419* Criteria for diagnosis of CF in the French Registry

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CF postnatal diagnosis is not always straightforward and this directly influences inclusion of patients in registries. Newborn screening programs allow very early diagnosis, often at a presymptomatic stage, increasing the number of equivocal diagnosis.

Aim: To evaluate diagnosis circumstances of patients enrolled in the French CF Registry database according to the recent CFF consensus recommendations (Farrell et al, 2008).

Methods: The French CF Registry has been collecting data since 1992. Diagnosis data at inclusion are sweat test (ST), CFTR mutations and symptoms.

Results: In 2006, 4994 patients were enrolled in the registry, 4886 were included in the analysis (exclusion of prenatal diagnosis). CF diagnosis was unquestionable in 4126 (84%) patients [abnormal ST (60%) and/or 2 CF-causing mutations (64%), clinical symptoms (72%)].

For the remaining 760 patients with 1 or 0 identified CF causing mutation, ST was intermediate, normal, unclassified or missing. At the time of enrolment, 68% had clinical symptoms suggestive of CF (table). Expanded genetic testing identified mutations in 527 patients (1 mutation, n = 461, 2 mutations, n = 66) but classification of these patients remains uncertain.

Conclusion: According to the recent CFF consensus recommendations, 84% of the French Registry's patients met the criteria for CF. Further analysis, in collaboration with the CF centres and the French Association of Neonatal Screening (AFDPHE), is under way to take into account enlarged data (pancreatic status, sputum culture) during follow-up monitoring to improve the patients' classification.

Symptoms	ST				
	Intermediate	Normal	Unclassified[a]	Missing data	Total
Yes	21	28	149	342	540
No	25	21	58	116	220
Total	46	49	207	458	760

[a] Due to lack of technique reference.

420* Extensive carrier testing and CF birth prevalence: evidence for a negative correlation

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Aim of the study was to evaluate if extensive CF carrier testing may be connected with the progressive decrease of CF birth incidence recorded in North Eastern Italy. From 1993 to 2007 an average 52,000 newborns per year underwent Neonatal Screening (NS), and 198 newborns with CF were detected (1/3937). A time related contraction in birth prevalence was confirmed, with an average annual percent decrease of 0.15 per 10,000 neonates (Poisson regression analysis p 0.003). In the NS area two sections were identified: the Western Region (WR), where CF carrier testing is not offered to couples from the general population, and the Eastern Region (ER), where CF carrier testing is widely offered to couples from the general population. In ER from 1995 to 2007 such testing practice has been steadily expanding, with a total of 87,721 CF carrier tests performed, 3460 carriers identified, and 238 carrier couples detected (data collection in progress). The prevalence of CF decreased by time ($p < 0.001$) but the rate of decrease was more enhanced in ER as suggested by the existence of a statistically significant ($p = 0.014$) interaction term between time and region in the Poisson regression model. The overall negative trend in North Eastern Italy is due to a contraction of CF births in its Eastern part. In ER a negative correlation was found between CF incidence and the number of carrier tests (p 0.012). Prenatal diagnosis data collection is in progress. These data support the hypothesis that carrier screening may modify the incidence of CF.

421 Rectal prolapse in CF: a population study

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Rectal Prolapse (RP) has long been recognised as a presenting feature of CF. Older literature suggested that it may have been caused by malnutrition and chronic diarrhoea. We investigated whether this relationship exists in a contemporary CF population, and whether any other features of CF are associated with RP at presentation.

The South and West CF Database currently registers all 1268 CF patients from 1995 to 2007 from a defined geographical area of England. For 1040 patients, data on presenting features and annual review findings have been contributed by their clinician. These data precede the adoption of universal neonatal screening.

65 (6.3%) presented with RP. The prevalences of other presenting features in those with RP were compared with the CF database population (n = 1040): steatorrhoea 28 (43%) vs. 273 (26%); failure to thrive 16 (25%) vs. 443 (43%); respiratory 12 (18%) vs. 441 (42%).

In 24 (37%) RP was the only presenting feature. All RP cases were pancreatic insufficient. For each RP case 2 age- and sex-matched controls whose CF presented with other symptoms were selected. There were no significant differences between cases and controls for: height, weight, % expected FEV1 (assessed at ages 6+, 10+ and 15+ years), prevalence of Delta-F 508 homozygosity. Cases acquired pseudomonas for the first time at an older age than controls (medians 6.5 vs. 2.5 years, $p = 0.021$). 12 cases and 23 controls died (n.s.).

We conclude that:

1. RP may be a presenting feature of CF in the absence of any other symptoms
2. RP is not associated with excessively poor nutrition and growth either at presentation or subsequently
3. RP is not apparently associated with more severe respiratory illness and may be associated with delayed acquisition of pseudomonas.

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422 The CFTRdele2,3 (21 kb) mutation is present in cystic fibrosis patients from Eastern Hungary

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Cystic fibrosis (CF) is the most common severe inherited monogenic disease in Caucasians. In addition of the most frequent deltaF508 mutation which is responsible for the 50–65% of the cases, more than 1300 different rare mutations are present in the CFTR gene.

The goal of this study was to determine whether a specific mutation with Slavic origin, namely CFTRdele2,3 (21 kb) is present among Eastern Hungarian CF patients.

For the mutation analysis, 43 patients with severe CF phenotype were selected and tested for the presence of the CFTRdele2,3 (21 kb) mutation using deletion specific primers. The deletion point was analyzed by DNA sequencing. The parents were also tested in the affected families. 4 patients of the 43 carried the CFTRdele2,3 (21 kb) mutation, all in heterozygous form and all together with deltaF508. In every analyzed families, the CFTRdele2,3 (21 kb) segregated trans with the deltaF508 mutation being all patients compound heterozygous for the two abovementioned mutations.

The CFTRdele2,3 (21 kb) mutation with Slavic origin is present in the Hungarian CF patients. Its combination with the deltaF508 is more frequent than any other previously tested mutation. Based on our data, it is recommended to include the CFTRdele2,3 (21 kb) mutation analysis in the Hungarian CF mutation testing panel.