A Decade Of Non-Cystic Fibrosis Bronchiectasis 1996-2006

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Abstract
This study aimed to determine the aetiology, clinical presentation, co-morbidity, severity and the lobar distribution of non cystic fibrosis bronchiectasis (NCFB). We performed a retrospective review of clinical, radiological, immunological and microbiological data from 92 non-CF patients with a High resolution thoracic CT (HRCT) diagnosis of bronchiectasis in the three Dublin Childrenâ s referral Hospitals for the period 1996-2006. Of 92 patients (50 female), the median age at diagnosis was 6.4 years. The aetiology of bronchiectasis was as follows; idiopathic 29 (32%), post-pneumonia 16 (17%), immune deficiency 15 (16%), recurrent aspiration 15(16%), primary ciliary dyskinesia 8 (9%), chronic aspiration with immune deficiency 5 (5%), post foreign body inhalation 2 (2%), tracheomalacia 1(1%) and Obliterative bronchiolitis 1(1%). Bronchial asthma and gastroesophageal reflux disease (GORD) were concurrently present in 18 (20%) and 10 (11%) respectively. Left lower lobe was commonly involved followed next by the right middle lobe. The common isolates were Haemophilus influenza (50), Streptococcus pneumoniae (34) and Staphylococcus aureus (14), Moraxella catarrhalis (9) and Pseudomonas auerginosa (8). Surgical interventions were performed in 23 (25%) of patients, lobectomy 11(12%), pneumectomy 2 (2%), laryngeal cleft repair 4 (5%), rigid bronchoscopy for foreign body removal 2(2%), Nissanâ s fundoplication 2(2%), tracheoesophageal fistula repair 2(2%). We conclude NCFB is under-recognised in Irish children and diagnosis is often delayed and Bronchial Asthma and GORD are common co morbidity. A high index of suspicion and early HRCT can expedite the diagnosis.

Introduction
Bronchiectasis is not a diagnosis in itself but a pathological description of abnormal irreversible airway morphology. The condition is characterised by dilated airway calibre and thickened bronchial walls [1]. Bronchiectasis not caused by cystic fibrosis (NCFB) is perceived to be rare in developed countries [2]. The fall in prevalence being attributed to improved socio-economic conditions, vaccinations and ease of access to antibiotics [3]. But NCFB remains an important cause of respiratory morbidity in the developing world [4-6]. Chronic infection is thought to play a pivotal role in the development of bronchiectasis; however the condition is widely believed to complicate underlying defects of host defence or pulmonary anatomic defects.

A vicious cycle of impaired mucociliary clearance, infection and inflammation has been proposed as the most likely mechanism by which irreversible airway damage occurs [7]. Plain chest radiographs are not sensitive enough to diagnose bronchiectasis, and when compared to High resolution thoracic CT (HRCT) there is agreement in only 5% of cases in paediatric series. HRCT is considered the gold standard method for the diagnosis of NCFB. The principal characteristics of the lesion on HRCT include: a) cross sectional diameter of one or more bronchi greater than that of adjacent pulmonary artery b) mucoid impaction within a dilated bronchus c) non-tapering bronchi in cuts parallel to the direction of travel d) bronchi visible adjacent to non mediastinal pleura [8]. Nikolaizik et al estimated that 1% of referrals to a specialist paediatric respiratory clinic in London had NCFB [9]. Later on, a prospective study conducted by Eastham et al reported that 9.6% of all referrals had NCFB [10]. The epidemiology and aetiology of NCFB has not been described in Irish children. The aim of this study was to determine the clinical presentation, aetiology, co-morbidity, severity and lobar distribution of NCFB in Irish children, diagnosed using HRCT. We report the experience of NCFB in the three Dublin Childrenâ s Hospitals from 1996-2006.

Methods
The hospital in-patient enquiry system (HIPE) is a soft ware programme used in the Irish health system to record clinical data and diagnosis for all discharges from the Irish public hospital service The computerized system was used to identify children (<18 years) with chronic bronchitis, bronchiectasis and chronic suppurative lung disease in order to identify cases of NCFB in the three Dublin Childrenâ s Hospitals for the period 1996-2006. Cases were verified following chart review, exclusion of CF and radiology review of each high resolution thoracic CT. Cystic fibrosis was excluded by a negative sweat test (sweat chloride < 60 mEq/l by quantitative pilocarpine iontophoresis and/or genotype with two mutations plus clinical signs and symptoms). Specific diagnostic evaluation was determined by each individualâ s clinical presentation. However the following investigations: (sweat test, sputum microbiology, differential white cell count, immunoglobulins, complement levels and specific antibody response to pneumococcus, haemophilus and tetanus) were performed in all children while extended immunologic evaluation, genetics, Mantoux test, lower oesophageal pH probe, pulmonary function tests, barium swallow, video fluoroscopy, bronchoscopy & BAL, ciliary beat frequency under light microscopy and nasal & bronchial brushings for ciliary ultra structure under electron microscopy were performed where clinically indicated.

Results
Ninety two (50 female) confirmed cases were identified who median age at diagnosis was 6.4 years (range 1.5-13 years). Chronic wet cough, wheeze and recurring respiratory tract infection were the commonest presenting complaints. Median age at onset of symptoms was 3.9 years (range 1-12 years). An underlying aetiology was determined in 68% (63) of children and no cause was identified in 32% (29). Post - pneumonia was commonest cause n=16 (17%), followed by immune deficiency n= 15 (16%) and chronic aspiration n= 15 (16%). Primary ciliary dyskinesia accounted for 8 (9%) (Table 1).

The commonest co-morbidities were asthma, n=18 (20%) and GORD n=10 (11%). In 23 children mean FEV1 was 82% of predicted value and FVC was 84% predicted value. Fifty one (55%) children had only one lobe involved. The most frequently affected location was the left lower lobe followed by the right middle lobe (Table 2). Haemophilus influenzae was the commonest sputum pathogen (Table 3). Airway clearance was recommended for all patients. Of 92, 23 (25%) underwent surgical intervention: lobectomy (11), pneumonectomy (2), laryngeal cleft repair (4), tracheo-oesophageal fistula repair (2), rigid bronchoscopy for removal of inhaled foreign body (2), and Nissanâ s Fundoplication (2). Eighteen children with asthma were at BTS guidelines step 2 or higher. Eight patients were receiving regular immunoglobulin replacement therapy for immune deficiency states.

Discussion
Over nine patients were discharged each year with a new diagnosis of NCFB. This study reflects the collective in-patient experience of the condition in Dublinâ s three childrenâ s hospitals (DCHs) over a decade and is probably a good surrogate for the situation in the Republic of Ireland. DCHs cater for most of the countryâ s tertiary respiratory paediatric referrals and one of the centres is the designated national centre for paediatric cardiothoracic and complex malformation surgery and hence it is assumed that all cases of NCFB requiring tertiary evaluation would have been captured in this study. However, HIPE data only reflects discharges and by definition the method would miss patients diagnosed as outpatients and those older children and adolescents in the care of chest physicians cared for in adult hospitals. Given these limitations, it would not valid to make any inferences regarding incidence & prevalence. Persisting high rates of childhood NCFB have been reported in Pacific Islands and Native Alaskans. Australian Aborigines living in remote locations have rates as high as 14.7 per 1000 children [11]. A prospective study in New Zealand reported an incidence of 3.7 per 100, 000 population aged under 15 years per year, which the authors concluded " too high" for a developed country [11]. In contrast, Finland has incidence of 0.5 per 100,000 children, which is relatively low [12].

Our findings in terms of aetiology, lobar distribution and sputum pathogens are similar to other studies [10,11]. Approximately one third of cases will have no specific underlying diagnosis [10,11]. In the future, it can be anticipated that the diagnostic yield will improve as our knowledge of immune dysfunction expands and better methods for diagnosing primary ciliary dyskinesia (PCD) and pulmonary aspiration emerge. The

diagnosis of PCD remains challenging and undoubtedly the condition remains under diagnosed. The estimated incidence of this autosomal recessive disorder is 1 in 15-20000 live births [13-15]. Early diagnosis and the institution of airway clearance and other specific therapies, where appropriate will preserve lung function and lead to less pulmonary morbidity in adulthood [16,17]. In the current series symptoms were present for almost three years before the diagnosis was made. The presence of wheeze may be incorrectly attributed to diagnosis of asthma thus leading to further delays in diagnosis. The matter is further complicated by the co-existence of asthma in 20% of the series, which is consistent with other reports [10,18]. Early diagnosis may lead to fewer lung resections and permanent loss of lung function. Milder forms of NCFB may resolve in younger children with appropriate conservative management.Our experience suggests that NCFB remains a significant problem in Irish children despite improvements in the countryâ s socio-economic status.

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Addendum

Bronchiectasis in Children

Bronchiectasis not caused by cystic fibrosis (NCFB) is considered an orphan disease. First described by Laennec in 1819, it is not a diagnosis in itself, but rather a description of abnormal airway morphology. The lesion occurs as the result of chronic infection in the context of impaired host defence or structural/ functional airway abnormality e.g. immunodeficiency, ciliary dyskinesia, chronic aspiration or tracheo-bronchmalacia, although one third of cases are idiopathic [1]. It is postulated that a vicious cycle of infection, inflammation and impaired muco-ciliary clearance leads to irreversible airway and parenchymal destruction. Most adult NCFB originates in childhood. It is estimated that 110,000 individuals are being treated for the condition in the USA [2]. The development of irreversible NCFB worsens the prognosis of the generating condition. NCFB in children remains a major problem in developing countries. However, In Ireland as living standards have improved its occurrence has undoubtedly reduced. However, there are no published comparative epidemiologic data.

The diagnosis may be difficult and is often delayed. Common to many studies of childhood bronchiectasis is the delay in diagnosis and the confusion of symptoms with those of asthma. A chronic wet cough or recurrent wet cough are prominent symptoms and should not be ignored. A poor response to asthma therapy should also prompt a clinician to consider referral to a respiratory paediatrician [3]. Plain chest X-rays may appear normal or show bronchial prominence only. Improved imaging with High-resolution CT has greatly facilitated the diagnosis of NCFB and it is now the gold standard diagnostic test. Using low radiation protocols on newer generation multi-slice scanners, the dose for a HRCT is only marginally more than a single CXR.

Despite advances in socio-economic conditions over the last 3-4 decades respiratory paediatricians continue to diagnose bronchiectasis with regularity. Almost 10% of all respiratory referrals to a specialist clinic in Newcastle, UK have been subsequently diagnosed with the condition [4]. In this issue, we report a retrospective review of the condition in the three Dublin childrenâ s hospitals over the last decade. More than 9 new cases were identified each year. The aetiology of NCFB in 92 cases was similar to other published series1,4. In a prospective evaluation of the prevalence of NCFB [5], we asked all the paediatricians in the Republic of Ireland to notify all cases of NCFB diagnosed on HRCT. Using data obtained from the Irish Paediatric Surveillance Card, we estimated that in 2006 the prevalence was 2.3 per 100,000. This compares with reported prevalences of 3.5 per 100,000 in New Zealand and 0.5 per 100,000 in Finland [6,7]. We feel our estimate is still too high for a developed country.

It is postulated that the initial lesion involves a chronic endobronchial infection that in turn leads to a reversible stage of bronchiectasis with thickening of the bronchial wall with mild dilatation. Greater degrees of airway and parenchymal damage lead to irreversible cystic change. Early recognition of the problem is vital because of the potential for the lesion in the transitional stage to regress. The lesion may respond to optimization of treatment of the generating condition, airway clearance and prompt treatment of acute respiratory infection with antibiotics.

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Comments:
