Lactate is measured amperometrically. The enzyme lactate oxidase, immobilized in the lactate biosensor, selectively converts lactate to pyruvate and hydrogen peroxide ($H_2O_2$). The liberated hydrogen peroxide is oxidized at a platinum electrode to produce a current which is proportional to the sample lactate concentration.

$$\text{L-Lactate} + O_2 \xrightarrow{\text{Lactate Oxidase}} \text{Pyruvate} + H_2O_2$$

$$H_2O_2 \xrightarrow{\text{Platinum electrode}} 2H^+ + O_2 + 2e^-$$

See below for information on factors affecting results. Certain substances, such as drugs, may affect analyte levels in vivo.\(^1\)

If results appear inconsistent with the clinical assessment, the patient sample should be retested using another cartridge.

**Intended Use**

The test for lactate, as part of the i-STAT System, is intended for use in the in vitro quantification of lactate in arterial, venous, or capillary whole blood.

**Contents**

Each i-STAT cartridge contains one reference electrode (when potentiometric sensors are included in the cartridge configuration), sensors for the measurement of specific analytes, and a buffered aqueous calibrant solution that contains known concentrations of analytes and preservatives. For cartridges that contain a sensor for the measurement of lactate, a list of reactive ingredients is indicated below:

- Lactate
- Lactate Oxidase

**Metrological Traceability**

The i-STAT System test for lactate measures L-lactate amount-of-substance concentration in the plasma fraction of arterial, venous, or capillary whole blood (dimension mmol L\(^{-1}\)) for in vitro diagnostic use. Presently, no international conventional reference measurement procedure or international conventional calibrator for lactate is available. Lactate values assigned to i-STAT’s controls and calibration verification materials are traceable to i-STAT’s working calibrator prepared from sodium L-lactate (Sigma-Aldrich Fluka, >99 % purity). i-STAT System controls and calibration verification materials are validated for use only with the i-STAT System and assigned values may not be commutable with other methods. Further information regarding metrological traceability is available from i-STAT Corporation.

**Expected Values**

<table>
<thead>
<tr>
<th>Test/Abbreviation</th>
<th>Units*</th>
<th>Reportable Range (arterial)</th>
<th>Reference Range (venous)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactate/Lac</td>
<td>mmol/L</td>
<td>0.30 – 20.00</td>
<td>0.36 – 1.25</td>
</tr>
<tr>
<td></td>
<td>mg/dL</td>
<td>2.7 – 180.2</td>
<td>3.2 – 11.3</td>
</tr>
</tbody>
</table>

---

1. See below for information on factors affecting results. Certain substances, such as drugs, may affect analyte levels in vivo.
To convert a lactate result from mmol/L to mg/dL, multiply the mmol/L value by 9.01.

The i-STAT reference ranges for whole blood listed above are similar to reference ranges derived from serum or plasma measurements with standard laboratory methods.

The reference range shown above is intended to be used as a guide for the interpretation of results. Since reference ranges may vary with demographic factors such as age, gender and heritage, it is recommended that reference ranges be determined for the population being tested.

* The i-STAT System can be configured with the preferred units.

**Clinical Significance**

Elevated levels of lactate are mainly found in conditions of hypoxia such as shock, hypovolemia, and left ventricular failure; in conditions associated with diseases such as diabetes mellitus, neoplasia, and liver disease; and in conditions associated with drugs or toxins such as ethanol, methanol, or salicylates.2

**Performance Characteristics**

The typical performance data summarized below was collected in health care facilities by health care professionals trained in the use of the i-STAT System and comparative methods.

Precision data were collected using NCCLS guideline EP5-A3. Duplicates of each level of control were tested on three lots of cartridges over 20 days for a total of 120 replicates.

Method comparison data were collected using NCCLS guideline EP9-A4. Venous blood samples, collected in sodium heparin Vacutainer® tubes, and arterial blood samples, collected in blood gas syringes, were analyzed in duplicate on the i-STAT System. In the plasma study, a portion of each specimen was centrifuged, and the separated plasma was analyzed on the comparative method.

Deming regression analysis5 was performed on the first replicate of each sample. In the method comparison table, n is the number of specimens in the data set, Sxx and Syy refer to the estimates of imprecision based on the duplicates of the comparative and the i-STAT methods respectively, Sy.x is the standard error of the estimate, and r is the correlation coefficient.*

Interference studies were based on NCCLS guideline EP7.6

*The usual warning relating to the use of regression analysis is summarized here as a reminder: For any analyte, “if the data is collected over a narrow range, the estimate of the regression parameters are relatively imprecise and may be biased. Therefore, predictions made from these estimates may be invalid”.3 The correlation coefficient, r, can be used as a guide to assess the adequacy of the comparative method range in overcoming this problem. As a guide, the range of data can be considered adequate if r>0.975.

<table>
<thead>
<tr>
<th>Precision Data (mmol/L)</th>
<th>Aqueous Control</th>
<th>n</th>
<th>Mean</th>
<th>SD</th>
<th>%CV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 1</td>
<td>120</td>
<td>6.35</td>
<td>0.08</td>
<td>1.21</td>
<td></td>
</tr>
<tr>
<td>Level 3</td>
<td>120</td>
<td>0.81</td>
<td>0.03</td>
<td>3.27</td>
<td></td>
</tr>
</tbody>
</table>
Method Comparison

<table>
<thead>
<tr>
<th>Method Comparison (mmol/L)</th>
<th>Radiometer ABL 725 (whole blood vs. whole blood)</th>
<th>Hitachi 917 (i-STAT whole blood vs. Hitachi plasma)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>47</td>
<td>47</td>
</tr>
<tr>
<td>Sxx</td>
<td>0.123</td>
<td>0.084</td>
</tr>
<tr>
<td>Syy</td>
<td>0.136</td>
<td>0.079</td>
</tr>
<tr>
<td>Slope</td>
<td>1.02</td>
<td>1.06</td>
</tr>
<tr>
<td>Int't</td>
<td>0.12</td>
<td>-0.32</td>
</tr>
<tr>
<td>Sy.x</td>
<td>0.18</td>
<td>0.17</td>
</tr>
<tr>
<td>Xmin</td>
<td>0.80</td>
<td>1.77</td>
</tr>
<tr>
<td>Xmax</td>
<td>14.20</td>
<td>14.24</td>
</tr>
<tr>
<td>r</td>
<td>0.998</td>
<td>0.997</td>
</tr>
</tbody>
</table>

Factors Affecting Results*

Special collection procedures are necessary to prevent changes in lactate both during and after the blood is drawn. For steady state lactate concentrations, patients should be at rest for 2 hours and fasting. Venous samples should be obtained without the use of a tourniquet or immediately after the tourniquet is applied. Both venous and arterial samples may be collected into heparinized syringes.

Samples for lactate should be analyzed immediately on drawing as lactate increases by as much as 70% within 30 minutes at 25 °C as a result of glycolysis.2

Interferent | Effect
---|---
Bromide 25 mmol/L (200 mg/dL) bromide will decrease lactate results by 40%.
Cysteine 6.4 mmol/L (101 mg/dL) cysteine will decrease lactate results by 11%.
Hydroxyurea (Droxia®, Hydrea®) Hydroxyurea may cause significant errors in the measurement of lactate with the i-STAT System. Consider using an alternative method to measure lactate when patients have been administered hydroxyurea. See note (1) below for typical uses of this drug and note (2) below for details of the interference.
Glycolic Acid: Glycolic acid can cause falsely increased lactate results on the i-STAT System. Preliminary studies indicated that 10 mmol/L glycolic acid increased lactate from 1.45 mmol/L to 3.41 mmol/L. See note (3) for details.

*It is possible that other interfering substance may be encountered. These results are representative and your results may differ somewhat due to test-to-test variation. The degree of interference at concentrations other than those listed might not be predictable.

Notes:

1) Hydroxyurea is a DNA synthesis inhibitor used in the treatment of various forms of cancer, sickle cell anemia, and HIV infection. This drug is used to treat malignancies including melanoma, metastatic ovarian cancer, and chronic myelogenous leukemia. It is also used in the treatment of polycythemia vera, thrombocytopenia, and psoriasis. At typical doses ranging from 500 mg to 2 g/day, concentrations of hydroxyurea in patients’ blood may be sustained at approximately 100 to 500 µmol/L. Higher concentrations may be observed soon after dosing or at higher therapeutic doses.

2) For every 100 µmol/L hydroxyurea in the whole blood sample, lactate will be increased by approximately 0.16 mmol/L, up to a whole blood hydroxyurea concentration of at least 921 µmol/L (maximum concentration tested). The magnitude of the bias is independent of the lactate level over a range of at least 2.8 mmol/L to 16.0 mmol/L.
3) Glycolic acid is a product of ethylene glycol metabolism. Unexpected increased lactate concentrations caused by glycolic acid may be a clue to the possibility of ethylene glycol ingestion as the cause of an otherwise unknown high anion gap metabolic acidosis.  

In a study of 35 patients who had ingested ethylene glycol, initial glycolic acid concentrations of 0 to 38 mmol/L corresponded to ethylene glycol levels of 0.97 - 130.6 mmol/L.

Acetaldehyde up to 0.6 mg/dL (0.14 mM), acetylsalicylic acid up to 50 mg/dL (2.8 mM), ascorbic acid up to 3 mg/dL (0.17 mM), β-hydroxybutyric acid up to 202 mg/dL (16 mM), dopamine up to 13 mg/dL (0.85 mM), formaldehyde up to 1.2 mg/dL (0.40 mM), glycine up to 98 mg/dL (13 mM), pyruvic acid up to 2.6 mg/dL (0.24 mM), and uric acid up to 25 mg/dL (1.5 mM) were tested and found not to interfere with lactate results. Hematocrit levels between 25 and 67% were tested and found not to interfere with lactate results.

References