Intended Responses

**SW-01** represents a positive specimen.

**SW-02** represents a negative specimen.

**SW-03** represents a borderline specimen for chloride (all collection techniques/ all instruments mean: 55.2 mmol/L) requiring repeat sweat chloride testing and/or CFTR mutational analysis for diagnosis. This specimen also represents a positive specimen for sodium (all collection techniques/ all instruments mean: 56.9 mmol/L), conductivity (all collection techniques/ all instruments mean: 66.5 mmol/L) and osmolality (all collection techniques/ all instruments mean: 212.7 mmol/kg). These results would require further testing (i.e., sweat chloride analysis) for diagnosis according to the Cystic Fibrosis Foundation. Manufacturers’ decision limits may differ.

Discussion

Sweat chloride testing and the diagnosis of cystic fibrosis.

Though cystic fibrosis (CF) was first fully described in 1938\(^1\), the discovery that CF patients lose excess salt in their sweat was reported in 1953.\(^2\) A test to measure chloride concentrations in sweat was soon developed, and this has evolved into a confirmatory test for the diagnosis of CF. It was not until the mid-1990s that newborn screening for CF was initiated in some states in the US. Following the discovery of the CF gene (cystic fibrosis transmembrane conductance regulator, CFTR) in 1985, the development of mutation testing for CF was started. Currently most states that screen for CF incorporate testing of a 25 (of >1500 mutations) mutation panel that is predicted to identify 99% of CF affected babies.

The measurement of chloride in sweat is used to confirm the diagnosis of CF. Sweat chloride levels greater than 60 mmol/L on two separate occasions are considered diagnostic. Sweat chloride concentrations in the borderline range, typically 40 - 60 mmol/L, present a more complicated diagnosis and require additional testing. A “normal” result is defined at less than 40 mmol/L. A major diagnostic challenge facing clinicians treating CF patients is the presence of normal sweat chloride results in patients with mild symptoms of CF, and who also have been found to have CF mutations.\(^3\) The same challenge exists for patients with borderline results.\(^4\) Therefore, the use of sweat chloride results remains a very useful tool for the diagnosis of CF, but it does have limitations.

The Cystic Fibrosis Foundation has developed criteria for the diagnosis of CF that are not limited to the use of sweat chloride results.\(^5\) These criteria require the presence of one or more of the following characteristic phenotypic features:

1. Chronic sinopulmonary disease (i.e. infections, cough, wheezing, radiograph abnormalities of the chest or sinuses)
2. GI and nutritional abnormalities (i.e. meconium ileus, pancreatic insufficiency, failure to thrive)
3. Salt loss syndromes
4. Azoospermia
Discussion

Or, a history of CF in a sibling plus laboratory evidence of a CFTR abnormality, identified by either sweat chloride testing or two CF mutations or in vivo demonstration of characteristic abnormalities in ion transport across the nasal epithelium.

The College’s 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 grading of sweat chloride results for the diagnosis of CF has not been implemented into the survey for the various reasons delineated above.

Stanley F. Lo, PhD
Chemistry Resource Committee

References