Eur J Pediatr (2008) 167:299–304
DOI 10.1007/s00431-007-0485-0

ORIGINAL PAPER

Nanoduct® sweat testing for rapid diagnosis in newborns, infants and children with cystic fibrosis

Marie-Claire Desax · Roland A. Ammann · Jürg Hammer · Martin H. Schoeni · Jürg Barben · On behalf of the Swiss Paediatric Respiratory Research Group

Received: 14 January 2007 / Revised: 21 March 2007 / Accepted: 21 March 2007 / Published online: 14 April 2007

Abstract Determination of chloride concentration in sweat is the current diagnostic gold standard for Cystic Fibrosis (CF). Nanoduct® is a new analyzing system measuring conductivity which requires only 3 microliters of sweat and gives results within 30 minutes. The aim of the study was to evaluate the applicability of this system in a clinical setting of three children's hospitals and borderline results were compared with sweat chloride concentration. Over 3 years, 1,041 subjects were tested and in 946 diagnostic results were obtained. In 95 children, Nanoduct® failed (9.1% failure rate), mainly due to failures in preterm babies and newborns. Assuming 59 mmol/L as an upper limit of normal conductivity, all our 46 CF patients were correctly diagnosed (sensitivity 100%, 95% CI: 93.1–100; negative predicted value 100% (95% CI: 99.6–100) and only 39 non CF's were false positive (39/900, 4.3%; specificity 95.7%, 95%CI: 94.2–96.9, positive predicted value 54.1% with a 95%CI: 43.4–65.0). Increasing the diagnostic limit to 80 mmol/L, the rate fell to 0.3% (3/900). CF patients had a median conductivity of 115 mmol/L; the non-CF a median of 37 mmol/L. In conclusion, the Nanoduct® test is a reliable diagnostic tool for CF diagnosis: It has a failure rate comparable to other sweat tests and can be used as a simple bedside test for fast and reliable exclusion, diagnosis or suspicion of CF. In cases with borderline conductivity (60–80 mmol/L) other additional methods (determination of chloride and genotyping) are indicated.

Keywords Sweat test · Conductivity · Cystic fibrosis · Paediatric

M.-C. Desax · R. A. Ammann · M. H. Schoeni
Department of Pediatrics, University of Berne,
Berne, Switzerland

J. Hammer
Pulmonology and Intensive Care,
University Children's Hospital Basel,
Basel, Switzerland

J. Barben (✉)
Paediatric Pulmonology, Childrens' Hospital,
CH-9006 St. Gallen, Switzerland
e-mail: juerg.barben@kispisg.ch

Abbreviations

CF	Cystic fibrosis
CI	Confidence interval
DC	Direct current
GA	Gestational age
IRT	Immune reactive trypsinogen
NCCLS	National Committee for Clinical Laboratory Standards
PPA	Post partal age
ROC	Receiver operating characteristics
SD	Standard deviation

Introduction

The diagnosis of cystic fibrosis (CF) is in most cases straightforward with one or more typical clinical features (or a positive newborn screening test result or a sibling with CF) and confirmation by either elevated sweat chloride levels or identification of two CF mutations using molecular genetic testing [20]. Performing a sweat test requires qualified technicians and strict adherence to guidelines [3, 12, 17]. Since the inception of the sweat test 50 years ago, [8] the pad method by Gibson and Cooke [11] using quantitative pilocarpine iontophoresis is still accepted to be the most accurate sweat test [16]. Although this test is well established, it is technically demanding and time consu-

ming, and it needs several steps in the procedure which are open to many sources of error [3]. The collection of a sufficient amount of sweat using various stimulation and different collecting systems is a well known difficulty in sweat testing procedures. Especially in newborns, it is sometimes difficult to collect the minimum acceptable volume (50 μL for the Wescor Macroduct® coil sweat collection system) or a minimum weight of sweat (75 mg for the Gibson-Cooke® procedure) within 30 minutes to ensure an average sweat rate of more than 1 g/m^2/min [9].

In the past, several attempts were made to improve the methods of stimulation, collection and analysis of sweat samples [4, 16, 19, 20]. The determination of conductivity in sweat as a test for approximation to electrolytes in a non selective manner has been shown to be as effective as the quantitative determination of sweat chloride or sodium concentrations. Several studies have demonstrated, that conductivity levels have an equal potential to discriminate diagnostically between CF and non-CF subjects [1, 13, 14, 19]. Compared to the classic Gibson and Cook procedure, testing for conductivity is easier to perform and requires a smaller sample of sweat.

Nanoduct® is a new diagnostic system that induces, collects and analyzes sweat in one step while the required electrodes and sensors are attached to the patient [21]. Compared to sweat volumes between 75 to 100 μl required by other systems, this system only needs 3 μl of sweat and test results are available within half an hour [1].

The aim of the study was to evaluate retrospectively the accuracy and applicability of the Nanoduct® test for daily use in a clinical setting.

Patients and methods

Patients

We consecutively used the Nanoduct® system in all patients requiring sweat testing referred to three tertiary paediatric clinics in Berne, Basel and St. Gallen (Switzerland). Results above 50 mmol/L were compared either with the conventional pad collection technique and determination of chloride according to Gibson and Cook, or with the Macroduct® system (Webster Sweat Collection System 3500) to collect sweat followed by coulometric chloride determination. In St. Gallen and Basel, sweat was collected by the Macroduct® capillary system and chloride was determined, and in Berne, sweat testing was done by conventional Gibson Cooke method. To increase the number of data, as it was requested in an editorial [10] to our recently published data, we integrated in the final analysis a data set of 111 subjects including 21 previously known CF patients [1]. Furthermore, data presented here also include results of a separate study which was done with babies and infants who were recruited from the Neonatology Department of the University of Berne and from the Newborn Unit of Lindenhofspital in Berne (born between June 2003 and June 2004) and who were tested by Nanoduct® only. The inclusion criteria for that part of the study were a newborn with a minimum weight of 1000 grams, healthy and/or with minor postnatale adaptation problems. Babies who had too small extremities for fixing the holders for the electrodes and babies who were ventilated or underwent vasoactive or steroid therapy were excluded. The parents were informed by the attending physician about the procedure and the purpose of the tests.

Informed consent was obtained from all parents (or patients) of the subjects who were separately recruited for study purposes (babies and infants, patients with previously diagnosed CF) and the study was approved by the local Ethics Committees. In all others the determinations were done as routine diagnostic procedure accepted by the laboratory services of the hospitals. The evaluation of the results on the basis for quality control measures and their publication were communicated to the patients.

Method

The Nanoduct® sweat analysis system (Wescor Inc., Logan, Utah, USA) incorporates the classical method of inducing sweat secretion by pilocarpine iontophoreses and a conductivity measurement in one single system and one step procedure [21]. During the whole manipulation for testing, the iontophoresis device and the flow cell which measures conductivity is attached to the patient by one wire connected to the Nanoduct® inducer/analyzer central unit.

The skin site, where electrodes will be fixed, is cleaned with alcohol and deionized water. The electrodes with an underlying pilocarpine discs Pilogel® (1.5% pilocarpine) at the anode are attached firmly with special holders, avoiding excessive tightness to the forearm or the leg. The sweat test can be performed either on the forearm or on a leg; the placement of the electrodes on the leg is approved by the National Committee for Clinical Laboratory Standards (NCCLS) when adequate contact on the forearm is difficult because of the patients size [17]. Iontophoresis is done by a controlled DC electric current supplied by the Nanoduct® inducer/analyzer system. After slow increase the current is maintained for 2 to 3 minutes at 0.5 mA. An automated signal on the electronic display of the system indicates the end. The electrode-gel assembly at the anode is removed from its holder, and the stimulated skin in the collecting area is washed free of salt with a cotton swab and deionized water and dried with fresh electrolyte free swabs. A disposable conductivity sensor is immediately inserted into the holder at the anode. The cathode electrode remains in

place to provide an ongoing electrical contact with the skin. Sweat analysis is then manually started on the central unit. The sweat emerging from the stimulated sweat glands is directed into the microconductivity cell within the sensor. A continuous-flow principle allows the initial sweating rate to be displayed in grams per square meter of skin surface and per minute (g/m^2/min). The small dimensions of the conductivity sensor allow a conductivity measurement to be obtained at a minimum production of only 3 μl of sweat. Within minutes, conductivity is displayed at the central unit expressed as millimole per liter (mmol/L). This value is approximated to a solution of sodium chloride that has the same conductivity as the sweat sample at the same temperature. The measured sweat conductivity has been shown to be about 15 mmol/L higher than the sweat chloride concentration because of additional anions such as bicarbonate and lactate [13, 21]. The manufacturer of the Nanoduct® system defines a cut-off value of > 80 mmol/L to diagnose CF and a cut-off value <60 mmol/L to exclude CF in children under 16 years [21]. The American Cystic Fibrosis Foundation (CFF) recommends to perform a quantitative sweat chloride test when conductivity of sweat is greater or equal to 50 mmol/L [5, 17].

Statistics

Descriptive statistics, graphical analysis, and analysis of difference between the different sweat tests by 2-sided paired t-test were performed with S-PLUS 6.0 (Insightful Corp, Seattle, Washington). The Fisher exact test was used for comparison of failure rates. The exact Wilcoxon-Mann-Whitney test was used for comparison of sweat test results using different procedures and collection times in patients with and without CF; 95% confidence intervals were calculated for the sensitivity and specificity of the new system with StatXact 5.0.3 (Cytel, Cambridge, Mass).

Results

Over a three-year period, the sweat test was performed in 1,041 subjects. The numbers of patients per centre and per age group of all subjects tested are shown in Table 1. Diagnostic results were obtained in 946 subjects: in 95 the test failed due to low sweat rate or technical problems (9.1% failure rate). As shown in Table 2, this was mainly due to the high failure rate (53%) in the newborns (<1 month). The failures occurred seven times due to technical problems (wrong wiring, the central unit did not start, the display was not conclusive) and in 88 times due to low quantity of sweating. These failures are immediately indicated by the central unit either as measurement failure or as low sweat rate.

In 46 patients, the diagnosis of CF was always confirmed by genetic testing; from these 46 CF patients, 21 (age 2 to 24 years old) were known before testing and were part of a previously published study including 111 patients [1]. Twenty-five CF patients were newly diagnosed, three in newborns below the age of one month, eight in the first year of life, 13 between one year and 16 years of age and in one adult.

Figure 1 shows the distribution of all the measured conductivity levels versus age in 946 subjects (CF patients included). The median conductivity level in non-CF subjects was 37.0 mmol/L (range, 2–108 mmol/L), and for CF patients 114.5 mmol/L (range 60–139 mmol/L). We found three patients with CF within a borderline zone (≥ 60 mmol/L, ≤ 80 mmol/L, see Fig. 2): Subject 1 was a 6-month-old child with pancreas insufficiency (homozygote for Q525X) who had a conductivity of 78 mmol/L and a chloride of 104 mmol/L. Subject 2 was a 12-year-old boy with pancreas sufficiency (F508del/R347H), who had a conductivity of 71 mmol/L and a chloride of 67 mmol/L. The third child was a 16-year-old boy with a conductivity of 60 mmol/L and a chloride of 54 mmol/L, who had a non-classic form of CF [15] with chronic rhinosinusitis and nasal polyps (heterozygous F508del and a new deletion 3271+39delG with four single nucleotide polymorphism). These three subjects were responsible for the extended range of values from 60–139 mmol/L in the CF patients.

Assuming an upper limit of a normal conductivity (as specified by the manufacturer) to be set at 59 mmol/L all our 46 CF patients are correctly diagnosed (sensitivity 100%, 95% CI: 93.1–100; negative predicted value 100% (95% CI: 99.6–100) and only 39 non CF's were false positive (39/900, 4.3%; specificity 95.7%, 95%CI: 94.2–96.9, positive predicted value 54.1% with a 95%CI: 43.4–65.0). In these 39 patients retesting in 26 gave mean conductivity of 26.2 mmol/L with a range of 5 to 52 mmol/L. In 13 patients, the diagnosis of CF was ruled out either by using genetic testing or normal chloride by conventional Macroduct® or Gibson and Cooke. This good result of Nanoduct® is also represented by the ROC (receiver operating characteristics) curve with an AUC (area under the curve) of 0.998 indicating excellent sensitivity and specificity for the Nanoduct® test. If the upper limit of

Table 1 Numbers of patients per centre and per age group

Age group	Basel	Berne	St. Gallen	Total
Newborns (< 1 month)	3	57	6	66
Infants (> 1 month, <1 yr)	44	129	64	237
Children (≥ 1 yr, <16 yrs)	117	335	238	690
Adults (≥ 16 yrs)	14	10	24	48
Total	178	531	332	1040

Table 2 Nanoduct failure rate per age group

Age group	Failure rate	Numbers
Newborns (< 1 month)	53%	35/66
Infants (>1 month, < 1 yr)	9.7%	23/237
Children (≥ 1 yr, < 16 yrs)	4.9%	34/690
Adults (≥ 16 yrs)	6.3%	3/48

normal is lowered down to 54 mmol/L the false positive rate is increases to 7.1% (64/900); and increasing the limit up to 80 mmol/L, the rate falls to 0.3% (3/900).

Newborns

In total we tested 66 newborns between birth and one month of age. From these, 49 neonates were recruited in the neonatal unit of University Hospital in Berne for testing the device in newborns of all gestational ages as early as possible. The rest of the newborns (n=17) were tested routinely as all other children in this study. In the 49 neonates 54 Nanoduct® tests were done (three double and one three times) in their first 4 weeks of life (Table 3). The mean gestational age (GA) of the neonates was 38.5 weeks (range, 32.4 to 43). 14 subjects were preterm babies, (birth before ending of the 37th week of gestation) the rest were born at term (after 37th week of gestation). The median weight was 3002 g (range 1825 g to 4340 g). In the term newborns successful sweat conductivity results were received 21 times (55%) and 17 times (45%) the test was not successful (Table 3). Among the 14 preterm babies, sweat could successfully be analysed only in three (21%). Based on all 54 determinations, the failure rate for Nanoduct® in this group of newborns was 52%. 23/49 babies had a weight under 3000 g and in 23 occasions sweat testing was performed within the first week post partum; this was at a median post partal age (PPA) of 12 days (range, 0.5 to 27 days).

In one baby of this group of neonates CF was newly diagnosed and confirmed by genotyping. The baby had a conductivity value of 124 mmol/L. In all babies in whom the test was successfully done, the mean conductivity value was 51 mmol/L with a range of 35 mmol/L to 76 mmol/L; only two times we measured values (71 mmol/L and 76 mmol/L) within the predefined borderline area of 60 to 80 mmol/L and both values were determined in the same baby who had a hyperbilirubinemia. A control test was performed on the 75th day postpartum and showed in a conductivity value of 54 mmol/L.

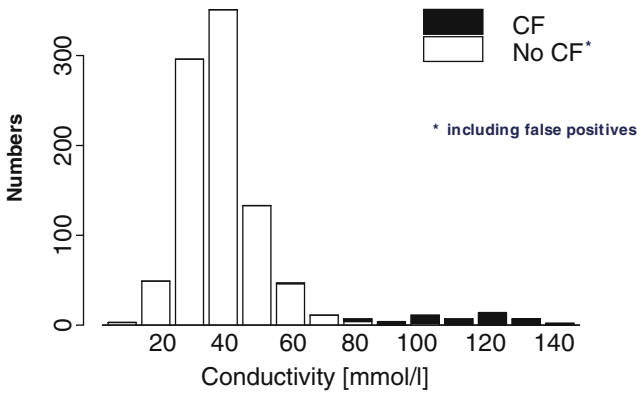

Fig. 1 Conductivity results of 946 subjects

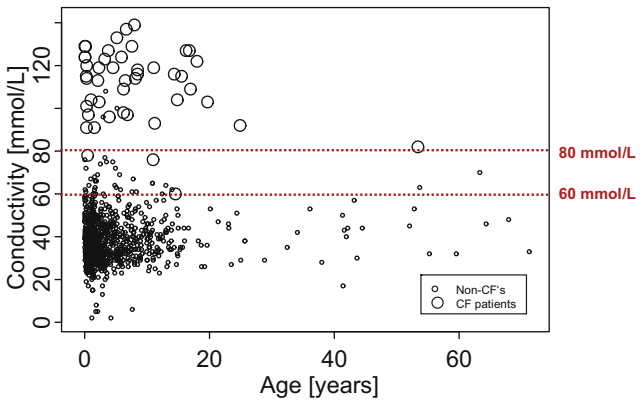

Fig. 2 Conductivity results of 946 subjects versus age

The duration for a successful Nanoduct® sweat test (from beginning of induction to the final result) in the newborns took on average of 19 minutes (range, 10 min. to 33 min). If there was no successful sweat collection within 45 minutes, the procedure was stopped. Significant statistical associations with successful determinations in newborns were found for GA ($p<0.01$), PPA ($p<0.001$), corrected GA ($p<0.001$), weight ($p<0.01$) and body temperature ($p<0.05$).

Based on these data we applied a mathematical model for calculating the best timing for Nanoduct® testing in babies The rule for the earliest time point to perform sweat collection aiming to reduce to a minimum of unsuccessful trials resulted in the following formula for the test age: PPA=(42-GA)/2 but most time not before the second day postpartum; this means that a baby born with a GA of 34 weeks can best be tested when it has reached a PPA of 4 weeks.

Table 3 Nanoduct sweat test in newborns

N=54*	Successful	Unsuccessful
Born at term (range 38.0 to 43.0 weeks of GA)	21 (55%)	17 (45%)
Prematurely born (range 32.4 to 37.6 weeks of GA)	5 (31%)	11 (69%)
Total determinations (range 32.4 to 43.0 weeks of GA)	26 (48%)	28 (52%)

*Indicated n=54 is the number of determinations done in 49 newborns

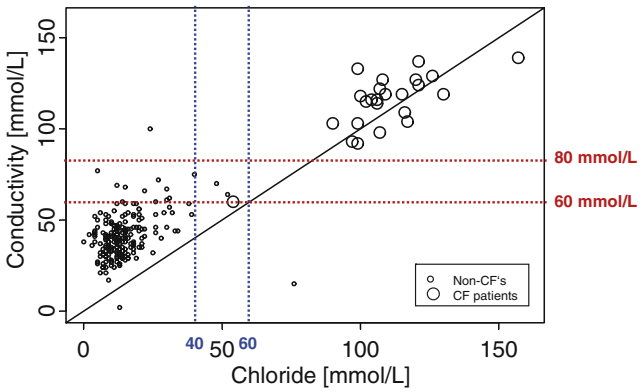

Fig. 3 Subset of 288 tests-Comparison with chloride determination using Macroduct

Nanoduct® versus Macroduct®

In a subgroup of 288 subjects, sweat conductivity measured with Nanoduct® was compared with sweat chloride concentrations using Macroduct® system for sweat collection. In Fig. 3 one can see that conductivity levels are slightly above the line of identity and that there is a good discrimination between CF and non-CF. This is in line with earlier reports of somewhat higher conductivity levels than chloride in sweat. Nanoduct® had a significantly ($p<0.001$) lower failure rate for getting a diagnostic result compared to the Macroduct® collection system (6.3% failures vs. 18.4%).

Conclusion

In this study we could demonstrate that the Nanoduct® sweat testing procedure is safe, fast, reliable and easy to use. It has, therefore, the potential for a point of care procedure i.e., at bedside in newborn units or in an outpatient setting where a sweat test is needed to confirm or exclude CF. It has furthermore the potential for fast and accurate assessment of a patient with positive IRT screening when awaiting genotyping results, provided that the child is not a preterm or a small for date. In all other situations, Nanoduct® testing is superior to other test methods due to the short time for having results at hands. This is the first report in the literature of a significant number of tests done with Nanoduct®. It also complements our first study [1] in so far that we extended the testing to newborns and even prematures and analyzed an extended dataset as it was requested in an editorial to our first study.

Assuming 59 mmol/L as an upper limit of normal conductivity, all our 25 new and 21 previously known CF patients were correctly diagnosed, and so far no false negative results of this test, as far as confirmational testing was done, were observed. We must assume that the reliability of Nanoduct® test system in patients with atypical clinical picture and certain specific genetic mutations going hand in hand with borderline sweat test results is the same as for other methods. It has been argued, that the determination of the quantitative chloride concentration in sweat must be kept for the gold standard of the CF diagnosis by sweat testing and that Nanoduct® can be used merely as a screening tool. However, these statements were based not on found results. They were deduced from conductivity determinations in sweat which was either collected by the Macroduct® coil system or by Nanoduct®. Several advantages are in favour of testing with Nanoduct®: during the procedure of iontophoresis the maximal current of 0.5 mA is sufficient and therefore is without side effects. The results are available within 30 minutes, the test specificity and sensitivity is excellent and the reliability is good [1]. As a point of care bedside test it can also be performed in babies who are in an incubator or connected to a monitoring system.

However, a few points have to be considered. Even though Nanoduct® sweat test was especially produced for newborns, its failure rate in our study is nevertheless still high despite showing a lower failure rate compared to the Macroduct® coil system or the conventional Gibson and Cooke method. In the subgroup of 288 subjects, where Nanoduct® was compared with Macroduct® collection system, Nanoduct® had a significantly ($p<0.001$) lower failure rate compared to the Macroduct® (6.3% failures vs. 18.4%), which was somewhat higher than in our first study (2.7% vs. 15.3%) [1] due to the high failure rate in preterm and small for date babies. Hammond et al. quoted a 0.7% failure rate for or the conventional Gibson and Cooke method compared with 6.1% using the Macroduct® collection system, however, only a few subjects were <1 month of age. According to the American National Committee for Clinical Laboratory Standards (NCCLS), the proportion of inadequate collection should not exceed 5%, unless many patients tested are <1 month of age [17]. Based on the current UK performance, a target failure rate of 5% is not unreasonable, and 10% should achieved by all [12].

So far, only one study comparing the Nanoduct® system with a quantitative pilocarpine iontophoresis has been published [18]. In this study, Nanoduct® produced a false negative result in nine of the 36 classical CF patients. However, these tests were performed with a batch of defective sensors, which rendered the study conclusions useless since conductivity determinations using liquid sweat collected into Macroduct® coils gave accurate test results. However, as a consequence of this study, the manufacturers have implemented a pre-testing system to quality control the sensors prior to sale.

A putative disadvantage of the test system might be the costs and waste of the disposable flow cell. In Switzerland the net costs for one test (including only disposable

material) is 40.35 SFr, i.e., 25.60 Euros. In some cases the child undergoing the test needs a permanent supervision. In addition, the statement of the NCCLS from 2000 [17] to exclude conductivity measures in a diagnostic setting except for screening is also hindering the use of the new developed Nanoduct® sweat test system as a diagnostic tool and should be reconsidered.

In summary we conclude that the Nanoduct® test system is a simple, fast, accurate and reliable sweat test system and can be recommended either for fast screening at bedside or as a standard diagnostic tool in the daily clinical setting. Based on our results with some limits of caution, we propose that all conductivity values determined by correct Nanoduct® technique need further clinical and genetic evaluation when the level exceeds 60 mmol/L. Classic CF is highly unlikely if conductivity is below 60 mmol/L whereas it is very likely above 80 mmol/L. As in all sweat testing systems, levels in the newborn or premature period are to be interpreted with more caution but can be used as an early fast diagnostic test. If the system indicates sufficient sweat rate and the result is below 60 mmol/L or over 80 mmol/L the appropriate conclusion can be drawn.

Part of this work has been presented at the European Respiratory Conference in Copenhagen, September 17–21, 2005, [2] at the European Cystic Fibrosis Conference in Copenhagen, June 14–18, 2006 [6] and at the annual Swiss Paediatric Society Meeting in Berne, 22–23, June 2006 [7].

Acknowledgements We thank PD Dr. M. Nelle, Neonatology Unit Dept. of Pediatrics, University of Berne and Dr. M. Travaglini, Neonatology Unit of Lindenhofspital, Berne, for their support to perform sweat tests in newborns.

If needed the genotyping was provided by the Molecular Genetic Laboratory of the University of Berne (Prof. Sabina Gallati), University of Basel (Prof. Peter Miny) and the University of Zurich (Prof. Wolfgang Berger).

No financial support was received by the Wescor Company.

References

1. Barben J, Ammann RA, Metlagel A, Schöni MH (2005) Conductivity determined by a new sweat analyzer compared with chloride concentrations for the diagnosis of cystic fibrosis. J Pediatr 146:183–188
2. Barben J, Desax MC, Ammann RA, Schöni MH (2005) Limitations of sweat conductivity determinations with Nanoduct analyzing system for rapid sweat testing in patients with cystic fibrosis. Eur Respir J 26:403s, (abstract)
3. Beauchamp M, Lands LC (2005) Sweat-testing: a review of current technical requirements. Pediatr Pulmonol 39:507–511
4. Carter EP, Barrett AD, Heeley AF, Kuzemko JA (1984) Improved sweat test method for the diagnosis of cystic fibrosis. Arch Dis Child 59:919–922
5. Cystic Fibrosis Foundation CDC (1993) Update 1. In. Bethesda: Cystic Fibrosis Foundation
6. Desax MC, Barben J, Hammer J, Ammann RA, Schöni MH (2006) Nanoduct sweat conductivity measurements in 1000 subjects. J Cystic Fibrosis 5:S105, (abstract)
7. Desax MC, Barben J, Hammer J, Ammann RA, Schöni MH (2006) Nanoduct sweat conductivity measurements: a good method for sweat testing in patients with cystic fibrosis. Swiss Med Wkly 136(Suppl 151):38S, (abstract)
8. di Sant'Agnese PA, Darling RC, Perera GA, Shea E (1953) Abnormal electrolyte composition of sweat in cystic fibrosis of the pancreas: clinical significance and relationship to the disease. Pediatrics 12:549–563
9. Eng W, LeGrys VA, Schechter MS, Laughon MM, Barker PM (2005) Sweat-testing in preterm and full-term infants less than 6 weeks of age. Pediatr Pulmonol 40:64–67
10. Funk MJ, LeGrys VA (2005) Testing diagnostic tests: why size matters. J Pediatr 146:159–162
11. Gibson LE, Cooke RE (1959) A test for concentration of electrolytes in sweat in cystic fibrosis of the pancreas utilizing pilocarpine by iontophoresis. Pediatrics 23:545–549
12. Green A, Elborn S, Fahie-Wilson MN, Kirk JM, Wallis CE, Weller P (2003) Guidelines for the performance of the sweat test for the investigation of cystic fibrosis in the UK. In. http://www.acb.org.uk
13. Hammond KB, Nelson L, Gibson LE (1994) Clinical evaluation of the macroduct sweat collection system and conductivity analyzer in the diagnosis of cystic fibrosis. J Pediatr 124:255–260
14. Heeley ME, Woolf DA, Heeley AF (2000) Indirect measurements of sweat electrolyte concentration in the laboratory diagnosis of cystic fibrosis. Arch Dis Child 82:420–424
15. Knowles MR, Durie PR (2002) What is cystic fibrosis? N Engl J Med 347:439–442
16. LeGrys VA (1992) Assessing quality assurance for sweat chloride testing. Clin Lab Sci 5:354–357
17. LeGrys VA, Rosenstein BJ, Doumas BT et al (2000) Sweat testing: sample collection and quantitative analysis; approved Guideline, 2nd edn. C34-A2. National Committee for Clinical Laboratory Standards
18. Losty HC, Wheatley H, Doull I (2006) The evaluation of a novel conductmetric device for the diagnosis of cystic fibrosis. Ann Clin Biochem 43:375–381
19. Mastella G, Di Cesare G, Borruso A, Menin L, Zanolla L (2000) Reliability of sweat-testing by the Macroduct collection method combined with conductivity analysis in comparison with the classic Gibson and Cooke technique. Acta Paediatr 89:933–937
20. Rosenstein BJ, Cutting GR, for the Cystic Fibrosis Foundation Consensus Panel (1998) The diagnosis of cystic fibrosis: a consensus statement. J Pediatrics 132:589–595
21. Webster HL, Quirante CG (2000) Micro-flowcell conductometric sweat analysis for cystic fibrosis diagnosis. Ann Clin Biochem 37:399–407