of the sound response of the external ear and ME can be imaged using the wide-band frequency. More specifically, WBT measurements are sensitive to changes in the ME status caused by external and ME disorders [283].

► Comparison with conventional tympanometry and diagnostic accuracy

It is not possible to simply compare the diagnostic accuracy between MFT and tympanometry using a single frequency (226 Hz). However, for the diagnosis of OME, WBT is reportedly superior to the conventional method in terms of sensitivity for differentiating effusion in the ME [284]. According to another study, WBT boasts a high diagnostic rate when combined with examination of otoacoustic emissions [285]. Furthermore, due to the extremely large amount of information that can be obtained by WBT, various analysis methods can be used to identify pathological conditions, including resonance frequency comparison and the use of averaged tympanogram data between certain frequencies.

► Future prospects

It has been reported that when OCT (described below) is combined with MFT for observing the ME, differences in absorbance can be seen depending on the viscosity of the accumulated fluid and the amount of fluid [286].

5.3. OCT for otology applications

OCT is a non-invasive optical imaging modality that produces depth-resolved images. It is an optical imaging test that enables high-resolution cross-sectional imaging of biological tissues and samples at clinically relevant depths [287,288].

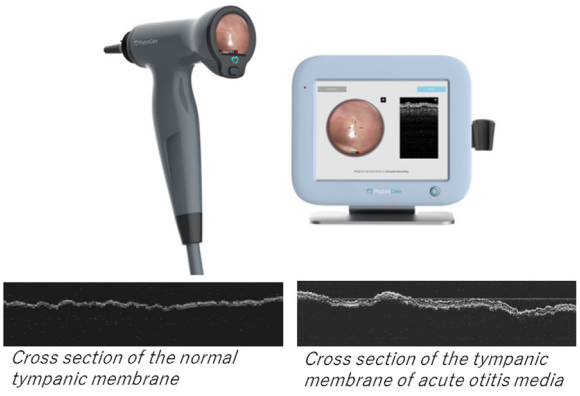

Fig. 12. Optical coherence tomography for otology.

OME is defined as "otitis media that can lead to hearing loss, characterized by the accumulation of exudate in the ME cavity, without perforation of the TM and without acute inflammatory symptoms, such as ear pain and fever." Therefore, differential diagnosis from AOM is important. However, the differential diagnosis is difficult in some cases in which only the findings of the TM are available. Improvement in this niche is also desired from the viewpoint of proper use of antibacterial drugs. Application of OCT as a new differential diagnosis method the in the field of otology has begun.

► Clinical application of OCT in the field of otology

ME OCT images were initially analyzed in animal studies but have since progressed to clinical applications [288,289]. At present, studies on OCT imaging in the field of otology are aimed at identifying pathologies of the TM and ME. Successive clinical studies on real-time OCT images of the TM have been reported. In these studies, the thicknesses of the normal TM and TMs in AOM and even chronic otitis media were measured from tomographic images, and biofilm images of the back of the TMs and accumulation of exudate in the ME were depicted (Fig. 12). These studies have concluded that OCT can contribute to highly accurate diagnosis of otitis media [290–294]. Moreover, it has been reported that OCT enables evaluation of biofilms on both sides of the TM before and after surgical intervention (TS tube insertion) [295].

► Future prospects

OCT for otology applications has great potential for future development. Further advances are expected, such as development of an intraluminal OCT catheter for ET evaluation, a functional hand-held OCT otoscope with vibrometer, a surgical microscope integrated with OCT, and a micro-OCT for *in vivo* imaging [296]. Recent years have seen widespread use of OCT devices equipped with Doppler vibrometers for evaluating the mobility of the auditory ossicles. Thus, OCT is also becoming useful for preoperative diagnosis of conductive hearing loss, such as in cases of otosclerotic disease [297].

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Declaration of Competing Interest

The authors declare no conflict of interest.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.anl.2022.12.004.

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