

## Have you measured lactate in your sick obstetrics and gynecology patients during the past year?

➡ Measuring lactate can facilitate the rapid identification of the sickest obstetrics and gynecology patients



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Lactate measurement is widely used in emergency departments (EDs) and intensive care units (ICUs) to facilitate the early diagnosis and management of sepsis, severe trauma, ischemic bowel, and necrotizing fasciitis. Measuring lactate levels is much less commonly utilized in the practice of obstetrics and gynecology; increasing measurement in our practices may improve our early recognition and treatment of women with severe sepsis and other serious diseases.

### Lactate physiology

The metabolism of glucose in the Embden-Meyerhof pathway results in the production of pyruvate and the high-energy compounds ATP and NADH. Pyruvate can enter 3 alternative metabolic pathways: 1) the mitochondrial Krebs cycle, 2) conversion to lactate in the cell cytosol, or 3) conversion back to glucose in the process of gluconeogenesis.

Under aerobic conditions, most pyruvate enters the Krebs cycle and little is converted to lactate. Molecular oxygen is an absolute requirement for Krebs cycle activity. Under anaerobic conditions, pyruvate cannot enter the Krebs cycle and is preferentially converted to lactate.<sup>1</sup>

An elevated lactate level is a sensitive marker for tissue hypoxia caused by a variety of diseases, including sepsis, trauma, ischemic bowel, and necrotizing fasciitis. With sepsis, additional mechanisms also contribute to the increase in lactate, including increased glycolysis, impaired lactate clearance, and activation of inflammatory cells that shift cellular metabolism toward lactate production.<sup>2,3</sup>

The normal range for venous plasma lactate in adults is 0.5 to

2.2 mM, although the normal range may vary because of differences in local laboratory methods. Arterial, capillary, and venous lactate are all highly positively correlated.<sup>4</sup> Venous lactate concentrations between 2.3 and 3.9 mM are suggestive of mild physiologic dysfunction, and values  $\geq 4.0$  mM are consistent with severe physiologic dysfunction. In hospitalized patients, sepsis is one of the most common causes of a lactate level  $\geq 4$  mM.<sup>5</sup>

In many patients with an elevated lactate concentration the anion gap is also increased—but this is not always the case. In fact, in one large observational study, among patients with sepsis and a lactate concentration  $\geq 4$  mM, approximately 25% had a normal bicarbonate level and normal anion gap.<sup>6</sup>

### Elevated lactate levels applied in obstetric and gynecologic practice

#### **CASE 1** Obstetric practice:

#### **Hernia identified during labor**

A 30-year-old woman (G1P0) presents in early labor at 37 weeks' gestation. Two years prior to the pregnancy she

## Instant Poll



Have you ever measured lactate on a woman in your practice? Did the lactate level help to guide diagnosis and treatment decisions?

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had a Roux-en-Y gastric bypass and lost more than 100 lb. In addition to reporting lower abdominal pain occurring during contractions, she reports the new onset of mid-epigastric pain. A surgical consult is requested. The initial white blood cell count is 6,290 per uL, and the lactate level is 1.0 mM.

The surgeon consulted orders a computed tomography (CT) scan with oral contrast, but the patient has difficulty retaining the oral contrast due to her nausea, delaying the performance of the CT scan. Three hours following admission a follow-up lactate measurement is 3.3 mM, and an emergency CT scan is performed.

The CT scan shows an internal hernia with swirling of the mesenteric vessels and twisting of the small bowel mesentery. An urgent cesarean delivery and repair of the internal hernia is performed.

The patient and her newborn do well postoperatively. The postoperative lactate level is 0.8 mM.

In pregnant women with a past history of a Roux-en-Y gastric bypass and abdominal discomfort who are in labor it is challenging to rapidly diagnose internal hernias and other bowel problems.<sup>7-9</sup> In this case, the increased lactate level from 1.0 mM to 3.3 mM raised concern for ischemic bowel and triggered the emergency CT and urgent exploratory laparotomy and cesarean delivery.

Up to 14% of maternal deaths in the United States are due to infection.<sup>10</sup> In many of these cases, there is a delay in sepsis recognition because previously healthy pregnant women with sepsis may not manifest classic signs such as fever, hypotension, or mental status changes until late in the disease course. Measurement of lactate can facilitate the early recognition of severe sepsis in pregnant women, thereby accelerating and focusing their treatment.<sup>11</sup>

To reduce mortality due to sepsis, aggressive intervention needs to occur within the first 6 hours following the onset of the infection.

**CASE 2 Gynecologic practice: Bacterial infection identified in the presence of abdominal pain and vomiting**

A 40-year-old woman presents to the ED 5 days following a myomectomy, with nausea, vomiting, and abdominal pain. Her vital signs reveal: temperature, 98.4°F (36.9°C); heart rate, 122 bpm; blood pressure, 115/70 mm Hg; and white blood cell count, 6,270 per uL. Her lactate level is 4.0 mM. She is admitted to the ICU with a presumptive diagnosis of severe sepsis and treatment with broad-spectrum antibiotics is initiated. Twenty-four hours following admission, gram-negative rods are identified in blood cultures that are later identified to be *Bacteroides fragilis*.

For the past 2 decades there has been a concerted national effort to reduce mortality caused by sepsis through early diagnosis and aggressive treatment of sepsis in an ICU setting. Observational studies have reported that an elevated lactate level is an excellent early biomarker for sepsis and may be observed prior to the onset of fever, elevated white blood cell count, or hypotension.<sup>6</sup> For example, in one large study of patients with sepsis and a lactate measurement  $\geq 4$  mM, only 50% of patients had a systolic blood pressure  $< 90$  mm Hg.

Elevated lactate levels also are associated with an increased risk of death. Among 13,932 consecutive patients admitted to an ICU in Alberta, Canada, the mortality rate among patients with a venous or arterial lactate  $> 2$  mM was 20%, compared with a mortality rate of

5% for patients with a lactate level  $\leq 2$  mM.<sup>12</sup> In a study of 1,278 patients with infection admitted to the hospital from the ED, mortality increased as baseline lactate concentration rose. For lactate concentrations of 0 to 2.4, 2.5 to 3.9, and  $\geq 4.0$  mM, mortality rates were 5%, 9%, and 28%, respectively.<sup>13</sup>

In patients with sepsis, serial measurement of lactate can help to guide treatment. In a randomized trial, 348 patients admitted to an ICU with a lactate  $\geq 3$  mM were randomly assigned to standard treatment, in which the clinicians had no knowledge of patients' lactate levels, or to an experimental group, in which the clinicians were provided lactate measurement results every 2 hours. Compared with clinicians in the control group, the clinicians with access to frequent lactate measurements administered more fluids and vasodilators to their patients. Compared with patients in the control group, the hospital mortality rate was lower when the clinicians had access to frequent lactate measurements (34% vs 44%, respectively; adjusted hazard ratio, 0.61; 95% confidence interval, 0.43–0.87;  $P = .0006$ ).<sup>14</sup>

### Elevated lactate levels in the fetus and newborn

The physiologic status of the newborn is routinely assessed with the Apgar score. Umbilical artery and venous blood gases, including measurement of pH, are often used as a corroborating biomarker. Most studies report that umbilical artery or vein lactate measurement is as useful as a pH measurement in assessing newborn physiologic status. The normal range of lactate in fetuses and newborns is not precisely defined, with values between 3.5 and 7 mM being cited as the upper limit of normal.<sup>15-18</sup>


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In many countries (but not the United States), in utero fetal status during labor is assessed by fetal scalp sampling of blood and measurement of either pH or lactate. Fetal scalp sampling is difficult and often very little blood is obtained, making it difficult to measure pH. A Cochrane review reported that in 2 randomized trials, fetal scalp sampling produced a successful measurement of lactate in 99% of attempts, while a pH result could only be obtained in

79% of cases due to an inadequate volume of blood or clotted blood.<sup>19</sup>

## Increased lactate measurement can help our patients

Measuring lactate in order to rapidly identify patients with major physiologic derangements is practiced widely in EDs and ICUs. There is significant opportunity to increase the use of lactate measurement in

obstetrics and gynecology. Increasing this use will help to rapidly identify women with severe sepsis and other diseases, leading to more rapid intervention and improved outcomes. 



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