

J.B. Wolffe

Memorial Lecture 1996

**Challenging beliefs:
Ex Africa Semper Aliquid Novi (Pliny 50AD)**



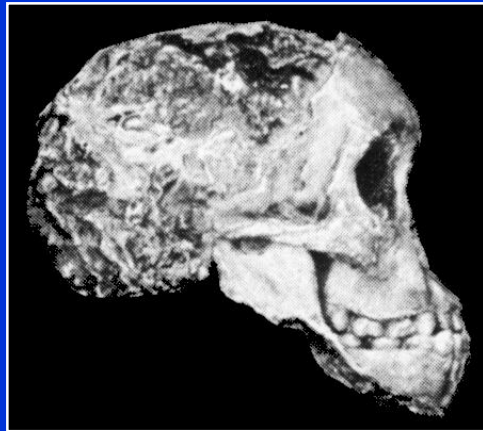
**SPORT
SCIENCE**
Institute of
South Africa

Professor Tim Noakes MBChB, MD, FACSM

**Discovery Health Chair of Exercise and Sports Science,
University of Cape Town and
Sports Science Institute of South Africa**

Why the title?

Ex Africa Semper Aliquid Novi
(Out of Africa, Always Something New)

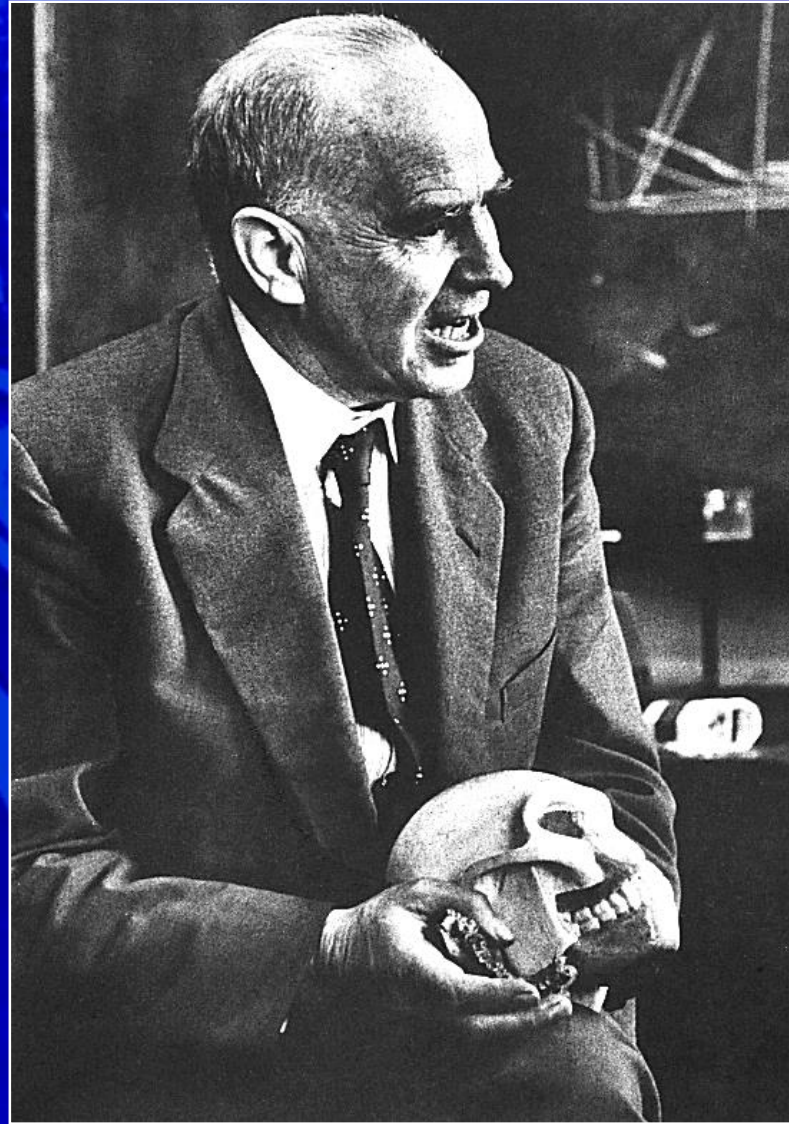


AFRICA
Cradle of Mankind

SUDAN
ETHIOPIA
UGANDA
KENYA
Olduvai Gorge
TANZANIA

JHB
Taung





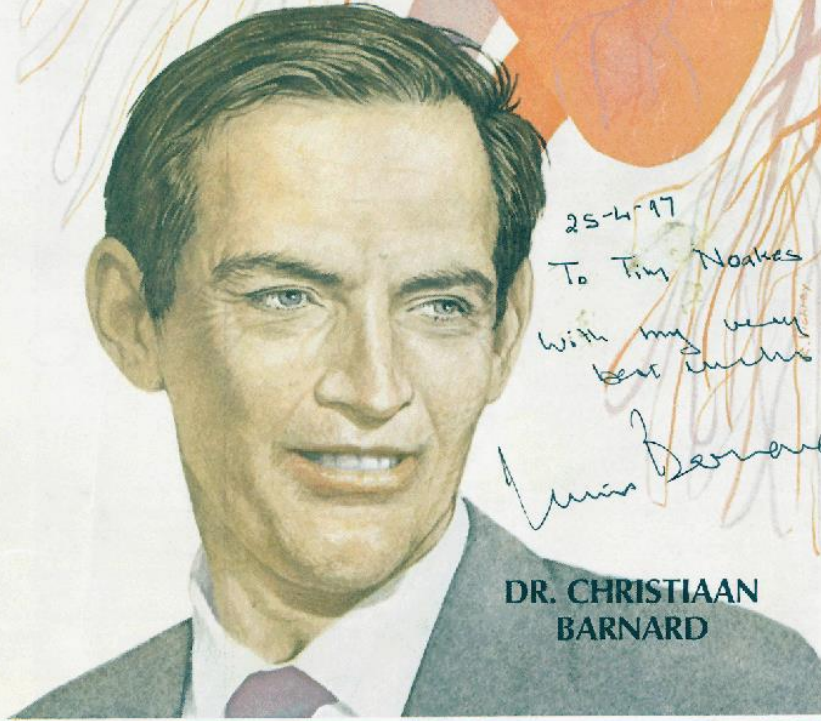
FIFTY CENTS *

DECEMBER 15, 1967

THE TRANSPLANTED HEART

TIME

THE WEEKLY NEWSMAGAZINE



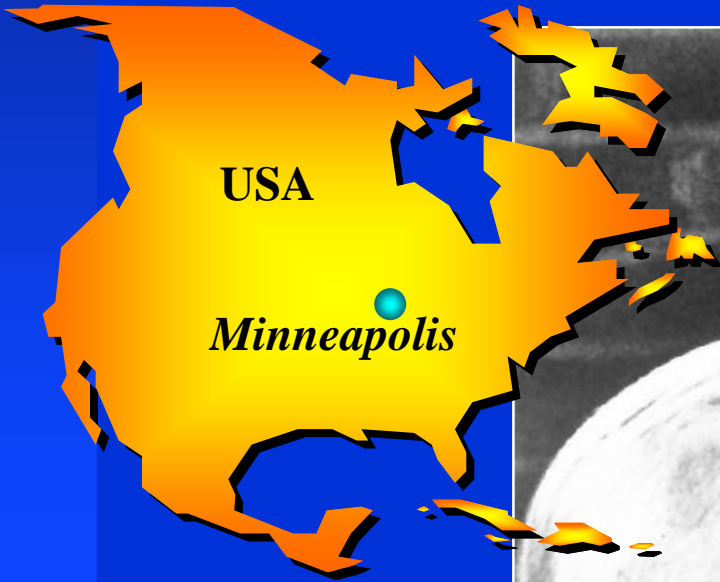
25-4-97
To Tim Noakes
With my very
best wishes
Christiaan Barnard

DR. CHRISTIAAN
BARNARD





World's first human heart transplant



**Prof. Owen
Wangensteen**



**Prof. Chris
Barnard**



Cape Town





Professor Chris Barnard

“Most of us think along straight lines, like a bus or a train or a tram. If the destination isn’t up on the board, few of us would know where we are going – and that applies even to scientific researchers who should know better. *We tend to let tradition lead us by the nose.* It takes an effort of will to break out of the mould.”

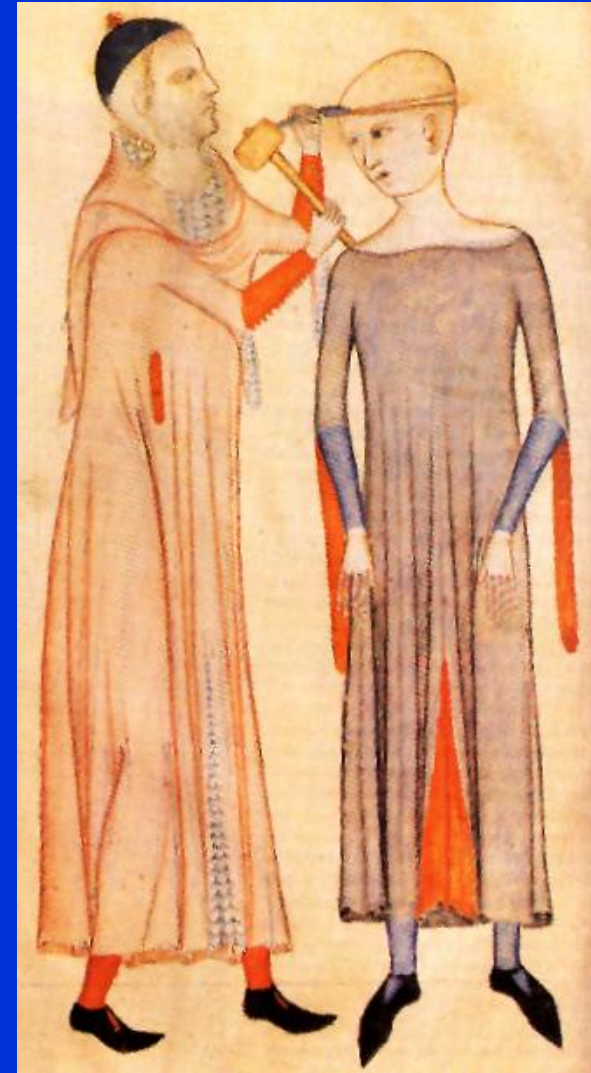


*D. Cooper (Ed): Chris Barnard by those who know him.
Vlaeberg, Cape Town, p.65, 1992.*



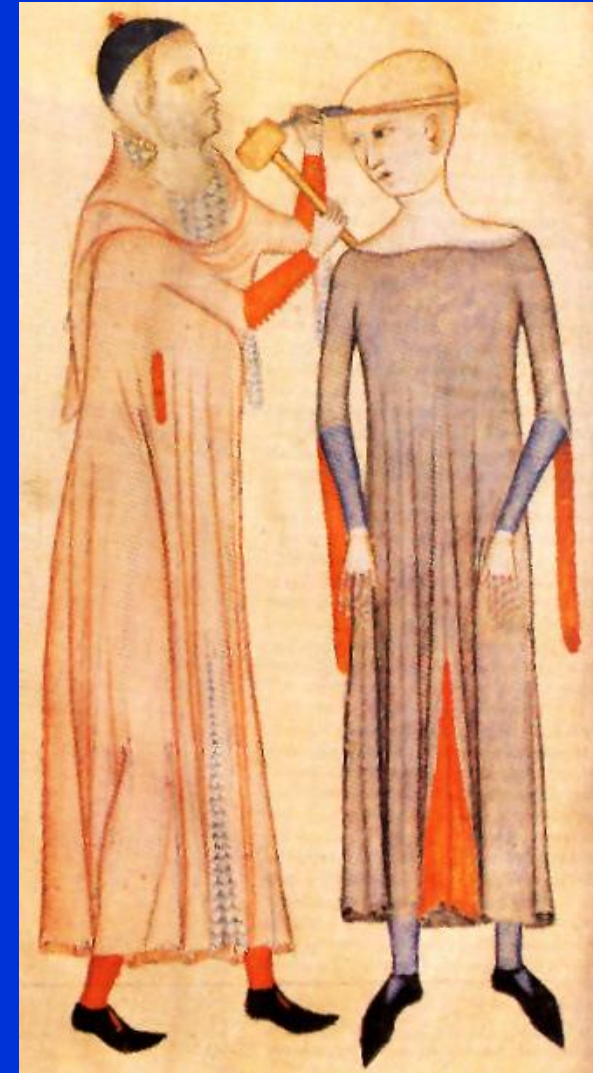
What my medical training taught me

- To understand the whole body



What my medical training taught me

- To understand the whole body
- Our level of ignorance





“The greatest single achievement of science in this most scientifically productive of centuries is the discovery that we are profoundly ignorant ... I wish there were some formal courses in medical school on Medical Ignorance; textbooks as well, although they would have to be very heavy volumes. We have a long way to go ...”

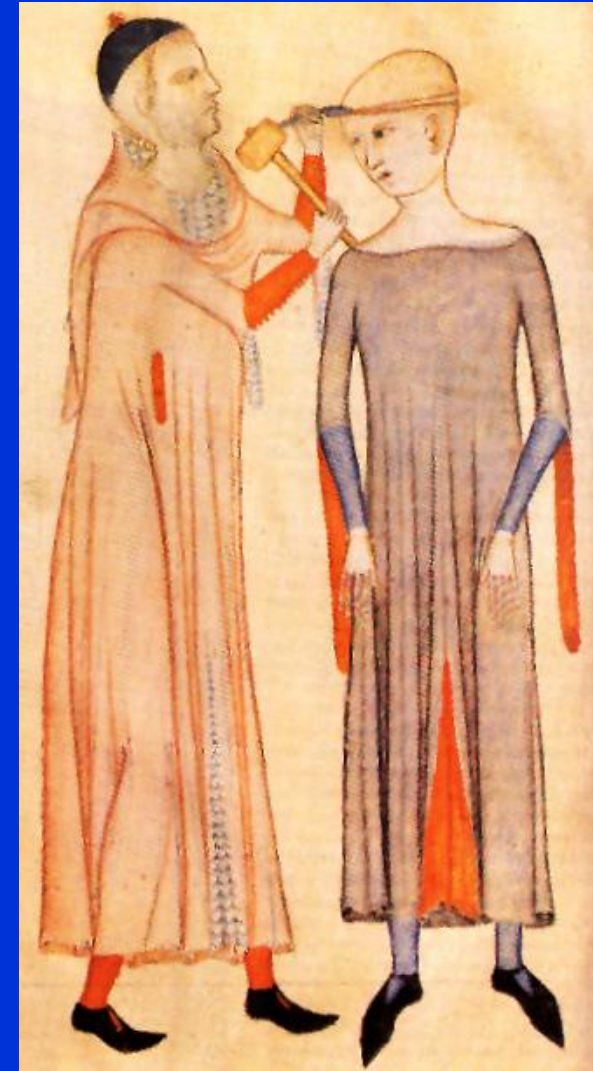


*Dr L. Thomas Medicine as a very old profession.
In Cecil Textbook of Medicine 17th edition; pp 9-11, 1985.*

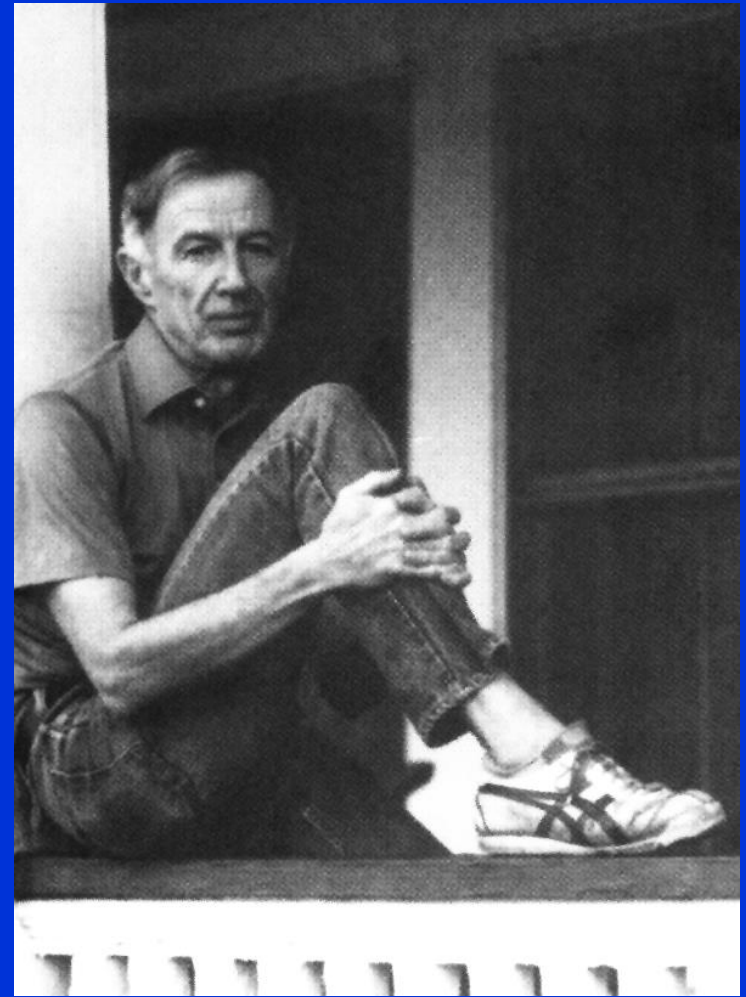


What my medical training taught me

- To understand the whole body
- Our level of ignorance
- To challenge the “truth”



“My students are dismayed when I say to them, ‘half of what you are taught as medical students will in 10 years have been shown to be wrong. And the trouble is, none of your teachers know which half!’”



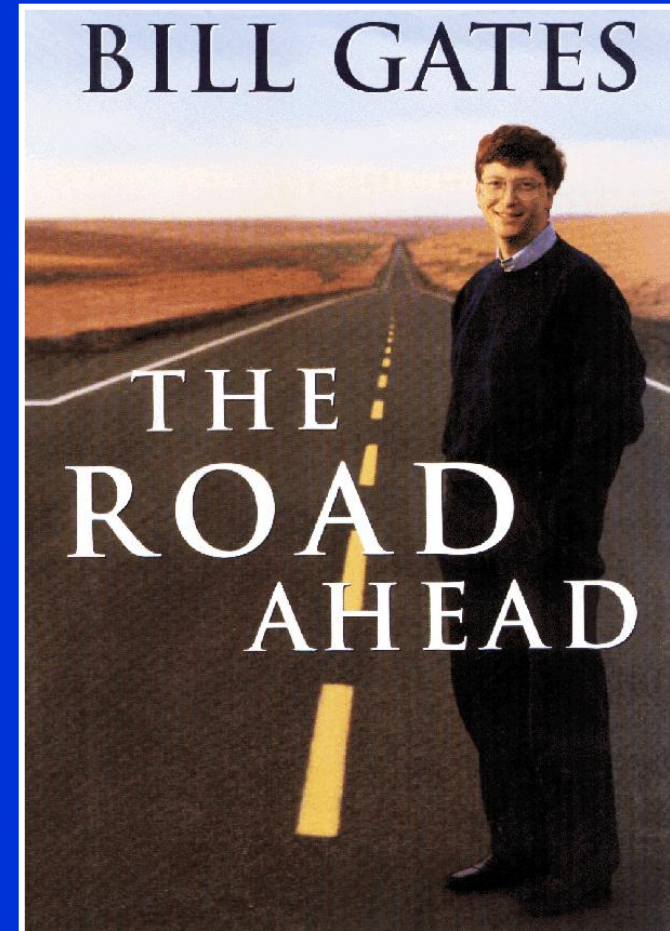
George Sheehan, MD, 1918-1993.

Dr S. Burwell Dean of Harvard Medical School. Quoted by Sir G. Pickering. BMJ 2; 113-116, 1956.



The goal of education

“The point of school is not to fill your mind with facts. The goal should be to learn how the world works, the underlying principles. You must study specifics in order to do that, but the specifics aren’t what you’re learning.”



Bill Gates, 1997.





**“The philosophies of one age
have become the absurdities
of the next”**

Sir William Osler

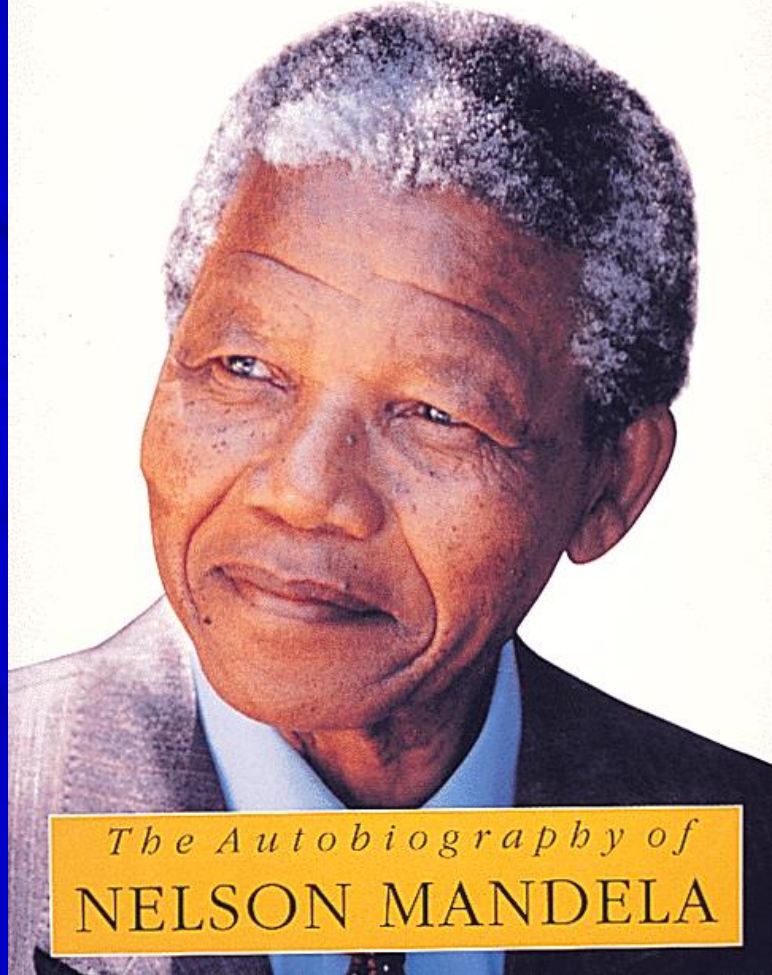


What South Africa teaches me

- Change



LONG WALK TO
FREEDOM



The Autobiography of
NELSON MANDELA



What South Africa teaches me

- Change
- Sport and national reconciliation





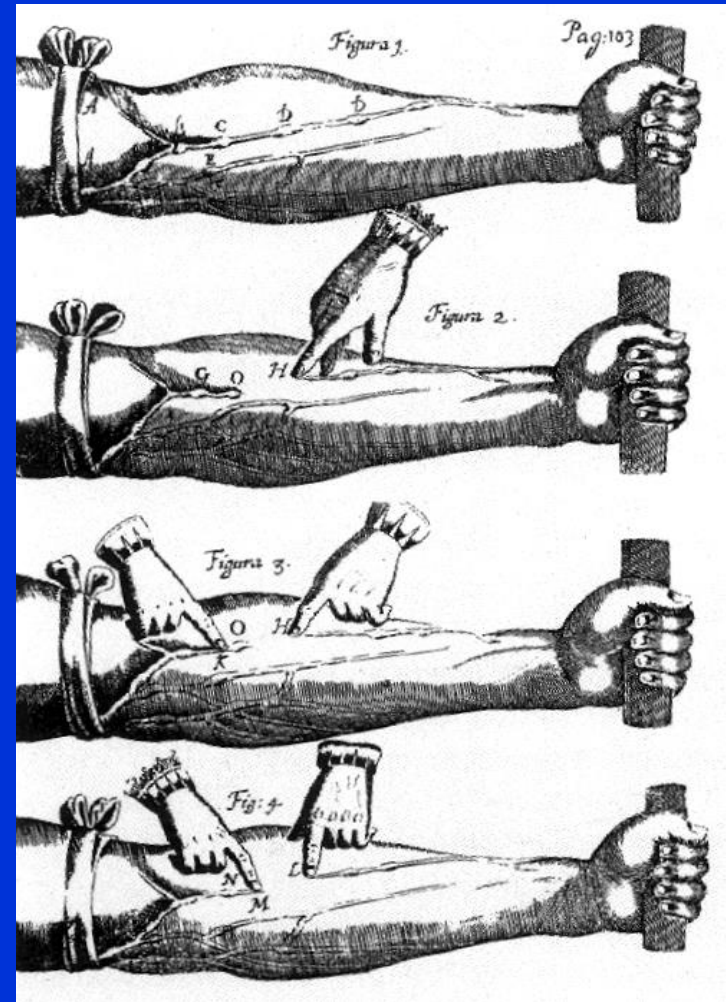
failed What my medical training [^] to teach me

- Scientific method
- Modern biochemistry
- Exercise physiology
- Sports medicine



What science has taught me

- The burden of disproof



The burden of disproof *

“A statement (a theory, a conjecture) has the status of belonging to the empirical sciences if and only if it is falsifiable.”

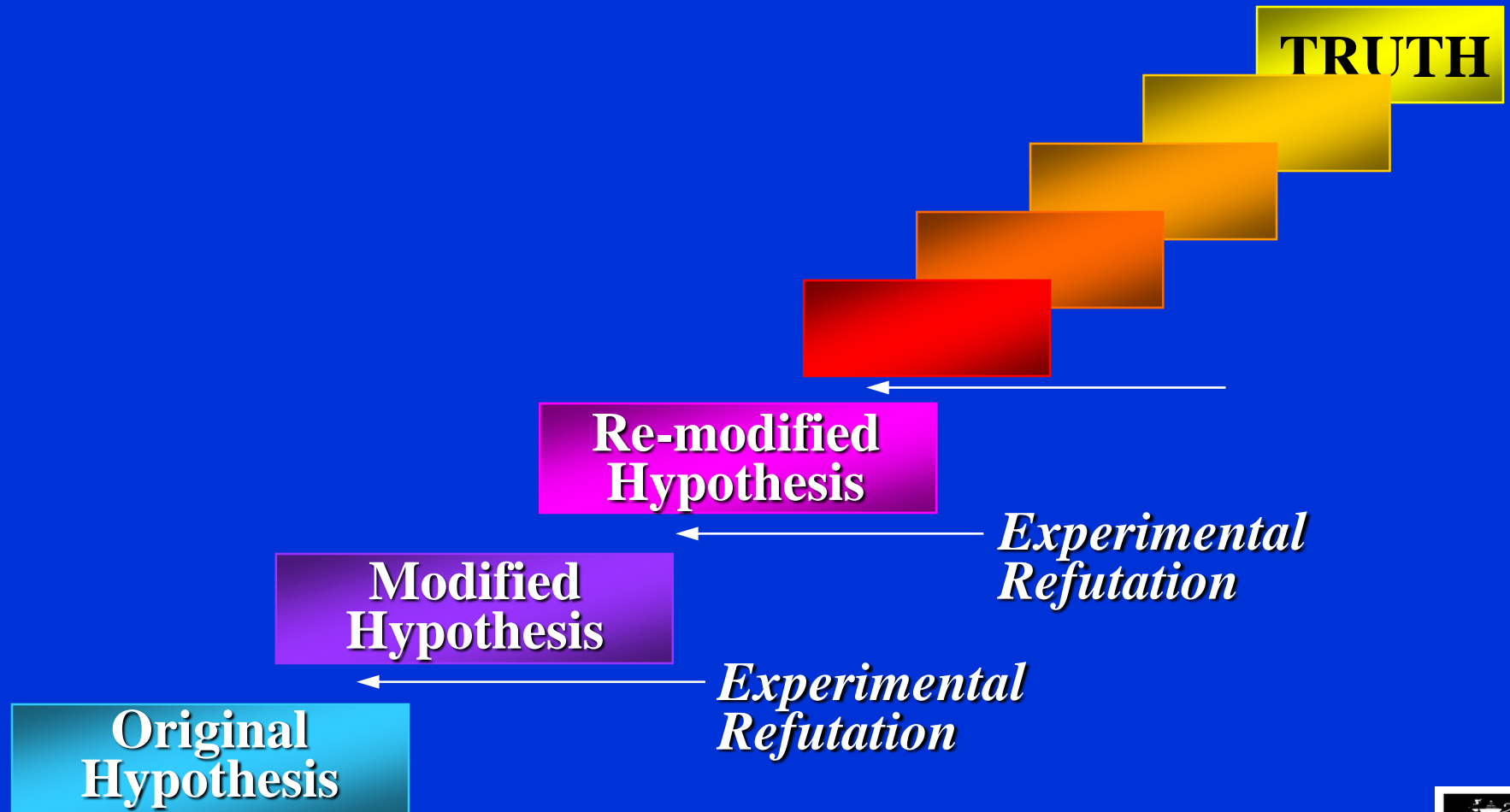
“A statement or theory is, according to my criterion, falsifiable if and only if there exists at least one potential falsifier – at least one possible basic statement that conflicts with it logically.”

*Sir K. Popper Realism and the Aim of Science.
Hutchinson, London. p XIX – XX, 1988.*

* *Victor Katch. Medicine and Science in Sports and Exercise 18; 593-595, 1985.*

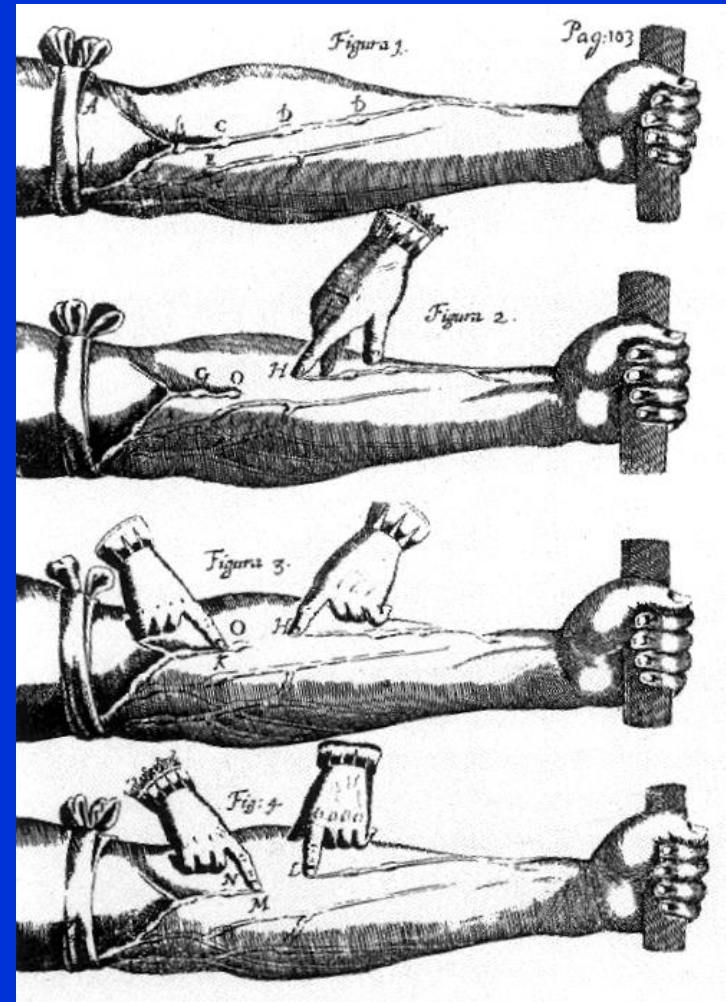


The process by which repeated refutations (falsifications) leads to the “truth”



What science has taught me

- The burden of disproof
- The development of paradigms (Intellectual models)



The development of paradigms (Intellectual models)

“Thinking people tend to develop some framework into which they try to fit whatever new idea they may come across; as a rule, they even translate any new idea which they meet into a language appropriate to their framework. **One of the most characteristic tasks of philosophy is to attack, if necessary, the framework itself.**”



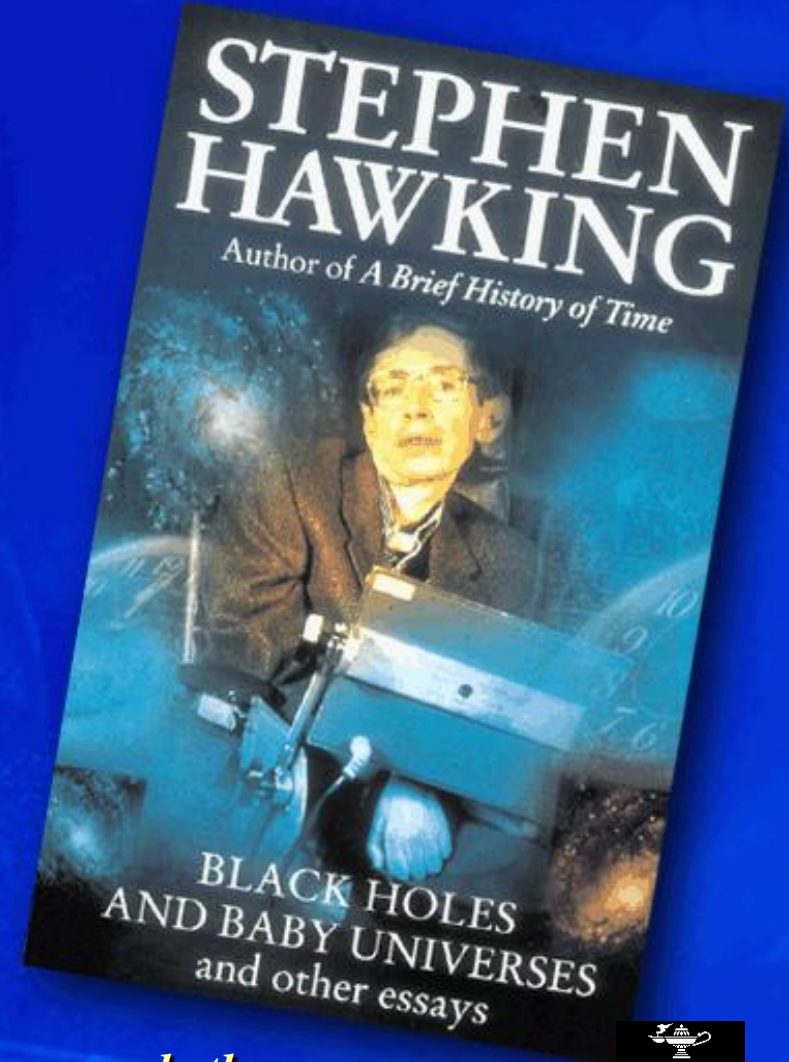
*Sir K. Popper Realism and the Aim of Science.
Hutchinson, London. p14, 1988.*



Model-dependent reality: Stephen Hawking

“A theory is a good.. *model* if it describes a wide class of observations and if it predicts the results of new observations. Beyond that it makes no sense to ask if it corresponds to reality, *because we do not know what is reality independent of a theory.*”

How can we know what is real, independent of a theory or model with which to interpret it?”

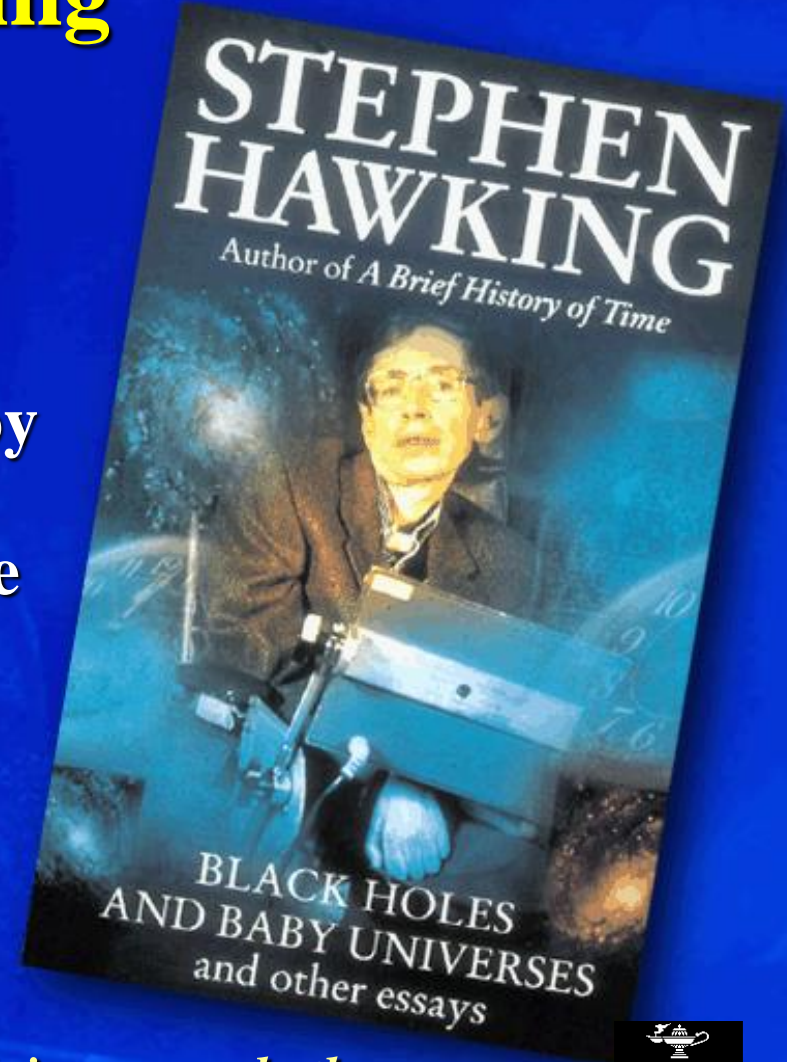


Stephen Hawking. Black Holes and Baby Universes and other essays. Bantam Books, London, p.38, 1993.



The theory (model) always comes first: Stephen Hawking

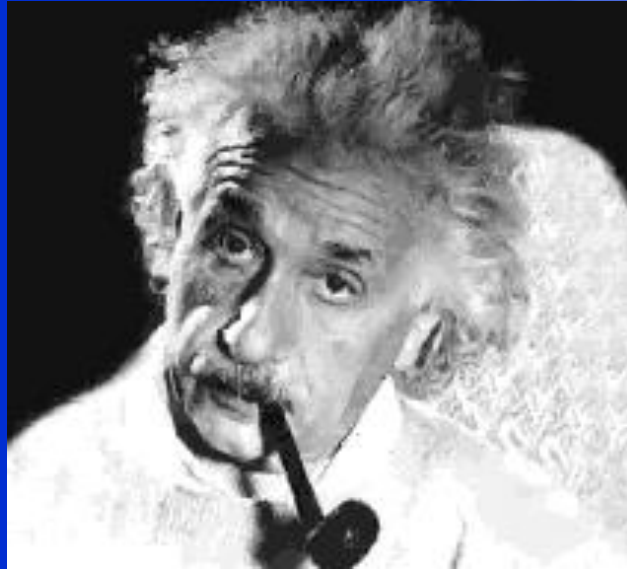
“*The theory always comes first*, put forward from the desire to have an elegant and consistent mathematical model. The theory then makes predictions, which can then be tested by observation. If the observations agree with the predictions, that doesn't prove the theory; but the theory survives to make further predictions, which are tested against observation. *If the observations don't agree with the predictions, one abandons the theory*”.



Stephen Hawking. *Black Holes and Baby Universes and other essays*. Bantam Books, London, p.36, 1993.



Scientific Truth according to Albert Einstein

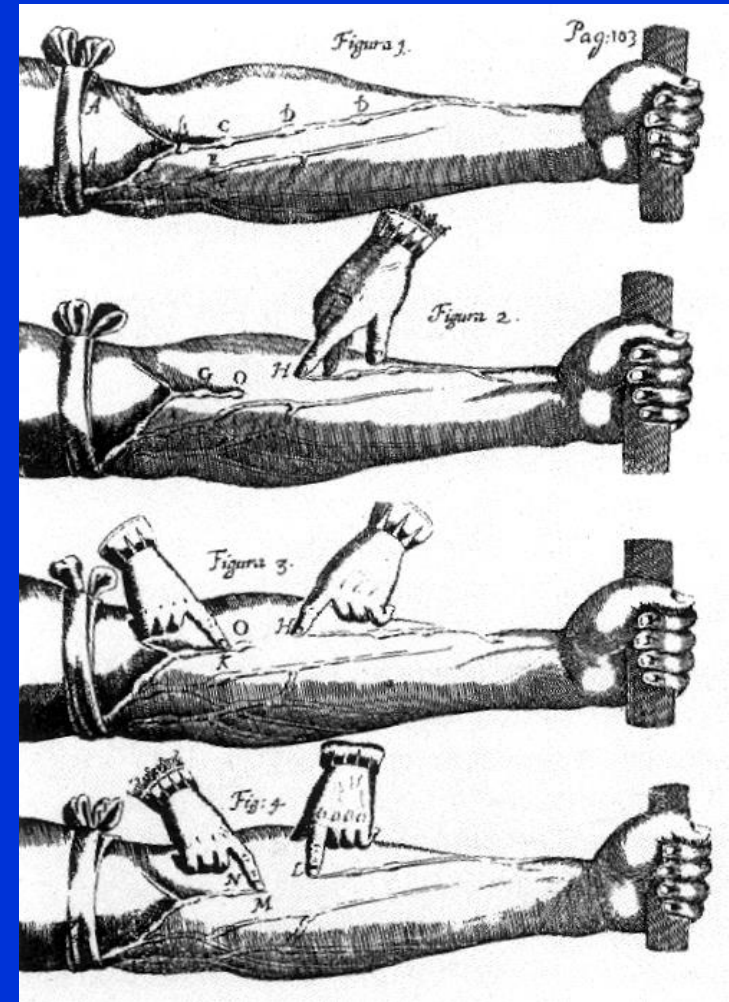


“No amount of experimentation can
ever prove me right;
a single experiment may at any time
prove me wrong”



What science has taught me

- The burden of disproof
- The development of paradigms (Intellectual models)
- The nature of “truth” in scientific endeavour



Truth in scientific endeavour

- Truth changes
- Truth is model dependent
- Truth reveals itself through refutation of the less-true



Why are novel ideas accepted with reluctance by the scientific community?



The preference for scientific orthodoxy

“At any given moment there is an orthodoxy, a body of ideas of which it is assumed that all right-thinking people will accept without question. It is not exactly forbidden to say this, that or the other, but it is “not done” to say it... Anyone who challenges the prevailing orthodoxy finds himself silenced with surprising effectiveness. A genuinely unfashionable opinion is almost never given a fair hearing, either in the popular press or in the high-brow periodicals.”



George Orwell. Introduction to 'Animal Farm', 1945.



Why new ideas are not accepted

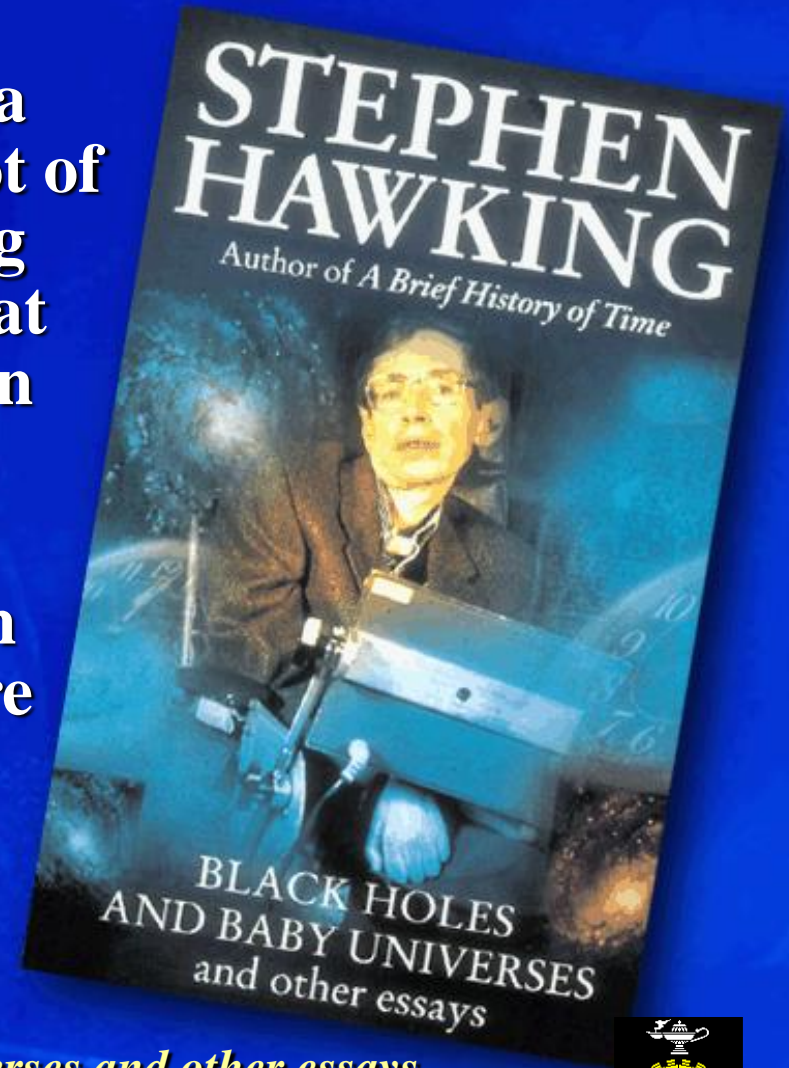
“A discovery is premature if its implications cannot be connected by a series of simple logical steps to canonical, or generally accepted, knowledge.”

Gunter Stent, Scientific American 227; 84-93, 1972.



Creaking and Ugly Edifices

“People are very reluctant to give up a theory in which they have invested a lot of time. They usually start by questioning the accuracy of the observations. If that fails, they try to modify the theory in an ad hoc manner. *Eventually the theory becomes a creaking and ugly edifice.* Then someone suggests a new theory in which all the awkward observations are explained in an elegant and natural manner”



Stephen Hawking. Black Holes and Baby Universes and other essays. Bantam Books, London, p.36, 1993.



Five Creaking and Ugly Edifices

The VO_2 Max. Hill

Muscle Hypoxia during Maximal Exercise

Anaerobic Threshold

Mitochondrial Adaptations and Exercise Performance

High Carbohydrate Diet and Exercise Performance



*What causes fatigue during
high intensity exercise of
short duration?*

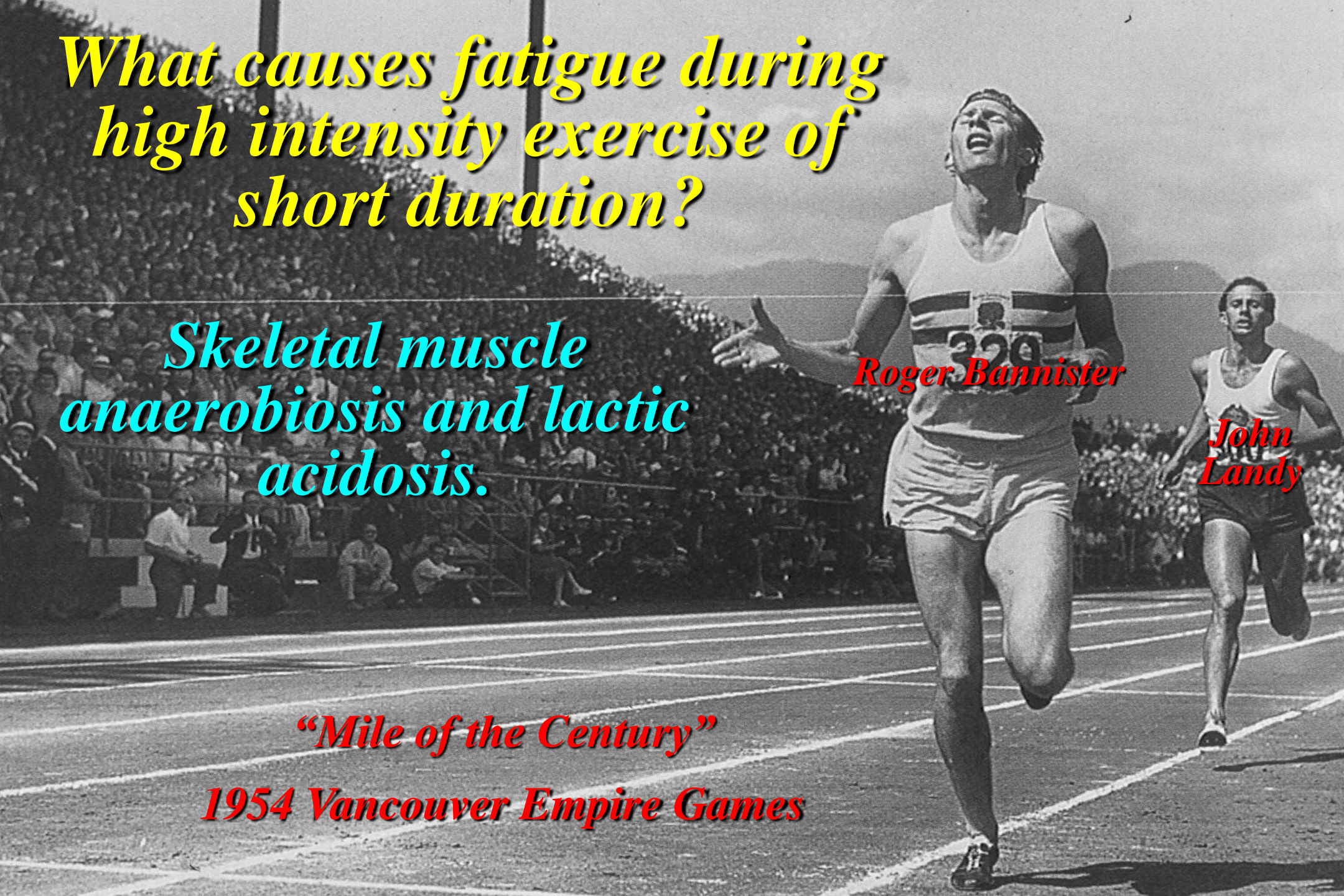
*Skeletal muscle
anaerobiosis and lactic
acidosis.*

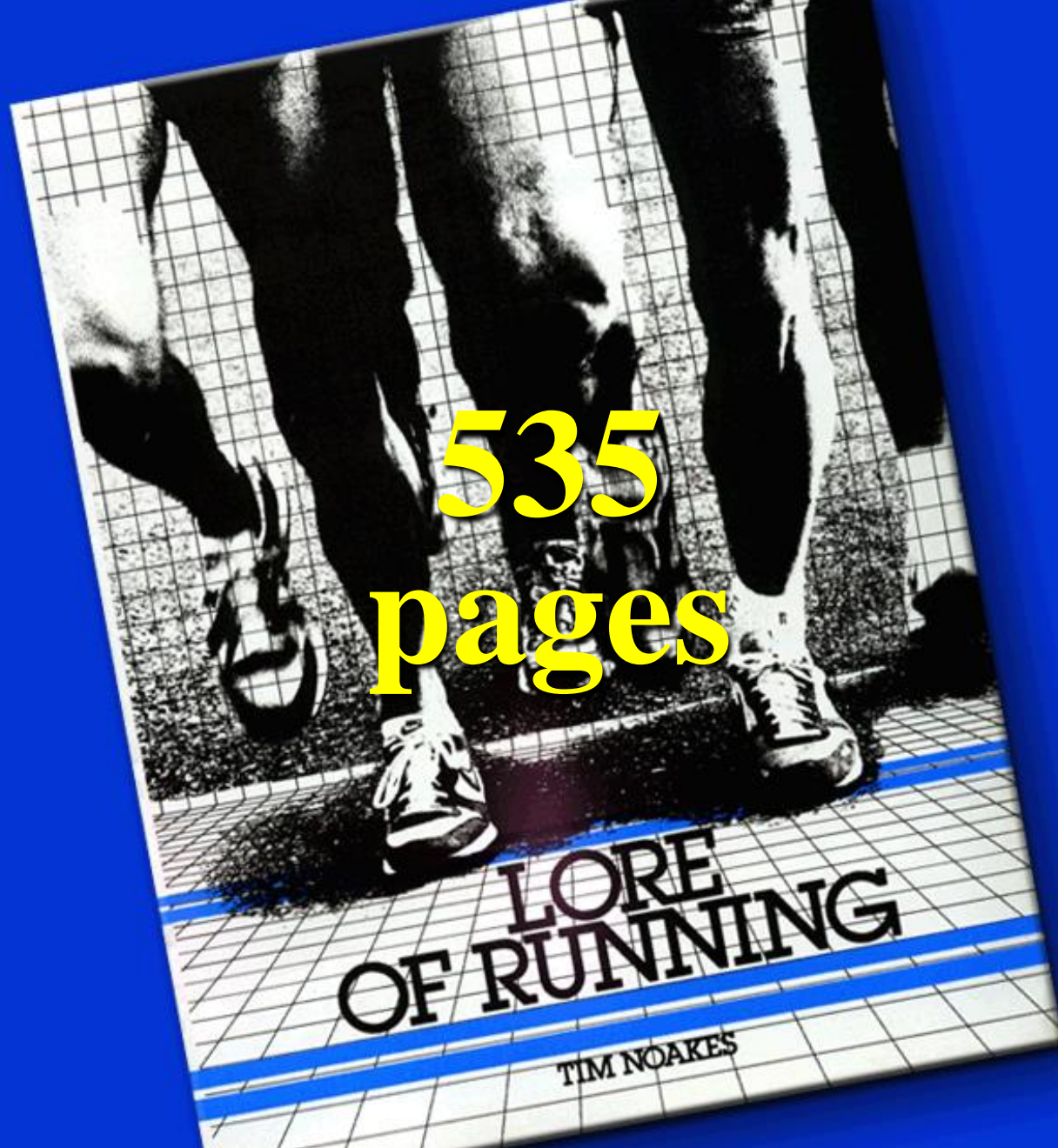
Roger Bannister

*John
Landy*

“Mile of the Century”

1954 Vancouver Empire Games

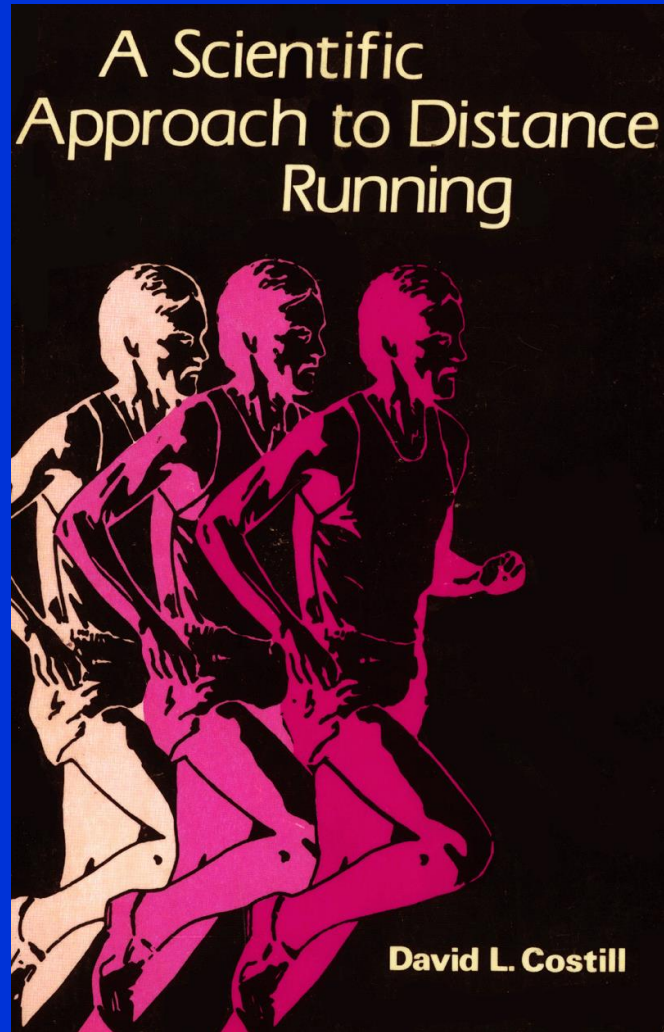




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Oxygen consumption and athletic performance

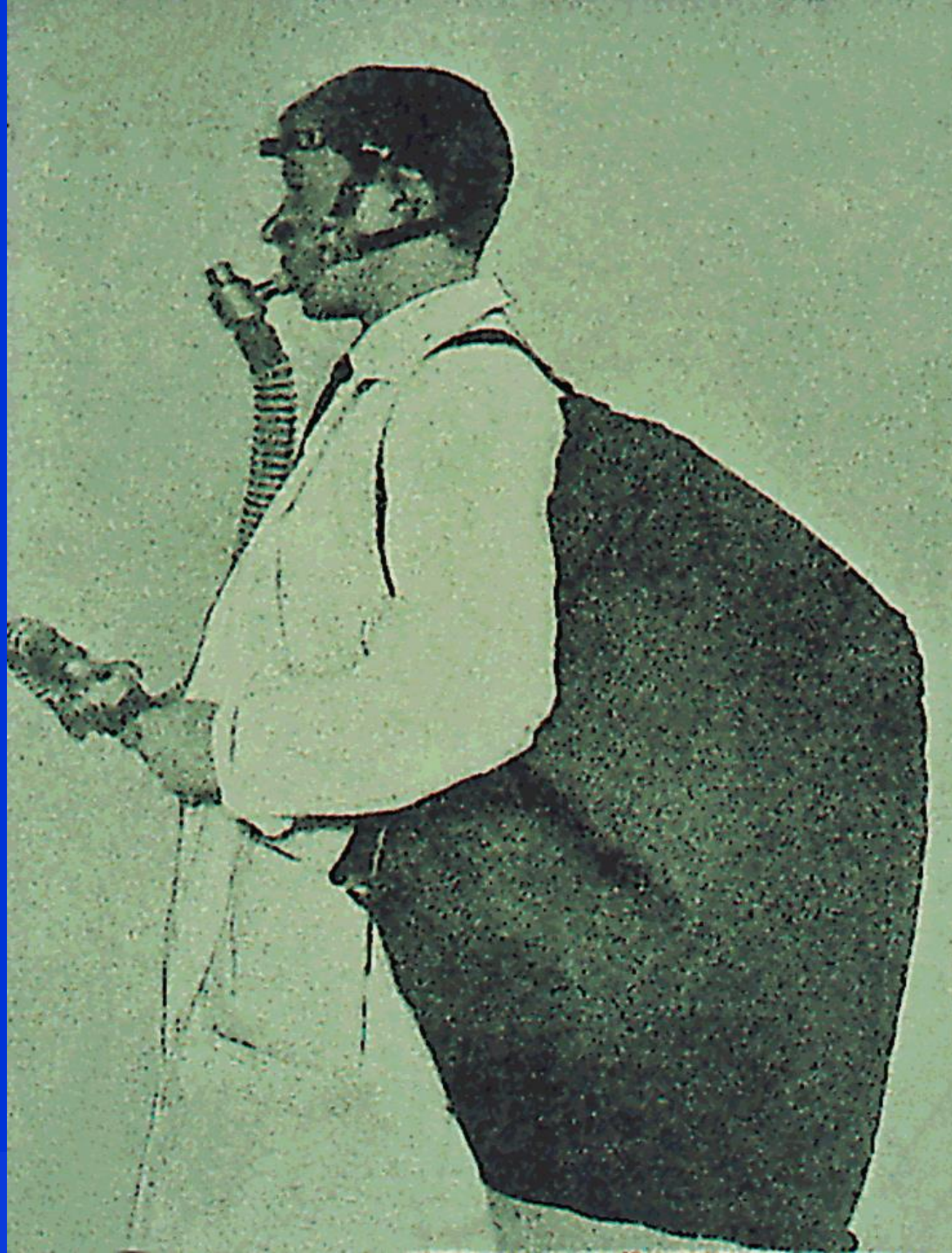


“Since the early work of Hill and Lupton (1923), exercise physiologists have associated the limits of human endurance with the ability to consume larger volumes of oxygen during exhaustive exercise.”

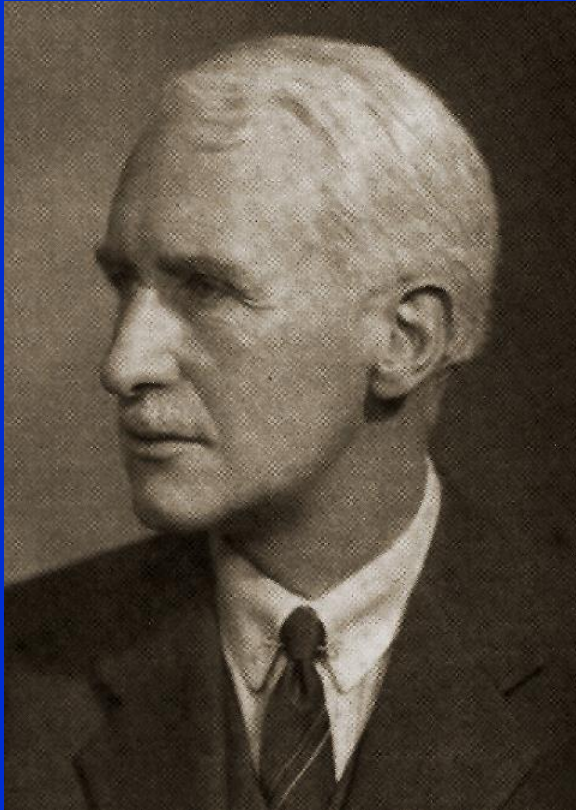


David Costill. A Scientific Approach to Distance Running. Tafnews, p.26, 1979.





Fatigue during exercise of progressively increasing intensity to exhaustion – (testing for maximum oxygen consumption)



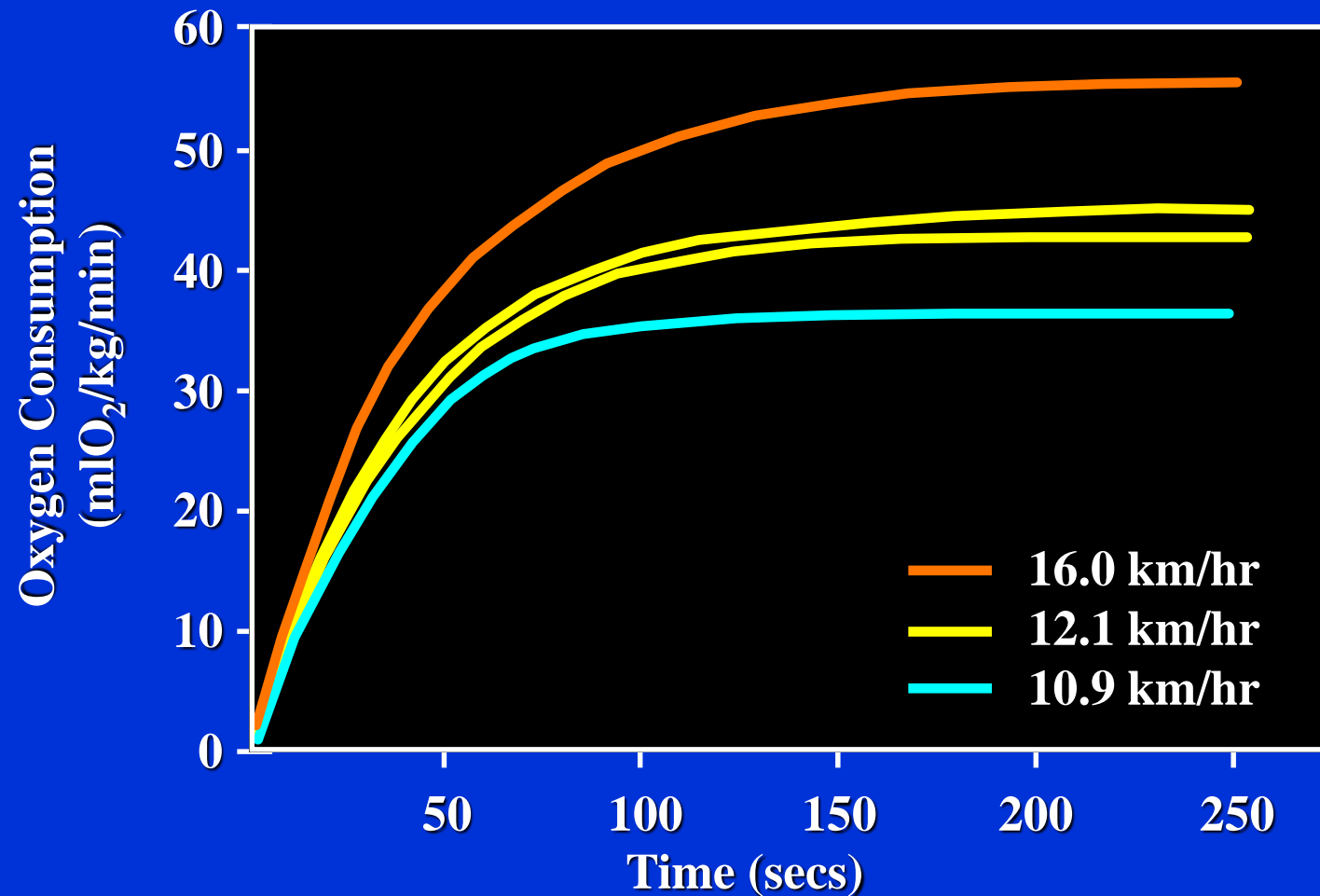
The classic Archibald Vivian Hill theory (1923-1935)

“Considering the case of running ... there is clearly some critical speed for each individual ... above which, the maximum oxygen intake is inadequate, lactic acid accumulating, a continuously increasing oxygen debt being incurred, fatigue and exhaustion setting in”.

*A.V. Hill, C.N.H. Long and H. Lupton
Proceedings of the Royal Society of Britain 97; 84-138, 1924.*



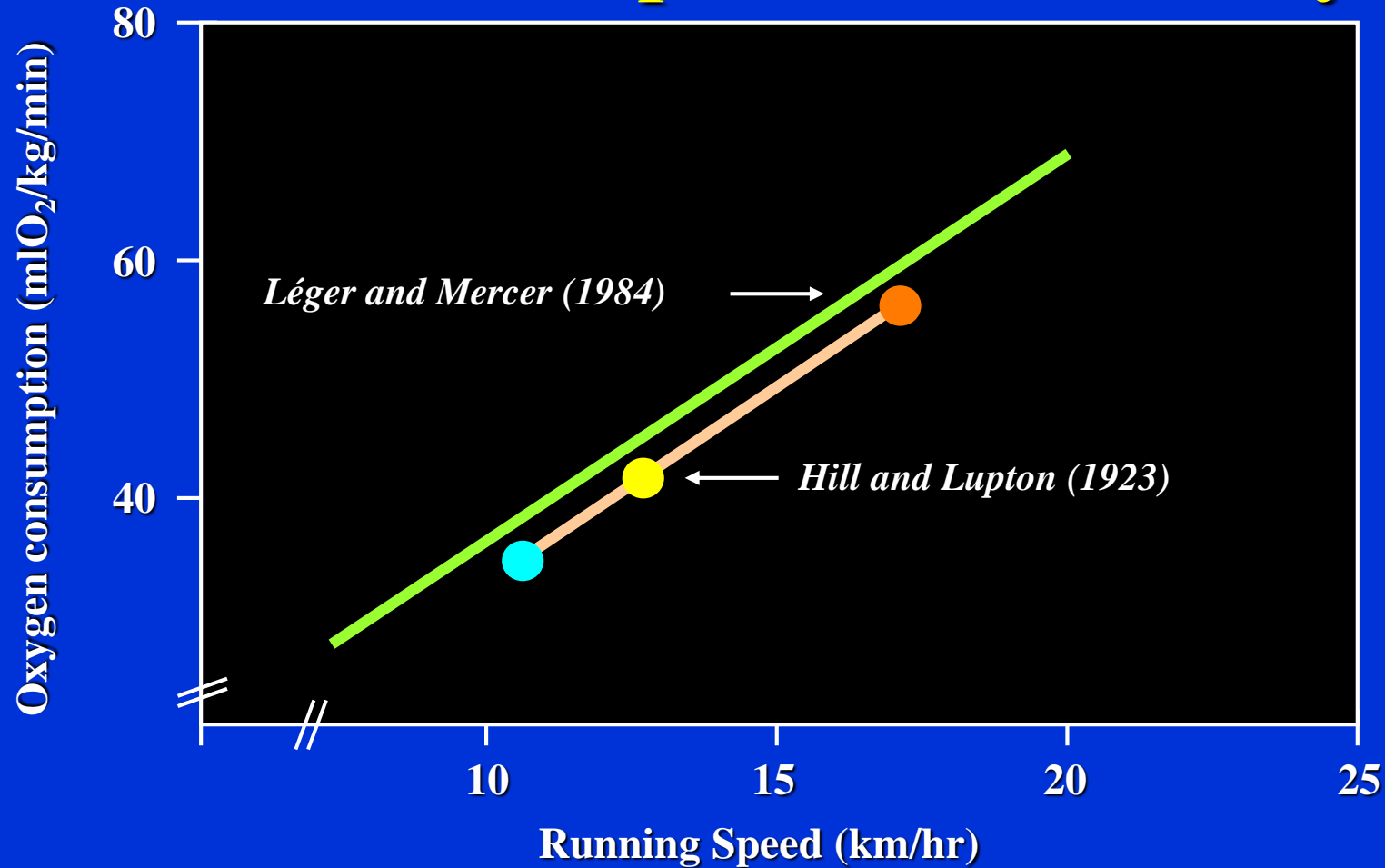
Early experiments



*A.V. Hill and H. Lupton.
Quarterly Journal of Medicine 16; 135 - 171, 1923.*



Absence of the plateau phenomenon in Hill and Lupton's 1923 study



T.D. Noakes. Medicine and Science in Sports and Exercise 20; 319 - 330, 1988.



**MEDICINE
& SCIENCE
IN SPORTS
& EXERCISE**

OFFICIAL JOURNAL
ISSN: 0195-9131

ORIGINAL INVESTIGATIONS

Implications of exercise testing for prediction of athletic performance: a contemporary perspective

Assumption.

Every single actin-myosin crossbridge is active during maximal exercise (complete muscle recruitment/activation).

...of a failure of muscle contractility (“muscle power”), which may be independent of tissue oxygen deficiency. The implications for exercise testing and the prediction of athletic performance are discussed.



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MEDICINE

& SCIENCE

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OFFICIAL JOURNAL
ISSN: 0195-9131

1996 J.B. WOLFFE MEMORIAL LECTURE

Challenging beliefs: *ex Africa semper*

Assumption.

There is complete muscle recruitment during all forms of exhaustive exercise.

myocardial ischemia during exercise in persons with heart failure, of hyperthermia during exercise in the heat, and of cerebral hypoxia during exercise at extreme altitude.



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VOL. 29, NO. 5, MAY 1997

MEDICINE & SCIENCE IN SPORTS & EXERCISE®

OFFICIAL JOURNAL OF THE AMERICAN COLLEGE OF SPORTS MEDICINE
ISSN: 0195-9131

response to the challenge

Maximal oxygen uptake: “classical” versus “contemporary” viewpoints

DAVID R. BASSETT, JR. and EDWARD T. HOWLEY

Exercise Science Unit, University of Tennessee, Knoxville, TN 37919

...When we weigh the scientific evidence on both sides of the issue, it appears that Hill’s views were amazingly accurate. Scientific investigations in the 70 years since Hill have served mainly to reinforce his paradigm and confirm that his scientific “hunches” were correct. Only relatively minor refinements to his theories have been needed.

In contrast, Noakes’ views are not supported by strong scientific evidence, and they raise numerous paradoxes and unresolved dilemmas.



VOL. 29, NO. 5, MAY 1997

MEDICINE & SCIENCE IN SPORTS & EXERCISE

OFFICIAL JOURNAL OF THE AMERICAN COLLEGE OF SPORTS MEDICINE
ISSN: 0195-9131

BASIC SCIENCES - *Commentary*

Maximal oxygen uptake: “classical” versus “contemporary” viewpoints: a rebuttal

TIMOTHY DAVID NOAKES

*Department of Exercise and Sports Science and Bioenergetics of Exercise
Research Unit of the Medical Research Council, University of Cape Town,
Sports Science Institute of South Africa, Newlands, 7700, SOUTH AFRICA*

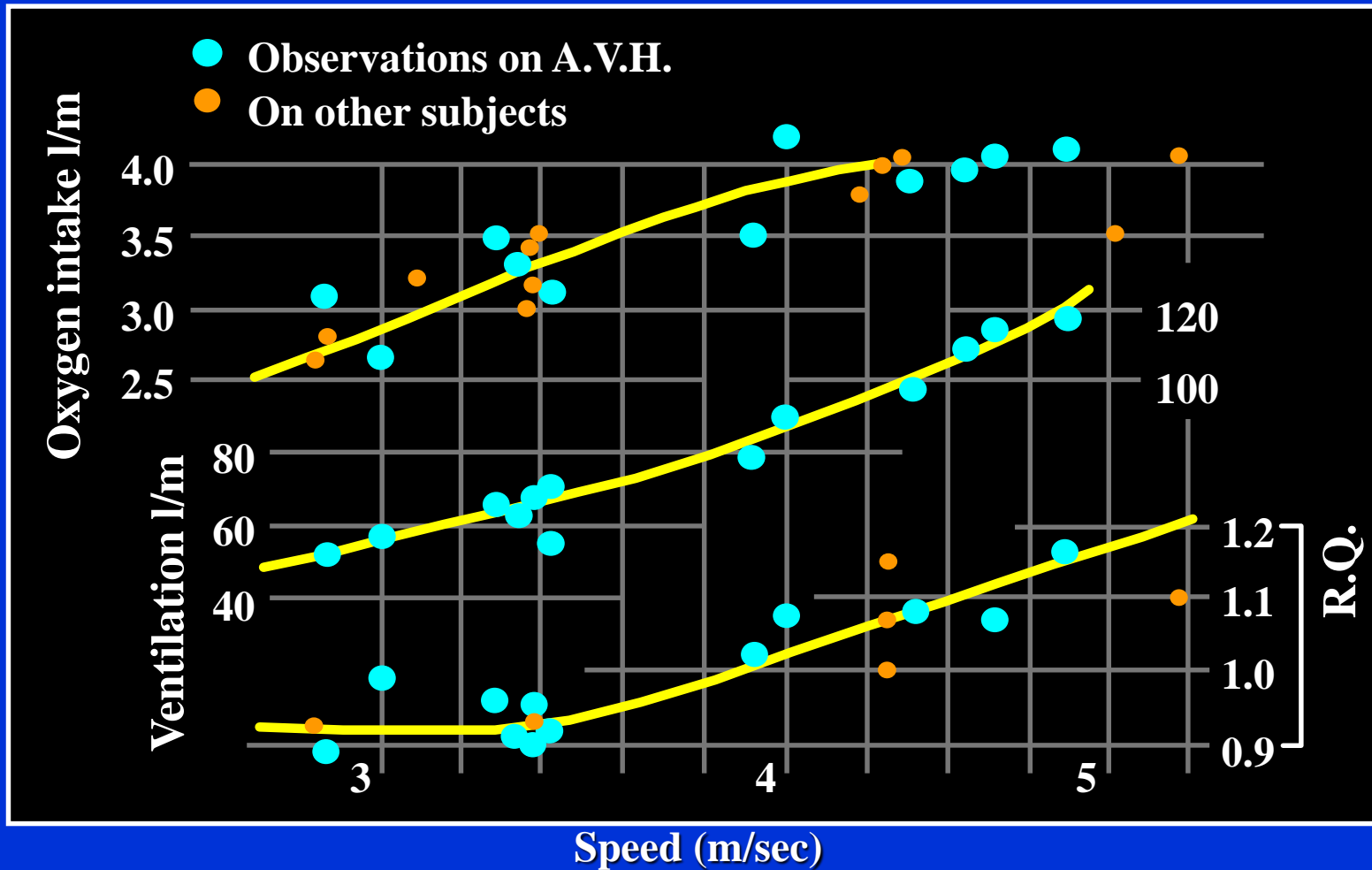

Williams & Wilkins
A HAWKERS COMPANY



Medicine and Science in Sports and Exercise 31; 1381 - 1398, 1998.



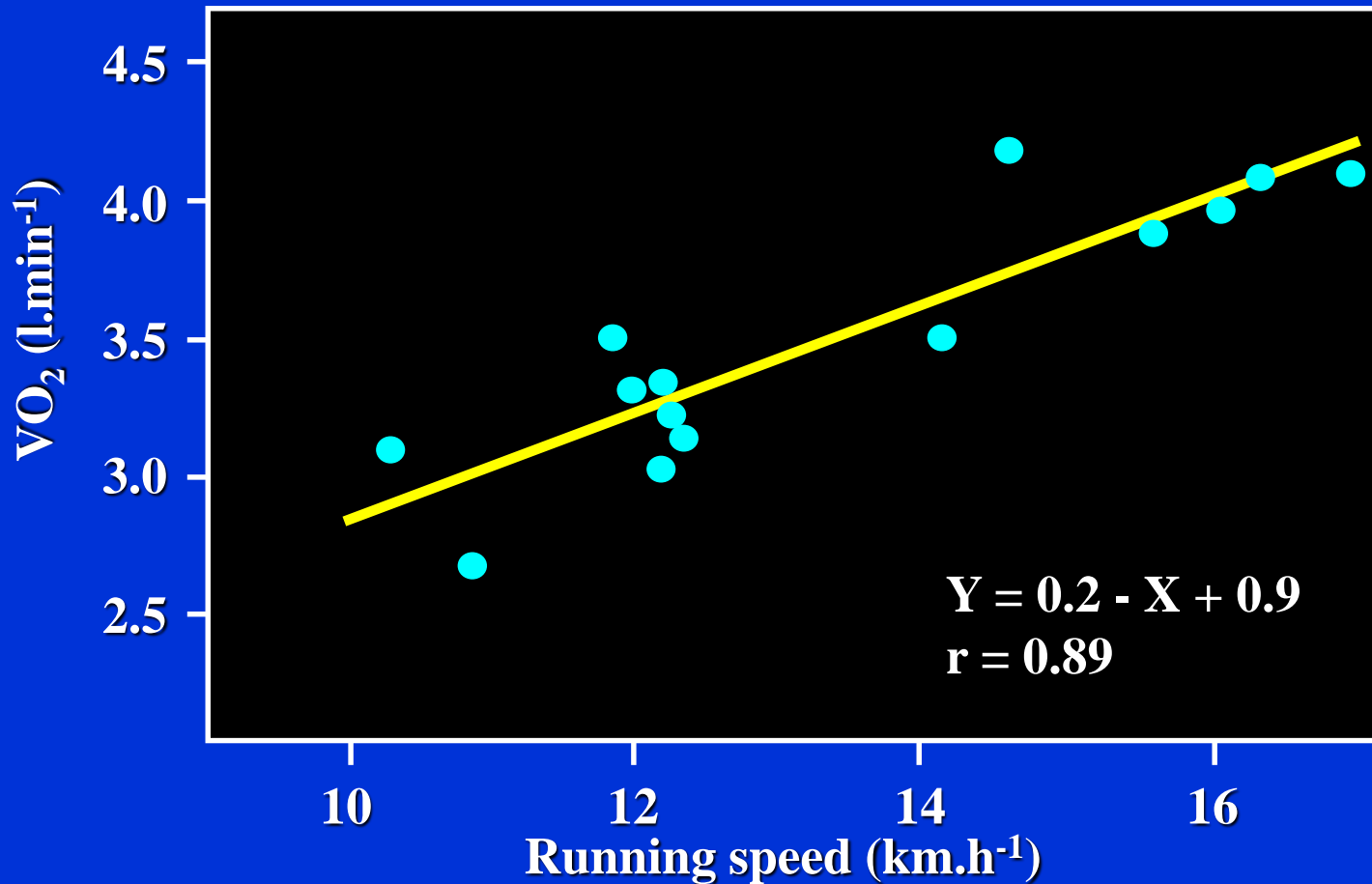
AV Hill's other evidence for the "Plateau Phenomenon"



A.V. Hill, C.N. Long and H. Lupton.
Proceedings of the Royal Society B 97: 157, 1924.



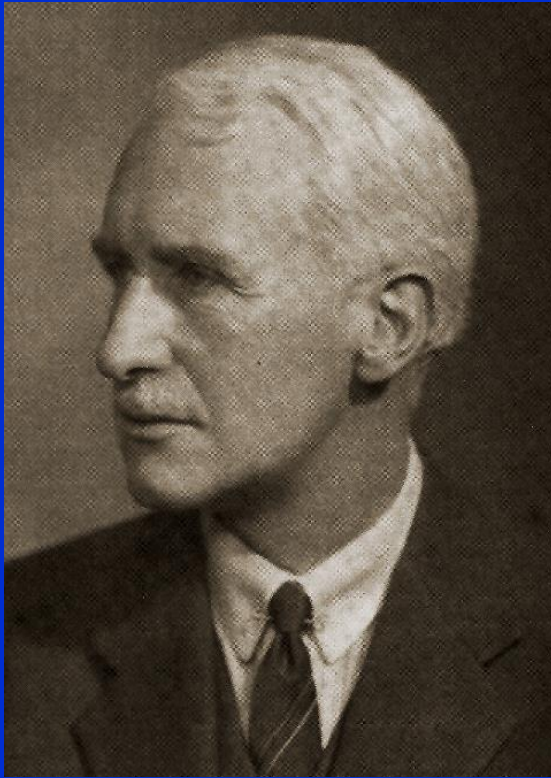
AV Hill's other evidence for the "Plateau Phenomenon"



*A.V. Hill, C.N. Long and H. Lupton.
Proceedings of the Royal Society B 97: 157, 1924.*



The universal VO_2 max concept of AV Hill



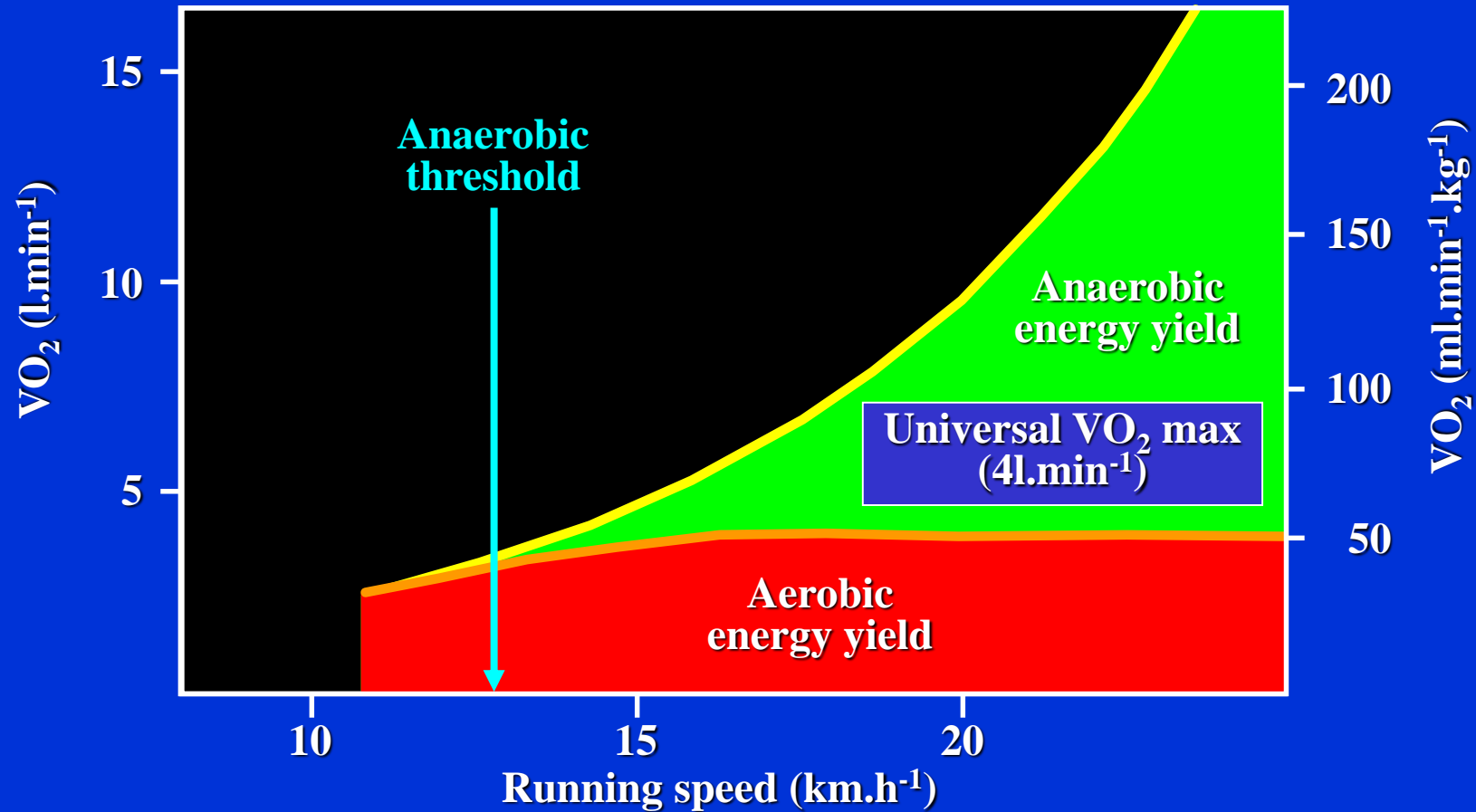
“The oxygen intake attains its maximum value, which in athletic individuals of about 73 kilograms body-weight *is strikingly constant (in the case of running) at about 4 litres per minute*”



*A.V. Hill, C.N. Long and H. Lupton.
Proceedings of the Royal Society B 97: 157, 1924.*



AV Hill believed that VO_2 rose exponentially with running speed



*Redrawn from A.V. Hill and H. Lupton
Quarterly Journal of Medicine 16; 157, 1923.*



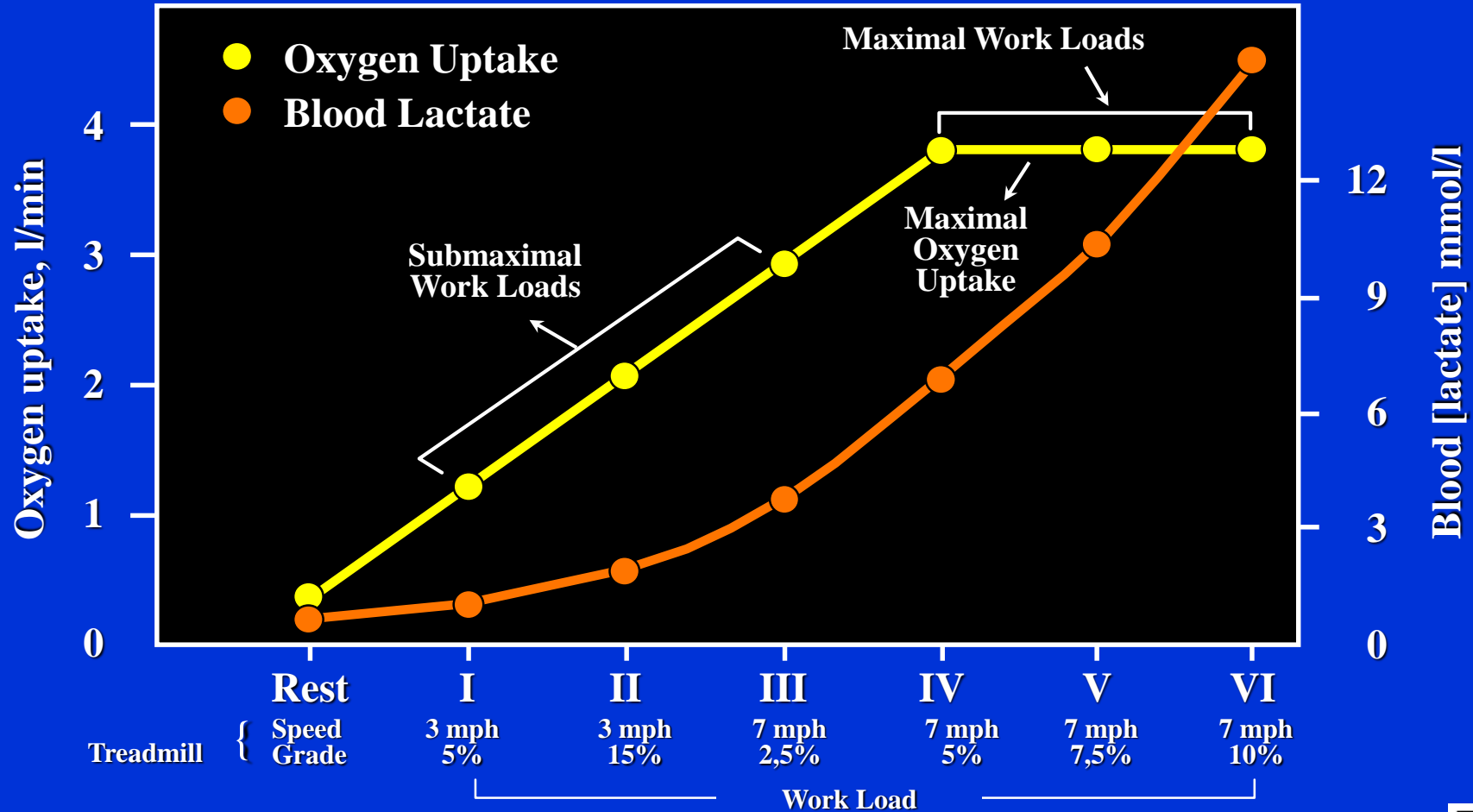
First description of the VO_2 max “Plateau Phenomenon” - 1955

“The classic work of Hill (20) has demonstrated that there is an upper limit to the capacity of the combined respiratory and cardiovascular systems to transport oxygen to the muscles. *There is a linear relationship between oxygen intake and workload until the maximum oxygen intake is reached.* Further increases in work load beyond this point merely result in an increase in oxygen debt and a shortening of the time in which the work can be performed”

*H.L. Taylor, E. Buskirk and A. Henschel
Journal of Applied Physiology 8: 73 - 80, 1955.*



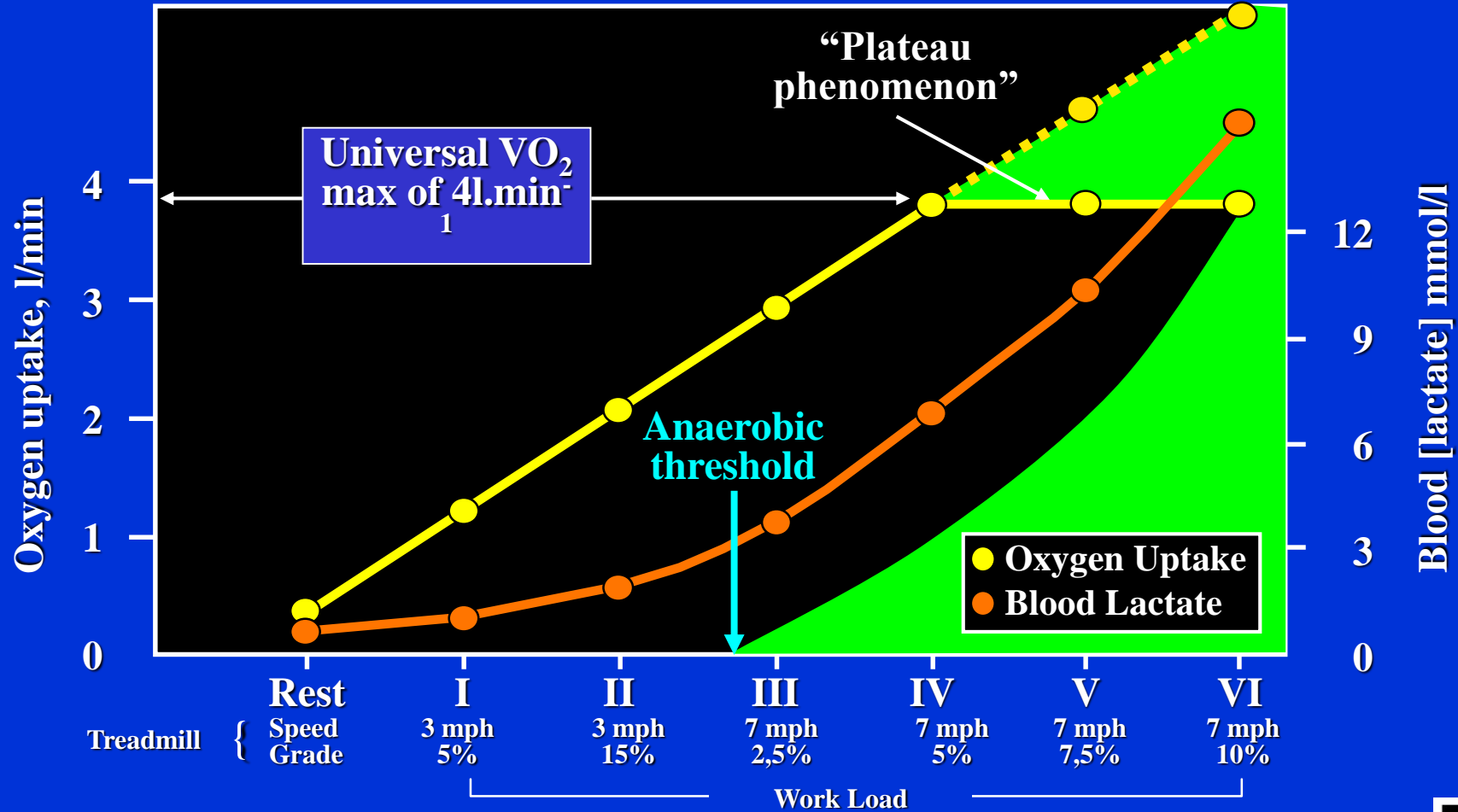
An early graphic depicting the “plateau phenomenon” - 1971



JH Mitchell and G Blomqvist
New England Journal of Medicine 284; 1018 - 1022, 1971.



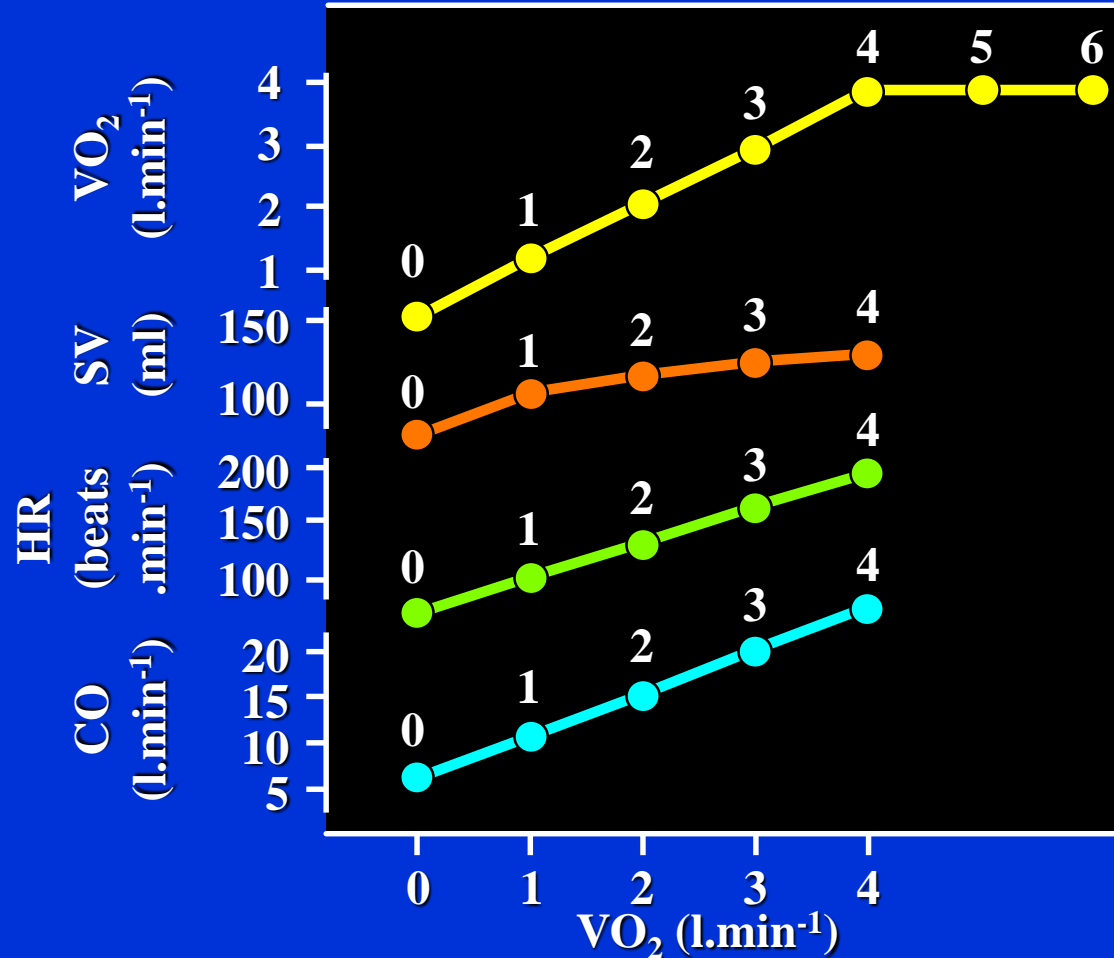
An early graphic depicting the “plateau phenomenon”



*JH Mitchell and G Blomqvist
New England Journal of Medicine 284; 1018 - 1022, 1971.*



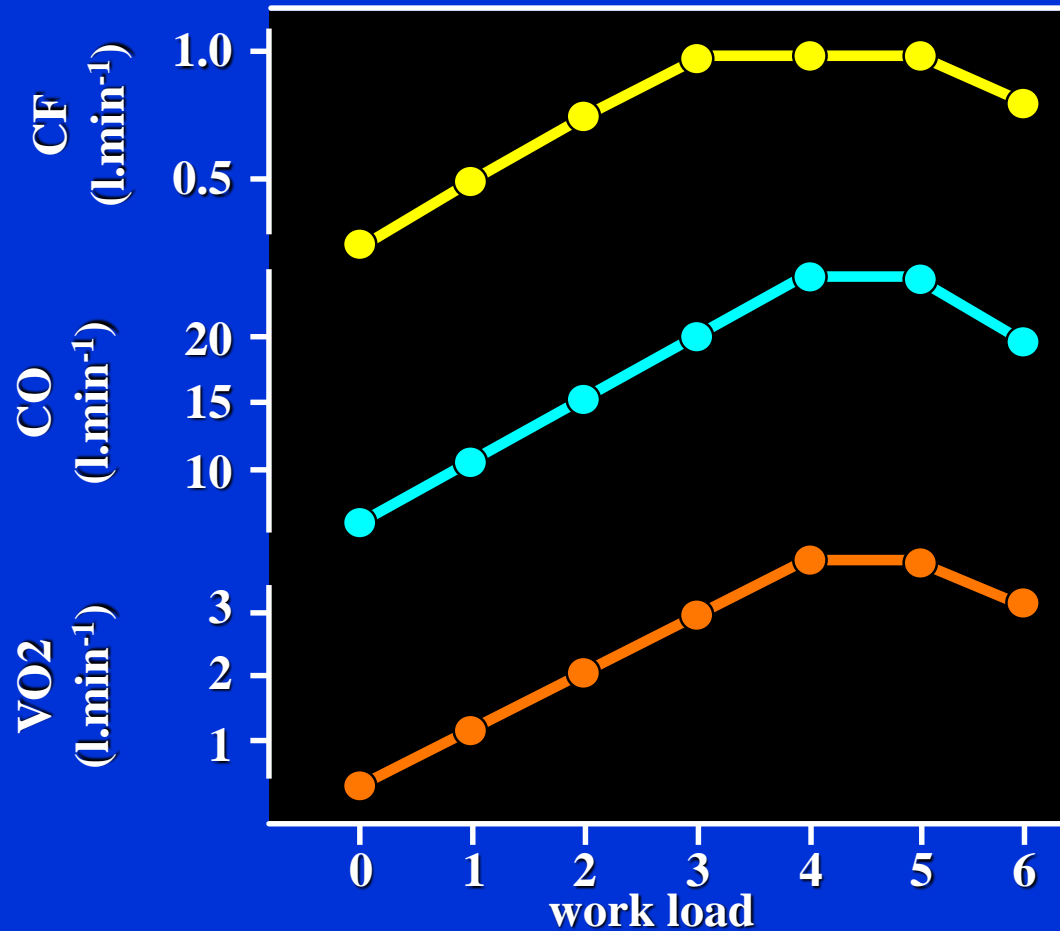
What happens to cardiovascular function beyond the “VO₂ Plateau”?



*Redrawn from J.H. Mitchell and G. Blomqvist.
New England Journal of Medicine 284: 1018 - 1022, 1971.*



A plateau in coronary flow must both cause and be caused by any “plateau” in cardiac output at the $\dot{V}O_2$ max.



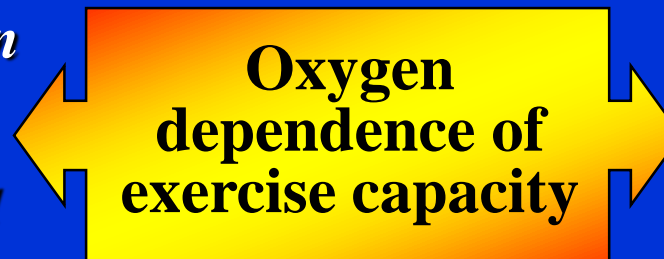
T.D. Noakes. Medicine and Science in Sports and Exercise 30; 1381 - 1398, 1998.



Intellectual evolution of the Cardiovascular/Anaerobic (Hill) model of Exercise Physiology and Athletic Performance

A.V. Hill	1923	Skeletal muscle anaerobiosis during exercise
D.B. Dill	1937	Oxygen use and superior athletic ability
H.L. Taylor	1957	The “plateau phenomenon” and the VO_2 max concept
K. Wasserman and B. Whipp	1964	The “anaerobic threshold” concept

Laboratory evaluation of athletic ability:
- VO_2 max
- anaerobic threshold

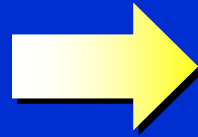
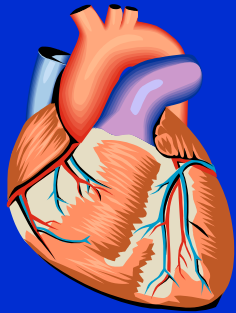


Cardiovascular contribution to exercise capacity:
- training
- blood doping
- dehydration
- disease



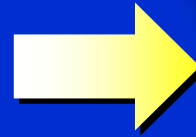
Mechanism of fatigue according to the A.V. Hill (Cardiovascular/Anaerobic) Model of Exercise Physiology

Heart



*Maximal
(Limiting)
cardiac
output*

Muscle



*Limiting
blood flow
to muscle*

Mitochondria



*Anaerobiosis
causes lactic
acidosis*

FATIGUE



The dual role of lactic acid in skeletal muscle contraction and fatigue: the teachings of A.V. Hill (1926)

“When a muscle is stimulated, a certain amount of lactic acid is liberated at certain surfaces within it. This, by some physical or chemical process still uncertain, causes a development of force and, if allowed, a shortening of the muscle. The acid is then rapidly neutralized, its effect passes off, and the muscle relaxes. The process can be repeated again and again until the available supply of alkali for neutralizing the acid has been used up, when the rapidly increasing acidity of the muscle stops its further activity. This stage is that of complete fatigue, and the amount of work which the muscle can perform depends on the degree to which it can tolerate acid before this stage is reached”



A.V. Hill. Scientific American, 224-225, (April) 1926.



The dual role of lactic acid in skeletal muscle contraction and fatigue: the teachings of A.V. Hill (1926)

“The acid slows the relaxation of the muscle. This last effect is very striking in short distance races. Where slower muscular relaxation, commencing within seven or eight seconds from the start, causes a progressive diminution in the maximum speed long before exhaustion.

This formation of lactic acid is the chemical reaction on which the whole of voluntary muscular activity depends”.



A.V. Hill. Scientific American, 224-225, (April) 1926.



The evolution of the peripheral fatigue model

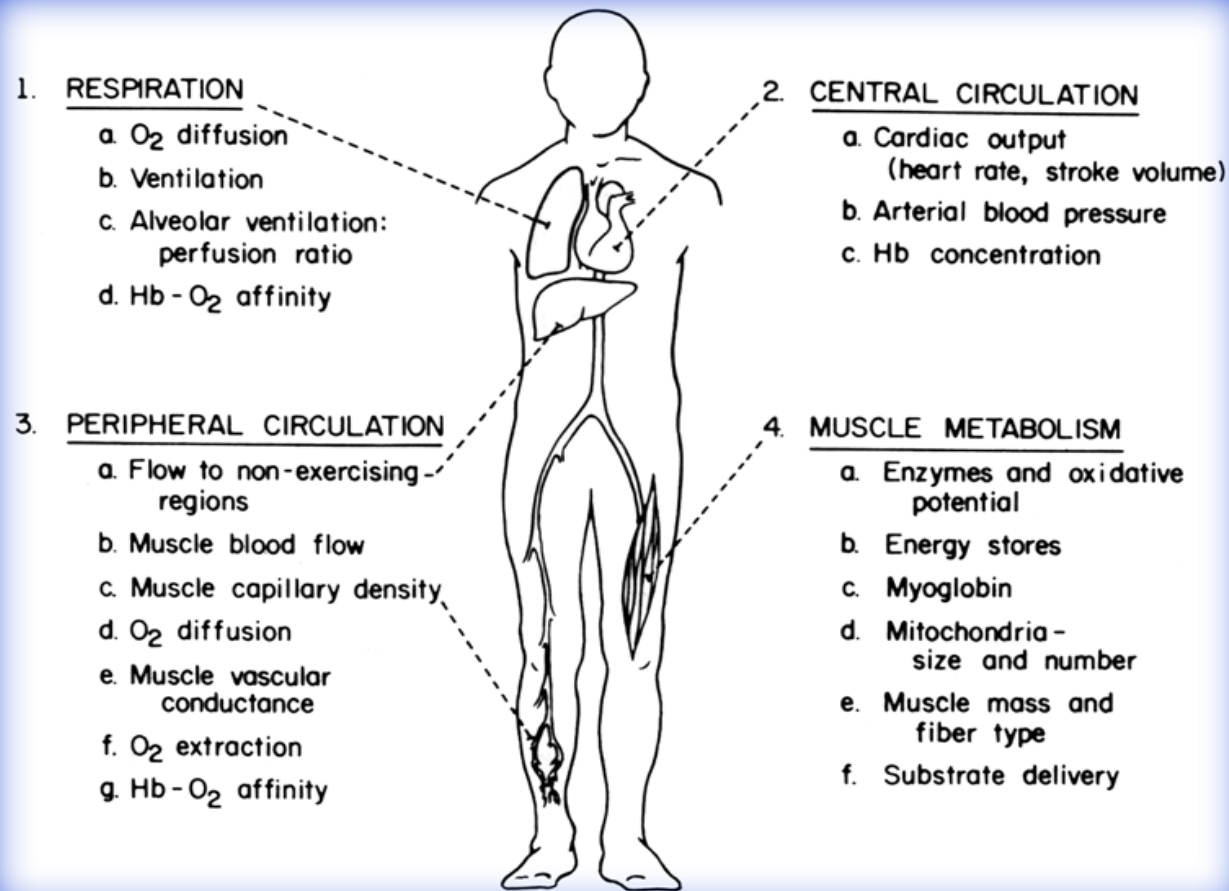
“First the sprinter very quickly creates what is termed an ‘oxygen debt’; and secondly, the valuable glycogen inside the muscle fibres is turned into poisonous lactic acid, the muscles become tired and stiff, dwindle in power, and finally refuse to function until the lactic acid has been turned back to glycogen during the recuperative processes of rest”.



F.A.M. Webster The Science of Athletics. Nicholas Kaye, London 1948 ; p 75.



What **limits** the ability to increase oxygen uptake?



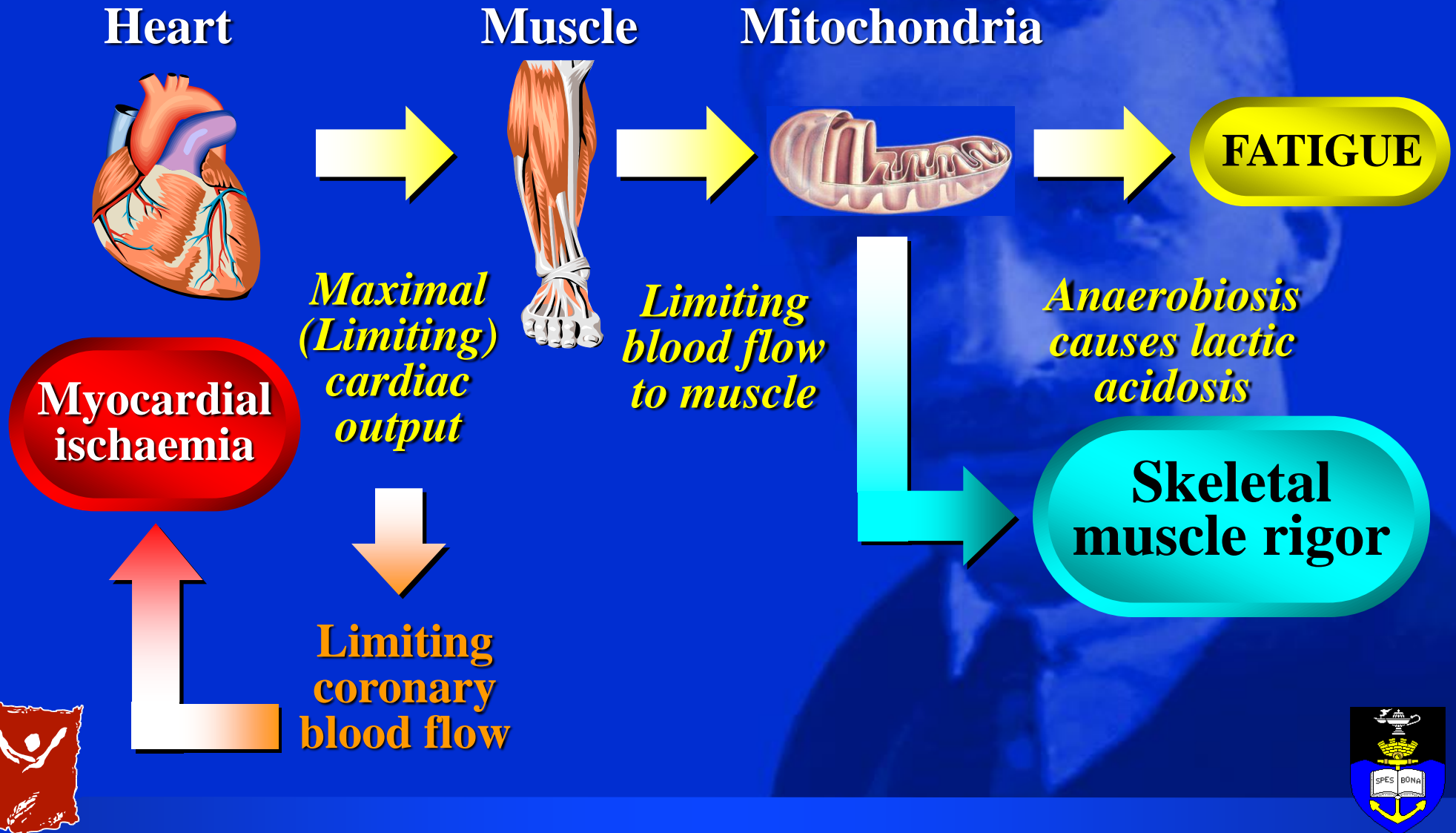
Loring B. Rowell. Human circulation.

Regulation during physical stress. Oxford University Press, New York, p.243 1986.

First published in Federation Proceedings 59; 1506-1513, 1980.



Skeletal muscle rigor is the more logical outcome of the A.V.Hill Model of Exercise Physiology



The British (Hill) theory that myocardial ischaemia limits the maximum cardiac output - 1924

“The enormous output of the heart of an able-bodied man, maintained for considerable periods during vigorous exercise, requires a large contemporary supply of oxygen to meet the demand for energy... *When the oxygen supply becomes inadequate, it is probable that the heart rapidly begins to diminish its output, so avoiding exhaustion*”

A. V. Hill, C.N. Long and H. Lupton.
Proceedings of the Royal Society B 96: 443, 1924.



The American (Dill) theory that myocardial ischaemia limits maximal exercise performance - 1931

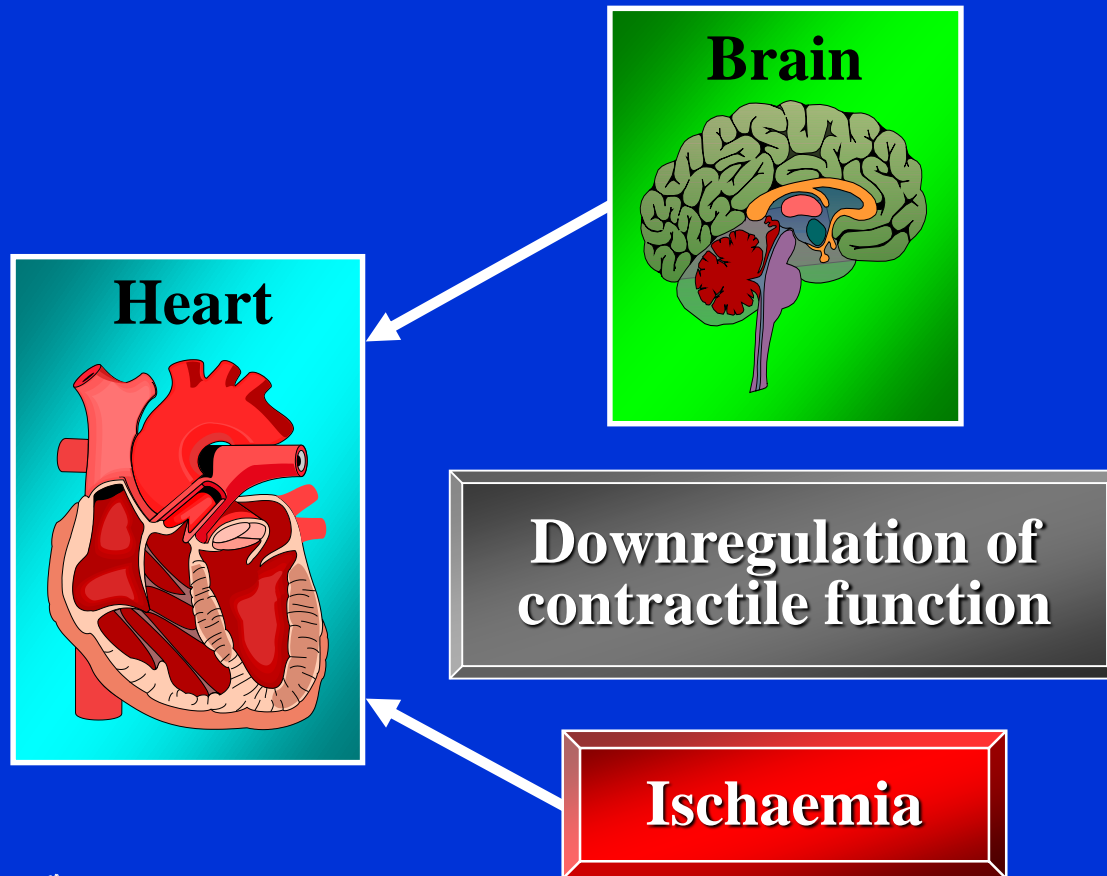
“The blood supply to the heart, in many men, may be the weak link in the chain of circulatory adjustments during muscular exercise, and as the intensity of muscular exertion increases, a point is probably reached in most individuals at which the supply of oxygen to the heart falls short of its demands, and the continued performance of work becomes difficult or impossible.”



A.B. Bock, D.B. Dill. The physiology of muscular exercise. 1931, p 15.



A.V. Hill's original "governor" to prevent the development of irreversible myocardial ischaemia during maximal exercise

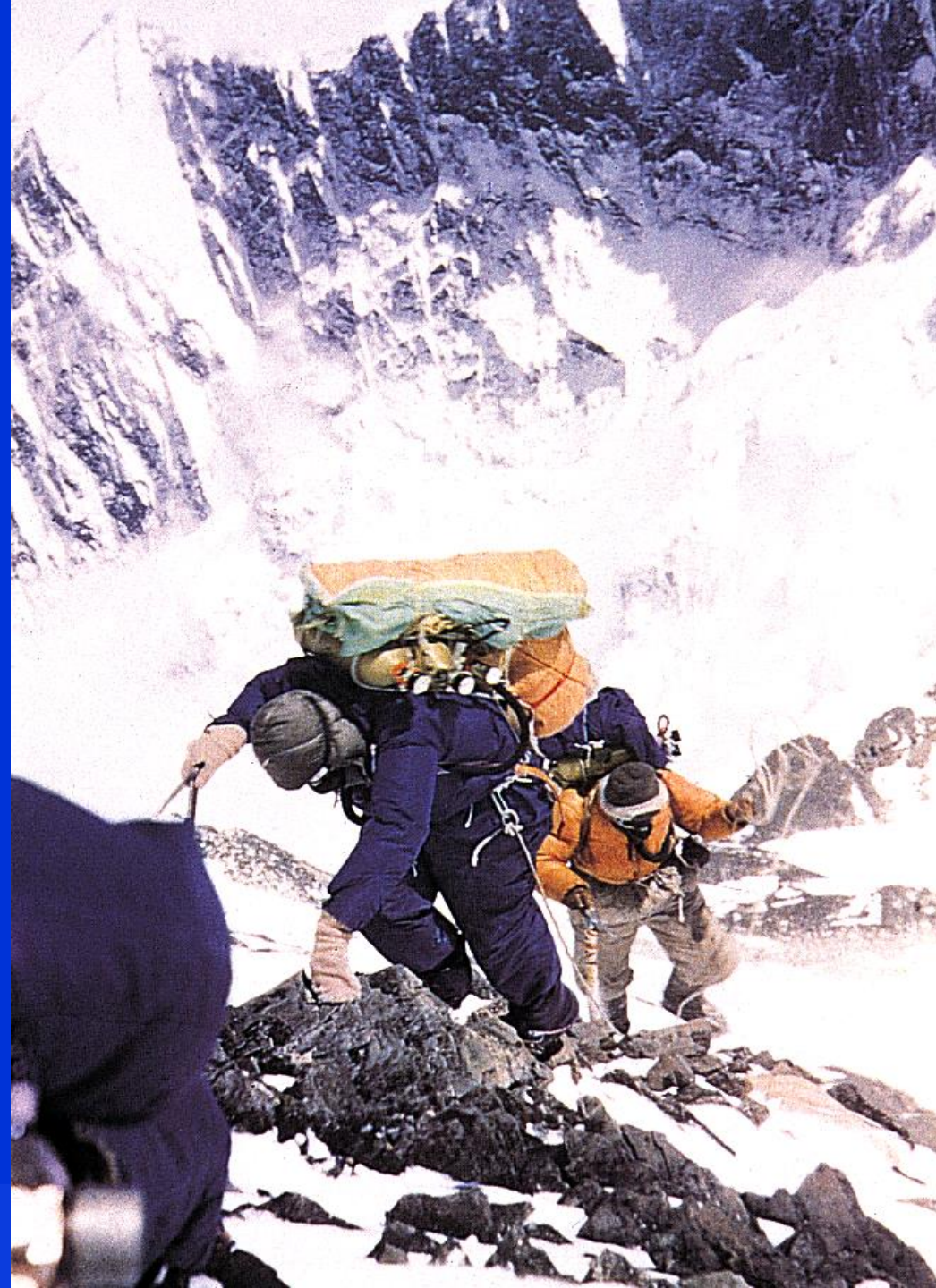


“ We suggest that... either in the heart muscle itself or in the nervous system, there is some mechanism (a “governor”) which causes a slowing of the circulation as soon as a serious degree of unsaturation occurs...”.



*A.V.Hill, C.N.H. Long and H.Lupton.
Proceedings of the Royal Society of Britain 97; 161-163, 1924.*





Climbing on Mount Everest

“Subjectively one was aware all the time of breathing near the maximum, and of weakness of the legs. Any increase in gradient, or deterioration in snow conditions, would bring one to a halt to recover breath.”



Dr Griffiths Pugh - Physiologist. British Everest Expedition, 1953.



Does the oxygen supply to the exercising muscles or to the heart limit exercise at altitude?

Physiological adaptations to maximal exercise at extreme altitude

If skeletal muscle regulates oxygen use:
Increased Reduced Unchanged

Output of heart

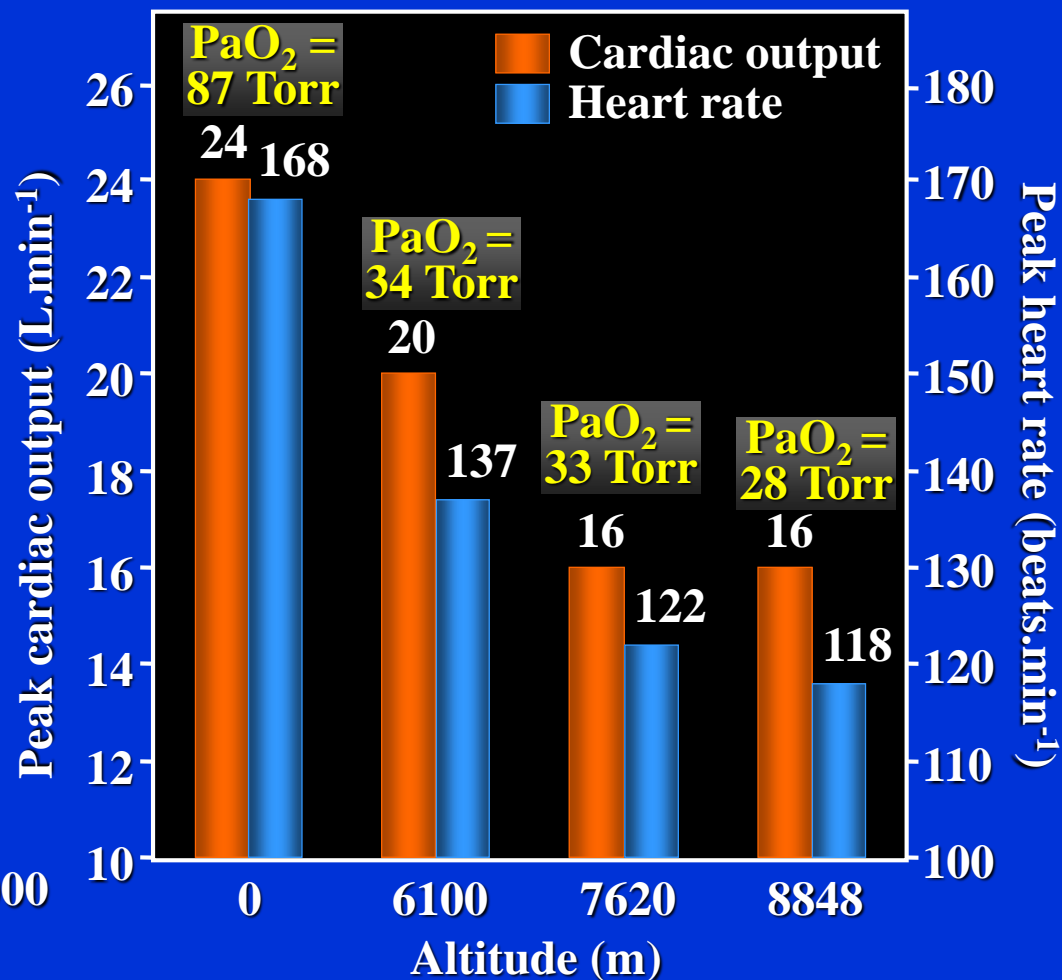
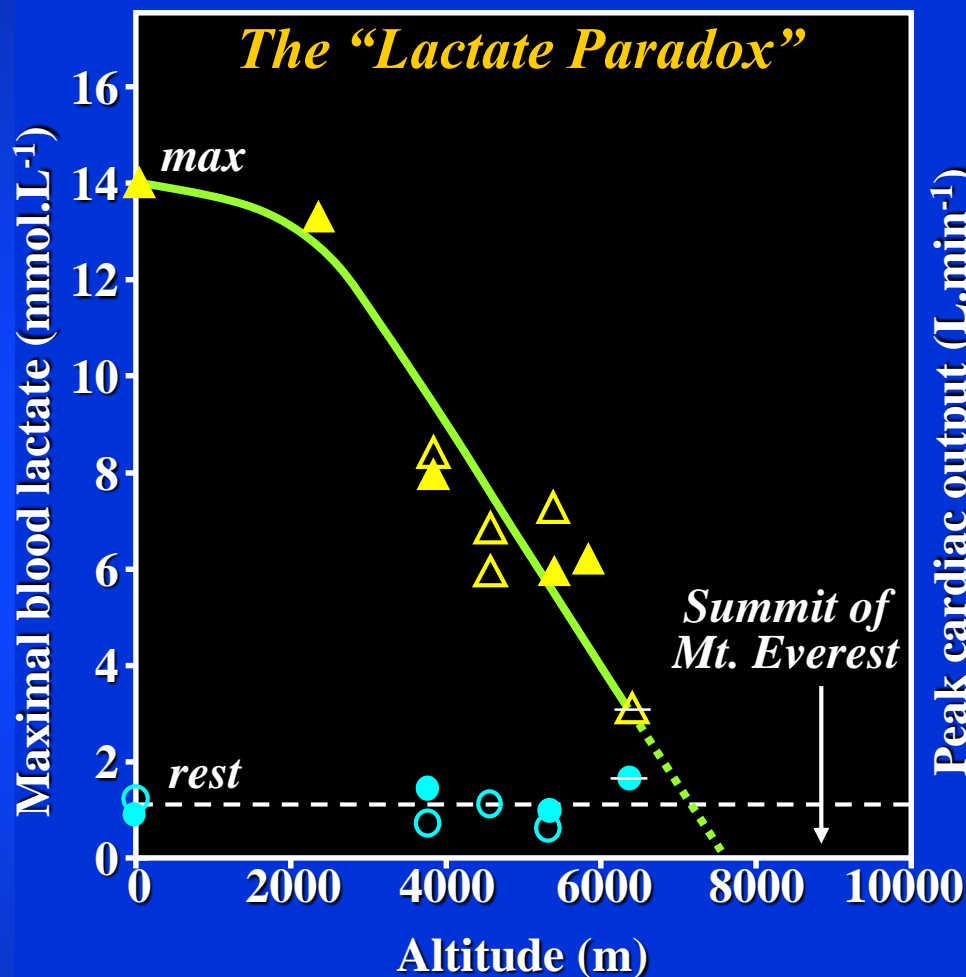
Blood O₂ content

O₂ requirement of exercising muscle

If the heart regulates oxygen use:
Reduced Reduced Reduced



The High Altitude paradox: Fatigue at low blood lactate concentrations and submaximal cardiac output



J.B. West. Federation Proceedings
45; 2953-2957, 1986.

J. Sutton et al. Journal of Applied Physiology 64; 1309-1321, 1988.



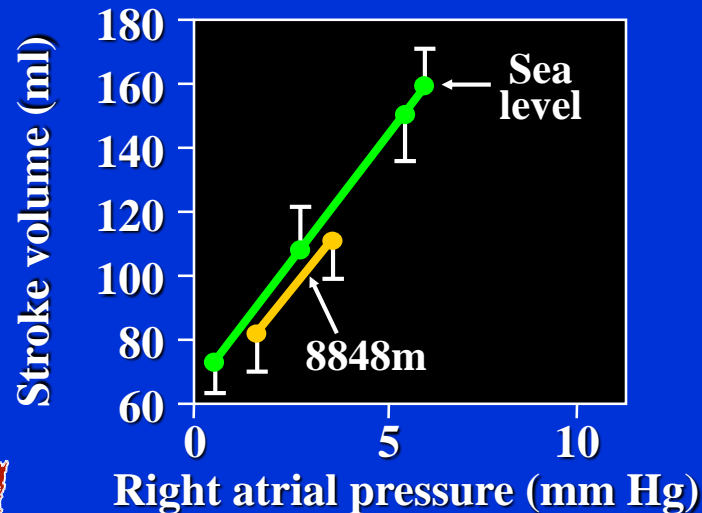
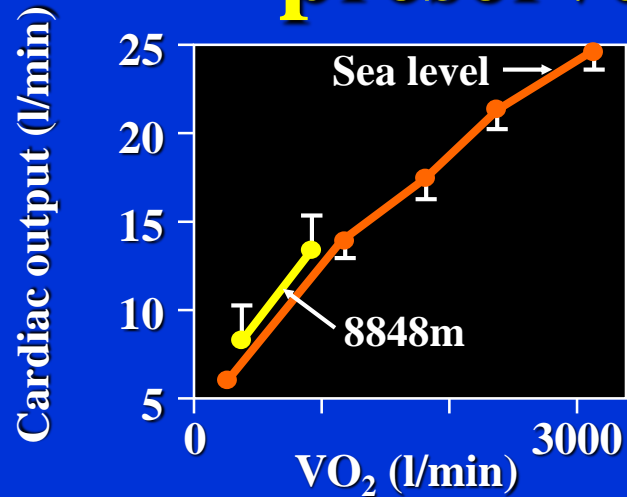
Peak Cardiorespiratory Measures at Different Altitudes: Operation Everest II

Altitude (m)	0	6100	7620	8848
Maximum Workrate (Watts)	300-360	180-210	120	120
paO ₂ (Torr)	87	34	33	28
Heart Rate (beats.min ⁻¹)	168	137	122	118
Cardiac Output (L.min ⁻¹)	24	20	16	16
Muscle [Lactate] (mmol.Kg ⁻¹)	105	90	45	20
Ventilation (L.min ⁻¹)	125	161	162	184

*J. Sutton et al. Journal of Applied Physiology 64:1309-1321, 1988.
H.Green et al. Journal of Applied Physiology 66:142-150, 1989.*



Myocardial contractile function is preserved at extreme altitude



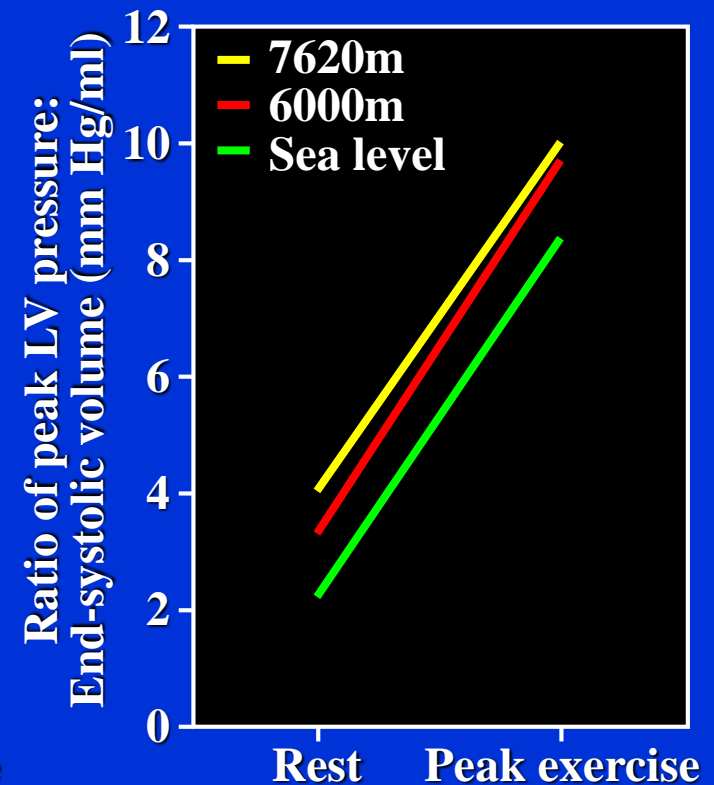
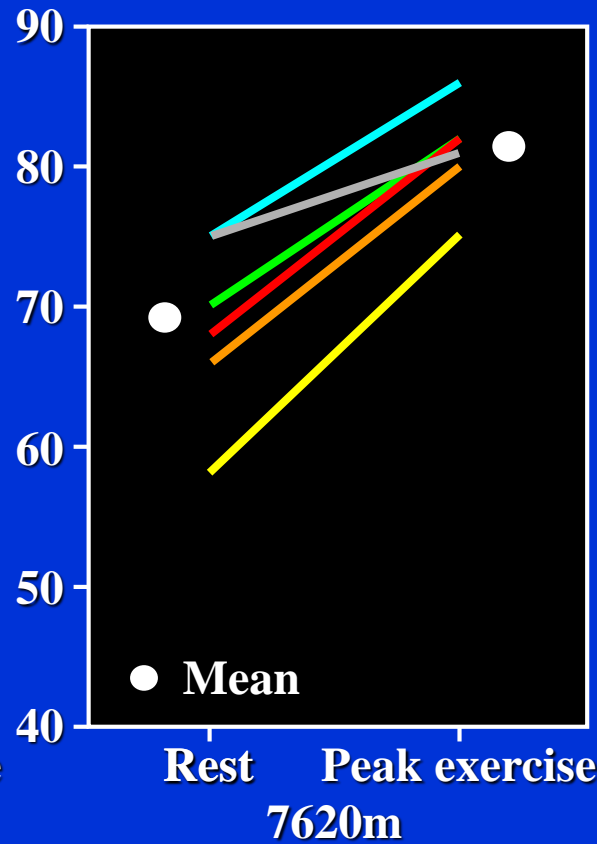
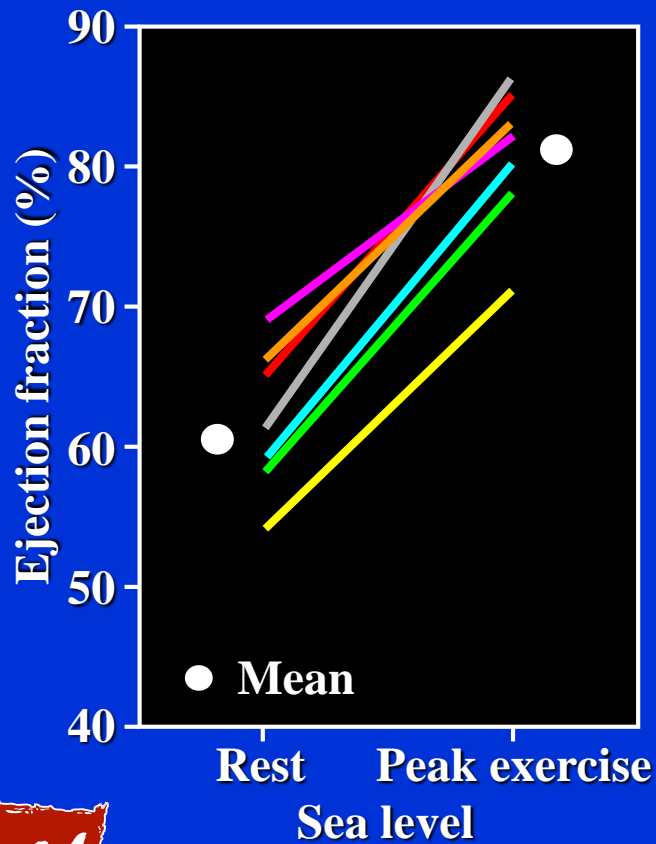
Conclusion:

“... cardiac rate, cardiac output, and myocardial contractile function were preserved at extreme altitude... reduced heart rates and cardiac outputs at maximum effort were *the result rather than the cause* of the reduced maximal O_2 uptake.”

J.T. Reeves et al. Journal of Applied Physiology 63;531 - 539, 1987.



“LV systolic function is not a limiting factor in compromising the exercise capacity of normal humans on ascent to high altitude, even to the peak of Mt. Everest.”



J. Suarez et al. American Journal of Cardiology 60; 137 - 142,1978



Conclusion

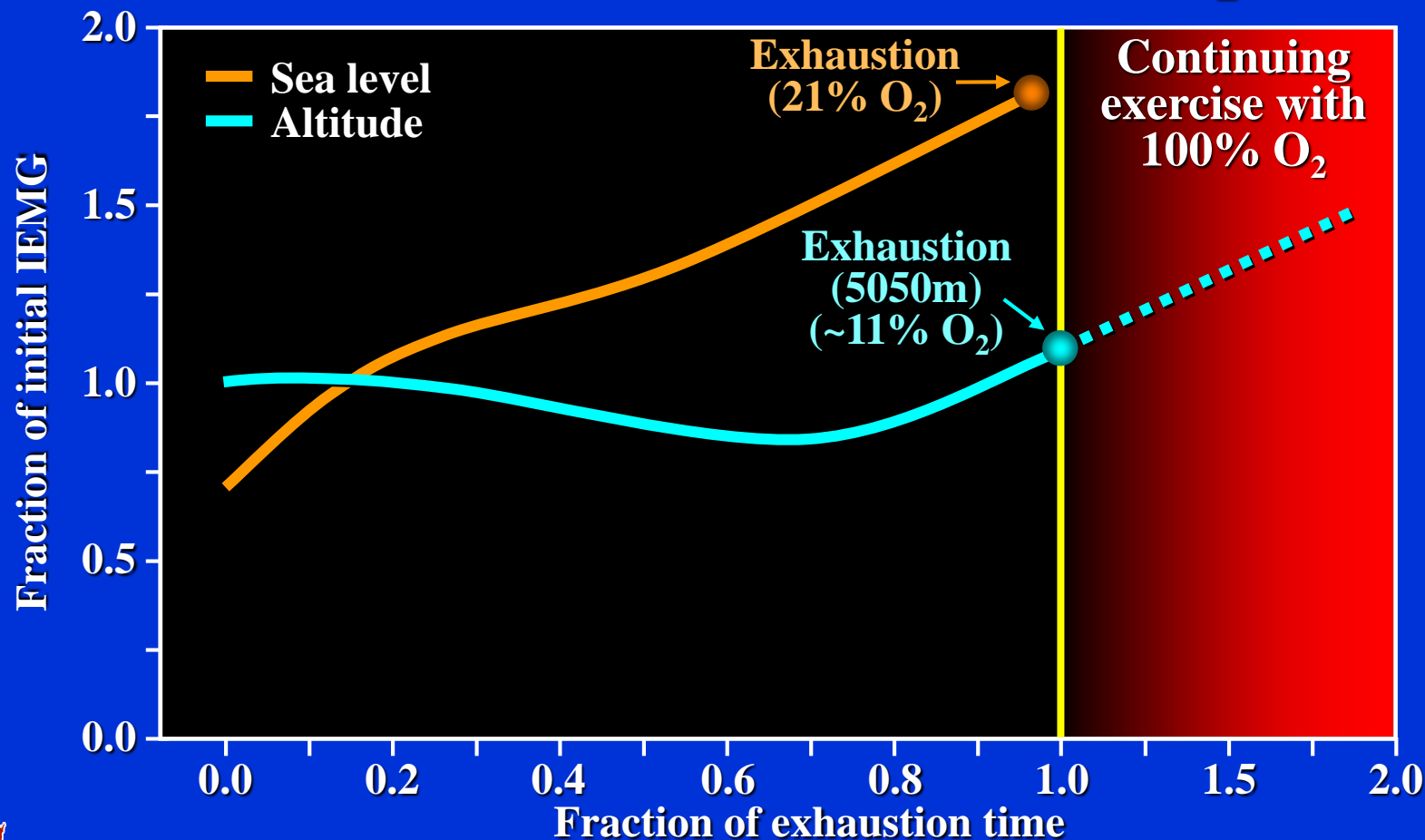
The heart makes no attempt to maximise O_2 delivery to skeletal muscle during maximal exercise at altitude.

There is no evidence for skeletal muscle anaerobiosis during maximal exercise at extreme altitude.

Hence exercise is terminated before anaerobiosis develops in either heart or skeletal muscle during maximal exercise (at extreme altitude).



Integrated EMG activity is reduced during maximal exercise at 5050m but increases acutely with administration of 100% O₂



*B. Kayser, M. Narici, T. Binzoni, B. Grassi and P. Cerretelli.
Journal of Applied Physiology 76; 634 - 640, 1994.*



The central nervous system limits exercise at altitude

“These results suggest that during chronic hypobaric hypoxia, the central nervous system may play a primary role in limiting exhaustive exercise and

m

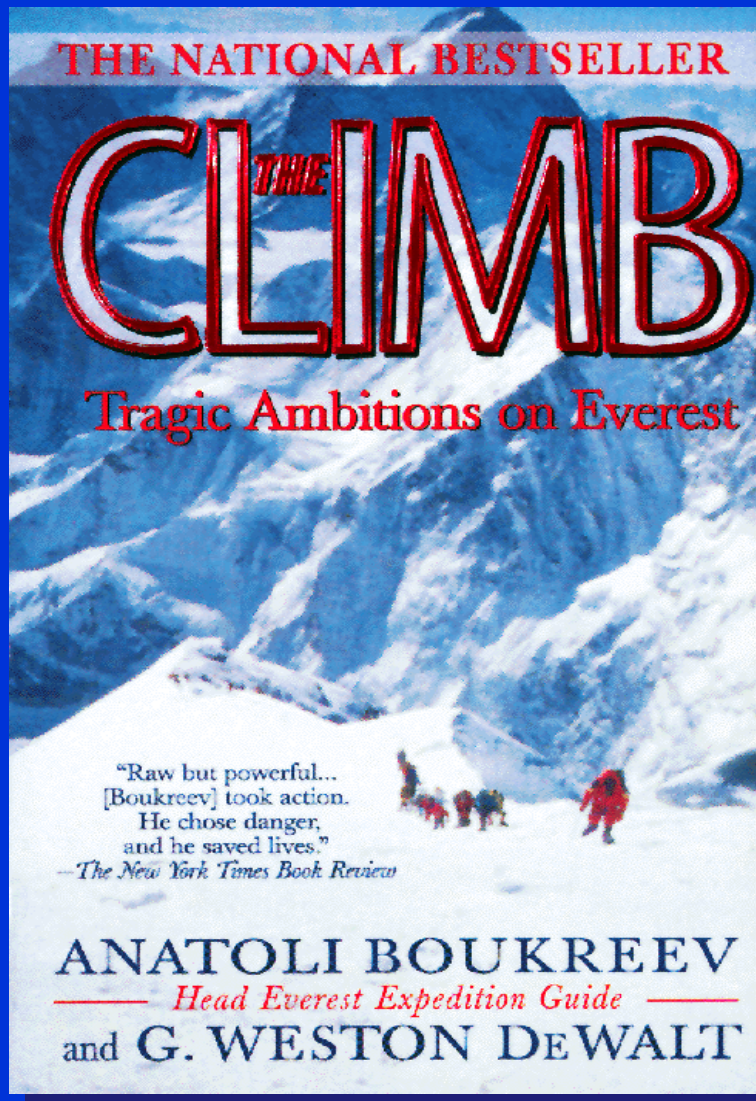
Conclusion.

Muscle recruitment is lower during maximal exercise at altitude than at sea level. Hence fatigue at altitude occurs without complete skeletal muscle recruitment.



*B. Kayser, M. Narici, T. Binzoni, B. Grassi and P. Cerretelli
Journal of Applied Physiology 76; 634-640, 1994.*





“We reminded (our clients) that they need to carefully monitor the conditions of their bodies, being constantly aware that at high altitude their sensations and reactions would not be altogether familiar. We could do our jobs as guides and monitor them, but only they would know *the interior truth*. We reinforced the importance of always maintaining a reserve, not allowing yourself to get totally depleted, being careful to understand that ‘I can’t’ usually means exactly that. You can’t and you shouldn’t. Stop, turn around, and save your life.”



The Climb - Tragic Ambitions on Everest
Anatoli Boukreev and G. Weston DeWalt, St Martin's Press, New York, 90-91, 1997.



H.T. Edwards' explanation of the "lactate paradox" at altitude

"The inability to accumulate large amounts of lactic acid at high altitudes suggests a protective mechanism preventing an already low arterial saturation from becoming markedly lower by shift of the O₂ dissociation curve through acid effect.

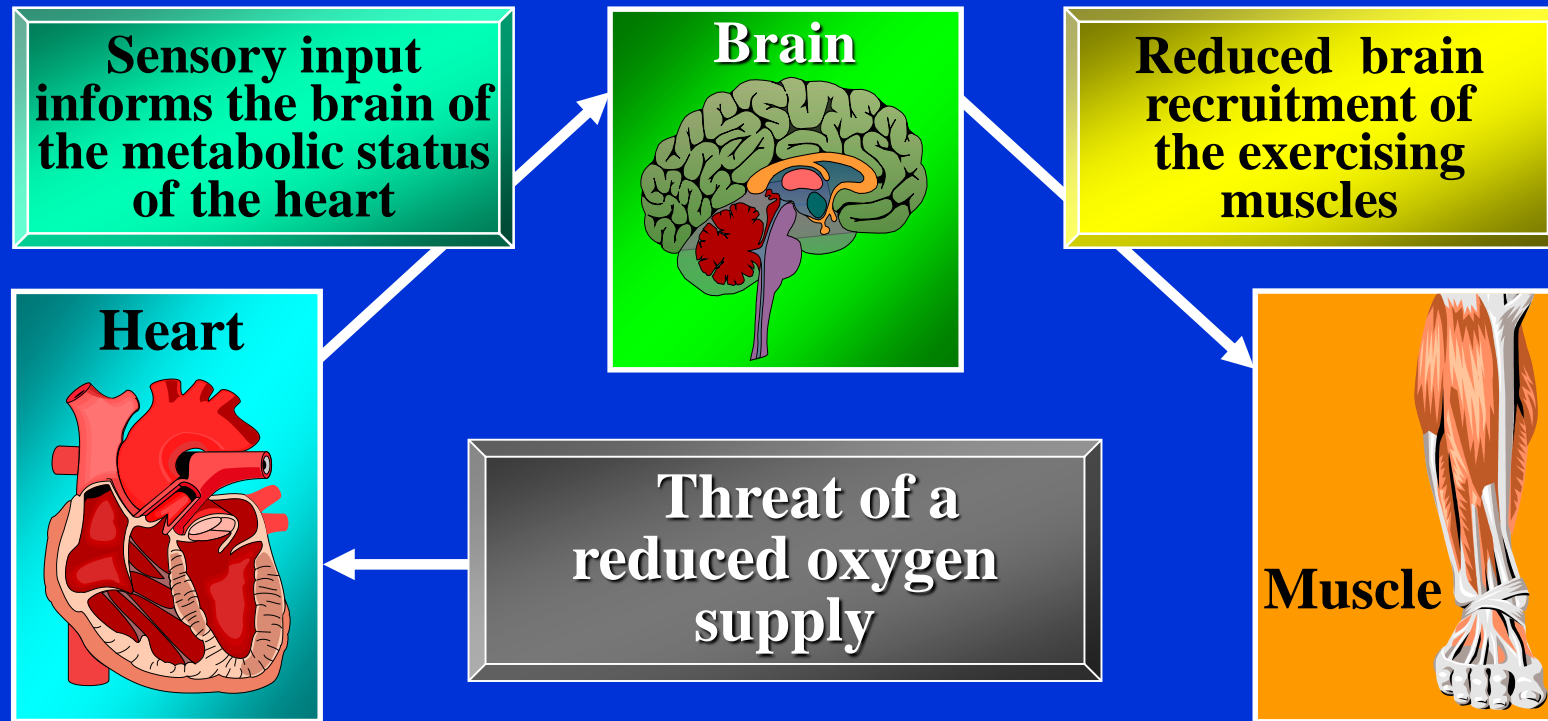
It may be that the protective mechanism lies in an inadequate oxygen supply to essential muscles, e.g. the diaphragm or the heart."



H.T. Edwards. American Journal of Physiology 116; 367 - 375, 1936.



Possible explanation for the “lactate” and “cardiac output” paradoxes during maximal exercise at altitude.



*T.D. Noakes. In: Cardiology at the Limits IV. Stanford Writers, Cape Town, 2001.
T.D.Noakes, J.E.Peltonen, H.Rusko. Journal of Experimental Biology 2001 (in press).*



What **limits** the ability to increase oxygen uptake?

Answer: The absence of a brain

1. RESPIRATION

- a. O₂ diffusion
- b. Ventilation
- c. Alveolar ventilation:



2. CENTRAL CIRCULATION

- a. Cardiac output
(heart rate, stroke volume)
- b. Arterial blood pressure

Assumption.

Complete muscle recruitment occurs during maximal exercise.

- conductance
- f. O₂ extraction
- g. Hb-O₂ affinity



- e. Muscle mass and fiber type
- f. Substrate delivery

Loring B. Rowell. Human circulation.

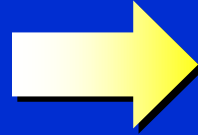
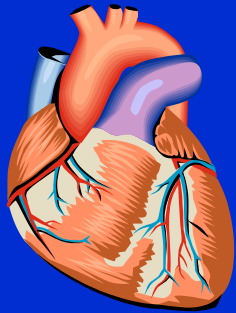
Regulation during physical stress. Oxford University Press, New York, p.243 1986.

First published in Federation Proceedings 59; 1506-1513, 1980.



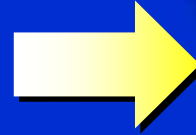
Mechanism of fatigue according to the A.V. Hill (Cardiovascular/Anaerobic) Model of Exercise Physiology

Heart



*Maximal
(Limiting)
cardiac
output*

Muscle



*Limiting
blood flow
to muscle*

Mitochondria



*Anaerobiosis
causing lactic
acidosis*

FATIGUE



Protective effect of lactic acid in fatiguing muscle contractions



The authors conclude:

“The accumulation of lactic acid protects against muscular fatigue” so that “in contrast to the often suggested role of acidosis as a cause of muscular fatigue, acidosis may protect against fatigue”.

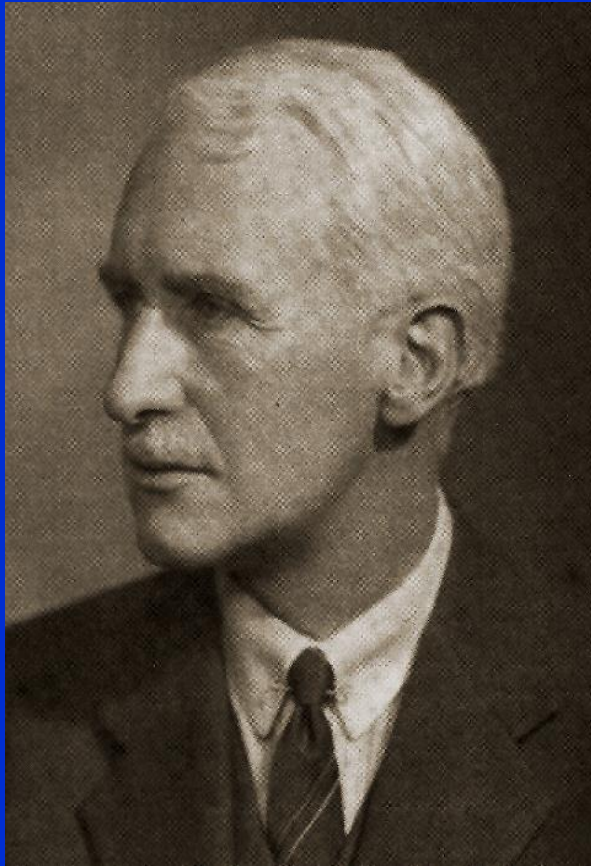


- Controls, n=2
- Lactic acid added together with the increase in $[K^+]$, n=6
- Lactic acid added after 90min at 11 mM K^+ , n=6

O. Nielsen, F. de Paoli and K. Overgaard. Protective effects of lactic acid on force production in rat skeletal muscle. Journal of Physiology, 536, 161-166, 2001.



AV Hill's Hypothesis on Hypotheses



“I have long believed, and am still inclined to believe, that all theories of muscle contraction are wrong. But they have been very useful in stimulating new research. In fact, many of the best theories are self destructive, by provoking fresh inquiry and leading to new facts which they cannot explain. The only useless theories are those that cannot be tested and can explain everything”



A.V. Hill. Trails and Trials in Physiology. 1965, p362-363.



Scandinavian Journal of
**MEDICINE &
SCIENCE IN
SPORTS**

Abstracts of the 4th Scandinavian
Congress on Medicine and Science in
Sports
November 5-8, 1998, Lahti, Finland

Volume 8 · Number 5 · Part 1
MUNKSGAARD

Review Article

Physiological models to understand exercise fatigue and the adaptations that predict or enhance athletic performance

TIMOTHY DAVID NOAKES

Bioenergetics of Exercise Research Unit of the Medical Research Council and the University of Cape Town, Sport Science Institute of South Africa, Newlands, South Africa



Scandinavian Journal of Medicine & Science in Sports 10: 123-145, 2000.

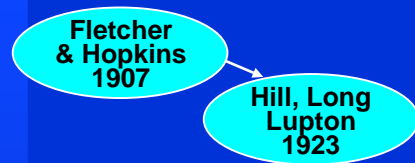


The family tree tracing the evolution of the different models in exercise physiology

Fletcher
& Hopkins
1907



The family tree tracing the evolution of the different models in exercise physiology



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|  CAN |  SWE |
|  DEN |  SWI |
|  GER |  UK |
|  ITALY |  USA |
|  RSA | |



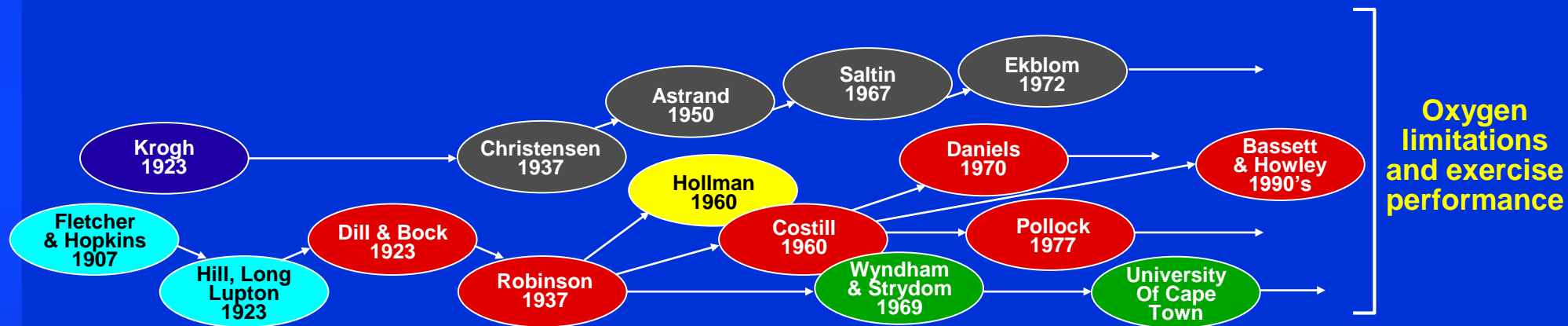
The family tree tracing the evolution of the different models in exercise physiology



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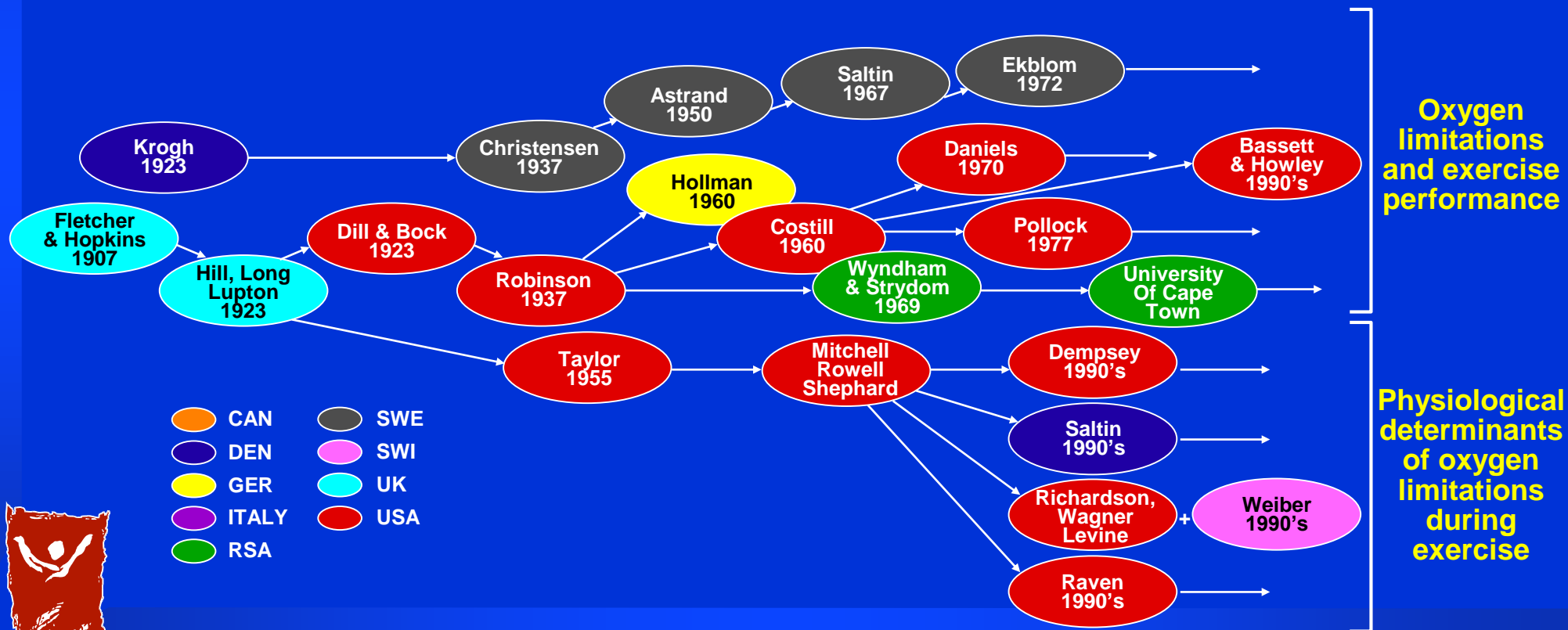
The family tree tracing the evolution of the different models in exercise physiology



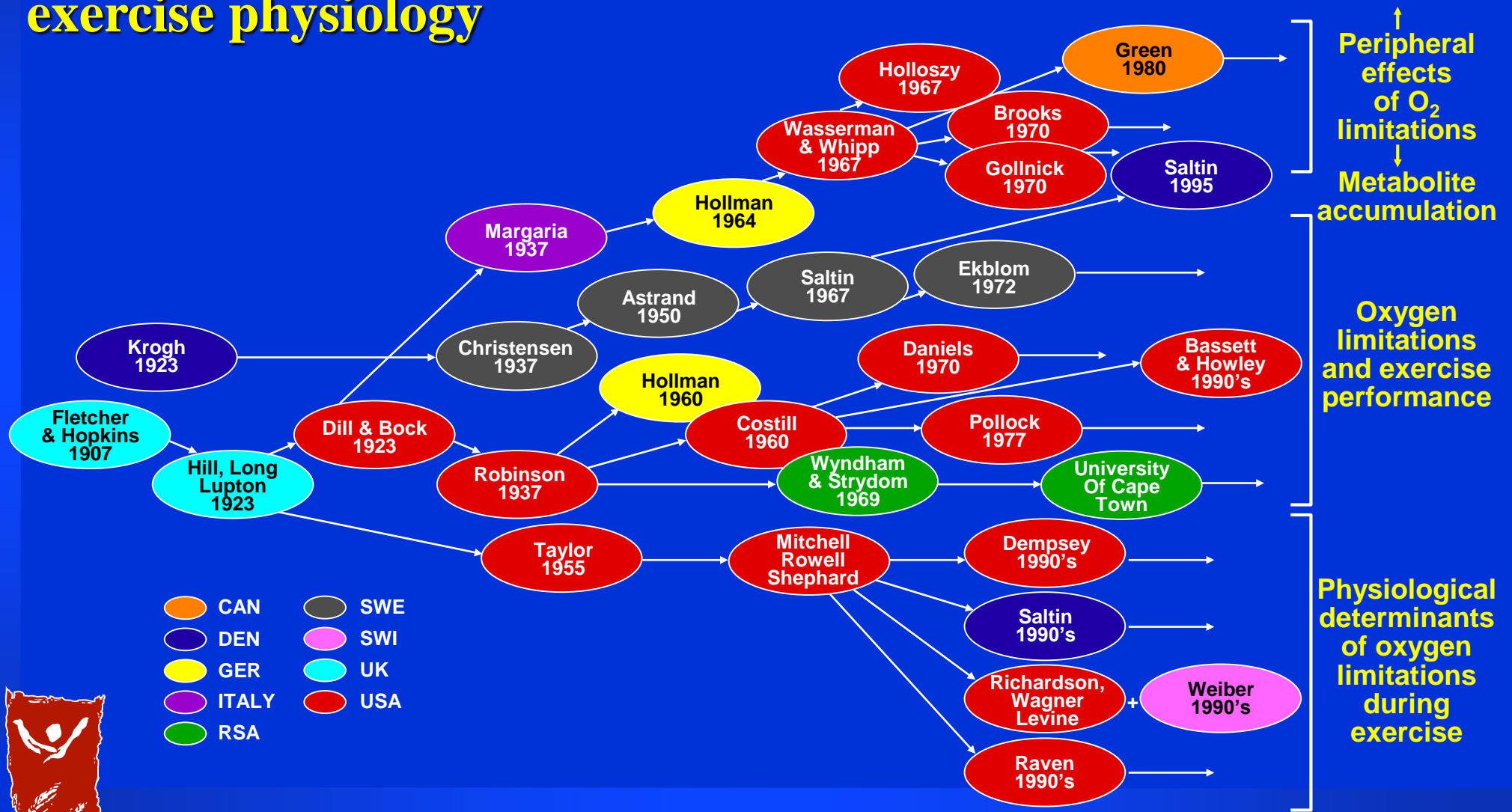
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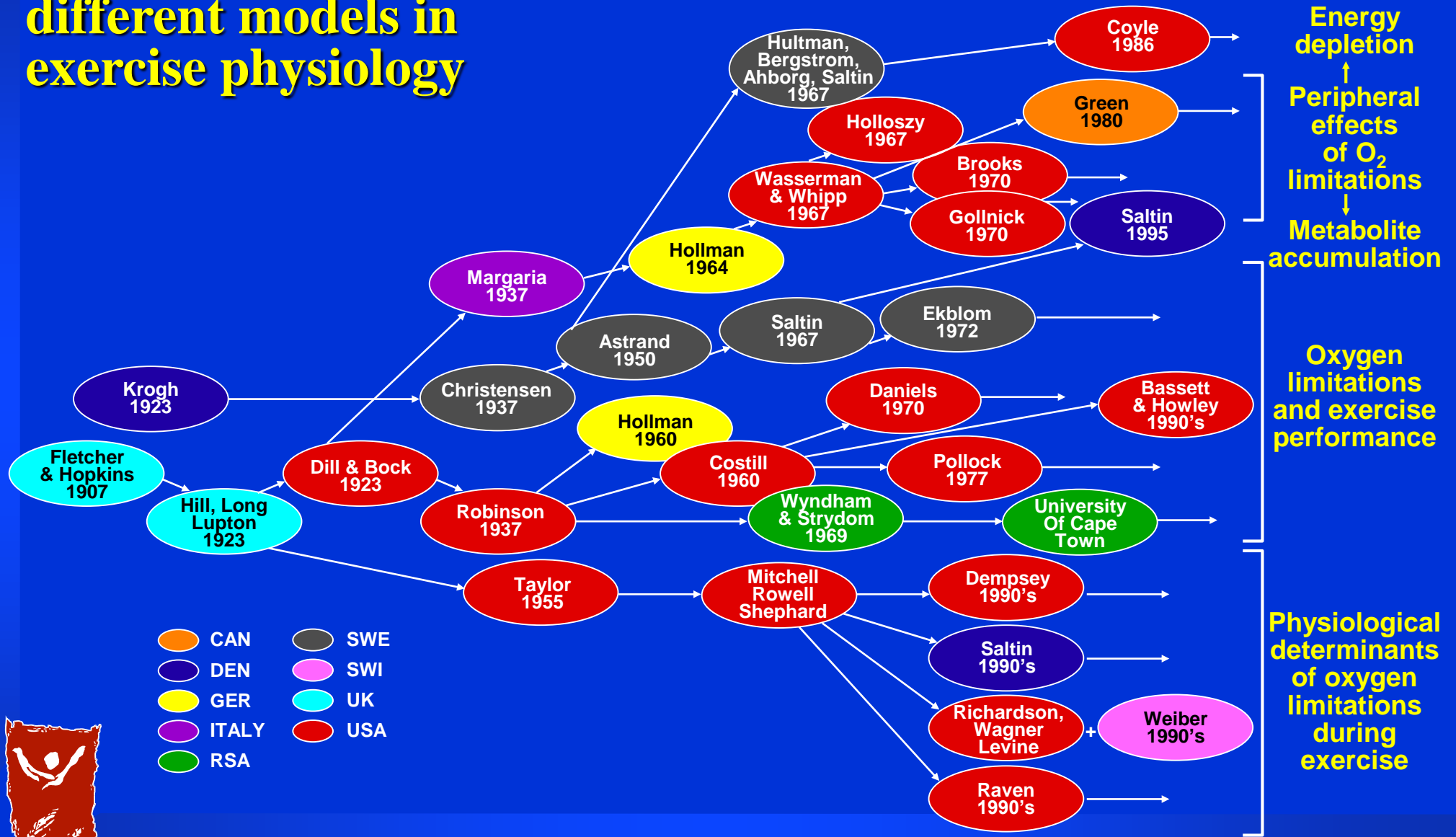
The family tree tracing the evolution of the different models in exercise physiology



The family tree tracing the evolution of the different models in exercise physiology



The family tree tracing the evolution of the different models in exercise physiology



Physiological Models of Exercise Performance

Cardiovascular / Anaerobic Model

The rate of supply of a **substrate (oxygen)** to muscle determines exercise performance

Energy Supply Model

The rate of supply of a **substrate (ATP)** to muscle determines exercise performance

Muscle Power Model

Muscle **strength**, or **muscle recruitment by the brain**, determines exercise performance

Energy Depletion Model

The rate of supply of **glucose from muscle glycogen** determines exercise performance

Biomechanical Model

The **economy / efficiency** of movement determines exercise performance

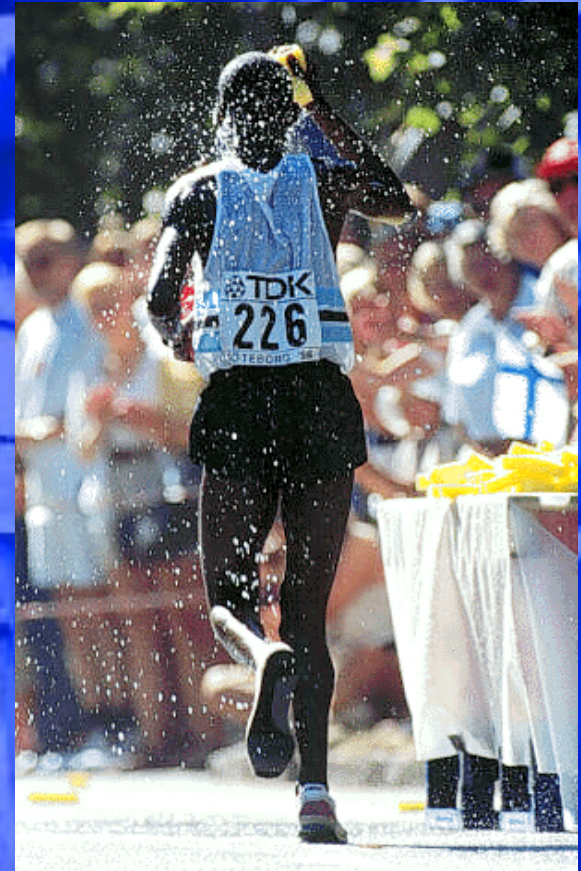
Psychological / Motivational Model

Conscious effort (motivation) determines exercise performance



Fatigue during prolonged submaximal exercise

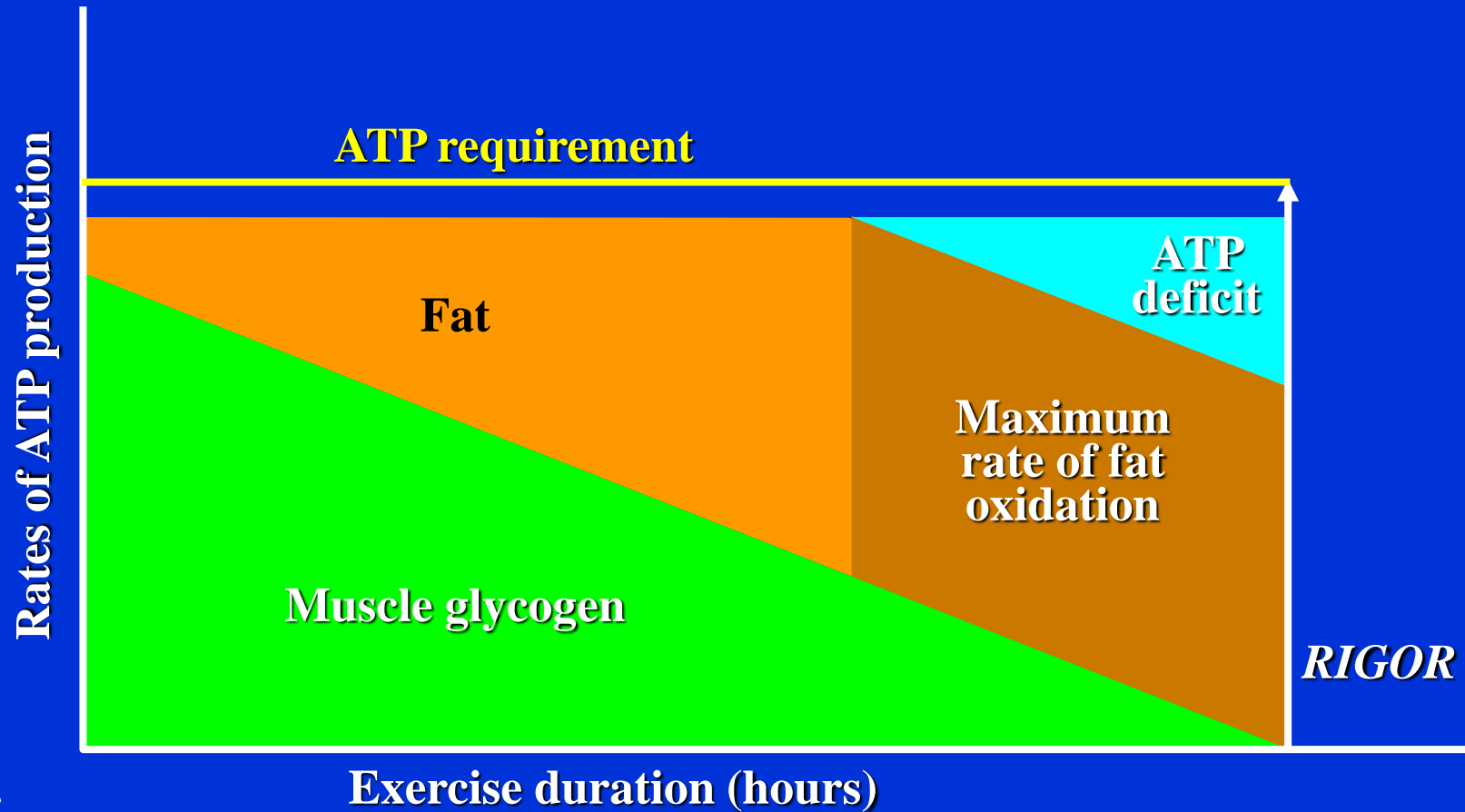
“When glycogen runs out... the muscle fails from lack of aerobic adenosine triphosphate (ATP) production. However plausible and attractive this theory is, it is unproven. ...what is clear is that, in glycogen-depleted muscle, ATP is being used up faster than it can be manufactured, and so force output is diminished”.



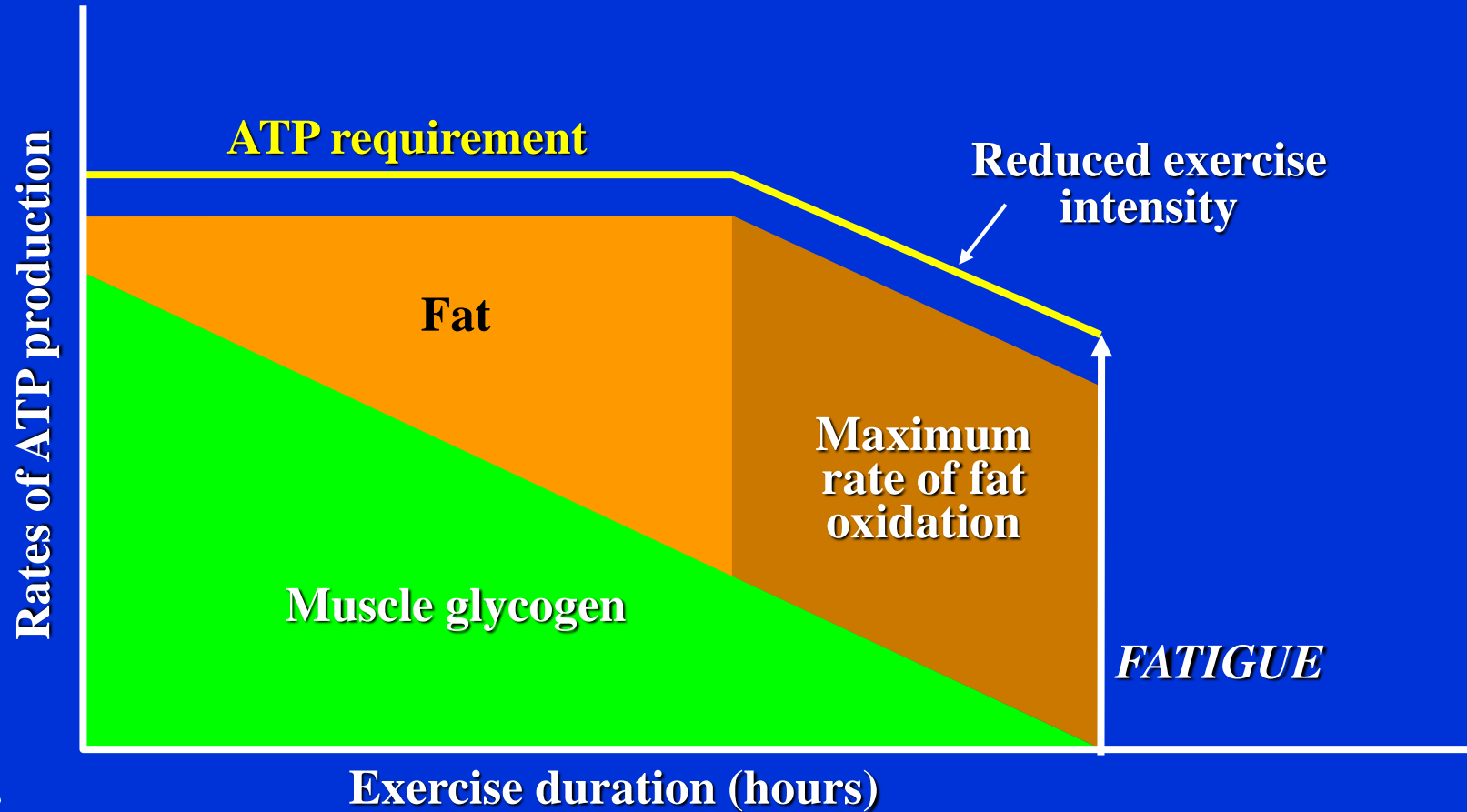
R.K. Conlee. Muscle glycogen and exercise endurance: A twenty-year perspective. Exercise and Sports Science Reviews 15; 1-28, 1987.



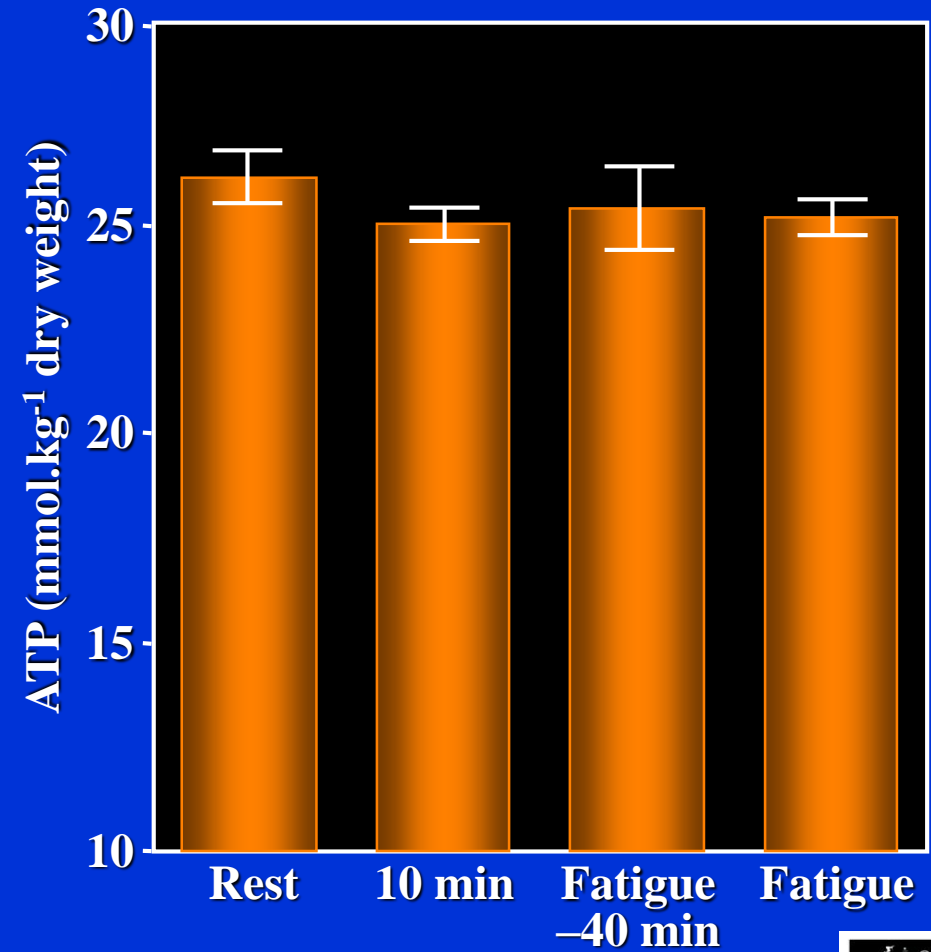
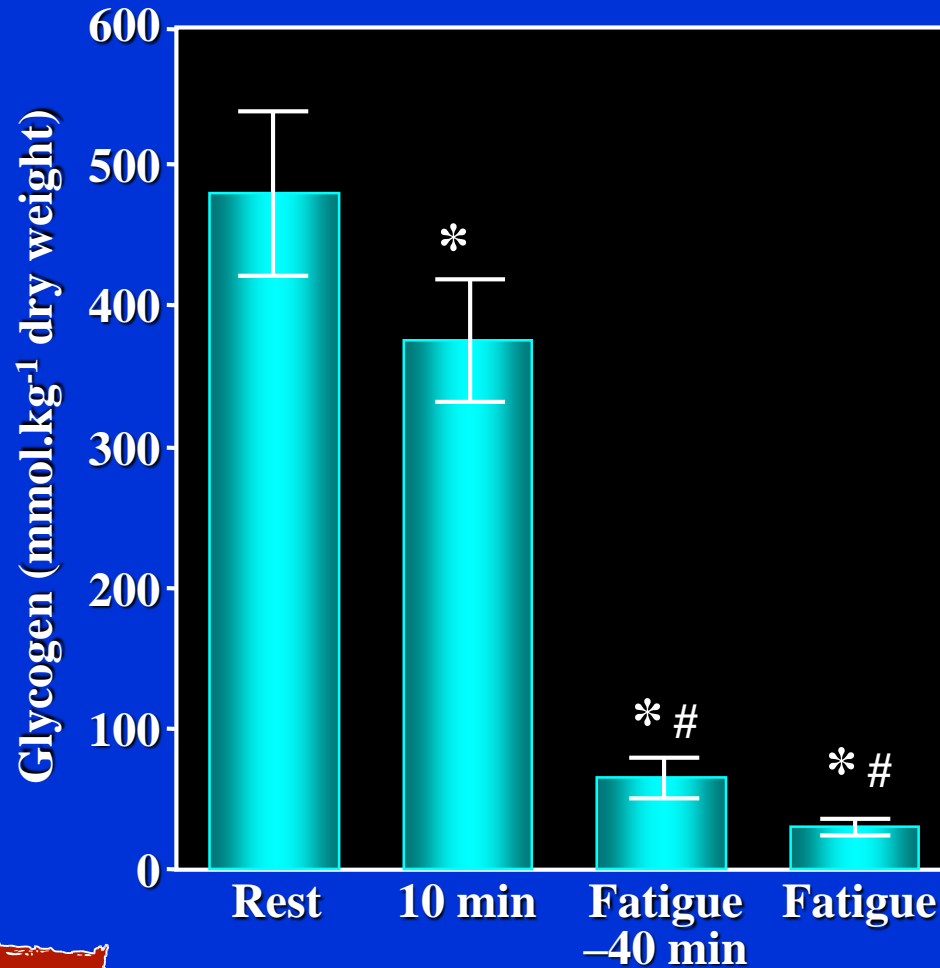
One theoretical flaw in the Energy Depletion Model of Exercise Physiology



The theoretical basis for the Energy Depletion Model of Exercise Physiology



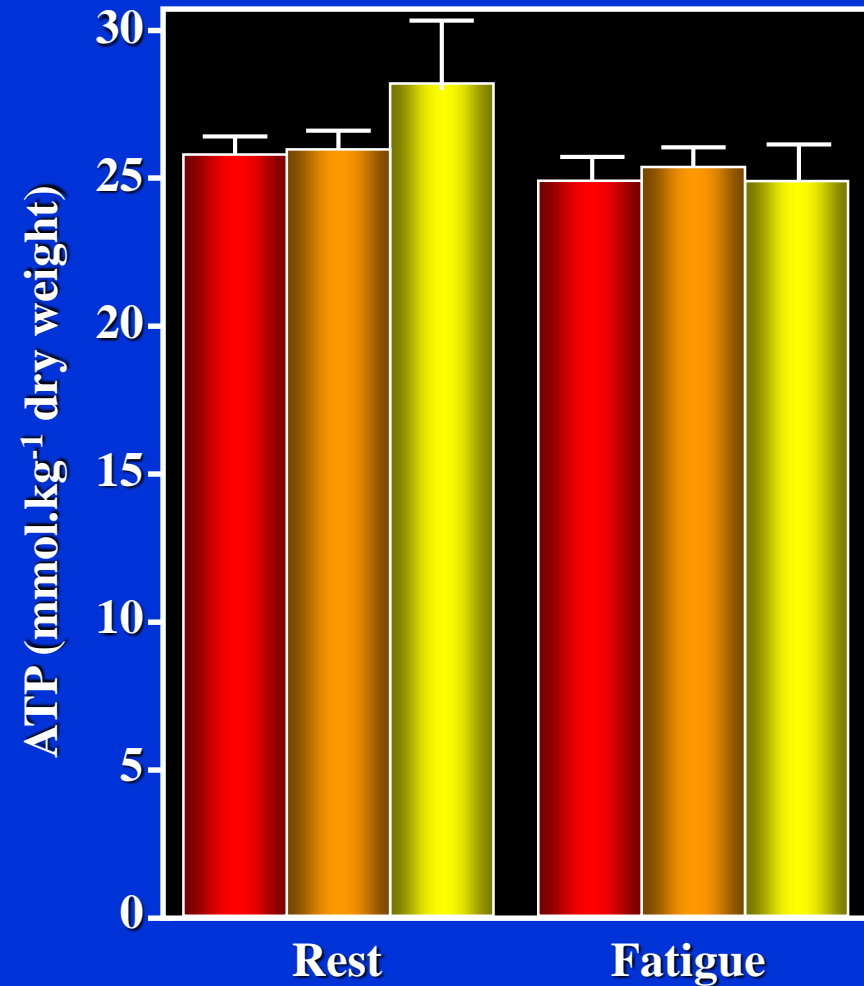
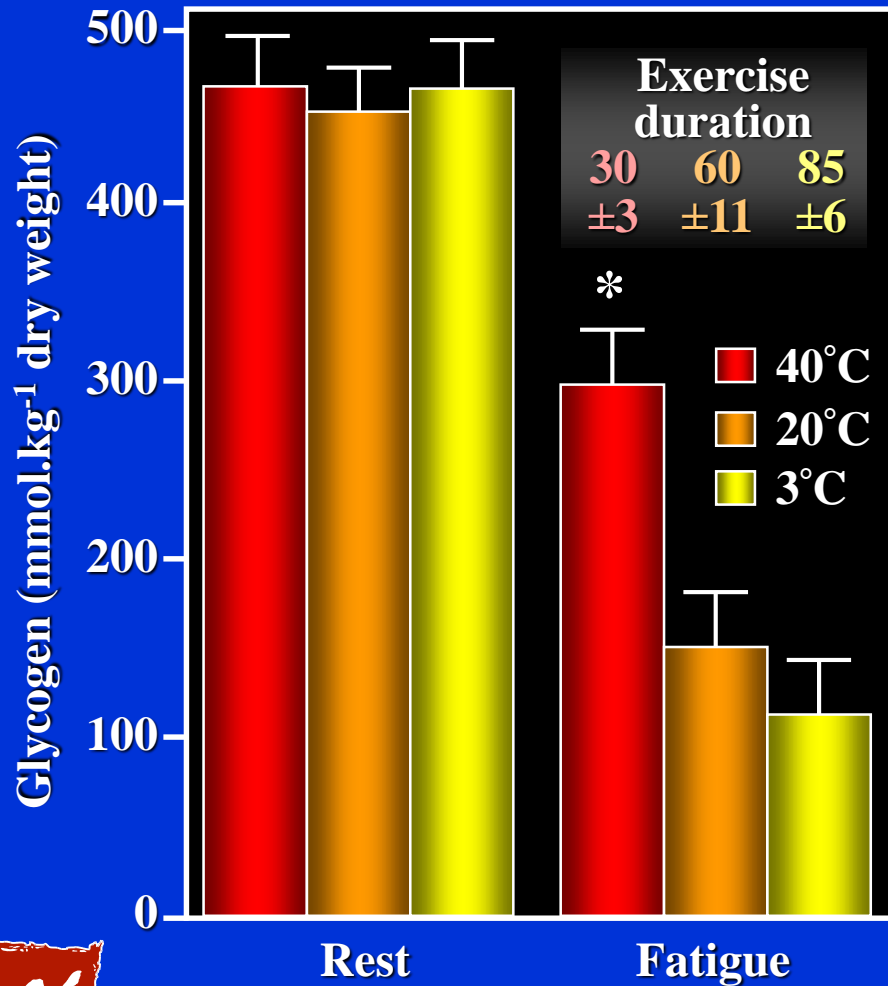
Fatigue during prolonged exercise: Protection of muscle [ATP]



M.A. Febbraio and J. Dancy. Journal of Applied Physiology 87; 2341-2347, 1999.



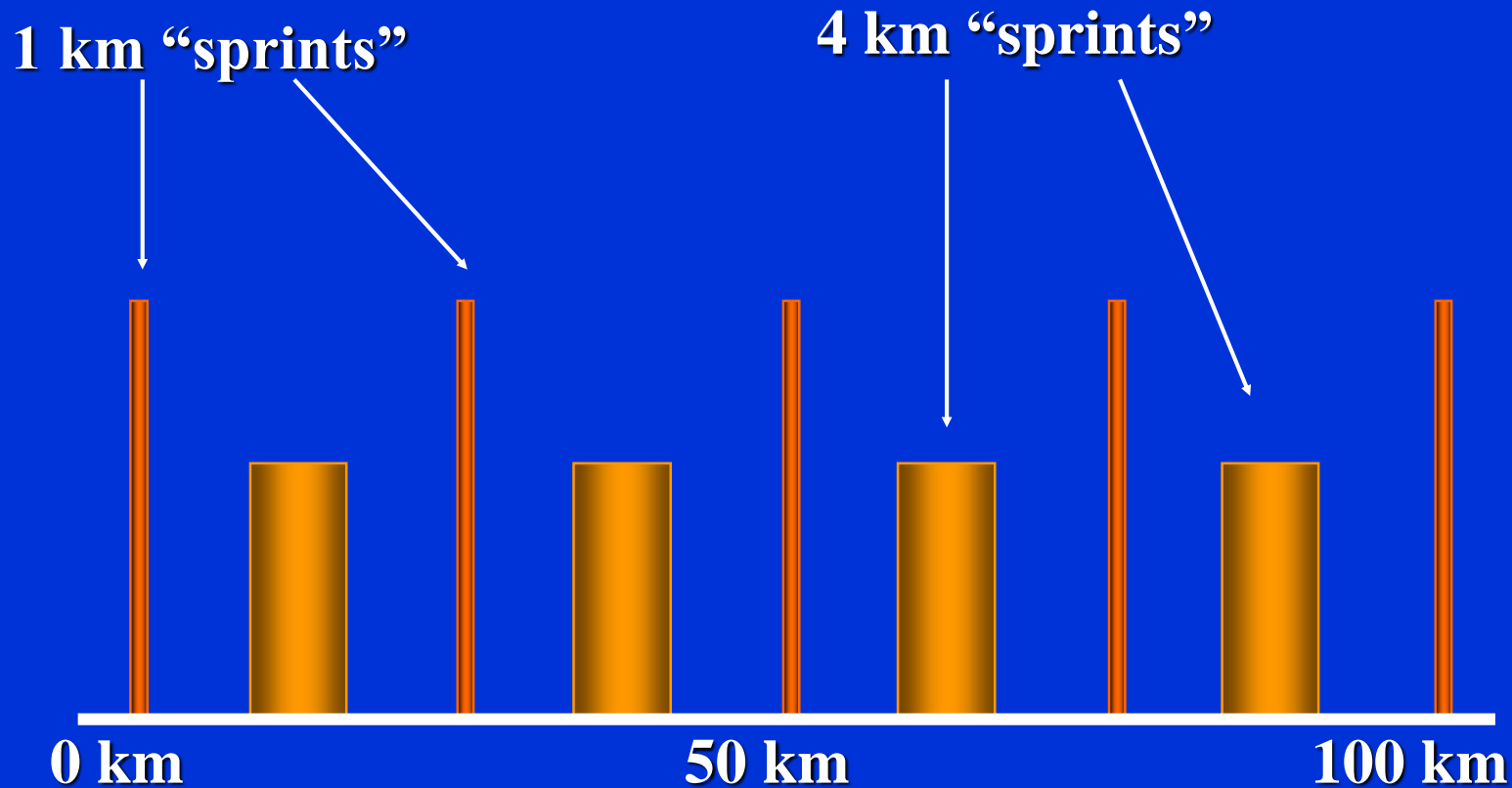
Fatigue during prolonged exercise in heat: Protection of muscle [ATP]



J.M. Parkin et al. Journal of Applied Physiology 86; 902-908, 1999.



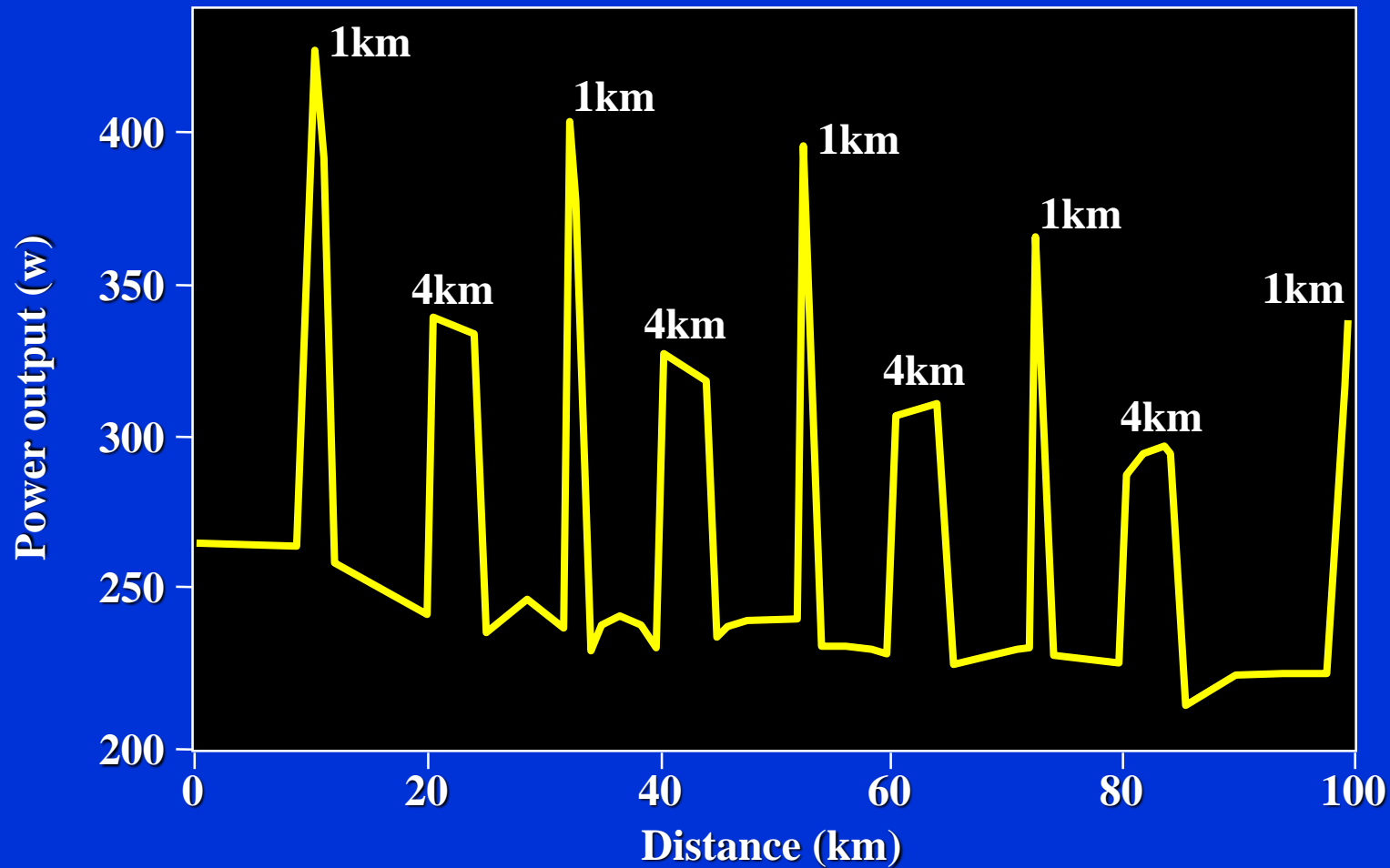
Protocol for measurement of neural activity during a 100km cycling time trial.



A. St Clair Gibson et al. American Journal of Physiology 281; R187-R196, 2001.



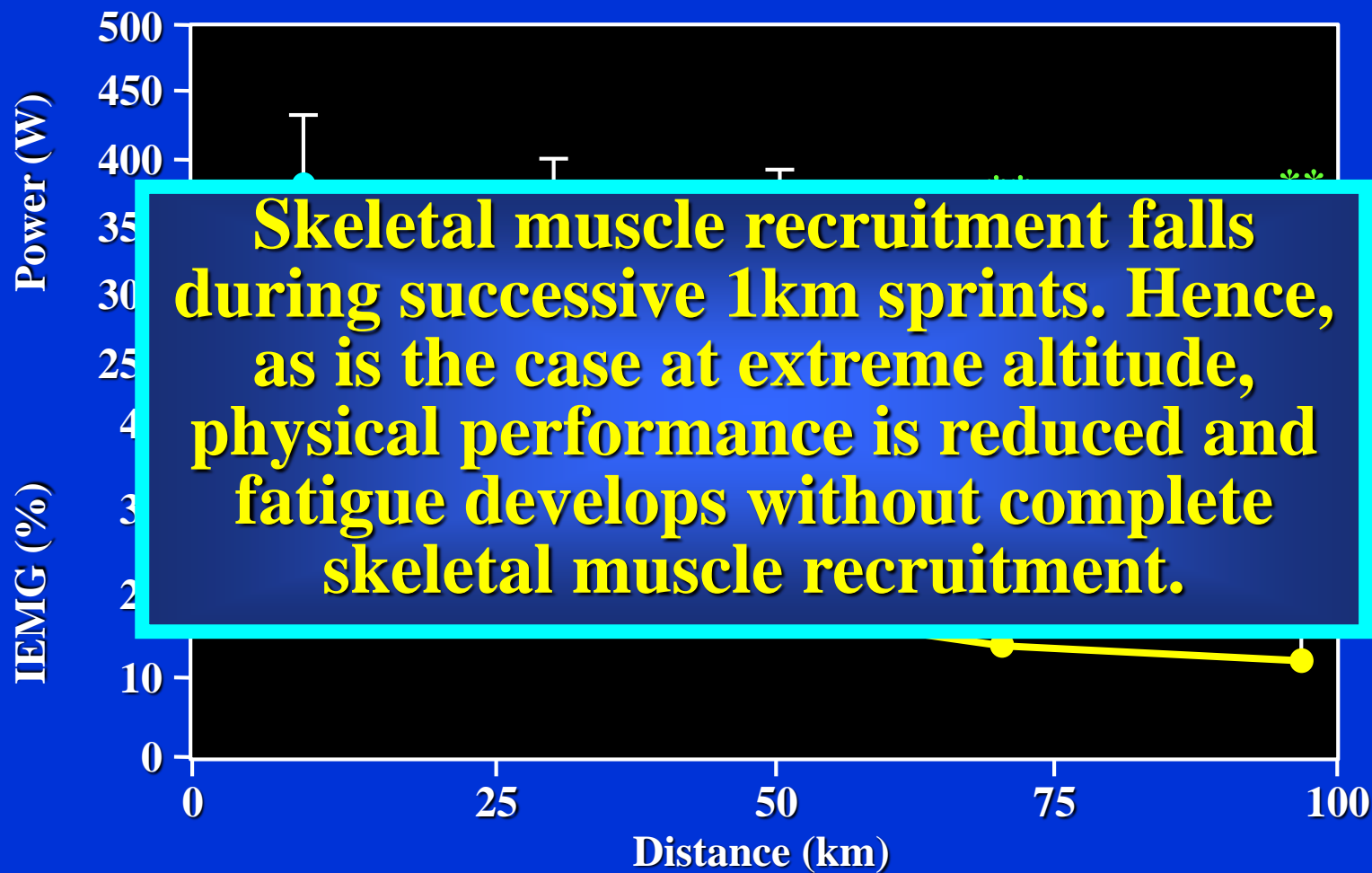
Power output falls during 1 and 4km sprints in a 100km cycling time trial.



A. St Clair Gibson et al. *American Journal of Physiology* 281; R187-R196, 2001.



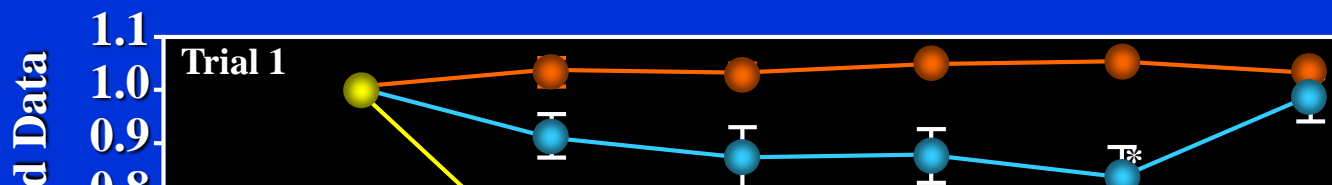
Equivalent falls in power and EMG activity during 1km sprints in a 100km cycling time trial.



A. St Clair Gibson et al. American Journal of Physiology 281; R187-R196, 2001.



Further evidence for centrally (brain) directed pacing strategy during 60 min time trial with 6 x 1km sprints.



Conclusion.

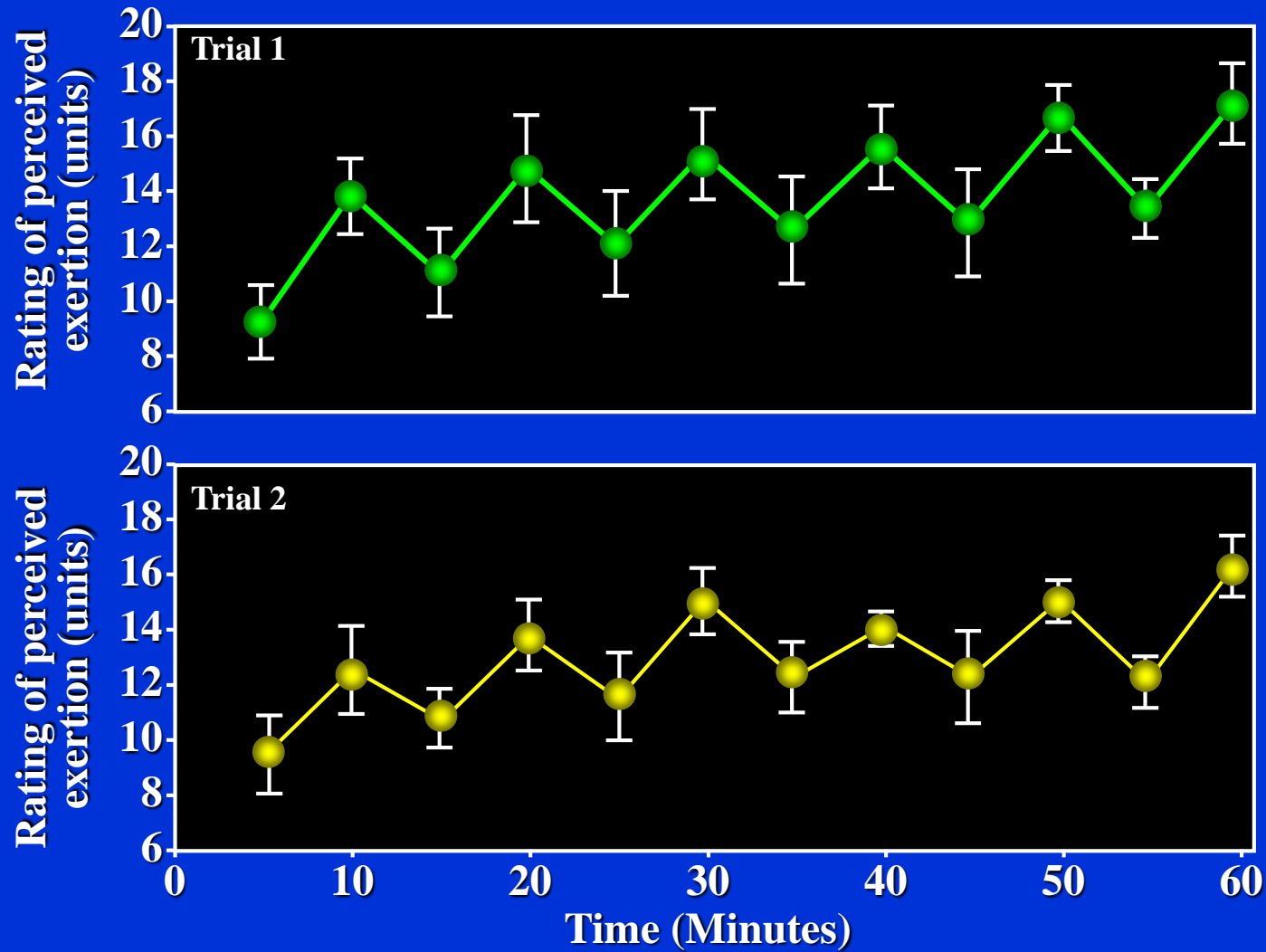
Complete muscle recruitment does not occur during voluntary exercise.



D. Kay et al. European Journal of Applied Physiology 84; 115-121, 2001.



Rating of perceived exertion is submaximal throughout 60 min time trial with 6 x 1km sprints



D. Kay et al. European Journal of Applied Physiology 84; 115-121, 2001.



Physiological Models of Exercise Performance

Cardiovascular /
Anaerobic Model

Energy Supply
Model

Muscle Power
Model

The rate of supply

The rate of supply

Muscle strength, or
power

The Central Governor Model.

Integrated Neuromuscular
Recruitment Model of Exercise
Physiology and Athletic
Performance

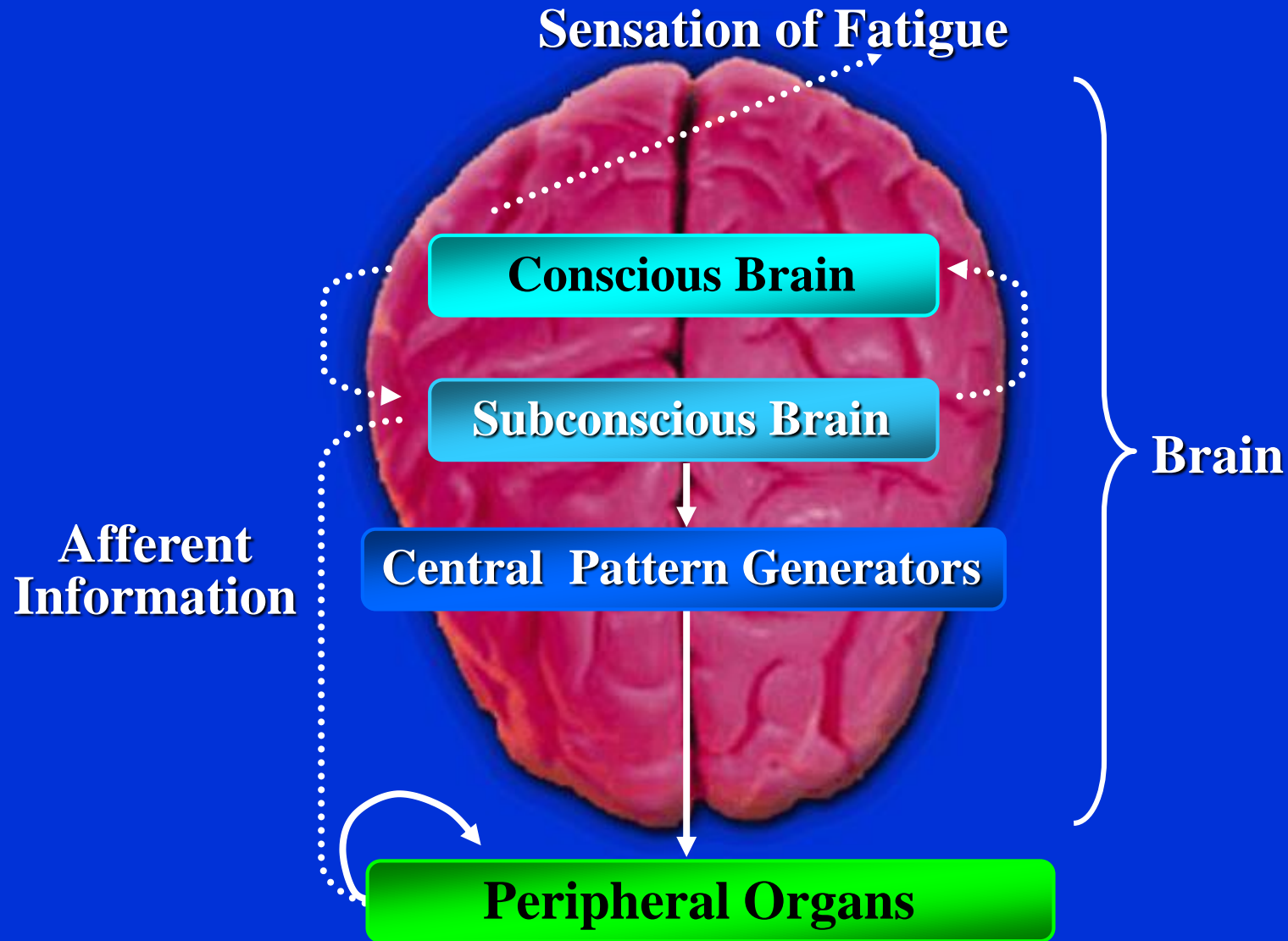
determines exercise
performance

determines exercise
performance

determines exercise
performance



Central Governor Model of Exercise.

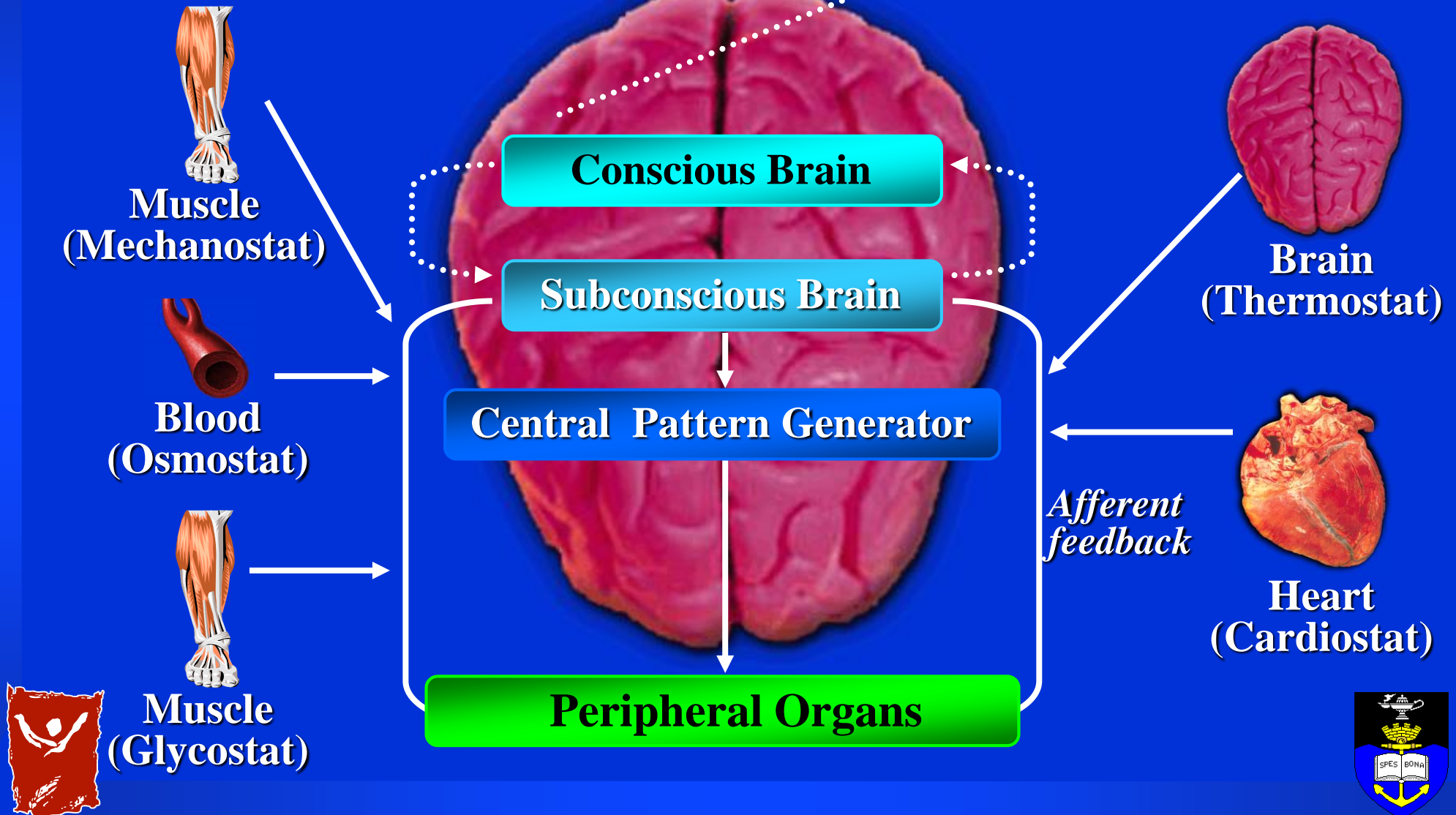


Ideas of Alan St Clair Gibson, 2001.



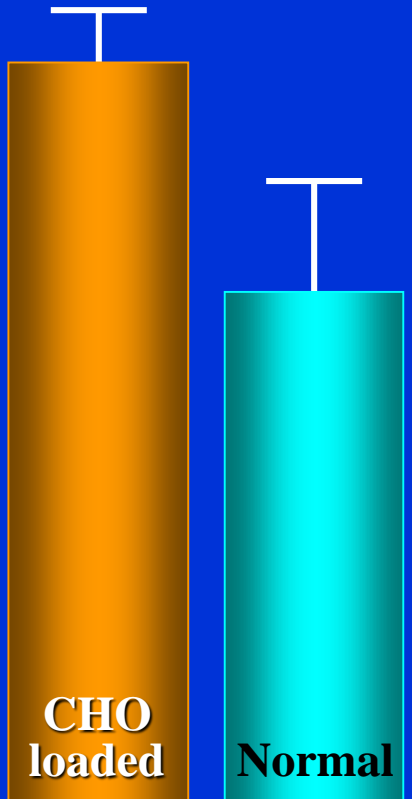
Central Governor Model of Exercise.

Sensation of Fatigue

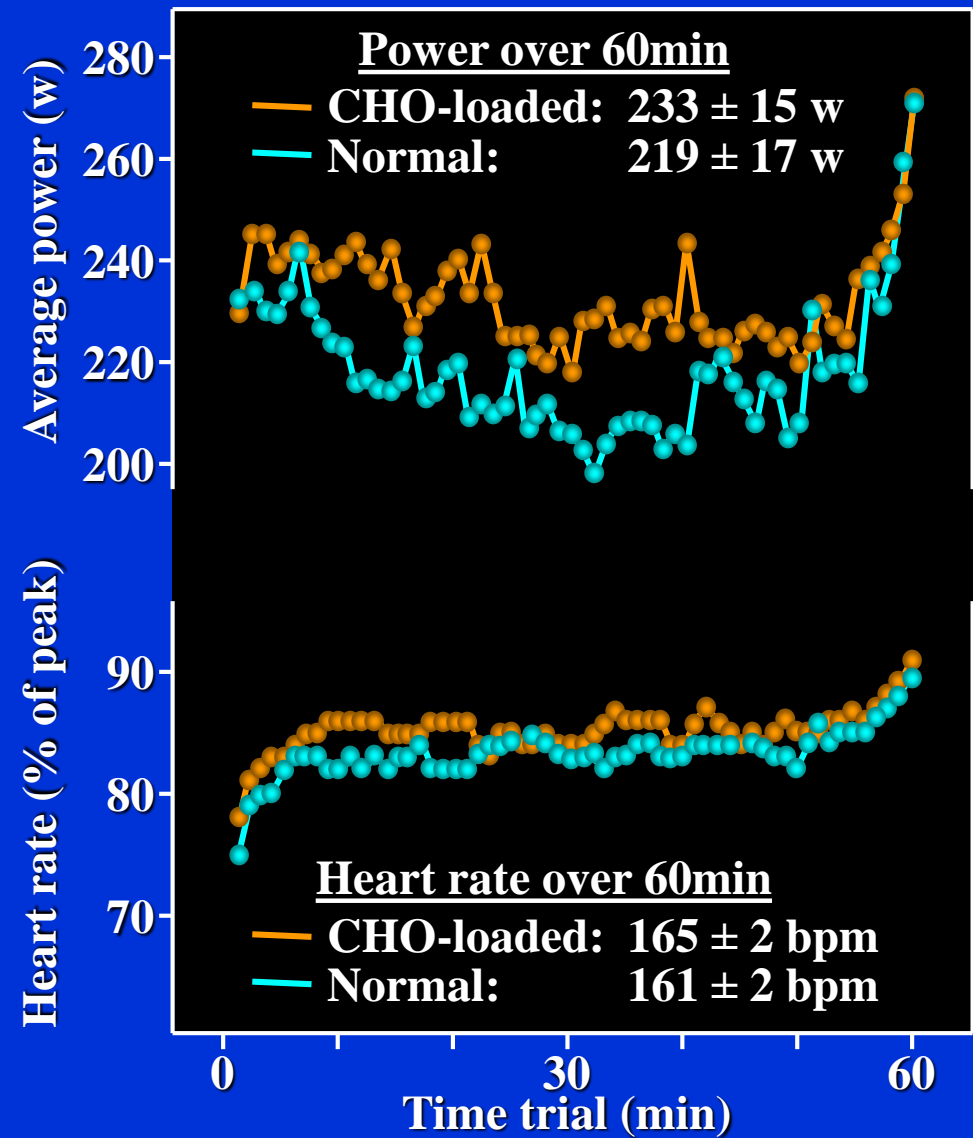


Evidence for the existence of a “Glycostat”.

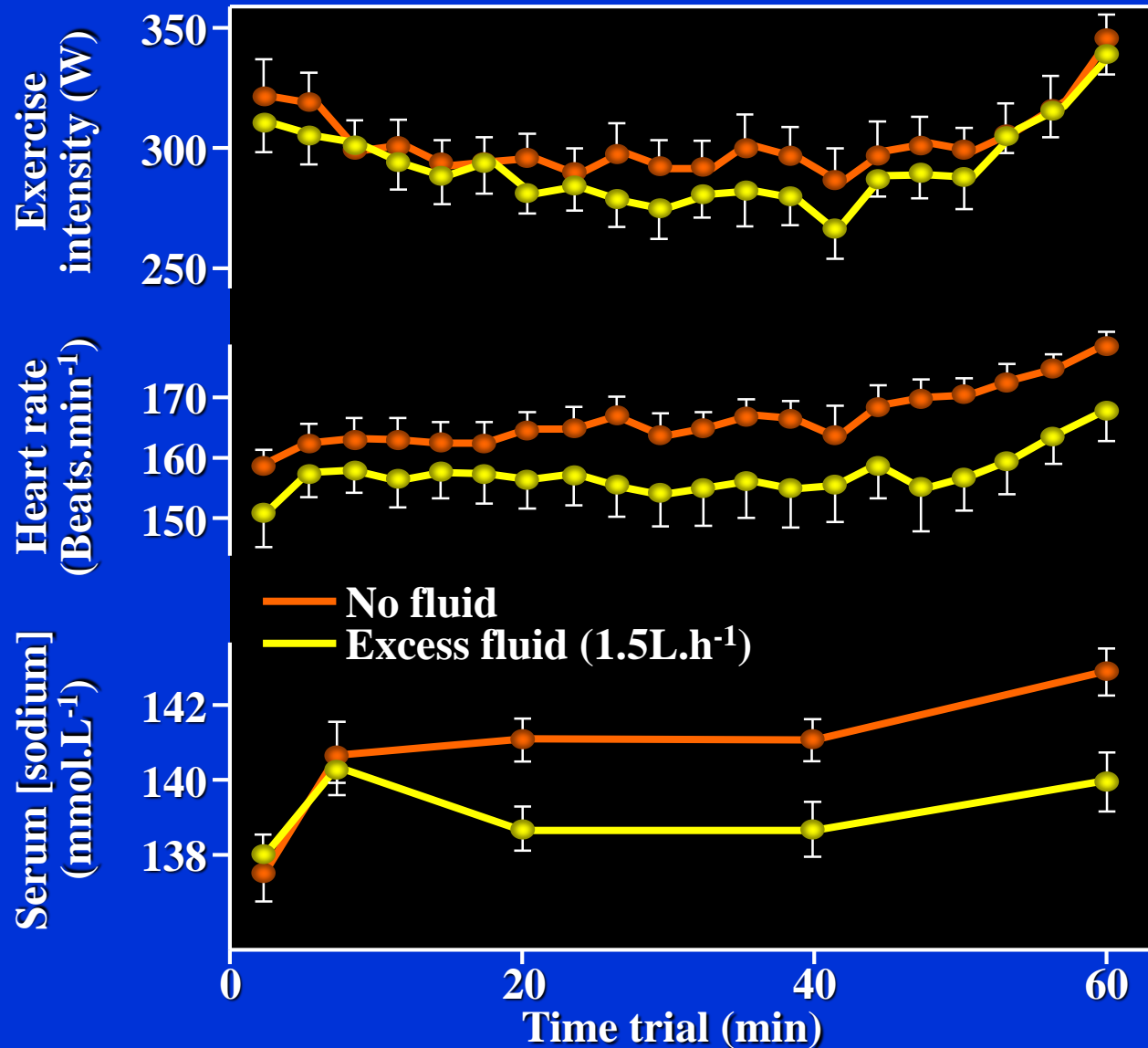
Pre-exercise muscle [glycogen] (mmol.Kg⁻¹ww)



Post-exercise muscle [glycogen] (mmol.Kg⁻¹ww)



Evidence for the existence of an “Osmostat”.



T.A. Robinson et al. *European Journal of Applied Physiology* 71; 153-160, 1995.



Barometric pressures, equivalent altitudes, and arterial blood gases during rest and maximal exercise from operation Everest II

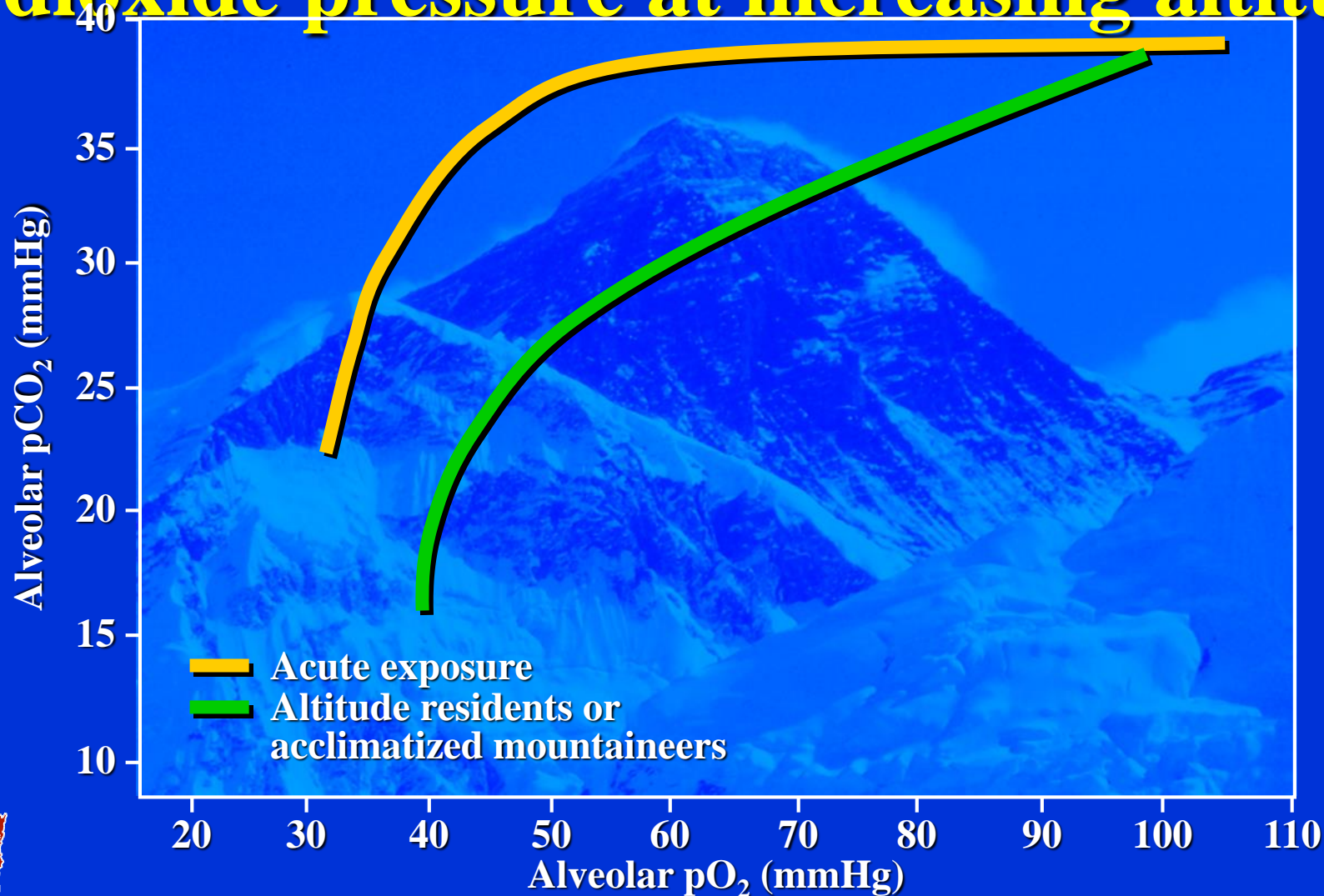
Baro- metric Pressure (torr)	Inspired PO ₂ (torr)	ICAO Altitude (ft)	ICAO Altitude (m)	Altitude on Mt. Everest (m)	Rest			Max Exercise		
					PaO ₂ (torr)	PCO ₂ (torr)	pH	PaO ₂ (torr)	PCO ₂ (torr)	pH
760	149	0	0	0	99	34	7.43	87	35	7.30
429	80	15,000	4572	4825	52	25	7.46	42	20	7.42
347	63	20,000	6096	6482	41	20	7.50	34	17	7.44
282	49	25,000	7620	8043	37	13	7.53	33	11	7.49
253	43	27,526	8390	8848	30	11	7.56	28	10	7.52



J.B. West. *High Life – A History of High Altitude Physiology and Medicine*, p.351, 1998.



Changes in alveolar oxygen and carbon dioxide pressure at increasing altitudes



H. Hultgren. High Altitude Medicine, p.16, 1997.



First ascent of Mount Everest without oxygen, 1978.

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Since the sensations of breathlessness occur at rest on the summit of Mount Everest, they are not the result of physical activity. Rather they must result purely from the effort necessary to maintain homeostasis, in particular, the ventilatory work required to maintain the PaO_2 above 28mmHg.



lung,

Messner, p.180, 1979.



Physiological Models of Exercise Performance

Cardiovascular /
Anaerobic Model

Energy Supply
Model

Muscle Power
Model

The rate of supply
of a substrate

The rate of supply
of a substrate

Muscle strength, or
muscle recruitment
by the brain

The Central Governor Model.

The crucial role of the brain
during exercise is to maintain
homeostasis

muscle glycogen
determines exercise
performance

movement
determines exercise
performance

(motivation)
determines exercise
performance



Physiological Models of Exercise Performance

Cardiovascular /
Anaerobic Model

Energy Supply
Model

Muscle Power
Model

The Central Governor Model.

As the biological work necessary to maintain homeostasis increases, the brain develops the sensation of fatigue, eventually terminating the exercise, even though homeostasis is still maintained.



Novel concepts from the Central Governor Theory

Questions that the Central Governor must answer include:

How much work do I have to do?

How much work do I still have to do?

Have I sufficient energy reserves to finish?

How do I feel about all of these?

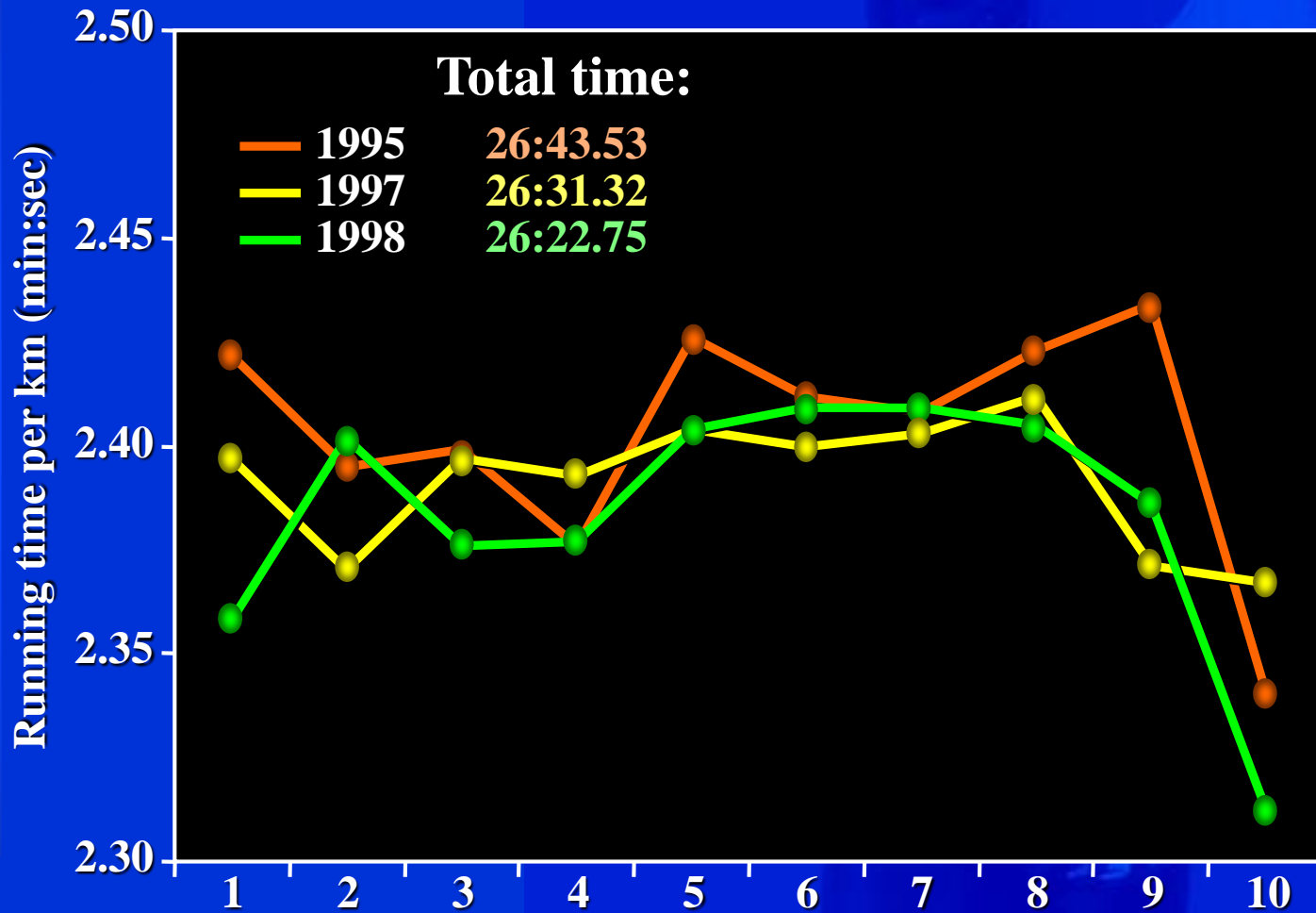
Will my muscles be damaged?

Will I become too hot?

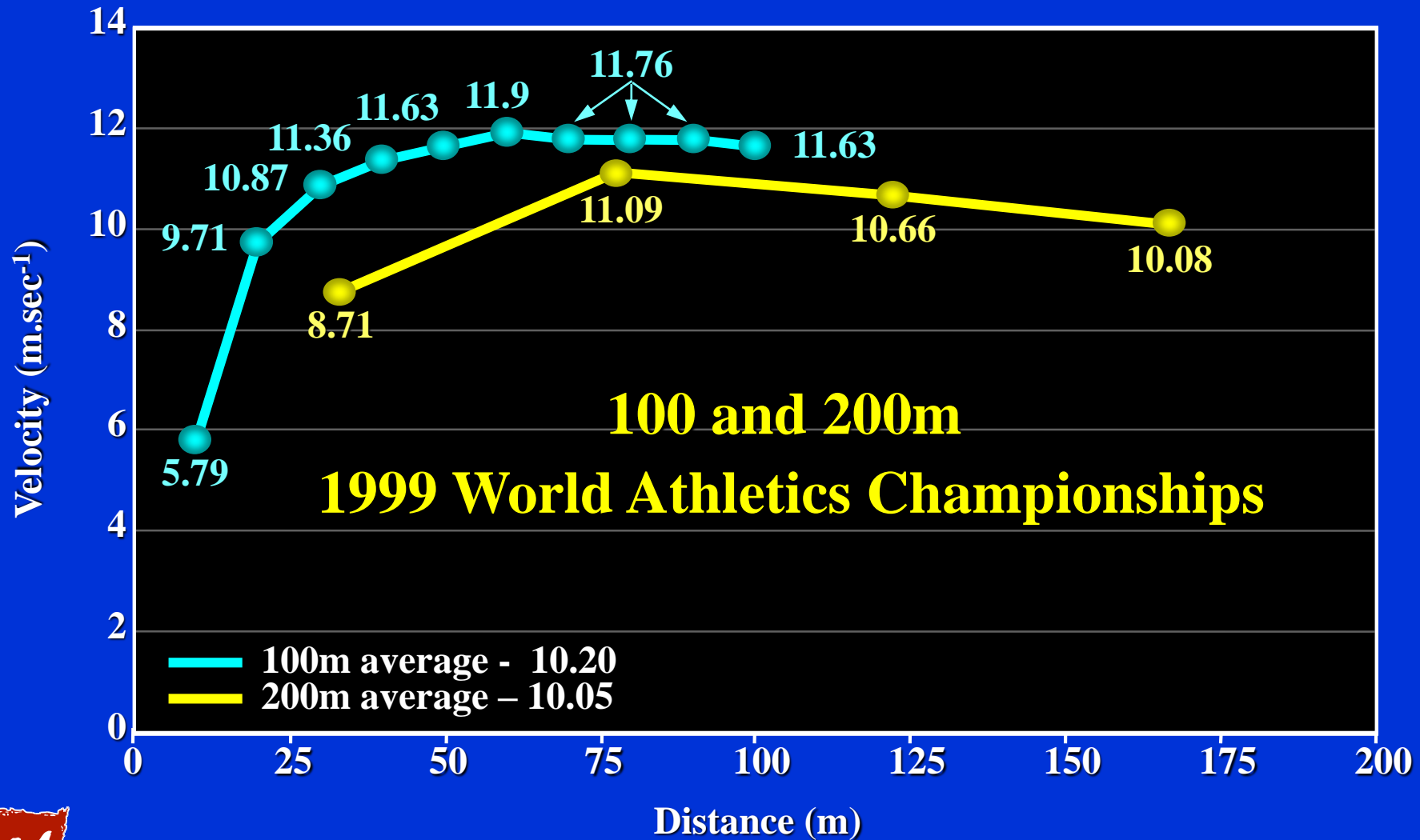


Ideas of Professor Vicki Lambert, 2001.

Time for consecutive 1 km splits during 3 world 10 000m record performances by Ethiopia's Haile Gebrselassie



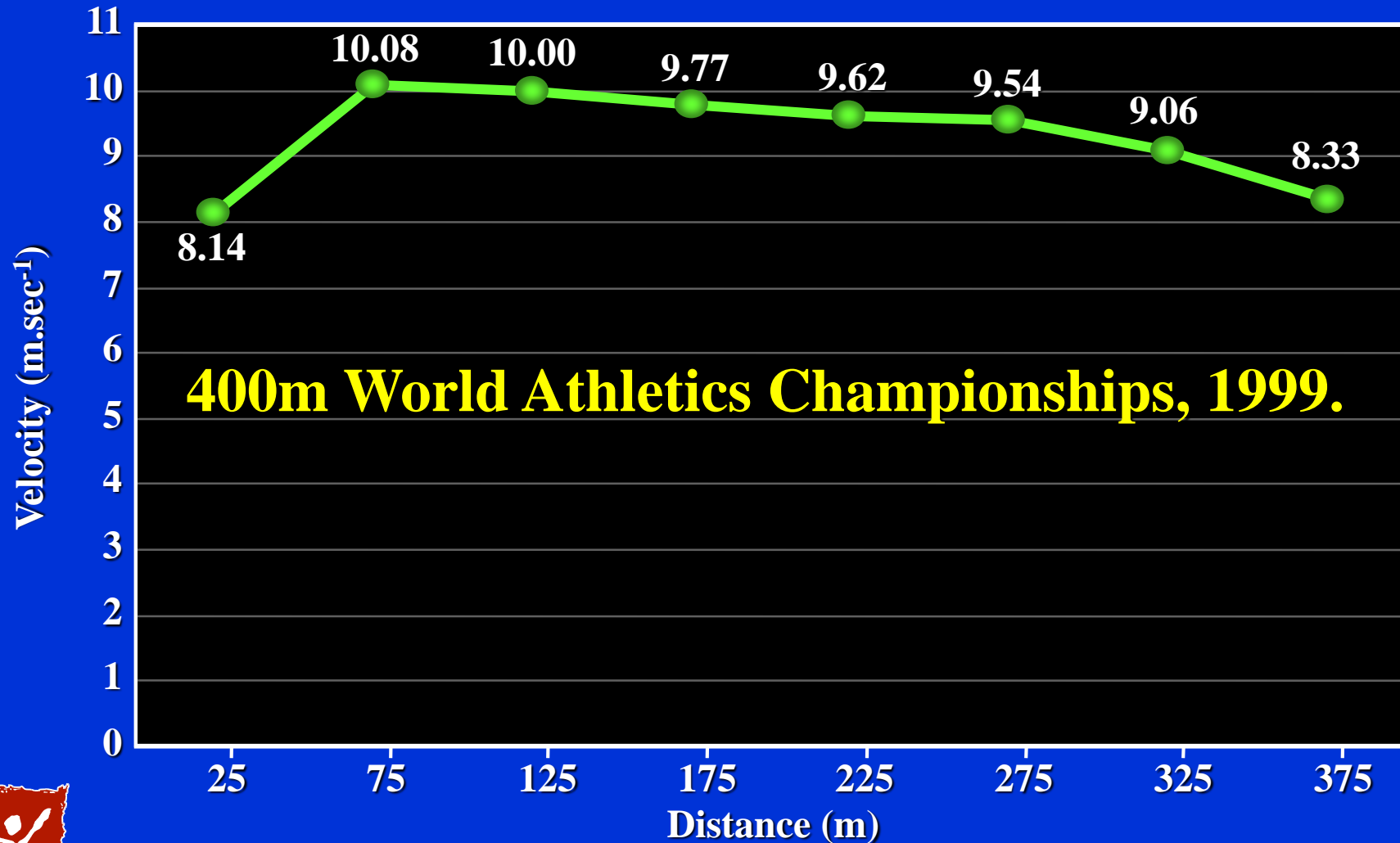
Pacing strategy of Maurice Green



New Studies in Athletics 1/2; 33 and 46, 2001.



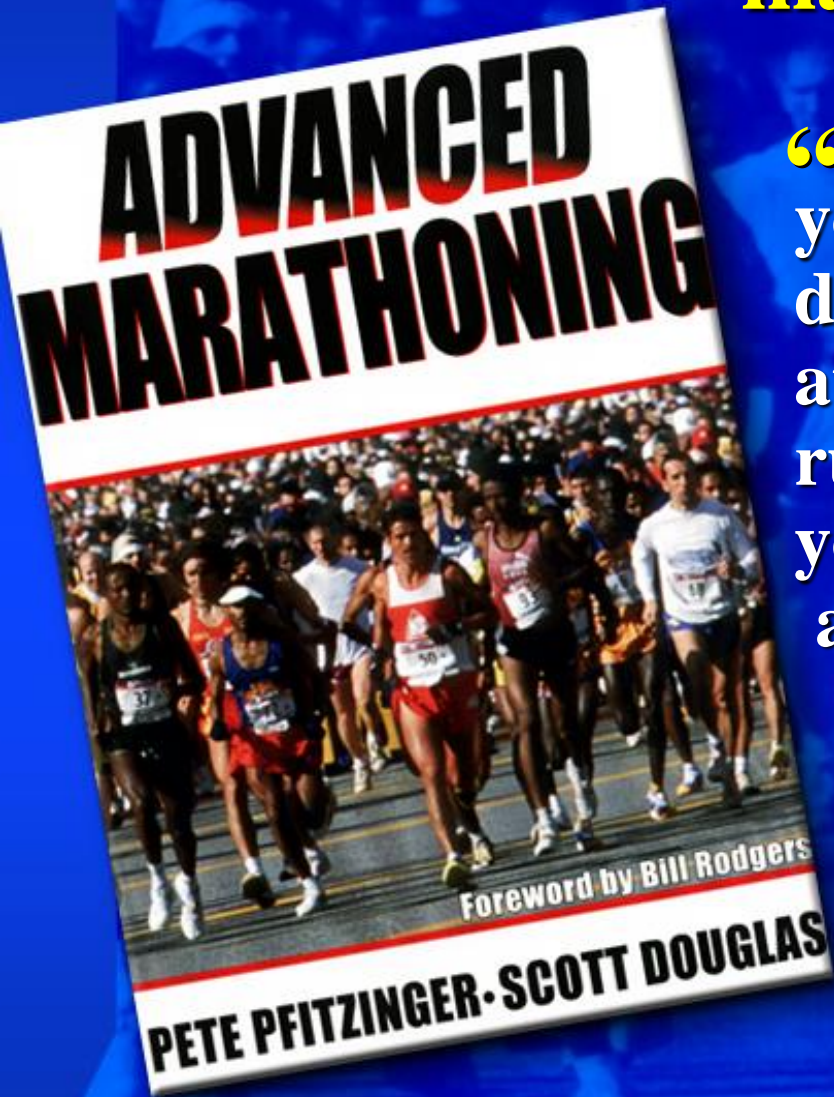
Pacing strategy of Michael Johnson.



New Studies in Athletics 1/2; 54, 2001.



Pete Pfitzinger's explanation for pacing during marathon running.



“ ... your marathon pace is very close to your lactate threshold pace, which is determined by your oxygen consumption at your lactate threshold and your running economy. If you run faster than your lactate threshold pace, then lactate accumulates in your muscles and blood; this occurrence deactivates the enzymes for energy production and makes you slow down. ”

P. Pfitzinger, S. Douglas. Advanced Marathon; 118-120, 2001.



Novel concepts predicted by the Integrated Neuromuscular Recruitment Model.

- The physiology of pacing, not fatigue, is the core issue for understanding exercise performance. The goal of pacing is to maintain homeostasis.
- Multiple, independent systems in the periphery provide sensory information to central motor command in the brain. The sum of this information determines the pacing strategy during exercise.
- Fatigue is solely a sensory perception but which may be expressed physically as an alteration in the pacing strategy.



Novel concepts predicted by the Integrated Neuromuscular Recruitment Model.

- Fatigue is therefore a measure of the central neural effort to maintain homeostasis.
- Finally, the role of the brain is to insure that exhaustion develops and exercise terminates, even though homeostasis is maintained.







EMIRATES  FLY EA

The common VO_2 max theory of Hill and Noakes

“Skeletal muscle recruitment and contractile function are regulated by an hierarchy of controls, specifically to prevent damage to any of a number of different organs.

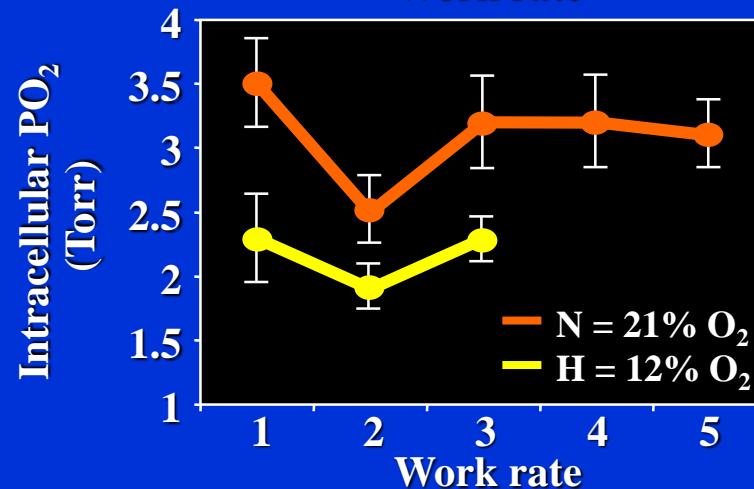
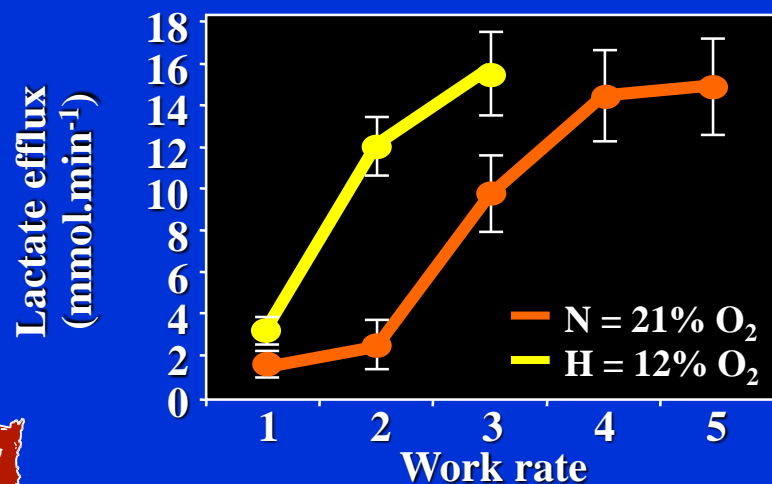
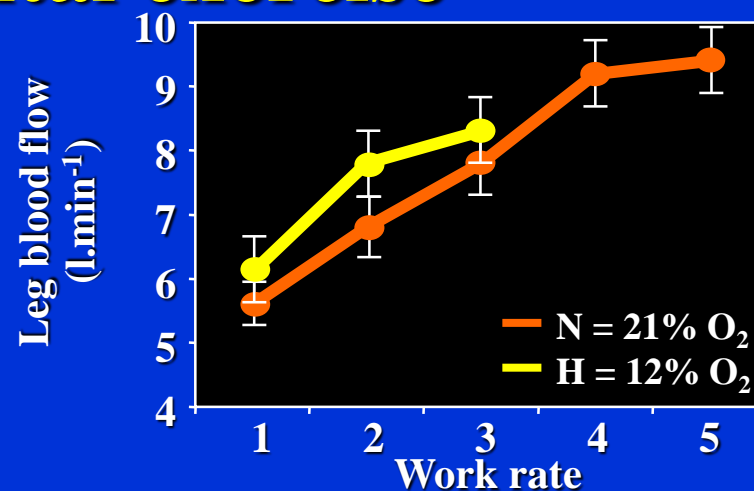
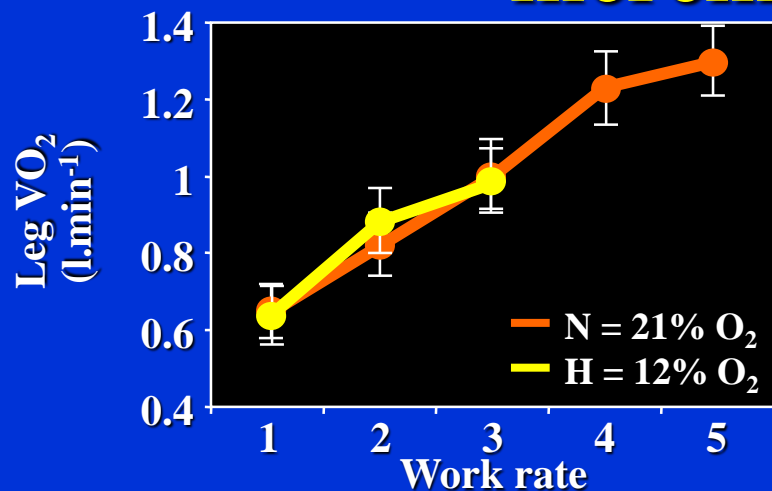
During maximal exercise, progressive myocardial ischaemia preceding skeletal muscle anaerobiosis, must be thwarted so that neither the heart, especially, nor skeletal muscle develops irreversible rigor and necrosis with fatal consequences”



T.D. Noakes Medicine and Science in Sports and Exercise 30; 1381 - 1398, 1998.



Biochemical evidence that skeletal muscle anaerobiosis does not occur during incremental exercise



R.S. Richardson et al. *Journal of Applied Physiology* 85; 627 - 634, 1998.



Biochemical evidence that skeletal muscle anaerobiosis does not occur during incremental exercise

“The major finding of his study is that intracellular PO_2 remains constant during graded incremental exercise in humans (50 - 100% of muscle VO_2 max)...”

“... these data demonstrate that, during incremental exercise, skeletal muscle cells do not become anaerobic... since intracellular PO_2 is well preserved at a constant level, even at maximal exercise.”



R.S. Richardson et al. Journal of Applied Physiology 85; 627 - 634, 1998.



Variables that are homeostatically regulated during exercise.

- Body temperature
 - pH
 - Arterial PO_2
 - Muscle glycogen
- Muscle eccentric force output
 - Muscle ATP
- Arterial Blood pressure

Variables that may determine exercise termination.

- Work of breathing
- Rate of CO_2 production etc



This slide needs to look at the idea that you did not find the plateau phenomenon in your studies. In addition you found that the treadmill speed was a good predictor of running performance – need a slide of those data that were published in 1990 in MSSE. This made you conclude that a “muscle factor” must be involved in performance. At the time you had no idea of what constituted recruitment as all assumed that recruitment was always 100%.



Road racing shoes – circa 1925



Paavo Nurmi display at the Helsinki Olympic Museum, Finland.



Here we need to discuss the idea of stochastic exercise. Most importantly this allowed the athlete to choose the workrate. We did not realise that this was the key issue at the time – not forcing the athlete to exercise according to the workrate that we had pre-set and which therefore allowed the brain to come into play.



This arose from the idea that fatigue is present early in exercise – for example when you repeatedly go up the same hill in competition, the effort seems to get harder with each successive effort. Hence the idea that fatigue does not develop only when you have finished the event but starts much earlier before the end of the effort.



At this time Roger Stewart and Elmarie Terblanche had developed a stochastic exercise machine and I was aware of it even reviewing Elmarie's thesis. Then there was the request to do research on a CHO loading product and I suggested that we should use a stochastic protocol for a change. Louise Burke then introduced the concept of the placebo into the trial.



Then there was the review of what limits performance during prolonged exercise and the realisation that the original studies were flawed. That led to Amanda's study which showed the effect of antecedent hypoglycaemia.



Need to remember the work of Andrew Bosch and Sandy Weltan and their finding that noradrenaline has some role perhaps as the SNS component of the reflex coming from muscle during exercise.



The studies of Nielsen confirm that the central governor works during exercise in the heat – as predicted by the JBWolffe lecture.

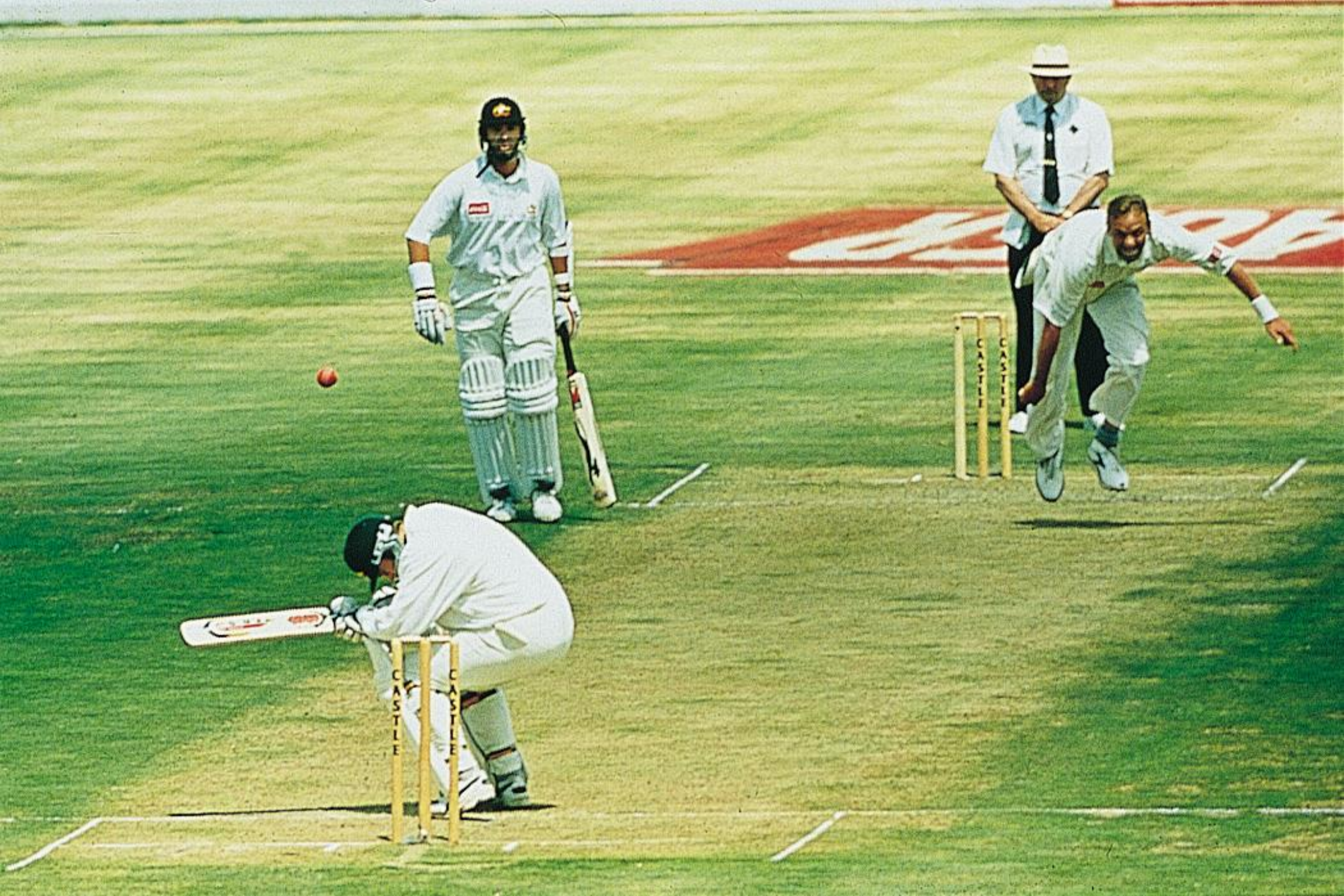


The study of Laurie Rauch fits here suggesting that there is a glycostat. At this point we speculated that the measurement of cell osmolality might be the variable that is sensed by the governor.



Here you need to refer to Bernd Heinrich's book and the concept of pacing by the birds that cross the Atlantic. Need some info on that as well.





A.V.Hill studies the effects of hyperoxia on oxygen consumption and respiration during exercise - 1924

C.N.H. Long: All-out stepping exercise



“It is necessary to assume that a rich oxygen mixture works primarily by increasing the saturation of the blood with oxygen ... this increased saturation must, therefore, in some manner increase the rate of circulation of the blood.... It would seem probable.... that the heart is able to regulate its output, to some extent, in accordance with the degree of saturation of the arterial blood, either of that which reaches it through the coronary vessels or by some reflex in other organs produced by a deficient oxygen supply. From the point of view of a well co-ordinated mechanism, some such arrangement is eminently desirable....”



*A.V.Hill, C.N.H. Long and H.Lupton.
Proceedings of the Royal Society of Britain 97; 161-163, 1924.*



????????

“... physical fitness cannot be defined nor can differences be detected by means of a few simple physiological measurements obtained during limited tests To do so results in focussing attention on some erroneous concept. Man is not a pulse rate, a rectal temperature, but a complex array of many phenomena... Into performance enters the baffling yet extremely important factor of motivation, the will-to-do.

This cannot be measured and remains an uncontrollable, quickly fluctuating, disturbing variable which may at any time completely alter the performance regardless of physical or physiologic state.”



Bean and Eichna; p.157, 1943.



Additional slides for this talk.

- 1. Lance Armstrong quote on his lactic acid causing him to feel pain.**
- 2. Tame Cheetah for the other talk on tired antelope.**
- 3. Re-do the slide of lactic acid and fatigue – new study from Copenhagen.**
- 4. The slide of the Japanese studies of gun shots and prolonged isometric exercises from Gandiva's paper**
- 5. Slide of Hopkins and Fletcher's data and conclusions.**



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“... physical fitness cannot be defined nor can differences be detected by means of a few simple physiological measurements obtained during limited tests To do so results in focussing attention on some erroneous concept. Man is not a pulse rate, a rectal temperature, but a complex array of many phenomena.... Into performance enters the baffling yet extremely important factor of motivation, the will-to-do.

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Bean and Eichna; p.157, 1943.





*What causes fatigue during
high intensity exercise of
short duration?*

**Wrong
question.**

*“It’s the brain not the
heart or lungs, that is the
critical organ, it’s the
brain”.*

Sir Roger Bannister, 1998.

“Mile of the Century”

1954 Vancouver Empire Games



Roger Bannister

*John
Landy*

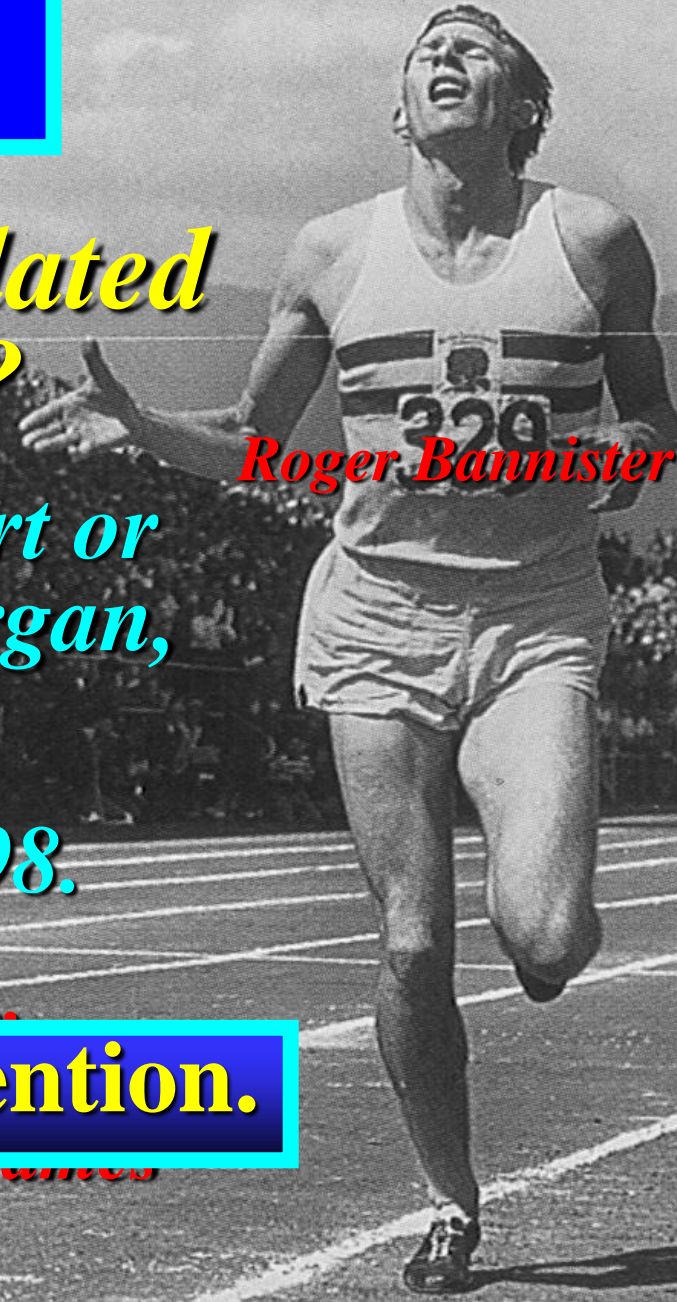
*More correct
question.*

*How is pacing regulated
during exercise?*

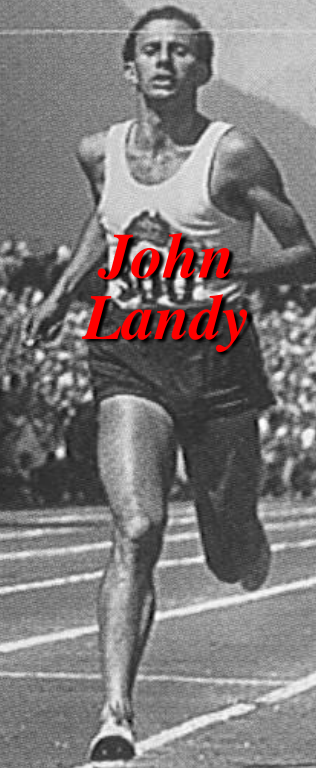
*“It’s the brain not the heart or
lungs, that is the critical organ,
it’s the brain”.*

Sir Roger Bannister, 1998.

Thank you for your attention.



Roger Bannister



*John
Landy*

*“It’s the brain not the heart or
lungs, that is the critical organ,
it’s the brain”.*
1954 Vancouver Empire Games

Correct question.

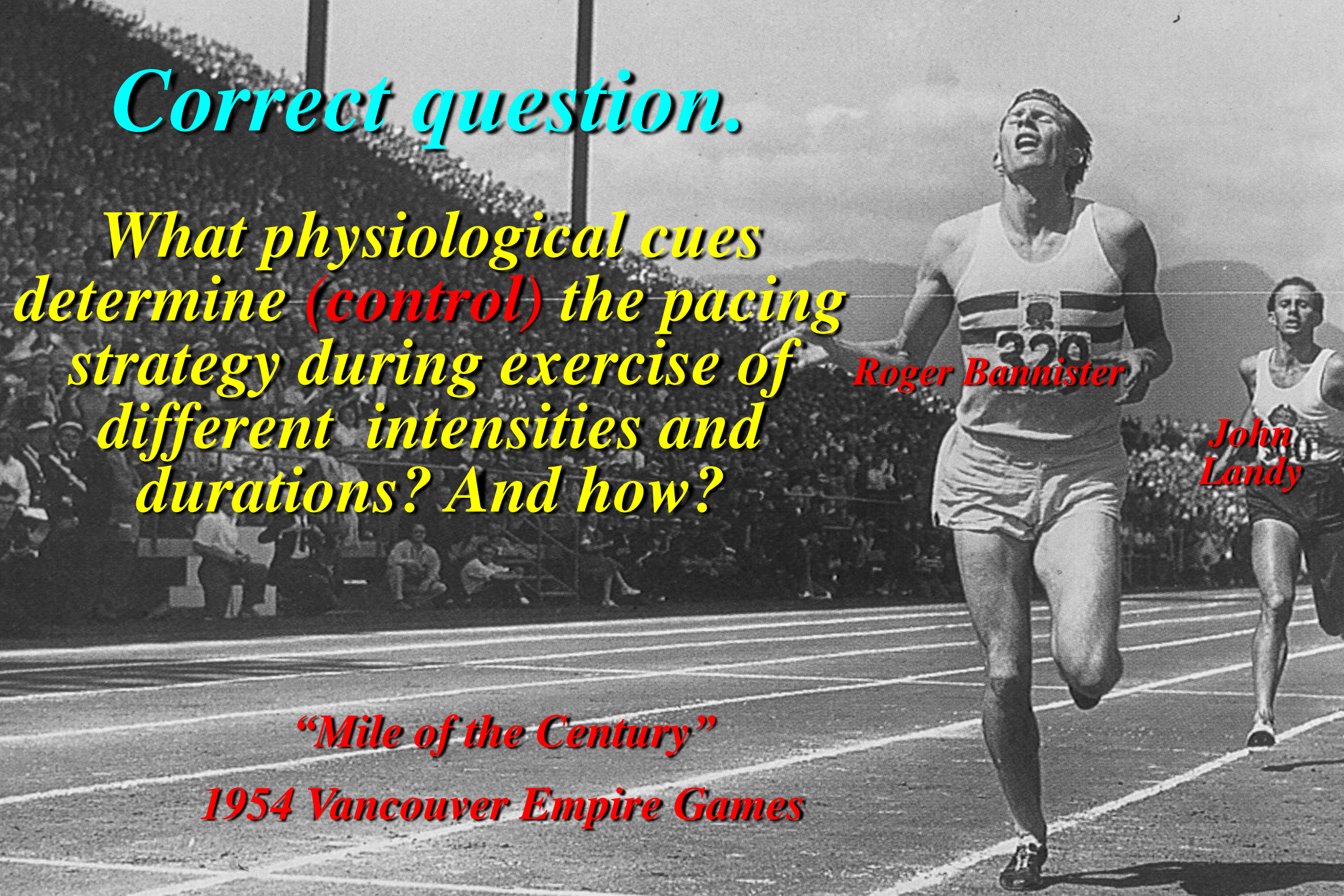
What physiological cues determine (control) the pacing strategy during exercise of different intensities and durations? And how?

Roger Bannister

John Landy

“Mile of the Century”

1954 Vancouver Empire Games



*What causes fatigue during
high intensity exercise of
short duration?*

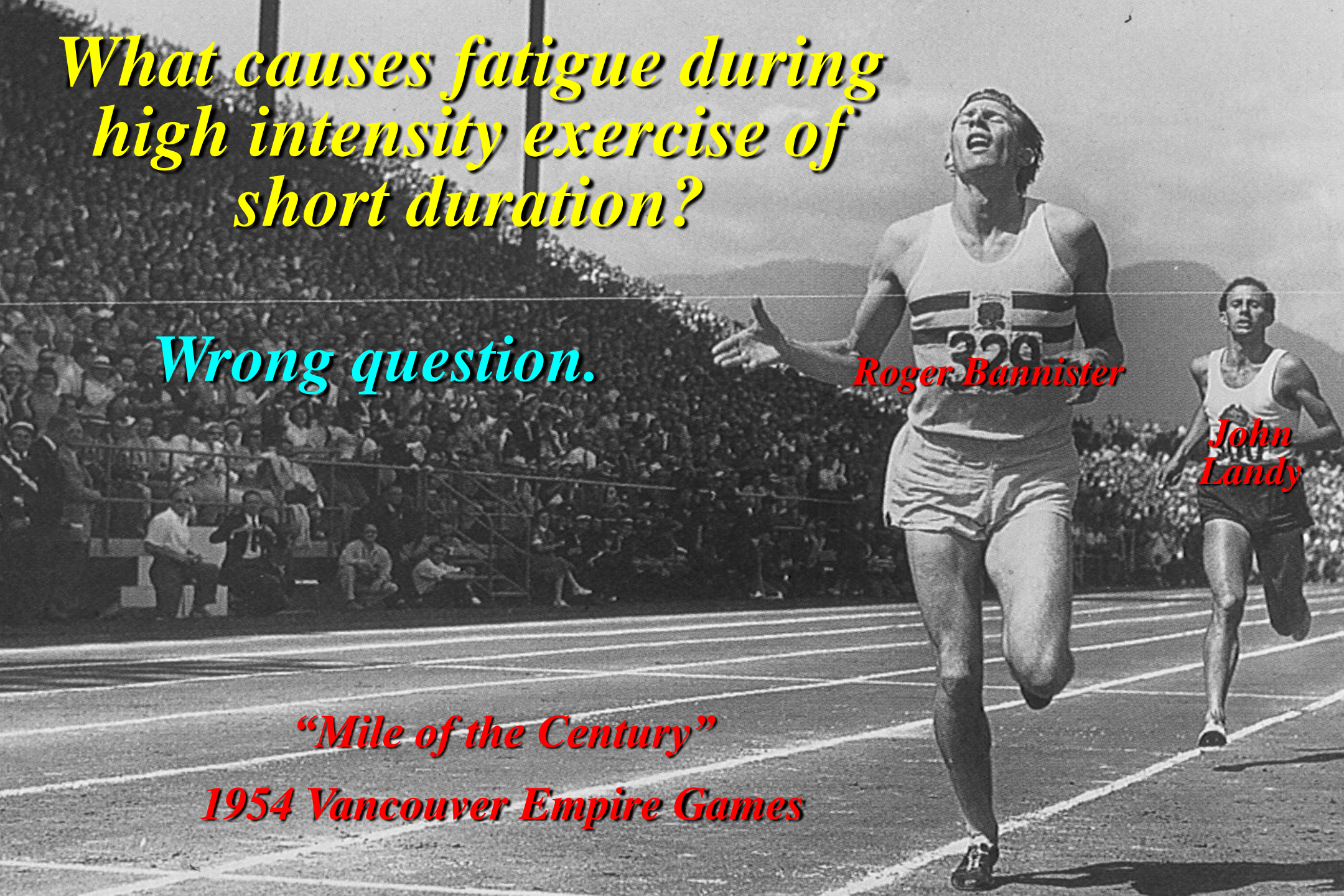
Wrong question.

Roger Bannister

*John
Landy*

“Mile of the Century”

1954 Vancouver Empire Games



Some key unresolved questions: Beyond 2001.

- What **controls** the peak work rate during maximal exercise with small and large muscle groups?
- **Solution:** Studies of hyperoxia show that it is not oxygen but a mechanoreceptor in either exercising muscles or the respiratory muscles.
- **Future studies:** Hyperoxia with helium to reduce the mechanical work of breathing will differentiate between the different possible mechanoreceptors.



Some key unresolved questions: Beyond 2001.

- What **controls** the pacing strategies during prolonged exercise lasting less than 60 minutes?
- **Solution:** More likely to be respiratory sensations during exercise of less than 1 hour.
- **Studies:** Hyperoxia with helium to reduce the mechanical work of breathing will identify whether respiratory cues are involved.



Some key unresolved questions: Beyond 2001.

- What **controls** the pacing strategies during prolonged exercise lasting more than 2 hours?
- Possible solutions:
 - Muscle chemoreceptors (glycostat).
 - Muscle mechanoreceptors.
 - Circulating factor – “Fatigueogen”.
 - Brain thermoreceptors.
 - If so – How do these factors act?



The story of Lore of Running

1972 - 2001

“It’s the brain not the heart or lungs, that is the critical organ, it’s the brain”.

Sir Roger Bannister, 1998.

“Mile of the Century”

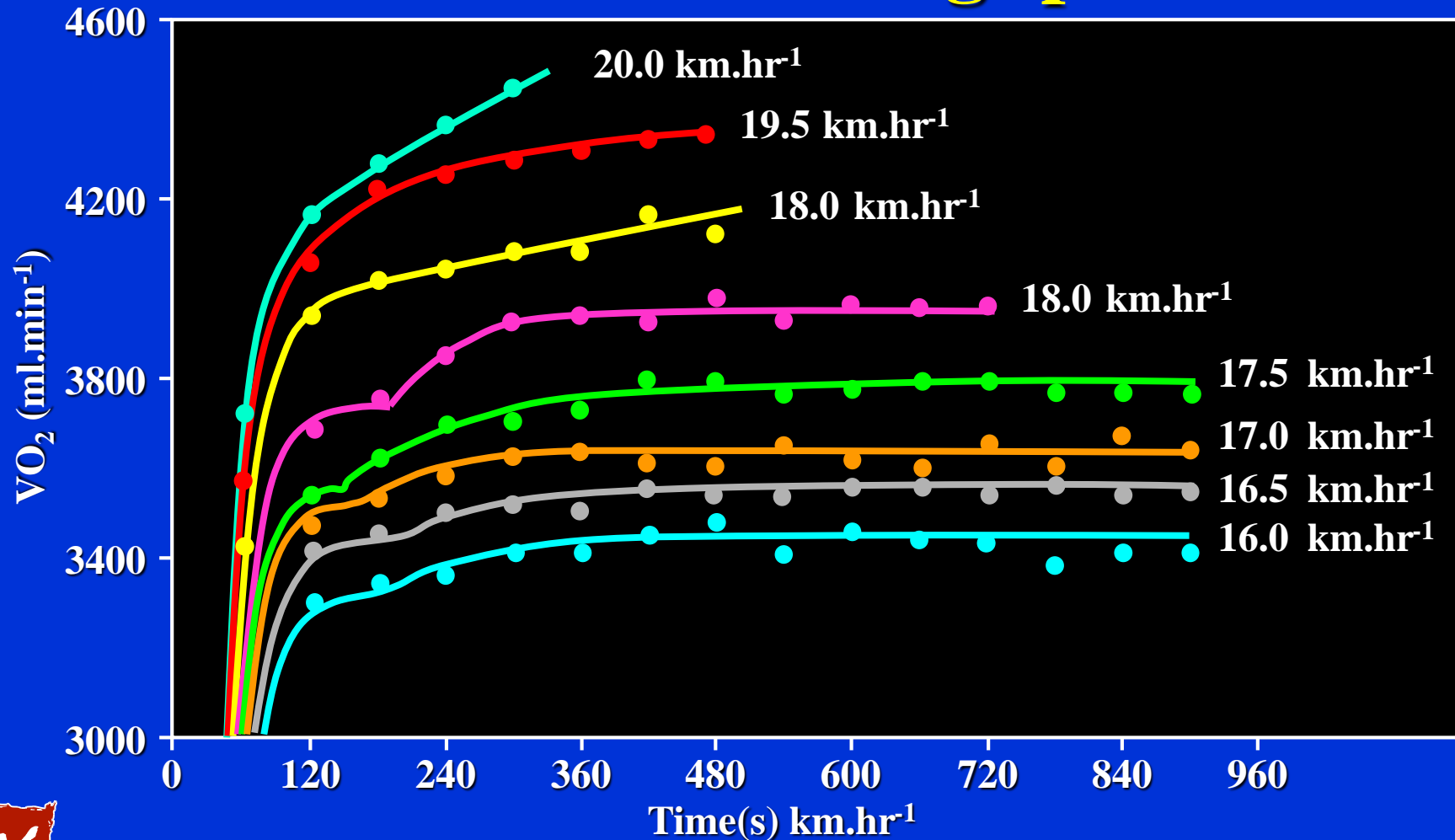
1954 Vancouver Empire Games



Roger Bannister

John Landy

Rate of rise of VO_2 during exercise at different running speeds



O. Bernard et al. European Journal of Applied Physiology 78; 578 - 585, 1998.

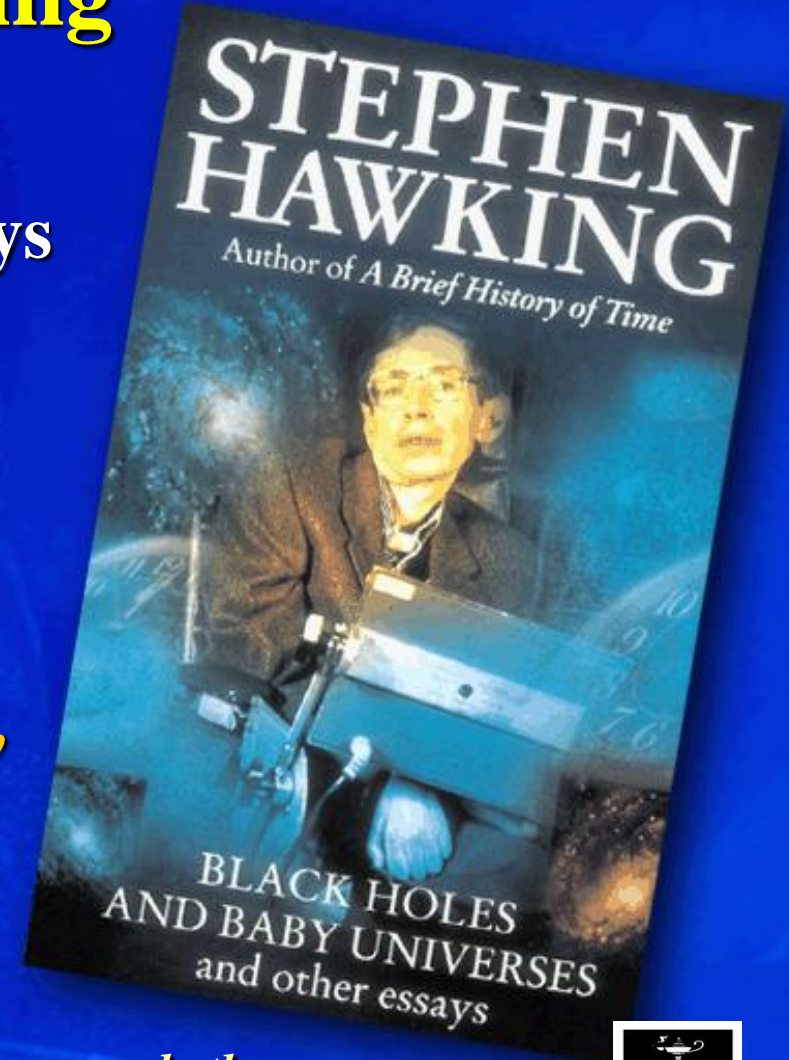


There is no other species on Earth that does science. It is, so far, entirely a human invention, evolved by natural selection in the cerebral cortex for one simple reason: it works. It is not perfect. It can be misused. It is only a tool. But it is by far the best tool we have, self-correcting, ongoing, applicable to everything. It has two rules. First: there are no sacred truths; all assumptions must be critically examined; arguments from authority are worthless. Second: whatever is inconsistent with the facts must be discarded or revised. We must understand the Cosmos as it is and not confuse how it is with how we wish it to be.



The theory (model) always comes first: Stephen Hawking

“In theoretical physics, the search for logical self-consistency has always been more important in making advances than experimental results. Otherwise elegant and beautiful theories have been rejected because they don't agree with observation, but *I don't know of any major theory that has been advanced just on the basis of experiment*”.

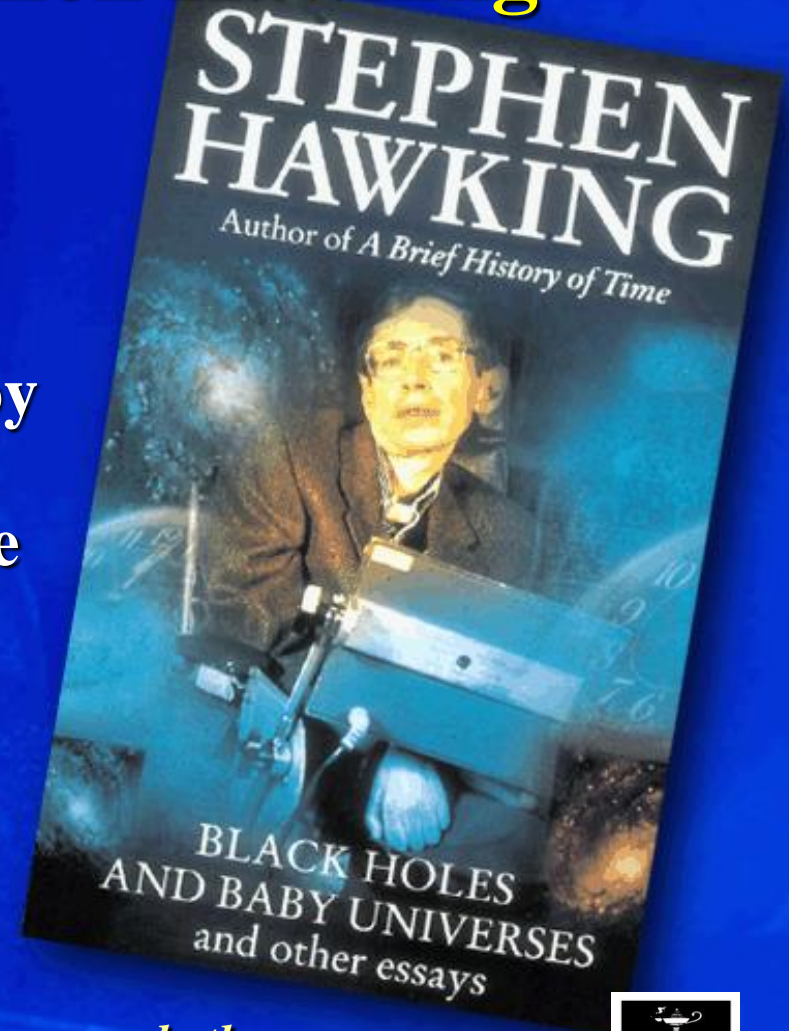


*Stephen Hawking. Black Holes and Baby Universes and other essays.
Bantam Books, London, p.36, 1993.*



If the facts do not fit the theory (model), abandon the theory: Stephen Hawking

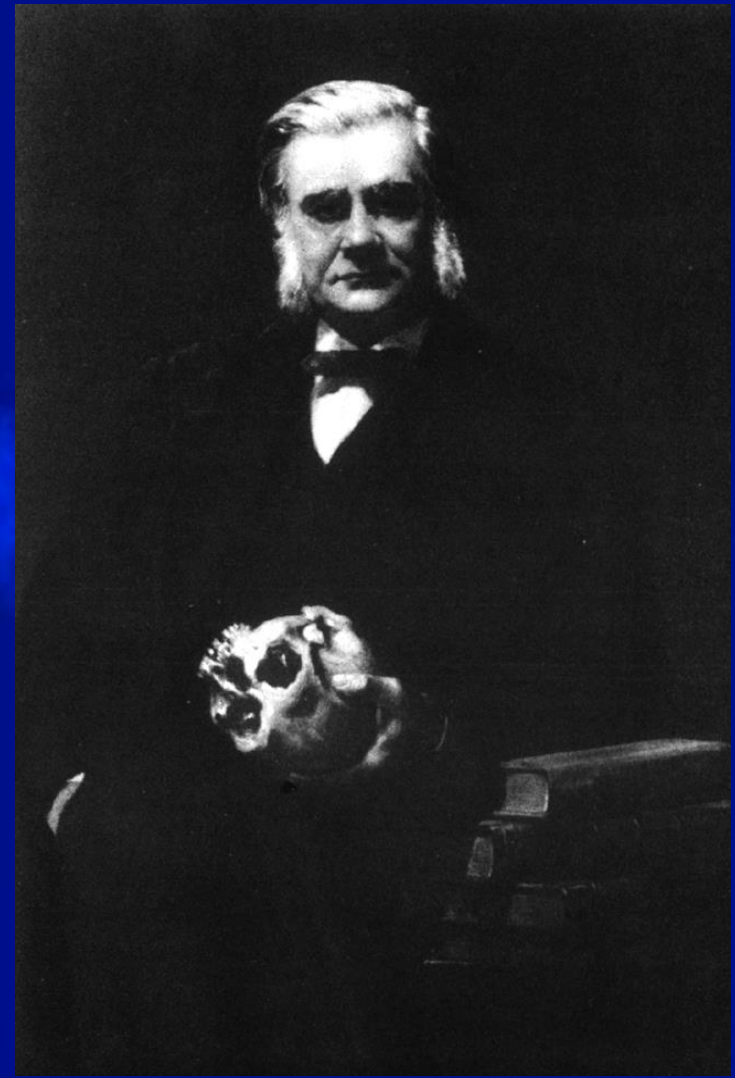
*“The theory always comes first, put forward from the desire to have an elegant and consistent mathematical model. The theory then makes predictions, which can then be tested by observation. If the observations agree with the predictions, that doesn’t prove the theory; but the theory survives to make further predictions, which are tested against observation. **If the observations don’t agree with the predictions, one abandons the theory”.***



*Stephen Hawking. Black Holes and Baby Universes and other essays.
Bantam Books, London, p.36, 1993.*



“The practical men believed that the idol whom they worship - rule of thumb - has been the source of the past prosperity, and will suffice for the future welfare of the arts and the manufactures. They were of the opinion that science is speculative rubbish; that theory and practice have nothing to do with one another; and that the scientific habit of mind is an impediment, rather than an aid, in the conduct of ordinary affairs.”



Thomas H. Huxley



Tyranny of knowledge axiom

“We already know how that works”



Sufficiency of Proof axiom

“Much less evidence is required to establish something as “fact” than to dislodge it.”



*Professor Stan Lindstedt, Professor of Biology,
Northern Arizona University*



Clifford's dictum

“It is wrong always, everywhere and for everyone to believe anything on insufficient evidence.”



W.W. Gibbs Beyond Physics. Renowned Scientists contemplate the evidence for God. Scientific American 279; August 10, 1998.



Do We Care About Truth?

“The truth is that we don’t know the truth. ... The trouble is that in modern America people often won’t search for what they fear they might find”.

Robert J. Samuelson. Newsweek. September 6, 1999

