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June 2001

C31-A2

Ionized Calcium Determinations: Precollection Variables, Specimen Choice, Collection, and Handling; Approved Guideline—Second Edition

This document addresses preanalytical considerations, such as patient condition, specimen choice, collection, and handling—that can influence the accuracy and clinical utility of ionized calcium measurements.

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

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C31-A2
Vol. 21 No. 10
ISBN 1-56238-436-8 Replaces C31-A
ISSN 0273-3099 Vol. 15 No. 20

Ionized Calcium Determinations: Precollection Variables, Specimen Choice, Collection, and Handling; Approved Guideline—Second Edition

Volume 21 Number 10

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Abstract

Ionized Calcium Determinations: Precollection Variables, Specimen Choice, Collection, and Handling; Approved Guideline—Second Edition (CLSI document C31-A2) is a guideline for specimen collection for ionized calcium determinations. The primary audience for this publication is personnel responsible for ionized calcium determinations. This document discusses the reasons for *in vivo* (nonpathologic) and *in vitro* changes in ionized calcium concentrations, and it presents recommendations for avoiding or minimizing these effects.

Clinical and Laboratory Standards Institute (CLSI). *Ionized Calcium Determinations: Precollection Variables, Specimen Choice, Collection, and Handling; Approved Guideline—Second Edition*. CLSI document C31-A2 (ISBN 1-56238-436-8). Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087, 2001.

Suggested Citation

CLSI. *Ionized Calcium Determinations: Precollection Variables, Specimen Choice, Collection, and Handling; Approved Guideline—Second Edition.* CLSI document C31-A2. Wayne, PA: Clinical and Laboratory Standards Institute; 2001.

Previous Editions:
November 1993, December 1995

Reaffirmed:
April 2007

Archived:
September 2016

ISBN 1-56238-436-8
ISSN 0273-3099

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Foreword

Ionized calcium determinations have proven to be clinically useful in the differential diagnosis of calcium disorders of endocrine origin, identification of hypercalcemia in various neoplasias, and managing the critically ill adult and neonatal patient. However, it is the responsibility of the laboratorian to choose which specimen is most appropriate for each clinical situation and how to collect and handle that specimen to ensure accuracy and clinical utility. This choice is complicated by the equilibrium between free (ionized) and bound calcium in blood, which is influenced by alterations in hydrogen ion and/or ligand concentrations. This guideline is designed to aid the laboratorian in determining the most appropriate specimen and its proper handling for each specific purpose.

Specifically, C31-A2 offers guidance in recognizing preanalytical factors that can affect ionized calcium determinations. The influence of patient conditions (e.g., physical activity, posture, meals, ventilation rate, and circadian variation) is considered in Section 5, while the advantages and disadvantages of whole blood, serum, and plasma are discussed in Section 6. The guideline also describes the selection of the collection site and device in Section 7. In Section 8, appropriate transportation, processing, and storage procedures are recommended.

References to pH-adjusted ionized calcium results are found throughout the guideline, and appropriate citations are provided.

Key Words

Ionized calcium, pH, preanalytical conditions, precollection variables, specimen choice, specimen collection, specimen transportation

Ionized Calcium Determinations: Precollection Variables, Specimen Choice, Collection, and Handling; Approved Guideline—Second Edition

1 Introduction

Ionized calcium is widely recognized as a better indicator of physiological calcium status in blood than total calcium. Generally, the reasons for measuring ionized calcium can be divided into three clinical categories: monitoring trends in acute or critical care, routine diagnostic care, and research. Generally, ionized calcium measurements for diagnostic purposes or research purposes require a high degree of accuracy.

This document describes the preanalytical variables for ionized calcium determinations and makes recommendations for minimizing the effects of these variables on the accuracy of ionized calcium measurements. Patient preparation and specimen handling options are presented, as well as the advantages and disadvantages of the various choices for specimen type, collection device, and technique. Recommendations are offered in each section.

2 Scope

This document addresses the preanalytical variables that can influence the accuracy and clinical utility of ionized calcium measurements.

3 Standard Precautions

Because it is often impossible to know which specimens might be infectious, all human blood specimens are to be treated as infectious and handled according to "standard precautions." Standard precautions are new guidelines that combine the major features of "universal precautions and body substance isolation" practices. Standard precautions cover the transmission of any pathogen and thus are more comprehensive than universal precautions which are intended to apply only to transmission of blood-borne pathogens. Standard precaution and universal precaution guidelines are available from the U.S. Centers for Disease Control and Prevention (*Guideline for Isolation Precautions in Hospitals*. Infection Control and Hospital Epidemiology. CDC. 1996;Vol 17;1:53-80.), [MMWR 1987;36(suppl 2S):2S-18S] and (MMWR 1988;37:377-382, 387-388). For specific precautions for preventing the laboratory transmission of blood-borne infection from laboratory instruments and materials; and recommendations for the management of blood-borne exposure, refer to NCCLS document M29—*Protection of Laboratory Workers from Instrument Biohazards and Infectious Disease Transmitted by Blood, Body Fluids, and Tissue*.

4 Definitions[a]

Circadian variation/chronobiological variation, diurnal variation, *n* – Variations in physiological parameters, including blood analyte concentrations, which are related to cyclic events, i.e., time of day, season of the year, and ingestion of meals.

Ionized calcium, *n* – The portion of calcium ions in the plasma water of whole blood that is not bound by protein or other molecules; **NOTE:** This parameter has also been called "free" or "ionic" calcium.

pH-adjusted ionized calcium, *n* – A calculated result empirically based on a measured pH and ionized calcium concentration, with the ionized calcium concentration normalized to a pH of 7.40; **NOTE:** These

[a] Some of these definitions are found in NCCLS document NRSCL8—*Terminology and Definitions for Use in NCCLS Documents.* For complete definitions and detailed source information, please refer to the most current edition of that document.

calculations exclusively compensate for *in vitro* increases in pH due to the loss of CO_2 and, therefore, help compensate for specimen handling errors. The pH-adjusted ionized calcium is included as an option in many of the commercial instruments currently available.

Plasma, *n* – The liquid part {of whole blood} remaining after the separation of the cellular elements ... in a receptacle containing an anticoagulant, or separated by continuous filtration or centrifugation of anticoagulated blood in an apheresis procedure.

Preanalytical variables, *n* – Events or circumstances that can alter the concentrations of analytes in a blood specimen before the actual measurement; **NOTE:** These can include patient preparation, specimen collection technique, specimen storage and transportation, and specimen handling.

Serum, *n* – The liquid remaining after treated whole blood has coagulated; **NOTE:** Observable after the clot and/or coagulum has retracted and/or has then been spun down in a centrifuge to separate the coagulum and cells from the liquid portion.

Skin puncture, *n* – Collection of capillary blood by producing a break in the skin in an area of the body with a high density of capillaries, e.g., fingertip or heel.

Titrated heparins, *n* – Typically, an aqueous or dry preparation of heparin salt, prepared with a fixed ratio of calcium to heparin, which minimizes changes to the concentration of ionized calcium, typically at 1.25 mmol/L; **NOTE:** When using these preparations to anticoagulate whole blood, the measured ionized calcium is unchanged, provided the calcium ion concentration of the blood specimen is at or near the concentration of calcium used in the preparation. Mixtures of lithium and zinc heparin are also currently used to limit calcium chelation by heparin.

Total calcium, *n* – The entire calcium concentration in plasma, including ionized calcium and calcium bound to proteins or other molecules, such as phosphate, bicarbonate, lactate, and citrate.

5 Precollection Variables: Influences of Physical Activity, Posture, Meals, Ventilation Rate, and Circadian Variation

While these variables can significantly alter the ionized calcium concentration under extreme conditions, they have a modest to insignificant effect when monitoring critically ill patients. However, because a high degree of accuracy is needed for ionized calcium measurements to diagnose a calcium disorder, these variables should be controlled to minimize variation in ionized calcium that is not related to the disease being investigated.

5.1 Effect of Physical Activity

The effect of moderate exercise on ionized calcium has been studied in persons during bicycling[1,2] and stair walking.[3] The mean increases reported in ionized calcium are 0.11 mmol/L after 10 minutes of bicycling,[1] 0.05 mmol/L after 10 to 15 minutes of bicycling,[2] and 0.02 mmol/L after 10 minutes of stair walking.[3] These changes appear to be related to changes in other constituents during exercise, e.g., decreased pH and bicarbonate and increased lactate, albumin, and total calcium.

5.2 Influences of Posture and Prolonged Bed Rest

While a change in posture has a proportionately greater effect on protein and protein-bound molecules, posture also affects the concentration of lower molecular weight ions. For example, as subjects change from a supine (lying) to a standing position, the following increases occur: ionized calcium 1.7%, total calcium 4.6%, hydrogen ion 2.9%, and albumin and total protein 12%.[4] Therefore, posture apparently has

Related NCCLS Publications[¶]

C46-P **Blood Gas and pH Analysis and Related Measurements; Proposed Guideline (2000).** This document provides clear definitions of the several quantities in current use, and provides a single source of information on appropriate specimen collection, preanalytical variables, calibration, and quality control for blood pH and gas analysis and related measurements.

H3-A4 **Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard — Fourth Edition (1998).** This document provides procedures for the collection of diagnostic specimens by venipuncture, including line draws, blood culture collection, and venipuncture in children. Includes recommendations on order of draw.

H4-A4 **Procedures and Devices for the Collection of Diagnostic Blood Specimens by Skin Puncture; Approved Standard —Fourth Edition (1999).** A consolidation of H4-A3 and H14-A2, this standard provides detailed descriptions and explanations of proper collection techniques, as well as hazards to patients from inappropriate specimen collection by skin puncture procedures.

H11-A3 **Procedures for the Collection of Arterial Blood Specimens; Approved Standard—Third Edition (1999).** This standard describes principles for collecting, handling, and transporting arterial blood specimens. The document is aimed at reducing collection hazards and ensuring integrity of the arterial specimen.

M29-A **Protection of Laboratory Workers from Instrument Biohazards and Infectious Disease Transmitted by Blood, Body Fluids, and Tissue; Approved Guideline (1997).** A consolidation of M29-T2 and I17-P, this document provides guidance on the risk of transmission of hepatitis viruses and human immunodeficiency viruses in any laboratory setting; specific precautions for preventing the laboratory transmission of blood-borne infection from laboratory instruments and materials; and recommendations for the management of blood-borne exposure.

NRSCL8-A **Terminology and Definitions for Use in NCCLS Documents; Approved Standard (1998).** This document provides standard definitions for use in NCCLS standards and guidelines, and for submitting candidate reference methods and materials to the National Reference System for the Clinical Laboratory (NRSCL).

[¶] Proposed- and tentative-level documents are being advanced through the NCCLS consensus process; therefore, readers should refer to the most recent editions.

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ISBN 1-56238-436-8