413. Airway infections in children: from risk factors to treatment

P4110

Quality of life after acute bronchiolitis in infancy Leif Bjarte Rolfsjord^{1,2,3}, Håvard Ove Skjerven^{1,2}, Petter Mowinckel¹, Kai-Håkon Carlsen^{1,2}, Egil Bakkeheim¹, Karin C.L. Carlsen^{1,2}. ¹Department of Paediatrics, Oslo University Hospital, Oslo, Norway; ²Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Norway; ³Department of Paediatrics, Sykehuset Innlandet Hospital Trust, Elverum, Norway

Acute bronchiolitis, parental allergic disease, atopic eczema, male gender and parental stress are risk factors for asthma development. Quality of life (QoL) may be reduced in children with allergic disease, but prospective studies on risk factors for reduced QoL in infants are lacking.

Aim: Are asthma risk factors, apart from acute bronchiolitis associated with QoL nine months after hospitalization for bronchiolitis?

Methods: The Infant Toddler Quality of Life Questionnaire (ITQOL(TM)) was sent to parents of 405 hospitalised infants included in a randomized clinical trial testing the efficacy of racemic adrenaline, the Bronchiolitis All SE-study. The 13 domains were analyzed by multiple linear regression including age at hospitalization, gender, atopic eczema, parental asthma and parental allergic rhinitis (risk factors).

Results: Risk factors were similar for the 209 infants (mean age 13.2 months) who did and the 196 who did not return the questionnaire. Reduced QoL was found for atopic eczema (Table 1), parental asthma and female gender (four, two and one domain, respectively), but increased in children with parental allergic rhinitis (one domain).

Effect on atopic eczema on QoL adjusted for asthma risk factors

Atopic eczema associated with	Change in QoL (95% CI)	p-values
Overall health	-9.8 (-16.4, -3.1)	0.004
Growth and development	-4.5 (-8.1, -1.0)	0.01
Discomfort	-14.5 (-25.7, -3.2)	0.01
Getting along	-12.5 (-18.7, -6.2)	< 0.001

Multiple regression of the risk factors, results of atopic eczema.

Age of hospitalization did not influence any scores. Conclusion: OoL nine months after hospitalization for acute bronchiolitis was negatively associated with atopic eczema, parental asthma and female gender.

P4111

Respiratory complication in children with dengue

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Dengue, emerging infectious disease, has been presenting more severe in the last years. In children the diagnosis is difficult. The morbimortality is related to the early recognition and appropriate management. The goal is to know the clinical and laboratory features of children with dengue, hospitalized in the pediatric emergency of the Antonio Pedro University Hospital. Were analyzed from 2006 to 2011 the records of 63 children, 25 (39.7%) of them with respiratory complication. All had pleural effusion: 17 (68%) to the right and 8 (32%) bilateral. The age ranged between 2 and 12 years (mean = 8.2), the most was female 16 (64%). The symptoms were: fever, abdominal pain, vomiting and headache. All had leukopenia and 23 (92%) thrombocytopenia. Ascite was found in 19 (76%) and thickening of the gallbladder in 5 (20%). Hypoalbuminemia in 15 (60%) and enzyme liver abnormalities in 21 (84%). The analysis was similar to that reported in the literature differing only in sex.

P4112

Additive effect of air pollution particulate matter and cigarette smoke on

pneumococcal adhesion to lower airway cells <u>Reetika Suri</u>¹, Naseem Mushtaq¹, Richard Waite², Jonathan Grigg¹. ¹Centre for Paediatrics, Blizard Institute of Cell and Molecular Sciences, London, United Kingdom; ²Centre for Immunology and Infectious Disease, Blizard Institute of Cell and Molecular Science, London, United Kingdom

Air pollution particulate matter (PM) and cigarette smoke (CS) are associated with increased vulnerability of children to bacterial pneumonia. In epidemiological studies, PM and CS are considered independent variables. We previously reported that PM10 (PM diameter <10µm) increases pneumococcal adhesion to lower airway cells. Here we assessed whether PM and CS additively increase the susceptibility of airway epithelial cells to pneumococcal infection. Monolayers of the alveolar epithelial cell line A549 were exposed to sub-optimal doses of PM10 or cigarette smoke extract (CSE) for 3 hrs. The pollutants were washed off and cells exposed to Streptococcus pneumoniae for 2 hrs at a multiplicity of infection (MOI) of 100. After vigorous washing, cells were detached and lysed. Adherent bacteria were assessed by quantitative culture. Data were compared by T tests.



Both PM10 and CSE stimulated pneumococcal adhesion. An additional increase in pneumococcal adhesion was caused by PM10 and CSE combined. No decrease in viability was observed by light microscopy. The data suggests that PM10 and CSE additively increase vulnerability of airway cells to pneumococcal infection. If confirmed in animal models, additive effects of PM10 and CSE should be considered in epidemiological studies. Individuals at risk are likely to be living in countries with high PM levels and high incidence of indoor smoking.

P4113

Neutrophil count trends in BAL samples from children being investigated for chronic cough

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Introduction: Investigating probable persistent bacterial bronchitis (PBB) with a bronchoscopy allows the identification of infectious agents and quantification of cellular responses in the paediatric population who rarely expectorate sputum under the age of 10.

Methods: Bronchoscopies in children carried out 2010-11 were identified and

a retrospective case notes analysis done to identify those performed because of chronic cough or proven/probable PBB. Bronchoalveolar lavage (BAL) samples were analysed for standard bacterial culture, viral PCR and neutrophil count (%). Results: 70 bronchoscopy BALs were analysed: 18.6% positive for bacterial and viral culture (B pos/V pos); 35.7% positive for bacteria but negative for viruses (B pos/V neg); 21.4% negative for bacteria but positive for viruses (B neg/V pos); (4) was performed with one-way ANOVA and Cuzick's test for trend. For the reasons of analysis the 4 groups were ordered as follows: group 1: B pos/V pos; group 2: B pos/V neg; group 3: B neg/V pos; group 4 B neg/Vneg. The 4 groups differ significantly (means \pm sd:45.7 \pm 30.7, 18.6 \pm 21.4, 20.4 \pm 22.9, 11.6 \pm 15.2, for groups 1, 2, 3, and 4, respectively, p=0.001). Furthermore, a significant trend was found across the 4 ordered groups (p=0.003).

Conclusion: The presence of bacteria and viruses is associated with a significantly more neutrophils and thus a greater degree of inflammation than that induced by bacteria alone and could explain why recurrent viral infections are a feature of PRR

P4114

Association between rhinovirus C infection and respiratory symptom severity in an unselected pediatric population, the EUROPA-study

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Rationale: -In a paediatric population hospitalized for bronchiolitis rhinovirus (RV) type C is associated with more severe respiratory symptoms as compared to other RV genotypes (Bizzintino,ERJ,'11). RV infections in infants are linked to the development of asthma but specific clinical features of RV-C infection in the general population are unknown. We therefore aim to study the occurrence and respiratory symptom severity associated with RV-C in an unselected paediatric population.

Methods: -This is a cross-sectional study from the prospective EUROPA birth cohort, aimed at early prediction of asthma (N=1207;0-3 years). Nose and throat swabs were collected in both asymptomatic infants and infants whose parents consulted the GP for wheeze or dyspnea. RV presence was tested using a 5'UTR rtPCR with genotyping based on the VP4/VP2 region. Symptom severity was assessed by parents scoring the presence and severity of 10 symptoms (range 0-50) and by clinicians using the validated PRAM-score (range 0-12).

Results: -102 infants (13.3±5.5 months) presented with an infection of whom 53% had a positive RV PCR. RV-A, B & C were found in 35%, 4% and 24% of cases, respectively. 2/17 asymptomatic infants tested positive for RV-A. RV genotypes did not differ significantly regarding symptom severity as scored by parents ($\mu \pm SD=14\pm 6.4$; p=0.75) and clinicians (1.5±1.9; 0.33).

Conclusion: -Rhinovirus-C infection occurred in 24% of the infants and is associated with similar symptom severity as other RV-genotypes. Since RV-C appears to be commonly involved in wheezy episodes not requiring hospitalization, it's association with future development of asthma needs to be examined.

P4115

Sodium sulfite enhances rhinovirus-induced chemokine production in airway epithelial cells

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Background: Sulfur dioxide is one of the most important air pollutants that can adversely affect respiratory system. RV is a major cause of common cold and is a major risk factor responsible for the exacerbation of asthma and chronic obstructive pulmonary disease. An epidemiological study suggested that interactions between sulfur dioxide and viral infections exacerbate respiratory disease. However, little is known about the mechanism underlying these interactions.

Objective: We investigated the effects of sodium sulfite on the production of RVinduced chemokines such as IL-8, RANTES and INF-gamma inducible protein-10 (IP-10) in airway epithelial cells in vitro.

Methods: A549 airway epithelial cells were pretreated with 2,500 µM sodium sulfite for 6 h at 37° and infected with RV-7 at 1×10^4 TCID₅₀/mL for 2 h at 33°. The medium was replaced with a virus-free medium, and the cells were incubated for 40 h at 33°. Cell culture supernatants and mRNA were harvested at 24 h and 48 h after sodium sulfite treatment. Production and mRNA expression of IL-8, RANTES, and IP-10 in these harvests were assessed by ELISA and real-time PCR. Results: RV induced the production and mRNA expression of IL-8, RANTES, and IP-10 in the A549 cells. Sodium sulfite did not affect the viability of A549 cells or RV replication under our experimental conditions. When the cells were pretreated with sodium sulfite prior to RV infection, production and mRNA expression of RV-induced IL-8, RANTES, and IP-10 were enhanced with no effect on cell viability or RV replication.

Conclusion: Our results suggest that sodium sulfite may potentiate the activity of RV-induced diseases by increasing the production of IL-8, RANTES, and IP-10.

P4116

Differential responses of monolayer and differentiated airway epithelial cell cultures to NTHi infection

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The innate defence functions of the lung require a patent airway epithelium and infections are often associated with epithelial defects and phenotypic alterations. Non-typeable Haemophilus influenzae (NTHi) one of the first bacterial species to infect children, reduces innate defences, allowing further colonisation with other pathogens, including RSV. We have established NTHi infections of lung derived cell lines and primary airway cells in differentiated cultures prior to the establishment of secondary infections with RSV as a model for paediatric RSV infection. A549, H292 and primary airway epithelial cells were grown in monolayer cultures in transwell inserts. Differentiated cultures of tracheobronchial epithelial (TBE) cells were grown at the ALI using established methods. The apical compartments of established cultures were infected with increasing doses of GFP tagged NTHi and followed for up to 7 days. Infection and cell viability was determined using confocal microscopy and bacterial counts at each time point. A549 and H292 cells, and undifferentiated primary cells became heavily infected and by day 7 almost complete loss of cells was associated with a loss of viable bacteria. Cytokine array studies showed that these cultures mounted limited cytokine responses. The ALI TBE cell cultures had an enhanced ability to overcome the same bacterial infections and this was associated with a marked cytokine response. This data suggests that differentiated epithelial cell cultures have an enhanced ability to overcome bacterial infection compared to monolayer cultures of epithelial cells. This is likely due to the innate defensive shield secreted from these complex cultures

P4117

Video-assisted thoracoscopic surgery (VATS) and percutaneous drain insertion (PDI) in childhood empyema

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Introduction: Pediatric parapneumonic effusion (PPE) incidence increases. Aims: To compare different treatment options in children with PPE. Methods: Retrospective analysis of children with PPE, admitted from 01/01/2007-

30/11/2011. PPE definition: \geq 1cm fluid on US or CT, and/or an opacity on chest X-ray of \geq 50% of the hemithorax. Exclusion criteria: age <6m., trauma, thoracotomy.

PDI and VATS were performed on clinical indication. VATS was reserved for patients (pts) with insufficient clinical improvement.

Pts were treated as follows: Group A: no PDI/VATS. Group B: PDI. Group C: VATS. Group D: PDI followed by VATS.

Results: 49 pts were included, F/M=23/26, median age 3.3y (range 0.8-14.8y); 15, 12, 11, and 11, in group A, B, C, and D, resp. Age, sex ratio and inflammatory parameters were similar in all groups.

Total length of stay (LOS) was similar for groups B, C and D, but shorter for group A (22 vs 18d, p=.023) Oxygen need was also shorter in group A compared to the others (4 vs 12d, p<.001). PDI was performed earlier than VATS (4 vs 9d, p=.011). Oxygen need and fever resolved earlier after intervention in group C than in group B (3 vs 8d, p=.009 and 1 vs 6d, p=.04, resp). Time to drain removal, LOS and duration of antibiotic treatment after intervention (3 vs 6d, p=.001; 11 vs 18d, p=.004; and 10 vs 18d, p=.001) were shorter in group C than in group B. ICU stay after intervention was similar in the 3 groups.

Conclusions: VATS is a good treatment option for PDI in children with PPE. Clinical improvement was faster with VATS than with PDI, indicating that early performed VATS might shorten LOS and duration of antibiotic treatment.

P4118

Cyst hydatid patients in a pediatric pulmonology department in Turkey <u>Ayse Tana Aslan</u>, Tugba Eyuboglu. *Gazi University, Pediatric Pulmonology, Ankara, Turkey*

Human hydatid disease due to *Echinococcus granulosus* is of worldwide importance in many countries.

The aim of this study is to review our experience in pediatric pulmonary hydatid cysts focusing on clinical symptoms, location of the cyst, type of the intervention, postoperative complications and long-term results.

Between January 2007- December 2011 there were 26 patients with Cyst Hydatid Disease (CH) at Gazi University Pediatric Pulmonology Department. There were

26 patients with a mean age of 12,8 (8-18) years. Hydatid cysts were localized in the lungs in 18 patients, in the liver in 14 patients. Nine patients have lung and liver CH together. Two patients have vertebral, one patient has splenic and one patient has surrenal involvement.

The most common symptoms were cough and chest pain. Cysts were found in right lung in 6 patients, in left lung in 7 patients and bilateral in 4 patients. The cysts were perforated into the bronchia in 3 patients.

Surgical treatment was performed in 15 patients. Cystotomy plus capitonage was the most frequent administered surgical technique. The mean hospitalization time was 14 days. There were no complication related to surgery such as pneumothorax and infection. Nine patients had PAIR.

All of the patients received albendazole therapy and 6 patients received praziquantel therapy. Mean follow-up time was 17.6 (1-52) months. Six patients left the follow-up.

There were two recurrence, one patient was with pulmonary CH and the other was with vertebral CH. 18 patients continue to follow-up of without recurrence.

Cyst hydatic is an important public health problem especially in countries where it is common in agriculture and animal husbandry.

P4119

Adjunct treatment of pneumonia in children 6-18 years old using a hand held sputum induction device

sputum induction device <u>Mary Aimee Uson</u>¹, Anjanette De Leon², Bobby Balete³, Leslie Mae Domagas⁴, Joyce Raymond Punzalan⁵. ¹Department of Pediatrics, Our Lady of Lourdes Hospital, Manila, Philippines; ²Department of Pediatrics, Our Lady of Lourdes Hospital, Manila, Philippines; ³Department of Pediatrics, Our Lady of Lourdes Hospital, Manila, Philippines; ⁵UP school of Statistics, University of Philippines, Diliman, Quezon City, Philippines

Pneumonia is consistently a leading cause of mortality and morbidity in the Philippines; treatment is mainly antimicrobial. Lung Flute is a safe, hand held device that helps effective induction of sputum. The objective of this study is to evaluate the effectiveness of Lung Flute in sputum induction for relief of cough in children 6-18 years old admitted for Pediatric Community Acquired Pneumonia (PCAP) PCAP B and PCAP C. Children ages 6-18 years old admitted with a diagnosis of PCAP B or PCAP C were included. Patients diagnosed with PCAP A, PCAP D and hyperreactive airway were excluded. Each subject was enrolled to Lung Flute group or Control group by systematic randomization. Patients in the Lung Flute group used Lung Flute 3x a day in addition to the treatment provided by the physician. Pretested questionnaire on cough was answered by both groups. McNemar test was used. Of the 35 subjects (CI 80%, alpha error 0.05), there were more males than females with a mean age of 9 years old. Majority admitted were diagnosed with PCAP B in Lung Flute group (73.4%) and Control group (85%). There was significant decrease in the frequency of cough on Day 2 (p value 0.048954) and significant improvement on the quality of cough on Day 2 (p value 0.002627) and Day 3 (p value 0.022961). Significant improvement on the quality of life on Day 1 and Day 2 was seen (p value 0.0004883, p value 0.002, p value 0.0000002384). Effective sputum induction was noted in both groups but earlier improvement was seen in the Lung Flute group. Lung Flute is an effective device in sputum induction and may someday be used as adjunct treatment of pneumonia.

P4120

Clinical characteristics of pediatric patients affected with human metapneumovirus who needed hospital admittance in the western region of Guatemala

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Introduction: Human Metapneumovirus (hMPV) was described for the first time on 2001 by van den Hoogen et al. as a cause of bronchiolitis in children, although a world spread pathogen, very little is known about its epidemiological behavior in latinamerican countries.

Aim: To review the clinical characteristics of children who needed admission to our hospital due to a respiratory infection caused by hMPV.

Methods: We included in this review all pediatric patients admitted during 2010 & 2011 suffering from a viral respiratory tract infection, and had a polymerase chain reaction positive to hMPV in a nasopharyngeal aspirate, sent to the CDC in the US, for its accurate classification.

Results: We reviewed 102 clinical files. 56 were female, mean age 16 months. Three symptoms were predominant in these patients: fever (n=89), cough (n=86) and respiratory distress (n=57). An alveolar radiological pattern on chest X rays was seen in 57% of the cases. White blood cell counts were normal although a discrete neutrophilia was observed in most cases. C reactive protein mean value 27 mg.dl. None required mechanical ventilation. Mean time hospitalization was 7.4 days. There was no mortality reported in all cases. During the year 2011, no hMPV infection was recorded, despite an intesive epidemiological surveillance.

Conclusions: hMPV is still an important cause of respiratory infection in children. Even though, during this review the mortality rate was null. It called our attention the bi anual pattern of appearance of this virus, because we did not record any hMPV case on 2011, but in this 2012 we are seeing a new increase in hMPV cases in our region

P4121

Acute lower respiratory tract infection and vitamin D status in children

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Childhood acute lower respiratory infection (ALRI) is one of the most common reason for morbidity and mortality especially in developing countries. Predisposing factors include season, nutrition, suboptimal immunization, lower socioeconomic status, prematurity, underlying disease, tobacco exposure and vitamin D deficiency. Vitamin D deficiency is the 25(OH)D levels below < 20 ng/ml, whereas vitamin D insufficiency is defined as 25(OH)D 21-30 ng/ml. In a study in Turkey the incidence of vitamin D deficiency in children was found 8% and insufficiency 25 5%

In this study we aimed to describe vit D status in children with lower respiratory infection. Between November 2010 and February 2011 63 children with acute lower respiratory infection between 0.5-5 years of age and 59 age matched children without respiratory symptoms were enrolled in the study. Both study and control groups received vitamin D prophylaxis for one year and they have no predisposing factors for ALRI. Vitamin D status of children with acute lower infection (mean 34,9 ng/ml) were compared with children without ALRI (mean 37,2 ng/ml). No difference was found between the patient and the control group (p=0,38). In the patient group 17 patients diagnosed to have ALRI again after February 2011 - after one year period. In terms of ALRI recurrence, statistically significant difference was found between vitamin D status normal and insufficient patients (p= 0,003). In conclusion although there was no association between vitamin D status and childhood ALRI, significant association was found between vitamin D status and ALRI recurrence. Larger serial studies are needed for precise results

P4122

Mycoplasma pneumoniae infection affects total eosinophil count, the serum level of ECP, and interleukin-5 in atopic children

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Background: A number of studies have outlined mechanisms by which mycoplasma infection may promote allergic lung inflammation. In addition, there is increasing evidence from human studies suggesting that mycoplasma infection contribute to asthma exacerbations, and severity with the change of cytokines. The present study evaluated the change of serum levels of eosinophil count, eosinophil cationic protein, and interleukin-5 in atopic children with Mycoplasma pneumonia infection.

Method: We recruited 137 children including 44 atopic children with mycoplasma pneumonia (Group 1), 34 non-atopic children with mycoplasma pneumonia (Group 2), 25 children with viral pneumonia (group 3), 34 non-atopic children with viral pneumonia with mycoplasma infection (Group 4). The change of total eosinophil count, serum levels of interleukin (IL)-5, eosinophil cationic protein were measured at admission and at recovery for each group by using commercial ELISA.

Results: The serum level of IL-5 at admission was increased at recovery in group 1 (114±51.1 pg/mL at admission, 143.2±68.4 pg/mL at recovery). However, Buserum eosinophil cationic protein concentrations were increased at clinical recovery compared to the mean serum concentration at admission(49.5 pg/mL at admission, 37.9 pg/mL at recovery in group 1; 38.2 pg/mL at admission, 27.8 pg/mL at recovery).

Conclusion: The outcomes of the present study implied changes of eosinophil and its mediators during Mycoplasma infection may be associated with the mechanism by which the Mycoplasma pneumoniae contribute to the development of airway hypersensitivity.

P4123

Is there a delay in diagnosis of post infectious obliterative bronchiolitis (PBO)?

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Background: PBO, an orphan lung disease results following an antecedent severe viral lower respiratory tract infection (LRTI), commonly due to adenovirus. The clinical symptoms of PBO are non-specific. This may result in a significant delay in diagnosis.

Methods: We retrospectively examined the medical records of children with PBO to determine the time from initial illness to diagnosis based on clinical and radiological criteria as follows:

1. History of antecedent viral LRTI

2. Evidence of airway obstruction (clinical or spirometry)

3. Radiological investigations consistent with PBO

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Results: Of the nine cases identified over last 17 years.adenovirus(n=7)was the main organism implicated in the initial infection in keeping with description in literature.Common referrals were for difficult or severe wheeze, exercise limitation. recurrent respiratory infections or bronchiectasis. The diagnosis was made earlier in children who had a persistent oxygen requirement or were admitted under the care of respiratory paediatricians.

Age at initial illness and at diagnosis

Age, months, Median (range)		
Initial severe LRTI Diagnosis confirmed	21 (12-54) 49 (18-171)	

Conclusions: There is a significant delay in diagnosis of PBO in our experience. Severe LRTI especially with adenovirus and a prolonged oxygen requirement at initial presentation followed by persistent respiratory symptoms should prompt further investigations.Confirmation of the diagnosis leads to better understanding of the disease for the child with the opportunity to network with other children with rare diseases, could lead to potentially disease modifying treatment like Azithromycin and avoid unnecessary treatment for asthma.

P4124

Pneumatocoeles that required surgery in childhood: Report of 2 cases V. Rozalia, Dimos Gidaris, Fotios Maris, Sofia Ioannidou, Dimitra Tzavella. 1st Pediatric Department, Aristotle University, Thessaloniki, Greece

Pneumatocoeles are thin-walled filled with air cystic lesions that have been recognized as a potential complication of pneumonia. Although, they are usually asymptomatic, they may enlarge and compress the adjacent lung and mediastinum. The aim of this report is to describe 2 cases of severe pneumonia complicated by pneumatocoeles that required surgical intervention. Case 1

A one year old girl presented with a 2 day history of pyrexia. Radiological investigation revealed a right sided consolidation with pleural effusion. Pleural fluid culture revealed staphylococcus aureus. Antibiotic treatment and drainage failed and a CT scan on day 21 revealed an enlarging pneumatocoele on the right causing mediastinal shift. The child developed acute respiratory failure; Successful decompression of the pneumatocoele was achieved after initial urgent needle aspiration. Radiologic resolution was complete 2 months post initial presentation. Case 2

A previously healthy 8 month old boy was admitted to our institution with a tension pneumatocoele following a severe necrotic pneumonia. Blood culture was positive for Pneumococcus type 3F. On auscultation there was dramatically decreased air entry on the left side. CXR and CT revealed hyperinflation, large air cyst causing mediastinal shift to the right. Conservative management was initially attempted, but when o-=xygen saturation decreased dramatically surgical excision (pneumonectomy) was decided. The patient is now asymptomatic 2 months post discharge

Conclusion: Tension pneumatocoeles, although rare, are a serious complication of pneumonia that may need surgical intervention when the patient is in critical condition