

# Cystic Fibrosis

## Evidence Update

November 2017

(Bimonthly)

Respecting everyone  
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Recognising success  
Working together  
**Our hospitals.**



## Training Sessions 2017

*All sessions are one hour*

### November (13.00)

2 <sup>nd</sup> Thu	Literature Searching
10 <sup>th</sup> Fri	Critical Appraisal
13 <sup>th</sup> Mon	Statistics
21 <sup>st</sup> Tues	Literature Searching
29 <sup>th</sup> Wed	Critical Appraisal

### December (12.00)

7 <sup>th</sup> Thu	Statistics
15 <sup>th</sup> Fri	Literature Searching



## Your Outreach Librarian: Jo Hooper

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## Updates

**NICE** National Institute for  
Health and Care Excellence

[Cystic fibrosis: diagnosis and management- guidance \(NG78\)](#)

Source: [National Institute for Health and Care Excellence - NICE](#) - 26 October 2017 -

Publisher: National Institute for Health and Care Excellence [Read Summary](#)

[Clinical referral: national standard protocol for cystic fibrosis](#)

Source: [GOV UK](#) - Source: [Public Health England](#) - 08 September 2017 - Publisher: Public Health England

[Piperacillin/Tazobactam 4 g/0.5 g powder for solution for infusion - Summary of Product Characteristics \(SPC\) - \(eMC\)](#)

Source: [electronic Medicines Compendium - eMC](#) - 08 November 2017

**This is just the first eMC Summary of Product Characteristics from your search. [See all](#)**

**BNF**

Source: [British National Formulary - BNF](#) - 25 October 2017

[Mucolytics for cystic fibrosis | Treatment summary](#)

[Oropharyngeal bacterial infections | Treatment summary](#)

[Proton pump inhibitors | Treatment summary](#)

[Nose infections, bacterial | Treatment summary](#)

[Respiratory system, drug delivery | Treatment summary](#)

[Aminoglycosides | Treatment summary](#)

 **Cochrane**  
Library

[Physical exercise training for cystic fibrosis](#)

Thomas Radtke, Sarah J Nevitt, Helge Hebestreit, Susi Kriemler

Online Publication Date: November 2017

[Autogenic drainage for airway clearance in cystic fibrosis](#)

Pamela McCormack, Paul Burnham, Kevin W Southern

Online Publication Date: October 2017

[Standard versus biofilm antimicrobial susceptibility testing to guide antibiotic therapy in cystic fibrosis](#)

Valerie Waters, Felix Ratjen

Online Publication Date: October 2017

[Interventions for treating distal intestinal obstruction syndrome \(DIOS\) in cystic fibrosis](#)

Jessica Green, Francis J Gilchrist, Will Carroll

Online Publication Date: September 2017

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OpenAthens login required. Register here: <https://openathens.nice.org.uk/>

[Cystic fibrosis: Overview of gastrointestinal disease](#)

Literature review current through: Oct 2017. | This topic last updated: Nov 05, 2016.

[Cystic fibrosis: Genetics and pathogenesis](#)

Literature review current through: Oct 2017. | This topic last updated: Oct 26, 2016.

[Cystic fibrosis: Hepatobiliary disease](#)

Literature review current through: Oct 2017. | This topic last updated: Oct 23, 2017.

[Cystic fibrosis: Treatment of acute pulmonary exacerbations](#)

Literature review current through: Oct 2017. | This topic last updated: Oct 06, 2017.

[Cystic fibrosis: Antibiotic therapy for chronic pulmonary infection](#)

Literature review current through: Oct 2017. | This topic last updated: Sep 21, 2017.

**Cystic  
Fibrosis Trust**

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08/11/2017 [Could the environment be having an effect on cystic fibrosis?](#)

03/11/2017 [Studies for Orkambi alternative show promising results](#)

03/11/2017 [Access to medicines - a winter of discontent is coming](#)

03/11/2017 [A look at the Accelerated Access Review response](#)

02/11/2017 [\(Moving and\) shaking up research](#)

26/10/2017 [How far away are we from saying goodbye to routine hospital visits?](#)

12/10/2017 [Wales extends access to Kalydeco](#)

12/10/2017 [Researchers develop tool that lights up around Pseudomonas](#)

05/10/2017 [Transplant opt out for England](#)



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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](mailto:library@uhbristol.nhs.uk)

## **Journal of Cystic Fibrosis**

**September 2017, Volume 16, Issue 5**

<http://www.cysticfibrosisjournal.com/current>

## **American Journal of Respiratory and Critical Care Medicine**

**October 15 2017, Volume 196, Issue 8**

<http://www.atsjournals.org/toc/ajrccm/current>

## **Thorax**

**November 2017, Volume 72, Issue 11**

<http://thorax.bmj.com/content/current>

## **Chest**

**October 2017, Volume 152, Issue 4**

<http://journal.chestnet.org/current>

## 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
- Psychological
- 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](mailto:library@uhbristol.nhs.uk)

### Medical

**Do cystic fibrosis centres with the lowest FEV<sub>1</sub> still use the least amount of intravenous antibiotics? A registry-based comparison of intravenous antibiotic use among adult CF centres in the UK**

**Author(s):** Hoo Z.H.; Campbell M.J.; Curley R.; Walters S.J.; Wildman M.J.

**Source:** Journal of Cystic Fibrosis; 2017

**Publication Type(s):** Article In Press

**Abstract:**Background: The Epidemiologic Study of Cystic Fibrosis using 1995-1996 and 2003-2005 data found that CF centres with lowest FEV<sub>1</sub> tended to use fewer intravenous antibiotics. We repeated the analyses using 2013-2014 UK CF registry data to determine if this was still the case. Methods: Analysing data for 2013 and 2014 separately, 28 adult CF centres were ranked according to median % age-adjusted FEV<sub>1</sub>. The top 7 centres were placed in the 'upper quarter' (best FEV<sub>1</sub>), the bottom 7 centres in 'lower quarter' (lowest FEV<sub>1</sub>), and the rest in 'middle half'. IV use was stratified according to %FEV<sub>1</sub>, then compared between the three groups. Results: Centres in the 'upper quarter' and 'middle half' used significantly more IV antibiotics compared to centres in the 'lower quarter' (van Elteren test P-value. 1 are still distinguished by lower use of intravenous antibiotics. Copyright © 2017 European Cystic Fibrosis Society.

**Glucose trajectories in cystic fibrosis and their association with pulmonary function**

**Author(s):** Reynaud Q.; Nove-Josserand R.; Durieu I.; Poupon-Bourdy S.; Touzet S.; Rabilloud M.

**Source:** Journal of Cystic Fibrosis; 2017

**Publication Type(s):** Article In Press

**Abstract:**Background: The prevalence of cystic fibrosis-related diabetes is increasing. This condition is potentially responsible for respiratory decline. Methods: At inclusion, then yearly (over three years), 111 children and 117 adults with cystic fibrosis had oral glucose tolerance and insulin tests at one (G1) and 2. h (G2). KmL analysis identified homogeneous G1 and G2 glucose trajectories. A linear mixed model quantified the relationships between trajectories and FEV<sub>1</sub> changes. Results: In children, there were three G1 and four G2 trajectories and FEV<sub>1</sub> decrease was not significantly different between G1 or G2 trajectories. In adults, two G1 and four G2 trajectories were identified and FEV<sub>1</sub> change was estimated at -0.85/year (95% CI: [-1.54; -0.17], p = 0.01) whatever the G1 trajectory and found significantly faster in the high and increasing G2 trajectory (-2.1/year, [-3.9; -0.2], p = 0.03). Conclusions: In case of persistent G2 abnormality, physicians should be alert for



clinical deterioration and intensify patient surveillance. Copyright © 2017 European Cystic Fibrosis Society.

### **Recent progress in translational cystic fibrosis research using precision medicine strategies**

**Author(s):** Cholon D.M.; Gentsch M.

**Source:** Journal of Cystic Fibrosis; 2017

**Publication Type(s):** Article In Press

**Abstract:** Significant progress has been achieved in developing precision therapies for cystic fibrosis; however, highly effective treatments that target the ion channel, CFTR, are not yet available for many patients. As numerous CFTR therapeutics are currently in the clinical pipeline, reliable screening tools capable of predicting drug efficacy to support individualized treatment plans and translational research are essential. The utilization of bronchial, nasal, and rectal tissues from individual cystic fibrosis patients for drug testing using in vitro assays such as electrophysiological measurements of CFTR activity and evaluation of fluid movement in spheroid cultures, has advanced the prediction of patient-specific responses. However, for precise prediction of drug effects, in vitro models of CFTR rescue should incorporate the inflamed cystic fibrosis airway environment and mimic the complex tissue structures of airway epithelia. Furthermore, novel assays that monitor other aspects of successful CFTR rescue such as restoration of mucus characteristics, which is important for predicting mucociliary clearance, will allow for better prognoses of successful therapies in vivo. Additional cystic fibrosis treatment strategies are being intensively explored, such as development of drugs that target other ion channels, and novel technologies including pluripotent stem cells, gene therapy, and gene editing. The multiple therapeutic approaches available to treat the basic defect in cystic fibrosis combined with relevant precision medicine models provide a framework for identifying optimal and sustained treatments that will benefit all cystic fibrosis patients. Copyright © 2017.

### **Approach to chronic abdominal pain in Cystic Fibrosis**

**Author(s):** Lusman S.S.; Grand R.

**Source:** Journal of Cystic Fibrosis; 2017

**Publication Type(s):** Article In Press

**Abstract:** Abdominal pain in individuals with CF is challenging for the patient as well as the physician, as the differential diagnosis can be complex. Most gastrointestinal manifestations of CF present with regional abdominal pain. Pain localization, which requires knowledge of gut development and innervation, is crucial to understanding the pathophysiology of abdominal pain in CF. The location of the pain, together with the clinical presentation, shapes the differential diagnosis and thus guides the evaluation and management. Copyright © 2017 European Cystic Fibrosis Society.

### **Gallbladder and bile duct disease in Cystic Fibrosis**

**Author(s):** Assis D.N.; Debray D.

**Source:** Journal of Cystic Fibrosis; 2017

**Publication Type(s):** Article In Press

**Abstract:** Cystic fibrosis (CF) is a multi-organ, clinically diverse disorder caused by mutations in the cystic fibrosis transmembrane conductance receptor (CFTR). Awareness of extra-pulmonary manifestations, including gastrointestinal and hepatobiliary disturbances, is an increasingly important part of providing high-quality care to patients with CF. Furthermore, biliary disorders, including gallbladder and bile duct disease, are common complications of CF. Therefore, a thorough

understanding and efficient clinical evaluation of the gallbladder and biliary tree is an important aspect of integrated care for the patient with CF in order to prevent progression of undetected pathology. This best practice article summarizes the basis for gallbladder and bile duct pathology, describes the context and clinical presentation of biliary disease, and provides recommended approaches to delivery of high-quality care for patients with CF. Copyright © 2017 European Cystic Fibrosis Society.

### **Cystic Fibrosis-related cirrhosis**

**Author(s):** Leung D.H.; Narkewicz M.R.

**Source:** Journal of Cystic Fibrosis; 2017

**Publication Type(s):** Article In Press

**Abstract:** While liver involvement is common in cystic fibrosis, the major liver disorder with impact on the clinical outcome of individuals with CF is the development of multilobular cirrhosis with progression to portal hypertension. Interestingly, this is a disorder primarily of children and adolescents. We review the proposed pathogenesis, clinical presentation, diagnostic work-up, medical and surgical management, and complications of CF cirrhosis. Copyright © 2017 European Cystic Fibrosis Society.

### **Cystic Fibrosis & disorders of the large intestine: DIOS, constipation, and colorectal cancer**

**Author(s):** Abraham J.M.; Taylor C.J.

**Source:** Journal of Cystic Fibrosis; 2017

**Publication Type(s):** Article In Press

**Abstract:** Since 1966 when the Cystic Fibrosis Foundation Patient Registry (CFFPR) was founded, clinicians have witnessed significant advances in both the quality and quantity of life for patients living with Cystic Fibrosis (CF). As patients with CF live longer and fuller lives, increasing encumbrances from gastrointestinal manifestations of CF will be observed. This article serves to discuss "below the diaphragm" concerns involving the large intestine (Distal Intestinal Obstruction Syndrome, Constipation, and Colorectal Cancer). Avenues for development and implementation of clinical care protocols, particularly regarding proactive management of known associated conditions and cancer screening, will continue to be refined in the coming years. It falls to the multidisciplinary CF care team to be actively engaged in addressing these concerns effectively as priority shifts from relative acuity (typically related to early nutrition and lung function) to the travails of longevity as the CF population continues to age. Copyright © 2017 European Cystic Fibrosis Society.

### **Cystic Fibrosis and gastroesophageal reflux disease**

**Author(s):** Maqbool A.; Pauwels A.

**Source:** Journal of Cystic Fibrosis; 2017

**Publication Type(s):** Article In Press

**Abstract:** Gastroesophageal reflux is common in children and adults with cystic fibrosis (CF). Pathological gastroesophageal reflux disease (GERD) is also frequent in patients of all ages with CF. This article reviews the pathophysiology, diagnostic work-up, management options, complications, and future directions in the evaluation and management of GERD - unique to and pertinent for - patients with CF in particular. Copyright © 2017 European Cystic Fibrosis Society.

### **Pharmacokinetic-pharmacodynamic target attainment analyses to determine optimal dosing of ceftazidime-avibactam for the treatment of acute pulmonary exacerbations in patients with cystic fibrosis**

**Author(s):** Bensman T.J.; D'Argenio D.Z.; Wang J.; Jayne J.; Beringer P.M.; Fukushima L.; Rao A.P.

**Source:** Antimicrobial Agents and Chemotherapy; 2017; vol. 61 (no. 10)

**Publication Type(s):** Article

**Abstract:** Acute pulmonary exacerbations (APE) involving *Pseudomonas aeruginosa* are associated with increased morbidity and mortality in cystic fibrosis (CF) patients. Drug resistance is a significant challenge to treatment. Ceftazidime-avibactam (CZA) demonstrates excellent in vitro activity against isolates recovered from CF patients, including drug-resistant strains. Altered pharmacokinetics (PK) of several betalactam antibiotics have been reported in CF patients. Therefore, this study sought to characterize the PK of CZA and perform target attainment analyses to determine the optimal treatment regimen. The PK of CZA in 12 adult CF patients administered 3 intravenous doses of 2.5 g every 8 h infused over 2 h were determined. Population modeling utilized the maximum likelihood expectation method. Monte Carlo simulations determined the probability of target attainment (PTA). An exposure target consisting of the cumulative percentage of a 24-h period that the free drug concentration exceeds the MIC under steady-state pharmacokinetic conditions ( $fT > MIC$ ) was evaluated for ceftazidime (CAZ), and an exposure target consisting of the cumulative percentage of a 24-h period that the free drug concentration exceeds a 1-mg/liter threshold concentration ( $fT > 1\text{mg/liter}$ ) was evaluated for avibactam (AVI). Published CAZ and CZA MIC distributions were incorporated to evaluate cumulative response probabilities. CAZ and AVI were best described by one-compartment models. The values of total body clearance (CL; CAZ CL, 7.53 +/- 1.28 liters/h; AVI CL, 12.30 +/- 1.96 liters/h) and volume of distribution (V; CAZ V, 18.80 +/- 6.54 liters; AVI V, 25.30 +/- 4.43 liters) were broadly similar to published values for healthy adults. CZA achieved a PTA ( $fT$ , 50%) of >0.9 for MICs of Copyright © 2017 American Society for Microbiology. All Rights Reserved.

### **The safety of lumacaftor and ivacaftor for the treatment of cystic fibrosis**

**Author(s):** Talamo Guevara M.; McColley S.A.

**Source:** Expert Opinion on Drug Safety; Nov 2017; vol. 16 (no. 11); p. 1305-1311

**Publication Type(s):** Review

**Abstract:** Introduction: Lumacaftor-ivacaftor is indicated for treatment of cystic fibrosis (CF) in patients homozygous for the Phe-508del cystic fibrosis transmembrane conductance regulator (CFTR) gene mutations. In clinical trials, treated patients showed improved pulmonary function, reduced pulmonary exacerbations, and other benefits. This article reviews safety of this therapy. Areas covered: Safety findings in ivacaftor, lumacaftor and combined therapy trials, and reported subsequently through post-approval evaluation, were accessed by PubMed and Google searches using key words 'VX-770', 'ivacaftor', 'VX-809', and 'lumacaftor'. Transaminitis was seen in ivacaftor and combination trials. Non-congenital cataracts were seen in pre-clinical animal studies and in children taking ivacaftor and combined therapy. Dyspnea occurs in some patients taking lumacaftor and combined therapy and usually resolves without stopping treatment. Lumacaftor is a strong inducer of CYP3A while ivacaftor is a CYP3A sensitive substrate. Combination therapy can decrease systemic exposure of medications that are substrates of CYP3A, decreasing therapeutic effect. Co-administration of lumacaftor-ivacaftor with sensitive CYP3A substrates or CYP3A substrates with narrow therapeutic index is not recommended. Expert opinion: Lumacaftor-ivacaftor therapy may be associated with ocular and hepatic side effects. Specific recommendations for monitoring are available. Dyspnea occurs, especially during initiation of treatment. Potential drug interactions should be evaluated in patients taking combination therapy. The risk benefit ratio of lumacaftor-ivacaftor favors therapy. Copyright © 2017 Informa UK Limited, trading as Taylor & Francis Group.

### **Ivacaftor withdrawal syndrome in cystic fibrosis patients with the G551D mutation**

**Author(s):** Trimble A.T.; Donaldson S.H.

**Source:** Journal of Cystic Fibrosis; 2017

**Publication Type(s):** Article In Press

**Abstract:**Ivacaftor use can lead to dramatic health improvements in cystic fibrosis (CF) patients with gating mutations. Here, we report five instances of dramatic clinical decline following withdrawal of ivacaftor in three individuals with the G551D-CFTR mutation. In each case, the patient's lung function and symptoms rapidly deteriorated after cessation of treatment. Awareness of this phenomenon should inform both clinical practices as well as the design of future clinical trials of highly active CFTR modulators. Copyright © 2017 European Cystic Fibrosis Society.

### **Lung transplantation in cystic fibrosis patients with difficult to treat lung infections**

**Author(s):** Dupont L.

**Source:** Current Opinion in Pulmonary Medicine; Nov 2017; vol. 23 (no. 6); p. 574-579

**Publication Type(s):** Review

**Abstract:**Purpose of review In cystic fibrosis (CF) patients with end-stage pulmonary disease, lung transplantation (LTx) remains a life-extending therapy with good outcome in most patients. Despite early concern about chronic pretransplantation infections in the context of posttransplantation immunosuppression, typical CF-associated organisms such as *Pseudomonas aeruginosa* turned out to be quite well manageable and associated with favorable outcomes in transplanted CF patients, even in patients with highly resistant strains. However, the situation is less evident with other pathogens. Recent findings *Burkholderia cenocepacia* is associated with reduced survival and regarded as a contraindication for LTx in most centers, other *Burkholderia* species are less problematic. Other resistant Gram-negative bacteria and methicillin-resistant staphylococcus aureus in CF patients are not regarded as a contraindication. Nontuberculous mycobacteria disease in CF patients does not preclude successful recovery after LTx, although postoperative complications can be expected in patients with *Mycobacterium abscessus* and specific management is indicated. Fungal species should be treated aggressively to limit morbidity after transplantation. Summary Despite its complexity, LTx is safe in most CF patients, with good outcomes if the pathogens that are present are identified and adequately treated. Copyright © 2017 Wolters Kluwer Health, Inc. All rights reserved.

### **Diagnosis, follow-up and treatment of cystic fibrosis-related liver disease**

**Author(s):** Van De Peppel I.P.; Bertolini A.; Bodewes F.A.J.A.; Verkade H.J.; Jonker J.W.

**Source:** Current Opinion in Pulmonary Medicine; Nov 2017; vol. 23 (no. 6); p. 562-569

**Publication Type(s):** Review

**Abstract:**Purpose of review To provide an insight and overview of the challenges in the diagnosis, follow-up and treatment of cystic fibrosis-related liver disease (CFLD). Recent findings The variable pathophysiology of CFLD complicates its diagnosis and treatment. A 'gold standard' for CFLD diagnosis is lacking. Over the past years, new techniques to diagnose features of CFLD, such as transient elastography, have been investigated. Although most of these tests confirm cystic fibrosis-related liver involvement (CFLI), they are, however, not suitable to distinguish various phenotypical presentations or predict progression to clinically relevant cirrhosis or portal hypertension. A combined initiative from the European and the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition has been started, aimed to obtain consensus on CFLD criteria and definitions. Currently, only ursodeoxycholic acid is used in CFLD treatment, although it has not been convincingly demonstrated to change the natural course of the disease. Drugs that

directly target cystic fibrosis transmembrane conductance regulator protein dysfunction show promising results; however, more long-term follow-up and validation studies are needed. Summary CFLD is an umbrella term referring to a wide variety of liver manifestations with variable clinical needs and consequences. CFLD with portal hypertension is the most severe form of CFLD due to its significant implications on morbidity and mortality. The clinical relevance of other CFLI is uncertain. Consensus on CFLD definitions is essential to validate new diagnostic tools and therapeutic outcome measures. Copyright © 2017 Wolters Kluwer Health, Inc. All rights reserved.

### **Cystic Fibrosis: A Risk Condition for Renal Disease.**

**Author(s):** Santoro, Domenico; Postorino, Adele; Lucanto, Cristina; Costa, Stefano;

**Source:** Journal of Renal Nutrition; Nov 2017; vol. 27 (no. 6); p. 470-473

**Publication Type(s):** Academic Journal

**Abstract:**Objective: Cystic fibrosis (CF) is the most common autosomal recessive disease affecting the Caucasian population, with a birth incidence ranging between 1:2,500 and 1:1,800. It is caused by mutations in the CF transmembrane regulator gene which is localized on 7 chromosomes. Renal disease is reported as a relatively rare complication in adult patient with CF. We evaluated proteinuria and chronic renal failure (CRF) in a population of patients with CF. Methods: A retrospective study was carried out in a referral center for CF at University of Messina in Italy. We identified all patients with renal disease, characterized by proteinuria and/or CRF, during the period 2007 to 2012 and reviewed their medical records to assess influence on renal disease of genotype, number of pulmonary exacerbation, pancreatic insufficiency, pulmonary function, CF-related diabetes, and antibiotics courses. Results: From a population of 77 adult patients with CF, we identified 9 patients with proteinuria (11.7%), and 11 patients (14.28%) with CRF. Mean age was 35.6 (+5.1 standard deviation) years, 55% were female and 33% had diabetes mellitus. Renal biopsy was performed in 3 patients because of nephrotic syndrome in 1 patient and proteinuria with renal failure in the other 2 patients. Renal amyloidosis was disclosed in 2, whereas IgA nephropathy in 1 patient. The  $\Delta F508$  mutation in homozygosis was present in 44% of patients with proteinuria (vs. 27% of our CF population, relative risk 2.07), whereas genotype  $\Delta F508/N1303K$  in 22%.  $\Delta F508$  allele mutation was present in 77.7% of proteinuric patients. Conclusions: Our study shows a higher prevalence of renal disease in patients with CF, than was previously described. The main reason may be related to increased life expectancy because of better management. Moreover, patients with  $\Delta F508$  homozygosis had higher risk of proteinuria.

### **Experience of using non-invasive ventilation as an adjunct to airway clearance techniques in adults with cystic fibrosis-A qualitative study.**

**Author(s):** Rodriguez Hortal, Maria Cecilia; Hedborg, Anna; Biguet, Gabriele; Nygren-Bonnier, Malin

**Source:** Physiotherapy theory and practice; Nov 2017 ; p. 1-12

**Publication Type(s):** Journal Article

**Abstract:**BACKGROUND Adults with cystic fibrosis (CF) suffer from abnormally thick mucus that is difficult to clear from the airways. Different airway clearance techniques (ACTs) can be used to clear secretions and non-invasive ventilation (NIV) can be used as an adjunct to these techniques. ACTs are ideally introduced at the time of diagnosis and thereafter modified throughout the patient's lifespan and disease progress. PURPOSE The research aim was to describe adult patients' views and experiences with using NIV as an adjunct to ACT. METHOD Eighteen adults with CF were interviewed about their experiences with using NIV during ACT. Semi-structured interviews were conducted and analyzed in accordance with qualitative content analysis. RESULT The results gave rise to the overall theme 'Becoming Friends with NIV' and six associated categories: 1) getting a sense of control and feedback; 2) getting support; 3) dealing with doubt; 4) finding the rhythm; 5) feeling the effects; and

6) finding their own motivation. The findings represent a learning process for adults during the implementation stages of NIV; the physiotherapist was found to play a key role in this process. CONCLUSION 'Becoming Friends with NIV' involves a learning process for adults with CF. To facilitate this learning process, different aspects should be taken into account so as to promote independence and self-management, which in turn allows the patient to experience the treatment as meaningful. The findings are relevant to physiotherapists working with adults and NIV, as improved insight into and understanding of the relationship may have a positive influence on the outcome and success of NIV usage.

### **Assessment of Liver Disease Progression in cystic Fibrosis Using Transient Elastography.**

**Author(s):** Gominon, Anne-Laure; Frison, Eric; Hiriart, Jean-Baptiste; Vergniol, Julien;

**Source:** Journal of pediatric gastroenterology and nutrition; Nov 2017

**Publication Type(s):** Journal Article

**Abstract:** OBJECTIVES Cystic fibrosis related liver disease (CFLD) can develop silently in early life and approximately 10% of children with cystic fibrosis (CF) become cirrhotic before adulthood. Clinical, biological and ultrasound criteria used to define CFLD often reveal liver involvement at an advanced stage. The aim of this retrospective study was to assess the progression of liver stiffness measurement (LSM) in pediatric CF patients. METHODS The change of LSM, expressed as kPa/year and %/year, was measured using transient elastography (TE, Fibroscan) in 82 CF children (median age: 6.8 years, IQR: 5.8). Mean time interval between the two LSM was 3.5 years. RESULTS Median initial liver stiffness was 3.7 kPa (IQR: 1.3), and then progressed by 0.23 kPa/year, i.e. 6%/year. The 7 patients who developed CFLD had a higher initial level of alanine aminotransferase (50 [IQR:15] vs 30 [IQR:18],  $p=0.0001$ ) and presented a more rapid progression of LSM (0.94 vs 0.23 kPa/year,  $p=0.02$ ). CONCLUSIONS This study shows that the slope of worsening of liver stiffness is greater in patients who will develop CFLD, suggesting that annual TE may be useful to detect risk of severe liver disease at an earlier stage.

### **Cost Effectiveness of Screening Individuals with Cystic Fibrosis for Colorectal Cancer.**

**Author(s):** Gini, Andrea; Zauber, Ann G; Cenin, Dayna R; Omidvari, Amir-Houshang; Hempstead, Sarah E; Fink, Aliza K; Lowenfels, Albert B; Lansdorp-Vogelaar, Iris

**Source:** Gastroenterology; Nov 2017

**Publication Type(s):** Journal Article

**Abstract:** BACKGROUND & AIMS Individuals with cystic fibrosis are at increased risk of colorectal cancer (CRC) compared to the general population, and risk is higher among those who received an organ transplant. We performed a cost-effectiveness analysis to determine optimal CRC screening strategies for patients with cystic fibrosis. METHODS We adjusted the existing MISCAN-Colon microsimulation model to reflect increased CRC risk and lower life-expectancy in patients with cystic fibrosis. Modeling was performed separately for individuals who never received an organ transplant and patients who had received an organ transplant. We modeled 76 colonoscopy screening strategies that varied the age range and screening interval. The optimal screening strategy was determined based on a willingness to pay threshold of \$100,000 per life-year gained. Sensitivity and supplementary analyses were performed, including fecal immunochemical test (FIT) as an alternative test, earlier ages of transplantation, and increased rates of colonoscopy complications, to assess if optimal screening strategies would change. RESULTS Colonoscopy every 5 years, starting at an age of 40 years, was the optimal colonoscopy strategy for patients with cystic fibrosis who never received an organ transplant; this strategy prevented 79% of deaths from CRC. Among patients with cystic fibrosis who had received an organ transplant, optimal colonoscopy screening should start at an age of 30 or 35 years, depending on the patient's age at time of transplantation. Annual FIT screening

was predicted to be cost-effective for patients with cystic fibrosis. However, the level of accuracy of the FIT in population is not clear. CONCLUSIONS Using a MISCAN-Colon microsimulation model, we found screening of patients with cystic fibrosis for CRC to be cost effective. Due to the higher risk in these patients for CRC, screening should start at an earlier age with a shorter screening interval. The findings of this study (especially those on FIT screening) may be limited by restricted evidence available for patients with cystic fibrosis

### **Prevalence of Fecal Incontinence in Adults with Cystic Fibrosis**

**Author(s):** Benezech A.; Bouvier M.; Vitton V.; Desmazes-Dufeu N.; Coltey B.; Reynaud-Gaubert M.

**Source:** Digestive Diseases and Sciences; Oct 2017 ; p. 1-7

**Publication Type(s):** Article In Press

**Abstract:**Background: Patients with cystic fibrosis (CF) are deemed at risk of developing urinary incontinence (UI) due to repeated coughing and other factors causing increased pressure on the pelvic floor. Fecal incontinence (FI) is probably derived from the same mechanism, but only very few data are available on its frequency. Aims: The aim of this study was to determine the prevalence of FI in an adult population with CF. Methods: This retrospective study was conducted from January 2012 to June 2014. Patients were recruited from Marseille referral center for adult CF. They were asked to fill in a self-completed anonymous questionnaire for symptom assessment of UI and FI. Clinical data and a detailed history of CF were also recorded. Results: A total of 155 out of 190 patients (92 females) of mean age 30.5 +/- 11 years completed the survey. Seventy-three patients (47%) were lung transplanted. Forty patients (25.8%) reported FI with a mean St Mark's score of 4.9 +/- 2. Thirty-five patients (22.6%) reported UI. Eighteen patients (11.6%) reported both FI and UI. FI was significantly more frequent in older patients (34.27 vs. 29.54 years,  $p = 0.03$ ) and in patients with associated UI ( $p = 0.001$ ). No relationship was found between respiratory, bacterial, nutritional status, transplantation, pancreatic status, practice of physiotherapy, delivery history, and FI. Conclusions: The high prevalence of FI in CF and its negative impacts need to integrate this symptom in the overall treatment of this pathology. The systematic early detection of FI may allow its rapid management and limit their consequences. Copyright © 2017 Springer Science+Business Media, LLC

### **Transient elastography and controlled attenuation parameter assessment of liver disease in children and young adults with cystic fibrosis: A 3 year longitudinal study**

**Author(s):** Mohanty P.; Wiggins S.M.; Nguyen D.; Harney S.; Jonas M.M.; Lee C.K.; Mitchell P.D.

**Source:** Hepatology; Oct 2017; vol. 66

**Publication Type(s):** Conference Abstract

**Abstract:**Background: Liver disease is the third leading cause of death in cystic fibrosis (CF) patients. Hepatic steatosis is a common, early sign of CF-related liver disease (CFLD). Controlled attenuation parameter (CAP), obtained during transient elastography (TE), can detect and quantify steatosis. Objective: To evaluate if serial LSM and CAP can be used to identify and follow progression of CFLD. Methods: This was a longitudinal cohort study of CF patients seen for routine outpatient care at Boston Children's Hospital. CAP and LSM were obtained at enrollment (January-October 2013) and annually up to 3 years. CFLD was defined per published criteria as: No CFLD, CFLD without portal hypertension (PHTN) and CFLD with PHTN. CFLD without PHTN criteria: recent ALT > 1.3xULN, on ursodiol, or abnormal liver echogenicity on imaging. CFLD with PHTN criteria: splenomegaly, esophageal varices on endoscopy, platelet count  $\geq 2$  and 74(30%) 18-25y] underwent baseline LSM; 127(51%) also had CAP. At enrollment, 158(64%) had no CFLD, 73(29%) CFLD without PHTN, and 18(7%) CFLD with PHTN. A total of 387 paired encounters were documented, 43(11%) reflecting a change in disease status. The median time between adjacent measurements was 12 months (IQR 10-15). Subjects with CFLD without PHTN at one encounter followed by CFLD with PHTN at the next

encounter saw a greater change in CAP than those whose status remained unchanged (40.06.6 dB/m, P14.4 vs 5.5+/-2.6 dB/m; P=0.19). There were no significant differences across adjacent encounters for LSM. Conclusion: In this 3 year study, CAP is able to detect changes in CFLD when there is no detectable change in liver fibrosis (Figure presented).

### **Allergic bronchopulmonary aspergillosis in cystic fibrosis: MR Imaging of airway mucus contrasts as a tool for diagnosis**

**Author(s):** Dournes G.; Berger P.; Delhaes L.; Montaudon M.; Chateil J.-F.; Marthan R.; Fayon M.

**Source:** Radiology; Oct 2017; vol. 285 (no. 1); p. 261-269

**Publication Type(s):** Article

**Abstract:** Purpose: To assess the diagnostic accuracy of mucus contrast characterization by using magnetic resonance (MR) imaging to discriminate allergic bronchopulmonary aspergillosis (ABPA) in cystic fibrosis (CF). Materials and Methods: The study was approved by the local Ethics Committee, and all patients or their parents gave written informed consent. One hundred ten consecutive patients with CF were screened between January 2014 and July 2015. All patients underwent a non-contrast material-enhanced MR protocol that included routine T1-weighted and T2-weighted sequences. The presence of mucus with both high T1 and low T2 signal intensities and the so-called inverted mucoid impaction signal (IMIS) sign was qualitatively and quantitatively assessed by two physicians who were blinded to all other data. The reference standard for a diagnosis of ABPA was the criteria of the Cystic Fibrosis Foundation Consensus Conference. ABPA status was followed up for 1 year. Reproducibility was assessed by using the kappa test, correlation was assessed by using the Spearman coefficient, and diagnostic accuracy was assessed by calculating the sensitivity and specificity of IMIS. Results: One hundred eight patients with CF were included (mean age, 20 years +/- 11 [standard deviation]; range, 6-53 years): 18 patients with ABPA and 90 patients without ABPA. At the lobar level, inter- and intrareader reproducibility were very good (kappa > 0.90). IMIS had 94% sensitivity (95% confidence interval [CI]: 73%, 99%) and 100% specificity (95% CI: 96%, 100%) for the diagnosis of ABPA. A complete resolution of IMIS was observed in patients with ABPA after 3 months of specific treatment that was significantly correlated with decrease in total immunoglobulin E level (rho = 0.47; P = .04). Conclusion: The IMIS sign was both specific and sensitive for the diagnosis of ABPA in CF. Allergic fungal inflammation appears to induce characteristic modifications of mucus contrasts that are assessable by using a noninvasive, contrast material-free, and radiation-free method. Copyright © RSNA, 2017.

### **Autogenic drainage for airway clearance in cystic fibrosis**

**Author(s):** McCormack P.; Burnham P.; Southern K.W.

**Source:** Cochrane Database of Systematic Reviews; Oct 2017; vol. 2017 (no. 10)

**Publication Type(s):** Review

Available at [Cochrane Database of Systematic Reviews](#) - from Cochrane Collaboration (Wiley)

**Abstract:** Background: Autogenic drainage is an airway clearance technique that was developed by Jean Chevaillier in 1967. The technique is characterised by breathing control using expiratory airflow to mobilise secretions from smaller to larger airways. Secretions are cleared independently by adjusting the depth and speed of respiration in a sequence of controlled breathing techniques during exhalation. The technique requires training, concentration and effort from the individual. It is important to systematically review the evidence demonstrating that autogenic drainage is an effective intervention for people with cystic fibrosis. Objectives: To compare the clinical effectiveness of autogenic drainage in people with cystic fibrosis with other physiotherapy airway clearance techniques. Search methods: We searched the Cochrane Cystic Fibrosis Trials Register, compiled from electronic database searches and handsearching of journals and conference abstract



books. We also searched the reference lists of relevant articles and reviews, as well as two trials registers (31 August 2017). Date of most recent search of the Cochrane Cystic Fibrosis Trials Register: 25 September 2017. Selection criteria: We identified randomised and quasi-randomised controlled studies comparing autogenic drainage to another airway clearance technique or no therapy in people with cystic fibrosis for at least two treatment sessions. Data collection and analysis: Data extraction and assessments of risk of bias were independently performed by two authors. The authors assessed the quality of the evidence using the GRADE system. The authors contacted two investigators for further information pertinent to their published studies. Main results: Searches retrieved 35 references to 21 individual studies, of which seven ( $n = 208$ ) were eligible for inclusion. One study was of parallel design with the remaining six being cross-over in design; participant numbers ranged from 17 to 75. The total study duration varied between four days and two years. The age of participants ranged between seven and 63 years with a wide range of disease severity reported. Six studies enrolled participants who were clinically stable, whilst participants in one study had been hospitalised with an infective exacerbation. All studies compared autogenic drainage to one (or more) other recognised airway clearance technique. Exercise is commonly used as an alternative therapy by people with cystic fibrosis; however, there were no studies identified comparing exercise with autogenic drainage. The quality of the evidence was generally low or very low. The main reasons for downgrading the level of evidence were the frequent use of a cross-over design, outcome reporting bias and the inability to blind participants. The review's primary outcome, forced expiratory volume in one second, was the most common outcome measured and was reported by all seven studies; only three studies reported on quality of life (also a primary outcome of the review). One study reported on adverse events and described a decrease in oxygen saturation levels whilst performing active cycle of breathing techniques, but not with autogenic drainage. Six of the seven included studies measured forced vital capacity and three of the studies used mid peak expiratory flow (per cent predicted) as an outcome. Six studies reported sputum weight. Less commonly used outcomes included oxygen saturation levels, personal preference, hospital admissions or intravenous antibiotics. There were no statistically significant differences found between any of the techniques used with respect to the outcomes measured except when autogenic drainage was described as being the preferred technique of the participants in one study over postural drainage and percussion. Authors' conclusions: Autogenic drainage is a challenging technique that requires commitment from the individual. As such, this intervention merits systematic review to ensure its effectiveness for people with cystic fibrosis. From the studies assessed, autogenic drainage was not found to be superior to any other form of airway clearance technique. Larger studies are required to better evaluate autogenic drainage in comparison to other airway clearance techniques in view of the relatively small number of participants in this review and the complex study designs. The studies recruited a range of participants and were not powered to assess non-inferiority. The varied length and design of the studies made the analysis of pooled data challenging. Copyright © 2017 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

### **Poor recovery from cystic fibrosis pulmonary exacerbations is associated with poor long-term outcomes**

**Author(s):** Sanders D.B.; Zhao Q.; Li Z.; Farrell P.M.

**Source:** Pediatric Pulmonology; Oct 2017; vol. 52 (no. 10); p. 1268-1275

**Publication Type(s):** Article

**Abstract:** Rationale: People with CF treated with IV antibiotics for a pulmonary exacerbation (PEX) frequently fail to recover to baseline FEV1. The long-term impact of these events has not been studied. Objectives: To determine if a patient's spirometric recovery after a PEX is associated with time to next PEX within 1 year, the spirometric recovery after the next PEX, and/or the number of PEX episodes in the next 3 years. Methods: We used data from the CF Foundation Patient Registry from 2004 to 2011. We randomly selected one PEX per patient that met inclusion/exclusion criteria.

Patients were defined as Non-Responders if their best FEV1 (in liters) recorded in the 3 months after the PEx was 1 (in liters) in the 6 months before the PEx. We compared Responders and Non-Responders using multivariable regression models. Results: We randomly chose 13 954 PEx episodes that met inclusion/exclusion criteria. A total of 2 762 (19.8%) patients were classified as Non-Responders. Non-Responders had a shorter median time to the next PEx, 235 (95%CI 218, 252) days, versus >365 days for Responders. Thirty-four percent of Non-Responders at the initial PEx were also Non-Responders at the next PEx, versus 20% of Responders at the initial PEx. Non-Responders had more PEx episodes over the next 3 years, 4.99 (95%CI 4.84, 5.13), than Responders, 3.46 (95%CI 3.41, 3.51). Conclusions: Poor recovery after a PEx is associated with a shorter time to the next PEx, increased risk of poor recovery at a second PEx, and more frequent subsequent PEx treatments. Copyright © 2017 Wiley Periodicals, Inc.

## Microbiological

### Developing a model for cystic fibrosis sociomicrobiology based on antibiotic and environmental stress

**Author(s):** Lopes S.P.; Pereira M.O.; Azevedo N.F.

**Source:** International Journal of Medical Microbiology; 2017

**Publication Date:** 2017

**Publication Type(s):** Article In Press

**Abstract:** Cystic fibrosis (CF) infections are invariably biofilm-mediated and polymicrobial, being safe to assume that a myriad of factors affects the sociomicrobiology within the CF infection site and modulate the CF community dynamics, by shaping their social activities, overall functions, virulence, ultimately affecting disease outcome. This work aimed to assess changes in the dynamics (particularly on the microbial composition) of dual-/three-species biofilms involving CF-classical (*Pseudomonas aeruginosa*) and unusual species (*Inquilinus limosus* and *Dolosigranulum pigrum*), according to variable oxygen conditions and antibiotic exposure. Low fluctuations in biofilm compositions were observed across distinct oxygen environments, with dual-species biofilms exhibiting similar relative proportions and *P. aeruginosa* and/or *D. pigrum* populations dominating three-species consortia. Once exposed to antibiotics, biofilms displayed high resistance profiles, and microbial compositions, distributions, and microbial interactions significantly challenged. The antibiotic/oxygen environment supported such fluctuations, which enhanced for three-species communities. In conclusion, antibiotic therapy hugely disturbed CF communities' dynamics, inducing significant compositional changes on multispecies consortia. Clearly, multiple perturbations may disturb this dynamic, giving rise to various microbiological scenarios in vivo, and affecting disease phenotype. Therefore, an appreciation of the ecological/evolutionary nature within CF communities will be useful for the optimal use of current therapies and for newer breakthroughs on CF antibiotherapy. Copyright © 2017 Elsevier GmbH.

### Bacterial overgrowth, dysbiosis, inflammation, and dysmotility in the Cystic Fibrosis intestine

**Author(s):** Dorsey J.; Gonska T.

**Source:** Journal of Cystic Fibrosis; 2017

**Publication Type(s):** Article In Press

### Ralstonia infection in cystic fibrosis

**Author(s):** Green H.D.; Bright-Thomas R.; Jones A.M.; Kenna D.T.; Turton J.F.; Woodford N.

**Source:** Epidemiology and Infection; Oct 2017; vol. 145 (no. 13); p. 2864-2872

**Publication Type(s):** Article

Available at [Epidemiology and Infection](#) - from ProQuest (Hospital Premium Collection) - NHS Version

**Abstract:** This study aimed to determine prevalence of *Ralstonia* spp. in cystic fibrosis patients, look for any evidence of cross infection and to describe clinical outcomes for patients infected by *Ralstonia* spp. Prevalence of *Ralstonia* spp. was calculated annually from 2008 to 2016. Pulsed-field gel electrophoresis was performed on 1 sample from patients with an isolation of *Ralstonia* spp. between 2008 and 2016. A prospective, longitudinal observational study of adult patients was performed with 12 months follow-up from recruitment. Prevalence of *Ralstonia* spp. rose from 0.6% in 2008 to 2.4% in 2016. In total 12 out of 14 (86%) patients with 1 isolation of *Ralstonia* spp. developed chronic infection. A pair and a group of three unrelated patients with epidemiological connections shared strains of *Ralstonia mannitolilytica*. Lung function of *Ralstonia* spp. infected patients was moderately to severely impaired. Prevalence of *Ralstonia* spp. is low but increasing. The risk of a patient developing chronic *Ralstonia* spp. infection following first acquisition is high and cross-infection may be possible. Whether *Ralstonia* spp. infection causes increased pulmonary exacerbation frequency and lung function decline needs to be evaluated in larger prospective studies.

**Procalcitonin, erythrocyte sedimentation rate and C-reactive protein in acute pulmonary exacerbations of cystic fibrosis**

**Author(s):** Loh G.; Skabelund A.; Ryaboy I.; French A.

**Source:** Clinical Respiratory Journal; 2017

**Publication Type(s):** Article In Press

**Abstract:** Introduction: Acute pulmonary exacerbations of cystic fibrosis (APECF) are a leading cause of morbidity and mortality among patients with cystic fibrosis (CF). APECF require frequent administration of antibiotics and subsequently lead to development of resistant organisms. Objectives: The aim of this study was to identify inflammatory markers that may help identify need for antibiotics and exacerbation as well as predict risk of exacerbations. Methods: A total of 17 patients were enrolled, and baseline erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and procalcitonin levels were obtained in addition to obtaining these levels during admissions for APECF. Results: A total of 28 APECF were recorded. ESR and CRP significantly increased during exacerbation (P Copyright © 2017 John Wiley & Sons Ltd.

**Ceftaroline pharmacokinetics and pharmacodynamics in patients with cystic fibrosis.**

**Author(s):** Barsky, Emily E; Pereira, Luis M; Sullivan, Keri J; Wong, Alanna; McAdam, Alexander J

**Source:** Journal of cystic fibrosis : official journal of the European Cystic Fibrosis Society; Nov 2017

**Publication Type(s):** Journal Article

**Abstract:** BACKGROUND Methicillin-resistant *Staphylococcus aureus* (MRSA) is a prevalent pathogen in patients with cystic fibrosis (CF) associated with increased morbidity. Ceftaroline fosamil is an intravenous (IV) cephalosporin with activity against MRSA. There are minimal data regarding dosing in the CF population. The objective of this study was to determine the pharmacokinetic and pharmacodynamic profile of IV ceftaroline in patients with CF. METHODS We conducted a single-center prospective study of children and young adults with CF receiving ceftaroline (15mg/kg IV up to 600mg every 8h) as part of treatment for a CF pulmonary exacerbation between June 2016 and April 2017. Seven patients were enrolled for a total of 10 treatment courses. For each treatment course, up to 8 plasma samples were assayed for ceftaroline using ultra-high performance liquid chromatography with mass spectrometry. Maximum plasma concentration, systemic clearance, and

elimination half-life were calculated. The area under the curve (AUC) above the minimum inhibitory concentration (MIC) and the percent time above the MIC (%T>MIC) were determined for each subject using MICs of 0.5, 1, and 2 µg/mL and the measured MIC if available. **RESULTS** The mean (SD) age for the 7 patients was 20.3 (8.0) years. Mean (SD) maximum plasma concentration of ceftaroline was 22.7 (9.6) µg/mL, systemic clearance 7.9 (3.3) L/h, and half-life 1.1 (0.4) hours. Using a MIC of 1 µg/mL, accepted as the MIC 90 of MRSA isolates, AUC above MIC mean (SD) was 53.6 (19.5) µg·h/mL, mean (SD) %T>MIC was 75.7 (10.4), and all subjects had >60%T>MIC. **CONCLUSIONS** In this cohort of CF patients, mean ceftaroline half-life was 1.1h, which is notably lower than the general population. The dosing regimen studied, which exceeds the recommended dosing in the non-CF population, was adequate to achieve >60% time above the MIC in all patients.

### **Viruses in cystic fibrosis patients' airways.**

**Author(s):** Billard, Lisa; Le Berre, Rozenn; Pilorgé, Léa; Payan, Christopher; Héry-Arnaud, Geneviève;

**Source:** Critical reviews in microbiology; Nov 2017; vol. 43 (no. 6); p. 690-708

**Publication Type(s):** Journal Article

**Abstract:** Although bacteria have historically been considered to play a major role in cystic fibrosis (CF) airway damage, a strong impact of respiratory viral infections (RVI) is also now recognized. Emerging evidence confirms that respiratory viruses are associated with deterioration of pulmonary function and exacerbation and facilitation of bacterial colonization in CF patients. The aim of this review is to provide an overview of the current knowledge on respiratory viruses in CF airways, to discuss the resulting inflammation and RVI response, to determine how to detect the viruses, and to assess their clinical consequences, prevalence, and interactions with bacteria. The most predominant are Rhinoviruses (RVs), significantly associated with CF exacerbation. Molecular techniques, and especially multiplex PCR, help to diagnose viral infections, and the coming rise of metagenomics will extend knowledge of viral populations in the complex ecosystem of CF airways. Prophylaxis and vaccination are currently available only for Respiratory syncytial and Influenza virus (IV), but antiviral molecules are being tested to improve CF patients' care. All the points raised in this review highlight the importance of taking account of RVIs and their potential impact on the CF airway ecosystem.

### **Group B streptococcus (GBS) is an important pathogen in human disease- but what about in cystic fibrosis?**

**Author(s):** Skolnik K.; Rabin H.R.; Parkins M.D.; Nguyen A.; Thornton C.S.; Waddell B.; Williamson T.

**Source:** BMC Infectious Diseases; Oct 2017; vol. 17 (no. 1)

**Publication Type(s):** Article

Available at [BMC Infectious Diseases](#) - from EBSCO (MEDLINE Complete)

**Abstract:** Background: Group B Streptococcus (GBS) is a common commensal capable of causing severe invasive infections. Most GBS infections occur in neonates (often as pneumonia). GBS can also cause infection in adults with diabetes and other immunological impairments but rarely leads to pneumonia in adults. GBS has occasionally been found in the sputum of Cystic Fibrosis (CF) patients, an inherited condition known for progressive lung disease. However, the epidemiology and clinical significance of GBS in CF are not understood. Methods: We retrospectively reviewed a large single-centre adult CF population with an associated comprehensive, prospectively collected bacterial biobank beginning in 1978. We identified all individuals with GBS isolated from their sputum on at least one occasion. The primary outcome was risk of pulmonary exacerbation (PE<sub>x</sub>) at the time of the first GBS isolate compared to the preceding visit. Secondary outcomes included determining: prevalence of GBS infection in a CF population, whether GBS infections were transient or persistent, whether GBS strains were shared among patients, change in % predicted FEV<sub>1</sub> at the

time of GBS isolate compared to the preceding visit, PEx frequency after the first GBS isolate, change in % predicted FEV1 after the first GBS isolate, and complications of GBS infection. Results: GBS was uncommon, infecting 3.5% (11/318) adults within our cohort. Only three individuals developed persistent GBS infection, all lasting > 12 months. There were no shared GBS strains among patients. PEx risk was not increased at initial GBS isolation (RR 5.0, CI 0.69-36.1, p=0.10). In the two years preceding initial GBS isolation compared to the two following years, there was no difference in PEx frequency (median 2, range 0-4 vs 1, range 0 to 5, respectively, p=0.42) or lung function decline, as measured by % predicted FEV1, (median -1.0%, range -19 to 7% vs median -6.0%, range -18 to 22%, p=0.86). There were no invasive GBS infections. Conclusion: In adults with CF, GBS is uncommon and is generally a transient colonizer of the lower airways. Despite the presence of structural lung disease and impaired innate immunity in CF, incident GBS infection did not increase PEx risk, PEx frequency, rate of lung function decline, or other adverse clinical outcomes. Copyright © 2017 The Author(s).

### **Early Respiratory Bacterial Detection and Anti-Staphylococcal Antibiotic Prophylaxis in Young Children with Cystic Fibrosis.**

**Author(s):** Hurley, Matthew N; Fogarty, Andrew; McKeever, Tricia M; Goss, Christopher H

**Source:** Annals of the American Thoracic Society; Oct 2017

**Publication Type(s):** Journal Article

Available at [Annals of the American Thoracic Society](#) - from EBSCO (MEDLINE Complete)

**Abstract:** RATIONALE Consensus is lacking regarding anti-staphylococcal antibiotic prophylaxis use for young children with cystic fibrosis. Prophylaxis is recommended in the UK, but recommended against in the US. OBJECTIVE To test the hypothesis that anti-staphylococcal antibiotic prophylaxis is associated with a decreased risk of Staphylococcus aureus acquisition, but no increased risk of Pseudomonas aeruginosa acquisition. METHODS We undertook a longitudinal observational study of children with cystic fibrosis who were recruited from birth (or their first registry entry in the period) and followed until the age of 4 years (1500 days) using UK CF Trust and US CF Foundation Registries, 2000-2009. Children were excluded if they had a culture positive for S. aureus or P. aeruginosa, or were receiving inhaled antibiotics, at first encounter. Time to first S. aureus and P. aeruginosa detection in the UK/US cohorts were compared using a Cox proportional hazards model. A UK-based analysis compared the same for those receiving flucloxacillin with those who received no prophylaxis. We included the following covariates: sex, age at registry entry, Dornase alfa use, genotype and center size. RESULTS The primary analysis consisted 1074 UK and 3677 US children. The risk of first detection was greater in US compared to UK for S. aureus (hazard ratio (HR) 5.79; 95% CI: 4.85, 6.90; p<0.001) and P. aeruginosa (HR 1.92; 95% CI: 1.65, 2.24; p<0.001). The UK analysis compared 278 children receiving flucloxacillin and 306 receiving no prophylaxis. Flucloxacillin was not associated with a reduced risk of S. aureus (HR 1.22; 95% CI: 0.74, 2.0; p=0.43), but was associated with an increased risk of P. aeruginosa (HR 2.53; 95% CI: 1.71, 3.74; p<0.001) detection. None of the covariates significantly affected the risk estimate in either analysis. CONCLUSIONS Risk of first detection of S. aureus and P. aeruginosa is greater in US compared to UK. In the UK, the risk of first P. aeruginosa detection is increased among those receiving flucloxacillin compared to those who received no prophylaxis. These observational findings should be explored in a randomized controlled trial.

### **Time-Kill Analysis of Ceftolozane/Tazobactam Efficacy Against Mucoïd Pseudomonas aeruginosa Strains from Cystic Fibrosis Patients.**

**Author(s):** Rac, Hana; Stover, Kayla R; Wagner, Jamie L; King, S Travis; Warnock, Henderson D

**Source:** Infectious diseases and therapy; Oct 2017

**Publication Type(s):** Journal Article

Available at [Infectious Diseases and Therapy](#) - from Europe PubMed Central - Open Access

**Abstract:**INTRODUCTIONMucoid Pseudomonas aeruginosa (MP) strains in cystic fibrosis (CF) patients are thought to initiate the chronic infection stage of CF and are associated with pulmonary function decline.OBJECTIVESThe purpose of this study was to assess the susceptibility of MP strains to ceftolozane/tazobactam and the efficacy of ceftolozane/tazobactam against MP strains compared with those for standard-of-care antipseudomonal antibiotics.METHODSTen clinical isolates of MP from CF patients were tested for susceptibility with Etest and time-kill analysis with ceftolozane/tazobactam compared with ceftazidime, cefepime, ciprofloxacin, meropenem, tobramycin, and polymyxin B. The physiologic free peak concentrations were used in the time-kill experiments.RESULTSCeftolozane/tazobactam minimum inhibitory concentrations ranged from 0.032 to 1.5 mg/L. In the time-kill analysis, the mean starting inoculum for the isolates was  $6.29 \pm 0.22$  log<sub>10</sub> colony forming units (CFU) per milliliter. On average, ceftolozane/tazobactam, cefepime, ciprofloxacin, meropenem, tobramycin, and polymyxin B all demonstrated bactericidal activity. With all isolates taken into account, polymyxin B, tobramycin, meropenem, and ceftolozane/tazobactam 3 g were the most potent, with reductions in inoculum of  $5.07 \pm 0.45$ ,  $4.58 \pm 2.2$ ,  $4.76 \pm 0.71$ , and  $4.17 \pm 0.94$  log<sub>10</sub> CFU/mL, respectively. Ceftolozane/tazobactam 1.5 g, cefepime, and ciprofloxacin reduced the starting inoculum by  $3.74 \pm 0.99$ ,  $3.42 \pm 1.4$ , and  $3.23 \pm 2.0$  log<sub>10</sub> CFU/mL, respectively. Despite 90% susceptibility, ceftazidime was bactericidal against seven of ten strains, with an average reduction in starting inoculum of  $2.91 \pm 2.2$  log<sub>10</sub> CFU/mL.CONCLUSIONCeftolozane/tazobactam activity against MP strains derived from CF patients was comparable to that of standard-of-care agents at both the 1.5-g dose and the 3-g dose. Further in vitro modeling and clinical trials are warranted.

#### **Incident Stenotrophomonas maltophilia infection and lung function decline in cystic fibrosis.**

**Author(s):** Barsky, Emily E; Williams, Kathryn A; Priebe, Gregory P; Sawicki, Gregory S

**Source:** Pediatric pulmonology; Oct 2017; vol. 52 (no. 10); p. 1276-1282

**Publication Type(s):** Journal Article

**Abstract:**OBJECTIVESTo determine whether incident detection of Stenotrophomonas maltophilia (SM) in patients with cystic fibrosis (CF) is associated with accelerated lung function decline and increased hospitalizations and to determine whether this effect is more pronounced in individuals with subsequent chronic infection.METHODSWe performed a longitudinal, retrospective single-center, pre-post study of 88 patients with CF, ages 6-51 years, with first positive respiratory culture for SM between 2008 and 2014. Rate of decline in FEV<sub>1</sub> and hospitalization rates prior to and following incident SM infection were analyzed using segmented regression analysis of interrupted time series.RESULTSMean (SD) age was 17.4 (9.2) years and the mean (SD) FEV<sub>1</sub> % predicted at acquisition was 90.0% (25.2). A total of 44% developed chronic SM infection. In regression analysis adjusted for clinical and demographic factors, there was worsening of the mean annual decline in FEV<sub>1</sub> % predicted from  $-1.79$  (95%CI:  $-2.43$ ,  $-1.15$ ) pre-acquisition to  $-2.14$  (95%CI:  $-2.61$ ,  $-1.67$ ) post-acquisition (P = 0.005). A significant change was observed in those with either subsequent intermittent or chronic infection. The mean annual hospitalization rate increased significantly in the subgroup with chronic infection from 0.46 (95%CI: 0.33, 0.60) to 0.88 (95%CI: 0.68, 1.07) (P = 0.007).CONCLUSIONSIn this single-center cohort, acquisition of SM in CF was associated with an acceleration in lung function decline. Among those with chronic colonization, acquisition was also associated with increased hospitalization rates.

#### **Incident Stenotrophomonas maltophilia infection and lung function decline in cystic fibrosis.**

**Author(s):** Barsky, Emily E; Williams, Kathryn A; Priebe, Gregory P; Sawicki, Gregory S

**Source:** Pediatric pulmonology; Oct 2017; vol. 52 (no. 10); p. 1276-1282

**Publication Type(s):** Journal Article

**Abstract:**OBJECTIVE To determine whether incident detection of *Stenotrophomonas maltophilia* (SM) in patients with cystic fibrosis (CF) is associated with accelerated lung function decline and increased hospitalizations and to determine whether this effect is more pronounced in individuals with subsequent chronic infection. METHODS We performed a longitudinal, retrospective single-center, pre-post study of 88 patients with CF, ages 6-51 years, with first positive respiratory culture for SM between 2008 and 2014. Rate of decline in FEV1 and hospitalization rates prior to and following incident SM infection were analyzed using segmented regression analysis of interrupted time series. RESULTS Mean (SD) age was 17.4 (9.2) years and the mean (SD) FEV1 % predicted at acquisition was 90.0% (25.2). A total of 44% developed chronic SM infection. In regression analysis adjusted for clinical and demographic factors, there was worsening of the mean annual decline in FEV1 % predicted from -1.79 (95%CI: -2.43, -1.15) pre-acquisition to -2.14 (95%CI: -2.61, -1.67) post-acquisition (P = 0.005). A significant change was observed in those with either subsequent intermittent or chronic infection. The mean annual hospitalization rate increased significantly in the subgroup with chronic infection from 0.46 (95%CI: 0.33, 0.60) to 0.88 (95%CI: 0.68, 1.07) (P = 0.007). CONCLUSIONS In this single-center cohort, acquisition of SM in CF was associated with an acceleration in lung function decline. Among those with chronic colonization, acquisition was also associated with increased hospitalization rates.

## Psychological

**Trajectories of caregiver burden in families of adult cystic fibrosis patients.**

**Author(s):** Wojtaszczyk, Ann; Glajchen, Myra; Portenoy, Russell K; Berdella, Maria; Walker, Patricia

**Source:** Palliative & supportive care; Oct 2017 ; p. 1-9

**Publication Type(s):** Journal Article

**Abstract:**OBJECTIVE Little is known about the experience of family caregivers of adults with cystic fibrosis (CF). This information is important for the identification of caregivers at risk for burden. METHODS This was a longitudinal analysis of survey data obtained from caregivers of adult CF patients participating in an early intervention palliative care trial. Caregivers completed the validated Brief Assessment Scale for Caregivers (BASC) repeatedly over a 28-month period. Mixed-effects modeling evaluated multivariate associations with positive and negative caregiver perceptions over time. RESULTS Of the 54 caregivers, 47.9% were spouses. The mean age was 50.9 years (SD = 13.2); 72.2% were women; 75.9% were married; and 63.0% were employed. At baseline, the BASC revealed large variations in positive and negative perceptions of caregiving. Although average scores over time were unchanging, variation was greater across caregivers than within caregivers (0.49 vs. 0.27, respectively). At baseline, the positive impact of caregiving in the sample was higher than the negative impact. Multivariate analysis revealed that patients' baseline pulmonary function and their full-time employment status predicted caregiver burden over time. SIGNIFICANCE OF RESULTS Caregivers of CF patients varied in their positive and negative caregiving experiences, although burden levels in individual caregivers were stable over time. When the disease was advanced, caregivers of CF patients experienced more overall burden but also more positive impact. This suggests that the role of caregivers may become more meaningful as disease severity worsens. In addition, full-time patient employment was associated with lower caregiver burden regardless of disease severity. This suggests that burden in CF caregivers may be predicted by financial strain or benefits conferred by patient employment. These associations require further investigation to determine whether highly burdened caregivers can be identified and assisted using tailored interventions.

## Nutritional

### **Nutrition: Prevention and management of nutritional failure in Cystic Fibrosis**

**Author(s):** Sullivan J.S.; Mascarenhas M.R.

**Source:** Journal of Cystic Fibrosis; 2017

**Publication Type(s):** Article In Press

**Abstract:**Close monitoring of nutritional status is critical to the overall health of a patient with CF. As part of routine CF care, measurement of weight and height (and calculation of weight/length or BMI as appropriate) should be performed and analyzed at each visit. Early recognition of nutritional risk is imperative and evaluation with a multidisciplinary team should be performed to assess for caloric intake, caloric malabsorption, and other causes of poor weight gain and growth. Many tools are available to use for intervention, including oral supplementation, behavioral interventions, medications, nutritional therapies, and enteral tube feeding. Copyright © 2017 European Cystic Fibrosis Society.

### **Body Weight and Body Mass Index in Patients with End-Stage Cystic Fibrosis Stabilize After the Start of Enteral Tube Feeding**

**Author(s):** Hollander F.M.; de Roos N.M.; Belle van Meerkerk G.; Teding van Berkhout F.

**Source:** Journal of the Academy of Nutrition and Dietetics; Nov 2017; vol. 117 (no. 11); p. 1808-1815

**Publication Type(s):** Article

**Abstract:**BACKGROUND: Enteral tube feeding (ETF) is widely used in patients with cystic fibrosis (CF) and end-stage lung disease, but previous studies have been limited to investigating whether ETF improves outcomes in patients with moderately or mildly impaired pulmonary function.OBJECTIVE: This study investigated body weight, body mass index (BMI; calculated as kg/m<sup>2</sup>), pulmonary function, and the presence of CF-related diabetes before and after the start of ETF.DESIGN: This was a retrospective observational study.PARTICIPANTS/SETTING: Data from 26 adult patients in an outpatient setting who had end-stage CF (19 women) and had been using ETF for at least 6 months between 2000 and 2014 were analyzed.MAIN OUTCOME MEASURES: Body weight, BMI, pulmonary function (forced expiratory volume in 1 second as percent of predicted) and incidence of CF-related diabetes from 6 months before to 6 months after starting ETF.STATISTICAL ANALYSES PERFORMED: Time effects were tested with one-way analysis of variance for data that were normally distributed and the Friedman test for non-parametric data. Correlations were tested with Pearson's r or Spearman's rho, depending on the distribution of the data.RESULTS: Mean body weight increased by 3.5 kg (95% CI 2.2 to 4.8 kg) after patients started ETF. In women, mean BMI decreased by 0.7 in the 6 months before the start of ETF (PCopyright © 2017 Academy of Nutrition and Dietetics. Published by Elsevier Inc. All rights reserved.

### **Methicillin-resistant Staphylococcus aureus in cystic fibrosis: How should it be managed?**

**Author(s):** Muhlebach M.S.

**Source:** Current Opinion in Pulmonary Medicine; Nov 2017; vol. 23 (no. 6); p. 544-550

**Publication Type(s):** Review

**Abstract:**Purpose of review Methicillin-resistant Staphylococcus aureus (MRSA) remains prevalent in people with cystic fibrosis (CF). As chronic infection is often associated with worse pulmonary outcomes, the organism is concerning to CF providers and patients. This review describes current epidemiology, our understanding of risk factors for MRSA infection, and relevant aspects of treatment with review of new and ongoing trials. Recent findings Prevalence ranges from a low of 3 to 4% in some European countries to a high of approximately 26% in the United States. Risk factors



for chronic MRSA infection include patient-specific factors such as genotype, pancreatic insufficiency, diabetes and antibiotic use; however, warmer climate also contributes to increased MRSA rates in CF and non-CF. In addition to retrospective reviews, a few clinical trials are being conducted or have been performed showing the successful short-term eradication of incident MRSA. Chronic MRSA remains challenging to eradicate and antibiotics should be dosed to adjust for CF-specific pharmacokinetics. Summary As chronic MRSA will remain a long-term challenge to treat, ongoing effort should focus on the prevention of transmission with a need to better understand patient's environmental and modifiable risk factors. Early treatment appears successful; however, protocols to achieve long-term clearance are lacking. Copyright © 2017 Wolters Kluwer Health, Inc. All rights reserved.

## Other

### **Pain is an underestimated symptom in cystic fibrosis**

**Author(s):** Masson A.; Kirszenbaum M.; Sermet-Gaudelus I.

**Source:** Current Opinion in Pulmonary Medicine; Nov 2017; vol. 23 (no. 6); p. 570-573

**Publication Type(s):** Review

### **Exercise assessment and training in cystic fibrosis: Can less achieve more?**

**Author(s):** Cox N.S.; Holland A.E.

**Source:** Journal of Cystic Fibrosis; 2017

**Publication Type(s):** Article In Press

### **Association between lung function, physical activity level and postural evaluation variables in adult patients with cystic fibrosis**

**Author(s):** Cherobin I.A.; Dalcin P.d.T.R.; Ziegler B.

**Source:** Clinical Respiratory Journal; 2017

**Publication Type(s):** Article In Press

### **Home monitoring of patients with cystic fibrosis to identify and treat acute pulmonary exacerbations eICE study results**

**Author(s):** Lechtzin N.; West N.E.; Allgood S.; Boyle M.P.; Mogayzel P.J.; Mayer-Hamblett N.

**Source:** American Journal of Respiratory and Critical Care Medicine; Nov 2017; vol. 196 (no. 9); p. 1144-1151

**Publication Type(s):** Article

Available at [American Journal of Respiratory and Critical Care Medicine](#) - from EBSCO (MEDLINE Complete)

### **Physical exercise training for cystic fibrosis.**

**Author(s):** Radtke, Thomas; Nevitt, Sarah J; Hebestreit, Helge; Kriemler, Susi

**Source:** The Cochrane database of systematic reviews; Nov 2017; vol. 11 ; p. CD002768

**Publication Type(s):** Journal Article Review

**Physical Activity Counseling for Children With Cystic Fibrosis.**

**Author(s):** Moola, Fiona J; Garcia, Eric; Huynh, Elizabeth; Henry, Lauren; Penfound, Shannon; Consunji-Araneta, Raquel; Faulkner, Guy Ej

**Source:** Respiratory care; Nov 2017; vol. 62 (no. 11); p. 1466-1473

**Provider Attitudes and Practices toward Sexual and Reproductive Health Care for Young Women with Cystic Fibrosis**

**Author(s):** Kazmerski T.M.; Sawicki G.S.; Borrero S.; Miller E.; Abebe K.Z.; Pilewski J.M.; Jones K.A.

**Source:** Journal of Pediatric and Adolescent Gynecology; Oct 2017; vol. 30 (no. 5); p. 546-552

**Publication Type(s):** Article

**Pregnancy outcome in women with cystic fibrosis-related diabetes**

**Author(s):** Reynaud Q.; Rousset Jablonski C.; Nove-Josserand R.; Durieu I.; Poupon-Bourdy S.

**Source:** Acta Obstetrica et Gynecologica Scandinavica; Oct 2017; vol. 96 (no. 10); p. 1223-1227

**Publication Type(s):** Article

**Patient and Provider Perspectives on Communication About Body Image With Adolescents and Young Adults With Cystic Fibrosis.**

**Author(s):** Helms, Sarah W; Christon, Lillian M; Dellon, Elisabeth P; Prinstein, Mitchell J

**Source:** Journal of pediatric psychology; Oct 2017; vol. 42 (no. 9); p. 1040-1050

**Publication Type(s):** Journal Article

**Understanding Treatment Adherence With the Health Belief Model in Children With Cystic Fibrosis.**

**Author(s):** Dempster, Nicole R; Wildman, Beth G; Masterson, Tracy L; Omlor, Gregory J

**Source:** Health education & behavior : the official publication of the Society for Public Health Education; Oct 2017 ; p. 1090198117736346

**Publication Type(s):** Journal Article

**Corrigendum to "Does current reporting of lung function by the UK cystic fibrosis registry allow a fair comparison of adult centres?" [J Cyst Fibros (2017) 585-591]**

**Author(s):** Nightingale J.A.; Osmond C.

**Source:** Journal of Cystic Fibrosis; 2017

**Publication Type(s):** Article In Press

## Exercise: Outcome Reliability

Inter-rater reliability	Intra-rater reliability	Test retest reliability
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Looks at the level of agreement between assessments by <i>one rater</i> of the same material at two or more different times.	
Refers to the level of agreement between the initial test results and the results of repeated measurements made at a later date.	
This measures the level of agreement between assessments made by <i>two or more raters</i> at the same time.	



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