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ARTICLE

Demographics of the UK cystic fibrosis population: implications for neonatal screening

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The objective was to determine the composition of the Cystic Fibrosis (CF) Population attending specialist UK CF centres in terms of age, gender, age at diagnosis, genotype and ethnicity. With the planned introduction of the national CF screening programme in the UK, cystic fibrosis transmembrane regulator (CFTR) mutations were compared between different ethnic groups enabling a UK-specific frequency of mutations to be defined. Data were analysed from the patient biographies held in the UK CF Database (see www.cystic-fibrosis.org.uk). The currently registered population of 5274 CF patients is 96.3% Caucasian with a male preponderance that significantly increases with age. The majority of the 196 non-Caucasian CF patients are from the Indian Subcontinent (ISC), of which one in 84 UK CF patients are of Pakistani origin. The commonest CFTR mutation, ΔF508, is found in 74.1% of all CF chromosomes. In the Caucasian CF population, 57.5% are ΔF508 homozygotes but the UK ISC CF population with only 24.7%, has significantly fewer ΔF508 homozygotes patients (95% confidence interval (CI) 0.2–0.4). The distribution of Caucasian patients with ΔF508/ΔF508, ΔF508/Other and Other/Other does not fit the expected distribution with a Hardy–Weinberg model unless those patients without a detected mutation are excluded ($P<0.001$). The UK CF Database has shown the UK CF population to have distinct characteristics separate from the North American and European CF Registries. The ISC group contains many mutations not recognised by current genetic analysis, and one in four ISC patients have no CFTR mutations identified. The CFTR analysis proposed for the screening programme would detect 96% of patients registered in the database, but is unlikely to achieve the desired >80% detection rates in the ethnic minority groups. Screen-positive, non-Caucasian infants without an identifiable CFTR mutation should be referred for a sweat test and genetic counselling when serum trypsinogen concentrations remain elevated after birth.
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Introduction

Cystic Fibrosis (CF) remains the commonest life-limiting autosomal recessive condition to affect the Caucasian UK population with a median age of death in the second decade for those born in the 1980s. There have been around 1000 individual CFTR mutations categorised since the landmark identification of the CFTR gene in 1989.[1] The application of new anti-microbial therapies and nutritional knowledge have seen the outlook for CF patients born today improve such that survival into the fourth and fifth decades is possible with specialist care. It is presently unknown whether survival will improve further with the introduction of neonatal screening for cystic fibrosis in Scotland in 2002/3, because the impact of the CFTR mutation on the subsequent pattern and severity of symptoms experienced by the patient remains controversial. With respect to neonatal screening, Farrell's Wisconsin cohort has shown some patient benefits of screening through long-term surveillance[2] but the controversy will only be settled by long-term analysis of trends using CF

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Table 1 Mode of presentation of the UK CF patients

Mode of presentation	*Percentage of total patient population* (%) (n=*5274*)	*Percentage of caucasian patient population* (%) (n=*5078*)	*Percentage of ISC patient population* (%) (n=*88*)
Failure to thrive/malnutrition	35.8	35.4	38.6
Lower respiratory tract infection	34.6	34.4	39.8
Steatorrhoea	29.0	28.9	28.4
Meconium ileus+/−distal intestinal obstruction syndrome	13.2	13.2	14.8
Screening	11.7	11.7	4.5
Family history	11.1	11.3	12.5
Other reason	4.4	4.4	3.4
Rectal prolapse	3.7	3.7	1.1
Unknown reason	2.7	2.8	2.3
Electrolyte imbalance	1.6	1.5	0
Sinus disease/polyps	0.7	0.6	1.1
Prolonged jaundice	0.5	0.5	2.3
Infertility	0.5	0.5	0

Table 2 Age at diagnosis of the UK CF patients

Age at diagnosis (years)	*Percentage of UK CF population* (%) (n=*5274*)	*Percentage of Caucasian UK CF population* (%) (n=*5078*)	*Percentage of UK CF patients from the ISC* (%) (n=*88*)
0–<1	63.1	63.0	71.6
1–<4	23.5	21.7	15.9
4–<7	5.6	5.8	3.4
7–<10	2.1	2.0	1.1
10–<40	5.4	5.4	8.0
40–<70	0.2	0.3	0.0
Unknown	1.8	1.9	0.0

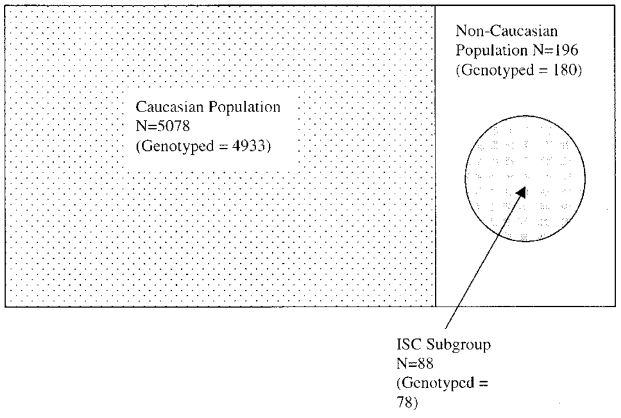

Figure 1 UK CF population subgroups. The registered UK population divided into the Caucasian and non-Caucasian Groups, including those patients who have been genotyped. The ISC Group are shown as a subgroup within the non-Caucasian Group, although the diagram is not to scale.

Registries. The UK CF Database contains such a registry within one of its modules and aims to analyse the clinical details of every cystic fibrosis patient in the United Kingdom who attends a specialist CF centre. This article presents the demographics of the currently registered UK CF population focusing on the gender, ethnicity, mode of presentation and genotypes of the 5274 patients from an estimated UK population of approximately 7500 patients.[3] The considerable impact of ethnicity on CFTR mutations in the UK is shown.

Methods

The UK CF Database was established at the Tayside Institute of Child Health, University of Dundee, Scotland in 1995. The patient's age, gender, parental ethnicity, genotype, and method of diagnosis were included in the Patient Biographies and entered into the database from 56 paediatric and adult CF clinics, and validated through the system of double data entry, range checking and error correction. Full details of all procedures are available at www.cystic-fibrosis.org.uk. We divided the UK CF population into two groups (Figure 1): the Caucasian Group and the non-Caucasian Group. Within the non-Caucasian Group, we created a subgroup called the ISC Group consisting of all Pakistani, Indian, Bangladeshi and Asian Other patients.

Data was analysed using Microsoft Access 97 software and included all patients registered by May 2001. Statistical

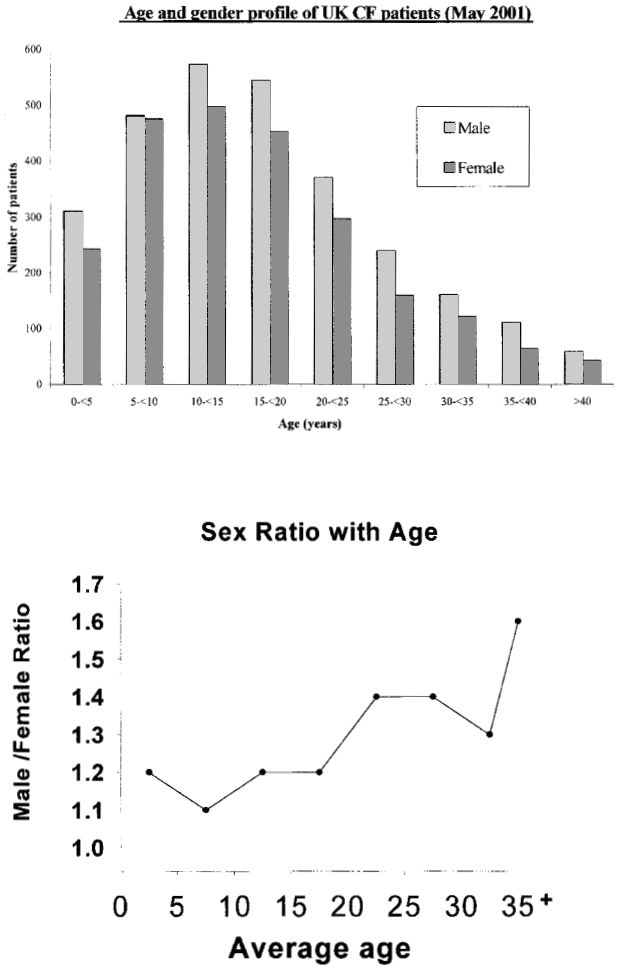

Figure 2 (**a**) Age and gender profile of UK CF patients; (**b**) Sex ratio by age. (**a**) The reduced number of patients in the 0– <5 age group occurs because not all of them have presented. (**b**) Exhibits the increasing male/female ratio with age.

analysis is shown with 95% confidence intervals for the difference between two population proportions.

Results

There were a total of 5274 patients entered into the UK CF database. The gender split in the UK CF population is 2881 male (54.6%) and 2393 female (45.4%) with a male/female ratio that increases with age (Figure 2a,b). It can be seen that 49.1% of the entire population is under 15 years of age, 40.0% lies between 15 and 30 years, and only 11.0% of the population are still alive over the age of 30 years. There were 5078 patients in the Caucasian Group (96.3%) and 196 in the non-Caucasian Group. This second group contains a subset of 88 patients forming the ISC group (63 Pakistani, 12 Indian, seven Bangladeshi and six Asian Other patients), the remainder comprising six Black Caribbean, three Black African and 99 others of mixed parentage. Therefore, one in every 27 UK CF patients has some non-Caucasian origin, with those of purely Pakistani origin accounting for one in 84 UK CF patients.

The main presenting features that lead a clinician to consider a diagnosis of cystic fibrosis are failure to thrive, lower respiratory tract infections, steatorrhoea, meconium ileus, distal intestinal obstruction syndrome, family history, rectal prolapse, the presence of nasal polyps, electrolyte imbalance, prolonged jaundice or infertility (Table 1). The Caucasian and ISC subgroups both demonstrated similar patterns of presentation. Neonatal screening accounted for 11.7% of all diagnoses.

The median age of diagnosis was 4 months (range 0 months to 61 years 8 months). A diagnosis of CF occurred in 86.7% of all patients before their fourth birthday, and 63.1% were diagnosed before their first birthday. Diagnosis of cystic fibrosis beyond the age of 10 years was seen in 5.7% of all patients. To assess whether ethnic origin had any effect on age at presentation, Caucasian and ISC patterns of presentation were compared (Table 2). For Caucasian CF patients (n=5078), 63.0% were diagnosed before their first birthday, 84.7% before their fourth birthday, and 5.6% beyond their 10th birthday. In the ISC subgroup (n=88), 71.6% of patients were diagnosed before their first birthday, 87.5% before their fourth birthday and 8.0% were diagnosed over the age of 10. There was no significant difference in the proportions of those diagnosed before 1 year of age in the Caucasian and ISC populations (95% Confidence Limits −0.02 and +0.19). UK CF patients of Black African or Black Caribbean origins (n=9) had a diagnosis rate of 77.8% before the age of four, and 22.2% over the age of 10, but the numbers were too small to undertake statistical analysis.

Genotype data was available on 4933 patients that permitted further comparison of Caucasian and ISC patients to test the hypothesis that the genotypes were similar (Table 3). Patients with two chromosomes containing the ΔF508 mutation account for 57.5% of the genotyped UK CF Caucasian population (n=4753) but only 24.7% of the genotyped UK ISC CF patients (n=78) (95% CI 0.2–0.4 in the difference between the proportions). In contrast, there are no F508 homozygotes in the Black African or Black Caribbean groups. Further differences are revealed in the ISC group with 4.7% showing ΔF508 heterozygous status where the other CFTR mutation is either a known disease-associated allele or as yet uncharacterised. Importantly, patients with two known CFTR mutations, neither of which are ΔF508 make up 35.3% in the ISC population, many of these being family specific mutations. Thus at 27.1% of the ISC patients, a much larger proportion has no identifiable CFTR mutation compared to the Caucasian patient population.

The Caucasian population contains 4753 patients who have had their genotype tested (319 patients have not been tested, and six refused). The proportions of Caucasian

Table 3 Genotypes of the UK CF Caucasian and ISC populations

Genotype	*Percentage of genotyped UK CF Caucasian population* n=*4753* (%)	*Percentage of genotyped UK CF ISC population* n=*78* (%)
ΔF508/ΔF508	57.5	24.7
ΔF508/Unknown	11.5	3.5
ΔF508/G551D	5.1	0.0
ΔF508/G542X	2.8	0.0
Unknown/Unknown	2.7	27.1
ΔF508/621+1G→T	2.0	1.2
ΔF508/R117H	2.0	0.0
ΔF508/1898+1G→A	1.0	0.0
ΔF508/1717-G→A	0.9	0.0
ΔF508/N1303K	0.8	0.0
ΔF508 ΔI507	0.8	0.0
ΔF508/R553X	0.6	0.0
ΔF508/R560T	0.6	0.0
ΔF508/Q493X	0.5	0.0
G551D/Unknown	0.4	0.0
Other/Other	2.8	15.3*
ΔF508/Other	6.7	0.0
Y569D/Y569D	0.0	8.2
L218X/L218X	0.0	3.5
1161delC/1161delC	0.0	3.5
R709X/V456A	0.0	2.4
G542X/G542X	0.4	2.4
Other/Unknown	1.0	3.5

The shaded areas represent the commonest genotypes in the ISC population. *Includes 1525-1G→T/1525-1G→T, Y569C/Y569D, G551D/G551D, 1525-1G→A/1525-1G→A, R1162X/R1162X, R01/07/R01/07, 2184insA/2184insA, Y568D/Y568D, 1VSB1-1/1VSB1-1, 1506M/1506M, 3849+10kbC→T/3849+10kbC→T and Q98X/Q98X.

patients with ΔF508/ΔF508, ΔF508/Other and Other/Other (where Other is either a known or an unknown non-ΔF508 mutation) were compared with expected values to see if the distribution fitted a Hardy–Weinberg model. From our data the maximum likelihood estimate of P is 0.751 (the proportion of ΔF508 in the population). Using our estimate of P to fit a Hardy–Weinberg model, we find that the observed number of ΔF508/ΔF508 and Other/Other is greater than expected. Wahlund's effect (http://darwin.eeb.uconn.edu/eeb348/lecture-notes/wahlund/wahlund.html) may partly explain the excess of ΔF508/ΔF508, but this influence would also affect the other groups. However, when we exclude those patients without easily detectable CFTR mutations (n=124), the data satisfies Hardy–Weinberg equilibrium using a χ^2 goodness-of-fit test (Observed : Expected ΔF508/ΔF508 2734 : 2755, ΔF508/Other 1674 : 1632 and Other/Other 221 : 242).

A total of 4933 patients have had their genotype tested, and Table 4 shows the gene frequency of different CFTR mutations amongst these 9866 chromosomes. We conducted a virtual study noting that the proposed Scottish screening programme includes a panel of 31 CFTR mutations (David Aitken, Guthrie Institute, Glasgow personal communication). These 31 mutations were compared with a 'virtual DNA kit' constructed from the 27 mutations shown in Table 4, composed of the 20 commonest mutations in the Caucasian Group and seven of the commonest mutations in the non-Caucasian Group. Amongst the different ethnic groups, Table 5 shows a comparison between the detection rates of at least one CFTR mutation using the 27-kit, the 31-kit and a virtual amalgam of 38 mutations (the 31-kit plus the additional seven non-Caucasian mutations used in the 27 kit). Overall, all the kits will detect 96% of all patients with at least one CFTR mutation, and 97% of pure Caucasians. Only those of purely Indian origin approach the >80% ideal threshold for a screening programme (detection rate 75%). Irrespective of the kit used, a detection rate of >87% will always occur in the mixed group and the screening programme will prove increasingly successful as the offspring of mixed relationships increase. Our data also shows that the 38-mutation kit performs no better than our proposed 27 kit for ethnic minorities. Irrespective of the final decision on the UK panel of mutations to be included, the index of clinical suspicion should remain high in the ISC, Black African or Black Caribbean patients who have no Caucasian parentage. Achieving a >80% detection rate for the UK patients in these ethnic groups is unlikely to be economically feasible due to the many individual/family specific mutations that would need to be included.

The regional distribution of CF patients, divided into three categories (ΔF508/ΔF508, ΔF508/Other and Other/Other) is shown in Table 6. The much greater proportion of Other/Other CF patients in Northern Ireland (and the corresponding drop in ΔF508/ΔF508) was statistically significant compared to every other region in the UK ($P<0.05$).

Discussion

The UK CF database has registered 5274 patients and characterises the majority of the CF specialist clinic population for the start of the new millennium. We have shown that the non-Caucasian CF population makes up 3.6% of the UK CF population and their range of CFTR mutations are markedly different to the Caucasian patients although they were diagnosed at similar ages and with similar symptoms.

Screening in the UK

Some of the best evidence for supporting a neonatal screening programme is based on Farrell's evidence for nutritional benefits.[2] The Cochrane review[4] found a second randomised controlled trial from the UK[5] that did not show a benefit to early diagnosis but is of interest that in the latter study, patients screened for CF were not all referred to a specialist centre for their care. Thus the criterion that appropriate treatment facilities should be in place post-screening was not met in this study.

Screening in Scotland is scheduled to commence in 2002/3. It is envisaged that the proposed screening programme will be based on a three-stage protocol.[6] In

Table 4 The commonest CFTR mutations in the UK

CFTR mutation	*Genotypes UK CF population (n=9866 chromosomes) gene frequency per 1000 genes*	*Genotyped UK Caucasian CF population (n=9506 chromosomes) gene frequency per 1000 genes*	*Genotyped UK CF ISC population (n=156 chromosomes) gene frequency per 1000 genes*
ΔF508	741.0	752.0	294.9
G551D	33.7	34.3	12.8
G542X	18.5	18.4	25.6
R117H	12.5	12.7	0.0
621+1G→T	12.7	12.7	6.4
1717-1G→A	5.8	5.8	0.0
1898+1G→A	5.7	5.9	0.0
N1303K	5.6	5.4	0.0
ΔI507	4.8	5.0	0.0
R560T	4.2	4.3	0.0
R553X	3.3	3.4	0.0
1154insTC	3.2	3.3	0.0
Q493X	2.8	2.9	0.0
3659delC	2.8	2.9	0.0
E60X	2.4	2.4	0.0
W1282X	2.7	2.7	0.0
P67L	2.1	2.1	0.0
G85E	2.1	2.0	0.0
V520F	1.6	1.7	0.0
1078delT	1.3	1.4	0.0
Y569D	1.5	0.0	96.2
L218X	0.6	0.0	38.5
1161delC	0.7	0.1	38.5
R1162X	0.9	0.6	19.2
R709X	0.4	0.2	12.8
3849+10kbC→T	1.2	0.8	19.2
S549R*	0.6	0.0	0.0

*S549R mutations appear in the non-Caucasian but not the ISC subgroup.

Table 5 CFTR detection rates in different ethnic groups

	Percentage with at least one of the 27 mutations	*Percentage with at least one of the 31 mutations*	*Percentage with at least one of the 38 mutations*
Total number of patients tested *n*=4933	96.4 (4755/4933)	95.8 (4724/4933)	96.3 (4749/4933)
Caucasian patients *n*=4753	97.2 (4620/4753)	96.9 (4606/4753)	97.1 (4614/4753)
Non-Caucasian patients *n*=180	75.0 (135/180)	65.6 (118/180)	75.0 (135/180)
ISC patients *n*=76	61.8 (47/76)	40.8 (31/76)	61.8 (47/76)
Pakistani patients *n*=52	61.5 (32/52)	38.5 (20/52)	61.5 (32/52)
Indian patients *n*=12	75.0 (9/12)	58.3 (7/12)	75.0 (9/12)
Bangladeshi patients *n*=6	50.0 (3/6)	16.7 (1/6)	50.0 (3/6)
Asian other patients *n*=6	50.0 (3/6)	50.0 (3/6)	50.0 (3/6)
Black African patients *n*=3	33.3 (1/3)	33.3 (1/3)	33.3 (1/3)
Black Caribbean patients *n*=6	50.0 (3/6)	50.0 (3/6)	50.0 (3/6)
Mixed origin *n*=95	88.4 (84/95)	87.4 (83/95)	88.4 (84/95)

Only those patients who have had genotype analysis are included; 335 patients had not had their genotype tested and six patients refused genotyping. Twenty of the CFTR mutations in the 31 panel also appear in the 27 mutations listed in Table 4. The additional eleven are S549N, 3849+4A→G, 3905insT, 2789+5G→A, Y122X, 711+1G→T, R347P, R347H, R334W, A455E and 3281AA→G. The following seven mutations appear in Table 4 but not in the 31 mutation panel; 1154insTC, E60X, P67L, Y569D, L218X, 1161delC and R709X.

Table 6 Regional distribution of genotypes: percentage of each region's CF population

	Scotland n=*697*	*Northern Ireland* n=*320*	*Wales* n=*143*	*Northern England* n=*1411*	*Southern England* n=*2366*
ΔF508/ΔF508	51.9%	39.4%	45.5%	51.4%	63.9%
ΔF508/Other**	40.3%	38.1%	44.8%	41.0%	29.1%
Other/Other**	7.7%	22.5%	9.8%	7.7%	6.9%

**=Non-ΔF508 CF causing mutations.

the first stage, a confirmed raised immunoreactive trypsinogen (IRT) level on a day 4–6 blood spot sample would be followed by a second stage DNA analysis for CFTR mutations from the same blood spot card. Individuals with two CFTR mutations will be referred with a definite diagnosis of CF. Infants with only one CFTR mutation, or those with a very high IRT and of non-Caucasian origin who have no identified CFTR mutation, would undergo a third stage repeat blood spot for IRT on day 27 of life. If the latter IRT is also raised, the infant has a high probability of CF and will be referred for sweat testing and genetic counselling. If not, the infant has a low probability of CF and the family will be offered genetic counselling alone. With current knowledge, CFTR mutation analysis cannot provide the full answer for all, but selective application of an IRT–IRT strategy is the only way of providing reasonable sensitivity, especially when screening non-Caucasian babies.

CFTR mutations in Caucasians

Large-scale CF studies have revealed common genotypes more prevalent in certain populations. Schwarz *et al* studied the distribution and frequency of Caucasian UK CFTR mutations in 1995[7] and listed 20 of the commonest mutations. Nineteen of these mutations feature in the commonest UK Caucasian 20 mutations listed in Table 4. Our data confirms the proportion of ΔF508 in the Caucasian population at 75.2%, comparable to the Schwarz value of 75.3%. There are similar frequencies for the more common mutations between our UK Caucasian CF data (Table 4) and the Schwarz data (respectively, G551D 3.43% and 3.08%; G542X 1.84% and 1.68%; 621+1G→A 1.27% and 0.93%; 1717-1G→A 0.58% and 0.57%). In North America, ΔF508 accounts for 71.2%, with G542X (2.4%), G551D (2.4%), W1282X (1.4%), N1303K (1.3%) and R553X (0.9%).[8]

Genotype frequencies in CF have previously been shown to fit a Hardy–Weinberg model in a smaller regional UK study.[9] In the current study, we find that the genotype frequencies only satisfy the Hardy-Weinberg equilibrium provided we exclude those without an identified CFTR mutation in the Other/Other category. This suggests that defects in non-CFTR genes may contribute to the CF phenotype. Our pragmatic exclusion of all patients with untyped mutations in CFTR from the Other/Other group will of necessity exclude some patients with very rare mutations that are not picked up by routine genetic tests (20 kit, 31 kit etc). This might explain why the new observed values now fall below the expected values in the Other/Other category.

When compared with a European CFTR geographic distribution,[10] the UK CF patients possess a greater proportion of ΔF508, G551D and 621+1G→T mutations, and a smaller proportion of G542X, N1303K, W1282X and R1162X mutations. In France, the five most common genotypes were ΔF508/ΔF508 (47.8%), ΔF508 /G542X (3.4%), ΔF508/N1303K (2.7%), ΔF508 /1717-1G→A (2.1%) and ΔF508/2789+5G→A (1.5%) (Desgeorges M, personal communication) which is different to the commonest genotypes found in the UK population (Table 3). N1303K and G542X occur at a frequency of around 5% in Italy.[11] In Germany, a study of 658 CF families revealed mutation frequencies of R553X (1.8%), N1303K (1.3%), G542X (1.1%), G551D (0.8%) and R347P (0.8%).[12] The frequency of CFTR mutations recorded for just over 1000 patients for the Irish CF Database include G551D in 7%, R117H in 2% and ΔF508 in 72% of patients.[13] In the white South African population, a paper based on 192 patients found that ΔF508 accounts for 76% of the mutations with 3272-26A→G (4%), 394delTT (3.6%) and G542X (1.3%) the other most common mutations.[14] It is suggested that the 3272-26A→G and 394delTT mutations are more common due to a founder effect in white South Africans of European descent. Northern Ireland has a much greater proportion of Other/Other CF patients (where neither mutation is ΔF508) and although there is a higher incidence of CF in Northern Ireland (one in 1850), the population frequency of ΔF508 is similar to other regions of the UK.[7]

CFTR mutations in the Non-Caucasian population

Cystic Fibrosis is being increasingly diagnosed in the non-Caucasian populations, and the range of presenting features is similar between Caucasian and ISC groups (Table 1). The genotypes of non-Caucasian patients often contain individual or family specific mutations along with mutations more commonly found in Caucasians due to admixture of the populations. A recent paper by Malone *et al*,[15] detected five novel CFTR mutations in 26 Pakistani patients and three of these mutations are reported in our 63 Pakistani patients. Malone's subgroup analysis of 14 Pakistani patients showed 32% of chromosomes had the ΔF508 mutation, similar to the 29% in our Pakistani patient data. In a small study of UK Asian CF patients,[16] Bowler *et al* reported that these patients appeared to have a poorer respiratory and nutritional status compared to age matched controls, and noted that only 44% (four out of nine) patients had the ΔF508 mutation. In Spencer's study of ethnic minority children in the West Midlands[17], 31% (4/13) of patients from the ISC had the ΔF508 mutation, but no other mutations were found. This study also found no overall delay in

diagnosis between the white European CF patients and the CF patients from ethnic minorities. Our data confirms this finding that there is no delay in diagnosis between the Caucasian and non-Caucasian groups. ΔF508 carrier status has been estimated at one in 238 women from North India (Kapoor V, personal communication), giving an estimated frequency of the homozygote at one in 228 000. In a later study of 13 Indian CF children, Kapoor found the ΔF508 mutation in 53.8% of chromosomes.[18] Our study represents the largest reported group of UK CF patients from the ISC and finds that one in four has no CFTR mutation identified. The relative infrequency of the most common CFTR mutations in the ISC patients has implications for the national CF screening programme. Screening for the commonest mutations will detect smaller proportions of non-Caucasian CF individuals than their Caucasian counterparts. Our 27-mutation virtual kit of mutations is particularly suited to detect mutations in the non-Caucasian as well as the Caucasian population, compared to the proposed 31-mutation kit or a combined kit of 38 mutations.

Differences in presentation between UK and North America

In common with CF populations studied in North America, Canada, Europe and Australasia, there is a male preponderance,[19–21] and half of the patients remain in the paediatric age group. The over 30s represent only one in 10 patients. Comparison of the mode of presentation between the UK CF Database (Table 1) and the North American CF Patient Registry[8] reveals (respectively) differences in the rates of lower respiratory tract infection (34.6% and 51.7%), failure to thrive/malnutrition (35.8% and 43.4%), steatorrhoea (29.0% and 35.3%), meconium ileus (13.2% and 20.8%) and screening (11.7% and 3.5%). It is noteworthy that the UK rate for presentation with meconium ileus (13.2%) is very similar to the Canadian data (13.4%).[21] In the UK, there were 63% patients diagnosed by 1 year of age (Table 2) compared to 70% in North America[8] and 56.4% from the Canadian Patient Data Registry.[22] In the UK CF Database, neonatal screening accounts for around one in 10 CF patients and the overall median age of diagnosis is 4 months, whilst in populations without screening, the mean age of CF diagnosis is reported at 5.7 months[23] and 11.7 months.[5]

Summary

The UK CF Database provides a framework for analysing the changing demographics of the CF population in the UK. The population is 96.4% Caucasian with a slight male preponderance. The commonest CFTR mutation, ΔF508, is found in 74.1% of CF patients' chromosomes, and ΔF508 homozygotes make up 57.5% of the Caucasian CF population. Detection of 96% of patients registered in the database is possible with the CFTR analysis proposed for the screening programme, but is unlikely to achieve the desired >80% detection rates in the ethnic minority groups. The National Screening programme for CF must take account of the different range of CFTR mutations in the non-Caucasian CF population, so that screening also benefits patients from ethnic minorities.

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