Cystic Fibrosis

Current Awareness Newsletter

May 2015
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New from the Cochrane Library Systematic Reviews on Cystic Fibrosis

PROTOCOL: **Interventions for improving adherence to treatment in cystic fibrosis**

Stephen Jones, Rachael Curley, Martin Wildman, Robert W Morton and Heather E Elphick

Online Publication Date: 21 April 2015

This is the protocol for a review and there is no abstract. The objectives are as follows:

The review aims to assess interventions aimed at promoting adherence to treatment in people with CF. Since there are various methods for measuring adherence, each with varying degrees of objectivity and accuracy, the review will also assess the effects of these interventions on clinical measures, such as lung function and quality of life, to allow a broader appraisal of efficacy. The review will also assess the disadvantages of the interventions such as cost and the length of time required to perform the intervention.

**Enteral tube feeding for cystic fibrosis**

Alison Morton and Susan Wolfe

Online Publication Date: 9 April 2015

Enteral tube feeding is routinely used in many cystic fibrosis centres when oral dietary and supplement intake has failed to achieve an adequate nutritional status. The use of this method of feeding is assessed on an individual basis taking into consideration the patients age and clinical status. **Objectives:** To examine the evidence that in people with cystic fibrosis, supplemental enteral tube feeding improves nutritional status, respiratory function, and quality of life without significant adverse effects.

**Potentiators (specific therapies for class III and IV mutations) for cystic fibrosis**

Sanjay Patel, Ian P Sinha, Kerry Dwan, Carlos Echevarria, Michael Schechter and Kevin W Southern

Online Publication Date: 26 March 2015

Cystic fibrosis is the most common inherited life-shortening illness in Caucasians and caused by a mutation in the gene that codes for the cystic fibrosis transmembrane regulator protein (CFTR), which functions as a salt transporter. This mutation most notably affects the airways of people with cystic fibrosis. Excess salt absorption by defective CFTR dehydrates the airway lining and leads to defective mucociliary clearance. Consequent accumulation of thick, sticky mucus makes the airway prone to chronic infection and progressive inflammation; respiratory failure often ensues.
Additionally, abnormalities with CFTR lead to systemic complications like malnutrition, diabetes and subfertility.

Since the discovery of the causative gene, our understanding of the structure and function of CFTR and the impact of different mutations has increased and allowed pharmaceutical companies to design new mutation-specific therapies targeting the underlying molecular defect. Therapies targeting mutation classes III and IV (CFTR potentiators) aim to normalise airway surface liquid and help re-establish mucociliary clearance, which then has a beneficial impact on the chronic infection and inflammation that characterizes lung disease in people with cystic fibrosis. These therapies may also affect other mutations.

**Objectives:** To evaluate the effects of CFTR potentiators on clinically important outcomes in children and adults with cystic fibrosis.

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**New from NICE**

**IN DEVELOPMENT:** Cystic fibrosis: diagnosis and management of cystic fibrosis

_Anticipated publication date: Feb 2017_

**Proposed technology appraisals**

**Suggested remit:** To appraise the clinical and cost effectiveness of lumacaftor in combination with ivacaftor within its marketing authorisation for treating cystic fibrosis in people who are homozygous for the F508del mutation

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**Recent Literature Searches on Cystic Fibrosis**

_Below is a sample of literature searches carried out by librarians for UH Bristol members of staff on the subject of Cystic Fibrosis. For further details get in touch: library@uhbristol.nhs.uk_

- CF and instigating non-invasive ventilation
- CF and dry powder antibiotics
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
- Psychological
- 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


Citation: Pediatric pulmonology, Apr 2015, vol. 50, no. 4, p. 340-343 (April 2015)

Author(s): Doumit, Michael, Jaffé, Adam

Abstract: This study aimed to assess the effectiveness of the Lung Flute in obtaining a sputum sample from children with cystic fibrosis (CF) that were not productive of sputum with coughing alone. Children attending an outpatient CF clinic who were not able to provide a sample with coughing alone were eligible. Each child used the Lung Flute on two occasions at least one month apart. The primary outcome was expectoration of a sputum sample. Secondary outcomes were sputum microbiology, time taken for the procedure, and ease of use of the device as assessed by the patient using a visual analogue scale (VAS), with 0/10 representing very easy and 10/10 representing very hard. Twenty-five children participated (15 males, mean age 12.7 range 6.5-17.9). Overall, a sputum sample was obtained on 26/50 (52%) uses of the device. In children that presented with a moist cough, a sample was obtained on 17/17 (100%) occasions, compared to 9/33 (27%) occasions when a child presented with a dry cough. A positive culture result for at least one known CF pathogen was found in 24/26 samples. Culture results from obtained samples resulted in management changes in 12 cases. Mean time taken to obtain a sample was 9.8 min (SD 2.2). Mean ease of use on the VAS was 1.5 (SD 1.6). The lung flute appears to be a clinically useful and easy device for sputum induction in children with CF. Further research comparing its effectiveness to other sputum induction methods is warranted. Pediatr Pulmonol. 2015; 50:340-343. © 2014 Wiley Periodicals, Inc. © 2014 Wiley Periodicals, Inc.

Title: Inhaled Antibiotics in Cystic Fibrosis (CF) and Non-CF Bronchiectasis.
Citation: Seminars in respiratory and critical care medicine, Apr 2015, vol. 36, no. 2, p. 267-286 (April 2015)

Author(s): Tay, George T P, Reid, David W, Bell, Scott C

Abstract: Bronchiectasis is a pathological diagnosis describing dilatation of the airways and is characterized by chronic lung sepsis. Bronchiectasis has multiple etiologies, but is usually considered in terms of whether it is due to the genetic disorder cystic fibrosis (CF) or secondary to other causes (non-CF bronchiectasis, NCFB). Inhaled antibiotics are used in bronchiectasis to suppress bacterial pathogens and reduce long-term lung function decline. The majority of the literature on inhaled antibiotics comes from studies on CF where the dominant bacterial pathogen in the airway is usually Pseudomonas aeruginosa. Thus, most aerosolized antibiotic regimens target this bacterium, but the emergence of molecular diagnostic methods has questioned this approach and more tailored strategies may need to be considered in CF based on the community composition of the lung microbiome. Similarly, the lung microbiome in NCFB has been found to be a complex polymicrobial one and the current practice of employing the same inhaled antibiotic regimes as are used in CF may no longer be appropriate in many patients. In this article, the use of inhaled antibiotics in CF and NCFB is considered in the light of improved understanding of the lung microbiome and why more tailored therapy may be needed based on molecular identification of the microbial pathogens present. The evidence for the use of currently available inhaled antibiotics and advances in inhaled drug packaging and delivery devices are discussed. Finally, the urgent need for prospective randomized clinical trials in CF and NCFB is highlighted and areas for future research identified.

Title: Epidemiology of infection and current guidelines for infection prevention in cystic fibrosis patients.

Citation: The Journal of hospital infection, Apr 2015, vol. 89, no. 4, p. 309-313 (April 2015)

Author(s): Schaffer, K

Abstract: The spectrum of bacterial pathogens encountered in cystic fibrosis (CF) lung disease has expanded over the last decade. In addition to established pathogens, such as Pseudomonas aeruginosa, Burkholderia cepacia complex and Staphylococcus aureus, novel Gram-negative non-fermenter bacteria and non-tuberculous mycobacteria have gained in clinical significance. Air sampling performed in inpatient and outpatient clinics, and analysis of cough aerosols expelled by CF patients provides evidence for potential airborne transmission of CF pathogens. Two outbreaks of 'Mycobacterium abscessus subsp. massiliense' have been reported among CF patients, raising the question of airborne transmission of non-tuberculous mycobacteria. In response to newer epidemiological evidence, international infection control guidance documents have changed. Guideline documents agree on the importance of specifications for ventilation when planning new CF inpatient facilities. New CF units should consider providing negative-pressure inpatient and outpatient rooms to diminish the risk of airborne contamination of ward corridors and communal areas. Air exchange rates of inpatient rooms and pulmonary function testing rooms need to be considered and optimized whenever possible. International guidelines disagree as to whether
patients should be requested to wear masks in the hospital environment. Copyright © 2015 The Healthcare Infection Society. Published by Elsevier Ltd. All rights reserved.

Title: Lung transplantation for cystic fibrosis: results, indications, complications, and controversies.

Citation: Seminars in respiratory and critical care medicine, Apr 2015, vol. 36, no. 2, p. 299-320 (April 2015)

Author(s): Lynch, Joseph P, Sayah, David M, Belperio, John A, Weigt, S Sam

Abstract: Survival in patients with cystic fibrosis (CF) has improved dramatically over the past 30 to 40 years, with mean survival now approximately 40 years. Nonetheless, progressive respiratory insufficiency remains the major cause of mortality in CF patients, and lung transplantation (LT) is eventually required. Timing of listing for LT is critical, because up to 25 to 41% of CF patients have died while awaiting LT. Globally, approximately 16.4% of lung transplants are performed in adults with CF. Survival rates for LT recipients with CF are superior to other indications, yet LT is associated with substantial morbidity and mortality (~50% at 5-year survival rates). Myriad complications of LT include allograft failure (acute or chronic), opportunistic infections, and complications of chronic immunosuppressive medications (including malignancy). Determining which patients are candidates for LT is difficult, and survival benefit remains uncertain. In this review, we discuss when LT should be considered, criteria for identifying candidates, contraindications to LT, results post-LT, and specific complications that may be associated with LT. Infectious complications that may complicate CF (particularly Burkholderia cepacia spp., opportunistic fungi, and nontuberculous mycobacteria) are discussed. Thieme Medical Publishers 333 Seventh Avenue, New York, NY 10001, USA.

Title: Airway clearance strategies in cystic fibrosis and non-cystic fibrosis bronchiectasis.

Citation: Seminars in respiratory and critical care medicine, Apr 2015, vol. 36, no. 2, p. 251-266 (April 2015)

Author(s): Main, Eleanor, Grillo, Lizzie, Rand, Sarah

Abstract: Many patients with cystic fibrosis (CF) and non-CF bronchiectasis present with common symptoms in clinical domains that appear to benefit from airway clearance strategies. These symptoms include chronic productive cough, retention of excessive, purulent mucus in dilated airways, impairment of normal mucociliary clearance (MCC), atelectasis, breathlessness, fatigue, respiratory inflammation, fever, infection, and airflow obstruction. Airway clearance strategies may involve singular and focused interventions for the purpose of removing secretions and improving lung recruitment and gas exchange in patients with atelectasis. Strategies may also involve indirect or adjunctive interventions that facilitate or enhance effective airway clearance at different ages or stages of the disease process, for example, inhalation therapy, exercise, oxygen therapy, or noninvasive ventilation. The aim is to optimize care by selecting any one or combination of these in responding intelligently and sensitively to individual and changing patient requirements during their lifetime. Currently, a solid evidence base does not exist for airway clearance strategies in CF and
Title: Effect of infection with transmissible strains of Pseudomonas aeruginosa on lung transplantation outcomes in patients with cystic fibrosis.

Citation: The Journal of heart and lung transplantation : the official publication of the International Society for Heart Transplantation, Apr 2015, vol. 34, no. 4, p. 588-593 (April 2015)

Author(s): Srour, Nadim, Chaparro, Cecilia, Vandemheen, Katherine, Singer, Lianne G, Keshavjee, Shaf, Aaron, Shawn D

Abstract: Compared with patients infected with unique strains of Pseudomonas aeruginosa, patients with cystic fibrosis who are infected with transmissible strains of P aeruginosa, such as the Liverpool epidemic strain, have a 3-fold greater risk of death or lung transplant. We aimed to determine if pre-operative infection with transmissible strains of P aeruginosa was similarly associated with poor health outcomes after lung transplant. We had prospectively identified and characterized endobronchial infections in 446 adult cystic fibrosis patients in Ontario, Canada, from September 2005 until December 2009. P aeruginosa isolated from sputum taken at 3-month intervals was genotyped, and patients were characterized as being infected with 1 of 2 transmissible strains or, alternatively, with unique strains of P aeruginosa. We monitored patients until 2013 and collected data on patients from the cohort who subsequently received a lung transplant. The primary outcome was survival after transplantation. We identified 56 lung transplant recipients from the cohort of 446 patients, including 18 infected with transmissible strains of P aeruginosa and 26 infected with unique P aeruginosa strains. Post-transplant survival at 3 years was 86% in the transmissible group and 84% in the unique group (p = 0.65). No significant differences between groups were found regarding bronchiolitis obliterans-free survival, the frequency of acute rejection episodes, the frequency of post-transplant respiratory tract infection, or the rate of change of post-transplant forced expiratory volume in 1 second. Pre-operative infection with transmissible strains of P aeruginosa is not associated with poorer post-transplant outcomes compared with patients infected with unique strains of P aeruginosa. Copyright © 2015 International Society for Heart and Lung Transplantation. Published by Elsevier Inc. All rights reserved.

Title: Clinical updates in cystic fibrosis-related diabetes.

Citation: Seminars in respiratory and critical care medicine, Apr 2015, vol. 36, no. 2, p. 236-250 (April 2015)

Author(s): Brennan, Amanda L, Beynon, Jennifer
Abstract: Improved clinical care has led to a dramatic increase in life expectancy for people with cystic fibrosis (CF). As they live longer, people with CF are therefore developing secondary complications. Cystic fibrosis-related diabetes (CFRD) is the commonest extrapulmonary complication of CF. Insulin deficiency is the primary defect in CFRD, but insulin resistance and impairment of the enteroinsular axis play contributory roles. CFRD affects 9% of people with CF aged 5 to 9 years, 26% aged 10 to 20 years, and up to 50% by the age of 30. The presence of CFRD is associated with accelerated decline in pulmonary function, poorer growth and nutritional status, and increased mortality. The need for early detection of abnormal glucose handling in CF is clear since it is linked with clinical decline. Patients with CFRD may be asymptomatic for many years, so it is recommended that screening be commenced at 10 years of age. Although oral glucose tolerance test is recommended, it is well recognized that early glucose handling abnormalities will not be detected and the chance to intervene early may be missed. Many centers are therefore using continuous glucose monitoring to refine the diagnosis and investigate real-life glycemic control. Future research will hopefully widen our understanding of the pathophysiology of CFRD and therefore the treatment options available. There are clearly some promising results suggesting the use of oral agents may prove beneficial in treating CFRD but insulin should remain the mainstay of treatment until these are further evaluated. Thieme Medical Publishers 333 Seventh Avenue, New York, NY 10001, USA.

Title: Safety, tolerability, and plasma exposure of tiotropium respimat(®) in children and adults with cystic fibrosis.

Citation: Journal of aerosol medicine and pulmonary drug delivery, Apr 2015, vol. 28, no. 2, p. 137-144 (April 2015)

Author(s): Konstan, Michael W, Sharma, Ashish, Moroni-Zentgraf, Petra, Wang, Fei, Koker, Paul

Abstract: People with cystic fibrosis (CF) suffer from chronic lung disease that is often treated with a bronchodilator. This trial evaluated the pharmacokinetics, safety, and tolerability of single and multiple doses of tiotropium inhaled via the Respimat(®) Soft MistTM Inhaler in patients with CF. Patients received a single dose (placebo, 2.5 μg, 5 μg, or 10 μg) and/or multiple doses (placebo, 2.5 μg, or 5 μg) of tiotropium daily for 28 days. Ninety-two patients, aged 5-57 years, were treated. All doses showed a satisfactory safety profile for adverse events, vital signs, laboratory evaluations, and physical examination. At steady-state, peak exposure to tiotropium was comparable between adult patients with CF and patients with chronic obstructive pulmonary disease. Tiotropium 2.5 μg or 5 μg inhaled via the Respimat(®) Soft MistTM Inhaler once daily was well tolerated in patients with CF.

Title: Management of pulmonary exacerbations in cystic fibrosis: still an unmet medical need in clinical practice.

Citation: Expert review of respiratory medicine, Apr 2015, vol. 9, no. 2, p. 183-194 (April 2015)

Author(s): Justicia, José Luis, Solé, Amparo, Quintana-Gallego, Esther, Gartner, Silvia, de Gracia, Javier, Prados, Concepción, Máliz, Luis
**Abstract:** Pulmonary exacerbation (PEx) is a hallmark of cystic fibrosis. Although several criteria have been proposed for the definition of PEx, no consensus has yet been reached. Very often, many PEx cases go unreported. A standardized and validated definition is needed to reduce variability in clinical practice. The pathophysiology of recurrent episodes remains unclear, and both onset and risk are multifactorial. PEx leads to increased healthcare costs, impaired quality of life and a cycle in which PEx causes loss of lung function, which predisposes to further episodes. The number of episodes affects survival. Although early diagnosis and aggressive treatment are highly recommended, measures to prevent the emergence of new PEx are even more important. In particular, inhaled antibiotics administered under new treatment schedules could play a key role in preventing exacerbations and thus delay decline in lung function and reduce mortality. The primary objective is zero exacerbations.

**Title:** Management of endocrine disease: Cystic fibrosis-related diabetes: novel pathogenic insights opening new therapeutic avenues.

**Citation:** European journal of endocrinology / European Federation of Endocrine Societies, Apr 2015, vol. 172, no. 4, p. R131. (April 2015)

**Author(s):** Barrio, Raquel

**Abstract:** Cystic fibrosis (CF) is a recessive genetic disease caused by mutations in the CF transmembrane conductance regulator (CFTR). CFTR is primarily present in epithelial cells of the airways, intestine and in cells with exocrine and endocrine functions. Mutations in the gene encoding the channel protein complex (CFTR) cause alterations in the ionic composition of secretions from the lung, gastrointestinal tract, liver, and also the pancreas. CF-related diabetes (CFRD), the most common complication of CF, has a major detrimental impact on pulmonary function, nutrition and survival. Glucose derangements in CF seem to start from early infancy and, even when the pathophysiology is multifactorial, insulin insufficiency is clearly a major component. Consistently, recent evidence has confirmed that CFTR is an important regulator of insulin secretion by islet β-cells. In addition, several other mechanisms were also recognized from cellular and animals models also contributing to either β-cell mass reduction or β-cell malfunction. Understanding such mechanisms is crucial for the development of the so-called 'transformational' therapies in CF, including the preservation of insulin secretion. Innovative therapeutic approaches aim to modify specific CFTR mutant proteins or positively modulate their function. CFTR modulators have recently shown in vitro capacity to enhance insulin secretion and thereby potential clinical utility in CFDR, including synergistic effects between corrector and potentiator drugs. The introduction of incretins and the optimization of exocrine pancreatic replacement complete the number of therapeutic options of CFRD besides early diagnosis and implementation of insulin therapy. This review focuses on the recently identified pathogenic mechanisms leading to CFRD relevant for the development of novel pharmacological avenues in CFRD therapy. © 2015 European Society of Endocrinology.

**Title:** Safety and pharmacokinetics of ciprofloxacin dry powder for inhalation in cystic fibrosis: a phase I, randomized, single-dose, dose-escalation study.
Citation: Journal of aerosol medicine and pulmonary drug delivery, Apr 2015, vol. 28, no. 2, p. 106-115 (April 2015)

Author(s): Stass, Heino, Delesen, Heinz, Nagelschmitz, Johannes, Staab, Doris

Abstract: Reliable, reproducible deposition to the lung is a major prerequisite for the clinical use of inhaled drugs. Ciprofloxacin dry powder for inhalation (ciprofloxacin DPI; Bayer HealthCare AG, Leverkusen, Germany) is an antibacterial therapy in development using Novartis' PulmoSphere™ technology (Novartis Pharma AG, Basel, Switzerland) for the targeted delivery of ciprofloxacin to the lung via a T-326 inhaler. This randomized, single-blind, placebo-controlled, dose-escalation study investigated the safety, tolerability, and pharmacokinetics of single-dose ciprofloxacin DPI (32.5 mg [n=6] or 65 mg [n=6]) and matching placebo (n=4) in adult patients with cystic fibrosis and stable pulmonary status (forced expiratory volume in 1 sec ≥30%) who were colonized with Pseudomonas aeruginosa. Peak sputum concentrations of 34.9 mg/L (range 2.03-229) and 376 mg/L (8.95-1283) for ciprofloxacin 32.5 mg and 65 mg, respectively, indicated targeting of ciprofloxacin DPI to the lung. This contrasted with low systemic exposure (peak plasma concentrations: 0.0790 mg/L [32.5 mg] and 0.182 mg/L [65 mg]). Single-dose ciprofloxacin DPI 32.5 mg or 65 mg was well tolerated with similar incidences of adverse events across all groups. No deaths, discontinuations, treatment-related serious adverse events, or clinically relevant changes in laboratory parameters, vital signs, or lung function tests were reported. Lung targeting with high pulmonary concentrations of ciprofloxacin combined with low systemic exposure was confirmed. These results support further study of ciprofloxacin DPI as a potentially more convenient alternative to nebulized antibiotic solutions for managing chronic lung infections.

Title: Comparing dosage adjustment methods for once-daily tobramycin in paediatric and adolescent patients with cystic fibrosis.

Citation: Clinical pharmacokinetics, Apr 2015, vol. 54, no. 4, p. 409-421, 0312-5963 (April 2015)

Author(s): Hennig, Stefanie, Holthouse, Franziska, Staatz, Christine E

Abstract: Several dosage adjustment methods are currently available to individualize intravenous tobramycin dosing. This study compared different methods in terms of their recommendations for dosage adjustment, their estimation of patients' pharmacokinetic parameter values and their ability to predict subsequent observed tobramycin concentrations following once-daily tobramycin treatment in children and adolescents with cystic fibrosis. Retrospective data from 172 patients treated at the Royal Children's Hospital (Brisbane, QLD, Australia) were analysed. To be included in the analysis, each patient had to have at least one pair of tobramycin plasma concentration-time measurements recorded over a dosing interval. One or both of the concentrations in the paired set were applied in each of the following dosage adjustment methods: (i) the Therapeutic Guidelines Aminoglycoside nomogram; (ii) the Massie nomogram; (iii) log-linear regression analysis; and two Bayesian forecasting software programs: (iv) TCIWorks and (v) DoseMe. All methods were compared in regard to their recommendations for tobramycin dosage adjustment. The latter three methods were also examined in terms of estimated pharmacokinetic parameter values and their ability to predict subsequent observed tobramycin concentrations. The Therapeutic Guidelines nomogram
recommended significantly greater mean doses for dosage adjustment (27.0 mg/kg) compared with all other methods (p ≤ 0.01), which gave similar mean dose recommendations (11.6-14.6 mg/kg); however, >20 % differences in doses on an individual level were seen on 20-35 % of occasions across all methods. The log-linear regression analysis method and the two Bayesian forecasting methods (TCIWorks and DoseMe) showed negligible bias but imprecision of around 20 % in predicting subsequent observed tobramycin concentrations. The Bayesian forecasting methods showed no significant difference in mean dose recommendations when using either one or two concentration measurements but increased imprecision in predicting subsequent observed tobramycin concentrations. The log-linear regression method and Massie nomogram are likely to be suitable alternative methods for tobramycin dosage adjustment when Bayesian forecasting software is unavailable. The Therapeutic Guidelines nomogram should not be used to aid dose adjustment of tobramycin therapy in children with cystic fibrosis.

Title: A rapid method for breath analysis in cystic fibrosis patients.

Citation: European journal of clinical microbiology & infectious diseases : official publication of the European Society of Clinical Microbiology, Apr 2015, vol. 34, no. 4, p. 745-751 (April 2015)


Abstract: For easy handling and speed of lung diseases diagnostics, approaches based on volatile organic compounds (VOCs), including those emitted by pathogenic microorganisms, are considered but currently require considerable sampling efforts. We tested whether easy-to-handle and fast detection of lung infections is possible using solid-phase microextraction (SPME) of 100 ml of exhaled breath. An analytical procedure for the detection of VOCs from the headspace of epithelial lung cells infected with four human pathogens was developed. The feasibility of this method was tested in a cystic fibrosis (CF) outpatient clinic in vivo. Exhaled breath was extracted by SPME and analyzed by gas chromatography-mass spectrometry (GC-MS). The compositions of VOCs released in the infection model were characteristic for all individual pathogens tested. Exhaled breath of CF patients allowed clear distinction of CF patients and controls by their VOC compositions using multivariate analyses. Interestingly, the major specific VOCs detected in the exhaled breath of infected CF patients in vivo differed from those monitored during bacterial in vitro growth. SPME extraction of VOCs from 100 ml of human breath allowed the distinction between CF patients and healthy probands. Our results highlight the importance of assessing the entire pattern of VOCs instead of selected biomarkers for diagnostic purposes, as well as the need to use clinical samples to identify reliable biomarkers. This study provides the proof-of-concept for the approach using the composition of exhaled VOCs in human breath for the rapid identification of infectious agents in patients with lower respiratory tract infections.

Title: Noninvasive methods, including transient elastography, for the detection of liver disease in adults with cystic fibrosis.

Citation: Canadian journal of gastroenterology & hepatology, Apr 2015, vol. 29, no. 3, p. 139-144 (April 2015)
Author(s): Sadler, Matthew D, Crotty, Pam, Fatovich, Linda, Wilson, Stephanie, Rabin, Harvey R, Myers, Rob P

Abstract: Liver disease is the third leading cause of mortality in patients with cystic fibrosis (CF). However, detection of CF-associated liver disease (CFLD) is challenging. To evaluate the diagnostic performance of noninvasive methods for the detection of CFLD with a focus on transient elastography (TE). Patients at the Adult CF Clinic of Calgary and Southern Alberta (n=127) underwent liver stiffness measurement (LSM) by TE using the FibroScan (FS, Ecosens, France) M probe; aspartate aminotransferase to platelet ratio index (APRI) and FibroTest (FT) scores were also calculated. The diagnostic performance of these tools for the detection of CFLD (defined as two or more the following criteria: abnormal liver biochemistry, hepatomegaly or sonographic abnormalities other than steatosis) were compared using the area under ROC curves. Forty-seven percent of the cohort was male. The median age was 27 years (interquartile range [IQR] 22 to 37 years) and body mass index 21 kg/m² (IQR 19 kg/m² to 23 kg/m²); 25% of patients were on ursodeoxycholic acid and 12% had undergone lung transplantation. The prevalence of CFLD was 14% (n=18). FS was successful in all patients; one (0.8%) patient had poorly reliable results (IQR/M >30% and LSM ≥7.1kPa). Compared with patients without CFLD (n=109), individuals with CFLD had higher median LSM according to FS (3.9 kPa [IQR 3.4 to 4.9 kPa] versus 6.4 kPa [IQR 4.4 to 8.0 kPa]), APRI (0.24 [IQR 0.17 to 0.31] versus 0.50 [IQR 0.22 to 1.18]) and FT scores (0.08 [IQR 0.05 to 1.5] versus 0.18 [IQR 0.11 to 0.35]); all P5.2 kPa, the sensitivity, specificity, positive and negative predictive values of LSM according to FS for detecting CFLD were 67%, 83%, 40% and 94%, respectively. FS, APRI and FT were useful noninvasive methods for detecting CFLD in adults.

Microbiological

Title: Whole-Genome Sequencing and Epidemiological Analysis Do Not Provide Evidence for Cross-transmission of Mycobacterium abscessus in a Cohort of Pediatric Cystic Fibrosis Patients.

Citation: Clinical infectious diseases : an official publication of the Infectious Diseases Society of America, Apr 2015, vol. 60, no. 7, p. 1007-1016 (April 1, 2015)

Author(s): Harris, Kathryn A, Underwood, Anthony, Kenna, Dervla T D, Brooks, Anthony, Kavaliunaite, Ema, Kapatai, Georgia, Tewolde, Rediat, Aurora, Paul, Dixon, Garth

Abstract: Mycobacterium abscessus has emerged as a major pathogen in cystic fibrosis (CF) patients and has been associated with poor clinical outcomes, particularly following lung transplant. We investigated the acquisition of this bacterium in a cohort of pediatric CF patients. Demographic and patient location data were used to uncover epidemiological links between patients with genetically related strains of M. abscessus that had been previously typed by variable-number tandem repeat profiling. Whole-genome sequencing was applied to 27 M. abscessus isolates from the 20 patients in this cohort to provide definitive data on the genetic relatedness of strains. Whole-genome sequencing data demonstrated that M. abscessus isolates from 16 patients were unrelated, differing by at least 34 single-nucleotide polymorphisms (SNPs) from any other isolate, suggesting that independent acquisition events have occurred. Only 2 clusters of very closely related (
Title: Functional and pharmacological induced structural changes of the cystic fibrosis transmembrane conductance regulator in the membrane solved using SAXS.

Citation: Cellular and molecular life sciences : CMLS, Apr 2015, vol. 72, no. 7, p. 1363-1375 (April 2015)

Author(s): Baroni, Debora, Zegarra-Moran, Olga, Moran, Oscar

Abstract: The cystic fibrosis transmembrane conductance regulator (CFTR) chloride channel is a membrane-integral protein that belongs to the ATP-binding cassette superfamily. Mutations in the CFTR gene cause cystic fibrosis in which salt, water, and protein transports are defective in various tissues. To investigate the conformation of the CFTR in the membrane, we applied the small-angle x-ray scattering (SAXS) technique on microsomal membranes extracted from NIH/3T3 cells permanently transfected with wild-type (WT) CFTR and with CFTR carrying the ΔF508 mutation. The electronic density profile of the membranes was calculated from the SAXS data, assuming the lipid bilayer electronic density to be composed by a series of Gaussian shells. The data indicate that membranes in the microsome vesicles, that contain mostly endoplasmic reticulum membranes, are oriented in the outside-out conformation. Phosphorylation does not change significantly the electronic density profile, while dephosphorylation produces a significant modification in the inner side of the profile. Thus, we conclude that the CFTR and its associated protein complex in microsomes are mostly phosphorylated. The electronic density profile of the ΔF508-CFTR microsomes is completely different from WT, suggesting a different assemblage of the proteins in the membranes. Low-temperature treatment of cells rescues the ΔF508-CFTR protein, resulting in a conformation that resembles the WT. Differently, treatment with the corrector VX-809 modifies the electronic profile of ΔF508-CFTR membrane, but does not recover completely the WT conformation.

To our knowledge, this is the first report of a direct physical measurement of the structure of membranes containing CFTR in its native environment and in different functional and pharmacological conditions.

Title: Missense variants in CFTR nucleotide-binding domains predict quantitative phenotypes associated with cystic fibrosis disease severity.

Citation: Human molecular genetics, Apr 2015, vol. 24, no. 7, p. 1908-1917 (April 1, 2015)

Author(s): Masica, David L, Sosnay, Patrick R, Raraigh, Karen S, Cutting, Garry R, Karchin, Rachel

Abstract: Predicting the impact of genetic variation on human health remains an important and difficult challenge. Often, algorithmic classifiers are tasked with predicting binary traits (e.g. positive or negative for a disease) from missense variation. Though useful, this arrangement is limiting and contrived, because human diseases often comprise a spectrum of severities, rather than a discrete partitioning of patient populations. Furthermore, labeling variants as causal or benign can be error prone, which is problematic for training supervised learning algorithms (the so-called garbage in, garbage out phenomenon). We explore the potential value of training classifiers using continuous-valued quantitative measurements, rather than binary traits. Using 20 variants from cystic fibrosis
transmembrane conductance regulator (CFTR) nucleotide-binding domains and six quantitative measures of cystic fibrosis (CF) severity, we trained classifiers to predict CF severity from CFTR variants. Employing cross validation, classifier prediction and measured clinical/functional values were significantly correlated for four of six quantitative traits (correlation P-values from $1.35 \times 10^{-4}$ to $4.15 \times 10^{-3}$). Classifiers were also able to stratify variants by three clinically relevant risk categories with 85-100% accuracy, depending on which of the six quantitative traits was used for training. Finally, we characterized 11 additional CFTR variants using clinical sweat chloride testing, two functional assays, or all three diagnostics, and validated our classifier using blind prediction. Predictions were within the measured sweat chloride range for seven of eight variants, and captured the differential impact of specific variants on the two functional assays. This work demonstrates a promising and novel framework for assessing the impact of genetic variation. © The Author 2014. Published by Oxford University Press. All rights reserved. For Permissions, please email: journals.permissions@oup.com.

Title: Evolutionary insight from whole-genome sequencing of Pseudomonas aeruginosa from cystic fibrosis patients.

Citation: Future microbiology, Apr 2015, vol. 10, p. 599-611 (April 2015)

Author(s): Marvig, Rasmus Lykke, Sommer, Lea M, Jelsbak, Lars, Molin, Søren, Johansen, Helle Krogh

Abstract: ABSTRACT The opportunistic pathogen Pseudomonas aeruginosa causes chronic airway infections in patients with cystic fibrosis (CF), and it is directly associated with the morbidity and mortality connected with this disease. The ability of P. aeruginosa to establish chronic infections in CF patients is suggested to be due to the large genetic repertoire of P. aeruginosa and its ability to genetically adapt to the host environment. Here, we review the recent work that has applied whole-genome sequencing to understand P. aeruginosa population genomics, within-host microevolution and diversity, mutational mechanisms, genetic adaptation and transmission events. Finally, we summarize the advances in relation to medical applications and laboratory evolution experiments.

Title: Bacterial phospholipases C as vaccine candidate antigens against cystic fibrosis respiratory pathogens: The Mycobacterium abscessus model.

Citation: Vaccine, Apr 2015, vol. 33, no. 18, p. 2118-2124 (April 27, 2015)

Author(s): Le Moigne, Vincent, Rottman, Martin, Goulard, Céline, Barteau, Benoît, Poncin, Isabelle, Soismier, Nathalie, Canaan, Stéphane, Pitard, Bruno, Gaillard, Jean-Louis, Herrmann, Jean-Louis

Abstract: Vaccine strategies represent one of the fighting answers against multiresistant bacteria in a number of clinical settings like cystic fibrosis (CF). Mycobacterium abscessus, an emerging CF pathogen, raises difficult therapeutic problems due to its intrinsic antibiotic multiresistance. By reverse vaccinology, we identified M. abscessus phospholipase C (MA-PLC) as a potential vaccine target. We deciphered here the protective response generated by vaccination with plasmid DNA encoding the MA-PLC formulated with a tetra functional block copolymer 704, in CF (ΔF508) mice.
Protection was tested against aerosolized smooth and rough (hypervirulent) variants of M. abscessus. MA-PLC DNA vaccination (days 0, 21, 42) elicited a strong antibody response. A significant protective effect was obtained against aerosolized M. abscessus (S variant) in ΔF508 mice, but not in wild-type FVB littermates; similar results were observed when: (i) challenging mice with the "hypervirulent" R variant, and; (ii) immunizing mice with purified MA-PLC protein. High IgG titers against MA-PLC protein were measured in CF patients with M. abscessus infection; interestingly, significant titers were also detected in CF patients positive for Pseudomonas aeruginosa versus P. aeruginosa-negative controls. MA-PLC DNA- and PLC protein-vaccinated mice cleared more rapidly M. abscessus than β-galactosidase DNA- or PBS- vaccinated mice in the context of CF. PLCs could constitute interesting vaccine targets against common PLC-producing CF pathogens like P. aeruginosa. Copyright © 2015 Elsevier Ltd. All rights reserved.

Title: Divergent, Coexisting Pseudomonas aeruginosa Lineages in Chronic Cystic Fibrosis Lung Infections.

Citation: American journal of respiratory and critical care medicine, Apr 2015, vol. 191, no. 7, p. 775-785 (April 1, 2015)

Author(s): Williams, David, Evans, Benjamin, Haldenby, Sam, Walshaw, Martin J, Brockhurst, Michael A, Winstanley, Craig, Paterson, Steve

Abstract: Pseudomonas aeruginosa, the predominant cause of chronic airway infections of patients with cystic fibrosis, exhibits extensive phenotypic diversity among isolates within and between sputum samples, but little is known about the underlying genetic diversity. To characterize the population genetic structure of transmissible P. aeruginosa Liverpool Epidemic Strain in chronic infections of nine patients with cystic fibrosis, and infer evolutionary processes associated with adaptation to the cystic fibrosis lung. We performed whole-genome sequencing of P. aeruginosa isolates and pooled populations and used comparative analyses of genome sequences including phylogenetic reconstructions and resolution of population structure from genome-wide allele frequencies. Genome sequences were obtained for 360 isolates from nine patients. Phylogenetic reconstruction of the ancestry of 40 individually sequenced isolates from one patient sputum sample revealed the coexistence of two genetically diverged, recombining lineages exchanging potentially adaptive mutations. Analysis of population samples for eight additional patients indicated coexisting lineages in six cases. Reconstruction of the ancestry of individually sequenced isolates from all patients indicated smaller genetic distances between than within patients in most cases. Our population-level analysis demonstrates that coexistence of distinct lineages of P. aeruginosa Liverpool Epidemic Strain within individuals is common. In several cases, coexisting lineages may have been present in the infecting inoculum or assembled through multiple transmissions. Divergent lineages can share mutations via homologous recombination, potentially aiding adaptation to the airway during chronic infection. The genetic diversity of this transmissible strain within infections, revealed by high-resolution genomics, has implications for patient segregation and therapeutic strategies.
Title: On the interactions between nucleotide binding domains and membrane spanning domains in cystic fibrosis transmembrane regulator: A molecular dynamic study.

Citation: Biochimie, Apr 2015, vol. 111, p. 19-29 (April 2015)

Author(s): Belmonte, Luca, Moran, Oscar

Abstract: The Cystic Fibrosis Transmembrane Regulator (CFTR) is a membrane protein whose mutations cause cystic fibrosis, a lethal genetic disease. We performed a molecular dynamic (MD) study of the properties of the nucleotide binding domains (NBD) whose conformational changes, upon ATP binding, are the direct responsible of the gating mechanisms of CFTR. This study was done for the wild type (WT) CFTR and for the two most common mutations, ΔF508, that produces a traffic defect of the protein, and the mutation G551D, that causes a gating defect on CFTR. Using an homology model of the open channel conformation of the CFTR we thus introduced the mutations to the structure. Although the overall structures of the G551D and ΔF508 are quite well conserved, the NBD1-NBD2 interactions are severely modified in both mutants. NBD1 and NBD2 are indeed destabilized with a higher internal energy (Ei) in the ΔF508-CFTR. Differently, Ei does not change in the NBDs of G551D but, while the number of close contacts between NBD1 and NBD2 in ΔF508 is increased, a significant reduction of close contacts is found in the G551D mutated form. Hydrogen bonds formation between NBDs of the two mutated forms is also altered and it is slightly increased for the ΔF508, while are severely reduced in G551D. A consequent modification of the NBDs-ICLs interactions between residues involved in the transduction of the ATP binding and the channel gating is also registered. Indeed, while a major interaction is noticed between NBDs interface and ICL2 and ICL4 in the WT, this interaction is somehow altered in both mutated forms plausibly with effect on channel gating. Thus, single point mutations of the CFTR protein can reasonably results in channel gating defects due to alteration of the interaction mechanisms between the NBDs and NBDs-ICLs interfaces upon ATP-binding process. Copyright © 2015 Elsevier B.V. and Société Française de Biochimie et Biologie Moléculaire (SFBBM). All rights reserved.

Title: Regulatory T-cell impairment in cystic fibrosis patients with chronic pseudomonas infection.

Citation: American journal of respiratory and critical care medicine, Apr 2015, vol. 191, no. 8, p. 914-923 (April 15, 2015)

Author(s): Hector, Andreas, Schäfer, Heike, Pöschel, Simone, Fischer, Alexandra, Fritzscheing, Benedikt, Ralhan, Anjali, Carevic, Melanie, Öz, Hasan, Zundel, Sabine, Hogardt, Michael, Bakele, Martina, Rieber, Nikolaus, Riethmueller, Joachim, Graepler-Mainka, Ute, Stahl, Mirjam, Bender, Annika, Frick, Julia-Stefanie, Mall, Marcus, Hartl, Dominik

Abstract: Patients with cystic fibrosis (CF) lung disease have chronic airway inflammation driven by disrupted balance of T-cell (Th17 and Th2) responses. Regulatory T cells (Tregs) dampen T-cell activation, but their role in CF is incompletely understood. To characterize numbers, function, and clinical impact of Tregs in CF lung disease. Tregs were quantified in peripheral blood and airway samples from patients with CF and from lung disease control patients without CF and healthy control subjects. The role of Pseudomonas aeruginosa and CF transmembrane conductance regulator (CFTR) in Treg regulation was analyzed by using in vitro and murine in vivo models. Tregs were decreased in
peripheral blood and airways of patients with CF compared with healthy controls or lung disease patients without CF and correlated positively with lung function parameters. Patients with CF with chronic P. aeruginosa infection had lower Tregs compared with patients with CF without P. aeruginosa infection. Genetic knockout, pharmacological inhibition, and P. aeruginosa infection studies showed that both P. aeruginosa and CFTR contributed to Treg dysregulation in CF. Functionally, Tregs from patients with CF or from Cftr(-/-) mice were impaired in suppressing conventional T cells, an effect that was enhanced by P. aeruginosa infection. The loss of Tregs in CF affected memory, but not naive Tregs, and manifested gradually with disease progression. Patients with CF who have chronic P. aeruginosa infection show an age-dependent, quantitative, and qualitative impairment of Tregs. Modulation of Tregs represents a novel strategy to rebalance T-cell responses, dampen inflammation, and ultimately improve outcomes for patients with infective CF lung disease.

Title: Targeted Correction and Restored Function of the CFTR Gene in Cystic Fibrosis Induced Pluripotent Stem Cells.

Citation: Stem cell reports, Apr 2015, vol. 4, no. 4, p. 569-577 (April 14, 2015)


Abstract: Recently developed reprogramming and genome editing technologies make possible the derivation of corrected patient-specific pluripotent stem cell sources-potentially useful for the development of new therapeutic approaches. Starting with skin fibroblasts from patients diagnosed with cystic fibrosis, we derived and characterized induced pluripotent stem cell (iPSC) lines. We then utilized zinc-finger nucleases (ZFNs), designed to target the endogenous CFTR gene, to mediate correction of the inherited genetic mutation in these patient-derived lines via homology-directed repair (HDR). We observed an exquisitely sensitive, homology-dependent preference for targeting one CFTR allele versus the other. The corrected cystic fibrosis iPSCs, when induced to differentiate in vitro, expressed the corrected CFTR gene; importantly, CFTR correction resulted in restored expression of the mature CFTR glycoprotein and restoration of CFTR chloride channel function in iPSC-derived epithelial cells. Copyright © 2015 The Authors. Published by Elsevier Inc. All rights reserved.

Title: Fungi in cystic fibrosis and non-cystic fibrosis bronchiectasis.

Citation: Seminars in respiratory and critical care medicine, Apr 2015, vol. 36, no. 2, p. 207-216 (April 2015)

Author(s): Moss, Richard B
**Abstract:** Bronchiectasis is a pathologic bronchial dilatation with loss of function that can result from multiple inflammatory and infectious injuries to the conducting airways of the lung. Molds, particularly the filamentous fungus Aspergillus fumigatus, have been implicated as a common cause of both cystic fibrosis (CF) and non-CF bronchiectasis, the latter primarily in patients with severe asthma. The pathogenesis of mold-associated bronchiectasis is usually due to atopic sensitization to mold allergens in the presence of active chronic endobronchial fungal infection with host innate and adaptive immune deviation to a Th2-dominated inflammation, a condition known as allergic bronchopulmonary aspergillosis (ABPA) (or allergic bronchopulmonary mycosis if a non-Aspergillus mold is implicated). Diagnostic criteria of ABPA continue to evolve, while treatment relies upon downregulation of the allergic inflammatory response with immunomodulatory agents and antifungal pharmacotherapy. Thieme Medical Publishers 333 Seventh Avenue, New York, NY 10001, USA.

**Title:** Genotypes and phenotypes in cystic fibrosis and cystic fibrosis transmembrane regulator-related disorders.

**Citation:** Seminars in respiratory and critical care medicine, Apr 2015, vol. 36, no. 2, p. 180-193 (April 2015)

**Author(s):** Bombieri, Cristina, Seia, Manuela, Castellani, Carlo

**Abstract:** Cystic fibrosis (CF) is characterized by remarkable variability in severity, rate of disease progression, and organ involvement. In spite of the considerable amount of data collected on the relationship between genotype and phenotype in CF, this is still a challenging matter of debate. Barriers to the interpretation of this connection are the large number of mutations in the CF transmembrane regulator (CFTR) gene, the difficulties in attributing several of them to a specific mode of dysfunction, and a limited number of the almost 2,000 mutations so far detected, which have been clinically annotated. In addition to that, the heterogeneity of clinical manifestations in individuals with the same CFTR genotypes indicates that disease severity is modulated by other genes and by environmental factors, of which the most relevant is possibly treatment in its aspects of appropriateness, early start in life, and adherence. The phenotype variability extends to conditions, named CFTR-related disorders, which are connected with CFTR dysfunction, but do not satisfy diagnostic criteria for CF. The current level of knowledge does not allow use of the CFTR genotype to predict individual outcome and cannot be used as an indicator of CF prognosis. This might change with the development of treatments targeting specific mutations and possibly capable of changing the natural history of the disease. Thieme Medical Publishers 333 Seventh Avenue, New York, NY 10001, USA.

**Title:** The findings of a clinical surveillance bronchoalveolar lavage programme in pre-school patients with cystic fibrosis.

**Citation:** Pediatric pulmonology, Apr 2015, vol. 50, no. 4, p. 327-332 (April 2015)

**Author(s):** Linnane, Barry, Vaish, Shashi, Clarke, Donna, O'Sullivan, Niamh, McNally, Paul
Abstract: Evidence suggests infection is present in the lower airways of young children with cystic fibrosis (CF), even when clinically stable. Oropharyngeal samples (OPS) are typically used for airway surveillance in these children but have been shown to have low positive predictive values and low sensitivity in detecting lower airway infection when compared with the reference standard, bronchoalveolar lavage (BAL). The aim of this study was to determine the prevalence of pathogens in lower airway samples detected as part of a pilot clinical BAL surveillance programme, in young children aged from one to six years old, and to ascertain if their detection resulted in a change in treatment. During the study 78 bronchoscopies were performed on 38 patients. The average age at the time of bronchoscopy was 2.7 years (range 0.3-7.0 year). A significant organism was detected in 58 (74.5%) BALs. Haemophilus influenzae was detected in 27 (34.6%) samples, 16 (20.5%) samples had Staphylococcus aureus, and nine (11.5%) had Pseudomonas aeruginosa. Change in treatment occurred after 46 (58.9%) BALs. This study suggests that, in young non-expectorating children with CF, routine surveillance bronchoscopy allows the detection of significant lower airway pathogens and provides the opportunity for targeted treatment of sub-clinical infection. Pediatr Pulmonol. 2015; 50:327-332. © 2014 Wiley Periodicals, Inc. © 2015 Wiley Periodicals, Inc.

Psychological

Title: Parents' responses to receiving sickle cell or cystic fibrosis carrier results for their child following newborn screening.

Citation: European journal of human genetics : EJHG, Apr 2015, vol. 23, no. 4, p. 459-465 (April 2015)

Author(s): Ulph, Fiona, Cullinan, Tim, Qureshi, Nadeem, Kai, Joe

Abstract: Universal newborn screening for sickle cell disorders and cystic fibrosis aims to enable the early identification and treatment of affected babies. Screening can also identify infants who are healthy carriers, with carrier results being the commonest outcome for parents and professionals to discuss in practice. However it is unclear what the effect will be on parents on being informed of their baby's carrier result. Semi-structured face-to-face interviews were conducted with a purposeful sample of 67 family members (49 mothers, 16 fathers, 2 grandparents) of 51 infants identified by universal newborn screening as carriers of cystic fibrosis (n=27) and sickle cell (n=24), across all health regions in England. Data were analysed by thematic analysis with subsequent respondent validation. Untoward anxiety or distress among parents appeared influenced by how results were conveyed, rather than the carrier result per se. Parents who had more prior awareness of carrier status or the possibility of a carrier result assimilated the information more readily. Being left in an information vacuum while awaiting results, or before seeing a professional, led some parents to fear that their child had a serious health condition. Parental distress and anxiety appeared mostly transient, subsiding with understanding of carrier status and communication with a professional. Parents regarded carrier results as valuable information and sought to share this with their families and to inform their children in the future. However parents needed greater support after communication of results in considering and accessing cascade testing, and negotiating further communication within their families.
Title: Friendship quality and health-related outcomes among adolescents with cystic fibrosis.

Citation: Journal of pediatric psychology, Apr 2015, vol. 40, no. 3, p. 349-358 (April 2015)

Author(s): Helms, Sarah W, Dellon, Elisabeth P, Prinstein, Mitchell J

Abstract: During adolescence, the significance of peer relationships peaks, and the presence and quality of dyadic friendships impact psychosocial outcomes. Yet, friendships have been studied infrequently among youth with chronic illness, particularly youth with cystic fibrosis (CF). The current aims were to (1) describe friendships among adolescents with CF, including number, duration, frequency of interactions, and positive/negative friendship qualities, and (2) explore associations between friendship quality, treatment adherence, and health-related quality of life. Participants (N = 42) reported on friendships with peers with and without CF; caregivers reported on adolescents’ adherence and quality of life. Friendships with CF-peers were less common and lower quality than friendships with non-CF peers. Both positive and negative friendship qualities were associated with adherence; positive friendship qualities were uniquely associated with quality of life. CF-related health promotion efforts may benefit from addressing the impact of friendships on adherence and quality of life. © The Author 2014. Published by Oxford University Press on behalf of the Society of Pediatric Psychology. All rights reserved. For permissions, please e-mail: journals.permissions@oup.com.

Title: Increased congregational support for parents of children with cystic fibrosis.

Citation: Journal of religion and health, Apr 2015, vol. 54, no. 2, p. 664-675 (April 2015)

Author(s): Szczesniak, Rhonda D, Zou, Yuanshu, Wetzel, J Denise, Krause, Neal, Grossoehme, Daniel H

Abstract: Positive health outcomes are related to adults’ religious congregational participation. For parents of children with chronic disease, structured daily care routines and/or strict infection control precautions may limit participation. For this exploratory study, we examined the relationship between congregational support and religious coping by parents of children with cystic fibrosis (CF) compared to parents for whom child health issues were not significant stressors. CF parents reported higher levels of emotional support from congregation members and use of religious coping. Within-group differences were found for CF parents by denominational affiliation. Congregational support for parents dealing with child chronic disease is important.

Title: Testing the feasibility and acceptability of a chaplaincy intervention to improving treatment attitudes and self-efficacy of adolescents with cystic fibrosis: a pilot study.

Citation: Journal of health care chaplaincy, Apr 2015, vol. 21, no. 2, p. 76-90 (2015 Apr-Jun)

Author(s): Cheng, Joy, Purcell, Hillary N, Dimitriou, Sophia M, Grossoehme, Daniel H
Abstract: Religious factors are known to contribute to treatment adherence in different patient populations, and religious coping has been found to be particularly important to adolescents dealing with chronic diseases. Adherence to prescribed treatments slows disease progression and contributes to desirable outcomes in most patients, and, therefore, adherence-promoting interventions provided by chaplains could be beneficial to various patient populations. The current article describes a pilot study to test the feasibility of a theoretically and empirically based chaplain intervention to promote treatment adherence for adolescents with CF. Cognitive interviews were conducted with adolescents with CF, and content analysis was used to identify themes, which informed revision of the intervention protocol. The authors thought that presenting the methods and results of this pilot study would be helpful for chaplains who want to conduct intervention research. The results indicated that the proposed intervention was acceptable and feasible to deliver in hard copy or an electronic platform.

Other

Title: Evaluation of a Multidimensional Cystic Fibrosis Transition Program: A Quality Improvement Initiative

Citation: Journal of Pediatric Nursing, Jan 2015, vol. 30, no. 1, p. 236-243, 0882-5963 (Jan-Feb 2015)

Author(s): Gravelle, Anna M, Paone, Mary, Davidson, A George F, Chilvers, Mark A

Abstract: The adequate preparation of cystic fibrosis (CF) youth for the transfer from pediatric to adult-based health care services is essential to meet the needs of this changing population. This paper describes the evolution of a transition clinic for patients with CF into a multidimensional quality improvement transition initiative. Three transition interventions (a patient transition clinical pathway; collaboration with the adult clinic; and a tool to measure transfer readiness) were sequentially implemented and evaluated. Each was found to be a valuable addition to a comprehensive transition protocol and today are endorsed as part of transition best practices.

Title: Imaging in cystic fibrosis and non-cystic fibrosis bronchiectasis.

Citation: Seminars in respiratory and critical care medicine, Apr 2015, vol. 36, no. 2, p. 194-206 (April 2015)

Author(s): Dodd, Jonathan D, Lavelle, Lisa P, Fabre, Aurelie, Brady, Darragh

Abstract: Bronchiectasis is defined as a permanent and progressive dilation of the airways, typically as a result of inflammation, infection, and subsequent repair. It typically presents with chronic cough, suppurative sputum production, and airway dilation. High-resolution computed tomography (HRCT) is now well established as the primary imaging tool for its investigation. Cystic fibrosis (CF) remains the most common autosomal recessive inherited disorder worldwide and its pulmonary hallmark is bronchiectasis. Although CF and non-CF bronchiectasis are different clinical entities, they
are typically imaged using HRCT and share many imaging aspects, and also some differences. Several important recent CT technology developments have improved the detection and characterization of bronchiectasis and its complications. Many CT aspects of radiation exposure have also undergone important enhancements in recent years resulting in significant dose reductions. This is particularly relevant in a pulmonary disease such as bronchiectasis, which often undergoes serial HRCT surveillance in contemporary practice. Several new CT clinical applications in bronchiectasis have been recently advanced, and CT is now being increasingly incorporated into investigative algorithms to assess bronchiectasis treatment effects. In this review, we assess the latest imaging features of CF and non-CF bronchiectasis, discuss radiation dose reducing methods and technology of the latest scanners, describe recent CT clinical applications, and explore the use of CT as a treatment surrogate in CF and non-CF bronchiectasis. Thieme Medical Publishers 333 Seventh Avenue, New York, NY 10001, USA.

Title: Effects of exercise intensity compared to albuterol in individuals with cystic fibrosis.

Citation: Respiratory medicine, Apr 2015, vol. 109, no. 4, p. 463-474 (April 2015)


Abstract: Although exercise is a vital component of the therapy prescribed to individuals with cystic fibrosis (CF), it is not a priority due to a finite amount of treatment time and the view that exercise is not as beneficial as pharmacological treatments by many individuals with CF. We sought to compare the therapeutic benefits of exercise and their prescribed bronchodilator albuterol. CF (n = 14) and healthy (n = 16) subjects completed three visits, a baseline screening with VO2 max test and two treatment visits. On the two treatment visits, subjects completed spirometry and diffusing capacity of the lungs for nitric oxide (DLNO) maneuvers either at baseline, 60, and 110 min post-albuterol administration, or at baseline and the midway point of three separate 15 min exercise bouts at low, moderate and vigorous intensity (25, 50 and 65% of the maximum workload, respectively). With moderate exercise the increase in DLNO was double (39 ± 8 vs 15 ± 6% change) and the level of bronchodilation similar (23% change) when compared to 110 min post-albuterol in individuals with CF. During exercise FVC became reduced (-309 ± 66 mL with moderate exercise) and the increase in FEV1 was attenuated (103 ± 39 vs 236 ± 58 mL, exercise vs. albuterol) when compared with the response to albuterol in individuals with CF. Epinephrine (EPI) release increased 39, 72 and 144% change with low, moderate and vigorous intensity exercise respectively for individuals with CF, but this increase was blunted when compared to healthy subjects. Our results suggest that moderate intensity exercise is the optimal intensity for individuals with CF, as low intensity exercise increases EPI less than 50% and vigorous intensity exercise is over taxing, such that airflow can be restricted. Although the duration of the beneficial effect is uncertain, exercise can promote greater improvements in gas diffusion and comparable bronchodilation when compared to albuterol. Copyright © 2014 Elsevier Ltd. All rights reserved.
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