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SHORT COMMUNICATION

The rise of lactic acid, from a pharmacist's laboratory to entry into the central nervous system

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Abstract
Brief historical review of lactic acid: since its discovery in the laboratory of Scheele, passing the role in muscle and systemically observed by scientists Friherre Jons Jakob Berzelius, Araki, Meyerhof, Margaria, Cori until joining and role in the Nervous System Central by scientists Davis, Brooks, Connet, Richardson, Donovan, Magistretti and Pellerin.

Keywords Lactate · Central nervous system · History of medicine

Brief historical review of lactic acid

Carl Wilhelm Scheele, the Swedish chemist, managed to isolate an element that he called "lactic" or "concerning milk" for the first time in relatively impure condition in 1780, while observing sample of acidic milk. He was actually identifying what would later be called "lactic acid".

However, the true chemical name of lactic acid is 2-hydroxypropanoic acid [1] (Fig. 1).

The impurity of Scheele's original sample brought about considerable criticism, to the extent that it questioned its actual existence. Several experts maintained that what Scheele had actually found was nothing more than an impure sample of acetic acid.

Around 1810, other chemists verified the presence of lactic acid in other organic tissues, such as fresh milk, bovine meat and blood [2].

Friherre Jöns Jakob Berzelius invented its chemical formula in 1833.

It was only stated in 1869 that lactic acid exists in several optical isomers (D- and L-isomers). The fermentation processes were the subject of the first scientific investigations about biochemistry and the production of lactic acid [2].

Later, Berzelius and then Araki showed that concentrations of lactic acid were also found in muscle tissue of exhausted animals and that the amount of lactic acid was directly proportional to the activation of the exercised muscle, a parameter that would later be associated with the availability of O_2 [2].

Studies carried out by Hill's group in London and by Meyerhof's group (from whom the glycolytic pathway in red blood cells takes its name) in Heidelberg, and later in 1933, by Margaria at Harvard, brought with them a decisive turning point for the life of lactic acid.

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Fig. 1 Image of some authors (missing authors have not been found) who have been dealing with lactic acid

These studies earned Hill and Meyerhof the prestigious Nobel Prize.

In a review from 1923, Hill and Meyerhof described the lactic acid cycle, describing the changeover from glucose to lactate and then back to glucose. The authors associated the production of lactic acid with the lack of oxygen and coined the term "oxygen deficit".

The concept of "oxygen deficit" was the hinge pin for understanding muscular physiology until a decade ago.

Although this was later found to be a mistaken concept, the data obtained by Hill and Meyerhof were the maximum that could be obtained with the knowledge and instruments available at that time. In fact, the existence of adenosine triphosphate (ATP) was still unknown, and to the contrary, it was believed that small amounts of lactic acid aided muscle contraction, while high concentrations worsened it [3].

The Cori couple (1929–1933), on the other hand, proved the existence of a cycle that took their name, the *Cori cycle,* wherein the lactate was converted into glycogen in the liver.

Davis (1985) noted that during muscle work carried out on average between 60 and 75% of VO_{2max}, the individuals examined showed an accumulation of lactate in their blood, thus hypothesizing the existence of an anaerobic threshold.

The theory of the anaerobic threshold did not clash with the concept of O_2 deficit postulated by Hill, and led him to think that when fast fibres were involved, with lower oxidation capacities, an oxygen deficit was formed.

Rodolfo Margaria (1901–1983), a milestone in the history of physiology, proved the role of lactic acid in muscle contraction.

He showed that the period of the oxygen debt is characterized by two phases: a first phase of rapid decrease in oxygen consumption and unchanged lactic acid concentration (alactacid oxygen debt with creatine phosphate resynthesis), and a second phase marked by the slow decrease in both oxygen consumption and lactic acid concentration (lactic acid debt with lactic acid removal [4].

In 1985 Brooks, and in 1986 Connet, observed the presence of lactate (given that, at physiological pH level, this molecule is found in ionic form) in the muscles of dogs stimulated in the presence of O_2.

Brooks noted that when the anaerobic threshold was reached, a certain quantity remains in the heart as a reserve.

Richardson later showed that the presence of lactate in the blood did not correlate with the partial pressure of O_2 but rather with its consumption (a phenomenon that can be seen at high altitude too).

These discoveries placed the consolidated theory of O_2 deficit as a possible explanation for the accumulation of lactic acid in doubt.

In the past, it was thought that lactate passed into circulation by simple diffusion, according to gradient, while Brooks hypothesized the existence of specific lactate vectors.

With his theory, Brooks explained that lactate was transported by the muscle fibrocell, that produces it, to another organ that uses it.

Brooks and Donovan understood that the main destiny of lactic acid during physical exercise is oxidation for energy purposes, even inside the muscle that produced it. Lastly,

they put forward the hypothesis that during resistance training it is possible to increase this capacity.

1994 was a turning point in the history of lactic acid. The studies started by Magistretti and Pellerin opened up the route towards the central nervous system for lactate and since then, the history of our ion has continuously evolved [5].

Compliance with ethical standards

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Ethical approval All procedures performed in studies involving human participants were in accordance with ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent For this type of study formal consent is not required.

References

1. Robergs RA, Ghiasvand F, Parker D (2004) Biochemistry of exercise-induced metabolic acidosis. Am J Physiol Regul Integr Comp Physiol 287(3):R502–R516
2. Gladden LB (2008) 200th anniversary of lactate research in muscle. Exerc Sport Sci Rev 36(3):109–115
3. Noakes TD, St Clair Gibson A (2004) Logical limitations to the "catastrophe" models of fatigue during exercise in humans. Br J Sports Med 38(5):648–649
4. Margaria R et al (1933) The possible mechanisms of contracting and paying the oxygen debt and the role of lactic acid in muscular contraction. Am J Physiol 106:689–715
5. Coco M (2017) The brain behaves as the muscle? Neurol Sci. https://doi.org/10.1007/s10072-017-3014-6