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Objectives: Recently we have developed a skin wipe test (SWT) that consists of a simple, fast and cheap procedure of obtaining unstimulated human sweat in CF diagnostics. In this work we present statistical data from a large groups of CF patients, CF carriers and controls.
Methods: The samples were obtained from multiple CF centers by wiping the subject's forearm with a cotton swab moisturized in 100 µl of deionized water and extracted in 400 µl of deionized water. Sweat samples were obtained from 113 patients diagnosed with CF, 46 CF carriers and 74 healthy controls. The samples were analyzed for their ionic content (Cl^-, K^+, Na^+) by capillary electrophoresis with contactless conductometric detection (CE-C4D) using a background electrolyte containing 20 mM 2-(N-morpholino)ethanesulfonic acid, 20 mM L-histidine, 2 mM 18-crown-6 and 30 µM CTAB.
Results: The ion ratios (Cl^-/K^+) in skin-wipe samples of CF patients (mean = 7.1, range 2.4–20.2), CF carriers (mean = 1.9, range 0.6–4.3) and healthy controls (mean = 1.6, range 0.5–4.0) were calculated. When the optimum calculated ion ratio cut-off value of 3.8 was used, high sensitivity (96%) and specificity (95%) were obtained. The area under curve (AUC) of ROC curve was 0.994. An extended ion ratio (($Cl^- + Na^+$)/K^+) lead to an improvement in the performance with the following data: CF patients (mean = 11.2, range 5.0–31.1), CF carriers (mean = 2.7, range 0.9–5.8) and healthy controls (mean = 2.6, range 0.9–8.9). When the optimum calculated cut-off value of 5 was used, 100% sensitivity and specificity of 93% were obtained. The AUC of ROC curve was 0.995.
Conclusion: The developed SWT is non-invasive, fast (5–7 min), simple and cheap (<0.2 EUR/sample) complementary CF diagnostic technique. Total ionic analysis by CE-C4D and use of ion ratio instead of Cl^- concentration has a great potential to be a suitable surrogate to standard Macroduct sweat test in CF diagnostics, particularly for cases when sufficient amount of sweat cannot be obtained.

WS04-2
Bêta-adrenergic sweat evaporimetric test in patients with an inconclusive diagnosis of cystic fibrosis

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Objectives: To evaluate whether assessment of bêta-adrenergic trans-epithelial water loss (βadr-TEWL) measured by evaporimetry, is useful to detect CFTR dysfunction in patients with an inconclusive diagnosis for cystic fibrosis (CF).
Methods: Patients with clinical symptoms suggestive of CF, borderline chloride (Cl^-) sweat concentration (30 to 59 mmol/L) and inconclusive genotypes were referred to our centre for epithelial functional evaluation including: (i) βadr-TEWL; (ii) nasal potential difference (NPD); (iii) intestinal current measurements (ICM), and extensive CFTR gene screening.
Results: Twenty five patients (18 children and 7 adults) were assessed. Their mean sweat Cl^- concentrations were 38 ± 14 mmol/L Cl^-. Reliable results were obtained in 25 patients for βadr TEWL (100%), 18 for NPD (72%) and 19 for ICM (76%). Low response after βadr-TEWL (CF cut-off <4.5 kg/h/m^2) was observed in 8 patients. Those had a NPD (87%) and ICM (63%) interpretable and in CF values. CF diagnosis was secondarily confirmed by evidence of 2 CF-causing mutations including rare CFTR mutations (75%). The 17 remaining patients had a βadr-TEWL response in the normal or heterozygote ranges (mean 25 ± 15 kg/h/m^2). In these 17 patients, this response was in accordance with the results of NPD (65%) and/or ICM (82%) and allowed to rule out a diagnosis of CFTR dysfunction. In the remainings, NPD and ICM could not be performed or were inconclusive. Genetic analysis revealed a second CFTR mutation only in one patient (G551D/L997F) presenting βadr-TEWL normal response (24.6 kg/h/m^2) and ICM residual Cl^- secretion.
Conclusion: For patients combining clinical symptoms suggestive of CF, borderline sweat Cl^- concentration and inconclusive genotypes, the βadr-TEWL test is valuable to determine CFTR dysfunction. It is also easier to perform and cheaper than NPD and ICM.
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WS04-3
A non-invasive version of the beta-sweat test

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Objectives: A bioassay for CFTR function describing a ratio between CFTR-dependent sweat rate, evoked by a β-adrenergic cocktail, and CFTR-independent sweat rate, induced by a cholinergic agent, was reported in small cohorts using multiple intradermal injections. The aims of this work is to validate a non-invasive version of the image-controlled β-adrenergic sweat test, and to build reference CFTR-dependent/-independent sweat rate ratios in larger cohorts.
Methods: Sweat secretion was initially stimulated by pilocarpine iontophoresis using a Macroduct (Wescor). The stimulated skin area was covered with an oil layer and sweat droplets were imaged for 10 minutes. A second iontophoresis was followed using atropine, to block the prior cholinergic stimulation, and isoproterenol plus aminophylline, to maximize intracellular cAMP. Images of blue eriogalucine-stained sweat droplets were recorded for 30 minutes.
Results: To avoid contamination of the β-adrenergic phase, pilocarpine was used at a much lower concentration than that used in the Gibson and Cooke test. Iontophoresis delivery of atropine, isoproterenol and aminophylline was achieved after assessing different drug concentrations, pH of solutions and stabilizers. Preliminary results on the kinetics of the responses showed that in healthy subjects, the β-adrenergic phase progresses overtime together with the cholinergic phase while in CF no progression of the blunted β-phase was observed.
Conclusion: These findings confirm that iontophoresis is adequate for drug delivery of the β-adrenergic cocktail and that the non-invasive version of the test allows a good discrimination between CF and controls.

WS04-4
Cystic fibrosis in black African children in South Africa: a case control study

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Objective: This study aimed to describe and compare the presentation and outcomes of Cystic Fibrosis(CF) in black African children to children with CF in South Africa(SA) with p. Phe508del genotype.
Methods: A retrospective case-controlled study was conducted among children with CF, in two CF Centres; Red cross War Memorial Children's Hospital in Cape Town and Charlotte Maxeke Academic Children's Hospital in Johannesburg from January 2000–August 2018. Presentation, genotype, nutrition and pulmonary function outcomes of black African children were compared with age, gender and date-of-diagnosis matched controls, homozygous (or heterozygous) with the p. Phe508del mutation.
Results: Thirty-four black African children (cases), were matched to 34 controls. Median age of diagnosis (5.5 months, IQR 2.0–15.0), gender