Saudi Journal of Medicine (SJM)
Scholars Middle East Publishers
Dubai, United Arab Emirates
Website: http://scholarsmepub.com/

ISSN 2518-3389 (Print)
ISSN 2518-3397 (Online)

Tonsillitis in Children Diagnosis and Treatment Measures

Abdullah D Alotaibi*
Department of Otolaryngology Head and neck surgery, College of Medicine, University of Hail, Saudi Arabia

***Corresponding author**
Abdullah D Alotaibi

Article History
Received: 17.12.2017
Accepted: 26.12.2017
Published: 30.12.2017

DOI:
10.21276/sjm.2017.2.8.4

Abstract: Tonsillitis is one of the most widely conditions that recurrently affect children in all ages during the childhood. The overall management of tonsillitis is complicated in regard to causes, specific diagnosis and appropriate treatment measures. Therefore, the aim of this review was to highlight the tonsillitis in children with particular stress on the diagnostic and treatment measure that are currently used to deal with pediatric tonsillitis. In conclusion, Bacteria is still the most causative agent with widely used antigen tests for confirmation. Tonsillectomy is still one of the most frequently performed surgical interventions in children.

Keywords: Tonsillitis; Tonsillectomy; Tonsils; Streptococci, Mononucleosis, Sore throat.

INTRODUCTION

Tonsillitis or throat infection is one of the most frequent health problems worldwide [1-3]. Tonsillitis is severe intermittent throat infections, which is characterized by five or more episodes of true tonsillitis a year, with episodes that are incapacitating and avert usual function. Beside bacteria as the main causes of tonsillitis, some viruses, and infectious mononucleosis, can be possible causes. Diagnosis of tonsillitis is clinical or/and laboratory, though sometimes, it can be challenging to differentiate viral from bacterial infections.

As more accurate tests take longer time to deliver the results, rapid antigen testing with a very low sensitivity is repeating used in the diagnosis of bacterial tonsillitis. Other causes include infectious mononucleosis from Epstein Barr virus (EBV) infection, cytomegalovirus (CMV), human immunodeficiency virus (HIV), hepatitis A, rubella and toxoplasmosis [4].

Tonsillectomy is still one of the utmost common surgical procedures for the treatment of tonsillitis in children. Tonsillitis and tonsillectomy are likely to have a distinct link where the incidence of one should reflect that of the other. While the entire incidence of tonsillectomy in a population may be extreme less than the total incidence of tonsillitis, a healthcare system should be capable to familiarize to upsurge rates of a specific surgical treatment when the specific sign for that treatment upsurges [5].

However, the aim of this review was to make available some updates in the diagnosis and treatment measures in childhood tonsillitis.

Tonsils

The tonsils contain immune-cells such as, germinal centers of B-lymphocytes, T-lymphocytes and other antigen presenting cells such as macrophages, which serves immune acquisition and defense [6-8]. Hence the core phase of the immune acquisition carry on up to the age of six, the *palatine tonsils* are physiologically hyperplastic at this stage [9]. At that time there is a shrinkage, which is revealed mostly in a regression up to the age of 12 [10, 11]. The palatine tonsils have a forceful blood flow from four diverse vessels. These vessels give out primarily to the superior and inferior tonsil pole, as well as the particular center of the tonsils sideways [6]. The tonsils have profound crypts to retain the organ exterior as huge as possible and to generate a detaching surface for potential antigens [12]. The crypts and their neighboring germinal centers are disconnected from each other by subtle connective tissue [13].

Etiology of Tonsillitis

The majority of cases of tonsillitis are caused by bacterial particularly beta-hemolytic and other streptococci. However, in tonsillitis related to infectious mononucleosis, the most common virus is the EBV, which present in 50% of children. CMV, hepatitis A, HIV, rubella and toxoplasmosis infections may also result in the clinical picture of infectious mononucleosis, which requires differential diagnosis [4].

With regard to bacterial infection, several germs were continuously incriminated due continuous advancement in detection methods [14-16]. At the time

of discovery of rheumatic fever, all cases of upper respiratory tract infections were thought to be caused by group A streptococcus [17,18], but later on there are anaerobes, such as *Fusobacterium necrophorum*, *Streptococcus intermedius* and *Prevotella melaninogenica* and *histicola* were incriminated [19-21]. When investigate the organisms that infect the tonsil in different phases of tonsillar life at times accurately, it was discovered that children before the age of eight years old have a tendency in the course of a diffuse, intracellular organism augmentation with interstitial abscesses [22], while a superficial bacterial accumulation at the edge of the crypts was verified in adults and adolescents [23]. The oral cavity and specially the furrowed tonsil is a reservoir for multiple pathogens including viruses, bacteria, parasites [24] and fungi [25]. These microbes belong to the transient flora and human lives in cooperation with them [19, 26]. However, more than 100 bacteria can be detected in the tonsils of children and adults with and without recurrent tonsillitis. Moreover, about 52 different bacterial strains can be identified in each patient, whether child or adult, whether ill or healthy. These bacterial strains represent 90% of the total pathogen load [19]. In the acute tonsillitis in children, the streptococcus was found to constitute up to 30% [27], followed by *Haemophilus influenzae* and *Neisseria* [19]. However, mixed infections (both bacterial and viral) may show similar clinical features [28].

Types of Tonsillitis

There are several types of tonsillitis acute, recurrent, and chronic tonsillitis, and peri-tonsillar abscess.

Acute Tonsillitis

It is also known as severe tonsillitis [29] or acute sore throat [4], is inflammation of the tonsils, which is caused by bacteria or virus with odynophagia. The condition is characterized by swelling and redness of the tonsils, may be with exudate, cervical lymphadenopathy and fever >38.3°C rectal [30, 31]. The odynophagia for 24 to 48 hours, resembles the symptoms of a common cold is excepted from the definition of acute tonsillitis [4].

Acute tonsillitis is an inflammatory process of the tonsillar tissues and is generally infectious in source. It is part of the spectrum of pharyngitis, which varies from localized tonsils' infection to widespread infection of the pharynx and usually affects young healthy adults. Simple sore throats secondary to viral or bacterial pharyngitis are mutual and commonly do not need hospital admission or antibiotic treatment. Caring management such as analgesia and sufficient hydration is usually necessary [32].

It is essential to differentiate the catarrhal angina with redness and swelling of the tonsils (early stage) from the follicular angina with stipple-like fibrin deposits from the lacunar angina with confluent deposits (late stage). This differentiation should be based on the stage and look of the deposits, or the exudate on the tonsils [33-38, 31]. Acute infections of the palatine tonsils mostly arise in children at school age, but patients of any age may be affected. Tonsillitis of viral cause is regularly treated with supportive care. Bacterial tonsillitis is most ordinarily caused by Streptococcus pyogenes. Poly-microbial infections and viral pathogens are also significant causes of infection [39].

Recurring Tonsillitis

Recurrent tonsillitis or recurrent throat infections [4], denotes recurrences of acute tonsillitis. This type of tonsillitis is defined if episodes of tonsillitis in one year evidenced in seven bacterial cultures, or five in two sequential years or three in three repeated years. In such conditions, the pause of the antibiotic leads to another bout of the bacterial infection within a few weeks, thus triggering it to return once more [40, 41]. On the other hand a single violence of acute tonsillitis can be caused by several diverse bacterial organisms [19, 22] and flash up again a few weeks after termination of an antibiotic treatment [42]. Reliant on the rate of recurrence and severity of such episodes, there is a clue for tonsillectomy.

Chronic Tonsillitis

This type is associated with chronic sore throat, in which the infection causes recurring tonsillitis. This type is usually associated with bad breath and persistent tender cervical nodes. Chronic tonsillitis describe the most common lesions contained by pharynx inflammatory pathology with multiple complications both local-regional and at the distance (glomerulonephritis, joint rheumatism, endocarditis, enteritis, etc.) [43-46]. Chronic tonsillitis can be also the site of some specific infections such as tuberculosis and syphilitic [45, 46]. Chronic tonsillitis usually describe focal tonsillitis, hypertrophic or scleroatrophic caseous cryptic tonsillitis as recurrent type, and simple hypertrophic tonsillitis soft type in children and hard type in adults [46].

In most of the cases of the hard chronic tonsillitis, the hypertrophic form occurs in adult and elder child, the tonsils were hypertrophied, congested, with reduced flexibility in the amygdalian space with apparent crypts eradicating spontaneous caseum, but also when they were compelled by spatula on the anterior pilier [47].

Peritonsillar Abscess (PTA) or Quinsy

It is an acute tonsillitis with formation of an abscess, typically on one side [48]. The intratonsillar, para-/peritonsillar or retrotonsillar spaces may be associated with abscess formation. When the acute tonsillitis is left untreated, the bacterial infection usually lead to peritonsillar abscess, which develops lateral to

the tonsillar region. The area of peritonsillar abscess appear with apparent abscess or a swollen zone with pus accumulation. Staphylococci, Streptococci, Haemophilus and Fusobacterium necrophorum are the most common pathogens responsible of peritonsillar abscess. No virus is involved. Altered voice quality, unease of mouth opening, coarse breath, fever and severe throat pain are the chief symptoms [49-51].

Diagnosis of Tonsillitis

The diagnosis of tonsillitis in children and adults usually start with clinical diagnosis [51]. Diagnosis of tonsillitis is based on a medical history to find out whether tonsillitis is recurrent and a physical exam of the throat. This can give clue whether the cause is bacterial or viral or other [52]. Pain, fever, primarily cough, hoarseness, and rhinorrhoea frequently occur in viral tonsillitis, while pain with lymph node swelling can occur in bacterial tonsillitis with mainly tonsils' exudate and fever >38.3°C [30]. Although streptococcal antigen test is less sensitive, but it can confirm the diagnosis of streptococci with 98% specificity. However, it was recommended that negative tests should be further confirmed with other more specific tests. Of the drawback of bacterial and viral RNA rapid tests, they can be positive in 10% of healthy children (usually asymptomatic chronic carriers of staphylococci and streptococci), who are absolutely don't require treatment [53-55]. Therefore, smears or these tests should only be performed on symptomatic patients [56]. At the initial phase, it is difficult to distinguish between viral and bacterial tonsillitis, particularly on considering that around 97.5% of cases, at least harbor one virus, even in the bacterial tonsillitis, adenovirus and parainfluenza virus may be found in about 47.5% of the cases [57-59].

However, it is recommended to get a tonsillar swab for rapid antigen testing rapid antigen detection (RAD) in children or adolescents with a history, signs and/or symptoms of suspected infection by group A beta-hemolytic streptococcus (GABHS). If RAD test result is negative in subjects where there is strong evidence or suspicion of infection, a bacterial culture should be done. In the case of a positive RAD test results, the bacterial culture is not compulsory for the high reliability and specificity of the tests [60-62].

The dosage of the anti-streptococcus antibodies Anti-streptolysin O (ASOT) is not recommended in the routine diagnosis of streptococcal pharyngitis since the existence of these antibodies reveals past infections and rather than ongoing infections [63]. Patients with raised ASO titers and recurrent tonsillitis episodes are known to be at greater risk for rheumatic heart disease [64]. Higher ASO titers can be detected in different clinical disorders other than the classic post-streptococcal related infections. In such cases it is not essential to be correlated with positive culture and or with inflammatory parameters [65].

Furthermore, differential diagnosis sometimes deemed important. Tonsils hyperplasia, dry air flows associated with turbinate hyperplasia [66], and allergy associated with chronic inflammation [67], in particular dust mite and mould allergy [68]. Tooth decay can lead to recurrent tonsillitis [69] and it was found that tonsil removal can positively affect pediatric periodontal disease [70]. In unilateral tonsillar hyperplasia, the differential diagnosis of lymphoma should be considered [71]. In pediatric unilateral tonsillitis, the differential diagnosis of Plaut-Vincent angina (caused by the spirochete *(Treponema vincentii* and *Fusobacterium nucleatum*) should be rolled out [72].

In acute tonsillitis, the diagnosis of scarlet fever and mononucleosis must be enlighten. Scarlet fever produced by streptococci group A, which is responsible for the production erythrogenic toxin, which results typical rash for scarlet fever [73].

Mononucleosis is caused by the EBV, particularly in children under the age of 10 years old. Although the disease is usually symptomless, but flu-like signs can occur in elderly people. Sometimes the disease occurs as a severe course with severe sore throat and swollen, coated tonsils and large lymph nodes, particularly in adolescents. Moreover, splenic enlargement, loss of appetite, chills, dry cough, nausea and night sweats can occur. However, the disease happens only once in one's life, but as with other herpes viruses, the EBV leftovers in the body for life and can be recurrently triggered again [74]. At present, there is still no approved vaccine for the EBV, but a number of working groups are doing research in this context [75, 76].

Treatment of tonsillitis

Antibiotic treatment

Penicillin still the treatment of choice for Streptococcus pyogenes tonsillitis, and amplified aminopenicillins have grown usefulness in performance with the growing incidence of beta-lactamase producing bacteria [39]. As a beta-lactam antibiotic therapy offers quite reliable protection against the feared rheumatic fever and glomerulonephritis. These conditions often lead specifically in developing countries to arthritis, myocarditis and death [77].

The penicillin, especially in children and adolescents, display the highest advantage for it being lowest cost. Cephalosporin is, however, more effective in children under the age of12 years and for chronic recurrent tonsillitis, as it can destroy more strains of streptococci [78]. Macrolides and clindamycin in children induce extra side effects with the similar effectiveness and thus it should be used only for confirmed penicillin allergy individuals [79]. Moreover, the short-term therapy with azithromycin (20 mg/kg) [80] for three days or clarithromycin and cephalosporin

for five days is equivalent to the long-term penicillin therapy with improved amenability [81].

Analgesics

For acute tonsillitis, the most common Non-steroidal anti-inflammatory is ibuprofen, which shows the top efficacy with the least side effects compared with paracetamol and acetylsalicylic acid [82]. Extra benefit of ibuprofen is extended period of action of 6-8 hours in comparison to paracetamol [83]. Diclofenac and ketorolac in children have less cut off sites and are metabolized rapidly, which necessitate the adjustment of the dose (higher dosage than in adults) [84]. Metamizol should be avoided as an analgesic in children because of the small but existing risk of agranulocytosis [85].

Steroids

The use of steroids in children displays a substantial enhancement in symptoms with slight side effects and without any effects on disease evolution [86]. The best consequences were realized in verified streptococcal pharyngitis for dexamethasone (10 mg), as well as betamethasone (8 mg) and prednisolone (60 mg) with a perfect decrease in the pain and feeling of illness that associated with acute tonsillitis [87].

Mouthwashes

Antiseptic mouthwashes with chlorhexidine or benzydamine show symptoms relief in children and adults [88]. Typical herbal gargles contain sage, thyme and chamomile, can lubricate and preserve the mucous membranes. However, several substances containing ethanol as an extraction solvent and are not approved for children <12 years old. Nasturtium and horseradish root are contained in some pharmaceuticals medications, which have antimicrobial, antiviral and antifungal properties [89].

Tonsillectomy

Is still one of the most common tonsillar surgery during childhood. A tonsillectomy in children before the age 6 years old should only be performed if the child suffers from recurrent acute bacterial tonsillitis. In all other cases such as hyperplasia of the tonsils, the low risk partial tonsillectomy should be the first line treatment. Postoperative pain and the risk of hemorrhage are lesser in partial tonsillectomy. Regardless of the fact that, tonsillotomy is performed by laser, radiofrequency, shaver, coblation, bipolar scissor or Colorado needle, open crypt and tonsil tissue that is left behind should be considered. Total extracapsular tonsillectomy is still considered in severely affected children with recurrent infections of the tonsils, allergy to antibiotics, PFAPA syndrome (periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis) and peritonsillar abscess. With regard to the frequency and seriousness of the recurrent tonsillitis the sign for tonsillectomy in children is necessary if seven or more well-documented, clinically significant, sufficiently treated episodes of throat infection happen in the past year, or five or more such episodes happen in each of the two previous years. Post-tonsillectomy bleeding may continue till the entire wound is totally healed, which is usually within three weeks. Life-threatening hemorrhages may arise after minor bleedings, which can spontaneously stop Most of the cases of fatal outcome after tonsillectomy were due to incorrect management of hemorrhage. In more younger children hemorrhage can be life-threatening due to the lower blood volume and the danger of aspiration with asphyxia. All "hot" procedures with laser, radiofrequency, coblation, mono- or bipolar forceps have a greater risk of late hemorrhage. The preoperative information about the surgery should be done with the child and the parents in a quiet and objective atmosphere with a written consent [77]. *Intracapsular/subcapsular or subtotal tonsillectomy*: involves the removal the lymphatic active tissue of the tonsil, including all crypts and follicles. However, the intracapsular tonsillectomy is partially associated with tonsillotomy [90].

Cryptolysis

Is a method in which the tonsil tissue ring is placed bare round the crypt superficially and the crypt shrinks in the path. The lymphatic active tissue leftovers existing and still intact [91]. Thermal or cryotherapy of the palatine tonsils: is the method in which the tonsil tissue is interstitially heated or cooled, which leads to scarring and subsequent shrinkage of the lymphatic tissues. Many procedures can be involve; interstitial (electro) coagulation to the palatine tonsils, laser coagulation, thermal coagulation, cryocoagulation, photodynamic therapy, ultrasound therapy, radiofrequency-induced thermotherapy, temperature-controlled tonsil treatment, tonsil thermotherapy [92-95].

In conclusion: Bacteria is still the most causative agent with widely used antigen tests for confirmation. Tonsillectomy is still one of the most frequently performed surgical interventions in children.

Acknowledgment

I would like to thank Professor Hussain Gadelkarim Ahmed for reviewing the manuscript.

REFERENCES

1. Lau, A. S., Upile, N. S., Wilkie, M. D., Leong, S. C., & Swift, A. C. (2014). The rising rate of admissions for tonsillitis and neck space abscesses in England, 1991–2011. *The Annals of The Royal College of Surgeons of England*, *96*(4), 307-310.
2. Klug, T. E. (2009). Peritonsillar abscess: clinical aspects of microbiology, risk factors, and the association with parapharyngeal abscess. *Clin Infect Dis*, *49*, 1467-72.
3. Borgström, A., Nerfeldt, P., Friberg, D., Sunnergren, O., & Stalfors, J. (2017). Trends and

changes in paediatric tonsil surgery in Sweden 1987–2013: a population-based cohort study. *BMJ open*, *7*(1), e013346.
4. Georgalas, C. C., Tolley, N. S., & Narula, A. (2009). Search date March 2009.
5. Millington, A. J., & Phillips, J. S. (2014). Current trends in tonsillitis and tonsillectomy. *The Annals of The Royal College of Surgeons of England*, *96*(8), 586-589.
6. Westermann, J. (2010). Organe des Abwehrsystems. In *Anatomie* (pp. 355-375). Springer Berlin Heidelberg.
7. Nave, H., Gebert, A., & Pabst, R. (2001). Morphology and immunology of the human palatine tonsil. *Anatomy and embryology*, *204*(5), 367-373.
8. Brandtzaeg, P. (2011). Immune functions of nasopharyngeal lymphoid tissue. In *Recent Advances in Tonsils and Mucosal Barriers of the Upper Airways* (Vol. 72, pp. 20-24). Karger Publishers.
9. Kaygusuz, I., Gödekmerdan, A., Karlidağ, T., Keleş, E., Yalçin, Ş., Aral, I., & Yildiz, M. (2003). Early stage impacts of tonsillectomy on immune functions of children. *International journal of pediatric otorhinolaryngology*, *67*(12), 1311-1315.
10. Kaygusuz, I., Alpay, H. C., Gödekmerdan, A., Karlidag, T., Keles, E., Yalcin, S., & Demir, N. (2009). Evaluation of long-term impacts of tonsillectomy on immune functions of children: a follow-up study. *International journal of pediatric otorhinolaryngology*, *73*(3), 445-449.
11. Perry, M. E., & Slipka, J. (1993). Formation of the tonsillar corpuscle. *Functional and developmental morphology*, *3*(3), 165-168.
12. Drucker, M., Drucker, I., Neter, E., Bernstien, J., & Ogra, P. L. (1978). Cell mediated immune responses to bacterial antigens on human mucosal surfaces. In *Secretory Immunity and Infection* (pp. 479-488). Springer, Boston, MA.
13. Perry, M. E., Jones, M. M., & Mustafa, Y. (1988). Structure of the crypt epithelium in human palatine tonsils. *Acta Oto-Laryngologica*, *105*(sup454), 53-59.
14. Al-Mazrou, K. A., & Al-Khattaf, A. S. (2008). Adherent biofilms in adenotonsillar diseases in children. *Archives of Otolaryngology–Head & Neck Surgery*, *134*(1), 20-23.
15. Drago, L., De Vecchi, E., Torretta, S., Mattina, R., Marchisio, P., & Pignataro, L. (2012). Biofilm formation by bacteria isolated from upper respiratory tract before and after adenotonsillectomy. *Apmis*, *120*(5), 410-416.
16. Jensen, A., Fagö-Olsen, H., Sørensen, C. H., & Kilian, M. (2013). Molecular mapping to species level of the tonsillar crypt microbiota associated with health and recurrent tonsillitis. *PLoS One*, *8*(2), e56418.
17. Matanoski GM, Price WH, Ferencz C. (1968). Epidemiology of streptococcal infections in rheumatic and non-rheumatic families. II. The inter-relationship of streptococcal infections to age, family transmission and type of group A. Am J Epidemiol, 87(1):190-206.
18. Feinstein AR, Levitt M. (1970). Tonsils and rheumatic fever. N Engl J Med. 2; 282(14):814.
19. Jensen, A., Fagö-Olsen, H., Sørensen, C. H., & Kilian, M. (2013). Molecular mapping to species level of the tonsillar crypt microbiota associated with health and recurrent tonsillitis. *PLoS One*, *8*(2), e56418.
20. Klug, T. E., Henriksen, J. J., Fuursted, K., & Ovesen, T. (2011). Significant pathogens in peritonsillar abscesses. *European journal of clinical microbiology & infectious diseases*, *30*(5), 619-627.
21. Klug, T. E., Henriksen, J. J., Fuursted, K., & Ovesen, T. (2011). Similar recovery rates of Fusobacterium necrophorum from recurrently infected and non-infected tonsils. *Dan Med Bull*, *58*(7), A4295.
22. Swidsinski, A., Göktas, Ö., Bessler, C., Loening-Baucke, V., Hale, L. P., Andree, H., ... & Lochs, H. (2007). Spatial organisation of microbiota in quiescent adenoiditis and tonsillitis. *Journal of clinical pathology*, *60*(3), 253-260.
23. Ramírez-Camacho, R., González-Tallón, A. I., Gómez, D., Trinidad, A., Ibáñez, A., García-Berrocal, J. R., ... & SanRomán, J. (2008). Environmental scanning electron microscopy for biofilm detection in tonsils. *Acta Otorrinolaringologica (English Edition)*, *59*(1), 16-20.
24. Mücke, W., Huber, H. C., & Ritter, U. (1994). The microbe colonization of the palatine tonsils of healthy school age children. *Zentralblatt fur Hygiene und Umweltmedizin= International journal of hygiene and environmental medicine*, *196*(1), 70-74.
25. Mitchelmore, I. J., Reilly, P. G., Hay, A. J., & Tabaqchali, S. (1994). Tonsil surface and core cultures in recurrent tonsillitis: prevalence of anaerobes and beta-lactamase producing organisms. *European Journal of Clinical Microbiology & Infectious Diseases*, *13*(7), 542-548.
26. Schwaab, M., Gurr, A., Hansen, S., Minovi, A. M., Thomas, J. P., Sudhoff, H., & Dazert, S. (2010). Human β-Defensins in different states of diseases of the tonsilla palatina. *European Archives of Oto-Rhino-Laryngology*, *267*(5), 821-830.
27. Brook, I., & Foote, P. A. (1986). Comparison of the microbiology of recurrent tonsillitis between children and adults. *The Laryngoscope*, *96*(12), 1385-1388.
28. Proenca-Modena, J. L., Valera, F. C. P., Jacob, M. G., Buzatto, G. P., Saturno, T. H., Lopes, L., ... & Tamashiro, E. (2012). High rates of detection of respiratory viruses in tonsillar tissues from children

with chronic adenotonsillar disease. *PLoS One*, *7*(8), e42136.
29. Lange, G. (1973). Angina and chronic tonsillitis--indications for tonsillectomy. *Zeitschrift für Allgemeinmedizin*, *49*(8), 366.
30. Stelter, K. (2014). Erkrankungen der Gaumenmandeln im Kindesalter. *Laryngo-rhino-otologie*, *93*(S 01), S84-S102.
31. Stuck, B. A., Windfuhr, J. P., Genzwürker, H., Schroten, H., Tenenbaum, T., & Götte, K. (2008). Tonsillectomy in children. *Deutsches Ärzteblatt International*, *105*(49), 852.
32. Bartlett, A., Bola, S., & Williams, R. (2015). Acute tonsillitis and its complications: an overview. *Journal of the Royal Naval Medical Service*, *101*(1), 69-73.
33. Berghaus, A. (2005). Chronic inflammation of the upper airways. Operation instead of antibiotic. *MMW Fortschritte der Medizin*, *147*(39), 27.
34. Berghaus A, Pirsig W. (1996). Mundhöhle und Pharynx. In: Berghaus A, Rettinger G, Böhme G, editors. Hals-Nasen-Ohren-Heilkunde. 1st ed. Stuttgart: Hippokrates Verlag;.
35. Borschmann, M. E., & Berkowitz, R. G. (2006). One-off streptococcal serologic testing in young children with recurrent tonsillitis. *Annals of Otology, Rhinology & Laryngology*, *115*(5), 357-360.
36. Fujikawa, S., Hanawa, Y., Ito, H., Ohkuni, M., Todome, Y., & Ohkuni, H. (1988). Streptococcal antibody: as an indicator of tonsillectomy. *Acta Oto-Laryngologica*, *105*(sup454), 286-291.
37. Kurien, M., Stanis, A., Job, A., & Thomas, K. (2000). Throat swab in the chronic tonsillitis: how reliable and valid is it?. *Singapore medical journal*, *41*(7), 324-326.
38. Stuck BA, Genzwürker HV. (2008) Tonsillectomy in children: preoperative evaluation of risk factors. Anaesthesist; 57(5):499-504.
39. Sidell D, Shapiro NL. (2012). Acute tonsillitis. Infect Disord Drug Targets, 12(4):271-6.
40. Szpunar, J., & RYBAKOWA, M. (1961). Electrophoretic Serum Studies Studies of Children with Frequently Recurring Acute Tonsillitis. *Archives of Otolaryngology*, *74*(3), 267-271.
41. Senska, G., Ellermann, S., Ernst, S., Lax, H., & Dost, P. (2010). Recurrent tonsillitis in adults: quality of life after tonsillectomy. *Deutsches Ärzteblatt International*, *107*(36), 622.
42. JENSEN, J. H., & LARSEN, S. B. (1991). Treatment of recurrent acute tonsillitis with clindamycin. An alternative to tonsillectomy?. *Clinical Otolaryngology*, *16*(5), 498-500.
43. Gaffney, R. J., & Cafferkey, M. T. (1998). Bacteriology of normal and diseased tonsils assessed by fine-needle aspiration: Haemophilus influenzae and the pathogenesis of recurrent acute tonsillitis. *Clinical otolaryngology and allied sciences*, *23*(2), 181-185.
44. Mattila, P. S., Tahkokallio, O., Tarkkanen, J., Pitkäniemi, J., Karvonen, M., & Tuomilehto, J. (2001). Causes of tonsillar disease and frequency of tonsillectomy operations. *Archives of Otolaryngology–Head & Neck Surgery*, *127*(1), 37-44.
45. Bailey, B. J., Johnson, J. T., Newlands, S. D., Calhoun, K. H., Curtin, H. D., & Deskin, R. W. (2006). Diagnosis and treatment of thyroid and parathyroid disorders. *Head & Neck Surgery Otolaryngology. Fourth edition. Philadelphia: Lippincott Williams & Wilkins*, 1630.
46. Bourbeau, P. P. (2003). Role of the microbiology laboratory in diagnosis and management of pharyngitis. *Journal of clinical microbiology*, *41*(8), 3467-3472.
47. Mogoantă, C. A., Ioniță, E., Pirici, D., Mitroi, M., Anghelina, F., Ciolofan, S., & Pătru, E. M. I. L. I. A. (2008). Chronic tonsillitis: histological and immunohistochemical aspects. *Rom J Morphol Embryol*, *49*(3), 381-386.
48. Dalton, R. E., Abedi, E., & Sismanis, A. (1985). Bilateral peritonsillar abscesses and quinsy tonsillectomy. *Journal of the National Medical Association*, *77*(10), 807.
49. Mazur, E., Czerwińska, E., Korona-Głowniak, I., Grochowalska, A., & Kozioł-Montewka, M. (2015). Epidemiology, clinical history and microbiology of peritonsillar abscess. *European Journal of Clinical Microbiology & Infectious Diseases*, *34*(3), 549-554.
50. 50-Wang Y-P, Wang M-C, Lin H-C, Chou P. The Impact of Prior Tonsillitis and Treatment Modality on the Recurrence of Peritonsillar Abscess: A Nationwide Cohort Study. Amar S, ed. *PLoS ONE*. 2014;9(10):e109887. doi:10.1371/journal.pone.0109887.
51. Klug, T. E. (2009). Peritonsillar abscess: clinical aspects of microbiology, risk factors, and the association with parapharyngeal abscess. *Clin Infect Dis*, *49*, 1467-72.
52. Proenca-Modena, J. L., Valera, F. C. P., Jacob, M. G., Buzatto, G. P., Saturno, T. H., Lopes, L., ... & Tamashiro, E. (2012). High rates of detection of respiratory viruses in tonsillar tissues from children with chronic adenotonsillar disease. *PLoS One*, *7*(8), e42136.
53. Tanz, R. R., & Shulman, S. T. (2007). Chronic pharyngeal carriage of group A streptococci. *The Pediatric infectious disease journal*, *26*(2), 175-176.
54. Wessels MR. (2011). Clinical practice. Streptococcal pharyngitis. N Engl J Med, 17; 364(7):648-55.
55. Roberts, A. L., Connolly, K. L., Kirse, D. J., Evans, A. K., Poehling, K. A., Peters, T. R., & Reid, S. D. (2012). Detection of group A Streptococcus in tonsils from pediatric patients reveals high rate of

asymptomatic streptococcal carriage. *BMC pediatrics*, *12*(1), 3.
56. Shulman, S. T., Bisno, A. L., Clegg, H. W., Gerber, M. A., Kaplan, E. L., Lee, G., ... & Van Beneden, C. (2012). Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. *Clinical infectious diseases*, *55*(10), e86-e102.
57. Drago, L., Esposito, S., De Vecchi, E., Marchisio, P., Blasi, F., Baggi, E., ... & Pignataro, L. (2008). Detection of respiratory viruses and atypical bacteria in children's tonsils and adenoids. *Journal of clinical microbiology*, *46*(1), 369-370.
58. Piacentini, G. L., Peroni, D. G., Blasi, F., Pescollderungg, L., Goller, P., Gallmetzer, L., ... & Boner, A. L. (2010). Atypical bacteria in adenoids and tonsils of children requiring adenotonsillectomy. *Acta oto-laryngologica*, *130*(5), 620-625.
59. Proenca-Modena, J. L., Valera, F. C. P., Jacob, M. G., Buzatto, G. P., Saturno, T. H., Lopes, L., ... & Tamashiro, E. (2012). High rates of detection of respiratory viruses in tonsillar tissues from children with chronic adenotonsillar disease. *PLoS One*, *7*(8), e42136.
60. Gurol, Y., Akan, H., Izbİrak, G., Tekkanat, Z. T., Gunduz, T. S., Hayran, O., & Yilmaz, G. (2010). The sensitivity and the specifity of rapid antigen test in streptococcal upper respiratory tract infections. *International journal of pediatric otorhinolaryngology*, *74*(6), 591-593.
61. Pelucchi, C., Grigoryan, L., Galeone, C., Esposito, S., Huovinen, P., Little, P., & Verheij, T. (2012). Guideline for the management of acute sore throat. *Clinical microbiology and infection*, *18*(s1), 1-28.
62. Tajbakhsh, S., Gharibi, S., Zandi, K., Yaghobi, R., & Asayesh, G. (2011). Rapid detection of Streptococcus pyogenes in throat swab specimens by fluorescent in situ hybridization. *European review for medical and pharmacological sciences*, *15*(3), 313-317.
63. Chiappini, E., Principi, N., Mansi, N., Serra, A., De Masi, S., Camaioni, A., ... & Speciale, A. M. (2012). Management of acute pharyngitis in children: summary of the Italian National Institute of Health guidelines. *Clinical therapeutics*, *34*(6), 1442-1458.
64. Sahin, M. S., Yalcin, M. U., & Kocyigit, D. (2016). Prevalence of rheumatic heart disease in patients with recurrent tonsillitis and elevated anti-streptolysin O titers. *International journal of pediatric otorhinolaryngology*, *89*, 133-135.
65. Ben-Chetrit, E., Moses, A. E., Agmon-Levin, N., Block, C., & Ben-Chetrit, E. (2012). Serum Levels Of anti-streptolysin O antibodies: their role in evaluating rheumatic diseases. *International journal of rheumatic diseases*, *15*(1), 78-85.
66. Berkowitz, R. G., & Mahadevan, M. (1999). Unilateral tonsillar enlargement and tonsillar lymphoma in children. *Annals of Otology, Rhinology & Laryngology*, *108*(9), 876-879.
67. Sadeghi-Shabestari, M., Moghaddam, Y. J., & Ghaharri, H. (2011). Is there any correlation between allergy and adenotonsillar tissue hypertrophy?. *International journal of pediatric otorhinolaryngology*, *75*(4), 589-591.
68. Karaca, Ç. T., Toros, S. Z., Noseri, H., Külekçi, S., Kalayck, Ç., Oysu, Ç., ... & Egeli, E. (2012). Role of allergy in children with adenotonsillar hypertrophy. *Journal of Craniofacial Surgery*, *23*(6), e611-e613.
69. Georgalas, C., Kanagalingam, J., Zainal, A., Ahmed, H., Singh, A., & Patel, K. S. (2002). The association between periodontal disease and peritonsillar infection: a prospective study. *Otolaryngology—Head and Neck Surgery*, *126*(1), 91-94.
70. Demir, U. L., Cetinkaya, B., Karaca, S., & Sigirli, D. (2013). The impacts of adenotonsillar hypertrophy on periodontal health in children: a prospective controlled pilot study. *American journal of otolaryngology*, *34*(5), 501-504.
71. Berkowitz, R. G., & Mahadevan, M. (1999). Unilateral tonsillar enlargement and tonsillar lymphoma in children. *Annals of Otology, Rhinology & Laryngology*, *108*(9), 876-879.
72. Gebhardt, B., Herrmann, K., Roessner, A., & Vorwerk, U. (2010). Differenzialdiagnostik der nekrotisierenden Tonsillitis. *Laryngo-rhino-otologie*, *89*(05), 266-269.
73. Lee, P. K., & Schlievert, P. M. (1991). Molecular genetics of pyrogenic exotoxin "superantigens" of group A streptococci and Staphylococcus aureus. In *Superantigens* (pp. 1-19). Springer Berlin Heidelberg.
74. Walther, L. E., Ilgner, J., Oehme, A., Schmidt, P., Sellhaus, B., Gudziol, H., ... & Westhofen, M. (2005). Die infektiöse Mononukleose. *Hno*, *53*(4), 383-394.
75. Cohen, J. I., Mocarski, E. S., Raab-Traub, N., Corey, L., & Nabel, G. J. (2013). The need and challenges for development of an Epstein-Barr virus vaccine. *Vaccine*, *31*, B194-B196.
76. Ruiss, R., Jochum, S., Wanner, G., Reisbach, G., Hammerschmidt, W., & Zeidler, R. (2011). A virus-like particle-based Epstein-Barr virus vaccine. *Journal of virology*, *85*(24), 13105-13113.
77. Stelter, K. (2014). Tonsillitis and sore throat in children. *GMS current topics in otorhinolaryngology, head and neck surgery*, *13*.
78. Casey, J. R., & Pichichero, M. E. (2004). Meta-analysis of cephalosporin versus penicillin treatment of group A streptococcal tonsillopharyngitis in children. *Pediatrics*, *113*(4), 866-882.
79. Chiappini, E., Principi, N., Mansi, N., Serra, A., De Masi, S., Camaioni, A., ... & Speciale, A. M.

(2012). Management of acute pharyngitis in children: summary of the Italian National Institute of Health guidelines. *Clinical therapeutics*, *34*(6), 1442-1458.

80. Cohen, R., Reinert, P., De La Rocque, F., Levy, C., Boucherat, M., Robert, M., ... & Bingen, E. (2002). Comparison of two dosages of azithromycin for three days versus penicillin V for ten days in acute group A streptococcal tonsillopharyngitis. *The Pediatric infectious disease journal*, *21*(4), 297-303.
81. Altamimi, S., Khalil, A., Khalaiwi, K. A., Milner, R. A., Pusic, M. V., & Al Othman, M. A. (2012). Short-term late-generation antibiotics versus longer term penicillin for acute streptococcal pharyngitis in children. *The Cochrane Library*.
82. van den Anker, J. N. (2013). Optimising the management of fever and pain in children. *International Journal of Clinical Practice*, *67*(s178), 26-32.
83. Hay, A. D., Redmond, N. M., Costelloe, C., Montgomery, A. A., Fletcher, M., Hollinghurst, S., & Peters, T. J. (2009). Paracetamol and ibuprofen for the treatment of fever in children: the PITCH randomised controlled trial. *Health Technol Assess*, *13*(27), 1-163.
84. Forrest, J. B., Heitlinger, E. L., & Revell, S. (1997). Ketorolac for postoperative pain management in children. *Drug safety*, *16*(5), 309-329.
85. Arencibia, Z. B., & Choonara, I. (2012). Balancing the risks and benefits of the use of over-the-counter pain medications in children. *Drug safety*, *35*(12), 1119-1125.
86. Hayward, G., Thompson, M. J., Perera, R., Del Mar, C. B., Glasziou, P. P., & Heneghan, C. J. (2012). Corticosteroids for the common cold. *Cochrane Database Syst Rev*, *8*(8).
87. Hayward, G., Thompson, M. J., Perera, R., Glasziou, P. P., Del Mar, C. B., & Heneghan, C. J. (2012). Corticosteroids as standalone or add-on treatment for sore throat. *The Cochrane Library*.
88. Cingi, C., Songu, M., Ural, A., Erdogmus, N., Yildirim, M., Cakli, H., & Bal, C. (2011). Effect of chlorhexidine gluconate and benzydamine hydrochloride mouth spray on clinical signs and quality of life of patients with streptococcal tonsillopharyngitis: multicentre, prospective, randomised, double-blinded, placebo-controlled study. *The Journal of Laryngology & Otology*, *125*(6), 620-625.
89. Ciuman, R. R. (2012). Phytotherapeutic and naturopathic adjuvant therapies in otorhinolaryngology. *European Archives of Oto-Rhino-Laryngology*, *269*(2), 389-397.
90. Walton, J., Ebner, Y., Stewart, M. G., & April, M. M. (2012). Systematic review of randomized controlled trials comparing intracapsular tonsillectomy with total tonsillectomy in a pediatric population. *Archives of Otolaryngology–Head & Neck Surgery*, *138*(3), 243-249.
91. Chang, C. Y., & Thrasher, R. (2012). Coblation cryptolysis to treat tonsil stones: a retrospective case series. *Ear, Nose & Throat Journal*, *91*(6), 238.
92. Chatziavramidis, A., Constantinidis, J., Gennadiou, D., Derwisis, D., & Sidiras, T. (2007). Volume reduction of tonsil hyperplasia in childhood with a surgical ultrasound device. *Laryngo-rhino-otologie*, *86*(3), 177-183.
93. Pfaar, O., Spielhaupter, M., Schirkowski, A., Wrede, H., Mösges, R., Hörmann, K., & Klimek, L. (2007). Treatment of hypertrophic palatine tonsils using bipolar radiofrequency-induced thermotherapy (RFITT). *Acta oto-laryngologica*, *127*(11), 1176-1181.
94. Coticchia, J. M., Yun, R. D., Nelson, L., & Koempel, J. (2006). Temperature-controlled radiofrequency treatment of tonsillar hypertrophy for reduction of upper airway obstruction in pediatric patients. *Archives of Otolaryngology–Head & Neck Surgery*, *132*(4), 425-430.
95. Zhu, X., Yang, H., Chen, X., Jin, Y., & Fan, Y. (2011). Temperature-controlled radiofrequency-assisted endoscopic tonsillectomy and adenoidectomy in children. *Lin chuang er bi yan hou tou jing wai ke za zhi= Journal of clinical otorhinolaryngology, head, and neck surgery*, *25*(12), 551-553.