Table 1 Variation in hypoxia and hypercapnia definition used between CF centres in the UK and Australasia (16 centres were unsure of the definitions)

Hypoxia	Hypercapnia
Frequent desaturations <90%	$Petco_2$ >6.7 kPa
Baseline Sao_2 <93%	CO_2 >6.7 kPa for >25% sleep study
Spo_2 <90% for >10% sleep study	$Tcco_2$ rise to 6.7 kPa or rise by 0.9 kPa during sleep
Spo_2 <92% for >5% sleep study	CO_2 >7 kPa

CO_2, carbon dioxide; $Petco_2$, end tidal carbon dioxide pressure; Sao_2, arterial oxygen saturations; Spo_2, non-invasive oxygen saturations; $Tcco_2$, transcutaneous carbon dioxide pressure.

There are no guidelines for the assessment of gas exchange or timing and mode of NIPPV initiation in patients with CF. The British Thoracic Society guideline states 'there is insufficient evidence to recommend its routine use in patients with CF'.[5] The aim of this study was to establish current practice with regard to investigation of respiratory failure, factors leading to NIPPV initiation and extent of the use of this modality across UK and Australasian (ANZ) paediatric CF centres.

A semi-structured questionnaire consisting of 21 closed and open-ended questions was sent to the lead CF consultant and CF physiotherapists of specialist paediatric CF centres in the UK (n=27) and ANZ (n=14). The response rate was 88% (25 UK centres, 11 ANZ centres), representing a total of 5954 children. Twenty-three children (0.39%) from 13 centres were using NIPPV (11 UK and 12 ANZ). The median (range) age of NIPPV initiation was 14 (6–17) years and the median (range) usage of NIPPV per night was 8 (3–10) h. Eleven of the 36 centres (31%) reported that they have a protocol for NIPPV initiation, but it was unclear whether this was specific for CF. The preferred mode of NIPPV was bi-level NIPPV (75%), followed by single-level preset pressure ventilation (19%), volume control single-level ventilation (3%) and continuous positive airways pressure (3%). Nasal masks were the most frequently used interface (47%), followed by full face masks (38%), mouthpieces (13%) and nasal pillows (2%).

Less than half of the CF centres (17/36) undertook CF sleep studies. Spo_2 monitoring alone was most commonly used (51% of centres), followed by Spo_2 and transcutaneous carbon dioxide monitoring (22%). Full polysomography was less frequently used as a first-line investigation (16.2%). Assessment of respiratory failure differed between childhood CF centres, with different definitions for hypoxia and hypercapnia in use (table 1).

The principal reasons for initiating NIPPV included in an acute exacerbation, as a bridge to transplant and as an adjunct to physiotherapy. There were 19 reported NIPPV failures in children with CF from 10 centres. Reasons for failure included claustrophobia, inability to tolerate pressure, discomfort, poor initial set-up, parent or patient anxiety and poor adherence. Four adverse advents were reported (issues with mask fitting and pressure sores, n=2; retained secretions, n=1; and pneumothorax, n=1).

NIPPV is rarely used in UK and ANZ paediatric CF populations, probably due to improved patient outcomes and the very low prevalence of respiratory failure in childhood CF. Bi-level NIPPV is the preferred mode of ventilation. However, there is no agreed definition of hypoxia and hypercapnia, no uniformity in assessing gas exchange and no standard protocol for the indications and institution of NIPPV in children with CF. As very few of the expected benefits of NIPPV have been proven, particularly in the paediatric CF population, and as there is a high frequency of NIPPV failure, the need for future research in this area is highlighted, beginning with the need for protocols to be developed and evaluated.

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REFERENCES

1. **Fauroux B,** Le Roux E, Ravilly S, *et al*. Long-term noninvasive ventilation in patients with cystic fibrosis. *Respiration* 2008;**76**:168–74.
2. **Young A,** Wilson J, Kotsimbos T. Randomised placebo controlled trial of noninvasive ventilation for hypercapnia in cystic fibrosis. *Thorax* 2008;**63**:72–7.
3. **Fauroux B,** Boule M, Lofaso F, *et al*. Chest physiotherapy in cystic fibrosis: improved tolerance with nasal support ventilation. *Pediatrics* 1999;**103**:E32–40.
4. **Holland AE,** Denehy L, Ntoumenopoulos G, *et al*. Noninvasive ventilation assists chest physiotherapy in adults with acute exacerbations of cystic fibrosis. *Thorax* 2003;**58**:880–4.
5. **British Thoracic Society**. BTS guideline: Non-invasive ventilation in acute respiratory failure. *Thorax* 2002;**57**:192–211.

Effects of omalizumab in Aspergillus-associated airway disease

The clinical spectrum of Aspergillus-associated airway diseases (AAAD) includes Aspergillus-induced asthma, allergic bronchopulmonary aspergillosis (ABPA) and bronchocentric granulomatosis. Corticosteroids are almost always used to suppress the immunological response to the fungal antigens.[1] Although there are no evidence-based alternative treatment options besides steroids, the well-known adverse effects of these drugs have prompted clinicians to look beyond this standard practice and several cases of ABPA patients with very positive outcomes after omalizumab therapy have been recently published.[2–6]

We recruited 18 patients (13 women; mean age 49±17 years) with AAAD (2 of them had been previously diagnosed with cystic fibrosis) from 11 Spanish hospitals. All of them had been treated with omalizumab for at least 16 weeks and they were receiving inhaled corticosteroids (daily dose 1351±554 μg budesonide or its equivalent) and a long-acting β2 agonist at the moment of omalizumab initiation. Seventeen patients were being treated with oral corticosteroids at a median daily dose of 16 mg prednisone or its equivalent (IQR 6–28) and 10 with itraconazole. The mean number of albuterol puffs per day was 3.5 (range 1–8). Prior to omalizumab administration, IgE levels were (median (IQR)) 698 IU/ml (478–977) and the median absolute count of eosinophils in blood was 610 mm^3 (317–1015). Sixteen of the 18 patients had CT-diagnosed bronchiectasis and fleeting pulmonary opacities were identified in 10 of them. All patients showed a delayed positive skin test for Aspergillus and 17 also developed an immediate response. Serum Aspergillus-specific IgE was found in all patients and precipitating antibodies in serum were observed in 10.

Omalizumab-treated patients were followed up for a median of 36 weeks (IQR, 28–42). The mean dose of omalizumab per week was 608±108 mg. No significant adverse effects were observed. The treatment was discontinued in five patients due to a lack of response and in another patient because of a positive test for pregnancy. The clinical and functional effects of omalizumab are summarised in table 1.

In this series, the largest reported to date, omalizumab has demonstrated a beneficial effect in reducing symptoms and exacerbations in a group of patients with AAAD. It

Table 1 Functional and clinical outcomes following omalizumab therapy

	Pretreatment	Post-treatment	p
FEV_1 (ml)	1360 (955–2200)	1850 (1270–2290)	0.08
FEV_1 (% predicted)	66% (39–73)	74% (70–84)	0.03
Annual rate of exacerbations	1 (1–4)	0 (0–1)	0.01
Daily symptoms (≥2 times per week)	15/18 patients (83%)	8/18 patients (44%)	0.04
Nocturnal symptoms (≥2 times per week)	15/18 patients (83%)	4/18 patients (22%)	0.04
Oral corticosteroids	17/18 patients (94%)	6/18 patients (33%)	0.0005
Itraconazole	10/18 patients (55%)	3/18 patients (16%)	0.037

Results are expressed as median with range in brackets or as a percentage. The Wilcoxon test was used to evaluate any significant differences ($p<0.05$) between continuous variables and the χ^2 test was employed for comparison of categorical variables.

also seems to improve pulmonary function even when oral corticosteroids were reduced or discontinued. Given the retrospective nature of this study and the small number of cases analysed, the results must be interpreted with caution. Although all patients met the criteria of APBA proposed by Rosenberg,[7] the differentiation between this entity and Aspergillus-induced asthma is problematic, so we decided to blanket them under the term 'Aspergillus-associated airway disease'. While the pathogenesis of ABPA remains not fully understood, IgE has been advocated as a key pathogenic mechanism of the disease. Since the total serum IgE level is a marker of immunological activity in ABPA, the attenuation of the hyper-IgE response seems to be a reasonable target. Further studies are warranted to clarify the utility of omalizumab in AAAD, especially in ABPA.

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REFERENCES

1. **Agarwal R.** Allergic bronchopulmonary aspergillosis. *Chest* 2009;**135**:805–26.
2. **Lin RY,** Sethi S, Bhargave GA. Measured immunoglobulin E in allergic bronchopulmonary aspergillosis treated with omalizumab. *J Asthma* 2010;**47**:942–5.
3. **Van der Ent CK,** Hoekstra H, Rijkers GT. Successful treatment of allergic bronchopulmonary aspergillosis with recombinant anti-IgE antibody. *Thorax* 2007;**62**:276–7.
4. **Quintás Vázquez LM,** Ortiz Piquer M, Pérez de Llano LA. Effective anti-immunoglobulin-E antibody treatment of a patient with allergic bronchopulmonary aspergillosis. *Arch Bronconeumol* 2009;**45**:207.
5. **Kanu A,** Patel K. Treatment of allergic bronchopulmonary aspergillosis (ABPA) in CF with anti-IgE antibody (omalizumab). *Pediatr Pulmonol* 2008;**43**:1249–51.
6. **Zirbes JM,** Milla CE. Longitudinal assessment of lung function from infancy to childhood in patients with cystic fibrosis. *Pediatr Pulmonol* 2009;**44**:330–9.
7. **Rosenberg M,** Patterson R, Mintzer R, *et al*. Clinical and immunologic criteria for the diagnosis of allergic bronchopulmonary aspergillosis. *Ann Intern Med* 1977;**86**:405–14.

CORRESPONDENCE

ABPA in adulthood: a CFTR-related disorder

In Western countries, allergic bronchopulmonary aspergillosis (ABPA) in childhood is very unusual beyond the context of cystic fibrosis (CF). It is presumed to be different in adulthood, although three studies[1–3] reported an increased frequency of cystic fibrosis transmembrane conductance regulator (CFTR) mutations in adults with ABPA. Out of the 63 patients investigated in these studies, none was reported as pancreatic insufficient, all had sweat chloride values <60 mmol/l, only two carried the intron 8 splice variant 5T and a single patient was found to be compound heterozygous for two CFTR mutations. However, Miller *et al* studied only 10 patients and did not sequence all CFTR exons, while the two other reports, including one from our institution, were hampered by the small number of mutations initially looked for (n=13 and 16, respectively). Accordingly, current guidelines for diagnosis of CF do not list ABPA as a suggestive phenotype feature nor even explicitly as a CFTR-related disorder.[4]

We hypothesised that extending DNA analysis to the >1300 mutations currently considered as potential CF causing (http://www.genet.sickkids.on.ca/cftr/app) would provide more accurate insights on the link between ABPA and CFTR in adulthood.

The characteristics of the study group are detailed in the princeps paper.[2] DNA samples were no longer available for 3 out of the 21 original patient cohort, one of whom had

Table 1 Relevant data and genetic findings in 18 adult patients with allergic bronchopulmonary aspergillosis (ABPA)

Subject no.	Age (years)*	Gender	Sweat (Cl^-) (mmol/l)	BC	CFTR mutations	
					Princeps study[2] †	Current study
1	30	M	17	+	F508del	F508del/D1152H
6	30	M	32	+		L997F/L997F
7	74	M	34	–		G576A/D443Y–R668C
8	55	M	36	+		R1070W/3659delC
2	65	M	33	+	F508del	F508del
3	64	M	6	+	G542X	G542X
4	58	F	8	+	R117H	R117H
5	63	F	NA	+	1717-1G→A	1717-1G→A
9	59	F	14	+		R75Q
10	47	F	19	+		L967S
11	68	F	21	+		I177F
12	67	F	34	–		V1153E
13	46	F	NA	+		
14	60	F	37	+		
15	84	M	23	+		
16	79	F	40	+		
17	63	M	15	+		
18	58	M	13	–		

*In 1997.
†Investigated set of mutations: F508 del, G542X N1303K, R117H, 621+1G→T, R334W, ΔI507, W1282X, R553X, R1162X, 1717–1G→A, G551D, 3849+10kbC→T; BC: bronchiectasis (high-resolution CT scan).
CFTR, cystic fibrosis transmembrane conductance regulator; F, female; M, male; NA, declined sweat testing.