MAYO CLINIC
Mayo Medical Laboratories

COMMUNIQUÉ

IMPROVING PATIENT CARE THROUGH ESOTERIC LABORATORY TESTING DECEMBER 2008

Preanalytic Laboratory Errors: Identification and Prevention

Quality systems are the mainstay of clinical laboratory management. The comprehensive laboratory testing process must be continually monitored and evaluated to ensure reliable test results and set the foundation for quality improvement. While such efforts have resulted in significant improvements in many of the processes, errors still occur. In order to implement corrections and improve the testing process, the laboratorian must identify the various sources of errors.

Laboratory testing can be divided into 3 phases as described in Table 1.

Preanalytic	• Patient variables
	• Specimen variables
	  • Collection
	  • Handling
	  • Processing

Analytic	• Performance of selected laboratory test

Postanalytic	• Test reporting variables
	  • Recording
	  • Reporting
	  • Interpreting

Table 1. *Three phases of laboratory testing*

Preanalytic Error Identification

A common assumption is that errors are most likely to occur in the analytical phase, the component of laboratory testing considered the most complex. Clinical laboratories invest considerable time and effort in maintaining quality control programs, participating in laboratory inspections, and complying with government regulations. In addition, significant advances in laboratory instrumentation and automation have improved the accuracy, reproducibility, and overall quality of the analytic phase. Contrary to popular belief, and perhaps as a consequence of the focus on technological improvements, it is actually the preanalytic phase in which most errors occur. Plebani and Carraro performed a large comprehensive study that determined—of all errors detected—68.2% originated in the preanalytic phase, compared with 18.5% in the postanalytic phase, and 13.3% during the analytic phase.[1] This group also found that, in more than

INSIDE THIS ISSUE

25% of all cases, the error resulted in unnecessary investigation or inappropriate patient care.

Identifying the phase when the most errors occur enables laboratories to focus their quality improvement efforts. Preanalytic variability, and postanalytic processes to a lesser degree, are areas where quality improvement will have significant positive impact on patient care and help ensure accurate and timely test results.

Preanalytic Error Prevention

Of all the errors, those that occur during the preanalytic phase are the most difficult to detect and correct. Therefore, for this type of error, the focus must be on prevention. To prevent preanalytic errors, the procedures for collection, handling, and processing prior to analysis, as well as the physiologic patient variables that may directly affect the test result, must be clearly understood (Table 2).[2]

Patient Variables

Specimen composition is influenced by any of the patient variables listed in Table 2. Some are controllable, some are not. The laboratory staff must be aware of these influences and minimize the effects when possible. For example, in the basal state, a patient is at rest and fasting. Collection of a blood specimen from a patient in that state minimizes the effect of diet, exercise, and other controllable factors.

Specimen Collection

Among the controllable preanalytic phase variables, specimen collection is perhaps the most critical.[3] Unacceptable specimens due to misidentification, insufficient volume to perform the assay, incorrect whole blood to anticoagulant ratio, or specimen quality issues (specimens that are hemolyzed, clotted, contaminated, or collected in the wrong container) account for the majority of preanalytic errors.[4,5] Hemolysis, lipemia, and icterus have variable effects on assays. The degree to which the accuracy of the assay is affected is both method and analyte dependent. Some assays are affected by very low levels of hemolysis, lipemia, or icterus, while there is minimal or no effect on other assays. Hemolysis interference may be analytic (the presence of hemoglobin interferes with the measurement of an analyte) or physiologic (caused by the release of the substance being measured from red cells into the serum or plasma). Two common examples of physiologic interference by hemolysis are potassium and aspartate aminotransferase (AST), assays that are very sensitive to the effects of hemolysis. Ideally, laboratory instruments have automated optical

Patient Variables	Specimen Collection Variables	Specimen Handling Variables
Diet	Posture	Hemolysis
Body mass	Diurnal variation	Lipemia
Age	Time of collection	Centrifugation
Medications	Fasting status	Processing time
Gender	Tourniquet	Temperature
Smoking	Presence of IVs	Sunlight
Pregnancy	Capillary vs venous	Evaporation
Exercise	Anticoagulants	Aliquoting
Race	Order of draw	Labeling
Dehydration		Transport conditions

Table 2. *Preanalytic variables*

Type of specimen	Definition
Acceptable plasma or serum sample	No known interfering substances
Hemolyzed sample	Visible hemolysis following centrifugation is defined as the presence of free hemoglobin in serum or plasma >100 mg/L. See Hemolysis chart (Figure 1)
Lipemic sample	Visible lipemia, turbidity due to elevated concentrations of lipids, usually translates to a triglyceride level >1000 mg/dL (whole blood) or >300 mg/dL (serum or plasma)
Icteric sample	Visible detection of icterus is variable and unreliable
Clotted sample	Those specimens that present with visible clots–either as a red cell clot in whole blood or a fibrin clot in plasma. Instrument flags, histograms indicating platelet clumps, and low platelet counts also suggest a clotted specimen.

Table 3. *Definition of specimen types*[6]

systems to detect serum or plasma free hemoglobin and prevent reporting of potassium and AST above defined levels of hemolysis.

Blood Specimens

A broad category of variables related to phlebotomy technique and procedures can introduce preanalytic error. The Clinical and Laboratory Standards Institute (CLSI) publication on procedures for the collection of blood specimens by venipuncture[7] establishes standards of care for those specimens collected via phlebotomy as described in the Appendix. A few studies have demonstrated that preanaltyic errors are less common when dedicated laboratory personnel collect blood samples as opposed to nursing or other health care personnel. Sheppard et al reported that when the phlebotomy was performed in an emergency department by dedicated laboratory technologists, there was a reduction in overall turn around time, and blood culture contamination rates dropped from 5.0% to 1.1%.[8] In addition, blood draws from indwelling catheters or during IV starts are more prone to hemolysis compared to venipuncture draws.[9]

Other Specimen Types

Preanalytic error prevention is also important in collection of specimens other that blood (eg, urine, stool, cerebral spinal fluid [CSF]). Mayo Medical Laboratories and the Department of Laboratory Medicine and Pathology at Mayo Clinic have worked collaboratively to establish guidelines for collection and handling of specimens. For 24-hour urine collections, stability studies are performed on all urine-based assays and 10 different types of preservative and temperature options are evaluated. A urine preservative chart developed from the studies enables the laboratory to select either temperature conditions or preservatives to maximize the number of tests that can be performed on a single 24-hour collection. By identifying all preservatives compatible for each test, many tests can be conducted from one 24-hour collection. Patients can then provide a single 24-hour collection for all urine tests ordered. The chart is available as a poster (supply #T492) that can be used in your laboratory. Additionally, 24-hour urine containers and preservatives for urine collection are supplied by Mayo Medical Laboratories.

Specimen Handling

How a specimen is handled from patient to laboratory is an area of potential error and mostly outside control of the testing laboratory. Careful handling of the specimen during transport and processing is imperative in maintaining the quality of a meticulously collected specimen. The means of transport, exposure to heat and cold, vibration, position of specimen tubes, and overall time to delivery can significantly affect test results. Detailed information for classifying, packaging, and shipping medical specimens to our laboratories for testing is available on the Mayo Medical Laboratories Web site (www.mayomedicallaboratories.com). Guidelines are updated as regulations, methods, and packaging materials change over time. We continually review and update procedures and supplies to improve specimen quality and reduce specimen-handling errors. All primary containers have been evaluated for the potential of leakage at high altitudes and our Styrofoam containers for long-term storage performance. For example, the polypropylene primary tube was tested to withstand air pressures at the equivalent of 50,000 feet (for air transport) and freezer tested to -70°C, and it remained leak-free. This tube

Approximate Hemoglobin Concentration (mg/dL)

General guidance for acceptance/rejection:
<50 mg/dL – not hemolyzed
>100 mg/dL – hemolyzed

Please refer to test specific information in the MayoAccess test catalog to determine if hemolyzed specimens will be rejected.

Figure 1. *Hemolysis chart for serum or plasma (available as supply item T598)*

has also been validated for direct placement on several testing instruments without aliquoting and relabeling, thus avoiding the errors associated with these practices. Mayo's shipping containers and guidelines are precisely designed to ensure that all medical specimens arrive at the testing facility:

- At the correct temperature for testing
- Intact in the container (without breakage or leakage)
- Within the time limits for the test
- In compliance with all applicable regulations

To define the instructions for transport and handling, Mayo Medical Laboratories validates all assays to establish performance characteristics under various conditions. In the preanalytic phase these parameters include analyte stability, acceptable specimen transport conditions, acceptable sample types, and storage time and temperature. To define alternate specimen types (eg, serum or plasma [heparinized, EDTA, and citrated plasma]) various specimen types from the same sample collection—covering a range of analyte concentrations—are run in the same assay and compared. To give clients optimal flexibility, we evaluate a number of possible anticoagulants for plasma samples. Analyte stability is examined at several specimen storage temperatures over time. The process includes at least 10 specimens with values within the analytic range. Specimens are stored frozen, refrigerated, and at room temperature for 1, 3, and 7 days. Frozen samples are analyzed through 1, 2, and 3 freeze-thaw cycles. Based on the outcomes, transport and storage temperatures are defined and used to delineating specimen requirements.

Specimen Transport

Most medical specimens sent to a reference laboratory such as Mayo Medical Laboratories are flown on passenger aircraft or cargo air carriers. A specimen that travels by air, falls under the aegis of the International Civil Aviation Organization (ICAO) and International Air Transportation Association (IATA) regulatory agencies. ICAO and IATA have established stringent rules to protect passengers and package handlers from exposure to potentially infectious substances. ICAO and IATA established 2 categories of specimens: Category A–Infectious Substances and Category B–Biological Substances. Each specimen type

requires specific packaging and handling procedures that are designed to protect anyone who has contact with the package. The shipper (laboratory sendout staff) must decide which category applies to each specimen based on these definitions:

> *Category A Substances:* An infectious substance transported in a form that, when exposure to it occurs, is capable of causing permanent disability, life-threatening illness or fatal disease to humans or animals. Examples include cultures of *Bacillus anthracis*, *Brucella abortus*, hepatitis B virus, and herpes B virus. An exposure occurs when an infectious substance is released outside of the protective packaging.
>
> *Category B Substances:* All specimens including urine, blood, swabs, and tissues, including those from patients known or suspected of being infected with HIV, hepatitis, and West Nile virus.

Packaging Overview

All specimens must be shipped in a leakproof container, regardless of risk group. Mayo Medical Laboratories provides several primary and secondary containers for packaging both category A and category B substances. For our clients' added convenience, the biohazard bags provided by Mayo Medical Laboratories are color-coded by temperature; white for ambient specimens, pink for refrigerate specimens, and yellow for frozen specimens. These bags also contain a piece of material capable of absorbing the full liquid content of the specimen(s) placed inside.

When shipping category A substances, the sendout personnel must package the specimen in a Mayo Medical Laboratories infectious mailer and temperature color-coded bag and the courier places the container in the Mayo Medical Laboratories shipping box.

For category B substances, the sendout laboratory is responsible for packaging specimens in the color-coded bags for the courier. The courier then prepares the shipper's documentation and boxes the specimens in a Mayo Medical Laboratories Styrofoam container and berry-colored shipping box. (Figure 2).

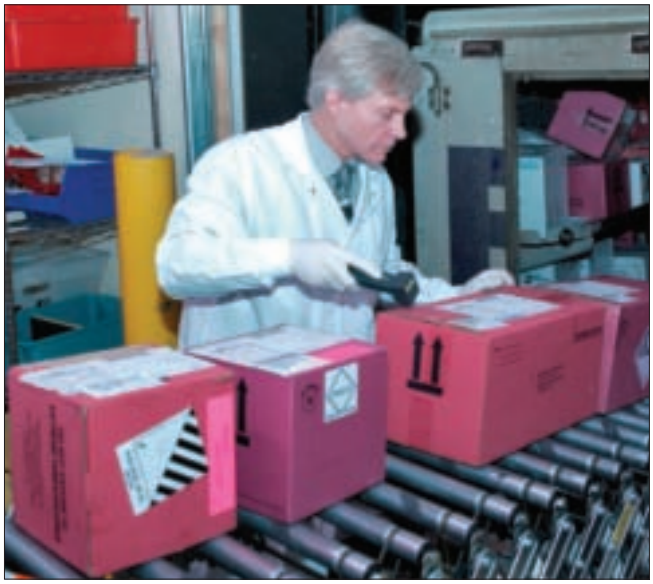

Figure 2. *Specimens arrive at Mayo Medical Laboratories in berry-colored shipping box*

Our transportation department provides detailed instructions for preparing medical specimens for shipping and works closely with clients, ground couriers, and air carriers to ensure that specimens arrive at Mayo Medical Laboratories in the most expedient, efficient, and safest manner possible. Instructions are available on our Web site (www.mayomedicallaboratories.com) or by calling the Transportation Department at 800-533-1710.

Specimen Acceptability

Upon arrival at Mayo, a specimen is initially evaluated to verify that transportation guidelines have been followed. Specimens are also evaluated for certain conditions that may render the sample unacceptable, based on the test ordered. Rejection criteria may include hemolysis, lipemia, clotted specimen, wrong specimen type, or unacceptable transport conditions. When conditions vary from established procedures, the testing laboratory is consulted to determine if the sample is acceptable to achieve accurate results. For example, several specific analytes cannot be accurately analyzed if a frozen sample has been thawed, even though thawing may be acceptable for other assays.

Conclusion

Preanalytic error prevention requires excellent communication and cooperation among all members of the health care team, from the phlebotomist who collects the specimen, to the courier who picks up the samples for transport to the testing laboratory, to the personnel receiving the specimen. The education of health care professionals involved in procedures for the collecting, handling, preparing, and transporting biological specimens is crucial to understanding the effects of preanalytic variables on specimen quality. Mayo Medical Laboratories works diligently to provide the necessary education, instructions, materials, and resources to assist our clients in educating their own health care teams. Optimal specimen condition and reliable results are achieved by collaboration between the collecting and receiving laboratories. With close attention to established procedures and instructions, preanalytic error is minimized. In turn, patient care improves.

Authored by Plumhoff EA, Masoner D, Dale JD

References

1. Plebani M, Carraro P: Mistakes in a stat laboratory: Types and frequency. Clin Chem 1997;43:1348-1351
2. Dale JC: Preanalytic variables in laboratory testing. Lab Med 1998;29:540-545
3. Lippi G, Salvagno GL, Montagnana M, et al: Phlebotomy issues and quality improvement in results of laboratory testing. Clin Lab 2006;52:217-230
4. Lippi G, Bassi A, Brocco G, et al: Preanalytic error tracking in a laboratory medicine department: results of a 1-year experience. Clin Chem 2006;52:1442-1443
5. Lippi G, Fostini R, Guidi GC: Quality improvement in laboratory medicine: extra-analytical issues. Clin Lab Med 2008;28:285-294
6. Lippi G, Banfi G, Buttarello M, et al: Recommendations for detection and management of unsuitable samples in clinical laboratories. Clin Chem Lab Med 2007;45(6): 728-736
7. Clinical and Laboratory Standards Institute. Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Sixth Edition. CLSI document 2007;H3–A6:Vol 27 No 26
8. Sheppard C, Franks N, Nolte F, et al: Improving quality of patient care in an emergency department. Am J Clin Pathol 2008;130:573-577
9. Lowe G, Stike R, Pollack M, et al: Nursing blood specimen collection techniques and hemolysis rates in an emergency department: analysis of venipuncture versus intravenous catheter collection techniques. J Emerg Nurs 2008;34:26-32

Appendix: Phlebotomy Procedure and Impact on Testing

	Procedural Steps	Impact on Testing
1	Prepare the accession order to identify all paperwork and supplies for each patient	Ensure prompt and accurate processing of forms and analysis of results
2	• Approach and identify the patient • Sanitize hands	• Identification of the patient is crucial for accurate test results • Reduce spread of infections
3	• Verify patient's fasting status, diet restrictions, and inquire if the patient has a latex sensitivity • Select appropriate gloves and tourniquet	• Some tests require fasting specimen or elimination of certain foods from the diet prior to blood draw • Hypersensitivity to latex can cause severe reaction. Use nonlatex supplies where appropriate.
4	Assemble necessary supplies and appropriate collection tubes according to test requests	• Inspect all supplies for defects and expiration dates • Select appropriate needle gauge • Select appropriate blood collection system
5	Position the patient	• For patient comfort and safety, collect specimens with the patient seated in an appropriate chair or lying down
6	Apply tourniquet and select the venipuncture site and vein	• Tourniquet placement should not exceed 2 minutes, which may result in hemoconcentration and erroneously increased levels of protein-based analytes, packed cell volume, and other cellular elements • Preferred site is antecubital fossa
7	Put on gloves	• Part of universal precautions to protect phlebotomists and other health care workers from exposure to blood-borne pathogens
8	Cleanse the venipuncture site and allow to dry	• Prevent microbiological contamination • Introduction of alcohol into specimen may cause hemolysis of specimen
9	Perform venipuncture; once blood flow begins, request the patient to open his/her hand	• Blood flow should be uninterrupted • Immediately mix collection tube containing additives by gentle inversion (end-to-end mixing 5–6 times) • Numerous inversions or vigorous shaking can cause hemolysis

10	Fill tubes using the correct order of draw	• Recommended order of draw
		  • Blood culture tube
		  • Coagulation tube (light-blue top)
		  • Serum tube with or without clot activator, with or without gel (red top)
		  • Heparin tube (green top)
		  • EDTA tube (lavender or pearl top)
		  • Glycolytic inhibitor tube (grey top)
		• Plastic or glass serum tubes containing a clot activator may cause interference in coagulation testing. Glass nonadditive serum tubes or plastic serum tubes without a clot activator may be drawn before the coagulation tube.

11	Release and remove the tourniquet	Remove as soon as possible after the blood begins to flow
12	Place the gauze pad over the puncture site	Cotton balls are not recommended because of the possibility of dislodging the platelet plug at the venipuncture site
13	Remove the needle, activate any safety feature, and dispose of the device	Follow manufacturer's directions
14	Apply pressure to the site, making sure bleeding has stopped and then bandage the arm	Watch for continued bleeding

15	Label the tubes and record time of collection	• The patient and the patient's specimen must be positively identified at the time of collection
		• Tubes must be labeled after filling with a label bearing at least the following:
		  • Patient's first and last names
		  • Identification number
		  • Date of collection
		  • Time of collection
		  • Identification of phlebotomist

16	Observe special handling requirements (if any)	• Special handling possibilities
		  • Specimen chilling
		  • Transport at 37 degrees C
		  • Protect from light

17	Send properly labeled blood collection tubes to the laboratory	Maintain proper transport conditions to preserve specimen integrity

Adapted from The Clotting Times 2004;4(1):4. Used with permission from Ledford-Kraemer, MR, Editor

2008–2009 Education Calendar

Upcoming Education Conferences . . .

Phlebotomy: Quality Service Begins with You
March 12-13, 2009
Mayo Clinic
Rochester, Minnesota

Coagulation Testing Quality
April 14-17, 2009
Marriott City Center
Minneapolis, Minnesota

16th International Surgical Pathology Symposium
May 5-8, 2009
SAS Radisson
Berlin, Germany

Practical Surgical Pathology
September 10-12, 2009
Mayo Clinic
Rochester, Minnesota

Clinical and Laboratory Update in Thrombosis and Anticoagulation
October 1-2, 2009
Kahler Hotel
Rochester, Minnesota

Integration Through Community Laboratory Insourcing
October 7-9, 2009
Hilton Orlando Bonnet Creek
Orlando, Florida

Continuous Process Improvement: Sharing our Lean Journey
November 5-6, 2009
Mayo Clinic
Rochester, Minnesota

Disease Management Strategies . . .

Cardiovascular Biomarkers—An Update
December 9, 2008
Presenter: Allan S. Jaffe, MD

Rheumatoid Arthritis: Recent Advances in Diagnosis and Management
February 10, 2009
Presenter: Harvinder S. Luthra, MD

Use of HPV in Cervical Cancer Screening
March 10, 2009
Presenter: Michael R. Henry, MD

Trace Metals: Evaluation for Heavy Metal Exposure or Nutritional Status
April 14, 2009
Presenter: Thomas P. Moyer, PhD

Cystic Fibrosis
May 12, 2009
Presenter: W. Edward Highsmith, Jr. PhD

Crohn's Disease
September 8, 2009
Presenter: TBD

Update on Diagnosis of Clostridium Difficile Infection
October 13, 2009
Presenter: Jon E. Rosenblatt, MD

Biochemical Testing Strategies for Thyroid Function
November 10, 2009
Presenter: George G. Klee, MD, PhD

Myocardial Infarction (MI) Controversies
December 1, 2009
Presenter: Allan S. Jaffe, MD

FOR MORE INFORMATION contact Mayo Medical Laboratories Education Department at 800-533-1710 or visit us at MayoMedicalLaboratories.com/education

COMMUNIQUÉ

MAYO CLINIC
Mayo Medical Laboratories

3050 Superior Drive NW
Rochester, Minnesota 55901
www.MayoMedicalLaboratories.com
800-533-1710

MC2831-1208

The *Communiqué* is published by Mayo Medical Laboratories to provide laboratorians with information on new diagnostic tests, changes in procedures or normal values, and continuing medical education programs and workshops.

A complimentary subscription of the *Communiqué* is provided to Mayo Medical Laboratories' clients. Please send address changes to communique@mayo.edu or *Communiqué*, Superior Drive Support Center, 3050 Superior Drive NW, Rochester, MN 55901, or call us at 800-533-1710.