Arrival Date: 06.03.2023 | | **Vol:** 8, **Issue:** 2 | **pp:** 254-259 | **Doi Number:** http://doi.org/10.5281/zenodo.7759770

THE IMPORTANT CONCEPT IN CHILDREN WITH CHRONIC COUGH: PROTRACTED BACTERIAL BRONCHITIS

ÇOCUKLUK ÇAĞINDA KRONİK ÖKSÜRÜKTE ÖNEMLİ BİR KAVRAM: UZAMIŞ BAKTERİYEL BRONŞİT

Belgin USTA GUC[1], Mehtap KILIÇ[2]

[1]Adana City Training and Research Hospital, Department of Pediatrics, Division of Pediatric Allergy and Immunology, Adana, Turkey.

[2] Samsun Private Pediatrics Clinic, Department of Pediatrics, Division of Pediatric Allergy and Immunology, Samsun, Turkey.

ABSTRACT

Objective: Chronic cough is a common problem in childhood. In chronic productive cough; there may be important underlying etiological causes such as protracted bacterial bronchitis (PBB), cystic fibrosis, primary ciliary dyskinesia, and immunodeficiencies. PBB is very important especially in terms of causing irreversible bronchiectasis in the long term. In our study, it was aimed to examine the history, clinical, radiological and laboratory findings and evaluation results of the patients over the age of 6 who were diagnosed with PBB in the clinical follow-up.

Materials-Methods: The documents of children over the age of 6 who applied to the pediatric allergy outpatient clinic between January 2021 and June 2022 for more than 4 weeks of productive cough were evaluated retrospectively.

Results: 48 patients aged 6-15.5 years were included in the study. The median age of the patients was 9.2 (6-15.5) years, 62.1% of them were male. The median duration of cough was 7 (4-10) weeks. On physical examination, respiratory sounds were normal in 56.25% of the patients, bilateral crepitant rales in 12 patients, and secretion rales in 9 patients. Considering the radiological findings; Chest X-ray was normal in 60.4% of the patients, peribronchial thickening was present in 35.4%, and chronic changes were present in 4.2%. Thoracic tomography was performed in 16 (33.3%) patients who did not respond to 2-week antibiotic treatment and 56.25% were found to be normal. Sputum culture was obtained in 47.9% of the patients; normal oropharyngeal flora was isolated in 6 patients, Streptococcus pneumonia in 3 patients and Haemophilus influenzae in 2 patients. The sputum culture of the other patients was negative. Antibiotics were given to the patients for 2 weeks in the first stage. In the first control, cough of 32 patients were resolved with treatment. Although the complaints of 8 patients decreased, their productive cough continued, the complaints of the other 8 patients relapsed within 2 weeks. The treatment of the patients was extended to 4 weeks and other etiological factors were re-evaluated. One of the patients was diagnosed with cystic fibrosis, the other was diagnosed with foreign body aspiration when the history was deepened, and pulmonary tuberculosis in 2 patients. IgA level of two patients was <0.1 mg/dl.

Conclusion: Many different underlying diseases can cause chronic productive cough in childhood. When inappropriate drug treatments are administered to the patients, irreversible complications such as bronchiectasis may develop. Protracted bacterial bronchitis, which has been described in recent years, is one of the important causes of chronic productive cough. It is very important to evaluate these patients diagnosed with PBB correctly and to follow up the treatment.

Keywords: Childhood, Chronic Cough, Protracted Bacterial Bronchitis

ÖZET

Amaç: Kronik öksürük çocukluk çağında sık karşılaşılan bir sorundur. Kronik balgamlı öksürükte; uzamış bakteriyel bronşit (UBB), kistik fibrozis, primer siliyer diskinezi, immün yetmezlikler gibi altta yatan önemli etyolojik nedenler olabilir. Özellikle uzun vadede geri dönüşsüz bronşiektaziye neden olması bakımından UBB oldukça önemlidir. Çalışmamızda klinik izlemde UBB tanısı alan 6 yaş üzeri hastalarımızın öykü, klinik, radyolojik ve laboratuvar bulgularıyla değerlendirme sonuçlarının incelenmesi amaçlandı.

Gereç-Yöntem: Ocak 2021 - Haziran 2022 arasında çocuk alerji polikliniğine 4 haftadan uzun süredir balgamlı öksürük sebebiyle başvuran 6 yaş üstü çocukların dosyaları retrospektif olarak değerlendirildi.

Bulgular: 6-15.5 yaş arasında 48 hasta çalışmaya dahil edildi. Hastaların ortanca yaşı 9,2 (6-15.5) yıl,%62,1'i erkekti. Öksürük ortanca süresi 7 (4-10) hafta idi. Fizik muayenede hastaların %56.25'inin solunum sesleri doğal iken, 12 hastanın bilateral krepitan ralleri, 9 hastanın sekresyon ralleri saptandı. Radyolojik bulgulara bakıldığında; hastaların %60.4'ünde akciğer grafisi normal, %35.4'ünde peribronşiyal kalınlaşma, %4,2'sinde kronik değişiklikler vardı. 2 haftalık antibiyotik tedavisine yanıt vermeyen 16 (%33.3) hastanın toraks tomografisi çekildi ve %56.25'i normal bulundu. Hastaların %47.9'u balgam kültürü verebildi, 6 hastada normal orofarinks florası, 3 hastada Streptococcus pneumonia ve 2 hastada Haemophilus influenza izole edildi, diğer hastaların balgam kültürü negatifti. Hastalara ilk aşamada 2 hafta boyunca antibiyotik verildi. İlk kontrolde 32 hastanın öksürükleri tedaviyle çözümlenmişti. 8 hastanın yakınmaları azalmakla birlikte balgamlı öksürükleri devam ederken, diğer 8 hastanın yakınmaları 2 hafta içinde tekrar başladı. Hastaların tedavileri 4 haftaya uzatıldı ve diğer etyolojik faktörler tekrar değerlendirildi. Hastaların birine Kistik fibrozis tanısı, bir diğerinin öyküsü derinleştirildiğinde yabancı cisim aspirasyonu, 2 hastaya da pulmoner tüberküloz tanısı kondu, iki hastanın IgA seviyesinin <0.1 mg/dl olduğu gözlendi.

Sonuç: Çocukluk çağında kronik balgamlı öksürüğe altta yatan birçok farklı hastalık sebep olabilmektedir. Hastalara uygun olmayan ilaç tedavileri uygulandığında bronşiektazi gibi geri dönüşü olmayan komplikasyonlar gelişebilmektedir. Son yıllarda tanımlanan uzamış bakteriyel bronşit kronik balgamlı öksürüğe sebep olan önemli nedenlerden biridir. UBB tanısı almış bu hastaların doğru şekilde değerlendirilmesi ve tedavinin izlemi oldukça önemlidir.

Anahtar Kelimeler: Çocukluk Çağı, Kronik balgamlı öksürük, Uzamış Bakteriyel Bronşit

***Sorumlu Yazar / Corresponding Author*:** Belgin USTA GUC, Uzm. Dr., Adana City Training and Research Hospital, Department of Pediatrics, Division of Pediatric Allergy and Immunology, Adana, Turkey**, E-mail:** defneusta@hotmail.com

Bu makaleye atıf yapmak için / Cite this article: Usta Guc B, & Kılıç M. (2023). The Important Concept in Children with Chronic Cough: Protracted Bacterial Bronchitis. *Gevher Nesibe Journal of Medical & Health Sciences*, 8(2), 254-259. http://doi.org/10.5281/zenodo.7759770

INTRODUCTION

Chronic cough is a common problem in childhood. Many etiological factors can cause chronic cough. One of these reasons is protracted bacterial bronchitis (PBB) (Ruffles et al., 2021). There are many studies on this concept, which was first defined in 2006 (Ruffles et al., 2021; Marchant et al.,2006; Narang et al.,2014; Chang et al., 2016). Since it is a concept that has developed in recent years, there is still no clear data for the prevalence of the disease. The diagnosis of PBB is a clinical definition. It is diagnostic for PBB that the complaints of a patient with productive cough lasting longer than four weeks are eliminated with antibiotic treatment given after other diagnoses that may cause a cough with sputum have been ruled out (Chang et al., 2016). Correct diagnosis is important as long-term antibiotics are required for treatment.

Chronic productive cough indicates increased secretion or impaired clearance in the respiratory tract. In these patients, sinusitis, PBB, Cystic fibrosis (CF), Primary ciliary dyskinesia (PCD), immunodeficiencies, recurrent aspirations, and specific lung infections such as tuberculosis are the most common causes(Shields, Doherty,2013; Chang et al.,2016). PBB is generally defined for preschool children. Differently, we aimed to evaluate PBB in the patient group over 6 years old. It is common to apply to general pediatrics and family physicians with complaint of chronic productive cough. It is known that bronchiectasis can develop in these patients in cases of misdiagnosis, inadequate treatment and recurrence (Chang et al.,2018). For this reason, it is very important to be more aware of the disease.

In this study, it was aimed to examine the history, clinical, radiological and laboratory findings and evaluation results of our patients over the age of 6 who were diagnosed with PBB in the clinical follow-up.

MATERIALS AND METHODS

The documents of 48 patients aged 6-18 years, who applied to Adana City Hospital Pediatric Allergy Department with the complaint of chronic productive cough between January 2021 and June 2022 and were diagnosed with protracted bacterial bronchitis, were retrospectively analyzed. Cough lasting longer than 4 weeks were considered chronic. An application was made to the Local Ethics Committee of Adana City Hospital in order to conduct the study. Informed consent was obtained from both parents at enrollment.

The diagnostic criteria, used in this study, were Modified clinical-based case definition (also termed PBB-clinical), which was explained in the article published by Chang et al in 2016 (Chang et al., 2016).

- Chronic productive cough (>4 weeks)
- Absence of symptoms or signs of other causes of productive cough
- Cough resolved following a 2-week course of an appropriate oral antibiotic (usually amoxicillin-clavulanate, 40-60 mg/kg/day)

The detailed history of the patients was taken and it was questioned whether the cough was productive, whether the complaints increased with exercise, whether there was a cough at night, whether there was a complaint of shortness of breath and wheezing, and whether rhinitis was accompanied by complaints. In addition, it was questioned whether the patient's complaints were accompanied by fever, whether the patient had weight loss, whether there was a history of foreign body aspiration, and whether there was a patient diagnosed with tuberculosis in the family members. Detailed physical examination was performed. Chest radiographs were taken at the first examination of all the patients. Pulmonary function test (PFT) with spirometry was applied to each patient who has a complaint of shortness of breath and wheezing.

In the first stage, if the patients had a productive cough, the patients were given antibiotic therapy for 2 weeks. Immune panel (level of serum IgG, gA, IgM) was studied from patients who were suggestive of immunodeficiency in the history and physical examination, and also the patients with productive cough who did not respond to antibiotic treatment. Advanced imaging (high-resolution chest tomography (HRCT)) was applied to patients with productive cough who did not respond to antibiotic treatment. Depending on history and physical examination results, tuberculin skin test, the mutation analysis in the CFTR gene were also performed. We followed our patients for 18 months

after their cough had resolved. Culture studies were performed in patients who were able to produce sputum.

Exclusion criteria: Patients with neuromotor development retardation, any known chronic lung disease like CF, asthma, interstitial lung disease, PCD, previously known immunodeficiency, swallowing dysfunction, the patients who have findings sinusitis on physical examination, and patients who do not come to regular follow-up were excluded from the study.

We used the following criteria for the diagnosis of CF and PCD.

Primary ciliary dyskinesia (PCD): When PICADAR scoring is done for PCD in patients presenting with chronic and recurrent productive cough, if the patient's score is ≥ 10 patients, it is evaluated as PCD with 90% probability (Behan et al., 2016).

Cystic fibrosis diagnosis; Although the diagnostic criteria vary for each age group, the clinical and imaging findings accompanying the patient's history, together with the sweat test and/or CFTR genetic analysis are used for the diagnosis of CF(Farrell et al.,2016).

Statistical analysis

Statistical analyzes were performed using SPSS version 20. Frequency and percentage values were used for categorical variables, mean ± standard deviation for normally distributed numerical variables, median and lowest-maximum values were used for non-normally distributed numerical variables. In statistical analysis, the significance level was accepted as $p<0.05$.

RESULTS

The median age of 48 patients with chronic productive cough was 9.2 (6-15.5) years. All patients, including 66.7% (n=32) male, had a productive cough at first admission. The median duration of cough was 7 (4-10) weeks. On physical examination, respiratory sounds were normal in 56.25% (n=27) of the patients, while crepitant rales were found in 12 patients and secretion rales in 9 patients. There was no significant difference between gender in terms of age at presentation ($p>0.05$) and duration of symptoms ($p>0.05$).

Considering the radiological findings; Chest X-ray was normal in 60.4% (n=29) of the patients, peribronchial thickening was found in 35.4% (n=17), and 4.2% (n=2) had chronic changes in the patient's chest X-ray. Thoracic CT was performed in 33.3% (n=16) patients who did not respond to 2 weeks of antibiotic treatment. Thoracic CT of 56.25% (n=9) of these patients was within normal limits; peribronchial thickening was found in 3 patients, atelectasis in 1 patient, and bronchiectasis in 2 patients.

Sputum culture could be obtained in 47.9% (n=23) of the patients, 52.2% (n=12) culture was negative. Microorganisms could be grown in 11 patients. Normal oropharyngeal flora was isolated in 6 patients, Streptococcus pneumonia in 3 patients, and Haemophilus influenza in 2 patients.

Antibiotics were given to all 48 patients for 2 weeks in the first phase. The cough of 40 patients were resolved with treatment at the follow-up visits 2 weeks later. Although the complaints of 8 patients decreased, their productive cough continued. The treatment of the patients was extended for 2 more weeks and other etiological factors were re-evaluated. Thoracic CT was performed in these patients. Immune panel was studied and no abnormal findings were found. Since one of the patients had a cousin in the family with a diagnosis of CF, genetic study was performed on the patient. A mutation was detected in the patient's Del F508 gene analysis. Tuberculin skin test was found > 15 mm in 2 of the patients, and chest imaging of these patients also had positive findings. The patients were referred to the pediatric infectious diseases department. In one of the patients, a history of foreign body aspiration (with peanut) was found upon further questioning, and the foreign body was removed by bronchoscopy. Complaints started again in 8 of 40 patients who did not have any problems at the first control, 2 weeks after the control. Thoracic CT was performed in these patients, and their treatment was completed in 4 weeks. Only 2 of these patients had an IgA level of <0.1 mg/dl.

DISCUSSION

Protracted bacterial bronchitis (PBB) is a clinical condition with inflammation that begins as a result of chronic infection in the airway. The most common finding in the patient is chronic productive cough. Delays in diagnosis and treatment may cause irreversible lung damage (Chang et al., 2008; Wurzel et al., 2016).

We diagnosed PBB in accordance with the in our patients who were not diagnosed with sinusitis or pneumonia, had no paranchymal inflammation or lobar involvement on direct chest X-ray, and no post nasal discharge was detected in physical examination, especially in patients with productive cough Since the patient with a diagnosis of sinusitis may have a productive cough, the patients were not included in the study when there were findings suggestive of sinusitis in the examinations of the patients.

According to Emiralioglu et al. in the retrospective study of 31 patients diagnosed with PBB by; 74% of the patients had normal lung sounds and 61% had normal chest X-rays (Emiroğlu et al., 2015). In the physical examinations of our patients, respiratory sounds were normal in 56.25%, while 12 patients had crepitant rales and 9 patients had secretion rales.

In a study conducted by Narang et al. flexible bronchoscopy with bronchoalveloar lavage (FB-BAL) fluid was examined both pathologically and microbiologically in 50 pediatric patients who presented with prolonged productive cough and no other underlying cause was found (Narang et al., 2014). Microorganism growth was observed in the BAL fluid culture of 82% of the patients, the authors reported that the most common growth was Haemophilus influenza, Moraxella catarrhalis, Staphylococcus aureus, and Streptococcus pneumonia (Narang et al., 2014). In addition, the authors reported that they most commonly observed bronchial wall thickening in the airway (Narang et al., 2014). In another study, the authors reported that the most frequently isolated microorganisms in the BAL fluid were 22.5% S. pneumonia and 16.1% H. influenza (Shields, Doherty, 2013; Emiroğlu et al., 2015). Neutrophil dominance was detected in BAL fluid cytology (Shields, Doherty, 2013). We could not obtain BAL fluid from our patients, we obtained sputum cultures from 47.9% of the patients, 11 of them had normal oropharyngeal flora growth, the other 3 patients were positive for S. pneumonia and 2 patients were positive for H. influenza.

Chang et al. developed the definition of PBB (Chang et al., 2016). First of all, they used the definition of “Original microbiologic-based case definition (also termed PBB-micro)”, but the authors reported that it is not possible in clinical practice to perform flexible bronchoscopy on every patient in order to make this definition, therefore they developed and modified the diagnostic criteria again(Chang et al., 2016). In addition, the authors have developed definitions for the patients in the different stuations over the years. “Original microbiologic-based case definition” (Chang et al., 2016) (also termed PBB-micro): Presence of chronic wet cough (>4 weeks), lower airway infection (recognized respiratory bacterial pathogens growing in sputum or at BAL at density of a single bacterial specifies > 104 colony-forming units/ml), and cough resolved following a 2-week course of an appropriate oral antibiotic (usually amoxicillin-clavulanate). “Modified clinical-based case definition” (also termed PBB-clinical): Presence of chronic wet cough (>4 weeks), absence of symptoms or signs of other causes of wet or productive cough, and cough resolved following a 2-week course of an appropriate oral antibiotic (usually amoxicillin-clavulanate). To explain Modified clinical-based case definition, the BAL component was replaced by "absence of other causes of wet/productive cough." Finally, the authors added the terms PBB-extended and Recurrent PBB to the literature (Chang et al., 2016).

The treatment duration of the patients with PBB was applied differently by different centers. In the first stage, we gave our patients amoxicillin-clavunate therapy for 14 days. As a matter of fact, unlike us, Kompare M et al. continued AB treatment for 4 weeks in 70 patients with PBB (Kompare, Weinberger, 2012). The 2008 BTS cough guidelines recommend that patients with PBB be given antibiotics for 4-6 weeks (Shields, 2008).

On the other hand, in a study by Donnelly et al. 51% of patients with PBB became completely asymptomatic after two weeks of antibiotic therapy. 13% of cases required antibiotic treatment for six weeks or longer (Donnelly et al., 2oo7). In the first stage, 40/48 of our patients resolved their complaints after 2 weeks of treatment, and productive cough continued in 8/48 of the patients. Therefore, the treatment was extended to 4 weeks.

A recent study reported that patients with a chronic wet cough that did not respond to 4 weeks of antibiotic therapy were more likely to have bronchiectasis on a thoracic CT scan (Goyal et al., 2014). In a multicenter study, wet cough was found in 63.9% of patients who applied for chronic cough, 41% of patients with wet cough were evaluated as PBB and 9% as bronchiectasis (Chang et al., 2012).

The most important limitation of our study; flexible bronchoscopy was not performed. For this reason, BAL fluid could not be taken from our patients. We were able to obtain sputum cultures from

only 47.9% (n=23) of our patients, and there was no growth in 12 of these patients. Patients with no growth in sputum culture were those who had used antibiotics before applying to us, so we thought that the culture was negative.

Cystic fibrosis is the most common OR inherited, life-limiting genetic disease in Caucasians. It is known that the incidence in the USA is 1/3500 live births. With infection, inflammation and permanent damage to the airway; it is the lung disease with the highest mortality and morbidity in childhood (Farrell et al., 2017). In a study about CF conducted by Accurso et al., 45% of CF patients were diagnosed by presenting with the complaint of chronic productive cough (Accurso et al., 2005). In a study from our country, CF was diagnosed in 20 of 563 patients who presented with chronic cough. While 11 of these patients were diagnosed before the age of two, 8 patients were diagnosed only after the age of six (Gedik et al., 2015).

In our study, only one patient was diagnosed with CF. because, the diagnosis age of CF patients is at a very early age, thanks to the CF screening test in the neonatal period, which has started in our country since 2015. While it was shown that the age at diagnosis of the patients with the CF screening program was 5 months, the age of diagnosis of our patient who was born before the screening program was 144 months. The importance of the screening program is clearly seen with the available data. In the meantime, sweat test could not be performed in our patient. However, Del F508 mutation was detected in the CFTR gene mutation analysis of the patient. The diagnosis was made by the presence of clinical findings, the compatibility of the history, and the detection of the mutation in the genetic examination. The patient with the diagnosis of CF was followed up in Department of Pediatric Pulmonology.

CONCLUSION

Chronic productive cough, which is frequently encountered in childhood, is very important in terms of underlying diseases. It is very important that these patients are diagnosed and treated correctly, especially since there is a possibility of irreversible bronchiectasis. Follow-up of these patients is necessary. PBB, which has been defined in recent years, should be considered in every patient presenting to a physician due to chronic productive cough.

Conflict of interest

The authors report no actual or potential conflicts of interest.

Funding

This study did not receive any specific grant or funding.

Authors Contributions

Plan, design: BUG, MK; **Material, methods and data collection:** BUG; **Data analysis and comments:** BUG; **Writing and corrections:** BUG, MK

REFERENCES

Anne B Chang 1, Colin F Robertson 2, Peter P Van Asperen 3, Nicholas J Glasgow 4, Craig M Mellis 5, I Brent Masters 6, Laurel Teoh 7, Irene Tjhung 8, Peter S Morris 9, Helen L Petsky 6, Carol Willis 6, Lou I Landau. A multicenter study on chronic cough in children : burden and etiologies based on a standardized management pathway. Chest 2012 Oct;142(4):943-950. doi: 10.1378/chest.11-2725.

Accurso FJ, Sontag MK, Wagener JSJTJop. Complications associated with symptomatic diagnosis in infants with cystic fibrosis. J Pediatr 2005;147(3):S37-S41. DOI: 10.1016/j.jpeds.2005.08.

Behan L, Dimitrov BD, Kuehni CE, et al. PICADAR: a diagnostic predictive tool for primary ciliary dyskinesia. European Respiratory Journal 2016 47: 1103-1112 DOI: 10.1183/13993003.01551-2015

Chang AB, Bush A, Grimwood K. Bronchiectasis in children: diagnosis and treatment. Lancet. 2018 Sep 8;392(10150):866-879. doi: 10.1016/S0140-6736(18)31554-X.

Chang AB, Oppenheimer JJ, Weinberger M, Rubin BK, Irwin RS. Children With Chronic Wet or Productive Cough--Treatment and Investigations: A Systematic Review. Chest. 2016;149(1):120-42. DOI: 10.1378/chest.15-2065

Chang AB, Redding GJ, Everard ML. Chronic wet cough: Protracted bronchitis, chronic suppurative lung disease and bronchiectasis. Pediatr Pulmonol 2008;43(6):519-31. DOI: 10.1002/ppul.20821

Chang AB, Upham JW, Masters JB, et al. Protracted bacterial bronchitis: The last decade and the road ahead. Pediatr Pulmonol. 2016 Mar;51(3):225-42. doi: 10.1002/ppul.23351.

Donnelly D, Critchlow A, Everard MLJT. Outcomes in children treated for persistent bacterial bronchitis. Thorax. 2007;62(1):80-4 DOI: 10.1136/thx.2006.058933

Emiralioglu N, Kiper N, Yalçin E, Ersöz DD, Özçelik U. Flexible bronchoscopy findings in children with protracted bacterial bronchitis. Turkiye Klinikleri J Pediatr, 26(2):39-43 DOI: 10.5336/pediatr.2016-53818

Gedik AH, Cakir E, Torun E, Demir AD, Kucukkoc M, Erenberk U, et al. Evaluation of 563 children with chronic cough accompanied by a new clinical algorithm. Ital J Pediatr. 2015;41:73. doi: 10.1186/s13052-015-0180-0.

Goyal V, Grimwood K, Marchant JM, et al. Does failed chronic wet cough response to antibiotics predict bronchiectasis? Arch Dis Child 2014;99:522–525. doi: 10.1136/archdischild-2013-304793

Kompare M, Weinberger M. Protracted bacterial bronchitis in young children: association with airway malacia. J Pediatr 2012; 160:88–92. DOI: 10.1016/j.jpeds.2011.06.049

Marchant JM, Masters IB, Taylor SM, Cox NC, Seymour GJ, Chang AB. Evaluation and outcome of young children with chronic cough. Chest 2006;129:1132–1141.doi: 10.1378/chest.129.5.1132

Narang R, Bakewell K, Peach J, Clayton S, Samuels M, Alexander J, et al. Bacterial distribution in the lungs of children with protracted bacterial bronchitis. PLoS One 2014;9(9):e108523. doi: 10.1371/journal.pone.0108523.

Shields M D, Bush A, Everard M L, et al. Recommendations for the assessment and management of cough in children. Thorax. 2008;63 (Suppl III): ii1–iii15. DOI: 10.1136/thx.2007.077370

Shields MD, Doherty GM. Chronic cough in children. Paediatric Respiratory Reviews. 2013;14(2):100-6. DOI: 10.1016/j.prrv.2012.05.002

Philip M Farrell, Terry B White, Clement L Ren, Sarah E Hempstead, Frank Accurso, Nico Derichs, Michelle Howenstine, Susanna A McColley, Michael Rock, Margaret Rosenfeld, Isabelle Sermet-Gaudelus, Kevin W Southern, Bruce C Marshall, Patrick R Sosnay. Diagnosis of Cystic Fibrosis:Consensus Guidelines from the Cystic Fibrosis Foundation. J Pediatr. 2017 Feb;181S:S4-S15.e1. doi: 10.1016/j.jpeds.2016.09.064.

Tom J C Ruffles, Julie M Marchant, Ian B Masters, Stephanie T Yerkovich, Danielle F Wurzel, Peter G Gibson, Greta Busch, Katherine J Baines, Jodie L Simpson, Heidi C Smith-Vaughan, Susan J Pizzutto, Helen M Buntain, Gregory Hodge, Sandra Hodge, John W Upham, Anne B Chang. Outcomes of protracted bacterial bronchitis in children: A 5-year prospective cohort study. Respirology. 2021 Mar;26(3):241-248. doi: 10.1111/resp.13950.

Wurzel DF, Marchant JM, Yerkovich ST, Upham JW, Petsky HL, Smith-Vaughan H, et al. Protracted Bacterial Bronchitis in Children: Natural History and Risk Factors for Bronchiectasis. Chest 2016;150(5):1101-8. DOI: 10.1016/j.chest.2016.06.030