Lactate: Friend or foe and implications for training and performance

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Is lactic acid to blame for Olympic pain?

Rowers can have a large build-up of acid in their muscles after a race.

Sportsmen and women pushing their bodies to the limit. That's what the Olympic Games are all about.
True or False?

It's the acid test for Mo! Lactate residue standing in Farah’s way in bid for double gold

By NEIL WILSON

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Taking its toll? Mo Farah could suffer from the lactic acid build up after performing in other events at such a high level.
Carl Wilhelm Scheele (1780)

Found lactic acid in sour milk

“lactic” – of or relating to milk

Real name: 2-hydroxypropanoic acid

Fig. 1. Chemical structures of lactic acid and the sodium salt of lactate. When the proton of the carboxylic acid functional group (-COOH) of lactic acid dissociates (COO⁻ + H⁺), a cation ionically interacts with the negatively charged oxygen atom of the carboxyl group, forming the acid salt lactate. In this example, the cation is sodium (Na⁺).
Integration of CHO and fat metabolism

Fats burn in a CHO flame!
Glyco[gen]olysis

Glycogen

Glucose → Pyruvate → Lactate

Mitochondria

[<1970's] Lack of Oxygen

CO₂ + H₂O

Lack of Oxygen
Lactate responses to exercise

![Graph showing lactate concentration over time during exercise with different conditions.](image-url)
AV Hill and Otto Meyerhof (1922)

Fig. 2. Archibald V. Hill (left) and Otto Meyerhof (right). Figures borrowed with permission of the Nobel Foundation.
Otto Meyerhof (1884-1951)

Nobel laureate who in the early 20th century cut a frog in half and put its bottom half in a jar. The frog’s muscles had no circulation - no source of oxygen or energy

Meyerhoff gave the frog’s leg electric shocks to make the muscles contract, but after a few twitches, the muscles stopped moving. Then, when Meyerhoff examined the muscles, he discovered that they were bathed in lactic acid

A theory was born: Lack of oxygen to muscles leads to lactic acid, which leads to fatigue
Archibald Vivian Hill, Nobel Laureate, 1922
Maximal oxygen uptake (\(\dot{\text{VO}_2}\text{max}\))
...The oxygen intake may attain its maximum and remain constant merely because it cannot go any higher owing to the limitations of the circulatory and respiratory system”

AV Hill, 1923
“...At higher speeds the requirement of the body for oxygen...cannot be satisfied...lactic acid accumulates, a continuous increasing oxygen debt being incurred, fatigue and exhaustion setting in”

AV Hill, 1923
Mechanism of fatigue according to the A.V. Hill (Cardiovascular/Anaerobic) Model of Exercise Physiology

Heart → Muscle → Mitochondria

Maximal (Limiting) cardiac output → Limiting blood flow to muscle → Limiting blood flow to muscle fibres causes anaerobiosis, stimulating muscle ‘lactic acid’ production

The lactic acid ‘poisons’ the muscle, causing (peripheral) fatigue

...The oxygen intake may attain its maximum and remain constant merely because it cannot go any higher owing to the limitations of the circulatory and respiratory system”

AV Hill, 1923

“...At higher speeds the requirement of the body for oxygen...cannot be satisfied...lactic acid accumulates, a continuous increasing oxygen debt being incurred, fatigue and exhaustion setting in”

AV Hill, 1923

Slides courtesy of Tim Noakes
Laboratory 1900s

Original bicycle ergometer used in Benedict's experiments to assess exercise energy metabolism.

Fig. 17.—Douglas's respiration apparatus. From "Journal of Physiology" (Cambridge University Press).
Anaerobic Threshold

Owles WH.

Alterations in the lactic acid content of the blood as a result of light exercise and associated changes in the CO$_2$-combining power of the blood and in the alveolar CO$_2$ pressure.

*J. Physiol* 69:214-237, 1930

...the first to establish that there was “a critical metabolic level” (later termed the “Owles’ point” above which an increase in blood lactate occurred

Owles’ experiment on himself showing the lactate concentration in venous blood after walking for 15-30 min at various speeds
“Lactate is the end product of the glycolytic sequence under anaerobic conditions and diffuses through the plasma membrane of the cell to the surroundings as waste. When muscle cells of higher animals function anaerobically during short bursts of exceptionally vigorous activity, lactate escapes from muscle cells into the blood in large quantities and is rebuilt to glucose in the liver during recovery”
Cori cycle

EXTRAHEPATIC TISSUES

Anaerobic glycolysis

Glucose → → → Lactate

Gluconeogenesis

Glucose ← ← ← Lactate

LIVER

(Physiol Rev 1931)
Anaerobic threshold and respiratory gas exchange during exercise

Karlman Wasserman et al. JAP 35(2):236-243, 1973

Methods: Incremental exercise 15 watts/min
n=85, 17-91 years
Expired O₂ and CO₂
AT was determined:

- non-linear increase in VE
- non-linear increase in VCO₂
- increase in end-tidal O₂ without a decrease end-tidal CO₂
- increase in R (the least sensitive)
Buffering of Lactic Acid in Blood

\[
\begin{align*}
H^+ + HCO_3^- & \rightarrow H_2CO_3 \\
& \rightarrow CO_2 + H_2O \\
LaH + NaHCO_3 & \rightarrow NaLa + CO_2 + H_2O
\end{align*}
\]

“Many investigations have revealed a fall in HCO_3^- concentration in plasma during exercise, which is equimolar to the rise in plasma lactate concentration…

…evidence of “lactic acid” accumulation; that is proof that La^- and H^+ enter the plasma or extracellular fluid together and that H^+ reacts with HCO_3^-”

…concept of ventilatory threshold depends on these relationships, because CO_2 production is associated with an increase in ventilation which may be used as an indirect indication of lactate production” Jones & Ehrsam 1982
Anaerobic threshold and respiratory gas exchange during exercise

Karlman Wasserman et al.

JAP 35(2):236-243, 1973

“The findings support the original hypothesis of Hill and Lupton (1923) that lactic acid is formed during exercise in the presence of tissue hypoxia; this process allows anaerobic mechanisms for ATP generation”
Inadequate $O_2$ delivery

Anaerobic Metabolism
  (↑ lactic acid)

Buffering
  ($↓ HCO_3^-$, $↑ VCO_2$, $↑ R$)

$V_E$

a) Non-linear increase
   (incremental work test)

b) Delayed steady state
   (constant work test)

Delayed steady state in $VO_2$
  ($↑ O_2$ deficit)

Respiratory compensation
for metabolic acidosis
  ($↓ PaCO_2$)

... $T(lact) = T(vent)$ and is caused by anaerobiosis
(absence of $O_2$) in muscle. Therefore, the $T(vent)$ has been called
the "anaerobic threshold" [T(an)]...
Anaerobic threshold and respiratory gas exchange during exercise
Karlman Wasserman et al.
JAP 35(2):236-243, 1973

But…
“refutation” of inadequate oxygen delivery!!!
THE ANAEROBIC THRESHOLD

Ivy et al.

Muscle respiratory capacity and fibre types as determinants of the lactate threshold

J. Appl Physiol 48:525, 1980
Determination of the anaerobic threshold by a noninvasive field test in runners

Conconi et al. 1982 (JAP: 52(4): 869-873)

Methods: Running on a 400m track 12-14km/h
n=210 runners
Determined AT using blood lactate
AT also determined using deflection in heart rate

Results: Good agreement between two methods
AT predicted actual race performance

Conclusion:
“…that AT is critical in determining the running pace in aerobic competitive events.”
Conclusion:
“…anaerobic threshold concept has been the subject of controversy during recent years. However, much of the debate has centred, not on the fundamental concepts, but on the descriptor of the concept. Regardless of semantic arguments, there is good reason to believe the anaerobic threshold concept will have enduring importance. Firstly, it has widespread utility because it can be measured noninvasively, using specific pulmonary gas exchange criteria. Secondly, it can be used to accurately predict exercise tolerance. …applications as diverse as determining the physiological potential of marathon runners and providing differential diagnostic information for patients with cardiopulmonary impairment.”
“The anaerobic threshold hypothesis fails because it requires the acceptance of three separate and invalid assumptions. …1) muscle lactate production results from oxygen-limiting ATP production; 2) changes in blood lactate concentration are due solely to changes in muscle lactate production; and 3) pulmonary ventilation tracks blood lactate level….Finding the inflection points in lines on graph paper is not likely to contribute to our understanding of metabolic and cardiopulmonary integration. Furthermore, insistence on the validity of the AT hypothesis is speculative at best, and at worse contributes to misunderstanding among those least prepared to interpret the literature”
Lactate metabolism - Traditional View

- immediate energy donor for muscle contraction
- primary factor in muscle soreness
- central cause of $O_2$ debt
- causative agent in muscle fatigue
- “dead-end” waste product
“The concentration of lactate in the blood is the result of (1) those processes which produce lactate and contribute to its appearance in the blood and (2) those processes which catabolize lactate after its removal from the blood. Consequently the concentration of lactate in the blood provides minimal information about the lactate production in muscle. …Lactate produced in skeletal muscle as a direct result of increased metabolic rate and glycolytic carbon flow…studies on dog gracilis muscle in situ clearly indicate that lactate production occurs in contracting pure red muscle for reasons other than an $O_2$ limitation…”
Reasons for lactate production

• Glycolysis proceeds faster than the mitochondria can process pyruvate

• Reduced cytosolic nicotinamide adenine dinucleotide (NADH + H⁺) cannot be reoxidised quickly enough by the mitochondria

NOT LACK OF OXYGEN
Lactate is an intermediate of carbohydrate metabolism. Lack of Oxygen inhibits the process.

Glycogen → Pyruvate → Lactate

Glucose

Lack of Oxygen

Mitochondria

CO₂ + H₂O
The Anaerobic Threshold: review of the concept and directions for future research

George A Brooks, 1985
MSSE 17(1): 22-31

“...T(lact) is clearly not due to sudden increase in production of lactate. The blood lactate response is a curve because the difference between Ra and Rd curves is a non-linear function of the VO₂”
Muscle - consumer of lactate

- Metabolic rate
- Blood flow (?)
- \([\text{La}]\) - gradient
- \([\text{H}^+]\) - ↓ pH increases lactate uptake
- Fibre type
  - Oxidative: oxidise LA
  - Glycolytic: make glycogen
- Exercise Training: ↑ with endurance

*Intra- and extra-cellular shuttles*
George A Brooks, 2000 MSSE
32(4): 790-99
Lactate clearance

- Liver (non-exercising muscle)
- Exercising muscle (oxidative fibres)

([LACTATE] production rate exceeds removal)

Intra- and extra-cellular shuttles
Mono-carboxylic Transporters (MCT)

- Lactate transporter protein
- Many isoforms (nine?) MCT1 for uptake and MCT4 for release
- Lactate co-transporter (one lactate & one H$^+$)
- MCT density and activity increased with training
Endurance training increases MCT1 and sprint training increases both MCT1 and MCT4.

How do MCTs work?

Lactate → MCT1 → Cell → MCT4 → Lactate
Mono-carboxylic Transporters (MCT)

Model of lactate shuttle

George Brooks
Intra- and extra-cellular lactate shuttles.
2000 Apr;32(4):790-9
“Until recently it was thought that lactate accumulation in skeletal muscle was largely a consequence of anaerobic metabolism, which occurs when the need for tissues to generate energy exceeds their capacity to oxidize the pyruvate produced in glycolysis. Recent metabolic studies, including 31P NMR analyses of the levels of phosphorylated intermediates in living muscle cells during exercise, suggest that lactate is actually an intermediate and not a metabolic “dead end”. These studies show that even in fully oxygenated muscle tissue, as much as 50% of the glucose metabolized is converted to lactate”
Conclusion

• Glycolytic metabolism
• Oxidative metabolism
• Lactate is the means by which the product of the one becomes the substrate of the other

George Brooks
*Intra- and extra-cellular lactate shuttles.*
Who do we believe?

friend or foe?
Do your athletes produce lactic acid?

- Yes
- No
Biochemistry of exercise-induced metabolic acidosis

Robert A. Robergs, Farzenah Ghiasvand, and Daryl Parker

1Exercise Physiology Laboratories, Exercise Science Program, Department of Physical Performance and Development, The University of New Mexico, Albuquerque, New Mexico 87131, and 2Exercise Science Program, California State University-Sacramento, Sacramento, California 95819

\[ \text{glucose} + 2 \text{ ADP} + 2 \text{ P}_i \rightarrow 2 \text{ lactate} + 2 \text{ ATP} + 2 \text{ H}_2\text{O} \quad (3) \]

\[ \text{glycogen}_n + 3 \text{ ADP} + 3 \text{ P}_i + 1 \text{ H}^+ \rightarrow \text{glycogen}_{n-1} \]
\[ + 2 \text{ lactate} + 3 \text{ ATP} + 2 \text{ H}_2\text{O} \quad (4) \]

Biochemistry of exercise-induced metabolic acidosis

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Fig. 10. Substrates and products of the ATPase reaction. This reaction is referred to as a hydrolysis reaction (ATP hydrolysis) due to the involvement of a water molecule. An oxygen atom, 2 electrons, and a proton from the water molecule are required to complete the free inorganic phosphate product of the reaction. The remaining proton from the water molecule is released into solution. Arrows pointing away from a bond represent bond/group removal. Arrows pointing to a bond represent addition of an atom/group.
Does lactate cause fatigue?

- Yes
- No
Biochemistry of exercise-induced metabolic acidosis

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“If muscle did not produce lactate, acidosis and muscle fatigue would occur more quickly and exercise performance would be severely impaired”

dosis during intense exercise has traditionally been explained by the increased production of lactic acid, causing the release of a proton and the formation of the acid salt sodium lactate. On the basis of this explanation, if the rate of lactate production is high enough, the cellular proton buffering capacity can be exceeded, resulting in a decrease in cellular pH. These biochemical events have been termed lactic acidosis. The lactic acidosis of exercise has been a classic explanation of the biochemistry of acidosis for more than 80 years. This belief has led to the interpretation that lactate production causes acidosis and, in turn, that increased lactate production is one of the several causes of muscle fatigue during intense exercise. This review presents clear evidence that there is no biochemical support for lactate production causing acidosis. Lactate production retards, not causes, acidosis. Similarly, there is a wealth of research evidence to show that acidosis is caused by reactions other than lactate production. Every time ATP is broken down to ADP and P_, a proton is released. When the ATP demand of muscle contraction is met by mitochondrial respiration, there is no proton accumulation in the cell, as protons are used by the mitochondria for oxidative phosphorylation and to maintain the proton gradient in the intermembranous space. It is only when the exercise intensity increases beyond steady state that there is a need for greater reliance on ATP regeneration from glycolysis and the phosphagen system. The ATP that is supplied from these nonmitochondrial sources and is eventually used to fuel muscle contraction increases proton release and causes the acidosis of intense exercise. Lactate production increases under these cellular conditions to prevent pyruvate accumulation and supply the NAD+ needed for phase 2 of glycolysis. Thus increased lactate production coincides with cellular acidosis and remains a good indirect marker for cell metabolic conditions that induce metabolic acidosis. If muscle did not produce lactate, acidosis and muscle fatigue would occur more quickly and exercise performance would be severely impaired.
Lactate: Friend or foe and implications for training and performance

Measure of fatigue but NOT the cause of fatigue and ... a measure of training intensity
Necessary Steps to Accelerate the Integration of Wearable Sensors Into Recreation and Competitive Sports

Peter Dilling, MS,1,2 Christian Stremel, MS,1,2 Billy Spearich, PhD,1,2 Shaun Subtelny, BS,3,4 Beja Marlo Pascho, MSc,5,6 Giuseppe Licci, PhD,3,6 Louis Kuller, MD, PhD7,8; and Yannis P. Pitsilados, MD, PhD, FACSM9,10,11
e-Celsius Performance®, is a miniaturised ingestible electronic pill that wirelessly transmits a continuous measurement of gastrointestinal temperature.

The data are stored on a monitor called e-Viewer Performance®. This device shows alerts if the measurement is outside the desired range. The activation box is used to turn the pill on from standby mode and connect with the monitor for data collection in either real time or by recovery from the internal memory of e-Celsius Performance®. Each monitor can be used with up to three pills at once to enable extended use. The monitor’s interface allows the user to download data to a PC/ Mac for storage. The pill is safe, non-invasive and easy to use, leaving the gastric system after one or two days, depending on individual transit time.
L. Messi, Captain of FC Barcelona and all-time goal scorer, P. Papoulis, SNF’s Deputy Group Director of Programs & Strategic Initiatives and J. Cardoner, FC Barcelona’s first Vice President, announce new grants for the development of SJD Pediatric Cancer Center.
**Results**  The NVF shoe improved running economy by $2.6 \pm 1.3\%$ compared with the NZM, $4.2 \pm 1.2\%$ compared with ADI, and $2.9 \pm 1.3\%$ when matched in weight of the ADI shoe. Among the 24 subjects, the difference in running economy over the four velocities between the NVF and NZM shoes ranged from $+0.50$ to $-5.34\%$, and $-1.72$ to $-7.15\%$ for NVF versus ADI. Correlations between changes in running economy and changes in biomechanical variables were either trivial or small, but unclear.

**Conclusion**  The NVF enhanced running economy compared with track spikes and marathon shoes, and should be considered a viable shoe option for track and road racing.
Seville, Spain, 25th February 2018
ZURICH MARATÓN SEVILLA

Seville, Spain, 25th February 2018

Current Pace: 03:33 min/km
Average Pace: 03:32 min/km
Distance: 4.21 km
Time: 00:14:54

Heart Rate: 201 bpm
Body Temperature: 11.5°C
Land Temperature: 62.373 VO₂ (mL/kg/min)
Humidity: 81.0%
Air Temperature: 9.41°C
Physilog® NanoCore™

“A motion lab-on-chip”

- Hardware: IMU sensing, processing, memory, communication
- Know-how from medical applications and Swiss luxury watch industry
- Miniaturisation at its best: Start of project: 18g -> **Now: 0.2g**
- Weight on shoe requires more effort than anywhere else
Wearable sweat sensor paves way for real-time analysis of body chemistry

Flexible plastic sensor sends molecular test results to a smartphone.

Linda Geddes

27 January 2016

Ali Javey, of the University of California, Berkeley, shows the flexible, wearable sweat-sensing device his team has created.
The Problem
Session 2: Latest innovations in monitoring vital data & sport performance
Vital data and performance monitoring – Movement and body analysis – Diagnostics of various parameters
14:55 h – 15:10 h
Necessary steps to accelerate the integration of wearables sensors into recreation and competitive sports
Prof. Dr. Yannis Pitsiladis, Professor of Sport and Exercise Science, University Brighton

IoT, Big Data and AI
Individual health data and data ownership – Genomic data and bio informatics – Predictive medicine
Moderated by Peter Dücking, Consultant, WT/Wearable Technologies

11:20 h – 11:40 h
New paradigms in precision health care with particular reference to telehealth and telecare
Dr. Ugo Riba, President, CIDIMU
Prof. Guiseppe Massaza, Full Professor in Physical Medicine and Rehabilitation, University of Turin and President of the Società Italiana Medici Manager (SIMM)

Session 5: Exercise – From idea to action
Public health guidelines and implementation – Exercise prescription – Digitalization
Swedish Physical activity on prescription- a role model for behavioral change?
Prof. Dr. med. Mats Börjesson, Department of Physiology at Institute of Neuroscience and Physiology, Sahlgrenska Academy

Panel Discussion: Exercise is Medicine – National action plans and learnings
Prof. Dr. med. Jürgen Steinacker, Chair European Initiative for Exercise is Medicine
Prof. Dr. med. Mats Börjesson, Department of Physiology at Institute of Neuroscience and Physiology, Sahlgrenska Academy
Necessary Steps to Accelerate the Integration of Wearable Sensors Into Recreation and Competitive Sports

Peter Dütting, MSc; Christian Stammel, MBA; Billy Sperlich, PhD; Shaun Sutehall, BSc; Borja Muniz-Pardos, MSc; Giscard Lima, BPhEd, MSc; Liam Kilduff, BSc, PhD; Iphigenia Keramitsoglou, MSc, PhD; Guoping Li, MD, PhD; Fabio Pigozzi, MD, PhD; and Yannis P. Pitsiladis, MMedSci, PhD, FACSM

Concluding Remarks
In the future, athletes will have the option to use an increasing number of wearables and each new device should add beneficial information to the training process with the goal of helping sports scientists and health care providers improve their athlete’s or patient’s performance. Sharing data between the athletes, exercise scientists, hardware and software engineers, and other stakeholders has the potential to improve wearable devices and technology for competitive athletes.