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Citation Classic

Forty-Five-Year Evolution of Stat Blood and Plasma Lactate Measurement to Guide Critical Care

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Featured Article: Marbach EP, Weil MH. Rapid enzymatic measurement of blood lactate and pyruvate: use and significance of metaphosphoric acid as a common precipitant. Clin Chem 1967;13:314–25.[2]

The measurement of oxygen deficits, which is reflected in the onset and severity of lactic acidosis, has had wide application in exercise physiology. Measurement of blood or plasma lactate, specifically the measurement of lactate/pyruvate ratios and subsequently excess lactate, became clinically important assays in the 1960s after these parameters were demonstrated to be of value in the evaluation and management of critically ill and injured patients. The measurements, although laborious and time-consuming, were regarded as quantitative with respect to the severity of anaerobic metabolism and therefore predictive of the prognosis of patients with major impairment in the blood circulation, especially during the states of low blood flow of circulatory shock *(1)*. Reduced oxygen availability associated with reduced blood flow, and therefore reduced tissue perfusion and consequent cellular hypoxia, triggered the production of lactic acid, the dead end of the energy chain.

Traditional measurements of lactate and pyruvate had been performed on deproteinized arterial blood with the colorimetric method of Barker and Summerson *(2)*, which typically required up to 8 h to complete. The time required constrained the usefulness of this measurement, the major role of which was that of an urgent ("stat") measurement to guide the clinician in the management of patients with immediately life-threatening injuries and illnesses.

Our effort therefore focused on the automation of lactate and pyruvate analyses to expedite the availability of the results, and we used a modification of the enzymatic technique for this purpose. Adding blood directly to a cold metaphosphoric acid solution (50 g/L) facilitated and expedited the analysis of both lactate and pyruvate, as described in our 1967 report highlighted here. The results were then available to the clinician within as little as 20 min, thereby realizing more closely the goals of a stat measurement *(3)*.

Because the initial intent of our effort was on the stat measurement of lactate and pyruvate and the computation of lactate excesses as proposed by Huckabee *(4)*, we initially analyzed both lactate and pyruvate *(1)*. When excess lactate was <1 mmol/L, 82% of the patients with clinical features of circulatory shock survived. If the concentration was between 1 and 2 mmol/L, 60% survived. If it was 2–4 mmol/L, 26% survived, and only 11% survived if the concentration of excess lactate exceeded 4 mmol/L.

Subsequent clinical studies provided persuasive data that routine measurement of pyruvate—to report the calculated "excess lactate" *(4)*—did not improve on the predictive value of lactate alone. The prognostic value of lactate measurement *(5)*, especially when serial measurements were obtained, increasingly served to guide the clinical management of critically ill patients. After the predictive value of the lactate measurement was widely confirmed, measurement of blood or plasma lactate was increasingly incorporated into stat measurements in panels for emergency and critical-care settings, which typically included blood gas, basic chemistry, and hematology analyses *(6)*.

Over the ensuing 20 years, electrode methods of lactate measurement further facilitated and expedited the measurement of and expanded the clinical demand for stat lactate measurements. The measurement of lactate has been incorporated into routine point-of-care testing in emergency and critical-care settings, in which a panel of results can be available within 5 min *(7)*. Lactate presently serves as the best-available single clinical measurement of the severity of the oxygen deficit reflecting failure of adequate substrate delivery; it is widely used to guide life-sustaining interventions in emergency and critical-care settings, specifically in diagnosing and estimating the severity of low-flow circulatory shock states.

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[2] This article has been cited more than 580 times since publication.
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