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Journal Tables of Contents

The most recent issues of the following journals:

- Journal of Cystic Fibrosis
- American Journal of Respiratory and Critical Care Medicine
- Thorax
- Chest

Click on the links for abstracts. If you would like any of these papers in full text then get in touch: library@uhbristol.nhs.uk

Journal of Cystic Fibrosis:
Vol.14, iss.6, November, 2015

http://www.cysticfibrosisjournal.com/current

Interferon response of the cystic fibrosis bronchial epithelium to major and minor group rhinovirus infection
Aline Schögler, Andrea B. Stokes, Carmen Casaulta,

CFTR potentiator therapy ameliorates impaired insulin secretion in CF patients with a gating mutation
Reuven Tsabari, Hila Iron Elyashar, Malena Cohen Cymberknowh, Oded Breuer, Shoshana Armo

Should we monitor exhaled NO to assess the restoration of CFTR function in CF patients

01 November 2015, 00:00:00
Intestinal Current Measurements Detect Activation of Mutant CFTR in Patients with Cystic Fibrosis with the G551D Mutation Treated with Ivacaftor

Simon Y. Graeber, Martin J. Hug, Olaf Sommerburg, Stephanie Hirtz, Julia Hentschel,
A 21-Year-Old Woman With Cystic Fibrosis, Abdominal Pain, and Recent Weight Loss

Kapnadak SG, Goss CH, Aitken ML
New from the Cochrane Library Systematic Reviews on Cystic Fibrosis

Cystic Fibrosis and Genetic Disorders Group

**Immunosuppressive drug therapy for preventing rejection following lung transplantation in cystic fibrosis**
Ian J Saldanha, Oluwaseun Akinyede, Karen A Robinson
Online Publication Date: November 2015

**Anti-IgE therapy for allergic bronchopulmonary aspergillosis in people with cystic fibrosis**
Kana R Jat, Dinesh K Walia, Anju Khairwa
Online Publication Date: November 2015

**Combination antimicrobial susceptibility testing for acute exacerbations in chronic infection of Pseudomonas aeruginosa in cystic fibrosis**
Valerie Waters, Felix Ratjen
Online Publication Date: November 2015
New from NICE

**Block scoping reports**

...constipation Lumacaftor in combination with ivacaftor for treating cystic fibrosis homozygous for the F508del mutation Azacitidine for treating...Iron overload - defasirox and deferiprone COPD- Roflumilast Cystic fibrosis- colistimethate sodium powder Depression - agomelatine...

**Published October 2015**

**List of technologies with approved Patient Access Schemes**

... Pseudomonas aeruginosa for adults and children over 6 with cystic fibrosis Forest Laboratories UK Simple Discount TA276... Pseudomonas aeruginosa for adults and children over 6 with cystic fibrosis Novartis Simple Discount TA278 Omalizumab...

**Published November 2015**

**Technology appraisal static list**

...decision TA266 Mannitol dry powder for inhalation for treating cystic fibrosis Oct 2015 Review decision TA268 Melanoma (stage III...powders for inhalation for treating pseudomonas lung infection in cystic fibrosis Oct 2015 Review decision TA287 Pulmonary embolism and...

**Published October 2015**

**MIB45: PneuX for preventing ventilator-associated pneumonia in intensive care**

...guidance excluded oral antiseptic treatments, severely immunocompromised patients, children under 16 years old and people with cystic fibrosis. The guidance states that measures should be taken to prevent VAP by reducing aspiration via subglottic secretion...

**Medtech innovation briefing Published November 2015**
Current Awareness Database Articles on Cystic Fibrosis

Below is a selection of articles on cystic fibrosis recently added to the healthcare databases, grouped in the following categories:

- Medical
- Microbiological
- Nutritional
- Other

If you would like any of the following articles in full text, or if you would like a more focused search on your own topic, then get in touch: library@uhbristol.nhs.uk

Medical

**Title:** Cystic Fibrosis Papers of the Year, 2013-2014.

**Citation:** Paediatric respiratory reviews, Oct 2015, vol. 16 Suppl 1, p. 9-11 (October 2015)

**Author(s):** Simmonds, Nicholas J

**Abstract:** Studies published in the last year in the field of cystic fibrosis have provided more data on the safety and efficacy of a number of therapies, including mutation-specific drugs. There have also been a number of publications on monitoring of early lung disease including the use of lung clearance index and magnetic resonance scanning. Evidence suggests early lung changes may remain relatively static over the first year of life. There are important outcome differences across national patient registries and there is also the increasing recognition of psychological illnesses and possible drug interactions as treatment becomes more complicated and survival improves. Copyright © 2015 Elsevier Ltd. All rights reserved

**Title:** Highlights of the 28(th) North American Cystic Fibrosis Conference 2014.

**Citation:** Paediatric respiratory reviews, Oct 2015, vol. 16 Suppl 1, p. 12-14 (October 2015)
Author(s): Nwokoro, Chinedu E C

Abstract: This is a selection of papers presented at the 28(th) North American Cystic Fibrosis Conference held in Atlanta in October 2014. The papers discussed are thought to be of particular interest to CF caregivers in the UK. Topics discussed include recent progress in the modification of the cystic fibrosis transmembrane regulator (CFTR), the potential of OligoG, a novel inhaled alginate mucolytic, and the changing approach to cystic fibrosis-related diabetes screening. Copyright © 2015. Published by Elsevier Ltd.

Title: Risk factors for acute kidney injury during aminoglycoside therapy in patients with cystic fibrosis.

Citation: Pediatric nephrology (Berlin, Germany), Oct 2015, vol. 30, no. 10, p. 1879-1888

Author(s): Downes, Kevin J, Patil, Neha R, Rao, Marepalli B, Koralkar, Rajesh, Harris,

Abstract: Aminoglycoside (AG) therapy is a common cause of acute kidney injury (AKI) in cystic fibrosis (CF) patients. The aim of this study was to identify factors associated with AKI during intravenous AG courses in this population. This was a matched case-control study utilizing two independent cohorts of hospitalized CF patients receiving ≥3 days of intravenous AG at Cincinnati Children’s Hospital Medical Center and Children’s of Alabama. All admissions with AKI (cases, N = 82) were matched to two randomly selected admissions without AKI (controls, N = 164) by center, gender, and age ±3 years of the case. AKI was defined as a 1.5-fold increase in the baseline serum creatinine (SCr) level or by an increase in SCr level of 0.3 mg/dL within 48 h. Admissions with AKI before day 4 or without at least weekly SCr monitoring were excluded from the analysis. Factors were compared between cases and controls using simple and multiple conditional logistic regression. Multivariable analysis identified receipt of an AG within 90 days prior to admission, longer duration of AG therapy, low serum albumin, and receipt of trimethoprim/sulfamethoxazole as independent risk factors for developing AKI. Infection with Staphylococcus aureus diminished the odds of developing AKI. This study identifies risk factors contributing to AG-associated AKI in CF patients. These findings can be used to anticipate high-risk scenarios and limit AKI in CF patients under clinical care.
Title: Pan-Resistant Achromobacter xylosoxidans and Stenotrophomonas maltophilia Infection in Cystic Fibrosis Does Not Reduce Survival After Lung Transplantation.

Citation: Transplantation, Oct 2015, vol. 99, no. 10, p. 2196-2202 (October 2015)

Author(s): Lobo, Leonard Jason, Tulu, Zeynep, Aris, Robert M, Noone, Peadar G

Abstract: The number of cystic fibrosis (CF) patients undergoing lung transplantation continues to grow, as does the prevalence of multidrug-resistant (MDR) gram-negative rods. However, the posttransplant survival of patients with MDR pathogens, specifically pan-resistant Achromobacter xylosoxidans and Stenotrophomonas maltophilia, is poorly characterized. This was a retrospective review of CF patients (n = 186; all age, > 16 years) transplanted at the University of North Carolina from 1990 through 2013. Respiratory cultures before transplantation were reviewed for Achromobacter xylosoxidans and Stenotrophomonas maltophilia and their antibiotic susceptibility patterns. Bacteria were defined as pan-resistant if they were resistant or intermediate to all antibiotics tested; otherwise, organisms were defined as MDR. Patients were divided into 5 groups: pan-resistant Achromobacter xylosoxidans (n = 9), MDR Achromobacter xylosoxidans (n = 15), pan-resistant Stenotrophomonas maltophilia (n = 5), MDR Stenotrophomonas maltophilia (n = 26), and CF patients without Achromobacter xylosoxidans, Stenotrophomonas maltophilia or Bulkholderia cenocepacia (n = 131). Survival was compared, and cause of death was described. The survival was similar between all cohorts (P = 0.29). Recurrence of the primary pathogen was the most common with pan-resistant Achromobacter xylosoxidans (100%) followed by MDR Stenotrophomonas maltophilia (46%), MDR Achromobacter xylosoxidans (33%), and finally, pan-resistant Stenotrophomonas maltophilia (20%). Death attributable to the primary pathogen was uncommon, occurring in 2 patients with MDR Stenotrophomonas maltophilia and 2 patients with MDR Achromobacter xylosoxidans. The CF patients with Achromobacter xylosoxidans and Stenotrophomonas maltophilia have similar posttransplant survival as compared to other CF patients, irrespective of their antibiotic susceptibility patterns. The presence of these organisms should not preclude lung transplantation.
**Title: NEW CYSTIC FIBROSIS DRUG.**

**Citation:** , 01 October 2015, vol./is. /(53-53), 15339300

**Author(s):** WALKER, TRACEY

**Abstract:** The article focuses on the approval of Vertex Pharmaceuticals’ lumacaftor/ivacaftor (Orkambi) drug by the U.S Food and Drug Administration (FDA). Topics discussed include use of the drug for treating cystic fibrosis (CF), views of Michael J. Sax, President at Pharmacy Group LLC, on the cost of drug, and impact of the drug on improving lung function.

**Title: Managing Pseudomonas aeruginosa respiratory infections in cystic fibrosis**

**Citation:** Current Opinion in Infectious Diseases, November 2015, vol./is. 28/6(547-556)

**Author(s):** Langan K.M., Kotsimbos T., Peleg A.Y.

**Abstract:** The management of P. aeruginosa respiratory infection in CF remains a challenging area, especially in the setting of multidrug resistance. The role of inhaled antibiotics continues to be expanded. Further research is required in the key areas of eradication and management of chronic infection and acute pulmonary exacerbations to identify those treatments that optimize long-term, clinical benefits.

**Title: Estimating body composition from skinfold thicknesses and bioelectrical impedance analysis in cystic fibrosis patients**

**Citation:** Journal of Cystic Fibrosis, November 2015, vol./is. 14/6(784-791)

**Author(s):** Alicandro G., Battezzati A., Bianchi M.L., Loi S., Speziali C., Bisogno A., Colombo C.
**Abstract:** Background: The accuracy of body composition estimates based on skinfold thickness measurements and bioelectrical impedance analysis (BIA) is not yet adequately explored in cystic fibrosis (CF). Using DXA as reference method we verified the accuracy of these techniques and identified predictors of body composition specific for CF. Methods: One hundred forty-two CF patients (age range: 8-31 years) underwent a DXA scan. Body fat percentage (BF%) was estimated from skinfolds, while fat free mass (FFM) from single-frequency 50 kHz BIA. Results: Bland-Altman analysis showed poor intra-individual agreement between body composition data provided by DXA and BF% estimated from skinfolds or FFM estimated from BIA. The skinfolds of the upper arm were better predictors of BF% than BMI, while compared to other BIA measurements the best predictor of FFM was the R-index (Height$^2$/Resistance). Conclusions: Due to poor accuracy at individual level, the estimates of body composition obtained from these techniques cannot be part of the standard nutritional assessment of CF patients until reliable CF-specific equations will become available. BMI has limited value in predicting body fatness in CF patients and should be used in combination with other predictors. Skinfolds of the upper arm and R-index are strongly related to BF% and FFM and should be tested in a large CF population to develop specific predictive equations.

**Title:** Prolongation of antibiotic treatment for cystic fibrosis pulmonary exacerbations

**Citation:** Journal of Cystic Fibrosis, November 2015, vol./is. 14/6(770-776),

**Author(s):** Waters V., Stanojevic S., Klingel M., Chiang J., Sonneveld N., Kukkar R., Tullis E., Ratjen F.

**Abstract:** Background: Pulmonary exacerbations frequently lead to an irrevocable loss of lung function in cystic fibrosis (CF) patients. Although extended antibiotic duration has not been shown to be associated with improved outcomes in CF overall, it is not known whether there is a subset of patients who may benefit from longer treatment courses. Methods: This was a retrospective cohort study, using the Toronto CF Database from 1997 to 2012, of CF individuals with pulmonary exacerbations requiring intravenous antibiotic treatment. We investigated factors associated with improvement in forced expiratory volume in 1 second.
(FEV\textsubscript{1}) in patients treated with <14days and >14days of antibiotic treatment. Results: A total of 538 pulmonary exacerbations in 253 patients were used for these analysis; 39% of these exacerbations fully recovered lung function at follow-up. Exacerbations were more frequently treated with >14days of antibiotics in older patients with lower FEV\textsubscript{1} at exacerbation and higher rates of B. cepacia complex infections. Subjects with exacerbations treated for >14days had a significantly greater increase in FEV\textsubscript{1} from day 14 to follow up compared to those with <14days (p<0.001). On multivariable analysis, smaller changes from days 0 to 14 of antibiotics and treatment duration>14days were associated with greater increases in FEV\textsubscript{1} from day 14 to follow-up. In those who received >14days of antibiotic therapy, smaller improvements in FEV\textsubscript{1} change from day 0 to 14 and younger age at exacerbation were significantly associated with a greater FEV\textsubscript{1} response from day 14 to end of treatment. Antibiotic treatment >14days was not associated with longer time to subsequent exacerbation. Conclusions: This study highlights that in the treatment of pulmonary exacerbations, maximum lung function is not achieved within 14. days in all patients, and that there is continued improvement beyond this period.

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**Title:** Randomized trial of efficacy and safety of dornase alfa delivered by eRapid nebulizer in cystic fibrosis patients

**Citation:** Journal of Cystic Fibrosis, November 2015, vol./is. 14/6(777-783),

**Author(s):** Sawicki G.S., Chou W., Raimundo K., Trzaskoma B., Konstan M.W.

**Abstract:** Background: Dornase alfa administered via jet nebulizer is indicated as a chronic respiratory medication for cystic fibrosis (CF) patients. Efficacy and safety of dornase alfa via an electronic nebulizer with vibrating membrane technology have not been formally assessed in randomized clinical trials. Methods: 87 CF patients (> 6. years) were randomized in a crossover study to receive dornase alfa 2.5. mg/d in 2-week periods with the Pari eRapid and Pari LC Plus jet nebulizers. The primary end point was comparison of forced expiratory volume in the first second. Safety, quality of life, and treatment satisfaction/preference were also compared between devices. Results: Lung function was equivalent between
nebulizers. Most domain scores from the Cystic Fibrosis Questionnaire-Revised and Treatment Satisfaction Questionnaire for Medication instruments were similar but patients strongly preferred the eRapid. Mean patient-reported administration times were shorter with the eRapid vs the LC Plus (2.7 vs 10.2 min). Adverse events were similar between devices. Conclusions: Administration of dornase alfa via the eRapid nebulizer resulted in comparable efficacy and safety, shorter nebulization times, and higher patient preference.

Title: Insulin secretion abnormalities in exocrine pancreatic sufficient cystic fibrosis patients

Citation: Journal of Cystic Fibrosis, November 2015, vol./is. 14/6(792-797)

Author(s): Wooldridge J.L., Szczesniak R.D., Fenchel M.C., Elder D.A.

Abstract: Background: The aim of this study is to assess insulin secretion in pediatric cystic fibrosis (CF) patients with exocrine pancreatic sufficiency. Methods: Glucose and insulin responses during an oral glucose tolerance test (OGTT) were measured in 146 CF patients. Patients were divided into exocrine sufficient (CF-PS) and insufficient (CF-PI) groups based on pancreatic enzyme usage and fecal elastase. A reference group included healthy, non-diabetic subjects. Results: All CF groups showed reduced insulin secretion as measured by insulinogenic index. The CF-PS patients had normal glucose tolerance. There was a direct correlation between BMI z-score and insulin area under the curve. Conclusion: Patients with CF have reduced insulin secretion during an OGTT regardless of exocrine pancreatic status. The abnormal insulin secretion in all CF patients may predispose them for glucose intolerance, particularly when challenged by inflammation, infection, or nutritional deficiency. In addition, the diminished insulin secretion may contribute to increased catabolism. Lastly, the CF-related diabetes (CFRD) screening guidelines should be followed by all CF patients regardless of pancreatic status.

Title: The influence of breathing mode on tobramycin serum levels using the I-neb AAD system in adults with cystic fibrosis
Abstract: Background: The clinical effectiveness of inhaled tobramycin depends on the dose reaching the desired regions of the lungs. This study evaluates the influence of breathing mode on tobramycin lung deposition using its pharmacokinetics as surrogate for deposition. Methods: In a randomized, open-label, crossover study lung deposition in 18 adult CF patients is evaluated following inhalation of tobramycin aerosol using the I-neb nebulizer with TBM (Tidal Breathing Mode) and TIM (Target Inhalation Mode) breathing patterns. Breathing in TIM forced the patient to inhale in a slow and deep manner. Patients were categorized in three subgroups according to their lung function: <. 59%, 60-79% or >. 80% of FEV1 predicted. Blood samples were collected in order to model tobramycin pharmacokinetics. Nebulization time was recorded. Results: Inhalation with TIM resulted in significantly higher maximum serum levels and area under the concentration-time curves (0-24h)<sub></sub>. Mean bioavailability of TIM relative to TBM was 1.53+-0.41. Mean nebulization time was reduced by half with TIM. Subgroup category did not affect the results. Conclusions: Slow and deep inhalation of aerosolized tobramycin resulted in higher lung deposition and shorter nebulization time compared to tidal breathing, regardless of the disease severity of the CF patient. Dutch trial register number NTR3109.

Title: Effects of Autogenic Drainage on Sputum Recovery and Pulmonary Function in People with Cystic Fibrosis: A Systematic Review

Citation: Physiotherapy Canada, 2015, vol./is. 67/4(319-326), 03000508

Title: Newborn screening for cystic fibrosis.

Citation: Expert review of respiratory medicine, Oct 2015, vol. 9, no. 5, p. 619-631

Author(s): Gonska, Tanja, Ratjen, Felix
**Abstract:** Newborn screening for cystic fibrosis (CF NBS) has been introduced in almost all of the Western countries, and most of the children with CF are now being identified via CF NBS before disease-related symptoms develop. This review summarizes the evidence that has been generated to date to support the benefit of CF NBS and the various screening algorithms that are used in different jurisdictions. A special focus is directed towards the challenges arising from false-negative and -positive screening results. Finally, we review the emerging data reporting on positively-screened newborns, in whom confirmatory sweat testing resulted in an inconclusive diagnosis for CF.

**Title:** Heart Involvement in Children and Adults with Cystic Fibrosis: Correlation with Pulmonary Indexes and Inflammation Markers

**Citation:** Heart Lung and Circulation, October 2015, vol./is. 24/10(1002-1010), 1443-9506;1444-2892

**Author(s):** Giacchi V., Rotolo N., Amato B., Di Dio G., Betta P., La Rosa M., Leonardi S.,

**Abstract:** Background: Cardiovascular involvement in Cystic Fibrosis (CF) is a not rare condition, although the prevalence of subclinical pulmonary hypertension (PH) and cardiac dysfunction is not known in the early stages of CF progression. The aim of our study was to assess cardiac involvement in children and adults affected by cystic fibrosis compared with healthy subjects of same age using echocardiography. Methods: Fifty-five patients, 25 adults and 30 children completed the study. We assessed FEV1 (Forced Expiratory Volume in one second), and carried out colour Doppler-echocardiography evaluating ejection fraction (EF) measurement of left ventricle, tricuspid annular plane systolic excursion (TAPSE) of right ventricle and pulmonary artery pressure (PAP). We compared the auxological, respiratory and cardiologic data with those of 16 adults and 34 children of the same age. Results: We discovered significantly different values of PAP between patients and controls in both children (p = 0.0001, r = - 0.62) and adults (p = 0.0001, r = - 0.63), whereas the EF and TAPSE showed significantly different values in only adults (p. = 0.0023 and p. = 0.0194 respectively). We found in both children and adults with CF an inverse correlation between PAP and FEV1 (p = 0.000, p = 0.001), Erythrocyte Sedimentation Rate (ESR) and FEV 1 (p =
0.015, \( r = -0.43; p = 0.009, r = -0.51 \), and highly sensitive C-reactive protein (hs-CRP) and FEV_1 \( (p = 0.007, r = -0.48; p = 0.001, r = -0.60) \). In adults we also detected direct correlation between PAP and hs-CRP \( (p = 0.008, r = 0.51) \) and PAP and ESR \( (p = 0.009, r = 0.51) \).

Conclusions: In paediatric-aged CF patients there are already early signs of potential heart impairment, represented by an increase of pulmonary blood pressure, and in adult age the systolic function of right ventricle may be impaired. We hypothesise that such cardiac impairments may gradually arise due to preceding chronic inflammation related to prior degeneration of lung function and thus it is very important to keep patients clinically stable and address chronic inflammation as early as possible in the progression of CF.

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**Title:** Renal diseases in adults with cystic fibrosis: a 40 year single centre experience

**Citation:** Journal of Nephrology, October 2015, vol./is. 28/5(585-591), 1121-8428;1724-6059

**Author(s):** Wilcock M.J., Ruddick A., Gyi K.M., Hodson M.E.

**Abstract:** Background: There is a sizable literature describing renal disease in patients with cystic fibrosis. Previous studies have focused on single disease processes alone, most commonly renal stone disease or acute kidney injury. In this study we report for the first time on the prevalence of all forms of renal disease in a cystic fibrosis population. Methods: A retrospective review of adult patients with cystic fibrosis attending the Adult Cystic Fibrosis Department at the Royal Brompton Hospital was carried out by searching the department’s database to identify patients with renal problems and subsequently retrieving clinical information from medical notes. Results: The prevalence of all renal diseases in our population was 5.1 %. The most commonly identified problem was renal stones. At 2.0 % the prevalence of renal stones in adult patients with cystic fibrosis was comparable to the general population. A range of other renal diseases were identified, the next most common being drug-induced acute kidney injury. Conclusions: A range of cystic fibrosis independent and attributable diseases has been identified but no cystic fibrosis specific disease. In contrast to other cystic fibrosis centres no increased prevalence of renal stones was found.
Title: Introduction: The remaining barriers to normalcy in cystic fibrosis

Citation: Pediatric Pulmonology, October 2015, vol./is. 50/(S1-S2), 8755-6863;1099-0496

Author(s): Murphy T.

Title: Inflammation and its genesis in cystic fibrosis

Citation: Pediatric Pulmonology, October 2015, vol./is. 50/(S39-S56), 8755-6863;1099-0496

Author(s): Nichols D.P., Chmiel J.F.

Abstract: The host inflammatory response in cystic fibrosis (CF) lung disease has long been recognized as a central pathological feature and an important therapeutic target. Indeed, many believe that bronchiectasis results largely from the oxidative and proteolytic damage comprised within an exuberant airway inflammatory response that is dominated by neutrophils. In this review, we address the longstanding argument of whether or not the inflammatory response is directly attributable to impairment of the cystic fibrosis transmembrane conductance regulator or only secondary to airway obstruction and chronic bacterial infection and challenge the importance of this distinction in the context of therapy. We also review the centrality of neutrophils in CF lung pathophysiology and highlight more recent data that suggest the importance of other cell types and signaling beyond NF-kappaB activation. We discuss how protease and redox imbalance are critical factors in CF airway inflammation and end by reviewing some of the more promising therapeutic approaches now under development.

Title: CFTR, bicarbonate, and the pathophysiology of cystic fibrosis

Citation: Pediatric Pulmonology, October 2015, vol./is. 50/(S24-S30)

Author(s): Borowitz D.

Abstract: The gene that encodes for the cystic fibrosis transmembrane regulator protein (CFTR) was identified in 1989, yet major pathophysiologic questions remain unanswered.
There is emerging evidence that CFTR is a bicarbonate channel, a driver of chloride-bicarbonate exchange and through its action on local pH, a regulator of other ion channels and of proteins that function optimally in a neutral environment. In both the respiratory and gastrointestinal (GI) tracts, bicarbonate drives ionic content and fluid on epithelial surfaces, allows mucins to unfold and become slippery, and contributes to innate immunity. In the GI tract bicarbonate neutralizes gastric acid to support digestion and absorption. When CFTR is dysfunctional, lack of bicarbonate secretion disrupts these normal processes and thus leads directly to the clinical symptoms and signs of CF. This article synthesizes evidence from cell, animal, and human investigations that support these concepts. Bicarbonate secretion does not seem to be the same in all tissues and varies with physiologic demand. Thus, tissue type and whether conditions are baseline or stimulated needs to be taken into account when evaluating the evidence concerning the role of bicarbonate in the pathophysiology of CF as a regulator of local pH. Basic and applied research that focuses on the role of CFTR-mediated bicarbonate secretion helps explain many of the diverse clinical manifestations that are CF.

Title: Personalized medicine for cystic fibrosis: Establishing human model systems

Citation: Pediatric Pulmonology, October 2015, vol./is. 50/(S14-S23), 8755-6863;1099-0496

Author(s): Mou H., Brazauskas K., Rajagopal J.

Abstract: With over 1,500 identifiable mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that result in distinct functional and phenotypical abnormalities, it is virtually impossible to perform randomized clinical trials to identify the best therapeutics for all patients. Therefore, a personalized medicine approach is essential. The only way to realistically accomplish this is through the development of improved in vitro human model systems. The lack of a readily available and infinite supply of human CFTR-expressing airway epithelial cells is a key bottleneck. We propose that a concerted two-pronged approach is necessary for patient-specific cystic fibrosis research to continue to prosper and realize its potential: (1) more effective culture and differentiation conditions for growing primary human airway and nasal epithelial cells and (2) the development of collective protocols for efficiently differentiating disease- and patient-specific induced
pluripotent stem cells (iPSC) into pure populations of adult epithelial cells. Ultimately, we need a personalized human model system for cystic fibrosis with the capacity for uncomplicated bankability, widespread availability, and universal applicability for patient-specific disease modeling, novel pharmacotherapy investigation and screening, and readily executable genetic modification.

Title: Lung clearance index in cystic fibrosis subjects treated for pulmonary exacerbations

Citation: European Respiratory Journal, October 2015, vol./is. 46/4(1055-1064), 0903-1936;1399-3003 (01 Oct 2015)

Author(s): Sonneveld N., Stanojevic S., Amin R., Aurora P., Davies J., Elborn J.S., Horsley A.

Abstract: Pulmonary exacerbations are important clinical events for cystic fibrosis (CF) patients. Studies assessing the ability of the lung clearance index (LCI) to detect treatment response for pulmonary exacerbations have yielded heterogeneous results. Here, we conduct a retrospective analysis of pooled LCI data to assess treatment with intravenous antibiotics for pulmonary exacerbations and to understand factors explaining the heterogeneous response. A systematic literature search was performed to identify prospective observational studies. Factors predicting the relative change in LCI and spirometry were evaluated while adjusting for within-study clustering. Six previously reported studies and one unpublished study, which included 176 pulmonary exacerbations in both paediatric and adult patients, were included. Overall, LCI significantly decreased by 0.40 units (95% CI -0.60 - 0.19, p=0.004) or 2.5% following treatment. The relative change in LCI was significantly correlated with the relative change in forced expiratory volume in 1 s (FEV1), but results were discordant in 42.5% of subjects (80 out of 188). Higher (worse) baseline LCI was associated with a greater improvement in LCI (slope: -0.9%, 95% CI -1.0 - -0.4%). LCI response to therapy for pulmonary exacerbations is heterogeneous in CF patients; the overall effect size is small and results are often discordant with FEV1.
Title: Sustained benefit from ivacaftor demonstrated by combining clinical trial and cystic fibrosis patient registry data

Citation: American Journal of Respiratory and Critical Care Medicine, vol./is. 192/7(836-842)

Author(s): Sawicki G.S., McKone E.F., Pasta D.J., Millar S.J., Wagener J.S., Johnson C.A.,

Abstract: Rationale: In clinical trials, patients with cystic fibrosis and a G551D mutation who received ivacaftor experienced improvements in pulmonary and nutritional outcomes. However, whether these improvements reflect a change in disease trajectory cannot be determined without longer-term analyses with an appropriate comparator population. Objectives: To examine, over a 3-year period, whether ivacaftor therapy affects pulmonary function and nutritional measures in patients with CF with aG551D mutation compared with patients with CF who are homozygous for the F508del mutation. Methods: A propensity score was used to match patients with CF greater than or equal to 6 years of age who have a G551D mutation and received ivacaftor in clinical trials for up to 144 weekswith data from patients in the U.S. Cystic Fibrosis Foundation Patient Registry who are homozygous for the F508del mutation. Matching was based on variables including age, sex, weight for age, height for age, body mass index for age, % predicted FEV1, and chronic therapies (dornase alfa, inhaled antibiotics, inhaled and oral corticosteroids). Measurements and Main Results: By calculating the annual estimated rate of decline in lung function for G551D patients receiving ivacaftor and comparing it with the rate of decline in lung function for matched F508del control patients, we show that the rate of lung function decline in G551D ivacaftor-treated patients was slower by nearly half. Moreover, treatment with ivacaftor is shown to improve body mass index and weight-for-age z scores for G551D patients over the 3-year analysis period. Conclusions: These findings suggest that ivacaftor is a disease-modifying therapy for the treatment of cystic fibrosis.

Title: A French multicentric study and review of pulmonary Nocardia spp. in cystic fibrosis patients

Citation: Medical Microbiology and Immunology, October 2015, vol./is. 204/4(493-504)
Author(s): Rodriguez-Nava V., Durupt S., Chyderiotis S., Freydiere A.-M., Karsenty J.,

Abstract: Some bacterial species recovered from the airways of cystic fibrosis (CF) patients are indisputably associated with lung infections, whereas the clinical relevance of others, such as Nocardia spp., remains unclear. Sixteen French CF cases of colonization/infection with Nocardia spp. were reviewed in order to evaluate the epidemiology, the clinical impact and the potential treatment of these bacteria, and results were compared to those of the literature. Five Nocardia species were identified, Nocardia cyriacea being the major species (50% of cases). At first isolation, Nocardia was the sole pathogen recovered in six patients. Seven patients presented pulmonary exacerbation. For 12 patients, antimicrobial treatment against Nocardia was started immediately, mainly based on cotrimoxazole (6 of the 12 cases). In this study, we highlight the heterogeneity of the clinical management of Nocardia spp. in CF. Guidelines for the clinical management of Nocardia infections in CF patients are proposed.

Title: Induced sputum in young healthy children with cystic fibrosis.

Citation: Paediatric respiratory reviews, Oct 2015, vol. 16 Suppl 1, p. 6-8 (October 2015)

Author(s): Forton, Julian

Abstract: Young children with CF are often asymptomatic and non-productive, yet CF lung disease occurs early in life. Cough swabs are used routinely to sample bacteria from the CF respiratory tract in non-productive healthy children; bronchoscopy is used to definitively sample the lower airway, but is an invasive procedure. Induced sputum is a non-invasive approach to sampling the lower airway. The article concentrates on how well it is tolerated in children, how successful it is in identifying respiratory pathogens, and how it may be important in routine surveillance if 16S technology is to be used in the clinical forum.

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Title: Cystic fibrosis in children and adults: Supplement to Paediatric Respiratory Reviews.
Title: Anabolic agent use in adults with cystic fibrosis.

Citation: Paediatric respiratory reviews, Oct 2015, vol. 16 Suppl 1, p. 28-30 (October 2015)

Author(s): Green, Heather D, Barry, Peter J, Jones, Andrew M

Abstract: The use of non-prescribed anabolic agents amongst non-athletes is increasing with young, adult males with cystic fibrosis (CF) in the highest risk demographic. There is evidence that anabolic agents increase weight and muscle mass in adults with a variety of catabolic conditions but there is no evidence for their use in hormone sufficient adults with CF. We report a case of anabolic agent use in a male adult with CF and review the clinical features of anabolic agent use with a focus on adults with CF. Copyright © 2015 Elsevier Ltd. All rights reserved.

Title: Pseudomonas aeruginosa in cystic fibrosis is potentially serious, and more than merely a marker for disease severity.

Citation: Paediatric respiratory reviews, Oct 2015, vol. 16 Suppl 1, p. 35-36

Author(s): Lenney, Warren

Title: Breakthrough therapies: Cystic fibrosis (CF) potentiators and correctors.

Citation: Pediatric pulmonology, Oct 2015, vol. 50 Suppl 40, p. S3. (October 2015)

Author(s): Solomon, George M, Marshall, Susan G, Ramsey, Bonnie W, Rowe, Steven M
Abstract: Cystic Fibrosis is caused by mutations in the Cystic Fibrosis Transmembrane conductance Regulator (CFTR) gene resulting in abnormal protein function. Recent advances of targeted molecular therapies and high throughput screening have resulted in multiple drug therapies that target many important mutations in the CFTR protein. In this review, we provide the latest results and current progress of CFTR modulators for the treatment of cystic fibrosis, focusing on potentiators of CFTR channel gating and Phe508del processing correctors for the Phe508del CFTR mutation. Special emphasis is placed on the molecular basis underlying these new therapies and emerging results from the latest clinical trials. The future directions for augmenting the rescue of Phe508del with CFTR modulators are also emphasized. Pediatr Pulmonol. 2015; 50:S3-S13. © 2015 Wiley Periodicals, Inc. © 2015 Wiley Periodicals, Inc

Title: Relationship Between Clinical Variables and Health-Related Quality of Life in Young Adult Subjects With Cystic Fibrosis.

Citation: Respiratory care, Oct 2015, vol. 60, no. 10, p. 1459-1468 (October 2015)

Author(s): Forte, Gabriele C, Barni, Gabriela C, Perin, Christiano, Casarotto, Fernanda C, Fagondes, Simone C, Dalcin, Paulo de Tarso Roth

Abstract: Health-related quality of life (HRQOL) has received much attention in patients with cystic fibrosis (CF). The goal of this study was to evaluate the association between clinical, lung function, sleep quality, and polysomnographic variables with 2 HRQOL questionnaires, the shorter-version World Health Organization Quality of Life (WHOQOL-BREF) and Cystic Fibrosis Quality of Life (CFQOL) questionnaires, in adult subjects with CF. In a cross-sectional study, 51 subjects underwent clinical evaluation and overnight polysomnography and answered WHOQOL-BREF, CFQOL, Pittsburgh Sleep Quality Index, and Epworth Sleepiness Scale questionnaires. In addition, pulmonary function tests, 6-min walk tests, and echocardiography were performed. For WHOQOL-BREF scores, the sleep quality index was associated with the physical domain; the percent-of-predicted 6-min walk distance (6MWD) and sleepiness scale were associated with the psychological domain; the percent-of-predicted FEV1 and sleep quality index were associated with the social relationship domain; and the sleep quality index was associated with the environment domain. For CFQOL scores, age at diagnosis, clinical score, and sleep quality index were associated with the physical
functioning domain; the percent-of-predicted 6MWD and pulmonary arterial systolic pressure were associated with the role domain; sex and sleep quality index were associated with the vitality domain; the apnea-hypopnea index was associated with the emotional functioning domain; sex and body mass index (BMI) were associated with the body image domain; the percent-of-predicted 6MWD and sleep quality index were associated with the health perception domain; age, sex, BMI, and arousal index were associated with the weight domain; age, sex, percent-of-predicted FEV1, percent-of-predicted 6MWD, and pulmonary arterial systolic pressure were associated with the respiratory symptom domain; and the clinical score was associated with the digestive symptom domain. The sleep quality index score, 6MWD, sleepiness scale score, and FEV1 were predictors of WHOQOL-BREF scores. Age at diagnosis, clinical score, sleep quality score, 6MWD, sex, apnea-hypopnea index, BMI, current age, arousal index, FEV1, and pulmonary arterial systolic pressure were predictors of CFQOL scores. Copyright © 2015 by Daedalus Enterprises.

Title: Baseline Ultrasound and Clinical Correlates in Children with Cystic Fibrosis.

Citation: The Journal of pediatrics, Oct 2015, vol. 167, no. 4, p. 862 (October 2015)

Author(s): Leung, Daniel H, Ye, Wen, Molleston, Jean P, Weymann, Alexander, Ling, Simon,

Abstract: To investigate the relationship between abdominal ultrasound findings and demographic, historical, and clinical features in children with cystic fibrosis (CF). Children age 3-12 years with CF without known cirrhosis, were enrolled in a prospective, multicenter study of ultrasound to predict hepatic fibrosis. Consensus ultrasound patterns were assigned by 3 radiologists as normal, heterogeneous, homogeneous, or cirrhosis. Data were derived from direct collection and US or Toronto CF registries. χ(2) or ANOVA were used to compare variables among ultrasound groups and between normal and abnormal. Logistic regression was used to study risk factors for having abnormal ultrasound. Findings in 719 subjects were normal (n = 590, 82.1%), heterogeneous (64, 8.9%), homogeneous (41, 5.7%), and cirrhosis (24, 3.3%). Cirrhosis (P = .0004), homogeneous (P < .0001), and heterogeneous (P = .03) were older than normal. More males were heterogeneous (P = .001). More heterogeneous (15.0%, P = .009) and cirrhosis (25.0%, P = .005) had CF-related diabetes or
impaired glucose tolerance vs normal (5.4%). Early infection with Pseudomonas aeruginosa (<2 years old) was associated with a lower risk (OR 0.42, P = .0007) of abnormal. Ursodeoxycholic acid use (OR 3.69, P < .0001) and CF-related diabetes (OR 2.21, P = .019) were associated with increased risk of abnormal. Unsuspected cirrhosis is seen in 3.3% of young patients with CF, heterogeneous in 8.9%. Abnormal ultrasound is associated with CF-related diabetes, and early P aeruginosa is associated with normal ultrasound. Prospective assessment of these risk factors may identify potential interventional targets. ClinicalTrials.gov: NCT01144507. Copyright © 2015 Elsevier Inc. All rights reserved.

**Microbiological**

Title: The microbiology of the cystic fibrosis upper and lower airway

Citation: Journal of Cystic Fibrosis, November 2015, vol./is. 14/6(e35)

Author(s): Dosanjh A.

Title: Role of nebulized amphotericin B in the management of allergic bronchopulmonary aspergillosis in cystic fibrosis: Case report and review of literature.

Citation: Journal of chemotherapy (Florence, Italy), Oct 2015, vol. 27, no. 5, p. 307-311

Author(s): Casciaro, Rosaria, Naselli, Aldo, Cresta, Federico, Ros, Mirco, Castagnola, Elio,

Abstract: To review the data available in literature about nebulized amphotericin B (AMB) in the treatment of allergic bronchopulmonary aspergillosis (ABPA) in cystic fibrosis (CF) and to report our experience in the use of this drug, with a particular therapeutic scheme. We used nebulized liposomal amphotericin B (L-AMB) in a patient affected by CF, complicated by ABPA. The previous combined treatment with oral steroids and azoles had no respiratory benefit and caused relevant side effects. Amphotericin B has always been well tolerated and
permitted a slight steroid tapering. We also observed benefits in pulmonary function and laboratory tests. Few data are available in literature about the use of nebulized AMB in CF and there are no RCTs evaluating antifungals in CF-ABPA. In our opinion, the reported case suggests that nebulized L-AMB could represent a possible strategy in ABPA management in CF patients.

**Title: Sinus biofilms in patients with cystic fibrosis: is adjusted eradication therapy needed?**

**Citation:** European Archives of Oto-Rhino-Laryngology, Oct 2015, vol./is. 272/9(2291-2297)

**Author(s):** Aanaes K., Eickhardt S., Johansen H.K., von Buchwald C., Skov M., Hoiby N.,

**Abstract:** The paranasal sinuses can be a focus for colonisation of the cystic fibrosis (CF) lungs with pathogens. In the sinuses, bacteria can adapt to the lung environment and enhance their antibiotic resistance, with biofilm formation thought to be the most important adaptive mechanism, causing recalcitrant disease. The presence of biofilms in CF sinuses is sparsely described. In this descriptive cross-sectional study, the sinus mucosa from 16 CF patients were analysed by fluorescence in situ hybridization using specific peptide nucleic acid (PNA-FISH) probes for Pseudomonas aeruginosa and Staphylococcus aureus to demonstrate the presence of biofilms. Small clusters of biofilm were visualised lining the sinus mucosa of CF patients. Biofilms were found in 10 out of 18 cases; 7 with intermittent lung colonisation, 2 chronically infected, and one lung transplanted patient. Finding P. aeruginosa biofilms in intermittently lung-colonised patients encourage us to intensify the attempt to eradicate pathogenic bacteria from the CF sinuses in an early stage using combined antibiotic therapy in the prolonged exposure of the sinus-mucosal surface.

**Title: Bacteriophage Delivery by Nebulization and Efficacy Against Phenotypically Diverse Pseudomonas aeruginosa from Cystic Fibrosis Patients**

**Citation:** Journal of Aerosol Medicine and Pulmonary Drug Delivery, October 2015, vol./is. 28/5(353-360)
Author(s): Sahota J.S., Smith C.M., Radhakrishnan P., Winstanley C., Goderdzishvili M.,

Abstract: Background: The rise in antibiotic-resistant Pseudomonas aeruginosa and the considerable difficulty in eradicating it from patients has re-motivated the study of bacteriophages as a therapeutic option. For this to be effective, host range and viability following nebulization need to be assessed. Host-range has not previously been assessed for the Liverpool Epidemic Strain (LES) isolates that are the most common cystic fibrosis-related clone of P. aeruginosa in the UK. Nebulization studies have not previously been linked to clinically relevant phages. Methods: 84 phenotypically variable isolates of the LES were tested for susceptibility to seven bacteriophages known to have activity against P. aeruginosa. Five of the phages were from the Eliava Institute (IBMV) and 2 were isolated in this study. The viability of the two bacteriophages with the largest host ranges was characterized further to determine their ability to be nebulized and delivered to the lower airways. Phages were nebulized into a cascade impactor and the phage concentration was measured. Results: The bacteriophages tested killed between 66%-98% of the 84 Liverpool Epidemic Strain isolates. Two isolates were multi phage resistant, but were sensitive to most first line anti-Pseudomonal antibiotics. The amount of viable bacteriophages contained in particles that are likely to reach the lower airways (<4.7 mum) was 1% for the Omron and 12% AeroEclipse nebulizer. Conclusions: Individual P. aeruginosa bacteriophages can lyse up to 98% of 84 phenotypically diverse LES strains. High titers of phages can be effectively nebulized.

Title: Surgical masks reduce airborne spread of Pseudomonas aeruginosa in colonized patients with cystic fibrosis

Citation: American Journal of Respiratory and Critical Care Medicine, October 2015, vol./is. 192/7(897-899)

Title: Pseudomonas aeruginosa quorum sensing molecules correlate with clinical status in cystic fibrosis

Citation: European Respiratory Journal, October 2015, vol./is. 46/4(1046-1054),

Author(s): Barr H.L., Halliday N., Camara M., Barrett D.A., Williams P., Forrester D.L.,

Abstract: Pseudomonas aeruginosa produces quorum sensing signal molecules that are potential biomarkers for infection. A prospective study of 60 cystic fibrosis patients with chronic P. aeruginosa, who required intravenous antibiotics for pulmonary exacerbations, was undertaken. Clinical measurements and biological samples were obtained at the start and end of the treatment period. Additional data were available for 29 of these patients when they were clinically stable. Cross-sectionally, quorum sensing signal molecules were detectable in the sputum, plasma and urine of 86%, 75% and 83% patients, respectively. They were positively correlated between the three biofluids. Positive correlations were observed for most quorum sensing signal molecules in sputum, plasma and urine, with quantitative measures of pulmonary P. aeruginosa load at the start of a pulmonary exacerbation. Plasma concentrations of 2-nonyl-4-hydroxy-quinoline (NHQ) were significantly higher at the start of a pulmonary exacerbation compared to clinical stability (p<0.01). Following the administration of systemic antibiotics, plasma 2-heptyl-4-hydroxyquinoline (p=0.02) and NHQ concentrations (p<0.01) decreased significantly. In conclusion, quorum sensing signal molecules are detectable in cystic fibrosis patients with pulmonary P. aeruginosa infection and are positively correlated with quantitative measures of P. aeruginosa. NHQ correlates with clinical status and has potential as a novel biomarker for P. aeruginosa infection.

Title: A case of failed eradication of cystic fibrosis-related sinus colonisation by Pseudomonas aeruginosa

Citation: BMC Pulmonary Medicine, October 2015, vol./is. 15/1(1), 1471-2466

Author(s): Linnane B., Kearse L., O’Connell N.H., Fenton J., Kiernan M.G., Dunne C.P.
**Abstract:** Background: Pseudomonas aeruginosa is a pathogen associated with cystic fibrosis that has potential to decrease lung function and cause respiratory failure. Paranasal sinuses are increasingly recognised as potential reservoirs for intermittent colonisation by P. aeruginosa. This case documents investigation and outcome of P. aeruginosa recurrence in a male paediatric patient over an eight year period. Case presentation: A 12 year old Irish male paediatric cystic fibrosis patient experienced intermittent culturing of P. aeruginosa from the oropharyngeal region, indicating chronic infection of the sinuses despite absence of symptoms, retaining good lung function, and normal bronchoscopy and bronchoalveolar lavage. However, P. aeruginosa was isolated from a sinus wash-out and was identified as a unique strain of P. aeruginosa that was also cultured from cough swabs. Despite treatment, successful eradication from the paranasal sinuses was not achieved. Conclusions: Few reports have addressed the paranasal sinuses as a reservoir for lung infection in cystic fibrosis patients despite increased recognition of the need to investigate this niche. In this case, attempts at eradication of P. aeruginosa present in paranasal sinuses including oral and nebulised antimicrobials proved unsuccessful. However, detection of P. aeruginosa in the paranasal sinuses instigated antimicrobial treatment which may have contributed to prevention of migration to the lower airways. Our outcome provides additional insight and may indicate utility of nasal lavage or nasal endoscopy in paediatric cystic fibrosis patients' annual review clinic visits.

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**Title:** An international, multicentre evaluation and description of Burkholderia pseudomallei infection in cystic fibrosis

**Citation:** BMC Pulmonary Medicine, October 2015, vol./is. 15/1, 1471-2466

**Author(s):** Geake J.B., Reid D.W., Currie B.J., Bell S.C., Bright-Thomas R., Dewar J., Holden S.

**Abstract:** Background: Several cases of Burkholderia pseudomallei infection in CF have been previously reported. We aimed to identify all cases globally, risk factors for acquisition, clinical consequences, and optimal treatment strategies. Methods: We performed a literature search to identify all published cases of B. pseudomallei infection in CF. In addition we hand-searched respiratory journals, and contacted experts in infectious diseases and CF
around the world. Supervising clinicians for identified cases were contacted and contemporaneous clinical data was requested. Results: 25 culture-confirmed cases were identified. The median age at acquisition was 21 years, mean FEV₁ % predicted was 60 %, and mean BMI was 19.5 kg/m². The location of acquisition was northern Australia or south-east Asia for most. 19 patients (76 %) developed chronic infection, which was usually associated with clinical decline. Successful eradication strategies included a minimum of two weeks of intravenous ceftazidime, followed by a consolidation phase with trimethoprim/sulfamethoxazole, and this resulted in a higher chance of success when instituted early. Three cases of lung transplantation have been recorded in the setting of chronic B. pseudomallei infection. Conclusion: Chronic carriage of B. pseudomallei in patients with CF appears common after infection, in contrast to the non-CF population. This is often associated with an accelerated clinical decline. Lung transplantation has been performed in select cases of chronic B. pseudomallei infection.

Title: Cystic fibrosis lung microbiome: Opportunities to reconsider management of airway infection

Citation: Pediatric Pulmonology, October 2015, vol./is. 50/(S31-S38),

Author(s): Caverly L.J., Zhao J., LiPuma J.J.

Language: English

Abstract: The importance of infection in the pathogenesis of cystic fibrosis (CF) lung disease has been long recognized, and the use of antibiotics targeting bacteria identified in cultures of respiratory specimens has played a critical role in improving outcomes for individuals with CF. Over the past ~15 years, the use of culture-independent methods to assess airway microbiology in CF has revealed complex and dynamic CF airway bacterial communities. Recent areas of investigation of the CF lung microbiome have included exploring how bacterial community structures change over time, particularly with respect to disease progression or pulmonary exacerbation, and in response to antibiotic therapies. This review will discuss what has been learned from these studies as well as how these findings offer opportunities to further refine management of CF airway infection.
Title: Persistent infection because of Pandoraea sputorum in a young cystic fibrosis patient resistant to antimicrobial treatment

Citation: Pediatric Infectious Disease Journal, October 2015, vol./is. 34/10(1135-1137)

Author(s): Puges M., Debelleix S., Fayon M., Megraud F., Lehours P.

Abstract: We report the case of a 13-year-old boy with cystic fibrosis with a pulmonary exacerbation concomitant to the first isolation of Pandoraea sputorum. The imipenem and trimethoprim-sulfamethoxazole treatments failed, with persistence of the bacteria, bronchial congestion and a decline in lung function. Pandoraea sp. is rarely isolated, with only 10 cases reported in France in 2011.

Nutrition

Title: Clinical audit results in earlier nutritional intervention in malnourished children with cystic fibrosis with improved outcome

Citation: Journal of Paediatrics and Child Health, October 2015, vol./is. 51/10(988-993)

Author(s): Ledder O., Oliver M.R., Heine R.G., Graham J., Volders E., Robinson P.J.

Abstract: Aim The association between nutritional status, pulmonary function and survival in cystic fibrosis (CF) is well established. A previous case series from the Royal Children's Hospital, Melbourne (RCH), demonstrated suboptimal referral practices and highlighted the importance of early nutritional interventions in children with CF. Various qualitative changes were made to our CF service, and this study assesses the effects of these practice changes timing of gastrostomy and clinical outcome in patients who underwent gastrostomy insertion. Method Clinical audit of all CF patients who had undergone gastrostomy insertion from 2002 to 2010 at Royal Children's Hospital. Clinical data, including nutritional parameters, respiratory function and survival, were collected at 2 years prior and 2 years post gastrostomy insertion. Data were compared with the previous study from 1989 to 1997. Results Patients with CF who underwent gastrostomy insertion between 2002 and
2010 (n = 22) had higher weight-for-age scores (-1.5 +/- 0.68 vs. -2.67 +/- 1.06; P = 0.0001) and higher forced expiratory volume in 1 s (68% +/- 22 vs. 52% +/- 18.5; P = 0.006), compared with the cohort from 1989 to 1997 (n = 37). These differences were maintained at 2-year follow-up. Pseudomonas aeruginosa colonisation rate was 100% in 1989-1997 vs. 41% in 2002-2010; P = 0.0001. The 2-year survival post-gastrostomy insertion improved from 70% to 100%; P = 0.004. Conclusion Earlier referral of patients in the recent cohort resulted in sustained improvements in weight-for-age and lung function. Survival at 2 years post-procedure was significantly improved. This study confirms the value of clinical audits and subsequent re-evaluation of clinical services.

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**Title:** Nutritional outcomes in cystic fibrosis - are we doing enough?

**Citation:** Paediatric respiratory reviews, Oct 2015, vol. 16 Suppl 1, p. 31-34 (October 2015)

**Author(s):** Connett, Gary J, Pike, Katharine C

**Abstract:** Although outcome data for individuals with cystic fibrosis (CF) have shown consistent improvements throughout the twentieth century, more recent national registry data suggests that outcomes have reached a plateau. Median values for nutritional outcomes in CF currently cluster around the fiftieth centile for the normal population. These data suggest that up to half of CF patients have sub-optimal body mass index (BMI) which might have a significant adverse impact on their respiratory status. BMI might be underestimating the extent to which more important lean body mass might also be reduced. Nutritional decline is a particular problem during adolescence and commonly persists into early adult life. Current treatment strategies to optimize nutrition include the use of high energy diets, proton pump inhibitors and optimal use of enzyme preparations including higher strength preparations to decrease pill burden. Whilst these are all of potential benefit, poor adherence to nutritional care recommendations is probably the greatest impediment to future health improvement. More effective strategies to impact on treatment adherence are needed. Copyright © 2015 Elsevier Ltd. All rights reserved.
**Psychological**

**Title:** Depression in cystic fibrosis; Implications of The International Depression/Anxiety Epidemiological Study (TIDES) in cystic fibrosis.

**Citation:** Paediatric respiratory reviews, Oct 2015, vol. 16 Suppl 1, p. 2-5

**Author(s):** Duff, Alistair J A

**Abstract:** Children and adults with chronic diseases, as well as their parents, are at increased risk for depression. Where people with CF do exhibit psychological distress it is linked to poorer adherence and pulmonary function, increased hospitalisations and healthcare costs and decreased quality of life. The International Depression Epidemiological Study (TIDES) evaluated depression and anxiety in CF patients and parent caregivers across eight European countries and the USA. Two national and one international data sets have been published. This paper summarises the findings, offers explanations for differences in results, and outlines the clinical implications with consideration given to if and how recommendations could be integrated into managing CF in the UK. Copyright © 2015 Elsevier Ltd. All rights reserved.

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**Other**

**Title:** Physical activity assessment in cystic fibrosis: A position statement

**Citation:** Journal of Cystic Fibrosis, November 2015, vol./is. 14/6(e25-e32), 1569-1993;1873-5010 (November 2015)

**Author(s):** O’Neill B., Kent L., Hulzebos E.H.J., Alison J., Arets B., Boas S., Bradley J.

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**Title:** Treatment and demographic factors affecting time to next pulmonary exacerbation in cystic fibrosis
Citation: Journal of Cystic Fibrosis, November 2015, vol./is. 14/6(763-769)

Author(s): Van Devanter D.R., Pasta D.J., Konstan M.W.

Title: Factors associated with response to treatment of pulmonary exacerbations in cystic fibrosis patients

Citation: Journal of Cystic Fibrosis, November 2015, vol./is. 14/6(755-762)

Author(s): Waters V.J., Stanojevic S., Sonneveld N., Klingel M., Grasemann H., Yau Y.C.W., Tullis E., Wilcox P., Freitag A., Chilvers M., Ratjen F.A.

Title: A comparison of respiratory and peripheral muscle strength, functional exercise capacity, activities of daily living and physical fitness in patients with cystic fibrosis and healthy subjects

Citation: Research in Developmental Disabilities, October 2015, vol./is. 45-46/(147-156)

Author(s): Arikan H., Yatar I., Calik-Kutukcu E., Aribas Z., Saglam M., Vardar-Yagli N., Savci S., Inal-Ince D., Ozcelik U., Kiper N.

Title: Eucapnic Voluntary Hyperventilation to Detect Exercise-Induced Bronchoconstriction in Cystic Fibrosis.

Citation: Lung, Oct 2015, vol. 193, no. 5, p. 733-738 (October 2015)

Author(s): Kirkby, Stephen E, Hayes, Don, Parsons, Jonathan P, Wisely, Clayton E, Kopp, Ben, McCoy, Karen S, Mastronarde, John G

Title: Induced sputum in young healthy children with cystic fibrosis.
Citation: Paediatric respiratory reviews, Oct 2015, vol. 16 Suppl 1, p. 6-8 (October 2015)

Author(s): Forton, Julian

Title: Critical timing of gastrostomy insertion in a child with cystic fibrosis.

Citation: Paediatric respiratory reviews, Oct 2015, vol. 16 Suppl 1, p. 19-21 (October 2015)

Author(s): Grime, Christopher J, Greenaway, Catherine, Clarke, Simon, Balfour-Lynn, Ian M

Title: Potential impact on fertility of new systemic therapies for cystic fibrosis.

Citation: Paediatric respiratory reviews, Oct 2015, vol. 16 Suppl 1, p. 25-27 (October 2015)

Author(s): Jones, Gareth Huw, Walshaw, Martin John

Title: The 29(th) Annual North American Cystic Fibrosis Conference.

Citation: Pediatric pulmonology, Oct 2015, vol. 50 Suppl 41, p. S1. (October 2015)
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