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370* Increasing incidence of cystic fibrosis being diagnosed in adulthood over time: an analysis of two decades of care

M. Weir[1], M. Parkins[1], J. Rendall[1], J.S. Elborn[1]. [1]*Belfast City Hospital, Belfast, United Kingdom*

Objectives: 5–10% of CF patients are diagnosed as adults. They often present with non-classical CF and suffer a milder clinical course. We postulate an increased incidence of adult CF diagnoses. We sought to determine if the adult CF, diagnostic characteristics and clinical course differed between 2000–2009 and 1990–1999.
Methods: Patients attending CF centres in Northern Ireland from 1990 with a diagnosis of CF after the age of 16 were identified. Comparison of their demographics and biostatistics was made and a F508del homozygous cohort used as a control.
Results: Fifty-two patients were identified. There was an increased incidence of individuals diagnosed with CF in adulthood in the latter decade (12 vs 40). Mean age at diagnosis was 30.4(±4.0) yrs in the 90's and 43.2(±2.7) yrs in the 00's ($p = 0.02$). The majority of patients presented with respiratory manifestations in both cohorts. Mean FEV_1% predicted at presentation in the 90's group 71.3% (±7.6) and the 00's group 76.9% (±4.1) ($p = 0.52$). Class 1–3 mutations represented 75% of the 90's group and 50% of the 00's ($p = 0.18$), Class 4 mutations 25% of 90's and 2.5% of 00's ($p = 0.03$) and unknown mutations accounted for 0% of 90's and 50% of 00's ($p = 0.002$). A comparison of FEV_1 % decline between the late diagnosis group (0.46 ml/yr) and F508del homozygous patients (1.64 ml/yr) ($p = 0.02$).
Conclusions: Owing to the increased recognition of the heterogeneity of CF, this diagnosis is increasingly being made in adulthood. The majority of patients in both cohorts presented with Bronchiectasis. While having a milder clinical course these patients still suffer a considerable burden of disease and have a declining respiratory status.

371* Evidence of decline in cystic fibrosis (CF) incidence: study over a 40-year period

V. Scotet[1], I. Duguépéroux[1], M.-P. Audrézet[2], G. Rault[3], M. Roussey[4], P. Saliou[2], C. Férec[1]. [1]*Inserm U613, Brest, France;* [2]*CHRU Morvan, Laboratoire de génétique, Brest, France;* [3]*CRCM, Roscoff, France;* [4]*CRCM, Rennes, France*

Newborn screening (NBS) allows a better appreciation of CF birth incidence that appears lower than in the past. Here we reported time trends in incidence of CF over a long period (40 years: 1970–2009) in an area where CF is frequent (Brittany, France) and where NBS is implemented since a long time (1989).
The study enrolled the CF patients born in Brittany since 1970. The cases born before the set up of NBS were registered through active enquiries and combination of data sources. Time trends in incidence rates were examined using Poisson regression and expressed by the average percent change (APC) with its 95% confidence interval (95% CI). The APC was derived from the formula ($[\exp(\text{beta}) - 1] \cdot 100$), beta representing the effect of time on the logarithm of the incidence rate.
Over the 40-year period, 569 CF children born in Brittany were registered, leading to a CF incidence rate of 1/2617. The mean number of cases born each year varied from 17.7 in the 1970's (decade 1970–79) to 11.8 nowadays (decade 2000–09). This corresponded to a decline in incidence rate of 29.0% (from 1/2260 to 1/3183). Poisson regression showed that the incidence rate decreased over the whole period (annual APC: −1.2%, 95% CI: [−1.8; −0.5], $p = 0.0012$), and especially since the availability of prenatal diagnosis in the 1980's (annual APC: −2.0%, 95% CI: [−3.7; −0.3], $p = 0.0216$).
This study highlights how the incidence of CF evolved in an area where CF is frequent and where prenatal screening is not underway. It reports a clear decline in incidence that results from a complex mixture of factors.
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372 Survival analysis of cystic fibrosis (CF) patients in the Moscow region of Russia in 2000–2010

S. Krasovsky[1], A. Cherniak[1], E. Amelina[1], A. Voronkova[2], V. Nikonova[2], N. Kashirskaya[2], N. Kapranov[2]. [1]*Pulmonology Research Institute, Moscow, Russian Federation;* [2]*Centre for Genetics, Cystic Fibrosis, Moscow, Russian Federation*

Introduction: Progressive improvement of survival in CF patients has been associated with the treatment in specialized centers.
Objectives: The aim of the study was to assess the median survival age of the patients in the Moscow region of Russia, followed in children and adult CF Centers of Moscow during the period 2000–2010.
Methods: A retrospective study was performed using the data about 371 patients from the National Registry. Statistical analysis was performed using Kaplan-Meier survival curves.
Results: We examined the data of 371 patients, 45 (12.1%) of whom died during the analyzed period (the age of death ranging from 4 months to 40 years). The median survival age was 35.7 years. There was no significant gender difference in the survival rate. The mean age was 13.2±9.6 yrs. The mean age at death was 16.8±8.4 yrs. 32.6% of the patients are over the age of 18.
Conclusion: A large increase in the Moscow Region CF patients' survival was observed during the last decade. 20 years of specialized treatment, performed in two Moscow centers are the reason for that, pointing out a survival advantage of specialized care.

373 p.F508del homozygosity and the genotype–phenotype relationship in Northern Greece

M. Fotoulaki[1], K. Vasilaki[1], M. Poulou[2], M. Tzetis[3], K. Tentzidou[1], F. Sotiriadou[1], S. Nousia-Arvanitakis[1]. [1]*Papageorgiou General Hospital, Thessaloniki, Greece;* [2]*Athens University, Thessaloniki, Greece;* [3]*Athens University, Athens, Greece*

p.F508del is the most common mutation in cystic fibrosis (CF). The **aim** of this study was to determine the prevalence of p.F508del and its relation to clinical manifestations in CF.
Methods: This is a single-CF unit retrospective study analyzing the genetic and clinical characteristics of 108 genotyped children from Northern Greece. Mutations were categorized as severe (p.F508del, c.1571delG, p.W1282X, p.G542X, c.1677delTA, p.N1303K, p.E822X, p.R553X, p.R334W, c.621+1G>T, Del exon 2–3(21kb), c.2183AA>G, c.1525–1G>A, p.G85E, p.D110H, R1158X, 1717–1G>A) or mild/variable (p.R347H, c.2789+5G>A, p.R1070Q, c.3272–26A>G, p.G1069R). In all patients, age at diagnosis, presenting symptoms, sweat-chloride concentrations, occurrence of dehydration, presence of diabetes, and liver disease were recorded.
Results: 25/108 patients (23.1%) were homozygous for p.F508del, 47/108 (43.5%) were p.F508del heterozygous (3/47 compound with a mild genotype), and 36/108 (33.3%) had other severe mutations. p.F508del was detected in 5/10 patients with meconium ileus (MI) (only 1/8 p.F508del homozygous). p.F508del was detected in 7/17 patients with dehydration and metabolic alkalosis (only 3/17 were p.F508del homozygous). p.F508del was detected in 13/18 patients with diabetes mellitus (DM) (only 5/18 p.F508del homozygous). Finally, p.F508del was detected in 7/12 patients with nodular biliary cirrhosis (NBC) (4/12p.F508del homozygous).
Conclusion: The presence of p.F508del homozygocity cannot predict prognosis in CF patients at the time of their diagnosis. p.F508del heterozygocity may also be related to a severe phenotype