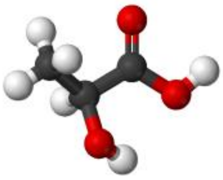
Εργαστήριο Κλινικής Εργοφυσιολογίας και Φυσιολογίας της Άσκησης, ΣΕΦΑΑ, ΔΠΘ

Γαλακτικό-Γαλακτικό Οξύ:

πολύτιμος μεταβολίτης της αναερόβιας γλυκόλυσης με μεγάλη προσφορά στον αθλητισμό και τους αθλούμενους

Σάββας Τοκμακίδης

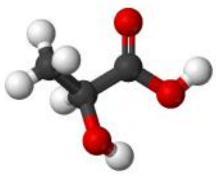
Δημοκρίτειο Πανεπιστήμιο Θράκης
Τμήμα Επιστήμης Φυσικής Αγωγής και Αθλητισμού

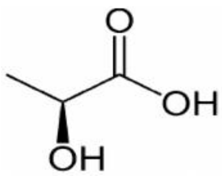


5ο Συνέδριο Βιοχημείας και Φυσιολογίας της Άσκησης
Κολλέγιο Αθηνών, Ψυχικό, 6-7 Νοεμβρίου 2015

Γαλακτικό-Γαλακτικό Οξύ:

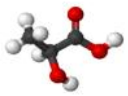
Ένας πολυσυζητημένος, παρεξηγημένος και πολύτιμος μεταβολίτης της αναερόβιας γλυκόλυσης με μεγάλη προσφορά στον αθλητισμό και τους αθλούμενους



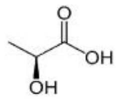


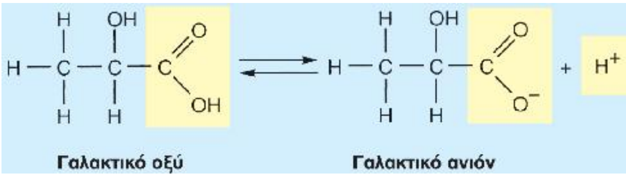
Γαλακτικό οξύ (συντακτικός τύπος: $CH_3CH(OH)COOH$ χημικός τύπος: $C_3H_6O_3$)

Γαλακτικό-Γαλακτικό Οξύ:



Δεν εντοπίζεται ως οξύ
Παράγεται ως οξύ
Ιονίζεται άμεσα
Γίνεται ιόν γαλακτικού
κατά 99,9%
Μετράμε γαλακτικό και όχι γαλακτικό οξύ



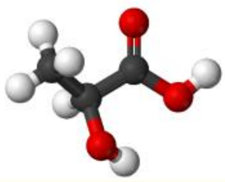


Μυϊκή κόπωση: τι φταίει H+ ή La-?

(τα υδρογόνα μας απαλλάσσουν από το δίλλημα)

Περιορίζουν τη μυϊκή λειτουργία
Μειώνουν την πρόσδεση των εγκάρσιων γεφυρών
Αναστέλλουν τη μέγιστη ταχύτητα συστολής
Αναστέλλουν τη δράση της ATPασης
Αναστέλλουν τη γλυκολυτική ροή
Αναστέλλουν τη σύνδεση Ca2+ με την τροπονίνη
Αναστέλλουν την επαναρρόφηση Ca2+ μεσω ATPασης

(μας λύνουν το πρόβλημα?)



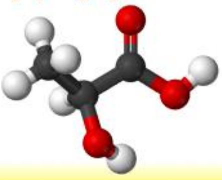
Γαλακτικό (La-):

Δεν προκαλεί μυϊκό κάματο

βοηθά-συμμετέχει-συνδράμει
και ενισχύει δυναμικά
τον ενεργειακό μεταβολισμό

παράγεται χωρίς οξυγόνο (αναερόβια)
δεν είναι όμως αναερόβιος μεταβολίτης
παράγεται και με την παρουσία οξυγόνου

Hill (1924): η έλλειψη οξυγόνου αυξάνει το γαλακτικό

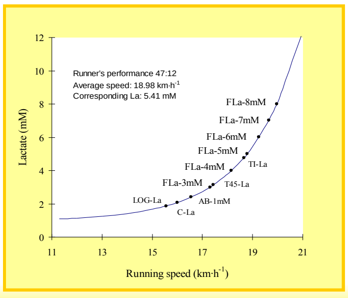


Γαλακτικό (La-):

Δεν εμφανίζει, δεν προκαλεί κατώφλια,
δεν δημιουργεί κατώφλια

Η δική σας επιλογή στην καμπύλη γαλακτικού
με τη γνώση των φυσιολογικών λειτουργιών

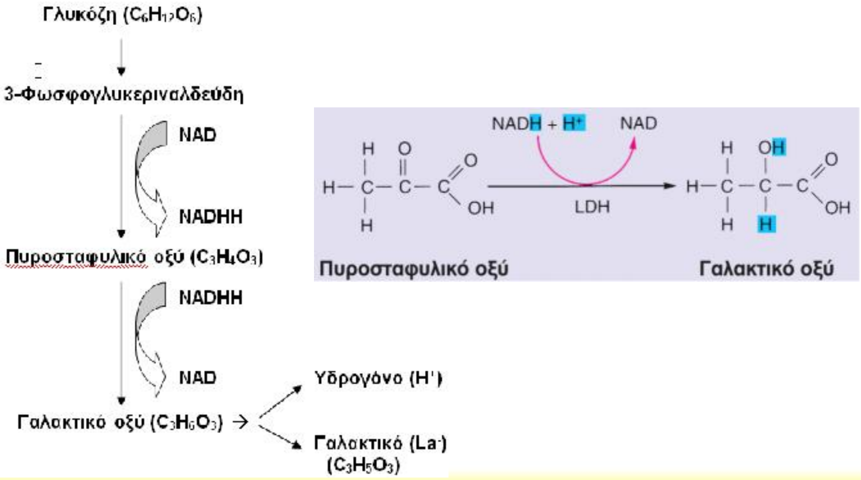
δημιουργεί το καλύτερο «κατώφλι»
δημιουργεί το δικό σας «κατώφλι»



Γαλακτικό:

Ως "αποδέκτης" υδρογόνων (NADHH-NAD)

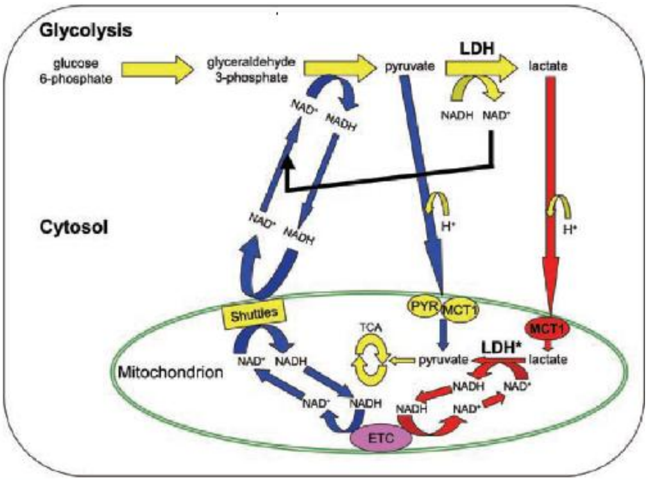
δίνει ζωή τον ενεργειακό μεταβολισμό



Άμεση μετάβαση και χρήση γαλακτικού

άμεση παροχή ενέργειας μέσω γαλακτικού

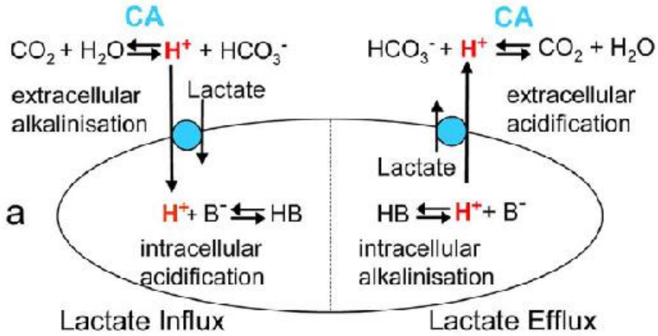
(lactate shuttle)



Gladden (2004) J Physiol 558.1 pp 5-30

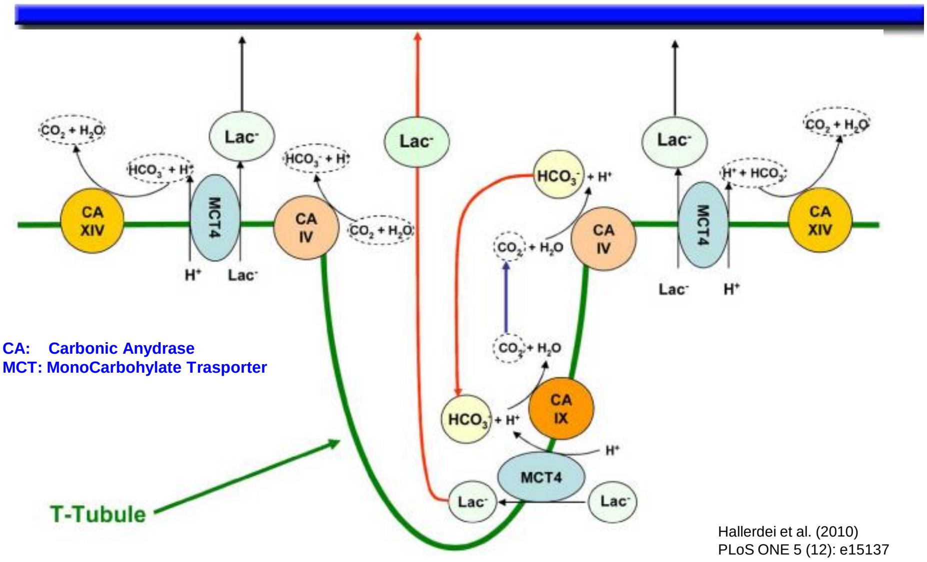
Μεταφορέας γαλακτικού – υδρογόνου (μεταβολική οξέωση – pH)

Sarcolemmal and T-Tubular Lactic Acid Transport



Hallerdei J, Scheibe RJ, Parkkila S, Waheed A, Sly WS, et al. (2010) T-Tubules and Surface Membranes Provide Equally Effective Pathways of Carbonic Anhydrase-Facilitated Lactic Acid Transport in Skeletal Muscle. PLoS ONE 5(12): e15137. doi:10.1371/journal.pone.0015137

Schematic cooperation of the MCT4 and the three membrane-bound CAs in lactic acid transport across the sarcolemma



Hallerdei et al. (2010)
PLoS ONE 5 (12): e15137

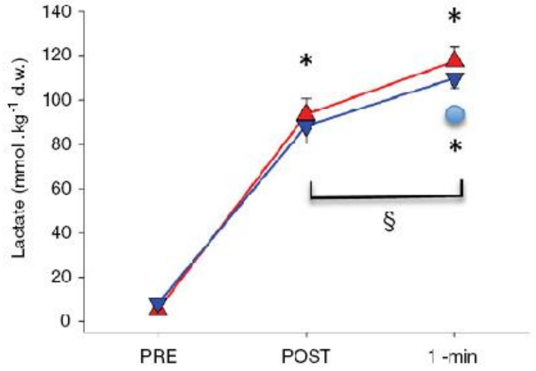
About half of lactic acid transport occurs via the surface membrane, supported by the buffering action of CA XIV and CA IV. The other half occurs via the T-tubular membrane and is supported by the buffering action of CA IX. The removal of lactic acid from the T tubules occurs by outward diffusion of lactate, while the H+ are transported out by an inward diffusion of HCO3 in combination with an outward diffusion of CO2, a CO2- HCO3 shuttle. This removal mechanism operates effectively in spite of the long diffusion distance from the T-tubule interior to the extracellular space due to very large concentration gradients of lactate and HCO3 that can build up along the T-tubule. These gradients and the mobility of protons are much smaller in the sarcoplasm of the fiber.

Ούτε το La- ούτε το Ph εύθυνεται για το μυϊκή κόπωση

Exhaustion is not due to lactate accumulation and the associated muscle acidification; neither the aerobic energy pathways nor the glycolysis are blocked at exhaustion.

Muscle lactate accumulation may actually facilitate early recovery after exhaustive exercise even under ischaemic conditions.

Exhaustion depends more on central than peripheral mechanisms



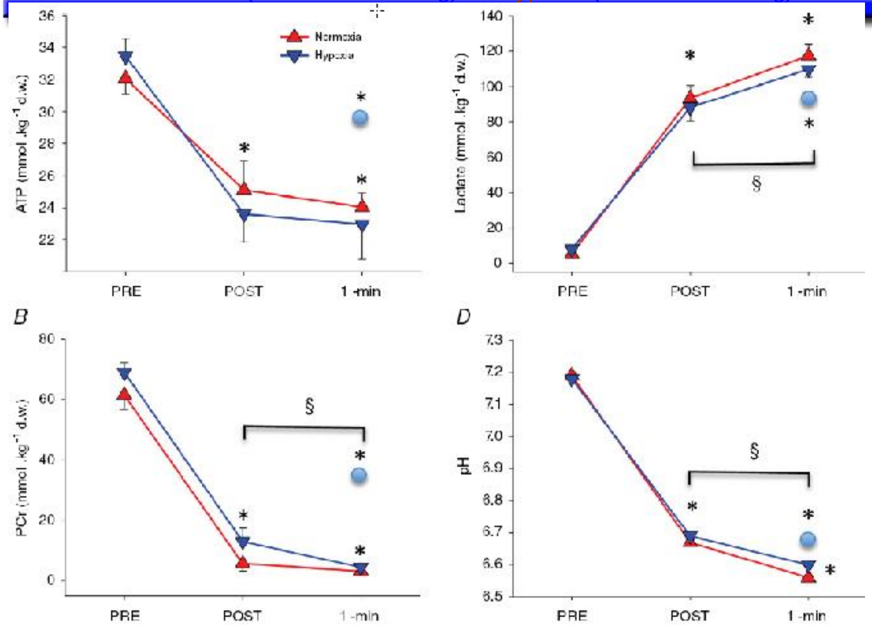
Normoxia (PIO2 = 143 mmHg) & hypoxia (PIO2 = 73 mmHg)

Occlusion in one leg. Biopsies (vastus lateralis) obtained 10 and 60 s after the end of the sprint

∗P < 0.05, compared with PRE; §ANOVA time effect POST vs. 1-min occlusion P < 0.05.

Morales-Alamo and others (2015) *J Physiol* DOI: 10.1113/JP270487

Normoxia (PIO2 = 143 mmHg) vs. hypoxia (PIO2 = 73 mmHg)

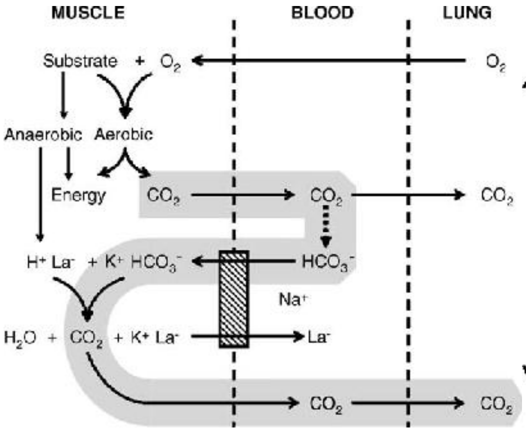


∗P < 0.05, compared with PRE; §ANOVA time effect POST vs. 1-min occlusion P < 0.05.

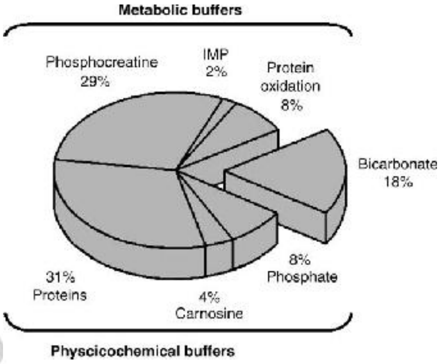
Morales-Alamo and others (2015) *J Physiol* DOI: 10.1113/JP270487

Το La- δεν παράγει μη-μεταβολικο CO2 κατά την άσκηση

Lactic acid buffering, nonmetabolic CO2 and exercise hyperventilation:
A critical reappraisal



Bicarbonate is not the main buffer of H+ in the muscle cell

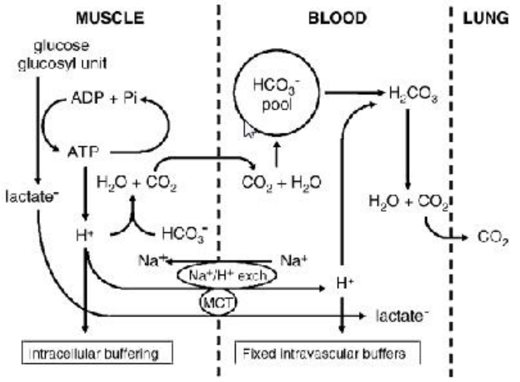


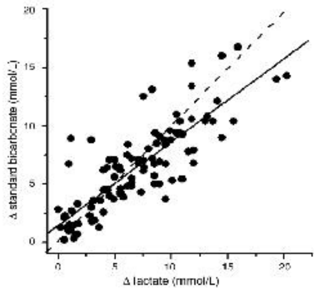
F. Peronnet, B. Aguilaniu / Respiratory Physiology & Neurobiology 150 (2006) 4–18

Το La- δεν παράγει μη μεταβολικό CO2 κατά την άσκηση

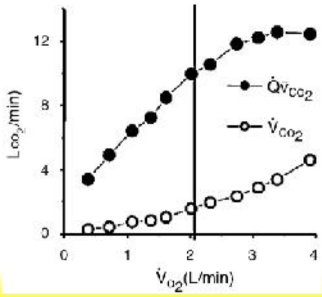
Lactic acid buffering, nonmetabolic CO2 and exercise hyperventilation:
A critical reappraisal

H+ buffering in the muscle, acid–base balance and hyper-ventilation in ramp exercise does not appear to be valid





The CO2 flow to the lungs levels off above AT



At the present time there is no comprehensive explanation for the control of ventilation in response to exercise below or above *AT*

«Αναερόβιο κατώφλι»

Σύνθεση-συνδυασμός αερόβιας ικανότητας δρομικής οικονομίας και αντοχής

Causes of lactate turnover during exercise

- intracellular function of glycogen metabolism
- function of cell-cell lactate shuttles

Causes of lactate turnover
(oxidative steady state)
optimal power output

- mitochondrial phosphorylation
- cytosol phosphorylation
  - oxidative energy
  - glycolytic energy

Lactate plays a key role in many intracellular functions during exercise

Consequences of the whole body and intramuscular lactate turnover

- The concept of anaerobic threshold (AT)
  - Lactate threshold (LT)
  - Ventilatory threshold (VT)

Consequences of lactate kinetics

- Lactate turning point
- Lactate breaking point
- Onset of Plasma Lactate Accumulation (OPLA)
- Onset of Blood Lactate Accumulation (OBLA)
- Maximal Steady State (MSS)
- Maximal Lactate Steady State (MLSS)

Question: Which is the proper one?

Consequences of lactate kinetics

- Log-Log threshold point
- Fixed lactate threshold points (2, 3, 4 mM)
- 1 mM above resting or exercise baseline
- Individual anaerobic threshold
- A tangent threshold point (45î or 51î)
- The slope index model (45î)

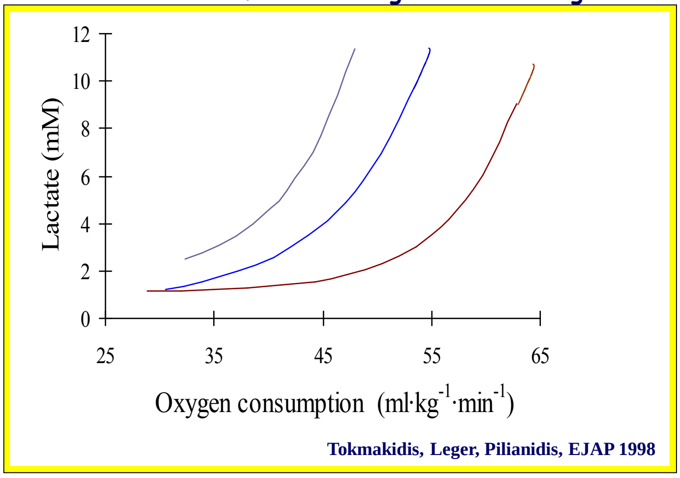
Question: Which is the proper one?

Consequences of lactate kinetics

- Transitional steady state
- Critical power
- Fatigue threshold
- Bicarbonate threshold
- Plasma ammonia threshold
- Electromyography (EMG) threshold
- Heart rate threshold (popular but invalid)

Question: Which is the proper one?

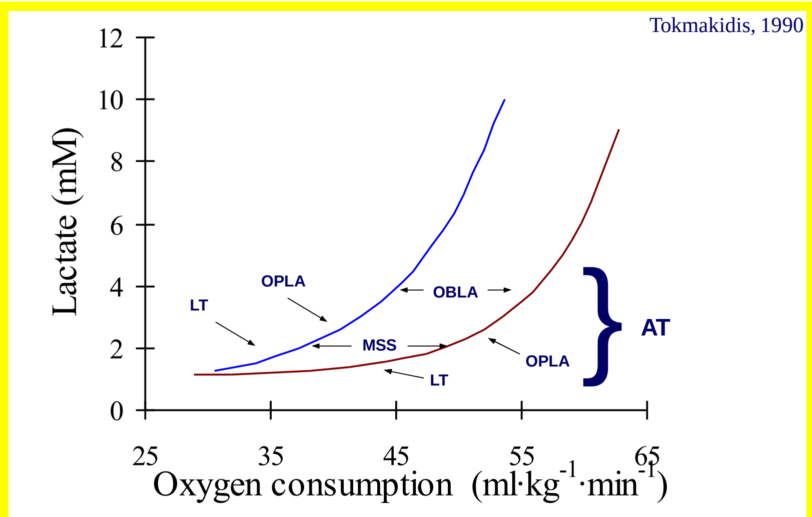
La curve shifts to the right with training



The rightward displacement of the La curve that occurs with training is partly due to the increase of the maximal speed or VO_{2max} values. Most of the time, when there is an increase in VO_{2max}, there is also an increase in AT.

Question:

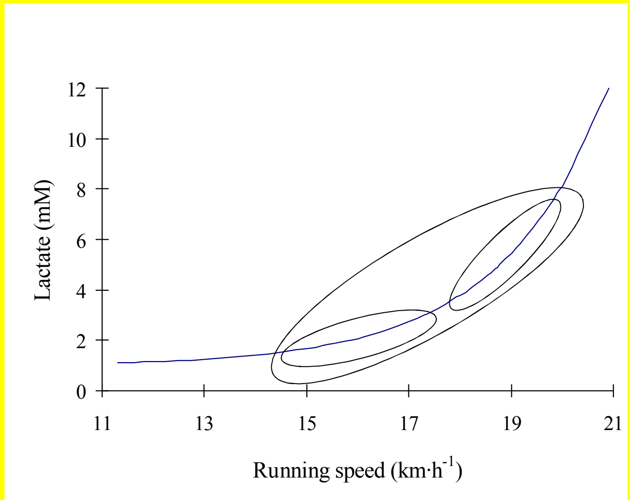
Which is the proper AT point?



Various AT points used in the literature give different intensities

Lactate threshold is considered to be a reliable and powerful predictor of performance

(Many reports have presented high correlation with running performance)

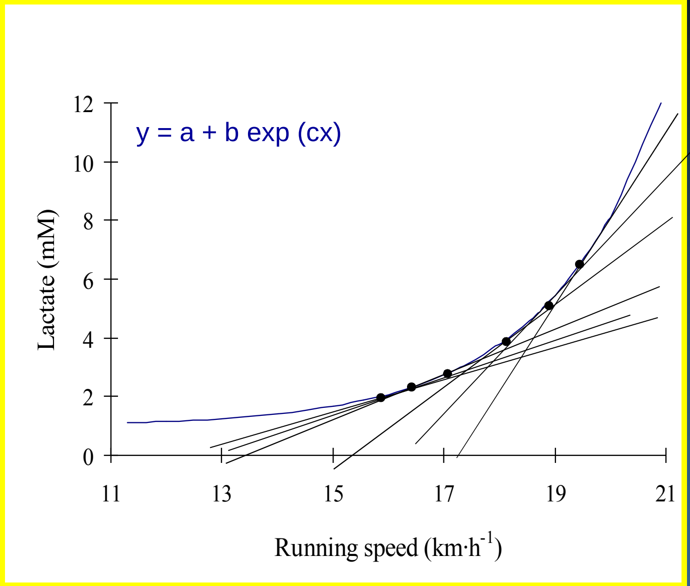


any point on the lactate curve correlates equally well with performance

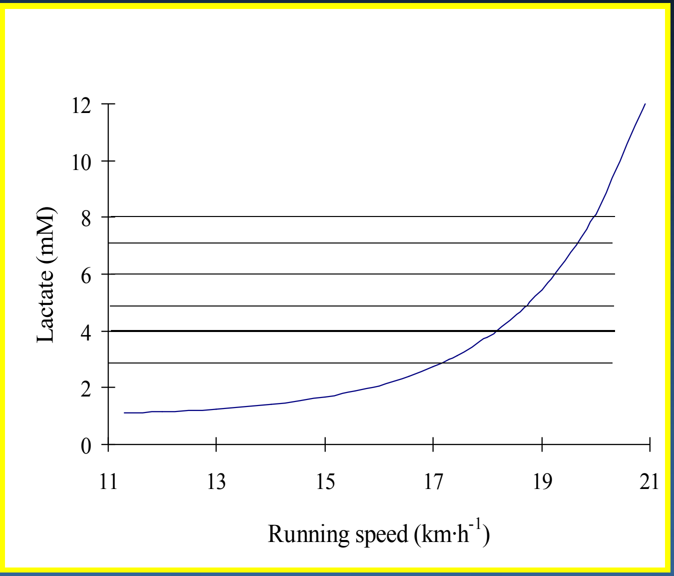
Selected AT points

- ✓ a conventional lactate threshold
- ✓ a fixed lactate level of 4 mM
- ✓ a point of 1 mM above baseline
- ✓ a log-log threshold point
- ✓ a slope index point

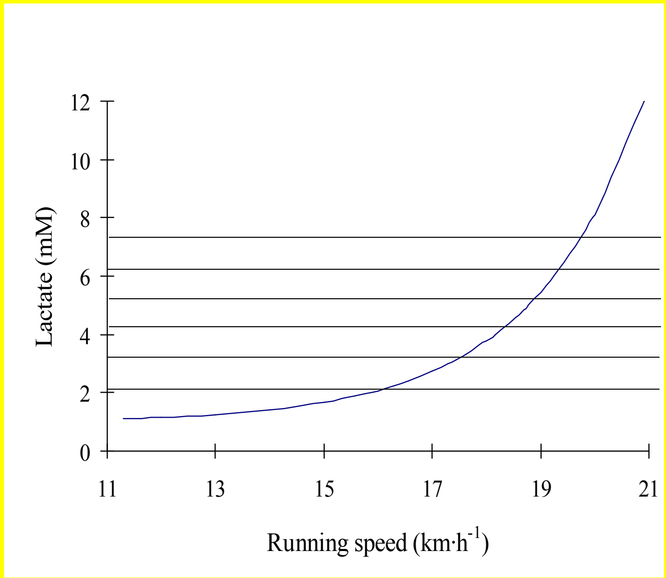
La data were fitted to a continuous nonlinear regression
(slope index model with specific tangents)



The fixed lactate concentration of 3-8 mM

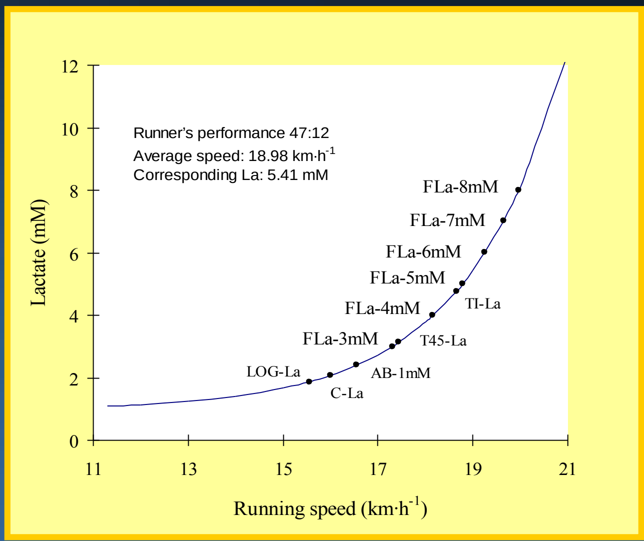


The lactate concentration of 1-6 mM above baseline



	15.000 m km·h^{-1} (n=19)	10.000 m km·h^{-1} (n=11)	20.000 m km·h^{-1} (n=16)	42.195 m km·h^{-1} (n=13)
FLa-3mM	0.930	0.929	0.889	0.907
FLa-5mM	0.949	0.934	0.911	0.917
FLa-6mM	0.949	0.932	0.910	0.915
FLa-7mM	0.948	0.930	0.908	0.913
FLa-8mM	0.946	0.928	0.905	0.911
AB-2mM	0.942	0.922	0.907	0.907
AB-3mM	0.944	0.922	0.908	0.905
AB-4mM	0.944	0.922	0.907	0.904
AB-5mM	0.943	0.921	0.905	0.903
AB-6mM	0.942	0.921	0.903	0.902
T30-La	0.923	0.988	0.888	0.865
T40-La	0.934	0.900	0.899	0.880
T50-La	0.938	0.908	0.900	0.890
T60-La	0.936	0.913	0.896	0.839
T70-La	0.926	0.915	0.881	0.886

Any lactate point can be used as a "threshold" or as a performance index



The knowledge of the physiological consequences of a chosen La level is what counts and not the AT point itself

The anaerobic threshold is expressed in different units

Absolute units of AT

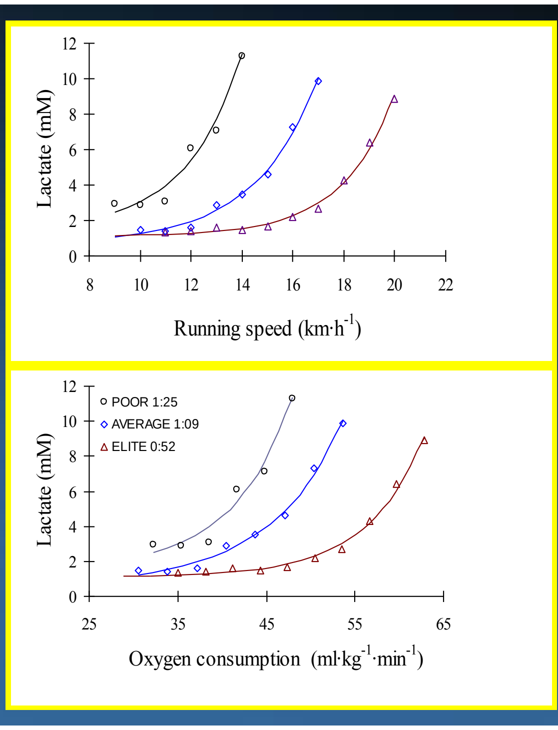
- running speed (km/h)
- VO_2 (ml/kg/min)

Relative units of AT

- % $SPEED_{max}$
- % VO_{2max}

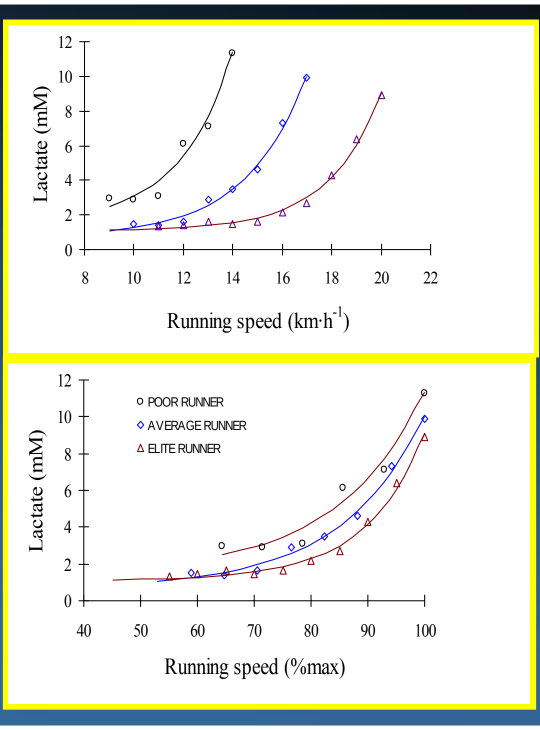
It is recognized that any AT point represents a sub-maximal value

AT - UNITS	AEROBIC POWER	RUNNING ECONOMY	ENDURANCE
SPEED $km \cdot h^{-1}$	YES	YES	YES
VO_2 $ml \cdot kg^{-1} \cdot min^{-1}$	YES	NO	?
% VO_2 max	NO	YES	?
% SPEED max	NO	?	?



The differences among the La curves are reduced when speed units are transformed in VO_2 units.

This is the effect of running economy which disappears when the speed units are expressed in VO2 units.

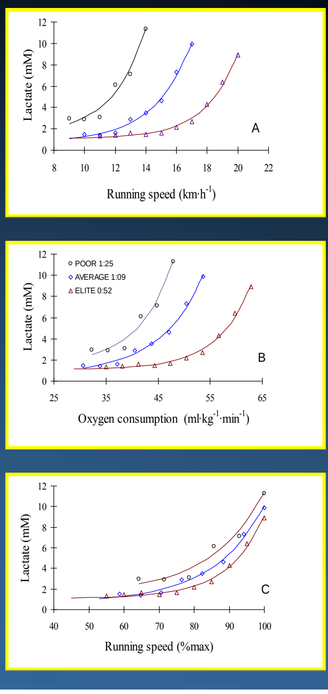


When AT is normalized according to the maximal running speed and it is expressed as %SPEEDmax, aerobic power, running economy and perhaps endurance are removed.

This in turn reduces the differences among runners and it eliminates the correlation between AT and performance.

	15.000 m $km \cdot h^{-1}$ (n=19)	10.000 m $km \cdot h^{-1}$ (n=11)	20.000 m $km \cdot h^{-1}$ (n=16)	42.195 m $km \cdot h^{-1}$ (n=13)
SPEED $km \cdot h^{-1}$				
C-La	0.921***	0.893***	0.869***	0.863***
LOG-La	0.868***	0.849***	0.827***	0.770**
TI-La	0.933***	0.906***	0.897***	0.906***
T45-La	0.937***	0.904***	0.900***	0.886***
FLa-4mM	0.948***	0.937***	0.910***	0.918***
AB-1mM	0.935***	0.923***	0.904***	0.914***
VO_2 $ml \cdot kg^{-1} \cdot min^{-1}$				
C-La	0.718***	0.557	0.687**	0.520
LOG-La	0.655**	0.518	0.661**	0.417
TI-La	0.834***	0.695*	0.829***	0.711**
T45-La	0.811***	0.656*	0.814***	0.668*
FLa-4mM	0.855***	0.743**	0.834***	0.729**
AB-1mM	0.812***	0.692**	0.797***	0.653*
% VO_2 max				
C-La	-0.319	-0.194	-0.280	-0.302
LOG-La	-0.214	-0.170	-0.120	-0.314
TI-La	-0.312	-0.050	-0.357	-0.356
T45-La	0.176	0.186	0.158	-0.019
FLa-4mM	0.139	0.212	0.057	0.018
AB-1mM	-0.031	0.095	-0.028	-0.164
% SPEED max				
C-La	-0.172	-0.035	-0.220	-0.221
LOG-La	-0.068	-0.024	-0.042	-0.210
TI-La	-0.219	0.056	-0.300	-0.300
T45-La	0.429	0.415	0.319	0.128
FLa-4mM	0.352	0.404	0.186	0.161
AB-1mM	0.217	0.325	0.109	-0.028

*** $P<0.001$; ** $P<0.01$; * $P<0.05$



AT - UNITS	AEROBIC POWER	RUNNING ECONOMY	ENDURANCE*	CORRELATION (r)
Tokmakidis et al., 1998				15.00 km
SPEED $km \cdot h^{-1}$	YES	YES	YES	0.95
VO_2 $ml \cdot kg^{-1} \cdot min^{-1}$	YES	NO	?	0.86
% VO_2 max	NO	YES	?	0.35
% SPEED max	NO	?	?	0.14
Weltman et al., 1987				3.20 km
SPEED $km \cdot h^{-1}$	YES	YES	YES	0.88
VO_2 $ml \cdot kg^{-1} \cdot min^{-1}$	YES	NO	?	0.79
Kumagai et al., 1982				16.09 km
VO_2 $ml \cdot kg^{-1} \cdot min^{-1}$	YES	NO	?	0.83
% VO_2 max	NO	YES	?	0.11
Rotstein et al., 1986				1.20 km
SPEED $km \cdot h^{-1}$	YES	YES	YES	0.74
% VO_2 max	NO	YES	?	0.14

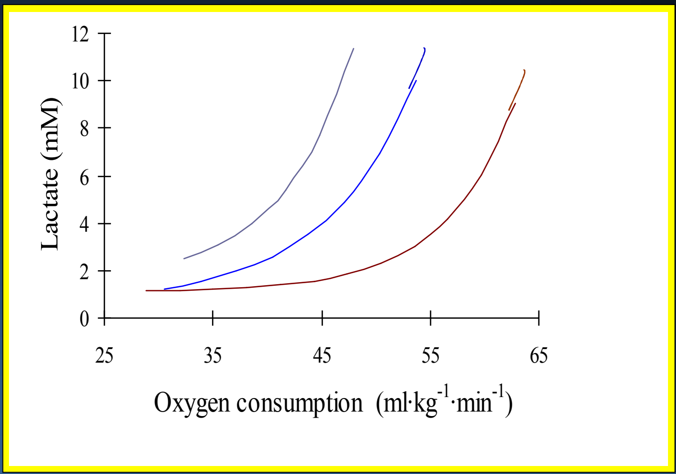
When AT was normalized for maximal speed or VO_{2max} values, the net results were not well correlated with performance. For this reason, the correlation between AT and performance is mostly reported in absolute speed or VO_2 units.

The absolute AT is a sub-maximal value that includes the value of VO_{2max}

Thus ...

the absolute AT is not independent of VO_{2max} as it has been considered

La curve shifts to the right with training



The rightward displacement of the La curve that occurs with training is partly due to the increase of the maximal speed or VO_{2max} values. Most of the time, when there is an increase in VO_{2max}, there is also an increase in AT.

References	Training period	Training effects (% differences)		
		Absolute AT units	Relative AT units	VO_{2max}
Sady et al. (1980)	8 weeks	37.0	2.7	26.5
		26.8	0.8	25.8
Raedy & Quinney (1982)	9 weeks	70.4	19.4	36.7
Gibbons et al. (1983)	8 weeks	15.2	0.2	14.8
Caldwell & Rauhala (1983)	3 months	21.0	7.6	12.4
Davis et al. (1979)	9 weeks	44.1	15.4	25.3

The identification of a unique threshold (AT point)
on the blood lactate concentration curve

There is no unique AT point on the La curve

Any point can be well correlated with performance

The unit effect and the anaerobic threshold

The relative importance of the threshold
as compared to VO_{2max} might not be as critical
when the AT point is expressed as $\%VO_{2max}$

Lactate turnover in exercise:
consequences and practical implications

- The properties of the lactate curve should not be overlooked

- The blood lactate response to exercise is a useful tool for exercise prescription

Thus, it is important to understand the physiological consequences of a chosen lactate level rather than to concentrate on an 'AT' for exercise prescription

Lactate kinetics at the lactate threshold in trained and untrained men

(Messonnier LA et al. J Appl Physiol 114: 1593–1602, 2013)

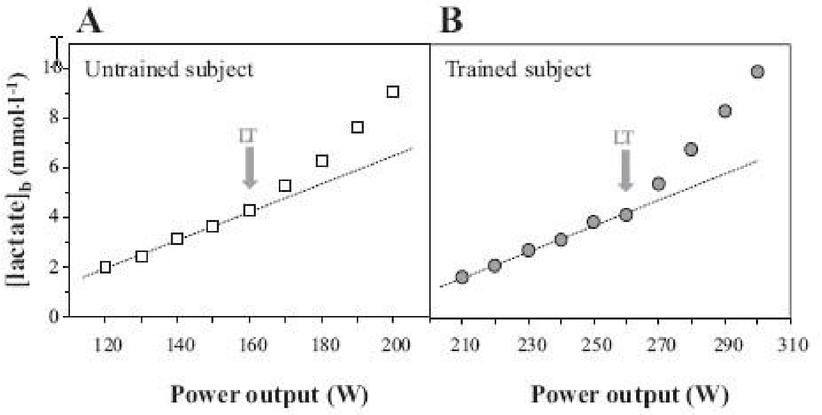


Fig. 1. Typical blood lactate evolution curves obtained in untrained (*A*) and trained (*B*) subjects during the lactate threshold (LT) determination test. Deviation from the dashed line is indicative of the acceleration in blood lactate accumulation (i.e., the LT). Of note, the dashed line should not be considered as demonstrating a linear relationship between blood lactate concentrations and power output.

Lactate kinetics at the lactate threshold in trained and untrained men

(J Appl Physiol 114: 1593–1602, 2013)

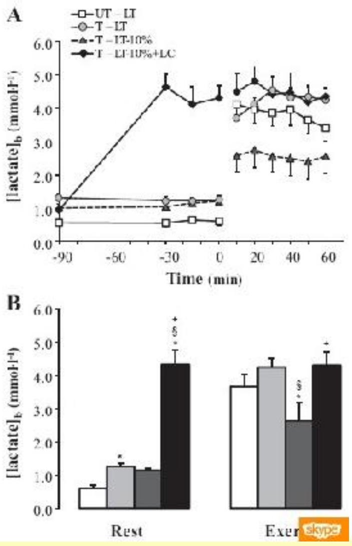
Table 1. *Physiological responses to maximal oxygen consumption and lactate threshold determination tests for untrained and trained subjects*

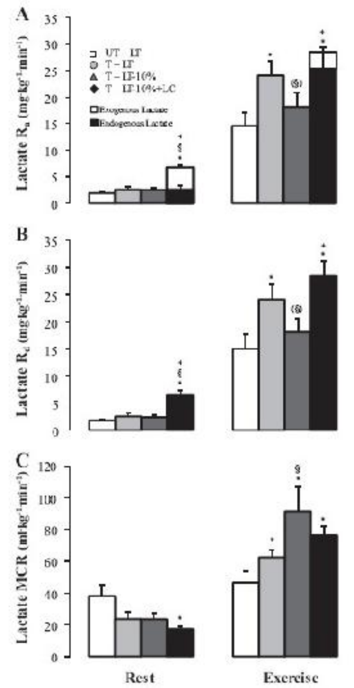
Variable	Untrained	Trained
Maximal oxygen consumption test		
fH_{max} (bpm)	189 ± 5	189 ± 3
VE_{max} (l/min)	115 ± 8	144 ± 13†
$\dot{V}O_{2max}$ (l/min)	3.7 ± 0.1	5.0 ± 0.3*
PO_{max} (W)	248 ± 7	357 ± 12*
Lactate threshold test		
fH at LT (bpm)	158 ± 5	168 ± 3
$\%fH_{max}$ at LT (%)	83 ± 3	89 ± 1
$\dot{V}O_2$ at LT (l/min)	2.57 ± 0.09	3.85 ± 0.21*
$\%\dot{V}O_{2max}$ (%)	69 ± 3	77 ± 2*
$[lactate]_b$ at LT (mmol/l)	4.3 ± 0.6	3.6 ± 0.6

Values are means ± SE; $n = 6$ for untrained and trained groups. Differences between groups: *$P < 0.05$; †$0.05 < P < 0.1$. fH_{max}, maximal heart rate; bpm, beats per minute; VE_{max}, maximal pulmonary ventilation; $\dot{V}O_{2max}$, maximal oxygen consumption; PO_{max}, $\dot{V}O_{2max}$-associated power output; fH at LT, heart rate at lactate threshold (LT); $\%fH_{max}$ at LT, percent of maximal heart rate at LT; $\dot{V}O_2$ at LT, oxygen consumption at LT; $\%\dot{V}O_{2max}$, percent of maximal oxygen consumption; $[lactate]_b$, blood lactate concentration.

were significantly higher in trained cyclists compared with untrained subjects ($P < 0.05$).

Exercise power outputs and relative metabolic rates during isotope tracer trials. Absolute POs during the LT trial in





Lactate kinetics in trained and untrained

(Messonnier LA et al. J Appl Physiol 114: 1593–1602, 2013)

Lactate rates of appearance (Lactate Ra) *(A) and disposal (Lactate Rd)* (*B*)*, and metabolic clearance rate of lactate (Lactate MCR) (C) at rest and* during 60 min of exercise at LT, LT-10%, and LT-10%LC in untrained and trained subjects. Values are means

Parentheses mean a trend (*P <0.10).*

Explanation of symbols:

Lactate threshold (LT), 10% below the LT workload (LT-10%), and LT-10% with a lactate clamp (LT-10%LC) in untrained (UT) and trained (T) subjects.

White squares indicate LT trial in UT subjects (UT-LT).
Dark grey circles, striated triangles, and black diamonds indicate LT, LT-10%, and LT-10%LC trials in T subjects (T-LT, T-LT-10%, and T-LT-10%LC, respectively).

Lactate kinetics at the lactate threshold in trained and untrained men

(Messonnier LA et al. J Appl Physiol 114: 1593–1602, 2013)

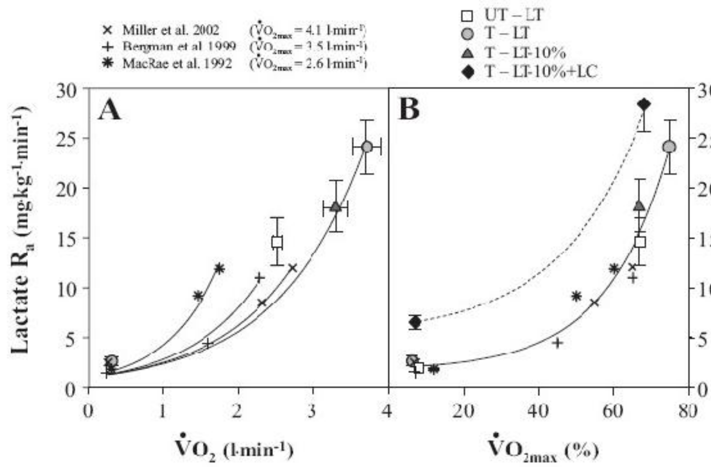


Fig. 5. Lactate R_a as a function of absolute ($\dot{V}O_2$) (*A*) and relative (to $\dot{V}O_{2max}$) (*B*) metabolic rates elicited at rest and exercise in the present and previous studies involving subjects with different physical fitness status. $\dot{V}O_{2max}$ values (means ± SE) of UT and T subjects are 3.7 ± 0.1 and 5.0 ± 0.3 liter/min, respectively.

Lactate kinetics at the lactate threshold in trained and untrained men

(Messonnier LA et al. J Appl Physiol 114: 1593–1602, 2013)

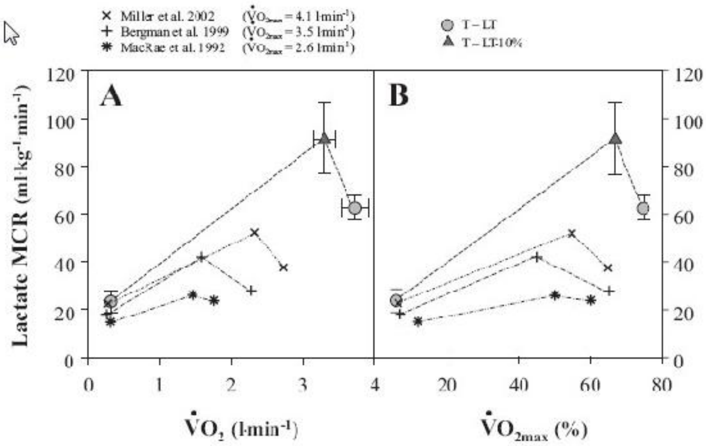
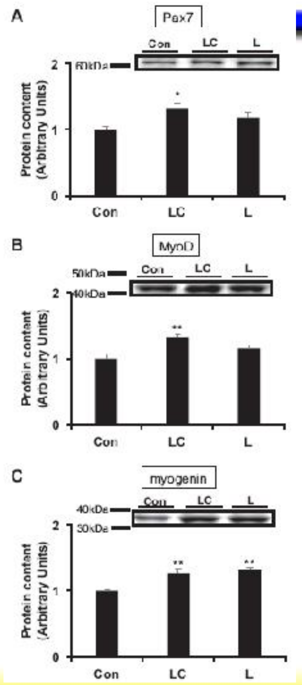


Fig. 8. Lactate metabolic clearance rate (MCR) as a function of absolute ($\dot{V}O_2$) (*A*) and relative (to $\dot{V}O_{2max}$) (*B*) metabolic rates elicited at rest and exercise in the present and previous studies involving subjects with different physical fitness status. See Fig. 2 for an explanation of symbols. $\dot{V}O_{2max}$ values (means ± SE) for UT and T subjects are 3.7 ± 0.1 and 5.0 ± 0.3 l/min, respectively.



Lactate-Caffeine Supplement Increases Muscle Mass

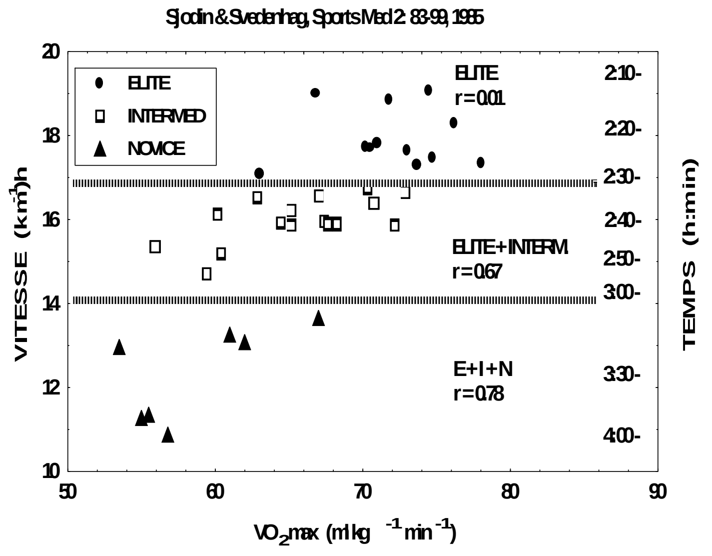
(*Oishi Y et al. J Appl Physiol 118: 742–749, 2015)*

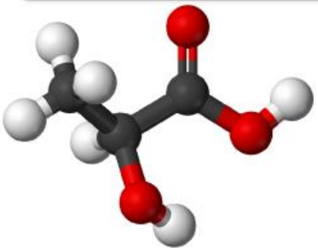
Effect of lactate or lactate-caffeine on satellite cell activity in C2C12 muscle cells.

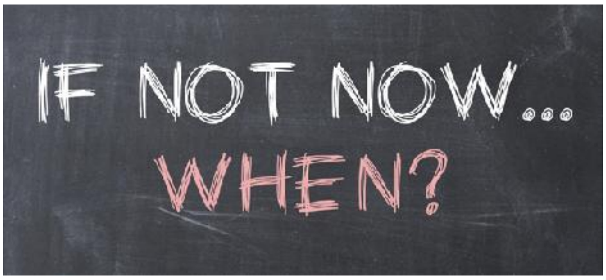
Protein expression of paired box protein (Pax7; *A), myogenic* differentiation factor (MyoD; *B), and myogenin (C) is shown with representative* immunoblots. C2C12 cells were incubated with media containing 10 mM sodium lactate 5 mM caffeine (LC) or 10 mM sodium lactate (L) for 6 h.

L increased myogenin expression compared with Cont.

LC significantly increased Pax7, MyoD, and myogenin expression compared with Con, and increased MyoD expression compared with L. **P <0.05, **P* <0.01 vs. Cont.






IF NOT NOW...
WHEN?