The most common genetic variant is F508del, it was found in 82 (74.2%) patients. In homozygous state - in 31 (25.8%) patients, in the heterozygous state - in 51 (42.5%) patients.
2184insA was found in 7 (5.8%) patients, 1677del TA, CFTR dele2,3, R1066C genetic- variants - in 5 (4.1%) patients each. E92K variant was found in 4 (3.33%) patients.
Conclusion: Genetic testing of 120 children with CF revealed 30 pathogenic *CFTR* variants with the dominance of the F508delta variant. It is necessary to continue the search for rare variants in the group of 120 presented patients and continue genetic testing in all other children with CF who have not been tested previously. This will allow the creation of a panel of the most common mutations and to increase the effectiveness of the first stage of genetic testing in Kazakhstan. It will also enable the expansion of pathogenetic treatment for CF patients.

P007

Genetic profile of cystic fibrosis in Morocco

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Objectives: Cystic fibrosis (CF) is the most common autosomal recessive genetic disorder in the Caucasian population. It is caused by mutations in the CFTR gene encoding the CFTR protein. The aim of this study was to determine the spectrum and frequency of known and novel mutations responsible for CF in Moroccan patients.
Methods: A retrospective study was conducted on 42 CF patients followed at the Pediatric Infectious Diseases Unit of the Mère-Enfants Abderrahim Harouchi Hospital in Casablanca, over a 9-year period from 2015 to 2024.
Results: A total of 26 mutations were identified in the 42 patients. The most common mutations were F508del (71%), E1104X (16.6%), R3437P (4.76%), along with other mutations recently identified in our department (7.64%).
Conclusion: This study provides a preliminary overview of the molecular landscape of CF in Morocco. It shows that CF is present in the country and is not limited to the Caucasian population. The results suggest that a tailored approach to molecular genetic diagnostic strategies should be.

P008

Large deletions account for about 4% of our patients with CF - should we include MLPA in newborn screening?

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Different ethnic groups have different distribution of mutation types for cystic fibrosis (CF), but common knowledge is for each country there is a set of mutations (covering roughly over 90% of mutations in the population). Classical sequencing technologies can't detect large rearrangements of the gene such an exon or more than one exon deletion and thus patients with such mutation can be misdiagnosed, especially with low or borderline sweat tests.
We present the data of all CF patients with at least one deletion, which comprise about 4% of all CF patients in the country. The gender and age distribution is 7 females and 4 males, 4 adults and 7 children. Only two patients were diagnosed as adults, one adult and two children were diagnosed at the ages of 4, 11 and 13 (albeit they had symptoms as early as infancy however, the sweat test and genetic confirmation took years) and the mean age for diagnosis of the rest 7 is 4 months (with the youngest one at birth – due to meconium ileus). Sweat tests were mostly borderline, and positive in only 3 patients. Six are eligible for modulator therapy, but in one of the cases the parents refused therapy. All four adult ladies are mothers – two with two children, two with one. Lung involvement severity differs, but 9 out of 11 had or still have persistent chronic *Pseudomonas aeruginosa* infection. None of the patients is with pancreatic sufficiency. Two patients have diabetes connected with CF and 6 have CF liver disease. At the moment all of them are relatively stable with none requiring oxygen support, non-invasive ventilation or to be listed for transplantation.
We advocate for multiplex ligation-dependent probe amplification (MLPA) assay to be included in Bulgarian neonatal screening program (once it starts), for we can suspect high percent of children with inconclusive screening diagnosis, actually to have large deletion and thus to miss CF in them.

P009

CFTR gene variants in the group of adult cystic fibrosis patients in Kazakhstan

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Background: CFTR genotyping for all people with cystic fibrosis (CF) is an important medical task for doctors in Kazakhstan.
Aim: To present the characteristics and frequency of various pathogenic variants of the CFTR gene in adult patients with CF in Kazakhstan.
Methods: Genetic testing was performed in 24 out of 32 adult patients with CF. Both mutations were detected in 18 (75%) patients, one in 6 (25%) patients.
Results: In 2024, the group of 17 genetically tested adult CF patients increased by 7 people due to the transfer from the pediatric group - 5 patients and diagnosis in adulthood - 2 patients.
The median age of patients was 23.9 years (min. 18, max. 44 years). In the group there are 15 women (62.5%) and 9 men (37.5%). There are 11 ethnic Russian patients (45.8%), 9 Kazakhs (37.5%), 1 Ukrainian (6%), 1 Pole (6%), 1 Korean (6%), and 1 Turk (6%).
15 variants of the CFTR gene were detected: F508del, V392G, G542X, R668C, R792X, H1054D, R1066C, N1303K, L1335P, 1677delTA, 2143delT, 3849+10kbC>T, c.274G>A, c.1766+2T>C, c.4111_4113dupGAA.
Allele frequency of the most common genetic variant F508del is 44% - 21 mutations, 6 in homozygous state and 9 in heterozygous state.
The vast majority of these mutations are eligible for pathogenic therapy.
Conclusion: The features of the CFTR variants distribution in adult CF patients in Kazakhstan are a lower frequency of F508del, a larger number of mild mutations. Further studies on CFTR genotyping in CF patients in Kazakhstan are needed.

P010

The evaluation of the genotype and phenotype relationship in patients with nasal polyps in the National Cystic Fibrosis Registry

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Objectives: We aimed to investigate the genotype and phenotype relationship of nasal polyp (NP) in Cystic Fibrosis Registry System of Turkiye (CFRT).
Methods: All children registered in the CFTR in 2023 were included in study. Patients were divided into two groups according to presentation of NP in any time. All clinical and demographic data were compared between the two groups. Patients with a history of NP were evaluated with Sinus-Nasal Quality of Life Survey-5 (SN-5).
Results: A total of 2258 patients were registered, 104 (4.6%) of them had NP (Group 1) and 2154 of them were without NP (Group 2). The current age was higher in Group 1 ($p<0.001$). There were no differences between the groups in terms of age of diagnosis, weight, height and BMI z-scores ($p>0.05$). The first and second sweat tests were higher in Group 1 ($p<0.05$). Mean FEV1(%) was 89 ± 24 in Group 1 and 82 ± 25 in Group 2 ($p=0.014$). There were no differences in terms of number of pulmonary exacerbations, hospitalizations and days of IV antibiotics in last year ($p>0.05$). Chronic colonization of MSSA and MRSA were more frequent in Group 1 ($p=0.013$, $p=0.001$, respectively). NP was the first presentation in 7 patients. 30 patients (28.8%) had recurrent NP. 91 (87.5%) received medical treatment, 42.3% of them regressed. 36 patients had surgical treatment (34.6%). Of the 34 patients who received modulator therapy, 13 had a reduction in NP. Trikafta use was more common in Group 1 ($p<0.001$). The F508del was detected more common in Group 1 ($p=0.007$). There was a negative corelation between the SN-5 score and FEV1% ($p=0.036$, $r=-0.205$) and positive correlation between the Visual Quality of Life Score and FEV1% ($p=0.035$, $r=0.208$).
Conclusion: Higher MSSA/MRSA colonization rates may contribute to increased chronic airway inflammation in patients with NP. The F508del mutation, linked to increased disease severity, could explain higher sweat chloride levels in these patients. Improved FEV1 in NP group might be due to higher use of Trikafta, suggesting benefits of modulator therapy. Notably, modulator therapy also appeared effective in reducing NP symptoms, highlighting the potential of targeted treatments in improving outcomes for CF patients with NP.

Diagnosis / Screening

P012

Implementation of the automated β-adrenergic Sweat Secretion Test in patients with inconclusive CFTR genetics and sweat chloride concentration

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Cystic fibrosis (CF) is caused by a dysfunctional CF transmembrane conductance regulatory protein (CFTR) and includes numerous gradations beyond classic CF. Diagnosis can be challenging since sweat chloride concentrations may be in the intermediate range and advanced electrophysiological measurements using intestinal current measurement (ICM) and nasal potential difference measurements (nPD) are limited to few centers and are restricted in their ability to differentiate between normal and high residual CFTR function.
The measurement of CFTR-dependent sweat secretion after β-adrenergic stimulation of the sweat gland, discovered in the 1980s, has not been established in routine clinical practice over the years due to difficulties in data collection, analysis, and standardization.
With our new automated recording and analysis of sweat bubble kinetics, we have simplified the performance of the β-adrenergic sweat secretion test and incorporated the test into our diagnostic work-up of patients with an unclear diagnosis. To date, we have studied 94 patients with clinically suspected CFTR dysfunction but inconclusive genetics and sweat chloride concentration, combining measurements of ICM and nPD with the SST to better understand CFTR function in vivo. Our results show that SST is a sensitive CFTR biomarker, especially in patients with high residual CFTR function. Patients report that the SST is a well-tolerated and pain-free procedure, and the test is simple and easy for the operator to learn. CFTR function in vivo showed organ-specific differences in many patients. Moreover, we used SST to monitor improvements in CFTR function in 13 patients with rare CFTR mutations where we have achieved off-label prescribing of ELX⁄TEZ⁄IVA. Furthermore, we have successfully used the test in children from 6 years of age.

P013

Understanding of sweat testing amongst adults living with cystic fibrosis: we've got work to do but don't sweat it

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Objectives: Lower sweat chloride levels (a surrogate marker for CFTR function) have been associated with better clinical outcomes. Sweat chloride is measured in the All-Wales Adult Cystic Fibrosis Centre (AWACFC) amongst those on CFTR modulator therapy at annual review. We assessed the understanding people with cystic fibrosis (PWCF) have of sweat testing and results.
Methods: Over a one-week period, 36 consecutive PWCF (17 female, 19 male) attending the AWACFC and taking CFTR modulators completed questionnaires on sweat testing.
Results: All given a questionnaire completed and returned it. All recalled having sweat tests. When asked to scale the test's acceptability from 1-10 (unacceptable to very acceptable), 33/36 (92%) answered 9 or 10. 1/36 (3%) would not want a sweat test in future.
When assessing understanding of sweat chloride
Results:

- 23/36 (64%) correctly identified the rationale for testing
- 13/36 (36%) knew their result
- 28/36 (78%) did not know normal test ranges
- Of the 8/36 who reported knowing normal ranges, 7 misidentified this

When rating their interest in sweat chloride results on a scale of 1-10, the median score was 8.
20/36 (56%) had never discussed their results with a healthcare professional.