

Volume XXIII Number 3 Fall 2008

In this Issue

Editor's Note 1

Potassium Pitfalls—An Update . . . 2

AAP Issues Clinical Report in
Response to Obesity Epidemic in
Children 3



Herman Hurwitz, M.D., F.C.A.P.
Senior Medical Director
Quest Diagnostics Philadelphia
Medical Director, Western Region

- Our Values**
- Quality
 - Integrity
 - Innovation
 - Accountability
 - Collaboration
 - Leadership

Editor's Note:

Laboratory testing involves three phases: preanalytic, analytic, and postanalytic.

The **preanalytic** phase includes:

- Patient identification
- Sample collection and preparation
- Sample processing and transport to testing location

The **analytic** phase includes:

- Sample testing

The **postanalytic** phase includes:

- Reporting of test results in a timely manner
- Delivery of test results to person(s) authorized to receive the results
- Presentation of test results in an understandable non-confusing format

Variables can affect any of the three phases of testing, sometimes leading to spurious results. The majority of testing inaccuracies occur in the preanalytic phase and, to a lesser extent, the postanalytic phase. Errors can also occur in the analytic phase but are less common, probably because the analytic phase is the most controllable phase of laboratory testing.

In this issue, we revisit what I euphemistically refer to as potassium pitfalls—the occurrence of a spurious serum or plasma potassium result—usually secondary to a preanalytic variable. Since our last discussion, internal studies performed by Raymond Gambino, M.D., Chief Laboratory Officer Emeritus at Quest

Diagnostics, have illuminated some more detail regarding potassium release from extremity muscle activity during phlebotomy.

Potassium is being released from our muscles all of the time, but it is being diluted in the total body water content and quickly recycled back into the cells. Potassium released from hand and forearm muscle activity is a problem, because the blood is being drawn at or near the site of release before it can be diluted. This physiologic release of potassium ions can lead to spurious potassium elevations and, just as importantly, can also mask low potassium levels. Since I still receive calls from physicians questioning the validity of elevated potassium results, I thought that it would be worthwhile to have an updated discussion about this topic.

On the first day of pediatric service rotation, every medical student learns that children are not just small adults. In many ways their physiology and responses to stimuli and stresses are quite different from those of adults. In past issues, we noted that atherosclerosis is a chronic process, starting in childhood. Atherosclerosis doesn't usually exhibit signs or symptoms, such as angina, stroke, myocardial infarction, or peripheral vascular disease, until adulthood. By the time atherosclerosis is evident, significant vascular damage has occurred and is often irreversible.

Fatty streaks—the first visible signs of fatty deposits occurring in the subintimal layer of the arteries—have been noted

continued on page 4

Potassium Pitfalls—An Update

The unexpected finding of an elevated serum or plasma potassium result has been the bane of the clinical pathologists' existence ever since the analyte was first measured in the laboratory. In spite of the improvements in the technology of electrolyte measurement, a spuriously elevated result is often due to a preanalytic variable—one that occurs prior to actual quantitation.

The red blood cell especially has a high intracellular concentration of potassium. Anything that might cause leakage of potassium into the extracellular environment will result in the artifactual elevation of serum or plasma potassium.

All individuals, physicians, phlebotomists, physicians' assistants, and nurse practitioners should read this refresher on the proper way to collect and handle a sample for serum or plasma potassium testing.

The causes of false serum or plasma potassium elevations (pseudohyperkalemia) are too numerous to review in this publication. Many of the spurious results are due to the release of potassium from intracellular sources, usually red blood cells or skeletal muscle. I will list the more common causes and refer the reader to the cited references for a more extensive review of the topic.

Also, included with this issue is the phlebotomy guide from the current Quest Diagnostics Directory of Services.

Specimen Collection Issues

- **Excessive finger movement** during sample collection releases potassium from skeletal muscle. This is updated from the previous issue to include fist clenching, hand pumping, or the use of soft squeeze balls. A recent Quest Diagnostics' internal study by Dr. Raymond Gambino suggests that the use of squeeze balls

is by far the worst offender.

- **Prolonged tourniquet application** causes rupture of red blood cells with the subsequent release of potassium. Release the tourniquet as soon as the vein is entered.
- **Betadine antiseptic** can result in pseudohyperkalemia. Remove betadine with 70% alcohol before venipuncture.
- **Improper order of draw** can cause carryover of potassium from anticoagulants to serum tubes. Draw anticoagulated tubes last.
- **Benzalkonium heparin-coated catheters** can interfere with some ion-selective electrodes. Be aware of the method that your laboratory uses.
- **Collection via small gauge needles**, such as butterfly needles, can cause trauma to red blood cells with resultant hemolysis and leakage of potassium. Avoid using small gauge butterfly or straight needles whenever possible.
- **Traumatic venipuncture** can cause trauma to red blood cells with hemolysis and leakage of potassium. Try to avoid traumatic venipuncture.
- **Improper tube inversion** can interfere with the clotting process. Plastic clot activator tubes require controlled inversion to ensure timely activation of clotting. Conversely, excessive vigorous inversion can traumatize red blood cells, causing hemolysis and leakage of potassium. Please see the Quest Diagnostics Proper Phlebotomy Techniques in this publication as well as the current Quest Diagnostics Directory of Services.
- **Mislabeled samples** can cause results to be reported on the wrong patient. Verify patient identification before drawing the sample, and properly identify the tube after the sample is obtained.

Processing/Handling/Transport Issues

- **Delays in processing and transport** can cause the release of potassium from red blood cells within 1 hour of collection.
- **Improper centrifugation** can cause lysis of red blood cells and leakage of potassium. Avoid running a fixed angle centrifuge for long periods of time or allowing heat buildup in any type of centrifuge.
- **Poor barrier formation in a gel barrier tube** can cause the leakage of red blood cells across the barrier. Follow the tube manufacturer's instructions carefully. If recentrifugation is necessary, follow the instructions below.
- **Recentrifugation in the original gel barrier tube** can cause mixing of the serum above and below the gel. If recentrifugation is necessary, aspirate the serum from the collection tube and recentrifuge in a clean, dry test tube.
- **Chilling whole blood beyond 2 hours** inhibits glycolysis, which provides energy to pump potassium into the red blood cells. Inhibiting glycolysis allows potassium to leak from the red blood cells. Do not chill the sample to 15°C for prolonged periods of time.

Physiologic Factors

- **Thrombocytosis** can cause spurious potassium elevation due to platelet release of potassium during the clotting process. Use plasma collected in lithium heparin to avoid this mechanism in patients with significantly elevated platelet counts.
- **Anticoagulant therapy and liver disease** induces delay in the clotting process. Allow at least 1 hour for good clot formation. Recentrifuging the tube can result in mixing serum above and below the gel barrier. See instructions for recentrifugation above.
- **Dehydration** can result in elevated serum or plasma electrolytes. Be

continued on page 3

sure that the patient is adequately hydrated.

- **Hyperventilation by an anxious patient** can cause a net efflux of potassium from the cells. Try to calm the patient before obtaining the sample.
- **Familial pseudohyperkalemia** is a genetic defect with linkage to a locus on chromosome 16. The result is the leakage of potassium through a defective red blood cell membrane in vitro. Check the family history. If positive, collect the sample in

lithium heparin and separate the plasma from the red blood cells immediately.

- **Serum and plasma potassium values** are different. Serum potassium values are higher than plasma potassium values due to the release of platelet potassium during clotting. Reports of differences in the literature vary from 0.1 to 0.4 meq/L. Be aware of the differences.

The reader is reminded to be alert to the many variables that can affect

serum or plasma potassium values. When appropriate, the first step to resolve an apparent discordance is to verify the result on the sample in question or a new sample.

(Becton Dickinson LabNotes 2003; **13**(3):1-11 — *Clin Chem* 1999; **45**(7):1091-1092 — *Lancet* 1979; **ii**:175-177 — *Lancet* 2002; **359**:848 — *MLO* 2005; **37**(11):39 — Quest Diagnostics Directory of Services 2008 — Personal communication, Raymond Gambino, MD)

AAP Issues Clinical Report in Response to Obesity Epidemic in Children

Cardiovascular disease (CVD) is the leading cause of mortality and morbidity in the United States. Most of the clinical burden occurs in adulthood. Research over the last 40 years increasingly has shown that the process of atherosclerotic CVD begins in childhood and is progressive throughout life. It also has become clear that an important genetic component produces susceptibility. In addition to the genetically determined atmosphere of vulnerability, environmental factors, such as diet and exercise, are equally, if not more, important in determining the course of atherosclerotic CVD. The AAP has retired the 1998 policy statement “Cholesterol in Childhood.”

In its most recent report, the academy notes that new data emphasize the negative effects of increased dietary intake of saturated and trans fats, as well as cholesterol and carbohydrate intake. Additionally, information has become available regarding the effects of the obesity epidemic, the metabolic/insulin resistance syndrome, and the decreased level of physical

activity and fitness on the risk of adult onset CVD. More factual knowledge is now available on the safety and efficacy of pharmacologic agents used to treat dyslipidemia. Much of this information was not available in 1998.

A number of studies have identified potential risk factors for adult CVD. The most robust risk factors include the following:

- A high blood concentration of low-density lipoprotein (LDL) cholesterol
- A low concentration of high-density lipoprotein (HDL) cholesterol
- Hypertension
- Diabetes mellitus, Type 1 or 2
- Cigarette smoking
- Obesity

Research in children and adolescents has shown that some of these risk factors may be present at a young age, and pediatricians must initiate a life-long approach to prevention of CVD in their patients. The focus of the AAP report is on improving lipid and

lipoprotein concentrations during childhood and adolescence in order to lower the lifelong risk of CVD. According to the AAP, the epidemic of obesity among children has increased the need for pediatric healthcare professionals to be knowledgeable of the risk factors for CVD and to implement the changes in the report into practice.

This discussion will be limited to the summary of the report. The reader is referred to the cited reference for an in-depth review of the subject at <<http://pediatrics.aappublications.org/cgi/reprint/122/1/198>>.

The AAP Summary states the following:

- The population approach to a healthful diet should be recommended to all children older than 2 years according to Dietary Guidelines for Americans. This approach includes the use of low-fat dairy products. For children between 12 months and 2 years of age for whom overweight or obesity is a concern or who have a family history of obesity, dyslipidemia, or CVD, the use of reduced-fat milk would be appropriate.
- The individual approach for children and adolescents at higher risk for CVD and with a high concentration of LDL includes recommended

continued on page 4

Editor's Note

continued from page 1

in autopsy studies of children as young as 4 to 5 years of age. Postmortem examinations of young, apparently healthy men killed in combat also have identified significant asymptomatic arterial plaque. Lipid screening in adults as an indicator of cardiovascular health and a guide to pharmacologic therapy for dyslipidemia is well established. The use of lipid screening and drug therapy of lipid abnormalities in children has been less clear.

Recently, the American Academy of Pediatrics (AAP) issued its report "Lipid Screening and Cardiovascular Health in Childhood." This clinical

report replaces the 1998 AAP policy statement on cholesterol in childhood, which has been retired. The AAP stated that the present report "has taken on new urgency given the current epidemic of childhood obesity with the subsequent increasing risk of type 2 diabetes mellitus, hypertension, and cardiovascular disease in older children and adults."

The AAP publication further notes that the screening of children and adolescents remains a targeted approach. Overweight children belong to a special risk category of children and are in need of cholesterol

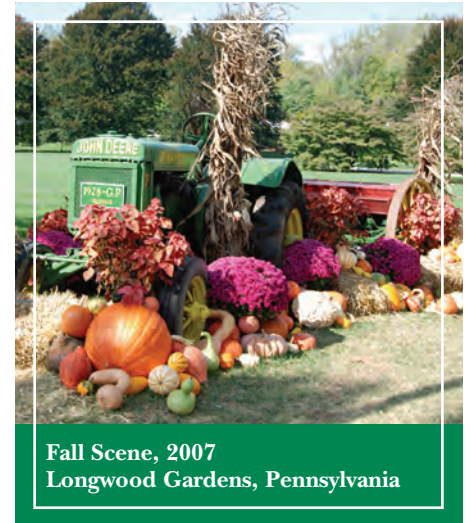
screening regardless of family history or other risk factors. The report reemphasizes the need for prevention of cardiovascular disease by following Dietary Guidelines for Americans and increasing physical activity. It also includes a review of the pharmacologic agents and indications for treating dyslipidemia in children. This review of the use of pharmacologic agents, such as bile acid resins, cholesterol absorption inhibitors, statins, fibrates, and niacin, has generated a great deal of discussion in the medical literature and the lay press.

AAP Issues Clinical Report in Response to Obesity Epidemic in Children

continued from page 3

changes in diet with nutritional counseling and other lifestyle interventions such as increased physical activity.

- The most current recommendation is to screen children and adolescents with a positive family history of dyslipidemia or premature (≤ 55 years of age for men and ≤ 65 years of age for women) CVD or dyslipidemia. It is also recommended that pediatric patients for whom family history is not known or those with other CVD risk factors, such as overweight (BMI ≥ 85 th percentile, < 95 th percentile), obesity (BMI ≥ 95 th percentile), hypertension (blood pressure ≥ 95 th percentile), cigarette smoking, or diabetes mellitus, be screened with a fasting lipid profile.
- For these children, the first screening should take place after 2 years of age but no later than 10 years of age. Screening before 2 years of age is not recommended.
- A fasting lipid profile is the recommended approach to screening, because there is no currently available noninvasive method to assess atherosclerotic CVD in children. This screening should occur in the context of well-child and health maintenance visits. If values are within the reference range on initial screening, the patient should be retested in 3 to 5 years.
- For pediatric patients who are overweight or obese and have a high triglyceride concentration or low HDL concentration, weight management is the primary treatment, which includes improvement of diet with nutritional counseling and increased physical activity to produce improved energy balance.
- For patients 8 years and older with an LDL concentration of ≥ 190 mg/dL (or ≥ 160 mg/dL with a family history of early heart disease or ≥ 2 additional risk factors present or ≥ 130 mg/dL if diabetes mellitus is present), pharmacologic intervention should be considered. The initial goal is to lower LDL concentration to < 160 mg/dL. However, targets as low as 130 mg/dL or even 110 mg/dL may be warranted when there is a strong family history of CVD, especially with other risk factors including obesity, diabetes mellitus, the metabolic syndrome, and other higher-risk situations.



Fall Scene, 2007
Longwood Gardens, Pennsylvania

News Credits

Herman Hurwitz, M.D., *Executive Editor*
Patricia Mellon, *Senior Editor*

Published quarterly by Quest Diagnostics Incorporated. Electronic copies are available at: www.questdiagnostics.com. All inquiries, suggestions, or comments should be addressed to Herman Hurwitz, M.D., F.C.A.P., Senior Medical Director, Quest Diagnostics Incorporated, 800 Business Center Drive, Horsham, PA 19044.

Telephone: 215.442.7673
Email: herman.s.hurwitz@questdiagnostics.com










Quest, Quest Diagnostics, the associated logo and all associated Quest Diagnostics marks are the trademarks of Quest Diagnostics. Copyright © 2008 Quest Diagnostics Incorporated. All rights reserved. www.questdiagnostics.com

All third party marks – ® and ™ – are the property of their respective owners.

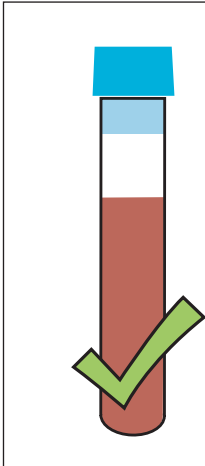
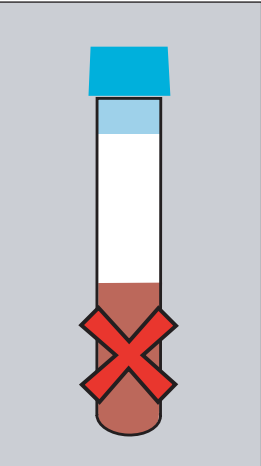
This newsletter is published quarterly by Quest Diagnostics as a service to the Medical Community.

Quest Diagnostics Proper Phlebotomy Techniques

Collect

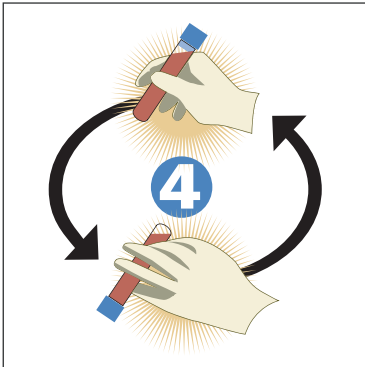
Stopper	Additive	Sequence
	YELLOW (CULTURE)	FIRST  LAST
	LIGHT BLUE	
	YELLOW	
	RED/BLACK	
	RED	
	GREEN	
	LAVENDER	
	GRAY	
TUBES WITH OTHER ADDITIVES		

* When using a winged blood collection set for venipuncture and a coagulation (citrate) tube is the first specimen to be drawn, a discard tube should be drawn first. The discard tube must be used to fill the blood collection set tubing's "dead space" with blood but the discard tube does not need to be completely filled. This important step will ensure maintenance of the proper blood-to-additive ratio of the blood specimen. The discard tube should be a nonadditive or coagulation tube.

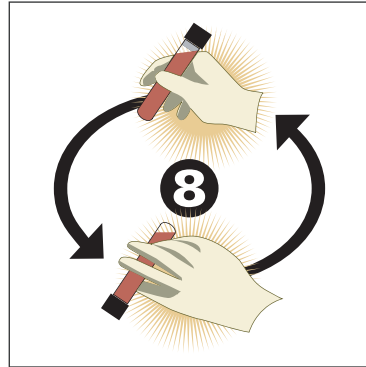



Mix Gently

Light blue tubes



All plastic tubes other than light blue



Separate

Do not use gel tubes for toxicology or drug testing

