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C34-A3

Sweat Testing: Sample Collection and Quantitative Chloride Analysis; Approved Guideline—Third Edition

This document addresses appropriate methods of collection and analysis, quality control, and the evaluation and reporting of test results.

A guideline for global application developed through the Clinical and Laboratory Standards Institute consensus process.

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Sweat Testing: Sample Collection and Quantitative Chloride Analysis; Approved Guideline—Third Edition

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Abstract

Clinical and Laboratory Standards Institute document C34-A3—*Sweat Testing: Sample Collection and Quantitative Chloride Analysis; Approved Guideline—Third Edition* is a guideline for the performance of the sweat test for the diagnosis of cystic fibrosis. The primary audience includes laboratory and clinical personnel responsible for collecting, analyzing, reporting, and evaluating sweat test results. Sweat stimulation, collection, and the quantitative measurement of sweat chloride are described along with quality assurance and result evaluation.

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Contents

Contents (Continued)

Foreword

The quantitative measurement of chloride in sweat (commonly called the “sweat test”) is used to confirm the diagnosis of cystic fibrosis (CF). With an approximate incidence of 1:3200, CF is the most common life-threatening genetic disease within the white population. It is an autosomal recessive disorder characterized by viscous secretions that affect the exocrine glands, primarily in the lungs and pancreas. Patients with CF have an increased concentration of sodium, chloride, and potassium in their sweat. The criteria for the diagnosis of CF include the presence of one or more characteristic phenotypic features, or a history of CF in a sibling, or a positive newborn screening test result; and an increased sweat chloride concentration by pilocarpine iontophoresis on two or more occasions, or identification of two CF-causing mutations or demonstration of abnormal nasal epithelial ion transport.[1,2]

The sweat test has been reported to have unacceptably high false-positive (up to 15%) and false-negative (up to 12%) rates attributable to inaccurate methodology, technical error, and patient physiology.[3-8] Comprehensive guidelines addressing the collection of sweat and the quantitative measurement of chloride in sweat are needed. Improvement in the performance of such tests can only occur when laboratory scientists and clinicians are aware of appropriate methods of collection and analysis, quality control, and evaluation of results. This document describes, in detail, the quantitative pilocarpine iontophoresis test for the determination of sweat chloride, including techniques to minimize the potential for false-positive and false-negative test results. Screening methods based on sweat conductivity are also mentioned. Other methods for measuring sweat electrolytes after pilocarpine iontophoresis exist but are not included in the guideline. Some of these methods are documented as having significant analytical problems.[3-8]

The Cystic Fibrosis Foundation requires that, at accredited Cystic Fibrosis Care Centers for diagnosis, sweating be stimulated by pilocarpine iontophoresis and collected in either gauze or filter paper, or microbore tubing followed by quantitative measurement of chloride.[2] At alternative sites, as a screening procedure, conductivity may be measured (see Section 10). Patients with a sweat conductivity value of 50 mmol/L (equivalent NaCl) or above should have a quantitative measurement of sweat chloride.[9,10]

This edition replaces the second edition approved guideline, C34-A2, which was published in 2000. Several changes have been made in this edition, including the following additions: a microvolume chloride procedure for sweat collected in coils; storage conditions for sweat; new reference ranges for infants; suggestions for enhancing sweat collection volume. It also includes sections on method validation and on developing and monitoring quality assurance and quality control.

Key Words

Chloridometer, iontophoresis, sweat chloride, sweat testing

Sweat Testing: Sample Collection and Quantitative Chloride Analysis; Approved Guideline—Third Edition

1 Scope

The following procedures are described: the stimulation and collection of sweat and the quantitative measurement of chloride; sweat stimulation by pilocarpine iontophoresis (specific precautions are noted); and sweat collection in filter paper, gauze, and microbore tubing. Sweat chloride (Cl^-) determination is described using coulometric titration. Screening methods based on sweat conductivity are also mentioned. Other methods for measuring sweat electrolytes after pilocarpine iontophoresis exist but are not included in the guideline. Some of these methods are documented as having significant analytical problems and also have limited diagnostic application.[3-8] Validation studies and quality assurance (QA) techniques are discussed, along with analytical and biological sources of error. The evaluation of sweat chloride test results to include reference intervals and diagnostic criteria are described, with an emphasis on the application of sweat chloride testing to newborn screening for cystic fibrosis (CF). This document is primarily directed towards laboratory and clinical personnel responsible for collecting, analyzing, reporting, and evaluating sweat chloride test results.

Because the sweat test has been reported to have unacceptably high false-positive and false-negative rates attributable to inaccurate methodology, technical error, and patient physiology,[3-8] comprehensive guidelines addressing the collection of sweat and the quantitative measurement of chloride in sweat are needed. Improvement in the performance of such tests can only occur when laboratory scientists and clinicians are aware of appropriate methods of collection and analysis, quality control (QC), and evaluation of results. This document describes, in detail, the quantitative pilocarpine iontophoresis test for the determination of sweat chloride, including techniques to minimize the potential for false-positive and false-negative test results.

2 Standard Precautions

Because it is often impossible to know what isolates or specimens might be infectious, all patient and laboratory specimens are treated as infectious and handled according to “standard precautions.” Standard precautions are guidelines that combine the major features of “universal precautions and body substance isolation” practices. Standard precautions cover the transmission of all infectious agents and thus are more comprehensive than universal precautions, which are intended to apply only to transmission of blood-borne pathogens. Standard and universal precaution guidelines are available from the US Centers for Disease Control and Prevention.[11] For specific precautions for preventing the laboratory transmission of all infectious agents from laboratory instruments and materials and for recommendations for the management of exposure to all infectious disease, refer to CLSI document M29.[12]

Currently, standard precautions for protection from transmissible infectious agents exempt sweat unless it contains visible blood. However, it is recommended that laboratory personnel wear powder-free gloves during sweat collection and analysis as routine practice, both for their protection and to prevent contamination of the sample.[11]

3 Terminology

3.1 A Note on Terminology

CLSI, as a global leader in standardization, is firmly committed to achieving global harmonization whenever possible. Harmonization is a process of recognizing, understanding, and explaining differences while taking steps to achieve worldwide uniformity. CLSI recognizes that medical conventions in the