ISSN: 2543-0343 Volume 4 Issue 3 July-September 2020

Pediatric Respirology and Critical Care Medicine

APPS
ASIAN PAEDIATRIC PULMONOLOGY SOCIETY

香港兒童呼吸及過敏學會
Hong Kong Society *of*
PAEDIATRIC RESPIROLOGY AND ALLERGY

www.appuls.org www.hkspra.org www.pedipulm.org.tw

Wolters Kluwer Medknow

SMOFlipid®
THE MIX FOR LIFE

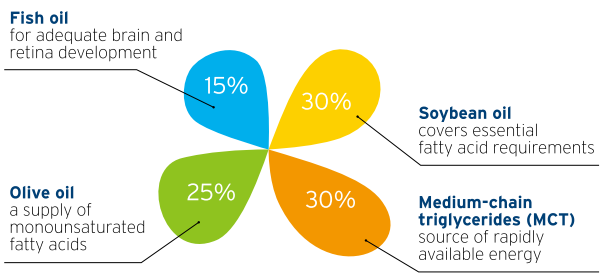
SMOFlipid®
Optimised care for the smallest patients

SMOFlipid® at a glance:

- Meets the high energy requirements of neonates
- Provision of an adequate supply of DHA (docosahexaenoic acid) for visual, neural, and mental development
- Favourable fatty acid pattern – More similar to human umbilical cord blood and human milk vs other lipid emulsions
- Improved antioxidant status [1,2]
- Positive impact on liver parameters [2-5]
- Promotes better weight gain and other health benefits [5,6]
- Safe and well tolerated [1,3,4,6]

References:
1. Deshpande G, Simmer K, Deshmukh M. J Pediatr Gastroenterol Nutr 2014;58(2):177-182.
2. Skouroliakou M, Konstantinou D, Koutri K et al. Eur J Clin Nutr 2010;64(9):940-947.
3. Rayyan M, Devlieger H, Jochum F et al. J Parenter Enteral Nutr 2012;36(1):81-94.
4. Tomsits E, Pataki M, Tölgyesi A et al. J Pediatr Gastroenterol Nutr 2010;51(4):514-521.
5. Skouroliakou M, Konstantinou D, Agakidis C et al. Nutr Clin Pract 2012;27(6):817-824.
6. Vlaardingerbroek H, Vermeulen MJ, Carnielli VP et al. J Pediatr Gastroenterol Nutr2014;58(4):417-427.
7. Biesalski HK. Vitamin E requirements in parenteral nutrition. Gastroenterology 2009; 137(5):92-104.

Meeting the special needs of neonates: A lipid emulsion combining the benefits of four different oils



+ additional vitamin E
(approx. 200 mg α-tocopherol/liter) to counteract lipid peroxidation and oxidative stress[7]

SMOFlipid® is as safe and well tolerated as soybean oil emulsion, beneficially influencing the fatty acid profile. Clinical studies and years of experience support the evidence of the positive health impacts of SMOFlipid.

SmofKabiven® contains SMOFlipid
Now approved for children ≥ 2 years

FRESENIUS KABI
caring for life

Fresenius Kabi Hong Kong Ltd.
Room 5001-5027, 50/F, Sun Hung Kai Centre,
30 Harbour Road, Wanchai, Hong Kong
Tel : (852) 2152 1330 Fax : (852) 2119 0815
www.fresenius-kabi.com

HK-DA-162-2020

Print ISSN: 2543-0343, E-ISSN: 2543-0351

Pediatric Respirology and Critical Care Medicine

Official Journal of Asian Paediatric Pulmonology Society, Hong Kong Society of Paediatric Respirology and Allergy, and Taiwan Society of Pediatric Pulmonology and Critical Care Medicine

Editorial Board

General Information

The journal

Pediatric Respirology and Critical Care Medicine is a journal for pediatricians to discuss the latest clinical practice and research in pediatrics and child health. It is the official Journal of Asian Paediatric Pulmonology Society, Hong Kong Society of Paediatric Respirology and Allergy, and Taiwan Society of Pediatric Pulmonology and Critical Care Medicine. The journal's full text is available online at http://www.prccm.org. The journal allows free access (Open Access) to its contents and permits authors to self-archive final accepted version of the articles on any OAI-compliant institutional/subject-based repository.

Abstracting and indexing information

The journal is registered with the following abstracting partners: Baidu Scholar, CNKI (China National Knowledge Infrastructure), EBSCO Publishing's Electronic Databases, Exlibris – Primo Central, Google Scholar, Hinari, Infotrieve, National Science Library, Netherlands ISSN center, ProQuest, TdNet, Wanfang Data.

Information for authors

The journal does not charge for submission, processing or publication of manuscripts and even for color reproduction of photographs. Please check http://www.prccm.org/contributors.asp for details. All manuscripts must be submitted online at http://www.journalonweb.com/prcm.

Advertising policies

The journal accepts display and classified advertising. Frequency discounts and special positions are available. Inquiries about advertising should be sent to Medknow Publications, advertise@medknow.com. The journal reserves the right to reject any advertisement considered unsuitable according to the set policies of the journal.

The appearance of advertising or product information in the various sections in the journal does not constitute an endorsement or approval by the journal and/or its publisher of the quality or value of the said product or of claims made for it by its manufacturer.

Permissions

For information on how to request permissions to reproduce articles/information from this journal, please visit www.prccm.org.

Disclaimer

The information and opinions presented in the Journal reflect the views of the authors and not of the Journal or its Editorial Board or the Society of the Publisher. Publication does not constitute endorsement by the journal. Neither the Pediatric Respirology and Critical Care Medicine nor its publishers nor anyone else involved in creating, producing or delivering the Pediatric Respirology and Critical Care Medicine or the materials contained therein, assumes any liability or responsibility for the accuracy, completeness, or usefulness of any information provided in the Pediatric Respirology and Critical Care Medicine, nor shall they be liable for any direct, indirect, incidental, special, consequential or punitive damages arising out of the use of the Pediatric Respirology and Critical Care Medicine. The Pediatric Respirology and Critical Care Medicine, nor its publishers, nor any other party involved in the preparation of material contained in the Pediatric Respirology and Critical Care Medicine represents or warrants that the information contained herein is in every respect accurate or complete, and they are not responsible for any errors or omissions or for the results obtained from the use of such material. Readers are encouraged to confirm the information contained herein with other sources.

Addresses

Editorial Correspondence
Prof. Gary Wing-kin Wong
Hong Kong Society of Paediatric Respirology and Allergy
4/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Wan Chai, Hong Kong.
E-mail: wingkinwong@cuhk.edu.hk
Website: www.prccm.org

Published by
Wolters Kluwer India Private Limited
A-202, 2nd Floor, The Qube, C.T.S. No.1498A/2
Village Marol, Andheri (East), Mumbai - 400 059, India.
Phone: 91-22-66491818
Website: www.medknow.com

Pediatric Respirology and Critical Care Medicine

Volume 4 ¦ Issue 3 ¦ July-September 2020

Contents

COVID – Resuming A New Norm

April 2021 sees the global mortality reaching 3 million and the ongoing vaccination campaign continues at full speed in the developed countries. What is worrying is the situation in developing countries where the availability of COVID vaccines remains scarce.

For children, COVID is usually mild and self-limited. However, it might not be the case for those with risk factors like young age or organ failure. Prof. E Lee and Prof. SJ Hong[1] presented a comprehensive account of the clinical spectrum of paediatric COVID. Co-infection is not uncommon in paediatric COVID leading to pneumonia and parapneumonic pleural effusion. Prof. YJ Wei and colleagues[2] reported their findings of follow-up lung functions after treatment with or without fibrinolytic. Early use of fibrinolytic was found to be associated with less abnormal lung functions at follow-up. This is certainly in line with the current recommendation regarding use of fibrinolytic in complicated pneumonia with effusion.

Other infections continue though at a lower rate because of the infection control measures. Tuberculosis is notably one of the most threatening infections especially in the developing countries already hammered by the COVID. Prof. W Anuntaseree and colleagues[3] reported an important observation that serum adenosine deaminase was not correlated with tuberculin skin test. So, MT 2 remains the investigation of choice, cheap and effective.

COVID sees a new norm in CME for doctors, i.e. telemedicine, webinar, zoom, etc. This new mode of communication allows a much cheaper and speedier information flow between doctors from different countries. I would appeal readers to send us the information about virtual conference held in your countries and we would disseminate to all members of APPS. Meanwhile, stay safe and well.

Daniel K. Ng

Department of Paediatrics, Hong Kong Sanatorium and Hospital, Hong Kong

Address for correspondence: Dr. Daniel K. Ng, Hong Kong Sanatorium and Hospital, 2, Village Road, Happy Valley, Hong Kong.
E-mail: daniel.kk.ng@hksh.com

Submitted: 19-Apr-2021
Accepted: 19-Apr-2021 **Published:** 06-May-2021

References

1. Lee E, Hong SJ. Clinical spectrum of pediatric coronavirus disease 2019 infection. Pediatr Respirol Crit Care Med 2020;4;34-6.
2. Anuntaseree W, Tangjitrapitak W, Sriphongphankul H, Ruangnapa K, Saelim K, Prasertsan P. Serum adenosine deaminase and tuberculin skin test in children with tuberculosis contact. Pediatr Respirol Crit Care Med;2020;4:37-40.
3. Wei YJ, Ju YT, Hsieh ML, Wu MH, Wu JM, Wang JN. A follow-up study for pulmonary function evaluation in children with complicated parapneumonic effusion. Pediatr Respirol Crit Care Med 2020;4:41-5.

Access this article online

Quick Response Code:

Website: www.prccm.org

DOI: 10.4103/2543-0343.315581

How to cite this article: Ng DK. COVID – Resuming a new norm. Pediatr Respirol Crit Care Med 2020;4:33.

Review Article

Clinical Spectrum of Pediatric Coronavirus Disease 2019 Infection

Eun Lee[1], Soo-Jong Hong[2]

[1]Department of Pediatrics, Chonnam National University Medical School, Chonnam National University Hospital, Gwangju, [2]Department of Pediatrics, Childhood Asthma Atopy Center, Humidifier Disinfectant Health Center, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

Abstract

Since December 2019, coronavirus disease 2019 (COVID-19) cases have been reported. The clinical features of COVID-19 in children are different from those in adults including morbidity and mortality. Even in infants and children, the clinical features are different according to ages in some cases. The children are commonly coinfected to diverse respiratory viruses, and therefore physicians, who take care of infants and children infected with COVID-19, have to consider diverse clinical aspects in their patients infected with COVID-19. In this review, we have summarized the clinical features of COVID-19 in children.

Keywords: Children, clinical, coronavirus disease 2019

Approximately 2% of coronavirus disease 2019 (COVID-19) infection has been occurred in children and adolescents.[1] The clinical spectrum of COVID-19 in children is milder than that in adults.[2] Furthermore, children have better outcomes than adults. The clinical manifestation of COVID-19 is similar to that of other viral respiratory infections; therefore, differential diagnosis is challenging. In a systematic review and meta-analysis, the most common symptoms in children were cough (mean prevalence: 49%, 95% confidence interval [95% CI]: 42%–56%), followed by fever (mean prevalence: 47%, 95% CI: 41%–53%),[3] although the prevalence of common symptoms varies according to the study population [Table 1]. In addition, there was no sex difference in the COVID-19 infection in children.[3] Although children with COVID-19 have a mild clinical course, some children require hospitalization for the management of COVID-19-associated symptoms. In a previous study, of the 157 children requiring hospitalization because of COVID-19 pneumonia, 38.2% (n = 60), 56.1% (n = 88), and 3.8% (n = 6) children exhibited mild, moderate, and severe pneumonia, respectively.[4] In the Italian Pediatric Research networks, among the 130 children with COVID-19, nine (6.9%) children required intensive care and one (0.8%) children with cerebral palsy required intubation; however, none of the children died.[5] In a multinational and multicenter cohort study in Europe involving 582 children and adolescents (mean age: 5.0 years, interquartile range [IQR] 0.5–12.0 years) infected with COVID-19, one (0.2%) child required extracorporeal membrane oxygenation.[6] Further, 8% (n = 48) of children required intensive unit care and 4% (n = 25) of children required mechanical ventilation for a median of 7 days.[6] In addition, four children died (case fatality rate: 0.69%, 95% CI: 0.20–1.82);[6] the severity of COVID-19 in this study slightly higher than the study performed in Italy.[6] Based on the finding of several studies on COVID-19 infection in children,[3-8] children with COVID-19 present with mild clinical symptoms; however, few children, especially those with comorbidities such as neurologic or respiratory diseases, experience severe clinical symptoms requiring intensive care with respiratory support.

Children of all ages are susceptible to COVID-19 infection. However, the clinical features of COVID-19 can differ

Address for correspondence: Dr. Soo-Jong Hong, Department of Pediatrics, Childhood Asthma Atopy Center, Humidifier Disinfectant Health Center, Asan Medical Center, University of Ulsan, College of Medicine, 88, Olympic-Ro 43-Gil, Songpa-Gu, Seoul 05505, Republic of Korea.
E-mail: sjhong@amc.seoul.kr

Submitted : 12-Oct-2020 **Revised :** 13-Oct-2020
Accepted : 27-Nov-2020 **Published :** 06-May-2021

How to cite this article: Lee E, Hong SJ. Clinical spectrum of pediatric coronavirus disease 2019 infection. Pediatr Respirol Crit Care Med 2020;4:34-6.

Access this article online

Quick Response Code:

Website: www.prccm.org

DOI: 10.4103/prcm.prcm_14_20

Table 1: Clinical characteristics of COVID-19 infection in children based on previous studies

Symptoms of COVID-19 infection in children[3]	Mean prevalence (95% CI) (%)
Cough	49 (42-56)
Fever	47 (41-53)
Sore throat	36 (30-42)
Vomiting or diarrhea	17 (12-21)
Rhinorrhea	9 (5-12)
Pneumonia	60 (54-66)
Intensive care	4 (1-6)
Prevalence of pneumonia severity in children requiring hospitalization because of COVID-19 infection[4]	
Mild	38.2
Moderate	56.1
Severe	3.8
Symptoms of COVID-19 in neonates and infants aged<1 year[5]	
Fever	10.6
Cough	6.3
Intensive care	6.8
Mortality rate	0.6

CI: Confidence interval

according to age.[9] In a systematic review of the clinical characteristics of COVID-19 in neonates and infants aged <1 year, the most common symptom was fever (17/160, 10.6%), followed by cough (10/160, 6.3%).[9] COVID-19 in this pediatric population tends to have a more severe clinical course than that in older pediatric populations. Furthermore, compared with older children, neonates, and infants aged <1 year have an increased requirement of intensive care (11/160, 6.8%) and a higher risk of mortality (1/160, 0.6%).[9] Nevertheless, most neonates and infants aged <1 year with COVID-19 infection had favorable outcomes.[9] In neonates, transmission from family members is the most important risk factor of COVID-19 infection.[3] On the other hand, in a systematic review and meta-analysis, only 6.3% of neonates born to mothers with confirmed COVID-19 were positive for COVID-19.[3] Even in children taking immunosuppressive medications, including immunomodulators and biologics, because of diverse chronic diseases such as kidney diseases and inflammatory bowel diseases, the clinical course of COVID-19 was mild.[10]

The household transmission rate of COVID-19 is different according to the age of the first documented case within a cluster.[11] The household transmission is high if the index patient is 10–19 years of age.[11] Many children with COVID-19 infection are asymptomatic before a diagnosis of COVID-19.[2,5] The viral shedding duration is associated with the presence and degree of respiratory symptoms of COVID-19 (mean: 11 days, IQR: 9–13 days in asymptomatic children vs. mean: 17 days, IQR: 12–23 days in symptomatic children).[2] Elevated levels of C-reactive protein (>3.0 mg/L) and procalcitonin (>0.05 ng/mL) were associated with the presence of symptoms in children with COVID-19 infection.[12] Children aged <6 years, especially those who aged <6 months, are at a higher risk of a severe COVID-19 than children aged ≥6 years.[5,12]

Diverse extrapulmonary symptoms can manifest in children with COVID-19 infection. COVID-19-related diseases are less frequent and aggressive in children than in adults.[13] Gastrointestinal symptoms including vomiting and diarrhea and headache have been reported in 21.6%–23.6%[4,12] and 3.4%[4] children with COVID-19 infection, respectively, compared to adults.

Although mild respiratory symptoms have been reported in most children and adolescents with COVID-19 infection, multisystem inflammatory syndrome in children (MIS-C) has been reported as a severe manifestation associated with host innate immunity in some children with COVID-19 infection.[14,15] MIS-C is defined according to the following criteria; age <21 years, serious illness requiring hospitalization, fever (>38.0°C) or subjective fever for at least 24 h, laboratory evidence of inflammation, multisystem organ involvement, including at least two systems, confirmed COVID-19 infection, or an epidemiologic link to a person with COVID-19 infection.[14,16] In a previous study, the most commonly involved system was the gastrointestinal system (vomiting, abdominal pain, and diarrhea; 45%–92%), followed by the cardiovascular system (myocardial dysfunction: 50%–80%), the hematologic system (deep vein thrombosis or pulmonary embolism, 76%), the mucocutaneous system (74%), and the respiratory system (respiratory insufficiency, 70%).[15] Furthermore, 80% (148/186) of patients with MIS-C received intensive care, 20% (37/186) required mechanical ventilation, and 2% (2/186) died.[15] Furthermore, 40% (74/186) of patients with MIS-C exhibited features of Kawasaki disease.[15] COVID-19-associated Kawasaki-like disease is different from the typical Kawasaki disease, in which the former is accompanied by a high prevalence of gastrointestinal symptoms and Kawasaki disease shock syndrome, which is defined by the presence of circulatory dysfunction and macrophage activation syndrome.[17,18] In previous studies, coronary artery dilatations were present in 8%–24% in COVID-19-associated Kawasaki disease or Kawasaki-like disease cases.[15,18] In one study from France, all of the children with COVID-19-associated Kawasaki-like disease were discharged after a mean hospitalization duration of 8 days (range: 5–17 days).[18]

In infants aged <1 year, the prevalence of fever, cough, and runny nose was significantly lower for COVID-19-associated pneumonia than for pneumonia associated with other virus infection such as influenza.[19] In addition, one study found that the mortality rate in infants with COVID-19-associated pneumonia was lower than that, in those with influenza and other coronavirus-associated pneumonia, although there was no statistical significance.[19] In addition, individuals with COVID-19 can be coinfected with other respiratory

viruses such as *Mycoplasma pneumoniae* and bacteria;[20] the prevalence of coinfection was 5% (29/582) in a European cohort[6] and 40% (8/20) in a Chinese cohort.[20] Therefore, screening for COVID-19 in children with respiratory symptoms is required,[21] even if other pathogenic respiratory viruses or bacteria have been detected.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in china: Summary of a report of 72 314 cases from the Chinese center for disease control and prevention. JAMA 2020;323:1239-42.
2. Han MS, Choi EH, Chang SH, Jin BL, Lee EJ, Kim BN, *et al*. Clinical characteristics and viral RNA detection in children with coronavirus disease 2019 in the republic of Korea. JAMA Pediatr 2021;175:73-80.
3. Mustafa NM, A Selim L. Characterisation of COVID-19 pandemic in paediatric age Group: A systematic review and meta-analysis. J Clin Virol 2020;128:104395.
4. Wu H, Zhu H, Yuan C, Yao C, Luo W, Shen X, *et al*. Clinical and immune features of hospitalized pediatric patients with coronavirus disease 2019 (COVID-19) in Wuhan, China. JAMA Netw Open 2020;3:e2010895.
5. Parri N, Magistà AM, Marchetti F, Cantoni B, Arrighini A, Romanengo M, *et al*. Characteristic of COVID-19 infection in pediatric patients: Early findings from two Italian Pediatric Research Networks. Eur J Pediatr 2020;179:1315-23.
6. Götzinger F, Santiago-García B, Noguera-Julián A, Lanaspa M, Lancella L, Calò Carducci FI, *et al*. COVID-19 in children and adolescents in Europe: A multinational, multicentre cohort study. Lancet Child Adolesc Health 2020;4:653-61.
7. Zhang C, Gu J, Chen Q, Deng N, Li J, Huang L, *et al*. Clinical and epidemiological characteristics of pediatric SARS-CoV-2 infections in China: A multicenter case series. PLoS Med 2020;17:e1003130.
8. Oualha M, Bendavid M, Berteloot L, Corsia A, Lesage F, Vedrenne M, *et al*. Severe and fatal forms of COVID-19 in children. Arch Pediatr 2020;27:235-8.
9. Raba AA, Abobaker A, Elgenaidi IS, Daoud A. Novel coronavirus infection (COVID-19) in children younger than one year: A systematic review of symptoms, management and outcomes. Acta Paediatr 2020;109:1948-55.
10. Marlais M, Wlodkowski T, Vivarelli M, Pape L, Tönshoff B, Schaefer F, *et al*. The severity of COVID-19 in children on immunosuppressive medication. Lancet Child Adolesc Health 2020;4:e17-8.
11. Park YJ, Choe YJ, Park O, Park SY, Kim YM, Kim J, *et al*. contact tracing during coronavirus disease outbreak, South Korea, 2020. Emerg Infect Dis 2020;26:2465-8.
12. Lu Y, Li Y, Deng W, Liu M, He Y, Huang L, *et al*. Symptomatic infection is associated with prolonged duration of viral shedding in mild coronavirus disease 2019: A retrospective study of 110 children in Wuhan. Pediatr Infect Dis J 2020;39:e95-9.
13. Licciardi F, Giani T, Baldini L, Favalli EG, Caporali R, Cimaz R. COVID-19 and what pediatric rheumatologists should know: A review from a highly affected country. Pediatr Rheumatol Online J 2020;18:35.
14. Dufort EM, Koumans EH, Chow EJ, Rosenthal EM, Muse A, Rowlands J, *et al*. Multisystem inflammatory syndrome in children in New York State. N Engl J Med 2020;383:347-58.
15. Feldstein LR, Rose EB, Horwitz SM, Collins JP, Newhams MM, Son MBF, *et al*. Multisystem inflammatory syndrome in U.S. children and adolescents. N Engl J Med 2020;383:334-46.
16. Whittaker E, Bamford A, Kenny J, Kaforou M, Jones CE, Shah P, *et al*. Clinical characteristics of 58 children with a pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2. JAMA 2020;324:259-69.
17. Verdoni L, Mazza A, Gervasoni A, Martelli L, Ruggeri M, Ciuffreda M, *et al*. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: An observational cohort study. Lancet 2020;395:1771-8.
18. Toubiana J, Poirault C, Corsia A, Bajolle F, Fourgeaud J, Angoulvant F, *et al*. Kawasaki-like multisystem inflammatory syndrome in children during the covid-19 pandemic in Paris, France: Prospective observational study. BMJ 2020;369:m2094.
19. Vanhems P, Endtz H, Dananché C, Komurian-Pradel F, Sanchez Picot V, Pneumonia Study GABRIEL members*. Comparison of the clinical features of SARS-CoV-2, other coronavirus and influenza infections in infants less than 1-year-old. Pediatr Infect Dis J 2020;39:e157-8.
20. Xia W, Shao J, Guo Y, Peng X, Li Z, Hu D. Clinical and CT features in pediatric patients with COVID-19 infection: Different points from adults. Pediatr Pulmonol 2020;55:1169-74.
21. Zhen-Dong Y, Gao-Jun Z, Run-Ming J, Zhi-Sheng L, Zong-Qi D, Xiong X, *et al*. Clinical and transmission dynamics characteristics of 406 children with coronavirus disease 2019 in China: A review. J Infect 2020;81:e11-5.

Original Article

Serum Adenosine Deaminase and Tuberculin Skin Test in Children with Tuberculosis Contact

Wanaporn Anuntaseree, Waroon Tangjitrapitak, Hansa Sriphongphankul, Kanokpan Ruangnapa, Kantara Saelim, Pharsai Prasertsan

Department of Pediatrics, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla, Thailand

Abstract

Background: The tuberculin skin test (TST) is used in children who have been in contact with tuberculosis (TB). The test has limitations in terms of operator variability and the need for a second visit at 48–72 h for interpretation. Serum adenosine deaminase (ADA) was studied in adults and found to have a strong correlation with TST. Until now no data are available in the pediatric population. **Objective:** To examine the correlation between serum ADA and the TST in children who had been in contact with TB. **Materials and Methods:** A prospective study was conducted at Songklanagarind Hospital in southern Thailand among children aged 2–15 years with a history of contact TB between 2016 and 2018. Serum ADA was obtained before performing the TST. Children with active TB disease were excluded from the analysis. **Results:** Sixty-seven children were enrolled. The serum ADA ranged from 9.3–43 IU/L. The overall correlation between serum ADA and TST was poor ($\rho = -0.03$, $P = 0.84$). However, a subgroup analysis excluding 32 children with TST size 0 mm and a high variation of serum ADA (10–37.6 IU/L) found that in the remaining children, serum ADA and TST had a moderate correlation with statistical significance ($\rho = 0.48$, $P = 0.004$). **Conclusions:** The correlation between serum ADA and TST in contact TB pediatric patients was poor. The cause of low correlation was due to a high variability of serum ADA level in children who had no reaction to TST.

Keywords: Latent tuberculosis infection, serum adenosine deaminase, tuberculin skin test

Introduction

The diagnosis and treatment of latent tuberculosis infection (LTBI) are key components of tuberculosis (TB) control. Children with LTBI are at high risk of developing active TB disease within 5 years after initial infection.[1] Contact investigation using a tuberculin skin test (TST) is the recommended method of identifying LTBI in children and adolescents.[2] The principle mechanism of the TST is a delayed-type hypersensitivity reaction, induced by the antigenic components of *Mycobacterium* TB (MTB).[3] A positive TST without evidence of active TB is defined as LTBI.[2] Although the TST is a simple and low-material procedure, the test has some limitations, notably operator variability and the time required, as the proper reading of the TST includes measuring and recording the diameter of the area of induration in millimeters 48–72 h after TST placement. In addition, TST specificity is reduced by the bacille Calmette-Guérin (BCG) vaccination.[4] As the test has low specificity, most positive reactions in low-risk individuals are false positives.

The interferon-gamma releasing assay (IGRA) is blood test that detects interferon-gamma released from T-lymphocytes after stimulation by MTB which has been studied as a possible alternative to the TST for the diagnosis of LTBI. A systematic review indicated that the IGRA had increased specificity for LTBI in children compared with TST, but varying sensitivities.[5] The IGRA is also much more expensive than the TST. Although the use of IGRA has been increasing, a recent study reported no clear evidence that would justify replacing the TST with the IGRA for detecting LTBI in children.[6]

Access this article online

Quick Response Code:

Website: www.prccm.org

DOI: 10.4103/prcm.prcm_12_20

Address for correspondence: Dr. Wanaporn Anuntaseree, Department of Pediatrics, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand.
E-mail: awanapor@medicine.psu.ac.th

Submitted : 29-Jun-2020 **Revised :** 04-Aug-2020
Accepted : 28-Dec-2020 **Published :** 06-May-2021

How to cite this article: Anuntaseree W, Tangjitrapitak W, Sriphongphankul H, Ruangnapa K, Saelim K, Prasertsan P. Serum adenosine deaminase and tuberculin skin test in children with tuberculosis contact. Pediatr Respirol Crit Care Med 2020;4:37-40.

Adenosine deaminase (ADA) is an enzyme that is involved in the metabolism of purine and catalyzes the deamination reaction from adenosine to inosine. There are two isoforms of ADA. ADA-1 is found in many tissues including red blood cells. ADA-2 is found only in macrophages and monocytes. The ADA-2 level is increased in patients with TB because of the stimulation of T-cell lymphocytes by mycobacterial antigens.[7] The ADA assay, which detects total ADA, has been widely used for the diagnosis of TB disease in adult due to its simplicity, low cost, and quickly available results. The specificity, sensitivity, and cut-off value in various body fluids of this assay have been studied and the results showed high accuracy for the screening test. Studies in children found that the serum activity of ADA was significantly higher in patients with TB compared to those without the disease.[8,9] However, these studies could not reveal any diagnostic value of serum ADA in LTBI.

Although serum ADA is widely used for the diagnosis of TB disease, the use of serum ADA for LTBI diagnosis is still lacking. Only one study has examined the correlation between serum ADA and TST for the diagnosis of LTBI in adults who had contact with TB patients, which reported an ADA cut point for LTBI diagnosis of 16 U/L with the sensitivity of 84% and specificity of 100%.[10] This suggests the possibility of using serum ADA as a diagnostic test for LTBI instead of TST or IGRA. However, there are to date no studies in pediatric populations to test the potential use of ADA to detect LTBI. The objective of this study was to examine the correlation of serum ADA and TST in children who had contact with a TB patient.

Materials and Methods

Study setting and design

A prospective study was conducted at the pediatric outpatient clinic of Songklanagarind Hospital, Songkhla province in southern Thailand.

Study population and sample size calculation

Children aged 2–15 years who attended at pediatric outpatient clinic from November 2016 to March 2018 with a history of contact with pulmonary TB patients were recruited. Children with immunodeficiency disease, malignancy, currently using anti-TB, or immunosuppressive medications and/or who had current respiratory symptoms or fever were excluded. The sample size was calculated based on an estimated correlation coefficient of 0.5, the total number of children required in this study was 29.

Data collection and study procedures

The children's caregivers were interviewed for a detailed history of TB contact as well as symptoms suggestive of TB and a physical examination was performed on all study subjects. Blood samples were collected to measure serum ADA using the conventional method,[11] which is a routine service in the hospital. After blood collection, a TST was performed by injection of 0.1 mL of the purified protein derivative from *Mycobacterium bovine* into the intradermal layer at the forearm and the size of any resulting induration was measured by a well-trained physician 48–72 h later. The largest transverse diameter was measured by a flexible ruler. Chest radiograph in the posteroanterior view was performed on all children and interpreted by a pediatric radiologist or pulmonologist.

Definitions

LTBI was defined as a positive tuberculin test (TST ≥10 mm) without evidence of active TB disease (normal physical examination and chest radiography).

A child was considered to have active pulmonary TB if there were any signs or symptoms suggestive of TB with abnormal chest radiography with or without positive sputum acid-fast bacilli stained or culture for TB.

Statistical analysis

EpiData version 3.1 (Odense, Denmark) was used to develop a database of all variables. The statistical analysis was performed using the R software 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria). Continuous variables are presented as mean and standard deviation (SD) or median and interquartile range (IQR) where appropriate. As the variables are not normally distributed, then the Spearman rank correlation was used for the correlational analysis. *P* values below 0.05 were considered statistically significant.

Ethical considerations

This study was approved by the Ethics Committee of the Faculty of Medicine, Prince of Songkla University, Thailand. All families were clearly informed of all study procedures before signing the consent form.

Results

Baseline characteristics of the contacted cases and index cases

During the study period, 77 children with a history of contact with TB patients were screened. Four children having TB diseases and six children having respiratory symptoms were excluded. Of the remaining 67 children who were analyzed, 46.3% were male and their mean age ± SD was 85.9 ± 44 months. Forty-five children (67.2%) were exposed to TB from their relatives. All of the children received BCG vaccine at birth. Ninety-two percent of the index cases were symptomatic and 68.7% had positive sputum acid-fast bacilli [Table 1].

Tuberculin skin test and adenosine deaminase results

The TST sizes ranged from 0 to 20 mm. Thirty-two patients (47.8%) had TST size 0 mm and 11 (16.4%) had a size deemed to indicate LTBI (TST size ≥10 mm). The serum ADA ranged from 9.3 to 43 IU/L, median 20.7 (IQR 17.4, 27.4).

The correlation between serum adenosine deaminase and tuberculin skin test

Spearman correlation indicated a poor correlation between serum ADA and TST (ρ = −0.03, *P* = 0.84) [Figure 1]. The 32 children with TST size 0 mm had a high variation of serum ADA (10–37.6 IU/L). We performed subgroup analysis by excluding these children. The result of the analysis on the remaining 35 children found that serum ADA and TST had a moderate correlation with statistical significance (ρ =0.48, *P* = 0.004) [Figure 2].

Table 1: Child and index case characteristics (*n*=67)

	n (%)
Child	
Male gender	31 (46.3)
Age (years)	
2-2.9	10 (14.9)
3-5.9	16 (23.9)
6-9	20 (29.9)
9-15	21 (31.3)
Growth	
Normal	55 (82.1)
Underweight	10 (14.9)
Obese	2 (3.0)
Index case	
Relationship with a child	
Parent	19 (28.3)
Relative	45 (67.2)
Other	3 (4.5)
Contact type	
Live in the same house	47 (70.1)
Live in separate house	20 (29.9)
Sputum AFB	
Unknown	8 (11.9)
Negative	13 (19.4)
Positive	46 (68.7)
Treatment status	
During treatment <2 weeks	44 (65.7)
During treatment ≥2 weeks	20 (29.8)
No treatment	3 (4.5)

AFB=Acid-fast bacilli

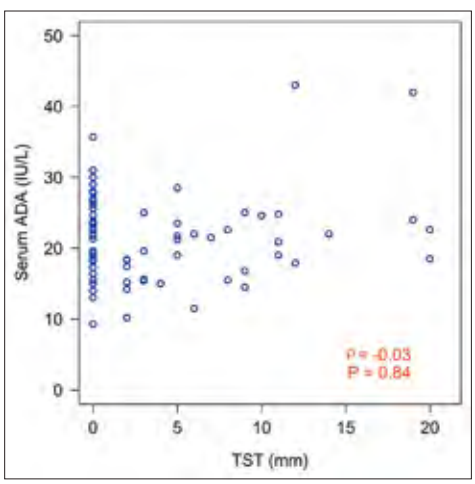


Figure 1: The overall correlation between serum adenosine deaminase and tuberculin skin test (*n* = 67).

Discussion

Our study in children who had been in contact with TB had three main findings. First, the overall correlation between serum ADA and TST was poor. Second, 47.8% of the children had no reaction with TST but had a high variation of serum ADA levels that ranged from 10 to 37.6 IU/L. Third, the subgroup correlation analysis, excluding children who had no reaction with TST, found that serum ADA and TST had a moderate correlation with statistical significance. The results of the study indicate that the factor that decreased the overall correlation between serum ADA and TST is children who had no reaction with TST.

The finding of poor overall correlation of serum ADA and TST in this study is different from a previous study in adults which found good correlation with high sensitivity and specificity. The author of that study suggested that a serum ADA of ≥16 IU/L is a strong predictor for a positive TST which can be used to diagnose LTBI.[10] However, our findings in children do not support the use of serum ADA instead of TST.

The point of interest in this study is the finding of a high variation of serum ADA in children who had no reaction to the TST. The possible causations could be explained in terms of factors affecting the TST and factors affecting serum ADA. For the factors affecting TST, the causes of the absence of a reaction to a TST can be classified into two categories. First are children who have never been exposed to MTB or who have a recent TB infection within 6–8 weeks of exposure. Second are false-negative results due to various reasons including age younger than 2 years, the presence of viral or bacterial infections, severe malnutrition, having diseases affecting lymphoid organs, and immunosuppressive drug use.[12] In our study, we excluded

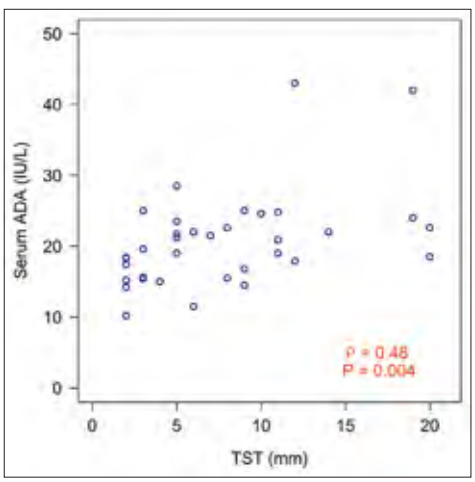


Figure 2: The correlation between serum adenosine deaminase and tuberculin skin test excluding children with tuberculin skin test size 0 mm (*n* = 35).

children who had conditions that could cause false-negative results from the study, so the remaining possibility is the first category, children who have never been exposed to MTB or who have a recent TB infection. However, we could not distinguish between these two conditions definitely, because we did not perform a follow-up TST to determine the tuberculin conversion.

For the factors affecting serum ADA, an increase in ADA activity can be seen in diseases associated with cellular system stimulation, such as viral infection, typhoid fever, infectious mononucleosis, liver disease, and malignancies.[13] In our study, we excluded sick children from the study recruitment, leaving the question of whether the increased serum ADA could be the result of TB infection.

When considering the negative TST together with high serum ADA, we arrived at a new hypothesis: Is it possible that serum ADA may be more sensitive and respond earlier to MTB exposure than TST in the pediatric population? There is some supporting evidence for this idea. In our study, we found that 65.7% of the index cases were during the first 2 weeks of treatment which could imply that the child has recently exposure. Furthermore, we found a moderate correlation between serum ADA and children who reacted to the TST. Hence, it is possible that serum ADA could be one of the markers of TB infection. Nevertheless, in our study, we could not definitely prove such a hypothesis. To prove that the serum ADA is more sensitive to MTB exposure than TST is challenging. Further studies with more comprehensive designs should be performed. Other screening tests such as IGRA are needed to identify the child with LTBI. Moreover, as the level of MTB exposure (the closeness and duration of exposure) is an important factor promoting airborne transmission, this should be used to test the hypothesis. If serum ADA is a better marker of TB infection than the TST, serum ADA should be correlated with the level of exposure to MTB. To test this, more extensive data collection for the levels of exposure is needed.

Our study had some limitations. First, we did not collect data on some factors associated with TST and ADA, such as recent live vaccinations which could have interfered with the results. Another limitation is that although diseases associated with high serum levels of ADA were excluded from the study, the exclusions were based on clinical manifestations which could have been missed in asymptomatic cases. In future studies, specific diagnostic tests should be performed to prevent this problem.

Conclusions

We observed a poor correlation between serum ADA and TST results in a pediatric population. These results indicate that serum ADA cannot replace the TST for the screening of LTBI in children. Further studies are needed to examine the hypothesis that serum ADA in the pediatric population is more sensitive to MTB exposure.

Financial support and sponsorship

This work was supported by the Faculty of Medicine, Prince of Songkla University, Thailand.

Conflicts of interest

There are no conflicts of interest.

References

1. World Health Organization. Latent tuberculosis infection: Updated and consolidated guidelines for programmatic management. 2018. Available from: https://apps.who.int/iris/bitstream/handle/10665/260233/9789241550239-eng.pdf;jsessionid=5657F195BD58E0D4771243343D43500F?sequence=1. [Last accessed on 2020 Sep 23].
2. Pediatrics Tuberculosis Collaborative Group. Targeted tuberculin skin testing and treatment of latent tuberculosis infection in children and adolescents. Pediatrics 2004;114:1175-201.
3. Huebner RE, Schein MF, Bass JB Jr. The tuberculin skin test. Clin Infect Dis 1993;17:968-75.
4. Seddon JA, Paton J, Nademi Z, Keane D, Williams B, Williams A, *et al*. The impact of BCG vaccination on tuberculin skin test responses in children is age dependent: Evidence to be considered when screening children for tuberculosis infection. Thorax 2016;71:932-9.
5. Zwerling A, van den Hof S, Scholten J, Cobelens F, Menzies D, Pai M. Interferon-gamma release assays for tuberculosis screening of healthcare workers: A systematic review. Thorax 2012;67:62-70.
6. Machingaidze S, Wiysonge CS, Gonzalez-Angulo Y, Hatherill M, Moyo S, Hanekom W, *et al*. The utility of an interferon gamma release assay for diagnosis of latent tuberculosis infection and disease in children: A systematic review and meta-analysis. Pediatr Infect Dis J 2011;30:694-700.
7. Gakis C. Adenosine deaminase (ADA) isoenzymes ADA1 and ADA2: Diagnostic and biological role. Eur Respir J 1996;9:632-3.
8. Kuyucu N, Karakurt C, Bilaloğlu E, Karacan C, Teziç T. Adenosine deaminase in childhood pulmonary tuberculosis: Diagnostic value in serum. J Trop Pediatr 1999;45:245-7.
9. Mishra OP, Yusaf S, Ali Z, Nath G, Das BK. Adenosine deaminase activity and lysozyme levels in children with tuberculosis. J Trop Pediatr 2000;46:175-8.
10. Phuenpathom W. The correlation of serum adenosine deaminase and tuberculin test for diagnosis of latent tuberculosis in close contact persons. Am J Respir Crit Care Med 2017;195:A3995.
11. Giusti G, Galanti B. Rapid colorimetric method for determination of some deaminase activities. Boll Soc Ital Biol Sper 1966;42:1312-6.
12. Lewinsohn DM, Leonard MK, LoBue PA, Cohn DL, Daley CL, Desmond E, *et al*. Official American Thoracic Society/infectious diseases society of America/centers for disease control and prevention clinical practice guidelines: Diagnosis of tuberculosis in adults and children. Clin Infect Dis 2017;64:111-5.
13. Salmanzadeh S, Tavakkol H, Bavieh K, Alavi SM. Diagnostic value of serum adenosine deaminase (ada) level for pulmonary tuberculosis. Jundishapur J Microbiol 2015;8:e21760.

Original Article

A Follow-Up Study for Pulmonary Function Evaluation in Children with Complicated Parapneumonic Pleural Effusion

Yu-Jen Wei[1], Ying-Tzu Ju[1], Ming-Lin Hsieh[1], Ming-Ho Wu[2], Jing-Ming Wu[1], Jieh-Neng Wang[1]

[1]Department of Pediatrics, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, [2]Department of Surgery, Tainan Municipal Hospital, Tainan, Taiwan

Abstract

Objectives: Although children with complicated parapneumonic effusions (CPEs) clinically improve within weeks after being discharged from the hospital, it remains unclear whether the injury and subsequent repair of the damaged lung allow a full return to premorbid lung function. We investigated the pulmonary function status in children whose CPE had been treated with different modalities. **Patients and Methods:** We therefore enrolled forty patients with a history of CPE: (1) patients treated with systemic antibiotics and conventional chest tube therapy only (control Group 1, $n = 11$); (2) patients treated with systemic antibiotics, conventional chest tube therapy, and intrapleural fibrinolytic therapy (Group 2, $n = 20$); and (3) patients treated with surgical intervention in addition to prior medical treatment (Group 3, the surgical rescue group, $n = 9$). Pulmonary function tests were done when patients had been discharged at least for 1 year. We used a spirometry test for pediatric pulmonary functions. **Results:** The basic demographic data of the three groups were not significantly different. The forced volume vital capacity (FVC) and forced expiratory volume in 1 s (FEV1) were significantly higher in Group 2 patients (percentage of the predicted value in FVC: 87.6% ± 8.5% versus 79.2% ± 13.4% (Group 1) vs. 77.6% ± 9.0% (Group 3)). Significantly, fewer Group 2 patients had abnormal pulmonary function ($P < 0.05$). **Conclusions:** Our data support a growing body of evidence that empyema in children may lead to reduced lung function later in life for a subset of patients.

Keywords: Complicated parapneumonic effusions, empyema, intrapleural fibrinolytic therapy, pulmonary function, surgical therapy

Introduction

Pleural effusions are common complications of pediatric bacterial pneumonias. They occur in 21%–91% of cases.[1,2] Failure to control the pleural process may lead to progressive disease and complicated parapneumonic effusions (CPEs) or empyema.[3-5] Children with CPE typically have compromised gas exchange, which must be managed with several days of hospitalization using systemic antibiotic treatment, chest tube drainage, intrapleural fibrinolytic therapy, or surgical intervention.[6] While most children clinically improve within a few weeks after they have been discharged from the hospital, it remains unclear whether the injury and subsequent repair of the damaged lung allow a full return to premorbid lung function.

There is increasing evidence that lower respiratory tract infections in childhood are associated with subsequent reduced lung function.[7-10] However, studies[11-14] on pulmonary function tests (PFTs) in children who have had empyema or pleural effusions report inconsistent findings, and not all studies on PFTs in children have found abnormalities after empyema.[15,16] Moreover, the dearth of follow-up pulmonary function studies preclude comparing the efficacy of different CPE treatment modalities. Our previous studies[17,18] showed that intrapleural fibrinolytic treatment is a safe and effective adjunct therapy, and that it should be attempted early on, when children are first diagnosed with CPE.

We hypothesized that breaking down the formation of fibrous pleural loculations as early as possible prevented additional

Access this article online

Quick Response Code:

Website: www.prccm.org

DOI: 10.4103/prcm.prcm_15_20

Address for correspondence: Dr. Jieh-Neng Wang, Department of Pediatrics, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, 138 Sheng Li Road, Tainan 70428, Taiwan.
E-mail: jiehneng@mail.ncku.edu.tw

Submitted: 14-Oct-2020 **Revised:** 21-Dec-2020
Accepted: 12-Jan-2021 **Published:** 06-May-2021

How to cite this article: Wei YJ, Ju YT, Hsieh ML, Wu MH, Wu JM, Wang JN. A follow-up study for pulmonary function evaluation in children with complicated parapneumonic pleural effusion. Pediatr Respirol Crit Care Med 2020;4:41-5.

lung damage. We therefore wanted to follow-up our previous patients by investigating the pulmonary function status in these children who recovered from CPE managed using different treatment modalities.

Patients and Methods

Patient selection

Potential study participants admitted to National Cheng Kung University Hospital for CPE between January 1, 1992, and January 31, 2005, were identified from our existing patient database.[17,18] Inclusion criteria based on the current definitions of CPE that required chest tube drainage included at least one of the following characteristics of pleural effusion: PH <7.2, glucose <40 mg/dL, total protein >5 g/dL, lactate dehydrogenase >1,000 IU/L, a grossly purulent appearance, or a positive Gram stain.[17-19] The exclusion criteria were one or more of the following: age <5 years at the time of the pulmonary function evaluation, discharged from the hospital because of CPE when <1 year old, or a medically significant history of diseases that affect lung function (excluding mild intermittent asthma). Patients who met the inclusion criteria were sent a letter asking whether they would be willing to participate in the study.

We divided the patients into three groups based on previous studies: those who had been given (1) systemic antibiotics plus conventional chest tube therapy only (conventional group); (2) systemic antibiotics, conventional chest tube therapy, and early intrapleural fibrinolytic therapy (either streptokinase or urokinase) (fibrinolytic Group); and (3) open chest surgical intervention (decortication, empyemectomy, or both) in addition to prior medical therapy (Surgical Rescue Group). The surgical intervention was done after 7 days of persistent fever (body temperature >38.0°C) despite appropriate therapy or because of a lung abscess proved by computer tomography of the chest. Indications for surgery remained the same during the entire study period.[17,18] To verify the referenced normal data in Zapletal *et al*.,[20] we enrolled thirty healthy age-matched children as a local control group.

Patients participating in the study filled in a questionnaire on their respiratory symptoms and medications since hospital discharge and were given a physical examination and a PFT. Their previous admission charts were reviewed to collect the basic information. The study protocol was approved by our institutional review board, and written informed consent was obtained from the patients' parents.

Pulmonary function testing

Spirometry, using standard procedures recommended by the American Thoracic Society (ATS),[21] was used to test pulmonary function in all participants (Model 2000 *Easy-One* Spirometer; NDD Medical Technologies, Andover, MA).[22] Each child was briefly instructed on the particulars of the test by the same technician, who was blinded to each patient's clinical history. Each testee's nose was sealed manually or with appropriately sized spirometry nose clips. All PFTs were completed between July 1 and September 30, 2006. All measured indices for spirometry are expressed as a percentage of the predicted normal values based on the results reported in Zapletal *et al*.[20]

Interpretation of pulmonary function test

Spirometry results that did not meet the ATS criteria for acceptability and reproducibility were excluded from the analysis.[23] Each participant's lung function test result was classified as *normal*, *obstructive,* or *restrictive.* We defined obstructive function as a predicted forced expiratory volume in 1 s (FEV_1)/forced volume vital capacity (FVC) ≤80% with either a predicted FEV_1 of ≤80% or a predicted mean forced expiratory flow during the middle half of the FVC ($FEF_{25–75}$) of ≥65%. The definition for restrictive function was an FVC ≤80%, with a normal or elevated FEV_1/FVC.[12]

Statistical analysis

We used a one-way ANOVA with *post hoc* test to compare, between each pair of groups, continuous variables: age at illness, age at PFT, body weight, body height, length of hospital stay for CPE, fever duration after initial treatment, and pulmonary function parameters. To compare category variables such as gender, CPE etiologies, and the number of patients with abnormal pulmonary function, we used a Chi-square test. For numbers <5, we used Fisher's exact test. Statistical significance was set at $P < 0.05$. Data are means ± standard deviation.

Results

From January 1, 1992, to January 31, 2005, we identified 72 patients who met our stipulated definition of CPE and who had received a complete course of treatment in our hospital. Forty-nine (68%) responded to our invitation and agreed to participate in this study. Five of the 49 had PFTs that did not conform to ATS guidelines, three had active symptoms of current respiratory disease, and one had a history of persistent asthma controlled with medication; all nine were thus excluded from the analysis. We finally enrolled and analyzed forty participants (16 boys and 24 girls; age range: 61–178 months; mean age: 90.1 ± 22.7 months).

The mean age at the time of illness was 43.5 ± 21.7 months (range: 8–130 months). There were 11 participants in the conventional Group, 20 in the fibrinolytic Group (11 had been given streptokinase, and 9 had been given urokinase), and 9 in the surgical rescue group (seven had been given conventional treatment before surgery and two had been given fibrinolytic therapy before surgery). In the surgical rescue group, eight participants had been given a lobectomy for lung abscess, and one had been given decortication only. Twenty (50%) participants had manifested culture-proven bacterial pathogens (*Streptococcus pneumoniae* [*n* = 17], *Pseudomonas aeruginosa* [*n* = 2], and *Staphylococcus aureus* [*n* = 1]). The physical examinations for all participants were normal, and all were clinically asymptomatic [Table 1]. Although participants in the surgical rescue group were significantly younger at the time of their illness, and the time from hospital discharge to the test was significantly shorter in the fibrinolytic Group, the age at PFT, gender, body weight, and body height did not significantly differ.

Table 1: Clinical characteristics and demographic data

	Group 1 ($n=11$)	Group 2 ($n=20$)	Group 3 ($n=9$)	Nonparticipants ($n=32$)
Gender (male/female)	5/6	6/14	5/4	20/12
Age at illness (months)	41.5±19.3	51.2±23.0	28.9±13.4$^{\mp}$	44.8±34.2
Duration of fever before admission (days)	6.4±3.3	6.5±3.6	5.0±3.6	7.0±3.4
White blood cell count (k/cm^2)	19163±6378	20035±14460	13578±4459	20871±11218
C-reactive protein (mg/L)	243.1±127.6	274.8±93.3	310.6±96.3	242.1±180.5
Light's classification (number of patients)	Class 3 (3)¶	Class 3 (4)¶	Class 3 (0)¶	Class 3 (13)¶
	Class 4 (7)¶	Class 4 (11)¶	Class 4 (3)¶	Class 4 (12)¶
	Class 5 (0)¶	Class 5 (2)¶	Class 5 (2)¶	Class 5 (1)¶
	Class 6 (1)	Class 6 (3)	Class 6 (4)	Class 6 (6)
Pleural effusion total protein (g/dl)	3.46±1.03	3.80±0.65	3.98±0.89	4.01±1.09
Pleural effusion lactate dehydrogenase (IU/L)	6284±4222	7422±3843	16549±11725	5622±6084
Total admission days (days)	14.7±5.1	15.5±5.2	23.4±9.2	15.0±4.3
Empyema culture results (number of patients)	*S. pneumoniae* (5)	*S. pneumoniae* (6)¶ *P. aeruginosa* (1)¶ *S. aureus* (1)	*S. pneumoniae* (6)¶ *P. aeruginosa* (1)¶	*S. pneumoniae* (8) *S. aureus* (2)¶ Group A *Streptococcus* (1)¶
Time from discharge to test (months)	57.1±14.1	34.3±10.1*,¶	61.0±23.9	N/A
Age at PFT (months)	98.7±17.8	85.5±24.1	89.9±24.3	N/A
Body weight at PFT (kg)	28.1±7.1	25.6±8.9	25.2±7.5	N/A
Body height at PFT (cm)	129.3±9.7	121.7±11.1	124.6±12.1	N/A
Lung parenchyma damage	Lung abscess (1)¶ Necrotizing poneumonia (1)¶	Lung abscess (2)¶ bronchopleural fistula (1)¶	Lung abscess (8)¶ Bronchopeural fistula (1)¶	

*P<0.05 (Group 2 compared with Group 3), ¶P<0.05 (Group 1 compared with Group 2), $^{\mp}P$<0.05 (Group 1 and 2 compared with Group 3).
PFT=Pulmonary function test, *S. pneumonia=Streptococcus pneumonia, S. aureus=Staphylococcus aureus, P. aeruginosa=Pseudamonus aeruginosa*

Thirty healthy children (15 boys and 15 girls; age range: 60–146 months; mean age: 84.4 ± 25.1 months) were enrolled as the local control group. There were no significant differences between the local control group and the fibrinolytic group. Both FVC and FEV_1 were significantly higher in the fibrinolytic group than in the surgical rescue group and conventional group (percentage of the predicted value in FVC: 87.6 ± 8.5 vs. 77.6 ± 9.0 vs. 79.2 ± 13.4; percentage of the predicted value in FEV_1: 89.7 ± 10.9 vs. 75.1 ± 17.4 vs. 80.5 ± 16.2) [Table 2]. Although FVC, FEV1, $FEF_{25–75}$, FEF_{25}, and FEF_{50} were higher in the conventional group than in the surgical rescue group, the differences were not significant. The fibrinolytic group had significantly fewer participants with abnormal pulmonary function than did the other two groups [Table 3; $P < 0.05$]. The proportion of parenchyma damage is higher in surgical group.

Discussion

Although empyema is not unusual in either adults or children, there are some differences. Empyema is rarely associated with any mortality in children in developed countries, and the long-term survival is excellent with surgical or medical treatment.[24-26] Therefore, attention should be paid to the recovery of pulmonary function. In this study, we found that up to 25% of children with CPE were classified as having abnormal pulmonary function, although they remained asymptomatic even after they had been discharged from hospital for at least 1 year. Our data support a growing body of evidence that, for a subset of patients, pediatric empyema leads to reduced lung function later in life.

Among studies[11,12,14-16,27] that have addressed the long-term outcomes of children who recovered from empyema, the most consistent findings are a complete clinical recovery with no residual symptoms, and a complete return to normal of chest X-rays. One study[26] found that even at 6 months posttreatment for empyema, nearly 90% of patients had abnormal chest X-rays; a more recent study[28] that reviewed ventilation-perfusion scans reported that the scan data were nearly normal.[28] Gocmen *et al*.[15] reported that patients given only conservative treatment had normal pulmonary function 3 months posttreatment, and Hoff *et al*.[16] reported normal pulmonary function in children with empyema treated with decortication. Other studies[12,14] reported evidence of restrictive patterns of lung function in children with a history of empyema. In the current study, although lung function was normal in most patients 2 years after discharge, ten of the forty patients still had evidence of abnormal pulmonary function (restrictive or obstructive pattern). Three possible reasons for the different findings in these studies are dissimilarities in PFT equipment, different reference standards, and a lack of consensus pediatric guidelines for defining obstructive and restrictive PFT patterns. Differences in the patient populations studied, including the severity of the pleural inflammation at the time of illness and the infectious agents causing the effusions, may also have contributed to the long-term effects on pulmonary function in

Table 2: Pulmonary function data

	Group 1 (n=11)	Group 2 (n=20)	Group 3 (n=9)	Healthy control group (n=30)
FVC (percentage of predicted value)	79.2±13.4	87.6±8.5*,¶	77.6±9.0	93.0±4.2
FEV_1 (percentage of predicted value)	80.5±16.2	89.7±10.9*,¶	75.1±17.4	93.4±8.7
FEV_1/FVC (percentage of predicted value)	97.8±8.2	99.4±9.3	91.9±14.3	100.3±6.6
FEF_{25-75} (percentage of predicted value)	84.4±14.4	88.4±16.0	75.8±12.9	91.7±5.8
FEF_{25} (percentage of predicted value)	85.3±10.1	87.0±12.3	81.1±14.5	89.8±8.4
FEF_{50} (percentage of predicted value)	82.3±13.6	89.5±16.6	80.8±13.7	92.2±7.6
FEF_{75} (percentage of predicted value)	80.3±11.5	83.8±14.2	82.7±16.7	86.9±6.5
PEF (percentage of predicted value)	85.4±11.9	87.2±8.2	82.1±15.7	90.2±7.7

*P<0.05 (Group 1 compared with Group 2), ¶P<0.05 (Group 2 compared with Group 3). FVC=Forced vital capacity, FEV_1=Forced expiratory volume in 1 s, FEF=Forced expiratory flow, FEF_{25-75}=Mean forced expiratory flow between 25% and 75% of FVC, FEF_{25}=Instantaneous forced expiratory flow when 25% of the FVC has been expired, FEF_{50}=Instantaneous forced expiratory flow when 50% of the FVC has been expired, FEF_{75}=Instantaneous forced expiratory flow when 75% of the FVC has been expired, PEF=Peak expiratory flow

Table 3: Number of patients with normal and abnormal pulmonary function

	Group 1 (n=11)	Group 2 (n=20)	Group 3 (n=9)	Total
Number of normal PFT	8	18	4	30
Number of abnormal PFT	3	2*	5	10
Restrictive type PFT	2	1	2	5
Obstructive type PFT	1	1	3	5

*P<0.05 (Fisher's exact test). PFT=Pulmonary function test

these study populations. In the present study, the initial clinical parameters in the surgical rescue group were more severe than in the other two groups, which may also be a morbidity cofactor for abnormal pulmonary function. In addition, there might have been a degree of selection bias in the study because the participants were not randomly selected patients but volunteers.

In this study, participants in the surgical rescue group had the lowest FVC and FEV_1. A possible explanation of why this was so may be that those patients had been given surgery only after medical therapy had failed. According to our previous management policy,[17,18] surgical intervention (decortication or lobectomy) was given only after a patient had 7 days of persistent fever (body temperature >38.0°C) despite appropriate therapy or because of a lung abscess identified by a computed tomography scan of the chest. At this stage, empyema may progress through a loculated, fibrinopurulent stage to the final organizing stage.[4,5] Therefore, early intervention to lyse fibrin deposits in the pleural space may improve long-term outcomes. This may also explain why participants in this study's fibrinolytic group had a better FVC than those in the conventional group. Our previous studies[17,18] showed that fibrinolytic therapy increased the volume of chest tube drainage concurrent with clinical improvement. Intrapleural administration of fibrinolytic agents has been proved to effectively lyse fibrous pleural material and to break down septa.[17-19,26,29] However, we could not exclude that open thoracotomy itself may disrupt chest-wall mechanics and affect lung function irrespective of the underlying indication for surgery. Recently, video-assisted thoracoscopic surgery (VATS) has been proposed[30] as a less invasive surgical technique suitable for primary procedures. The exact point at which thoracoscopy becomes useful in the management of pleural sepsis remains unclear and is even less well defined than the role of fibrinolytics.[26]

In the present study, ten of the forty patients had evidence of abnormal pulmonary function (restrictive or obstructive pattern) as late as 2 years after they had been discharged from hospital. This restrictive pattern may reflect residual parenchymal or pleural disease in which loculations that bridge the parietal and visceral pleura have not completely resolved and thus prohibit full lung expansion. Another study[12] suggested that bacterial infection may injure and scar airways, which will lead to persistent obstruction in growing children. However, the limitation of lung function was mild in this subset of patients and appeared to be clinically insignificant with no abnormalities detected on physical examinations; none of the patients was taking daily respiratory medicine. To screen for high-risk patients, a follow-up PFT is, therefore, important. Spirometry is the most commonly used PFT for patients with CPE. A portable spirometer is more convenient than a standard spirometer for clinical recordings pulmonary function.[22]

The major limitation of this study is that our study population was small. Studies with much larger populations are necessary to verify our conclusions. All of our study participants underwent a single lung function assessment several years after they had been discharged from the hospital. It would have been beneficial to have begun longitudinally monitoring their lung function from soon after discharge. This would have helped us determine whether lung function initially recovers before subsequently deteriorating or whether it fails to recover at all.

Conclusions

This study showed that although all the study participants who had recovered from empyema were asymptomatic, there was still a relatively high incidence of study participants with abnormal pulmonary function, especially those who had needed and been given more invasive surgical intervention. Perhaps the latter had presented with a more severe clinical condition. Our data also indicate that early intervention to lyse fibrous pleural effusion leads to, or is at least correlated with, better pulmonary function outcomes. Because we had no follow-up pulmonary function data from patients who underwent mini-invasive procedures, such as VATS, to confirm our findings, it is necessary to evaluate the follow-up pulmonary function data of more patients who were given different types of treatments.

Acknowledgment

This work was supported by intramural grant NCKUH-10903044 from National Cheng Kung University Hospital, Tainan, Taiwan. The institute supports the pulmonary function test lab, statistical analysis, and publication charge.

Financial support and sponsorship

This study was supported by intramural grant NCKUH-10903044 from the National Cheng Kung University Hospital.

Conflicts of interest

There are no conflicts of interest.

References

1. Freij BJ, Kusmiesz H, Nelson JD, McCracken GH Jr. Parapneumonic effusions and empyema in hospitalized children: A retrospective review of 227 cases. Pediatr Infect Dis 1984;3:578-91.
2. Taryle DA, Potts DE, Sahn SA. The incidence and clinical correlates of parapneumonic effusions in pneumonococcal pneumonia. Chest 1978;74:170-3.
3. Krishnan S, Amin N, Dozor AJ, Stringel G. Urokinase in the management of complicated parapneumonic effusions in children. Chest 1997;112:1579-83.
4. Sahn SA. Use of fibrinolytic agents in the management of complicated parapneumonic effusions and empyemas. Thorax 1998;53 Suppl 2:S65-72.
5. Sahn SA. Management of complicated parapneumonic effusions. Am Rev Respir Dis 1993;148:813-17.
6. Hardie WD, Roberts NE, Reising SF, Christie CD. Complicated parapneumonic effusions in children caused by penicillin-nonsusceptible *Streptococcus pneumoniae*. Pediatrics 1998;101:388-92.
7. Kjellman B. Pulmonary function in children with *Mycoplasma pneumoniae* pneumonia. Infection 1976;4:71-4.
8. Noble V, Murray M, Webb MS, Alexander J, Swarbrick AS, Milner AD. Respiratory status and allergy nine to 10 years after acute bronchiolitis. Arch Dis Child 1997;76:315-9.
9. Johnston ID, Strachan DP, Anderson HR. Effect of pneumonia and whooping cough in childhood on adult lung function. N Engl J Med 1998;338:581-7.
10. Johnston ID. Effect of pneumonia in childhood on adult lung function. J Pediatr 1999;135:33-7.
11. McLaughlin FJ, Goldmann DA, Rosenbaum DM, Harris GB, Schuster SR, Strieder DJ. Empyema in children: Clinical course and long-term follow-up. Pediatrics 1984;73:587-93.
12. Kohn GL, Walston C, Feldstein J, Warner BW, Succop P, Hardie WD. Persistent abnormal lung function after childhood empyema. Am J Respir Med 2002;1:441-5.
13. Fishman AP, Elias JA, Fishman JA, Grippi MA, Kaiser LR, Senior RM, editors. Fishman's Pulmonary Diseases and Disorders. 3rd ed. New York, NY: McGraw Hill; 1998.
14. Redding GJ, Walund L, Walund D, Jones JW, Stamey DC, Gibson RL. Lung function in children following empyema. Am J Dis Child 1990;144:1337-42.
15. Gocmen A, Kiper N, Toppare M, Ozcelik U, Cengizlier R, Cetinkaya F. Conservative treatment of empyema in children. Respiration 1993;60:182-5.
16. Hoff SJ, Neblett WW 3rd, Heller RM, Pietsch JB, Holcomb GW Jr., Sheller JR, *et al*. Postpneumonic empyema in childhood: Selecting appropriate therapy. J Pediatr Surg 1989;24:659-63.
17. Yao CT, Wu JM, Liu CC, Wu MH, Chuang HY, Wang JN. Treatment of complicated parapneumonic pleural effusion with intrapleural streptokinase in children. Chest 2004;125:566-71.
18. Wang JN, Yao CT, Yeh CN, Liu CC, Wu MH, Chuang HY, *et al*. Once-daily versus twice-daily intrapleural urokinase treatment of complicated parapneumonic effusion in pediatric patients: A randomised, prospective study. Int J Clin Pract 2006;60:1225-30.
19. Robinson LA, Moulton AL, Fleming WH, Alonso A, Galbraith TA. Intrapleural fibrinolytic treatment of multiloculated thoracic empyemas. Ann Thorac Surg 1994;57:803-13.
20. Zapletal A, Samanek M, Paul T. Lung function in children and adolescents. Method, reference values. Prog Respir Res 1987;22:1-22.
21. American Thoracic Society. Standardization of Spirometry 1994 Update. Am J Respir Crit Care Med 1995;152:1107-36.
22. Mortimer KM, Fallot A, Balmes JR, Tager IB. Evaluating the use of a portable spirometer in a study of pediatric asthma. Chest 2003;123:1899-907.
23. American Thoracic Society. Lung function testing: Selection of reference values and interpretative strategies. American Thoracic Society. Am Rev Respir Dis 1991;144:1202-18.
24. Thomson AH, Hull J, Kumar MR, Wallis C, Balfour Lynn IM. Randomised trial of intrapleural urokinase in the treatment of childhood empyema. Thorax 2002;57:343-7.
25. Chapman SJ, Davies RJ. Recent advances in parapneumonic effusion and empyema. Curr Opin Pulm Med 2004;10:299-304.
26. Sonnappa S, Cohen G, Owens CM, van Doorn C, Cairns J, Stanojevic S, *et al*. Comparison of urokinase and vido-assisted thoracoscopic surgery for treatment of childhood empyema. Am J Respir Crit Care Med 2006;174:221-7.
27. Wise MB, Beaudry PH, Bates DV. Long-term follow-up of *Staphylococcal pneumonia*. Pediatrics 1966;38:398-401.
28. Mew RC, Jaffe A, Biassoni L, Sonnappa S. Ventilation-perfusion scans in children treated for empyema. Thorax 2009;64:273.
29. Simpson G, Roomes D, Heron M. Effects of streptokinase and deoxyribonuclease on viscosity of human surgical and empyema pus. Chest 2000;117:1728-33.
30. Coote N. Surgical versus non-surgical management of pleural empyema. Cochrane Database Syst Rev 2005;3:CD010651.

Erratum: Cystic Fibrosis in Asia

In the article titled "Cystic fibrosis in asia", published on pages 8-12, Issue 1, Volume 4 of Pediatric Respirology and Critical Care Medicine[1], the list of authors and affiliations is incorrectly written as:

"Shakil Ahmed[1], Gary Cheok[2], Anne E N Goh[3], Aye Han[4], SJ Hong[5], Wahyuni Indawati[6], A R M Lutful Kabir[7], SK Kabra[8], Harutai Kamalaporn[9], Hyung Young Kim[10], Shen Kunling[11], Sorasak Lochindarat[12], Mohammad Ashkan Moslehi[13], Anna Marie Nathan[14], Daniel Ng[15], Nguyen Ng The Phung[16], V Singh[17], Masato Takase[18], Rina Triasih[19], Zen-Kong Dai[20]";

"[1]Department of Pediatrics, Shaheed Suhrawardy Medical College, Dhaka, Bangladesh, India

[2]Yee Wui Medical Centre, Macau SAR, China

[3]Department of Paediatrics, KK Women's and Children's Hospital, Singapore

[4]Department of Paediatrics, University of Medicine, Yangon, Myanmar

[5]Department of Pediatrics, Childhood Asthma Atopy Center, Humidifier disinfectant Health Center, Asan Medical Center, University of Ulsan College of Medicine Seoul, Republic of Korea

[6]Respirology Division, Child Health Department, Jakarta, Indonesia

[7]Department of Pediatrics, Ad-din Women's Medical College, Dhaka, Bangladesh, India

[8]Department of Pediatrics, All India Institute of Medical Sciences, New Delhi 110029, India

[9]Department of Pediatrics, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

[10]Department of Pediatrics, Pusan National University Yangsan Hospital, Pusan, Republic of Korea

[11]Department of Respiratory, Beijing Children's Hospital, Capital Medical University, Beijing, China

[12]Department of Pediatric Intensive Care and Respiratory Medicine, Queen Sirikit National Institute of Child Health Bangkok, Thailand

[13]Pediatric Interventional Pulmonology Division, Department of Pediatric, Shiraz University of Medical Sciences, Shiraz, Iran

[14]Department of Pediatrics, University Malaya, Kuala Lumpur, Malaysia

[15]Department of Pediatrics, Hong Kong Sanatorium and Hospital, Hong Kong SAR, China

[16]Department of Pediatrics, University of Medicine and Pharmacy at Ho Chi Minh City, Vietnam

[17]Kalawati Saran Children Hospital, Lady Hardinge Medical College, New Delhi 110029, India

[18]Department of Pediatrics, Nippon Medical School Tama-Nagayama Hospital, Tokyo, Japan

[19]Department of Pediatrics, Dr. Sardjito Hospital, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia

[20]Department of Pediatrics, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Taiwan"

The correct list of authors and their affiliations should read as:

"Shakil Ahmed[1], Gary Cheok[2], Anne E N Goh[3], Aye Han[4], SJ Hong[5], Wahyuni Indawati[6], A R M Lutful Kabir[7], SK Kabra[8], Harutai Kamalaporn[9], Hyung Young Kim[10], Shen Kunling[11], Sorasak Lochindarat[12], Mohammad Ashkan Moslehi[13], Anna Marie Nathan[14], Daniel Ng[15], Nguyen Ng The Phung[16], V Singh[17], Masato Takase[18], Rina Triasih[19], Zen-Kong Dai[20] , Mahesh Babu Ramamurthy[21]";

"[1]Department of Pediatrics, Shaheed Suhrawardy Medical College, Dhaka, Bangladesh, India

[2]Yee Wui Medical Centre, Macau SAR, China

[3]Department of Paediatrics, KK Women's and Children's Hospital, Singapore

[4]Department of Paediatrics, University of Medicine, Yangon, Myanmar

[5]Department of Pediatrics, Childhood Asthma Atopy Center, Humidifier disinfectant Health Center, Asan Medical Center, University of Ulsan College of Medicine Seoul, Republic of Korea

[6]Respirology Division, Child Health Department, Jakarta, Indonesia

[7]Department of Pediatrics, Ad-din Women's Medical College, Dhaka, Bangladesh, India

[8]Department of Pediatrics, All India Institute of Medical Sciences, New Delhi 110029, India

[9]Department of Pediatrics, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

[10]Department of Pediatrics, Pusan National University Yangsan Hospital, Pusan, Republic of Korea

[11]Department of Respiratory, Beijing Children's Hospital, Capital Medical University, Beijing, China

[12]Department of Pediatric Intensive Care and Respiratory Medicine, Queen Sirikit National Institute of Child Health Bangkok, Thailand

[13]Pediatric Interventional Pulmonology Division, Department of Pediatric, Shiraz University of Medical Sciences, Shiraz, Iran

[14]Department of Pediatrics, University Malaya, Kuala Lumpur, Malaysia

[15]Department of Pediatrics, Hong Kong Sanatorium and Hospital, Hong Kong SAR, China

[16]Department of Pediatrics, University of Medicine and Pharmacy at Ho Chi Minh City, Vietnam

[17]Kalawati Saran Children Hospital, Lady Hardinge Medical College, New Delhi 110029, India

[18]Department of Pediatrics, Nippon Medical School Tama-Nagayama Hospital, Tokyo, Japan

[19]Department of Pediatrics, Dr. Sardjito Hospital, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia

[20]Department of Pediatrics, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Taiwan

[21]Department of Pediatrics, National University Hospital, National University of Singapore, Singapore"

The "How to cite this article" section should read correctly as "Ahmed S, Cheok G, N Goh AE, Han A, Hong S J, Indawati W, Lutful Kabir A R, Kabra S K, Kamalaporn H, Kim HY, Kunling S, Lochindarat S, Moslehi MA, Nathan AM, Ng D, The Phung NN, Singh V, Takase M, Triasih R, Dai ZK, Ramamurthy MB. Cystic fibrosis in asia. Pediatr Respirol Crit Care Med 2020;4:8-12".

Reference

1. Ahmed S, Cheok G, N Goh AE, Han A, Hong S J, Indawati W, Lutful Kabir A R, Kabra S K, Kamalaporn H, Kim HY, Kunling S, Lochindarat S, Moslehi MA, Nathan AM, Ng D, The Phung NN, Singh V, Takase M, Triasih R, Dai ZK. Cystic fibrosis in asia. Pediatr Respirol Crit Care Med 2020;4:8-12.

DOI: 10.4103/2543-0343.315580

Similac®
Total Comfort

LEADING THROUGH HMO INNOVATION

SIMILAC® TOTAL COMFORT

WITH 2'-FL HMO

FOR A BROAD SPECTRUM OF INTOLERANCE ISSUES

UPGRADED FORMULA

UNIQUE DUAL-PATHWAY CARBOHYDRATE BLEND
Non-competing carbohydrate pathways improve digestion and adsorption[2]

NEW
HMO NTs pHF

DUAL IMMUNE BLEND
UNIQUE COMBINATION OF PHF AND DUAL IMMUNE BLEND DESIGNED FOR **REDUCING ALLERGENICITY** AND **OPTIMIZING IMMUNE RESPONSE**

CLINICALLY PROVEN

FOR A FAST RELIEF OF GI INTOLERANCE SYMPTOMS IN **1 DAY**[1] & SUSTAINED THE IMPROVEMENT OVER **28 DAYS**[1]

Similac Mom	Similac	Similac Total Comfort	PediaSure
LACTATION COMPLETE NUTRITION FORMULA[3]	BREAKTHROUGH IMMUNE-NOURISHING HMO+ + NTs△ FORMULA	4X WITH 2'-FL HMO+ SPECIALIZED FORMULA FOR A BROAD SPECTRUM OF INTOLERANCE ISSUES	CLINICALLY PROVEN CHILD GROWTH FORMULA

*Refers to 100% Partially-Hydrolysed Whey Protein formula can help reduce the risk of cow's milk protein intolerance, 98% Lactose Free formula can help reduce the risk of lactose intolerance, 0% Palm Olein Oil formula can help reduce the risk of dry and hard stools, and the prebiotics can help soften the stools. + HMO : Human Milk Oligosaccharide 2'-FL (20 mg / 100ml), not from Human milk. △ NTs: Nucleotides (2.9 mg / 100ml) ◎ NTs: Nucleotides (Stage 1 : 5.8 mg/100 ml , stage 2 : 2.1mg / 100ml)

1.Reverri EJ, et al. 2018 2.Southgate DA, et al. Am J Clin Nutr 1995;62:2035-210S 3. Abbott Similac® Mom contains most of the nutrients mentioned in National Institutes of Health (NIH) on the important maternal nutrients during lactation, including protein, DHA (12.5mg/100ml), folic acid, and 18 vitamins and minerals. Suggest to have 2 servings per day with a balanced diet, while staying active and relaxed to support breastfeeding.

IMPORTANT NOTICE: Breastfeeding is the best source of infant nutrition. Good maternal nutrition is important for preparation and maintenance of breastfeeding. When infant formulas are to be used, a mother should be aware of the negative effect on breastfeeding along with the financial and social implications of formula feeding, the difficulty of reversing the decision not to breastfeed, and the care that must be taken to prevent partial formula feeding from interfering with lactation. A healthcare professional should be consulted before initiating formula feeding.

商品圖片只供參考。

P21-COM-1-0216

FOR HEALTHCARE PROFESSIONALS' REFERENCE ONLY

Abbott 雅培

Turn down their ***symptoms***

BE PROACTIVE. CONTROL ASTHMA

SERETIDE

salmeterol/fluticasone propionate

Safety Information: Seretide should be used with caution in patients with pre-existing cardiovascular disease.

SERETIDE

INDICATIONS Asthma *Accuhaler/Inhaler:* Regular treatment of asthma in children & adults, where the use of a bronchodilator plus an inhaled corticosteroid (ICS) is appropriate. **COPD** (Only for Adults) *Accuhaler:* SERETIDE accuhaler 50mcg/250mcg and SERETIDE accuhaler 50mcg/500mcg are indicated for the maintenance treatment of COPD, including emphysema and chronic bronchitis in patients where the use of a combination product is considered appropriate. Inhaler: SERETIDE Inhaler 25/125mcg and SERETIDE Inhaler 25/250mcg are indicated for the symptomatic treatment of patients with severe COPD (FEV1<–50% predicted normal) and a history of repeated exacerbations who have significant symptoms despite r egular beta-2 agonist bronchodilator therapy. SERETIDE is not indicated for the initiation of bronchodilator therapy in COPD. **DOSAGE AND ADMINISTRATION** For oral inhalation only. The dose should be titrated to the lowest dose at which effective control of symptoms is maintained. Patients should be given the strength of SERETIDE containing the appropriate fluticasone propionate dosage for the severity of their disease. **Asthma** *Accuhaler: Adults & adolescents ≥ 12 years:* 50mcg salmeterol (SALM) & 100mcg, or 250mcg, or 500mcg fluticasone propionate (FP) twice daily. *Children ≥ 4 years:* 50mcg SALM & 100mcg FP twice daily. *Inhaler: Adults & adolescents ≥ 12 years:* Two inhalations of 25mcg salmeterol (SALM) & 50mcg, or 125mcg, or 250mcg fluticasone propionate (FP) twice daily. *Children ≥ 4 years:* Two inhalations of 25mcg SALM & 50mcg FP twice daily. **COPD** *Accuhaler: Adults & ≥ 18 years:* 50mcg SALM & 250mcg, or 500mcg FP twice daily. *Inhaler: Adults & ≥ 18 years::* Two inhalations of 25mcg SALM & 250mcg FP twice daily or two inhalations of 25 SALM & 125mcg FP twice daily may be considered in patients who are at greater risk of inhaled corticosteroid adverse effects. **Elderly & patients with renal/hepatic impairment:** No need to adjust dose. **CONTRAINDICATIONS** Hypersensitivity to any of the ingredients. **WARNINGS AND PRECAUTIONS** Not for relief of acute symptoms. For patients with COPD cessation of therapy may be associated with symptomatic decompensation and should be supervised by a physician. If the current SERETIDE dosage failed to adequately control asthma, the patient should be reviewed by a physician. Sudden and progressive deterioration in control of asthma is potentially life-threatening and the patient should be reviewed by a physician. Do not stop treatment abruptly. Caution in patients with: thyrotoxicosis; active/quiescent pulmonary tuberculosis; history of diabetes mellitus; pre-existing cardiovascular disease; predisposing low levels of serum potassium. Systemic effects include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract and glaucoma, for asthma patients the dose of inhaled corticosteroid is titrated to the lowest dose at which effective control is maintained. There was an increased reporting of pneumonia in studies of patients with COPD receiving SERETIDE. Regular height monitoring is recommended in children receiving prolonged ICS treatment. SERETIDE Accuhaler contains lactose (which contains milk protein). **INTERACTIONS** Avoid all β-blockers in asthma patients. Concomitant use of FP and ritonavir should be avoided. Care is advised when co-administering potent CYP3A4 inhibitors (e.g. ketoconazole). **PREGNANCY AND LACTATION** Only consider use of drugs during pregnancy & lactation should if the expected benefit to the mother is greater than any possible risk to the foetus or child. No data on human fertility. Animal studies indicate no effects of fluticasone propionate or salmeterol xinafoate on male or female fertility. **ADVERSE REACTIONS** Hoarseness/dysphonia; throat irritation; candidiasis of the mouth & throat; oesophageal candidiasis; palpitations; headache; tremor; muscle cramps; cardiac arrhythmias; cutaneous hypersensitivity reactions; paradoxical bronchospasm; facial & oropharyngeal oedema; contusions. Pneumonia (in COPD patients). **OVERDOSE** If higher than approved doses of SERETIDE are continued over prolonged periods, significant adrenocortical suppression is possible.

Please refer to the SERETIDE full prescribing information for warnings, precautions, interactions, pregnancy, lactation, adverse reactions and overdose. Abbreviated PI (GDS 34 for Seretide inhalers and GDS32 for Seretide Accuhalers) Please read the full prescribing information prior to administration. Full prescribing information is available on request from GlaxoSmithKline Ltd, 23/F, Tower 6, The Gateway, 9 Canton Road, Tsimshatsui, Kowloon, Hong Kong or Level 20, AIA Tower, Nos 251A – 301 Avenida Comercial De Macau, Macau.

For adverse events reporting, please call GlaxoSmithKline Limited at (852) 3189 8989 (Hong Kong) or (853) 2871 5569 (Macau) or email to HK Adverse Event mailbox: HKAdverseEvent@gsk.com

PM-HK-FPS-ADVT-210001 (02/23)
Date of preparation: 9 Mar 2021

"Smart Pediatric Pulmonology: From Asia to the World"

APPS/TPPCC Joint Congress 2021

6th Annual Scientific Congress of Asian Paediatric Pulmonology Society (APPS)
23th Annual Conference of the Taiwan Society of Pediatric Pulmonology and Critical Care Medicine (TPPCC)
12th Annual Scientific Congress in Pediatric Pulmonology for Three Places across the Strait

Sep.18-19,2021
APPS/TPPCC Joint Congress 2021

第六屆亞洲兒童胸腔醫學會年度大會
第二十三屆台灣兒童胸腔暨重症醫學會年會
第十二屆海峽兩岸三地學術研討會

歡迎踴躍投稿

Welcome for Abstract Submission
Clinical studies, Laboratory investigations, Challenge cases are all welcome

Don't miss the opportunity to submit your abstract for the APPS 2021 and take a part in the Young Investigator Award and Top Poster Award Competition (https://www.2021-apps.com)
See you in Kaohsiung ,Taiwan in September 2021!

free registration fee with submission

Abstract Submission Date
Starting date : 2021/01/01
Deadline : 2021/07/31

Onsite and Online Hybrid Meeting

APPS
ASIAN PAEDIATRIC PULMONOLOGY SOCIETY

台灣兒童胸腔暨重症醫學會

APPS / TPPCC Joint Congress 2021

SMART PEDIATRIC PULMONOLOGY

FROM ASIA TO THE WORLD

1. 6th Annual Scientific Congress of Asian Paediatric Pulmonology Society (APPS)
2. 23th Annual Conference of the Taiwan Society of Pediatric Pulmonology and Critical Care Medicine (TPPCC)
3. 12th Annual Scientific Congress in Pediatric Pulmonology for Three Places across the Strait

Date 2021 9.18–9.19

Venue
Kaohsiung Medical University Hospital 6F, Building E

Organiser | Taiwan Society of Pediatric Pulmonology and Critical Care Medicine
Asian Paediatric Pulmonology Society

Co-organisers | Kaohsiung Medical University Hospital