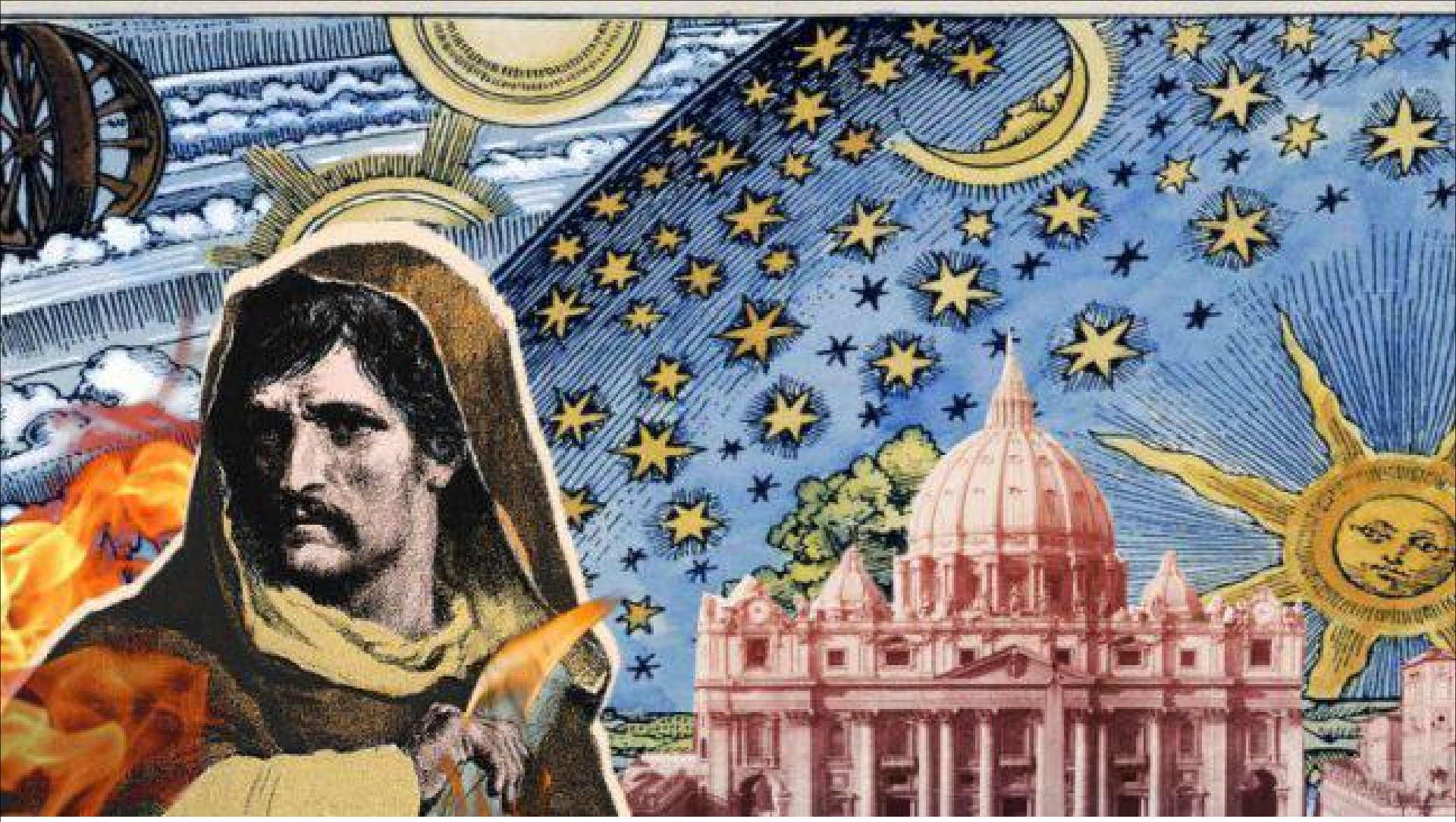


XI congresso nazionale
simeu

Lattati nel paziente critico: stiamo rincorrendo una chimera?

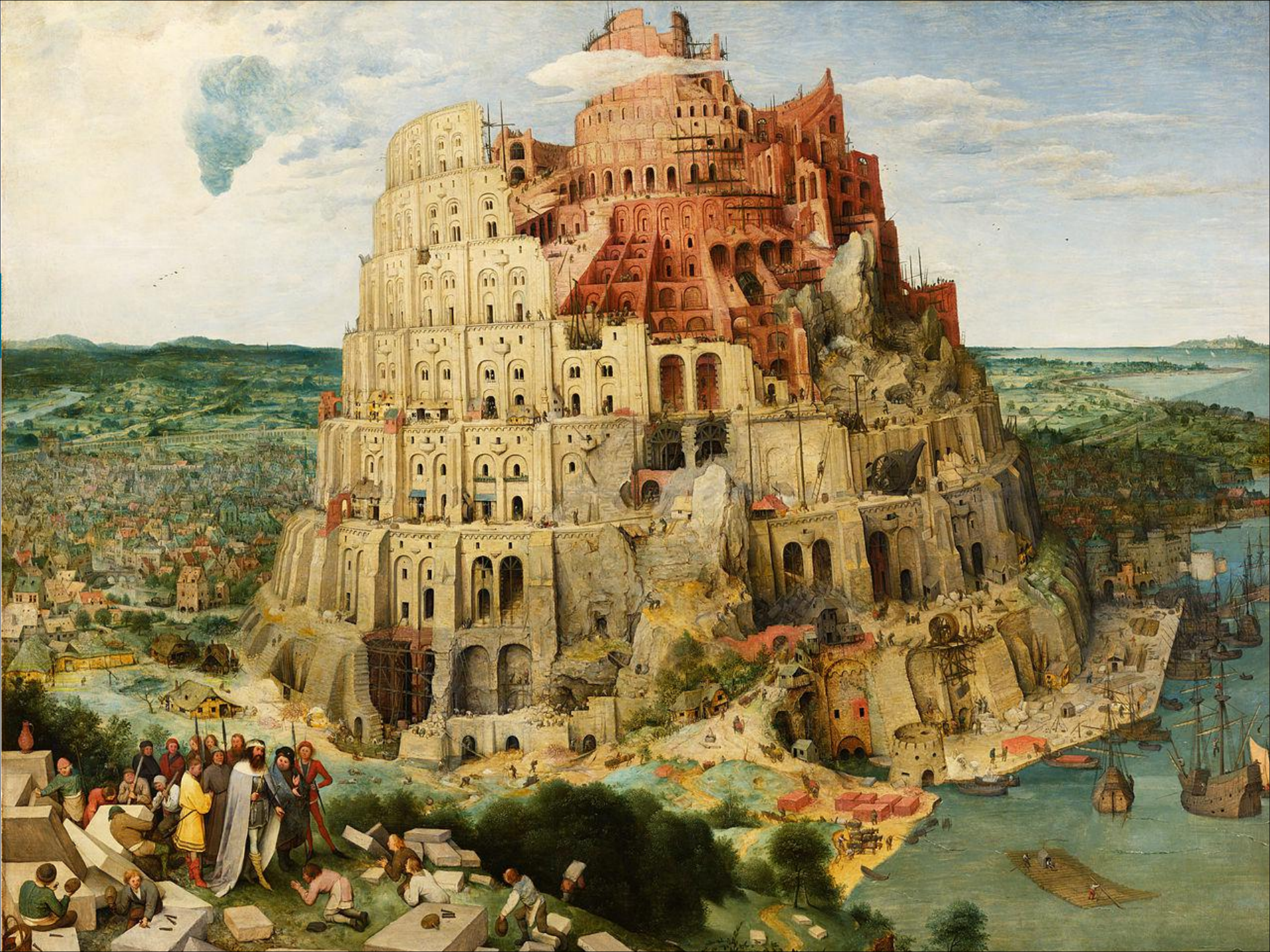
Dr. Matteo Borselli – DEA Ospedale Misericordia - Grosseto

COMPARE QUANDO LA RISPOSTA DEL CORPO ALL'INFEZIONE E' COMPLICATA DA ABNORME RISPOSTA IMMUNE

20.000.000 / anno

Prevalenza: 37% dei pz in ICU

Prima patologia per impatto economico negli USA



Journal of Thoracic Disease

J Thorac Dis. 2016 Jul; 8(7): 1388–1390.
doi: 10.21037/jtd.2016.05.55
PMCID: PMC4958885
PMID: 27501243

New clinical criteria for septic shock: serum lactate level as new emerging vital sign

Su Mi Lee and Won Suk An

Commentary | Open Access

Lactate in the critically ill patients: an outcome marker with the times

H Bryant Nguyen

Critical Care 2011 **15**:1016
https://doi.org/10.1186/cc10531
Published: 5 December 2011

3-Hour Bundle

1. Measure Lactate Level

Background

Hyperlactatemia is typically present in patients with severe sepsis or septic shock and may be secondary to anaerobic metabolism due to hypoperfusion or other complex factors. The prognostic value of raised blood lactate levels has been well established in septic shock patients[1], particularly if the high levels persist.[2,3] In addition, blood lactate levels have been shown to have greater prognostic value than oxygen-derived variables.[4] Obtaining a lactate level is essential to identifying tissue hypoperfusion in patients who are not yet hypotensive but who are at risk for septic shock.

LATTATI

MARKER DI IPOSSIA TISSUTALE

PRODOTTO DI METABOLISMO ANAEROBIO

NORMALIZZAZIONE DEI LATTATI

IPERLATTATEMIA

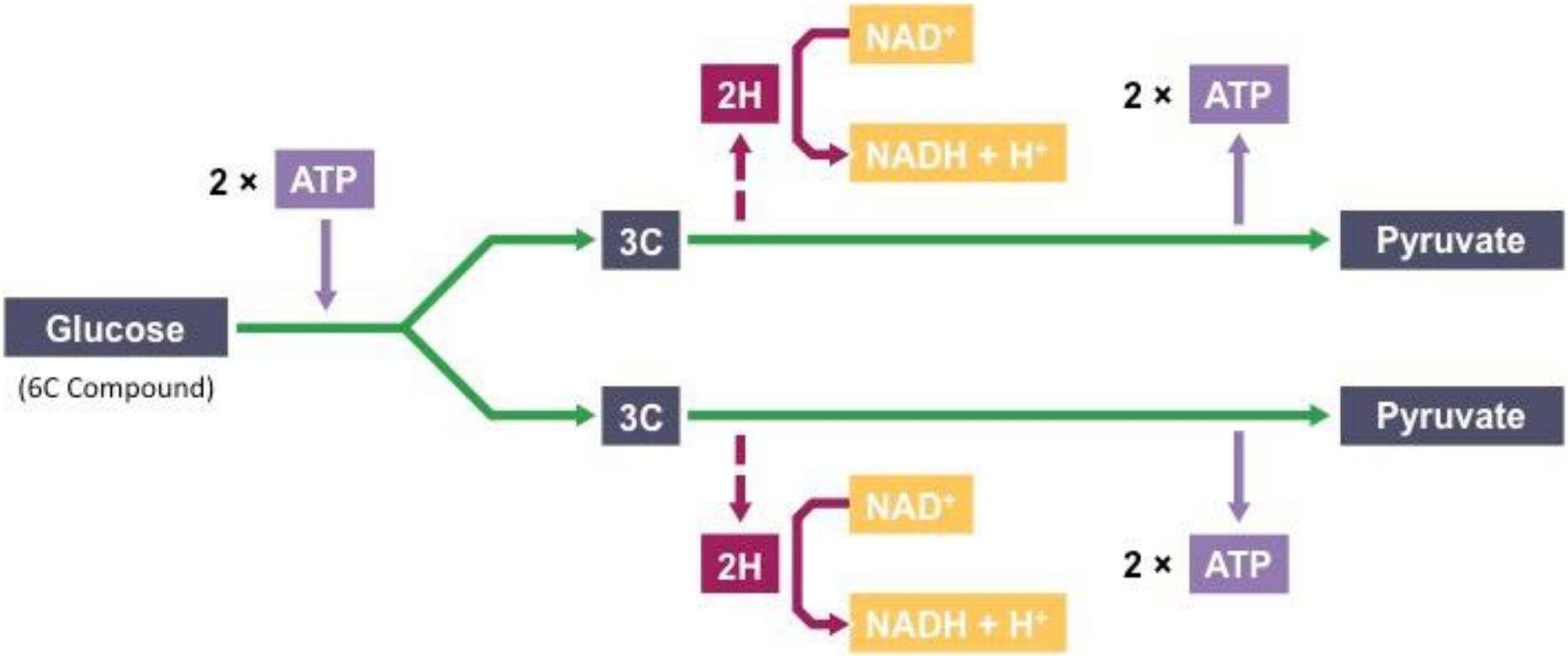
≠

IPOPERFUSIONE

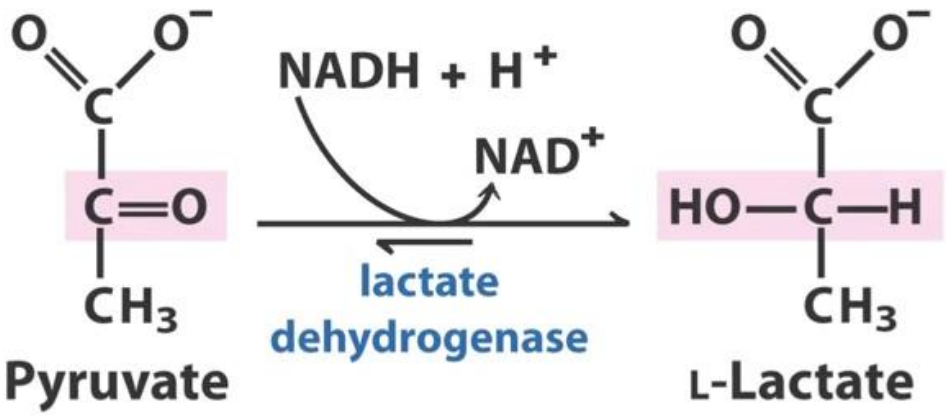
IPERLATTATEMIA

=

RISPOSTA ADATTATIVA



Net Gain: 2 × ATP ; 2 × NADH + H^+ (+ 2 × pyruvate)

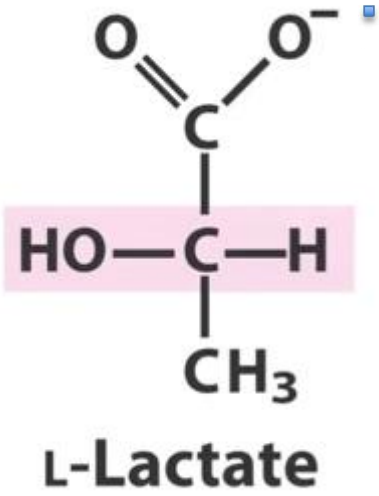


Mediata da LDH che mantiene rapporto 10:1

Libera NAD+ (accettore di elettroni)

Ogni condizione che aumenta la produzione di Piruvato aumenta la generazione di Lattati.

La produzione di Lattato consuma 2 protoni (*J Mol Cell Cardiol* 1997;9[11]:867)



L-Lactate

PRODUZIONE

20 mmol/kg al giorno

CLEARANCE
60-120 mmol/h
(tutto il sangue può essere ripulito in alcuni minuti)

OSSIDAZIONE
(ciclo di Krebs)

50% dei lattati a riposo
Fino all'80% sotto sforzo

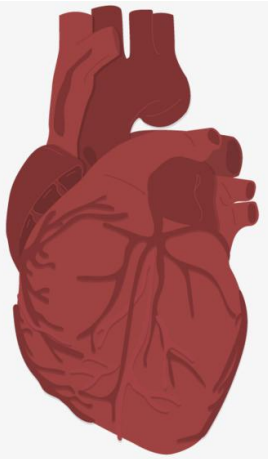
[LATTATO] upregola i trasportatori di membrana mitoncondriale e la LDH mitocondriale

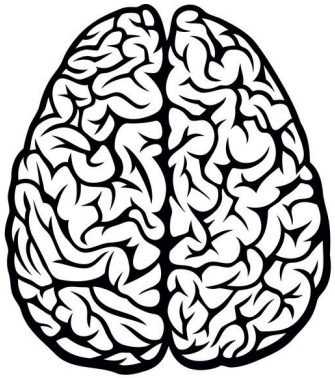
+ Lattato + Krebs

CARBURANTE?

Metabolizza lattati a riposo

Durante shock quasi l'intero fabbisogno energetico viene erogato dall'ossidazione dei LATTATI





Fino al 25% dell'energia è fornita dai LATTATI nei momenti di stress

Esiste uno 'shuttle' astrocita-neuroni (nei primi avviene la glicolisi, nei secondi il Krebs)

LATTATI

=

MARKER DI IPOSSIA TISSUTALE

PRODOTTO DI METABOLISMO ANAEROBIO

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Arterial Blood Gases and Oxygen Content in Climbers on Mount Everest

Michael P.W. Grocott, M.B., B.S., Daniel S. Martin, M.B., Ch.B., Denny Z.H. Levett, B.M., B.Ch., Roger McMorrow, M.B., B.Ch., Jeremy Windsor, M.B., Ch.B., and Hugh E. Montgomery, M.B., B.S., M.D., for the Caudwell Xtreme Everest Research Group*

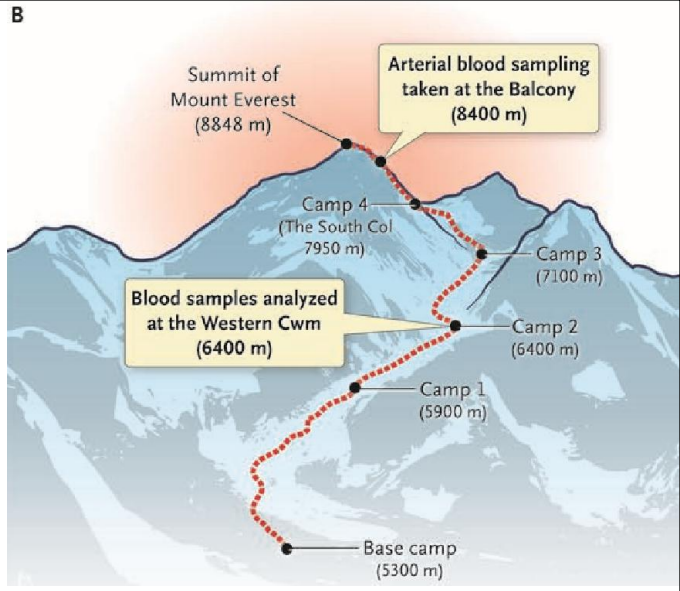


Table 2. Arterial Blood Gas Measurements and Calculated Values for Pulmonary Gas Exchange from Four Subjects at an Altitude of 8400 m, during Descent from the Summit of Mount Everest.*

Variable	Subject No.				Group Mean
	1	2	3	4	
pH	7.55	7.45	7.52	7.60	7.53
PaO_2 (mm Hg)†	29.5	19.1	21.0	28.7	24.6
$PaCO_2$ (mm Hg)†	12.3	15.7	15.0	10.3	13.3
Bicarbonate (mmol/liter)‡	10.5	10.67	11.97	9.87	10.8
Base excess of blood‡	−6.3	−9.16	−6.39	−5.71	−6.9
Lactate concentration (mmol/liter)	2.0	2.0	2.9	1.8	2.2
SaO_2 (%)‡	68.1	34.4	43.7	69.7	54.0
Hemoglobin (g/dl)§	20.2	18.7	18.8	19.4	19.3
Respiratory exchange ratio¶	0.81	0.74‖	0.72	0.70	0.74
PAO_2 — mm Hg†**	32.4	26.9	27.4	33.2	30.0
Alveolar–arterial oxygen difference — mm Hg†	2.89	7.81	6.44	4.51	5.41

aps American Physiological Society | JOURNAL of Applied Physiology

Lactate efflux from exercising human skeletal muscle: role of intracellular P_{O_2}

RUSSELL S. RICHARDSON,[1] ELIZABETH A. NOYSZEWSKI,[2]
JOHN S. LEIGH,[2] AND PETER D. WAGNER[1]
[1]*Department of Medicine, University of California, San Diego, La Jolla, California 92093-0623; and* [2]*Department of Radiology, University of Pennsylvania, Philadelphia, Pennsylvania 19104-6021*

Summary

This investigation illustrates that in hypoxic or normoxic exercise conditions net muscle lactate efflux is independent of intracellular P_{O_2}. The former increases while the latter remains constant during progressive incremental exercise. Although the latter observations indicate that a role for intracellular P_{O_2} as a modulator of metabolism cannot be ruled out, arterial epinephrine levels are closely related to skeletal muscle lactate efflux in normoxia and hypoxia and, thus, may be a major stimulus for the observed rise in muscle lactate efflux during progressively intense exercise and for the elevated lactate efflux in hypoxia.

Crit Care Med. 1994 Apr;22(4):640-50.

Skeletal muscle partial pressure of oxygen in patients with sepsis.

Boekstegers P[1], Weidenhöfer S, Kapsner T, Werdan K.

Author information

Abstract

OBJECTIVE: In order to obtain direct evidence for tissue hypoxia in patients with sepsis oxygen, partial pressure was measured within skeletal muscle. Furthermore, serial intermittent and continuous measurements of skeletal muscle PO2 in patients with sepsis were used to find out whether skeletal muscle oxygenation may change in the course of sepsis and depends on the severity of sepsis.

DESIGN: Prospective study.

SETTING: Intensive care unit of a university hospital.

PATIENTS: Intensive care patients (n = 98) with sepsis (group 1, n = 39; group 4, n = 28), limited infection (group 2, n = 16), and cardiogenic shock (group 3, n = 15).

INTERVENTIONS: Pulmonary artery catheterization; standard antibiotic therapy and volume replacement.

MEASUREMENTS AND MAIN RESULTS: Skeletal muscle PO2 was determined by polarographic needle electrodes or catheter probes. In patients with sepsis (n = 67), no evidence for skeletal muscle hypoxia was obtained from the PO2 distribution within biceps muscle. Mean skeletal muscle PO2 was increased in patients with sepsis (group 1, 48 torr [6.4 kPa]) compared with patients with limited infection (group 2, 28 torr [3.7 kPa]), $p < .001$) and with patients with cardiogenic shock (group 3, 22 torr [2.9 kPa], $p < .001$). Serial measurements of the PO2 distribution during seven consecutive days in another 28 patients (group 4) with sepsis showed that a more severe degree of sepsis was associated with an increase of mean skeletal muscle ($p < .001$). These results were confirmed by continuous measurements of mean skeletal muscle PO2, using PO2 catheters.

CONCLUSIONS: In patients with sepsis, oxygen transport to skeletal muscle was not critically reduced. Serial intermittent and continuous measurements of skeletal muscle PO2 showed that skeletal muscle PO2 increased in relation to the severity of the stage of sepsis. Our findings suggest that oxygen utilization within skeletal muscle decreased with deterioration of sepsis, thereby increasing skeletal muscle PO2.

THE LANCET

Relation between muscle Na^+K^+ ATPase activity and raised lactate concentrations in septic shock: a prospective study

Bruno Levy, Sébastien Gibot, Patricia Franck, Aurélie Cravoisy, Pierre-Edouard Bollaert

Summary

Background Hyperlactataemia during septic shock is often viewed as evidence of tissue hypoxia. However, this blood disorder is not usually correlated with indicators of perfusion or diminished with increased oxygen delivery. Muscles can generate lactate under aerobic conditions in a process linking glycolytic ATP supply to stimulation of Na^+K^+ ATPase. Using in-vivo microdialysis, we tested whether inhibition of Na^+K^+ ATPase can reduce muscle lactate.

LATTATI ELEVATI
NORMALE PO2 TISSUTALE

aminoacid conversion to pyruvate. Nevertheless, evidence seems to implicate accelerated aerobic glycolysis, a definite state when the rate of glucose metabolism exceeds the oxidative capacity of the mitochondria. Accelerated aerobic glycolysis is induced by an endogenous or exogenous catecholamine and an inflammatory state. Gore and colleagues[12] showed that pyruvate production and oxidation are enhanced in septic patients. The rise in pyruvate concentration will ultimately drive lactate production by a mass effect.

ANNALS OF SURGERY
Vol. 224, No. 1, 97–102

Lactic Acidosis During Sepsis Is Related to Increased Pyruvate Production, Not Deficits in Tissue Oxygen Availability

Dennis C. Gore, M.D.,* Farook Jahoor, Ph.D.,† Jacqueline M. Hibbert, Ph.D.,* and Eric J. DeMaria, M.D.*

From the Department of Surgery, Medical College of Virginia, Richmond, Virginia; and the Department of Pediatrics, Baylor College of Medicine,† Houston, Texas*

Objective

The purpose of this study was to quantitate the derangements in intermediary carbohydrate metabolism and oxygen use in severely septic patients in comparison with healthy volunteers.

Summary Background Data

It commonly has been assumed that the development of lactic acidosis during sepsis results from a deficit in tissue oxygen availability. Dichloroacetate (DCA), which is known to increase pyruvate oxidation but only when tissue oxygen is available, provides a means to assess the role of hypoxia in lactate production.

Methods

Stable isotope tracer methodology and indirect calorimetry was used to determine the rates of intermediary carbohydrate metabolism and oxygen use in five severely septic patients with lactic acidosis and six healthy volunteers before and after administration of DCA.

Results

Oxygen consumption and the rates of glucose and pyruvate production and oxidation were substantially greater ($p < 0.05$) in the septic patient compared with healthy volunteers. Administration of DCA resulted in a further increase in oxygen consumption and the percentage of glucose and pyruvate directed toward oxidation. Dichloroacetate also decreased glucose and pyruvate production, with a corresponding decrease in plasma lactate concentration.

Conclusions

These findings clearly indicate that the accumulation of lactate during sepsis is not the result of limitations in tissue oxygenation, but is a sequelae to the markedly increased rate of pyruvate production. Furthermore, the substantially higher rate of pyruvate oxidation in the septic patients refutes the notion of a sepsis-induced impairment in pyruvate dehydrogenase activity.

Concepts in Emergency and Critical Care

Roger C. Bone, MD, *Section Editor*

Reevaluation of the Role of Cellular Hypoxia and Bioenergetic Failure in Sepsis

Richard S. Hotchkiss, MD, Irene E. Karl, PhD

(*JAMA*. 1992;267:1503-1510)

JAMA®

The Journal of the American Medical Association

Sepsis is frequently characterized by a number of metabolic abnormalities: increased plasma lactate concentration, metabolic acidosis, increased glycolysis, and an abnormal "delivery-dependent" oxygen consumption. Two hypotheses have been advanced to explain these metabolic abnormalities: (1) cellular hypoxia resulting from abnormal microcirculatory blood flow or (2) defect(s) in energy-producing metabolic pathways of cells. Results of our studies on rat muscle, liver, heart, brain, and plasma suggest that there is no evidence of bioenergetic failure in these septic tissues and that the increase in lactate production is not necessarily due to cellular hypoxia. The adequacy of cellular oxygenation and bioenergetics was verified using in vivo phosphorus 31 nuclear magnetic resonance spectroscopy, [^{18}F]fluoromisonidazole, and microfluorometric enzymatic techniques. Findings from these studies as well as results from several clinical investigations indicate that neither hypothesis can adequately account for the metabolic features typical of sepsis and that the pathophysiology of sepsis awaits further clarification. These studies and important clinical implications are discussed.

(*JAMA*. 1992;267:1503-1510)

CLINICAL IMPLICATIONS

Perhaps the most important implication of the present review is that the hypothesis that sepsis results in systemic, ie, multiorgan, cellular hypoxia,[74,78-80] may be incorrect. Several investigative groups have proposed that the multiple organ failure that occurs in patients with sepsis is due to a substantial cumulative tissue oxygen debt that may be difficult to recognize.[79,80] In addition, these investigators argue that effective therapy for the patient with sepsis should consist of maximizing oxygen delivery to supranormal values in an attempt to reverse the presumed cellular hypoxia.[79,80] Our results using an animal model of sepsis as well as findings from the clinical studies of patients with sepsis discussed in the present report do not support the concept of systemic cellular hypoxia. It is important to note, however, that cellular hypoxia/ischemia is *not* excluded in the gastrointestinal tract or kidney. Although

Intensive Care Med (2007) 33:495–502
DOI 10.1007/s00134-006-0523-9

EXPERIMENTAL

Bruno Levy
Arnauld Mansart
Chantal Montemont
Sebastien Gibot
Jean-Pierre Mallie
Veronique Regnault
Thomas Lecompte
Patrick Lacolley

Myocardial lactate deprivation is associated with decreased cardiovascular performance, decreased myocardial energetics, and early death in endotoxic shock

Experimental data demonstrate that lactate production in the muscle is linked to epinephrine stimulation of the Na^+/K^+-ATPase pump [4]. In human septic shock we have demonstrated that muscle is a net producer of lactate, and that this production is totally inhibited by ouabain, thus confirming a Na^+/K^+-ATPase-dependent mechanism while clearly independent of tissue hypoxia [5]. Muscle

MODELLO ANIMALE

SOMMINISTRATO B-Bloccante e DCA (stimola PDH)

RIDUZIONE DEI LATTATI

COLLASSO CARDIOVASCOLARE

AUMENTO MORTALITA’

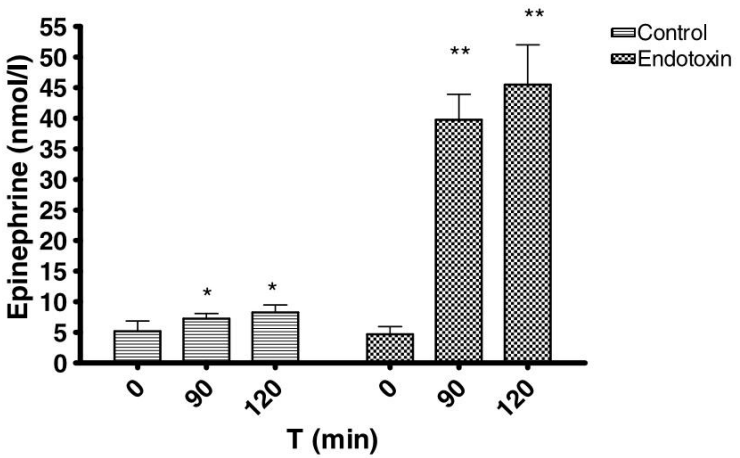


Fig. 1 Plasmatic concentrations of epinephrine. Epinephrine concentrations were measured before and during endotoxic. $*p < 0.01$ vs. t_0, $**p < 0.01$ vs. controls

Intensive Care Med (2007) 33:495–502
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EXPERIMENTAL

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Myocardial lactate deprivation is associated with decreased cardiovascular performance, decreased myocardial energetics, and early death in endotoxic shock

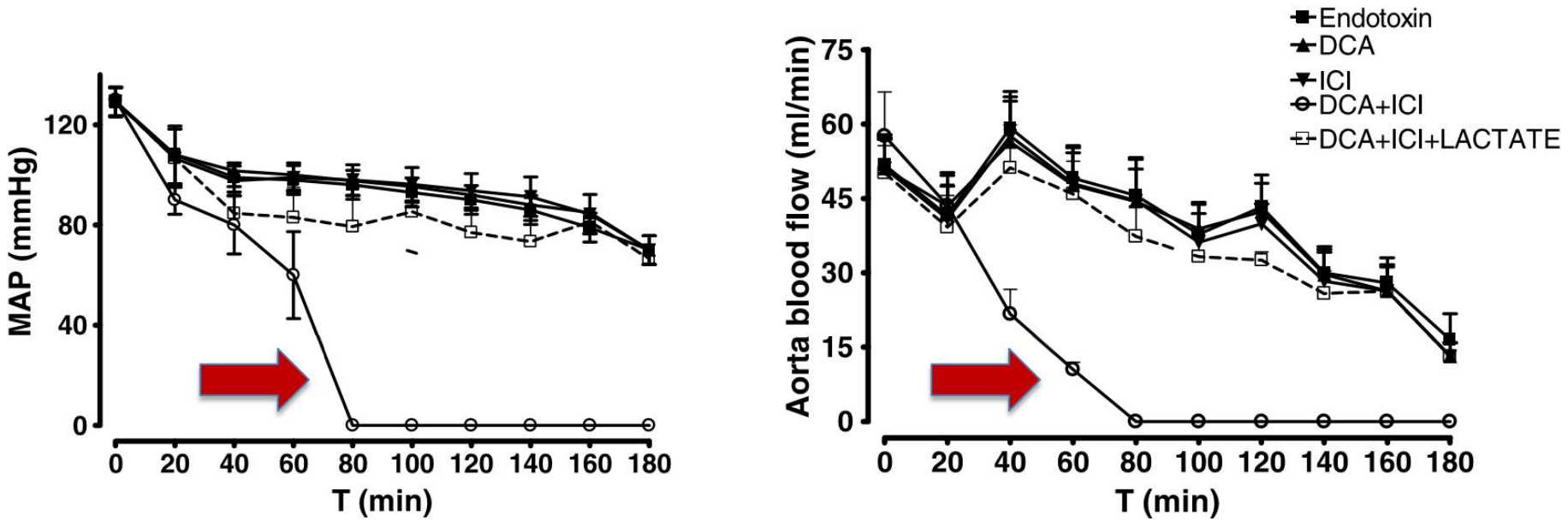

Fig. 3 Course of mean arterial pressure (*MAP*) and aorta blood flow in rats treated by either endotoxin, endotoxin plus ICI-118551, endotoxin plus dichloroacetate (*DCA*), endotoxin plus ICI-118551 plus DCA and endotoxin plus ICI-118551 plus DCA plus lactate. Neither DCA nor ICI-1185551, a selective β_2-blocker, changed MAP or aorta blood flow compared to endotoxin alone. The combination DCA and ICI-118551 dramatically decreased MAP and aorta blood flow and led to early death ($p < 0.01$). The addition of lactate blunted the effects of ICI plus DCA on hemodynamics ($p < 0.01$)

GLICOSI e GLICOGENOLISI AEROBIA INDOTTA DAL DRIVE ADRENERGICO	**Il metabolismo dei carboidrati eccede la capacità del ciclo di Krebs di lavorare il Piruvato**
AUMENTATO CATABOLISMO	**Gli Aminoacidi vengono trasformati in Piruvato**
RUOLO DELLA POMPA Na^+/K^+ ATPasi	**Consuma ATP** **ADP stimola Glicolisi e fa produrre Lattati**

the CONCLUSIONS

IPERLATTATEMIA E' COMUNE NEI PAZIENTI SETTICI ED E' UN MARKER DI MORTALITA' E DI SEVERITA' DI MALATTIA

IPERLATTATEMIA POTREBBE NON ESSERE UN MARKER DI IPOSSIA

IPERLATTATEMIA POTREBBE ESSERE UN MARKER DI RISPOSTA ALLO STRESS DA PARTE DELL'ORGANISMO

LA SEPSI NON PUO' ESSERE TRATTATA IN MANIERA STANDARDIZZATA MA SECONDO LE NECESSITA' DEL PAZIENTE