Revised reference intervals for sweat chloride interpretation

Recommendations for interpreting sweat chloride concentrations from the Cystic Fibrosis Foundation (1) and in the newly revised CLSI Sweat Testing document C34-A3 (2), have been changed for infants up to 6 months in age. This modification is primarily due to the implementation of newborn screening for CF. An increasing number of infants are being tested for sweat chloride concentrations. Keep in mind that infants identified by screening often do not have clinical features exhibited by "older" patients, thus the sweat chloride test has an increased role in diagnosing infants for CF.

Studies of sweat chloride testing in infants have demonstrated that the age at which testing is done is an important consideration when interpreting the sweat chloride value. Based on the available data on sweat chloride test results in healthy and CF-affected infants, the following sweat chloride (Cl^-) reference intervals are recommended for infants up to and including 6 months: $Cl^- \leq 29$ mmol/L is within a normal range; $Cl^- = 30$ to 59 mmol/L is intermediate; and $Cl^- \geq 60$ mmol/L is indicative of CF. As more data emerges from newborn screening programs, the upper limit of the normal reference interval may need to be lowered. Although sweat chloride values are generally ≥ 60 mmol/L in infants with CF, lower values including concentrations < 30 mmol/L can occur. Individuals with intermediate or borderline results should have sweat chloride testing repeated and be referred to a CF center with expertise in the diagnosis of CF in infancy. Further evaluation should include an early detailed clinical assessment, more extensive cystic fibrosis transmembrane conductance regulator (CFTR) gene mutation analysis, and repeat sweat chloride testing and follow-up at 6- to 12-month intervals until the diagnosis is clear.

The SW-05 specification was set to provide a result in the 30-40 mmol/L range. Since no age was provided for its interpretation, a negative or borderline result was considered acceptable.

Laboratories are encouraged to engage in conversations with their CF physicians to properly implement these recommended reference intervals.

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1. Farrell PM, Rosenstein BJ, White TB, Accurso FJ, Castellani C, Cutting GR, et al. Guidelines for Diagnosis of Cystic Fibrosis in Newborns through Older Adults: Cystic Fibrosis Foundation Consensus Report. J Pediatr 2008;153:S4-S14.

2. 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.