Another study on urinary incontinence - this time on younger patients. In recent years the physiotherapists have taken an increasing interest in bladder dysfunction in CF. Girls with CF aged 11 to 17 years were studied and urinary incontinence was reported by 17/51 (33%) girls, compared with only 4/25 (16%) of those with asthma and 2/27 (7%) healthy controls. The problem was associated with increasing severity of lung disease. (also described in adults with CF by Cornacchia et al, 2001 above[PubMed]; Orr A et al. BMJ; 322:1521). [PubMed]

Armmani Prasad (figure 39) is the senior Physiotherapist at the CF Unit Great Ormond Street Hospital for Children, London and one the leading CF physiotherapists in the UK and internationally. She has written extensively on CF and also been an invited speaker at many conferences both in the UK and abroad and regularly advises the CF Trust on matters relating to CF care.


Inhaled hypertonic saline (7%) acutely increases mucociliary clearance and, in short-term trials, improves lung function in people with cystic fibrosis. Peter Bye (figure 40) of St Vincent’s Hospital Sydney, and Mark Elkins (figure 41) and their colleagues tested the safety and efficacy of inhaled hypertonic saline after a bronchodilator in a long-term double-blind, parallel-group trial over 48 weeks. The rate of change (slope) in lung function did not differ significantly between the treated and control groups but the absolute difference in lung function between groups was significant (P=0.03) when averaged across all post-randomization visits. The hypertonic-saline group also had a 56% reduction in pulmonary exacerbations. This study was funded by the US CF Foundation and received considerable attention.

A similar short term study from Chapel Hill, USA showed similar benefit in mucus clearance and FEV1 (6.62% increase) but not when used with amiloride which was considered to inhibit osmotically driven water transport (Donaldson SH et al. NEJM 2006; 354:241-250). [PubMed]

Subsequently 7% saline was shown to be tolerated by infants with CF when assessed by infant respiratory function tests and clinically (Subbarao P et al, Pediatr Pulmonol 2007; 42:471-476. [PubMed]) and will be subjected to a multicentre trial funded by the CF Foundation.

The great interest in these findings stemmed partially from the fact that here was a way of
correcting the low salt situation, postulated by Boucher to be a major cause of the fluid deficit and airway mucociliary clearance problems in CF. Also the treatment is inexpensive compared with other very expensive mucolytics such as rhDNase.


Three patients with CF had superior vena cava syndrome (thrombosis in the large vein entering the heart) due to the presence in the vessel of a foreign body i.e. the implantable venous access device. Although these devices proved to be a major overall advance since their introduction in the mid-Eighties, a variety of complications have been reported particularly if the devices are not cared for by experts and these include infection and various vascular clotting problems even paradoxical embolisation (Espiritu JD, Kleinhenz ME. Mayo Clin Proc 2000; 75:1100–1102), [PubMed] Experience at CF centres shows that this particular complication is not rare and most have experienced one or two cases.


Prevalence of chronic *P. aeruginosa* infection in one of the seven Belgian CF centres was very low and only half the national level; overall 19.8% for all the children and adults but only 2.8% in patients below 18 years. This was attributed to cohorting patients according to their microbiological status and particularly to the widespread and frequent use of inhaled antibiotics over the previous 15 years; also patients were seen by the same paediatric pulmonologist.

This is an impressive report showing a 2.8% prevalence of chronic *P. aeruginosa* infection in children at this Belgian CF clinic - a prevalence in stark contrast to many published results for example the incidence reported in both the US and UK patient registries.


A previous study had been performed with plasma derived inhibitor (McElvaney et al, 1991 above[PubMed]). In this present study recombinant human ATT was used in a Phase II trial of rAAT at various dose levels. This drug was safe but, disappointingly, had little effect on neutrophil elastase activity and other markers of inflammation. As a result, there was no further work in CF from this group. However, later a similar trial from Germany (Griese, M. et al, Eur Respir J 2007; 29:240–50. [PubMed]) did show some reduction of inflammatory markers although no change of respiratory function. These authors suggested that the clear reduction of airway inflammation after ATT treatment may precede pulmonary structural changes; also the ATT deposition region, either bronchial or peripheral, may play a minor role for ATT inhalation in patients with cystic fibrosis. So it is likely there may be further developments in relation to CF.

**2006** Littlewood JM, Wolfe SP, Conway SP. Diagnosis and treatment of intestinal malabsorption in cystic fibrosis. Pediatr Pulmonol 2006; 41:35–49. [PubMed]

A detailed review of the present management of malabsorption based on some 25 years experience at the Regional Paediatric CF Centre in Leeds. We have been very fortunate in Leeds in having a number of outstanding paediatric dietitians since Anita MacDonald (now Chief Dietitian at Birmingham Children’s Hospital) played a major part in building up the Regional Paediatric CF Unit at St James’s during the Eighties.

Sue Wolfe, the present chief paediatric dietitian, (figure 42) and Alison Morton (figure 11 - see Conway et al, 2000 above) chief dietitian on the adult CF unit, at St James's Leeds have made a major contribution to the nutritional aspects of CF and now have vast practical and research experience. Much of our nutritional and gastrointestinal work was in collaboration with members of Professor Monty Losowsky’s University Department of Medicine in St James's where there was a very productive collaboration between the adult gastroenterologists and our CF team. Particular mention going to the late Dr Jerry Kelleher the chief biochemist and his colleague Mr Mike Walters.


Data from CF Foundation registry on 15,651 patients was analysed and showed that the high risk CFTR genotype carried a twofold increased risk of death compared to those with low risk genotype. Of patients who died, the high risk median age of death was 24.2 years and low risk 37.6 years. Although reassurance can be provided for patients in the low risk group there is...
substantial phenotypic variability. The outlook for people with CF is mainly determined by the treatment they receive although a minority do have mutations which are associated with milder disease; these are often associated with pancreatic sufficiency and a much later presentation and diagnosis.


The proportion of older people with CF who have recurrent troublesome abdominal symptoms is as high as 20-30% in some clinics. In this study patients were encouraged to drink plenty of water through the night and assessed with regard to abdominal symptoms for 3 months before and after starting this regimen. The frequency and severity of pain was reduced as was the medication required, emergency room visits and hospitalisations and even episodes of acute pancreatitis.

This is a simple measure which would be likely to reduce the pain which, in our experience, is commonly due to constipation and faecal accumulation in the lower ileum and colon even though the patient does not complain of constipation i.e. defined as the passage of infrequent hard stools.

This child (figure 43) complained of troublesome recurrent central abdominal pain; but neither she nor her parents complained of any disturbance in her bowel habit. However, her abdominal pain resolved completely when she was treated with laxatives (Littlewood et al, Pediatr Pulmonol 2006; 41:35-49). [PubMed]

So this suggestion of increasing fluid intake is simple, cheap and potentially very useful measure to reduce the incidence of abdominal pain in adults with CF. An extremely economical, and apparently effective, way of improving quality of life. An additional reason for persisting abdominal symptoms could be the presence of inflammation of the bowel which has been shown in a number of recent studies by breath tests, inflammatory markers in the stools, endoscopic means and most recently by capsule visualisation.


On the grounds that the authors considered that inhaled steroids are widely used despite lack of evidence, this study was to test the safety of withdrawal of inhaled corticosteroids with the hypothesis this would not be associated with an earlier onset of acute chest exacerbations. Patients during the 2-month run-in period, received fluticasone; they then took either fluticasone or placebo for 6 months. There was no difference in time to first exacerbation in the two groups. So in this study population (applicable to a surprising 40% of patients with cystic fibrosis in the UK), it appears safe to consider stopping inhaled corticosteroids.

It would be wise to consider the individual patient’s clinical history prior to their starting inhaled steroids before considering withdrawing the treatment. Note that the summary does not mention the 24 patients whose steroids the clinicians were unwilling to stop. They had more asthma, more were atopic and they had more exacerbations and were in a worse condition. Many of these patients are considerably, even dramatically, improved when they commence inhaled steroids. Trials of N=1 are obviously useful in this clinical situation.

Dr Ian Balfour-Lynn (figure 43) is consultant paediatrician at the Royal Brompton Hospital, London. He is involved in both patient care and CF research.


rhDNase (Pulmozyme) is a major component of treatment for people with CF but some patients show little or no response and hence fail to benefit from this important drug. In this study the biochemical properties, physical properties, and degradation by rhDNase-1 of sputum obtained from clinical responders and non-responders were compared; also the ability of magnesium to reactivate rhDNase-1 in DNA solutions and in sputum was investigated.

The effect of oral magnesium supplements on magnesium levels in the sputum of patients with CF was also examined. Sputum from clinical responders was extensively degraded in vitro on incubation with rhDNase-1, while sputum from clinical non-responders was not degraded: the median decrease in sputum elasticity in the two groups was 32% and 5%, respectively.

Sputum from clinical responders contained significantly higher concentrations of magnesium than sputum from non-responders (2.0 mM v 1.3 mM; p = 0.020). Sputum that could not be degraded by rhDNase-I became degradable after preincubation with magnesium. The effect of magnesium on rhDNase-I activity was mediated through actin. Oral intake of magnesium enhanced the magnesium concentration in the sputum of CF patients. So increasing the magnesium
One further supportive study by Rosenecker J et al. (Airway surface liquid contains endogenous DNase activity which can be activated by exogenous magnesium. Eur J Med Res 2009; 14:304-308. [PubMed]). They found BAL samples degraded plasmid DNA only after pre-incubation with magnesium. When analyzing the exhaled breath condensate the samples obtained from the healthy volunteers showed no DNase activity even after pre-incubation with magnesium, whereas in one of the two samples obtained from CF patients contained DNase activity after pre-incubation with magnesium. The authors concluded that increasing the magnesium concentration in the airway surface liquid by aerosolisation of magnesium solutions or oral magnesium supplements could improve the removal of highly viscous mucus in chronic lung disease by activating endogenous DNase activity.

Professor Kris De Boeck (figure 44) of University Hospital Leuven, Belgium is a leading, very active researcher and clinician in the CF field. Potentially a very useful paper which could benefit the 30-50% of patients who fail to show a significant response to rhDNase. [PubMed]

In people with CF inhaled heparin 50,000 IU twice daily had no effect on FEV1, sputum clearance or inflammatory markers. Ledson et al (Eur Respir J 2001; 17:36-38) from Liverpool had reported that inhaled heparin had no effect on 6 patients with CF who had B. cepacia infection. The present authors stated that Heparin thins sputum by decreasing the mucin molecule amino group negative charge, altering its intermolecular hydrogen bonding, and ionically shielding its polyionic moieties. It also has an anti-inflammatory effect within the lung“.

It seems unlikely that this will prove to be a significant advance in treatment. Although the authors suggested that heparin was safe and future evaluation of larger doses over a longer period may be warranted, it is perhaps significant that neither of the CF centres involved in these studies are using the heparin treatment on a regular basis.


Detailed metabolic and ultrasound studies of 29 adult patients with CF, 20 heterozygotes (CF-H) and 30 controls (C). 21% of those with CF and 15% of CF-H had kidney stones. Those with CF had elevated uric acid but no other differences compared with heterozygotes and controls. Lower urine volume and acidic pH produced super saturation of CF urine with uric acid in contrast to heterozygotes and controls. The authors considered high risk dietary advice or medication aimed at reducing risk of stones.

In another series of people with CF 13% had history of renal stones – many were recurrent. People with CF in this present series had a high risk of nephrolithiasis, although we did not recognise this complication through the Eighties although this series was of adults. There have been sporadic reports since 1964 (Gebala A. Pol med Sci Hist Bull 1964; 51:149-154 [PubMed]; Turner et al, 2000 above; Bertenshaw C et al, 2007 for acute renal failure below). Earlier Bohles & Michalk (Helv Paediatr Acta 1982; 37:267-272). [PubMed] found patients with CF showed increased urinary concentrations of oxalate, phosphate, xanthine and uric acid, and decreased concentrations of magnesium and citrate, comparable to concentrations found in patients with calcium oxalate stones. However, compared to stone bearing controls their urine calcium concentration was markedly decreased. They suggested that hypocalciuria in CF seems to protect against nephrolithiasis despite the presence of lithogenic factors.


Inhaled nitrous oxide was safe and effective in reducing trauma and the effects of needle phobia and being offered to children with CF for procedural pain in the district general hospital at Wolverhampton.

Dr Rosie Rayner (figure 45), the paediatrician, was previously the CF Research Fellow in Nottingham. The use of nitrous oxide had been previously reported at CF Meetings by this team from Wolverhampton (Williams V et al, Cyst Fibros 2004; 3: S100 Poster 376; also Maddison JC et al, Poster 377; original report by Mills HL & Redmond AOB, 2001 above).

Sixty one prepubertal children were either treated with growth hormone or were controls. After 1 yr, growth hormone treated children had significantly greater gain in height, weight, lean body mass, and bone mineral content. They had fewer hospitalizations and an improvement in CF quality of life but there was no difference in pulmonary function between groups. After cessation of GH treatment, there was a sustained effect for increased height and weight velocity, as well as accrual of bone mineral.

Although there was a significant favourable effect for the growth hormone treatment there are few children who receive or indeed now require this treatment (also Hardin et al, 2001 above).


Thirty-eight patients with an average age of 30 years (range 18-55yrs) with CF-related diabetes for 20 years (0-31yrs) were screened for diabetes complications at the Copenhagen CF Centre. Because of chronic pulmonary infections, the majority of patients were regularly treated with aminoglycoside and cyclosporine was given to those who had lung transplants. Since the pharmacological treatment of lung transplant patients could influence metabolic regulation and renal function, the results were given separately for nontransplanted (n = 29) and transplanted (n = 9) CF patients.

Nine of these diabetic patients (27%) had retinopathy, two of whom had proliferative retinopathy requiring laser treatment. Lung transplantation did not affect the prevalence of retinopathy. In 29 non-transplanted patients, nine had hypertension, three microalbuminuria, and one elevated creatinine; none had macroalbuminuria. In transplanted patients (9), eight had hypertension, two had microalbuminuria, and none had macroalbuminuria; seven of the nine had elevated plasma creatinine, and severely reduced glomerular filtration rate was significantly more frequent.

So a high frequency of diabetic retinopathy was found in patients with insulin-treated CF-related diabetes, stressing the need for a regular screening program as in type 1 diabetes. Severely impaired kidney function was common in lung transplant patients, probably secondary to cyclosporine treatment but many would also have had life long regular courses of intravenous aminoglycosides. As age increases so do complications. Eventually the majority of older people with CF will develop diabetes and it is clear that eventually many will develop diabetic complications particularly retinopathy. The added complications associated with immunosuppressant drugs in those who have had lung transplants and the effects of repeated courses of aminoglycosides contribute to the high frequency of renal complications.


The purpose of this study from Paris was to develop a molecular method to characterise both paternal and maternal CFTR alleles in DNA from circulating fetal cells (CFCs) isolated by ISET (isolation by size of epithelial tumour/trophoblastic cells). This protocol was validated in 12 pregnant women, at 11 to 13 weeks of gestation, whose offspring had a 1 in 4 risk of CF. Results showed that one fetus was affected, seven were heterozygous carriers of a CFTR mutation, and four were healthy homozygotes. These findings were consistent with those obtained by chorionic villus sampling (CVS).

This test affords a reliable method prenatal diagnosis for high risk couples and avoids the risks associated iatrogenic miscarriage with chorionic biopsy (also note Fetal DNA detected at 13 weeks of a Q890X carrier fetus by Gonzalez-Gonzalez MC et al. Prenatal diagnosis 2002; 22:946-948. [PubMed])


Six patients with CF (median age 14 years) underwent splenectomy with a splenorenal shunt operation – 3 for massive splenomegaly and three to control variceal bleeding after several sessions of sclerotherapy. Lung function remained stable, and there was an overall reduction of respiratory tract infections. The youngest patient, however, died of overwhelming septicemia during treatment with steroids.

Sometimes the spleen is so large in people with CF that the size is a physical handicap causing respiratory embarrassment and considerable abdominal distension in addition to the systemic effects of hypersplenism. A boy with CF of 15 years in Leeds had a spleen weighing over 3 kg removed by the late Prof Giles with great improvement in his respiratory function and general health (Gilbert J et al. Splenectomy for massive splenomegaly in cystic fibrosis with improvement in pulmonary status. Scand J Gastroenterol 1987; 23 (Suppl 143):177).


During one year patients with CF were randomized either to aerosolized Pulmozyme daily or to no Pulmozyme. The number of positive respiratory cultures was higher in the untreated group (82%) compared with the treated group (72%) (p<0.05). The most striking difference was found for Staphylococcus aureus, with a prevalence of 30% in the untreated group compared with 16% in the treated group (p<0.0001). Pulmonary function (FEV1) in the treated group showed a
significant increase of 7.3% compared to 0.9% in the untreated group (p<0.05). Long term DNase treatment was beneficial to CF patients without chronic lower respiratory tract infection, with fewer positive respiratory cultures, leading to reduced demand for antibiotics and to improved lung function.

A useful study from Copenhagen showing inhaled rhDNase reduced the likelihood of a positive respiratory culture. This finding provides additional support for starting all patients on the treatment at an early age, where inhaled treatment is practical, as occurs now in some centres.


Fifty adult patients at Stanford University Medical Center with a diagnosis of bronchiectasis and/or pulmonary NTM infection were prospectively characterized by sweat chloride measurement, comprehensive mutational analysis of CFTR, and sputum culture results. A new diagnosis of cystic fibrosis (CF) was established in 10 patients (20%). Sweat chloride concentration was elevated > 60 mEq/dL (diagnostic of CF) in seven patients (14%), and from 40 to 60 mEq/dL in eight patients (16%). The frequency of CFTR mutations was elevated above that expected in the general population: heterozygous DeltaF508 (12% vs 3%), R75Q (14% vs 1%), and intron 8 ST (17% vs 5 to 10%).


A report of 57 CF patients, many of whom were in their teens, who had liver transplants. Post-transplant survival was high and poor respiratory function was the main risk factor for early death; in the short-term, respiratory function significantly improved in most patients. Transplantation was considered to be the appropriate treatment for patients with advanced CF-related liver disease and preserved pulmonary function and an FEV1 over 50% predicted.

Further general European experience of liver transplantation in people with CF confirming the good results since the first report of Mieles LA et al. (1989 above) [PubMed]


The aim of this review was to determine the evidence available to support the efficacy of isolation (or segregation) practices in preventing, delaying or reducing the risk for CF patients of acquiring P. aeruginosa and B. cepacia. In the absence of studies with an experimental, controlled design, the efficacy of isolation practices in preventing the transmission of respiratory pathogens in CF remains unproven. However, it is no surprise that the observational studies reviewed seem to support the implementation of isolation (or segregation) measures to reduce the risk of transmission of B. cepacia and P. aeruginosa in CF patients.

There is now certainly enough published evidence to support patient segregation according to microbiological status and a controlled trial would be quite unethical. The delay in introducing patient segregation and the occurrence of cross infection in some CF centres has provided adequate information that the practice is fully justified!!!


A report of six patients with CF with respiratory deterioration that did not respond to appropriate antibiotic treatment. All had had A. fumigatus in their sputum cultures but did not fulfill the accepted criteria of allergic bronchopulmonary aspergillosis (ABPA). Treatment with antifungal agents was followed by improvement in their clinical condition. The authors suggest that in patients with CF, A. fumigatus should be considered as a pathogen that may directly cause respiratory exacerbations (rather than by only causing an allergic reaction as in ABPA). Antifungal therapy should be considered when deteriorating respiratory function is not responding to antibacterial therapy and A. fumigatus is growing in sputum cultures.

Problems with Aspergillus were becoming increasingly common and it is experience in both Leeds and Copenhagen that as the prevalence of chronic Pseudomonas falls, as a result of early eradication therapy, the number of patients growing Aspergillus increases. There is also increasing evidence that, although, at times manifest as typical ABPA, the presence of the fungus in the airways can also cause a subtle deterioration in respiratory function or, as in the present report, even cause an acute bronchial infection which should be treated with appropriate anti-fungal drugs.


Non-typeable Haemophilus influenzae (NTHi) commonly infects patients with CF, especially early in childhood and biofilms were common in bronchoalveolar lavage fluid decreasing susceptibility to antibiotics; also respiratory cells exhibited inflammatory and host defence responses - evidence of
a dynamic host-pathogen interaction. There are implications both for understanding early CF lung disease pathogenesis and for the treatment of early, asymptomatic colonization of patients with CF with *H. influenzae*.

*H. influenzae* at times persists in serial respiratory cultures despite antibiotic treatment or soon reappears after such treatment. It is undoubtedly a pathogen for people with CF who become chronically infected. This warrants vigorous attempts to eradicate the organism, if necessary by intravenous antibiotics if oral treatment fails, an approach analogous to the treatment of early *P. aeruginosa*. Many CF units would now treat and attempt to eradicate any pathogen grown from the CF airways whether or not there were symptoms which are a very crude indicator of endobronchial infection.

2006 Gibson RL, Retsch-Bogart GZ, Oermann C, Milia C, Pilewski J, Daines C, Ahrens R, Leon K, Cohen M, McNamara S, Callahan TL, Markus R, Burns JL. Microbiology, safety, and pharmacokinetics of aztreonam lysinate for inhalation in patients with cystic fibrosis. Pediatr Pulmonol 2006; 41:656-665. [PubMed] Aztreonam lysinate for inhalation (AI) is a novel monobactam formulation for chronic pulmonary *Pseudomonas aeruginosa* infections in CF. The activity of AI was retained against multiple CF isolates after nebulisation via eFlow nebuliser, and the activity was not inhibited by CF sputum. All 12 adult subjects and 11 of 12 adolescents tolerated the inhaled antibiotic. These data were supportive of the continued development of aztreonam lysinate for treatment of patients with CF. Original aztreonam was not tolerated as an inhalation but the lysinate is suitable for nebulisation. This study also confirms that nebulisation does not denature the product. Phase III trials were completed by 2008 (Retsch-Bogart et al, 2008below) [PubMed] [PubMed] and by 2009 the product licensed in Europe and Canada; and in the USA in 2010.

2006 Lording A, McGraw J, Dalton A, Beal G, Everard M, Taylor CJ. Pulmonary infection in mild variant cystic fibrosis: implications for care. J Cyst Fibros 2006; 5:101-104. [PubMed] Few reports document the condition of the airway in infants and young children with apparent "mild" disease. A retrospective cohort study was carried out comparing frequency of bacterial isolates and clinical outcomes in eleven compound heterozygotes for DeltaF508 and a second mild mutation, mainly R117H, with a matched group of DeltaF508 homozygotes. *Staphylococcus aureus* was isolated in 8 of the 11 patients with mild variant disease and *Pseudomonas aeruginosa* found in 7 (64%), although the frequency of positive cultures was significantly less (2.8/year) than the DeltaF508 homozygotes (6.1/year). Shwachman scores were significantly higher in patients with mild mutations (94(74-92) vs. 88 (77-91)); there was also a small but significant difference in chest radiograph (Chrispin-Norman) scores although little difference in lung function.

This is a timely paper from Sheffield UK stressing that most patients with so-called mild variant CF will nonetheless have bacterial isolates from their airway cultures requiring antibiotic therapy three to four times a year. Infection with both *S. aureus* and *P. aeruginosa* is common. Also they are slowly deteriorating with respect to respiratory function. Anti-staphylococcal prophylaxis for the first three years should be considered. It is vitally important these mild patients are followed carefully by a team experienced in CF care and treated vigorously to prevent their changing into severe cases. They deserve just as careful treatment and follow-up as those with more obvious symptoms and signs.

2006 Poustie VJ, Russell JE, Watling RM, Ashby D, Smyth RL. CALICO Trial Collaborative Group. Oral protein energy supplements for children with cystic fibrosis: CALICO multicentre randomised controlled trial. BMJ 2006; 332(7542):632-636. [PubMed] In 102 children with cystic fibrosis, aged between 2 and 15 years, who were moderately malnourished, the effects of oral protein energy supplements in addition to their usual dietary advice were compared with dietary advice alone, for 12 months. The authors concluded that the long term use of oral protein energy supplements did not result in a significantly better improvement in nutritional status or other clinical features and so oral protein energy supplements should not be regarded as an essential part of the management of children with CF.

This multi centre trial was supported by the UK CF Trust. At the time over 50% of children with CF in the UK were taking regular (expensive) proprietary dietary supplements with only sparse evidence of their efficacy. Although this trial showed that dietary advice to increase the intake of normal food was of equivalent value, the supplements were still widely used as one way of dealing with the eating problems so common in small children with CF and in improving energy intake in adults (White et al, J Cyst Fibros 2004; 3:1-7). [PubMed] So the outcome of the trial appeared to have only minimal effect on the use of the supplements in the UK.

2006 Kalnins D, Ellis L, Corey M, Pencharz PB, Stewart C, Tullis E, Durie PR. Enteric-coated pancreatic enzyme with bicarbonate is equal to standard enteric-coated enzyme in treating malabsorption in cystic fibrosis. J Pediatr Gastroenterol Nutr 2006; 42:256-261. [PubMed] To compare the efficacy of an enteric-coated buffered pancreatic enzyme containing 1.5 mEq of bicarbonate per capsule with a conventional enteric-coated enzyme capsule in cystic fibrosis patients with signs or symptoms of moderate to severe malabsorption. The authors found that in the doses used, nutrient absorption of patients taking the buffered preparation offered no advantage over a conventional preparation.

The addition of bicarbonate or acid suppressing drugs was recommended to protect the active enzymes from gastric acid before the acid resistant enzymes became available in the early...
Eighties. With the introduction of the acid resistant microspheres (e.g. Pancrease and Creon) acid suppression was required infrequently and only recommended if malabsorption was difficult to control even with doses equivalent to 10,000IU lipase/kg/day.

Daina Kalnins (figure 46) is Academic and Clinical Specialist Dietitian, Respiratory Medicine Manager, Clinical Dietetics at the Hospital for Sick Children in Toronto, Ontario. In addition to many research publications on CF she has co-authored several books on nutrition, including The Hospital for Sick Children’s Better Food for Kids and Better Baby Food, which won The International Cookbook Revue Award (2001).


Several studies have reported omega-3 and omega-6 fatty acid imbalances in patients with cystic fibrosis. Whether these imbalances contribute to, or are manifestations of, the pathophysiology of CF is unknown. This study by John Lloyd-Still and colleagues from Chicago was to determine bioavailability, tissue accretion, and safety of a large dose of an algal source of docosahexaenoic acid (DHA) triacylglycerol and to observe the effects on lung function in patients with CF. Twenty subjects with CF (8 to 20 yrs of age) were randomly assigned to receive algal oil providing 50 mg of DHA per kilogram per day (1 to 4.2 g of DHA per subject per day) or placebo for 6 months. The authors found that algal DHA triacylglycerol oil is readily absorbed well tolerated, and increases blood and tissue DHA levels in patients with CF. No adverse developments were associated with this large dose of DHA oil. The authors concluded that larger studies of longer duration are needed to determine whether DHA supplementation results in any clinically significant benefits in patients with CF. Subsequently a report from Belgium failed to show any clinical improvement after a year’s supplementation with a DHA rich algal oil (Van Biervliet S et al. Prostaglandins Leukot Essent Fatty Acids 2008; 78:109-115. [PubMed]).

Dr John Lloyd Still (figure 47) is one of the leading figures in CF care and research in N. America and has been involved in CF and paediatric gastroenterology for many years since he qualified at Guys Hospital in London in 1960. After qualifying he worked in London in paediatrics and eventually moved to Boston where he worked with Harry Shwachman. He is now in charge of the CF care at the Rush University Medical Center, Chicago. He edited a major textbook on CF in 1983 to which most of the leading authorities on CF in North America at the time contributed (Textbook of Cystic Fibrosis. Lloyd-Still J D. John Wright PSG Inc. 1983). He is particularly interested in, and has published widely on, the gastroenterological and nutritional aspects of CF.


The purpose of this study was to determine the association between long-term use of azithromycin, now taken by many patients with CF, and change over time in macrolide susceptibility of *Staphylococcus aureus* and Haemophilus spp. The authors found that erythromycin resistance in *S. aureus* increased from 6.9 to 53.8% and clarithromycin resistance in Haemophilus spp. from 3.7 to 37.5%. Resistance but also isolation rates were strongly related to azithromycin use. So over a 4 year period, azithromycin maintenance therapy in the CF population was associated with an increase in macrolide resistance in *S. aureus* and Haemophilus spp. which was not unexpected.


A Chinese girl of 16 years old was diagnosed as having CF at the age of 14 years. A heterozygous novel missense mutation of 699 C --> A, which results in the amino acid change of N189K, was identified in exon 5. In addition, a heterozygous 3821 - 3823 delT mutation in exon 19 was found in CFTR.

CF is very rare on Chinese people; only twenty were reported from 1974 to 2004 were also reviewed in this paper. DelF508 mutation was not found in any of the nine cases whose CFTR mutations were analyzed and suggests that the genotype of Chinese CF may be different from those in Europe and N America.

This search identified 15 trials on the subject but the reviewers considered only 3 trials, involving 69 participants, were eligible for inclusion. The reviewers considered that there was evidence from two randomised controlled trials, of "questionable methodological quality", that treatment of early *P. aeruginosa* infection with inhaled tobramycin resulted in microbiological eradication of the organism from respiratory secretions more often than placebo and that this effect may persist for up to 12 months, however incomplete data from one of the trials precluded an accurate analysis. One randomised controlled trial of oral ciprofloxacin and nebulised colistin versus usual treatment was identified (Valerius et al, 1991 above) but the reviewers considered this trial was of "poor methodological quality. The results suggested treatment of early infection results in microbiological eradication of *P. aeruginosa* more often than usual treatment, after two years. The reviewers considered that there was insufficient evidence to determine whether antibiotic strategies for the eradication of early *P. aeruginosa* decrease mortality or morbidity, improve quality of life, or are associated with adverse effects compared to placebo or standard treatment. From the three trials included in this review, there was some evidence that antibiotic treatment of early *P. aeruginosa* results in short-term eradication but it remains uncertain whether there is clinical benefit to people with cystic fibrosis.

The conclusions of this Cochrane review were quite out of keeping with the clinical experience of most experienced CF clinicians and the study was soundly criticised by Prof. Neils Holby who regarded further trials as unwarranted. The opinion of an experienced and respected clinician such as the late Christian Koch was representative of current opinion (quoted in entry on Valerius et al, 1991 above). There was by the time of this review (2006) a wealth of evidence that avoidance of chronic *P. aeruginosa* infection improved clinical condition and increased survival - evidence that the reviewers did not consider (Kerem et al, 1990; Henry et al, 1992; Hudson et al, 1993; Pamucku et al, 1995 above; Frederiksen et al, 1996; CF Foundation Patient Registry 1996; Frederiksen et al, 1997 above; Kosorok et al, 2001). Presumably this evidence was ignored as it did not directly concern eradication of *P. aeruginosa*. The conclusions of this Cochrane review were quite out of keeping with the clinical experience of most experienced CF clinicians and the study was soundly criticised by Prof. Neils Holby who regarded further trials as unwarranted. The opinion of an experienced and respected clinician such as the late Christian Koch was representative of current opinion (quoted in entry on Valerius et al, 1991 above). There was by the time of this review (2006) a wealth of evidence that avoidance of chronic *P. aeruginosa* infection improved clinical condition and increased survival - evidence that the reviewers did not consider (Kerem et al, 1990; Henry et al, 1992; Hudson et al, 1993; Pamucku et al, 1995 above; Frederiksen et al, 1996; CF Foundation Patient Registry 1996; Frederiksen et al, 1997 above; Kosorok et al, 2001). Presumably this evidence was ignored as it did not directly concern eradication of *P. aeruginosa*. It is important to stress that eradication of early *P. aeruginosa* infection, to prevent or delay chronic infection, is one of the most important aspects of therapy and acquisition of chronic infection should now be regarded as avoidable and represent a failure of therapy (Drittanti et al, 1996 above).

In cystic fibrosis (CF), chronic infection of the airways with Achromobacter xylosoxidans have become more frequent. The pathogenic role of this is yet unclear. METHODS: A retrospective case-control study of all patients chronically infected with A. xylosoxidans for at least 3 years. 15 patients (6 males) with chronic A. xylosoxidans infection were matched by age, FEV(1) and body mass index z-score to 15 controls (7 males) at the time of establishment of chronic infection. Eight patients harboured a common A. xylosoxidans strain, indicating either cross-infection or a common source. CONCLUSION: A. xylosoxidans may lead to a decline in lung function in a subgroup of chronically infected CF patients characterised by a rapid increase in specific precipitating antibodies. Cross-infection may possibly occur.

A useful review from the Copenhagen CF Centre of a relatively new problem in people with CF:

Stool specimens from 30 consecutive patients with CF, aged 1-44, and from 30 healthy similarly aged subjects were tested for the H. pylori antigen by specific monoclonal antibodies and for CD toxins by Tox A/B assay and Tox A assay. CF patients were assessed clinically and tested for specific H. pylori serum antibodies and for mutations. In CF patients, the prevalence of H. pylori antigen was 16.6% (5/30), compared to 30% (9/30) in controls. Of the 26 CF patients with PI, only 2 (7.6%) were infected by H. pylori, compared with 3 of the 4 (75%) patients with PS (P=0.001). H. pylori infection was diagnosed in 3 of 5 (60%) CF patients carrying mild mutations, compared to 1 of 25 (4%) CF patients carrying severe mutations (P=0.01). Fourteen of 30 (46.6%) stool specimens from CF patients tested positive in the ToxA/B assay, and 3 of 14 tested positive for ToxA. No significant differences in antibiotic use, severity of lung disease, PI, chronic abdominal pain, or genotype were found between the two groups. None of the controls was positive for CD toxins. Prevalence of H. pylori infection in CF patients was lower than in similarly aged non-CF controls. CF patients with PI or a history of distal intestinal obstruction syndrome and those carrying mutations associated with a severe phenotype were protected against H. pylori infection. Almost half of the CF patients were asymptomatic carriers of CD producing mostly toxin B. More studies are needed to confirm our results in a larger group of CF patients.

This paper confirms the previously reported low incidence of H. pylori in people with CF:

Tuberculosis is a rare occurrence in CF. Second author is Jean Feigelson of Paris who published his first paper on CF on 1963 ([(PubMed)]).

Pneumothorax is a known complication in cystic fibrosis (CF), associated with poor outcome. Records of CF patients with pneumothorax at the Royal Children's Hospital, Melbourne between

The History of Cystic Fibrosis by Dr James Littlewood OBE
1990 and 2004 were reviewed, and the characteristics, sputum culture results, lung function, treatment, and outcome for the 11 patients who had pneumothoraces were described.

This is a useful report as pneumothorax is now rare in children with CF.

The objectives of this study were to determine the prevalence of morphometric vertebral fractures in a large cohort of adult cystic fibrosis (CF) patients, and to examine the association between fractures and bone mineral density (BMD). DESIGN: Cross-sectional retrospective study. SETTING: A tertiary care academic hospital. Seven percent of adult patients with CF had vertebral fractures as determined by morphometry. Subjects in the fracture group had both clinically and statistically higher BMD as measured by DXA. Our findings raise the intriguing possibility that BMD may not be useful in identifying CF patients with fractures.

A representative cross sectional analysis of serum antibodies against three Pseudomonas antigens (alkaline protease, elastase, and exotoxin A) was performed in 183 patients with CF of mean age 16.7 years and FEV1 85.9% predicted. The results were correlated with microbiological results from the previous 2 years to calculate sensitivity, specificity, positive and negative predictive values. The following 2 years were assessed to determine prognostic predictive values. The authors concluded regular determination of serum antibodies may be useful in CF patients with negative or intermittent but not with positive P aeruginosa status. A rise in antibody titres indicates probable infection and eradication treatment may be initiated even in the absence of microbiological detection of P aeruginosa.

The papers evaluating the use of Pseudomonas antibodies in CF have appeared regularly since the Seventies when Neils Hoiby showed by crossed immunoelectrophoresis that a rising antibody was a bad sign (Hoiby N, Axelsen NH. Identification and quantitation of precipitins against Pseudomonas aeruginosa in patients with cystic fibrosis by means of crossed immunoelectrophoresis with intermediate gel. Acta Path Microbiol Scand 1973; 81:298-308). [PubMed] In Leeds, influenced by Hoiby’s work, we evaluated their use in the mid Eighties (Brett MM, Ghoneim ATM, Littlewood JM. Serum antibodies to Pseudomonas aeruginosa in cystic fibrosis. Arch Dis Child 1986; 61:1114-1120. [PubMed] in series of studies by Moira Brett and found them to be very useful. Basically the absence of antibodies was reassuring that Pseudomonas was not present in the airways and a rising titre in chronically infected patients indicated the need for more aggressive treatment.

A novel strategy for delivering low doses of steroids for long periods through the infusion of autologous erythrocytes loaded with dexamethasone has been recently set up. A recent study suggested the feasibility of therapy with low doses of corticosteroids delivered through engineered erythrocytes in CF patients. This study presents a further analysis of safety and efficacy of this therapy. Nine patients in the experimental group received the treatment once a month for a period of 24 month. Patients did not develop diabetes, cataract, or hypertension, or other typical side effects of steroid treatment during the follow up period. There was a constant improvement of FEV1 in patients undergoing the experimental treatment compared to a gradual decrease of the same parameter in the standard therapy group (P = 0.04). The average of clinic and radiological indexes did not vary. The number of infective relapses that have required antibiotic intravenous therapy was not different in the two groups, although the average of these episodes was slightly higher in the experimental therapy group. The authors concluded intraerythrocyte corticosteroid treatment may stabilize the respiratory function in CF patients but is often considered too invasive by patients. The results obtained by our study may help planning an experimental, controlled, randomised study. A sample size of 150 patients per group would be sufficient for demonstrating such a difference with a 95% confidence interval and a power of 90%.

A novel method for administering anti-inflammatory treatment with dexamethasone to people with CF. However, there were no further studies up to 2011.

A report of a 30-year-old woman with cystic fibrosis (CF) chronically infected with Pseudomonas aeruginosa who delivered and breast-fed a healthy boy. While breast-feeding the woman had to undergo an i.v. antibiotic course with tobramycin, due to pulmonary exacerbation. Tobramycin was not detected in her milk and lactation could be continued. This is the first time that the presence of tobramycin in the milk of a CF woman during i.v. administration has been investigated.

This is useful information even though only an isolated case report - particularly as pregnancy becomes more common in women with CF.

2006 Mulheran M. Hyman-Taylor P. Tan KH. Lewis S. Stableforth D. Knox A. Smyth A. Absence of cochleotoxicity measured by standard and high-frequency pure tone

We undertook assessment of hearing in patients with cystic fibrosis who were taking part in a large randomized controlled trial of once- versus three-times-daily tobramycin for pulmonary exacerbations of cystic fibrosis (the TOPIC study). Complete pre- and post treatment standard audiological data were obtained for 168/219 patients. We found no significant differences in hearing thresholds when they were assessed at the baseline, at the end of treatment, and at follow-up 6 to 8 weeks later were compared. In addition, no significant differences in hearing thresholds were detected between treatment regimens. Similar results were obtained for the subset of 63/168 patients who underwent high-frequency auditory audiometry. We conclude that for a single 14-day course of tobramycin treatment in patients with cystic fibrosis with no preexisting auditory deficit, no measurable effect on hearing was apparent with either once- or three-times-daily treatment. Estimation of the cumulative cochleotoxict risk in cystic fibrosis patients due to repeated aminoglycoside therapy, as evidenced by the patients excluded from this study due to hearing loss, also requires further characterization.


Although bronchial artery embolization (BAE) is effective in the acute control of recurrent or major hemoptysis in adults with cystic fibrosis, outcomes after embolization are not well known. Of 297 patients with cystic fibrosis hospitalized from 1990 to 2004, 30 patients (mean age, 26.7+/−9.2 years) presented with major or persistent hemoptysis that required 42 BAE sessions. These patients were compared with a control group of 27 patients without hemoptysis requiring embolization who were matched for age, sex, and forced expiratory volume in 1 second (FEV1). Hemoptysis stopped within 24 hours after BAE and there were no major complications. The change in the slope of FEV1 after the BAE or matching date was significantly worse in the embolization group (P=.0007). At last follow-up, nine and one patients, respectively, had undergone lung transplantation in the BAE and control groups (P=.002). The 5-year survival rates without lung transplantation were 31% and 84%, respectively, in the BAE and control groups (hazard ratio, 5.95; P=.002). Sixty-two percent of patients were free of hemoptysis 5 years after BAE. The number of collateral arteries was the only factor associated with the risk of death or recurrent hemoptysis (P=.001). Despite the effectiveness of embolization in controlling recurrent or major hemoptysis, adults with cystic fibrosis who have undergone BAE for hemoptysis are at much higher risk of respiratory function aggravation, death, and the need for lung transplantation than those who have not undergone BAE for hemoptysis. They are more likely to die or to undergo lung transplantation than to present with recurrent major hemoptysis.

This is useful extensive experience of treating haemoptysis in people with CF. As to be expected the patients with haemoptysis had more severe chest involvement and generally a worse prognosis but the procedure was successful and free of major complications with regard to the controlling the bleeding.


Four separate categories of chronic Pseudomonas aeruginosa (Pa) infection in children with cystic fibrosis (CF) have been previously defined, based on airway cultures taken over the previous year. The aim of the present study was to evaluate this definition in the current authors' paediatric and adult CF clinic using clinical, immunological and lung function parameters. During follow-up, out of 193 patients, 55 (34%) CF patients had never been infected with Pa, 27 (17%) were free of Pa, 29 (18%) were intermittently infected and 51 (31%) were chronically infected. Disease severity markers, such as lung function, were significantly worse in the chronic group, especially in the paediatric population. Differences in adult patients were smaller and no longer significant. Pa antibodies differed strongly between the groups, and were very high (mean+/-sd 55.4+/−5.5) and highly statistically significant from all other groups in the chronic group. They were low and different from all other groups in the never group (1.8+/−0.6). Pa antibodies did not differ between the free of Pa and the intermittent group. In conclusion, the current authors confirmed an agreement between Pseudomonas aeruginosa status according to the new definition and clinical status, as well as with the level of Pseudomonas aeruginosa antibodies.

Although these authors agreed with the Leeds criteria for evaluating Pseudomonas infection, there was still considerable differences in the criteria used for chronic PA infection.


Laboratory evidence suggests that vitamin A could have a protective effect on respiratory status in patients with cystic fibrosis (CF). This study shows a significant correlation between serum vitamin A concentrations and every aspect of lung function tested in 38 patients with stable CF. Serum vitamin D and vitamin E concentrations were also measured but did not show any significant correlations with lung function.

This is interesting as Dorothy Andersen initially likened the changes in the bronchial epithelium to the epithelial metaplasia found in vitamin A deficiency and for some years considered that the pulmonary problems were related to the changes in the bronchial epithelium leading to a infection - i.e. the condition was primarily the result of intestinal malabsorption resulting in vitamin
deficiency. The authors of the present paper note this is the first study showing a definite relationship between vitamin A levels and respiratory function tests in CF.


We performed a retrospective analysis of patients who underwent lung transplantation from December, 1992 through July, 2005 at our tertiary care medical center. Of the 215 patients who received lung transplantation, 17 (7.9%) developed gastric bezoars confirmed by upper endoscopy. Cystic fibrosis was the leading indication for lung transplantation (n=145), and 11% of cystic fibrosis patients (16 of 145) formed gastric bezoars after transplant. Additionally, 94% of patients with bezoars (16 of 17) had cystic fibrosis (P=0.02), with the exception being a subject with primary ciliary dyskinesia. No patient who underwent lung transplant for another indication was found to have a bezoar. The mean time to diagnosis was 34 days, with two-thirds of bezoars diagnosed within one month after transplant. The annual incidence was unchanged during the study period. Gastric bezoars are common in cystic fibrosis patients after lung transplantation. The etiology is likely multifactorial, related to gastric motility, respiratory secretions, and medications. Further investigation is needed to understand the pathogenesis of bezoar formation in this selected population, and strategies for primary prevention may be beneficial.

This complication seems to be relatively common after transplants in people with CF who are known to have abnormal gastric motility.


To assess outcome of assisted ventilation in cystic fibrosis (CF) patients with acute respiratory failure (ARF), to identify risk factors associated with poor outcome and to compare long-term outcome of CF children who were mechanically ventilated for ARF with unventilated CF controls. A retrospective cohort study in two large CF centres in the Netherlands. Thirty-one CF patients required assisted ventilation for ARF between January 1990 and March 2005. All five children (under 2 years of age) and seven adults (27%) survived. CF patients younger than 2 years old, who are ventilated because of ARF, have a good prognosis and their long-term outcome seems identical to unventilated CF controls. ARF in adult CF patients still is associated with high mortality, especially among patients with acute on chronic respiratory failure.

The resort to assisted ventilation has changed over the years now there is the possibility of transplantation; prior to the mid Eighties before the first successful transplantsations ventilation was regarded as inappropriate.


Neutrophilic airway inflammation is a hallmark of cystic fibrosis (CF). As high oxidant producers, airway neutrophils contribute largely to the systemic redox imbalance seen in CF. In turn, this chronic and profound imbalance can impact circulating neutrophils before their migration into Airways. Indeed, in 18 CF patients with stable disease, blood neutrophils were readily deficient in the pivotal antioxidant glutathione (P = 0.003, compared with 9 healthy controls). In a phase 1 study, this deficiency was improved (P = 0.025) by the glutathione prodrug N-acetylcysteine, given orally in high doses (0.6 to 1.0 g three times daily, for 4 weeks). This treatment was safe and markedly decreased sputum elastase activity (P = 0.006), the strongest predictor of CF pulmonary function. Consistently, neutrophil burden in CF Airways was decreased upon treatment (P = 0.003), as was the number of airway neutrophils actively releasing elastase-rich granules (P = 0.005), as measured by flow cytometry. Pulmonary function measures were not improved, as expected with short-term treatment. After excluding data from subjects without baseline airway inflammation, positive treatment effects were more pronounced and included decreased sputum IL-8 levels (P = 0.032). Thus, high-dose oral N-acetylcysteine has the potential to counter the intertwined redox and inflammatory imbalances in CF.

Conflicting views on the effect of N-acetylcysteine appear despite the Cochrane conclusion that it is of no benefit in CF.


Cystic fibrosis (CF) patients with advanced lung disease are at risk for developing pulmonary vascular disease and pulmonary hypertension, characterized by progressive exercise intolerance beyond the exercise-limiting effects of airways disease in CF. We report on a patient with severe CF lung disease who experienced clinically significant improvements in exercise tolerance and pulmonary hypertension without changing lung function during sildenafil therapy.

Sildenafil has been reported to have a favourable effect on the DF508 mutation although no clinical trials have been reported (by 2011). Here the drug is used to treat pulmonary hypertension which is common in severe CF lung disease.


As the life expectancy of patients with cystic fibrosis increases, unusual complications including...
amyloidosis are increasingly recognised. We report three cases of amyloidosis including a unique case presenting with a hemorrhagic and thrombotic diathesis. This complication of amyloidosis has never been reported in cystic fibrosis.

There are sporadic reports of amyloidosis in people with CF since the Seventies. Considering the prolonged severe sepsis present in many patients the number of reports are relatively infrequent. See topics for Castile R, et al. Amyloidosis as a complication of cystic fibrosis. Am J Dis Child 1985; 139:728-732. [PubMed]


Inhaled colistin is commonly used in patients with cystic fibrosis (CF), but only limited data are available to define its pharmacokinetic profile. We performed a multicentre study in 30 CF patients to assess sputum, serum and urine concentrations after a single dose of 2 million units of colistin administered by inhalation. In a subgroup of patients we also compared the efficacy of two different nebulizers for administration of inhaled colistin. Serum concentrations of colistin reached their maximum 1.5 h after inhalation and decreased thereafter. Serum concentrations were well below those previously reported for systemic application in all patients. A mean 4.3+-1.3% of the inhaled dose was detected in urine. Elimination characteristics did not differ significantly from those previously reported for systemic application. A positive correlation was found between forced expiratory volume in 1 s (FEV1) in per cent predicted and both AUC and maximal colistin concentrations in serum (Cmax). Maximum sputum concentrations were at least 10 times higher than the MIC breakpoint for Pseudomonas aeruginosa proposed by the British Society for Antimicrobial Chemotherapy. Although sputum drug concentrations decreased after a peak at 1 h, the mean colistin concentrations were still above 4 mg/L after 12 h. No differences were seen in polymyxin E sputum concentrations, for CF patients between the two nebulizer systems.

The authors concluded the low systemic and high local concentrations of colistin supported the use of inhaled colistin in CF patients infected with P. aeruginosa. This was reassuring as inhaled colistin had been increasingly used since the first report of its use in eradicating early Pseudomonas infection in CF (Littlewood et al, Nebulised colomycin for early Pseudomonas colonisation in cystic fibrosis. Lancet 1985; 1: 865. [PubMed] No pharmacokinetic studies were done before we gave inhaled colomycin in the early Eighties to see if it would clear early Pseudomonas infection!


The coughing paroxysms of patients with cystic fibrosis may occasion neurological symptoms. Although cough syncope is well-known, and is associated with headache and paralysis, a migrainous mechanism has not been reported. We reviewed the medical records, autonomic testing results, and responses to treatment in two cystic fibrosis patients with similar presentations of cough-induced impairment of consciousness followed by headache and paralysis. A 24-year-old woman and an unrelated 38-year-old man, both with cystic fibrosis, developed post-tussive neurologic deficits. Both patients reported infrequent dramatic spells, always preceded by major hemoptysis, and associated with left-sided paralysis, transient blindness, nausea, and severe pulsating headaches. Autonomic testing demonstrated only postural tachycardia and a near-vasodepressor episode in the woman, and mild, generalized sympathetic dysfunction in the man. Treatment for presumptive migraine with aura with verapamil nearly eradicated symptoms in both patients. Discontinuation of verapamil in the woman was associated with symptom recurrence and a stroke, with significant persistent residual left hemiparesis. In conclusion, cough-induced neurologic deficits were previously reported with cystic fibrosis, without clear understanding of the mechanism of impairment of consciousness. Based on the cases presented here, we hypothesize a migrainous mechanism in both of our patients. The pathophysiology that links the hemoptysis to the spells deserves further investigation.

Another type of neurological complication resulting from pulmonary problems in people with CF.


This is the first reported use of pulse intravenous methylprednisolone in the treatment of ABPA in CF. We present the clinical course of four children with CF and severe ABPA, in whom pulse methylprednisolone was used to manage the disease because of relapses and marked side effects on high-dose oral corticosteroids. Methylprednisolone pulses achieved disease control in 3 of the 4 children. However, troublesome side effects were experienced, in some cases necessitating discontinuation of therapy. Pulse methylprednisolone may represent a treatment option for children with CF and ABPA, where ABPA fails to respond adequately to routine therapy.


A six-year-old healthy female with cystic fibrosis (CF) and pancreatic sufficiency presented with cough, weight loss, and lung function decline. Further history suggested obstructive sleep apnea, and nocturnal polysomnography (NPSG) confirmed this. Adenotonsillectomy resulted in resolution of clinical symptoms with return of normal lung function. This case establishes that obstructive sleep apnea syndrome (OSAS) may be a potential cause of lower airway inflammation and resulting weight loss in the young CF population.
It is useful to remember that increase in respiratory symptoms and signs in CF may be related to the upper respiratory tract which may be obstructed by the huge tonsils and adenoids. In such cases adenotonsillectomy may be followed by dramatic improvement even in young children not only in overnight oxygen saturations but also in weight increase and general wellbeing.