Improving Quality and Turnaround Time of Clinical Chemistry Specimens Using Plasma

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BD
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Main Tasks of the Laboratory

- Perfect Service
- Very Reliable Results
- Highly Sensitivity and Specificity
- Cost Effective
- Broad Spectrum of Tests
- Small Amount of Sample
- FAST TAT

Specimen Quality
How Important is TAT?

- TAT represents top 3/5 categories listed by physicians as the most important

*TAT = 36.5%

<table>
<thead>
<tr>
<th>Service Category*</th>
<th>Respondents, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality/reliability of results</td>
<td>1191 (31.7)</td>
</tr>
<tr>
<td>Routine test TAT</td>
<td>554 (14.8)</td>
</tr>
<tr>
<td>Inpatient stat test TAT</td>
<td>455 (12.1)</td>
</tr>
<tr>
<td>Test menu adequacy</td>
<td>409 (10.9)</td>
</tr>
<tr>
<td>Outpatient stat test TAT</td>
<td>361 (9.6)</td>
</tr>
<tr>
<td>Accessibility of pathologists</td>
<td>160 (4.3)</td>
</tr>
<tr>
<td>Critical value notification</td>
<td>152 (4.0)</td>
</tr>
<tr>
<td>Clinical report format</td>
<td>90 (2.4)</td>
</tr>
<tr>
<td>Accessibility of laboratory staff</td>
<td>90 (2.4)</td>
</tr>
<tr>
<td>Esoteric test TAT</td>
<td>81 (2.2)</td>
</tr>
<tr>
<td>Staff courtesy</td>
<td>71 (1.9)</td>
</tr>
<tr>
<td>Phlebotomy services</td>
<td>58 (1.5)</td>
</tr>
<tr>
<td>Laboratory management responsiveness</td>
<td>34 (0.9)</td>
</tr>
<tr>
<td>Accessibility of laboratory manager</td>
<td>26 (0.7)</td>
</tr>
<tr>
<td>Courier services</td>
<td>22 (0.6)</td>
</tr>
</tbody>
</table>

* TAT indicates turnaround time.

How Important is TAT?

- TAT is on the bottom for level of satisfaction

<table>
<thead>
<tr>
<th>Service Category</th>
<th>No. of Institutions</th>
<th>10th</th>
<th>50th (Median)</th>
<th>90th</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality/reliability of test results</td>
<td>138</td>
<td>75.0</td>
<td>89.9</td>
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<td>Staff courtesy</td>
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<td>100.0</td>
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<td>Accessibility of laboratory staff</td>
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<td>66.7</td>
<td>87.6</td>
<td>100.0</td>
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<td>Accessibility of pathologist</td>
<td>137</td>
<td>69.6</td>
<td>87.5</td>
<td>100.0</td>
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<tr>
<td>Critical value notification</td>
<td>138</td>
<td>66.7</td>
<td>85.4</td>
<td>95.7</td>
</tr>
<tr>
<td>Accessibility of laboratory manager</td>
<td>136</td>
<td>65.6</td>
<td>84.6</td>
<td>100.0</td>
</tr>
<tr>
<td>Phlebotomy services</td>
<td>136</td>
<td>60.0</td>
<td>84.4</td>
<td>100.0</td>
</tr>
<tr>
<td>Test menu adequacy</td>
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<td>84.6</td>
<td>97.2</td>
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<td>Laboratory management responsiveness</td>
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<tr>
<td>Esoteric test TAT</td>
<td>136</td>
<td>33.3</td>
<td>54.5</td>
<td>80.0</td>
</tr>
</tbody>
</table>

* Higher percentile ranks indicate better relative performance.
† TAT indicates turnaround time.

### How Important is TAT?

<table>
<thead>
<tr>
<th>Most Important Category</th>
<th>Respondents, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stat test TAT</td>
<td>2432 (37.8)</td>
</tr>
<tr>
<td>Accuracy of test results</td>
<td>981 (15.2)</td>
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<tr>
<td>Abnormal results notification</td>
<td>523 (8.1)</td>
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<td>Telephone courtesy</td>
<td>487 (7.6)</td>
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<td>Phlebotomy responsiveness</td>
<td>455 (7.1)</td>
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<td>Phlebotomy courtesy toward patients</td>
<td>404 (6.3)</td>
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<tr>
<td>Routine test TAT</td>
<td>364 (5.7)</td>
</tr>
<tr>
<td>Ability to answer telephone questions</td>
<td>292 (4.5)</td>
</tr>
<tr>
<td>Promptly answered phones</td>
<td>183 (2.8)</td>
</tr>
<tr>
<td>Phlebotomy courtesy toward nursing</td>
<td>94 (1.5)</td>
</tr>
<tr>
<td>Laboratory management responsiveness</td>
<td>94 (1.5)</td>
</tr>
<tr>
<td>Accessibility of laboratory management</td>
<td>71 (1.1)</td>
</tr>
<tr>
<td>Laboratory POC support</td>
<td>55 (0.9)</td>
</tr>
</tbody>
</table>

* TAT indicates turnaround time; POC, point of care.

- Stat TAT represents most important category listed by nurses

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How Important is TAT?

- TAT is on the bottom for level of satisfaction

Table 4. Distribution of Percentage of Very Satisfied/Usually Satisfied Ratings for Each Interaction Category

<table>
<thead>
<tr>
<th>Category</th>
<th>10th</th>
<th>50th (Median)</th>
<th>90th</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accuracy of test results</td>
<td>79.2</td>
<td>90.9</td>
<td>97.9</td>
</tr>
<tr>
<td>Phlebotomy courtesy toward patients</td>
<td>64.3</td>
<td>86.5</td>
<td>98.0</td>
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<tr>
<td>Phlebotomy courtesy toward nursing</td>
<td>58.5</td>
<td>80.4</td>
<td>95.5</td>
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<tr>
<td>Abnormal results notification</td>
<td>60.4</td>
<td>79.4</td>
<td>91.8</td>
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<tr>
<td>Laboratory POC support</td>
<td>45.0</td>
<td>74.3</td>
<td>92.3</td>
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<tr>
<td>Telephone courtesy</td>
<td>51.5</td>
<td>74.0</td>
<td>88.0</td>
</tr>
<tr>
<td>Ability to answer telephone questions</td>
<td>48.5</td>
<td>73.3</td>
<td>89.4</td>
</tr>
<tr>
<td>Promptly answered phones</td>
<td>44.0</td>
<td>72.0</td>
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</tr>
<tr>
<td>Routine test TAT</td>
<td>40.9</td>
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<tr>
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<td>85.0</td>
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<tr>
<td>Laboratory management responsiveness</td>
<td>35.7</td>
<td>63.7</td>
<td>83.2</td>
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<tr>
<td>Stat test TAT</td>
<td>26.0</td>
<td>49.0</td>
<td>73.7</td>
</tr>
</tbody>
</table>

* Higher percentile ranks indicate better relative performance.
† POC indicates point of care; TAT, turnaround time.

Current Serum vs Plasma Option

Chemistry

Clot activator
30 min clot time

Centrifuge
1,100 - 1,300g
10 min

Serum

Lithium Heparin
Mix and spin

Centrifuge
1,100 - 1,300g
10 min

Plasma
How To Reduce TAT?

- Fast Analytical Phase
- Speed Up Sample Transport
- Reduce Preanalytical Handling & Processing
- Use Plasma
Polling Question

Which sample does your laboratory use?

A. Only serum
B. Only plasma
C. Mainly serum with some plasma
D. Mainly plasma with some serum
E. Almost even split
F. Don’t know
Turnaround Time

➢ Recommended clotting times for serum blood collection tubes generally range from 30-60 minutes.

➢ Use of plasma allows laboratories to process and test specimens upon receipt, while avoiding latent fibrin formation due to incomplete clotting.
Serum Specimen Quality

➢ Specimen quality has been another factor prompting some laboratories to switch to plasma.

➢ Serum specimens are subject to latent fibrin formation when clotting is inadequate.
  ➢ insufficient clotting time
  ➢ patients receiving anticoagulant or thrombolytic therapy

➢ Fibrin can range from thin strands to large cloud-like masses.
Fibrin / Micro clots

- Visible clot
- Fibrin mass
- Fibrin strands
- “Microclots”

**SERUM**
Incomplete clotting fibrin

**PLASMA**
Micro clots from filtered heparinized specimen
Fibrin and Gel globules

• Can cause significant disruption to instrument operation and process workflow.
Issues Due To Fibrin

➢ Physical obstruction of sampling probe
➢ Insufficient sampled volume
➢ Gradual deposition of fibrin in reaction chambers or pathways
➢ Interference with measurement systems or reagents

➢ Potential consequences: instrument downtime, failure to provide test results, or erroneous test results.
## Fibrin – Instrument Operation

<table>
<thead>
<tr>
<th>Location</th>
<th>Event</th>
<th>Type of Interference</th>
<th>Potential Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sampling Probe</td>
<td>Aspiration of fibrin causing probe obstruction</td>
<td>Physical</td>
<td>- Sampling problem, insufficient quantity aspirated</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Erroneous results</td>
</tr>
<tr>
<td>Reaction Pathway or Reaction Chamber</td>
<td>Aspiration of &quot;micro clots&quot; not sufficiently large to obstruct probe</td>
<td>Physical, chemical or immunological</td>
<td>- Gradual deposition of fibrin in reaction pathway; &quot;plaque&quot;</td>
</tr>
<tr>
<td></td>
<td>Latent fibrin formation inside instrument</td>
<td></td>
<td>- Build up leads to obstruction</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Even with no obstruction, potential interference from light scattering or reagent interference</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Erroneous results</td>
</tr>
</tbody>
</table>
Addressing Fibrin Issues

➢ Approaches to minimize the impact of fibrin in serum specimens often require user intervention, increase TAT, and may not be recommended.

➢ To help reduce these issues, some laboratories have switched to plasma.

➢ However, plasma specimens also have unique characteristics concerning specimen quality and integrity.
Plasma Trends

➢ World wide generally increasing use of plasma

➢ Increasing use of plasma in some European countries

➢ US also increasing number of labs are moving to plasma due to TAT
Plasma Trends
Gel Movement

The presence of a solid clot in serum gel tubes also leads to a difference in the movement of gel during centrifugation.

**Serum:** Gel must move up and around the clot, against the tube wall.

**Plasma:** Gel moves up in pieces similar to a ‘lava lamp’.
Simulated Gel Movement

serum tube

plasma tube
Plasma Specimen Quality

- Separation of blood based on density gradient:
  platelets (least dense) > white blood cells > red blood cells (most dense)

- Platelets most abundant followed by WBC
- Fibrin – where present, generally exists in form of thin strands
- May lead to formation of 'microclots'
Plasma Specimen Quality

• As a result of the potential for variable amounts of cells, platelets, fibrin, and WPM, heparin plasma is generally a more complicated matrix to manage than serum.

• A proper understanding of the factors that influence plasma specimen quality is needed.
What type of specimens are these?
Ideal Plasma Specimen

• Ideal plasma specimen would be one which is cell/platelet free and in which the anticoagulant functions to inhibit clotting and fibrin formation for extended periods of time

• Often not attained with heparin plasma specimens
Problem:
Supernatant Balance

TAT

Specimen Quality
Plasma Test Results

In general, most assays in clinical chemistry are compatible with both serum and heparin plasma, (85 – 95% of chemistry assays) and test results are sufficiently equivalent that the same reference ranges can be used.

However for certain assays or test methods, plasma specimens may be unacceptable, or differences in results may be sufficient to warrant a change in reference range.
Specimen effects due to clotting

- Clotting is proteolytic process
- During clotting, some cells will lyse

Serum Potassium around 0.7 mmol/L higher than plasma
Serum ref range: 3.5 – 5.2 mmol/L
Plasma ref range: 3.5 – 4.5 mmol/L
Potassium and phosphorus increased in serum due to release from cells/platelets during clotting.

A linear correlation has been shown between platelet count and the increase in serum potassium.


Total Protein

➢ Slightly increased in plasma due to presence of fibrinogen.


Other Tests

➢ Differences in certain enzymes (e.g., LD, ALKP, AST) may be seen.

➢ Lithium/sodium increased with use of lithium or sodium heparin.

➢ Interference from fibrinogen may also make plasma an unsuitable specimen for certain protein analysis methods (e.g., SPEP - protein electrophoresis).

➢ Heparin may interfere with certain immunoassays.

Effects over Time

- Reduced stability in plasma of certain common analytes that are involved in cell/platelet-mediated metabolic processes and/or are present in higher concentrations in cells or platelets.

- Serum-plasma differences may be evident with these analytes depending on plasma cell/platelet content and time between centrifugation and testing.
Heparin plasma specimens with increased cell/platelet concentrations exhibit reduced stability of certain common analytes.

Analytes affected are involved in cell/platelet-mediated metabolic processes and/or are present in higher concentration in cells or platelets.

### Table 6. Storage Stability of Selected Analytes in Lithium Heparin Plasma (mean ± sd)*

<table>
<thead>
<tr>
<th>ANALYTE</th>
<th>UNITS</th>
<th>TIME 0</th>
<th>TIME 24h</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td><strong>Allquot from Non-Gel Tube</strong></td>
<td><strong>Gel Tube</strong></td>
</tr>
<tr>
<td>Glucose</td>
<td>mg/dL</td>
<td>100.8 ± 50.8</td>
<td>98.3 ± 50.8</td>
</tr>
<tr>
<td>Potassium</td>
<td>mmol/L</td>
<td>3.87 ± 0.26</td>
<td>3.96 ± 0.27</td>
</tr>
<tr>
<td>Carbon Dioxide</td>
<td>mmol/L</td>
<td>20.6 ± 2.2</td>
<td>19.6 ± 2.0</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>mg/dL</td>
<td>3.06 ± 0.56</td>
<td>3.11 ± 0.55</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>mg/dL</td>
<td>134.4 ± 91.1</td>
<td>131.8 ± 88.7</td>
</tr>
<tr>
<td>GGT</td>
<td>U/L</td>
<td>32.9 ± 51.2</td>
<td>33.1 ± 49.9</td>
</tr>
<tr>
<td>AST</td>
<td>U/L</td>
<td>21.6 ± 7.4</td>
<td>22.5 ± 7.1</td>
</tr>
<tr>
<td>LD</td>
<td>U/L</td>
<td>139.1 ± 16.6</td>
<td>154.8 ± 16.5</td>
</tr>
</tbody>
</table>
Dependence on Handling and Test Methodology

The occurrence and magnitude of serum-plasma differences can depend on specimen handling and processing procedures and/or the specific instrument/assay methodology used.

Plasma specimens may also exhibit an increased frequency of duplicate errors with certain instrument/test combinations, due to platelets, cell aggregates, or microclots.


Fibrin – Test Interference

- Falsely elevated Troponin-I due to fibrin in serum samples.¹
- Duplicate errors in LD due to micro clots or cell aggregates in plasma samples.²
- Erroneous FSH results caused by insufficient clotting of serum specimens and fibrin formation within analyzer reaction vessel.³

Serum vs. Plasma

- nearly cell-free
- good storage stability for most analytes
- wide range of assays available

- shorter TAT: can be centrifuged immediately
- faster gel movement in gel tubes
- more reproducible gel barrier formation
- increase supernatant yield 15-20% > serum
Serum vs. Plasma

- longer TAT
- instrument or test interference from fibrin, esp. with anticoagulation therapy
- may cause pseudohyperkalemia
- analytical variation due release from cells/platelets during clotting

- Higher cell counts
- reduced storage stability for certain analytes
- fibrin formation during storage
- interference from anticoagulant
- interference from fibrinogen
BD Barricor™

Introduction

What is BD Barricor™?

- BD Barricor™ is a single-use, plastic evacuated tube with a mechanical separator
- Used to collect, separate, transport and process venous blood specimens
- Provides a high-quality plasma sample for chemistry determinations and TDM monitoring for *in vitro* diagnostic use
BD Barricor™
Mechanical separator

Elastomer top

High-density base

Insert separator TDM compatible
BD Barricor™
How it Works