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Educational Discussion: Sweat Chloride Testing in Infants

2015-B Sweat Analysis Survey (SW)

The measurement of sweat electrolyte concentrations has been the mainstay for diagnosing cystic fibrosis (CF) since a standardized procedure, known as the Gibson-Cook method, was established in 1959. Results from the measurement of chloride concentrations in sweat should be interpreted in relation to the patient's age and clinical picture. The criteria for the diagnosis of CF include the presence of one or more characteristic phenotypic features, or a positive newborn screening test result and an increased sweat chloride concentration by pilocarpine iontophoresis on two or more occasions, or a history of CF in a sibling plus laboratory evidence of a Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) abnormality, identified by either sweat chloride testing or identification of two CF-causing mutations or an in vivo demonstration of abnormal nasal epithelial ion transport.

Studies of sweat chloride testing in infants have demonstrated that the age at which testing is performed is an important consideration in interpreting sweat chloride values. Based on the available data on sweat chloride test results in healthy and cystic fibrosis affected infants, the Cystic Fibrosis Foundation recommends the following sweat chloride ranges for infants up to six months: ≤29 mmol/L is the normal range; 30 to 59 mmol/L is intermediate; ≥60 mmol/L is indicative of CF. Although sweat chloride values are generally greater than 60 mmol/L in infants with CF, lower values can also occur and any value greater than or equal to 30 mmol/L should be considered abnormal, requiring further patient evaluation.

Based on the available data on sweat chloride test results beyond infancy, the Cystic Fibrosis Foundation recommends the following sweat chloride ranges for individuals 6 months of age or older: CF is very unlikely in individuals with sweat chloride ≤39 mmol/L; 40-59 mmol/L is intermediate; ≥60 mmol/L is indicative of CF. Individuals with intermediate results should undergo repeat sweat testing and further evaluation.

The College of American Pathologists' Sweat Analysis Proficiency Testing Survey is designed to evaluate the performance of the analytical measurement of sweat chloride. It does not evaluate the sweat collection process, a crucial procedure requiring skilled personnel. The SW-A and SW-B mailings of 2015 contained instructions to participants to interpret the results assuming the specimens were taken from a 1-month-old infant. These interpretations were not formally evaluated but are provided for informational purposes.

In the 2015 A mailing (SW-A) most participants interpreted the results correctly across all concentration ranges. However, specimen SW-02 (all method mean of 34.8 mmol/L) should have been interpreted as "borderline" for a 1-month-old infant and would require repeat sweat chloride testing and/or CFTR mutational analysis for diagnosis. The majority of participants (67-89 %, depending on the methodology) responded correctly. The remaining participants responded incorrectly (negative) which may have been due to a failure to follow kit instructions or a failure to implement the reference intervals for infants less than 6 months of age.

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Excerpt from SW-A 2015 PSR, specimen SW-02

Chloride – mmol/L (mEq/L)

Collection Technique/ Instrument	No. Labs	Mean	S.D.	C.V.	Median	Low Value	High Value
All Collection Techniques/							
All Instruments **	283	34.8	2.6	7.6	35	27	43
Macroduct Coils							
Bayer 925	12	34.5	2.4	6.9	34	32	40
Labconco/Buchler Digital Chloridometer	99	34.8	2.6	7.6	34	27	43
Wescor ChloroChek	46	34.3	1.3	3.7	34	31	36
Pre-Weighed Filter Paper							
Labconco/Buchler Digital Chloridometer	17	36.2	2.5	6.8	36	31	40
Pre-Weighed Gauze							
Labconco/Buchler Digital Chloridometer	46	35.4	3.1	8.6	35	28	43

Chloride Interpretation

Collection Technique/ Instrument	Negative		Borderline		Positive	
	No.	%	No.	%	No.	%
Macroduct Coils						
Bayer 925	4	33.3	8	66.7	-	-
Labconco/Buchler Digital Chloridometer	29	29.6	68	69.4	1	1.0
Wescor ChloroChek	10	22.2	35	77.8	-	-
Pre-Weighed Filter Paper						
Labconco/Buchler Digital Chloridometer	2	11.1	16	88.9	-	-
Pre-Weighed Gauze						
Labconco/Buchler Digital Chloridometer	12	25.0	36	75.0	-	-

Participants should be reminded that the use of the infant-specific ranges are strongly recommended by the Cystic Fibrosis Foundation, the Clinical and Laboratory Standards Institute and the College of American Pathologists. The B mailing (SW-B) did not contain any specimens that would have been interpreted differently based on age.

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References:

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2. Farrell, Philip M., et al. "Guidelines for diagnosis of cystic fibrosis in newborns through older adults: Cystic Fibrosis Foundation consensus report." *The Journal of Pediatrics* 153.2 (2008): S4-S14.

3. CLSI. *Sweat Testing: Sample Collection and Quantitative Chloride Analysis; Approved Guideline-Third Edition*. CLSI document C34-A3. Wayne, PA: Clinical and Laboratory Standards Institute; 2009.

4. Comeau, Anne Marie, et al. "Guidelines for implementation of cystic fibrosis newborn screening programs: Cystic Fibrosis Foundation workshop report." *Pediatrics* 119.2 (2007): e495-e518.