Oxygen Delivery - Hb

Cardiac output x Hb x % Sat O2

Preload

Effective blood volume
Capacitance
Obstruction
Septal shift
IV fluid
    volume
    C.O.P.

Pump failure

Arrhythmias
Ischaemia
Valvular problems
Septal shift

Afterload

RAA adaptaion
Sepsis
Valvular problems
Pulmonary embolism
Hypertension
Shunts

Heart rate

Anaemia

Fe def
Dilutional
Inflammatory
Vitamin deficiency
Aplastic

Abnormal Hb

Sickle cell
Thalassaemia
met Hb
CO Hb

Hemolysis

free Hb and NO
Pulmonary hypertension
Hypercoagulability

Hyperviscosity

PRV
Acclimatisation

Inspired O2

Altitude
Hyperbaric O2

Hypoventilation

Decreased respiratory drive
    drug induced
CVA
Fatigue (asthma)
Obstruction
    Sleep apnoea syndrome
    Decreased consciousness

Ventilation/perfusion abnormalities

Shunt
    Pneumonia
    Pulmonary oedema
Dead space
    Pulmonary embolism
    Fat embolism
Mixed
    COPD
    Asthma

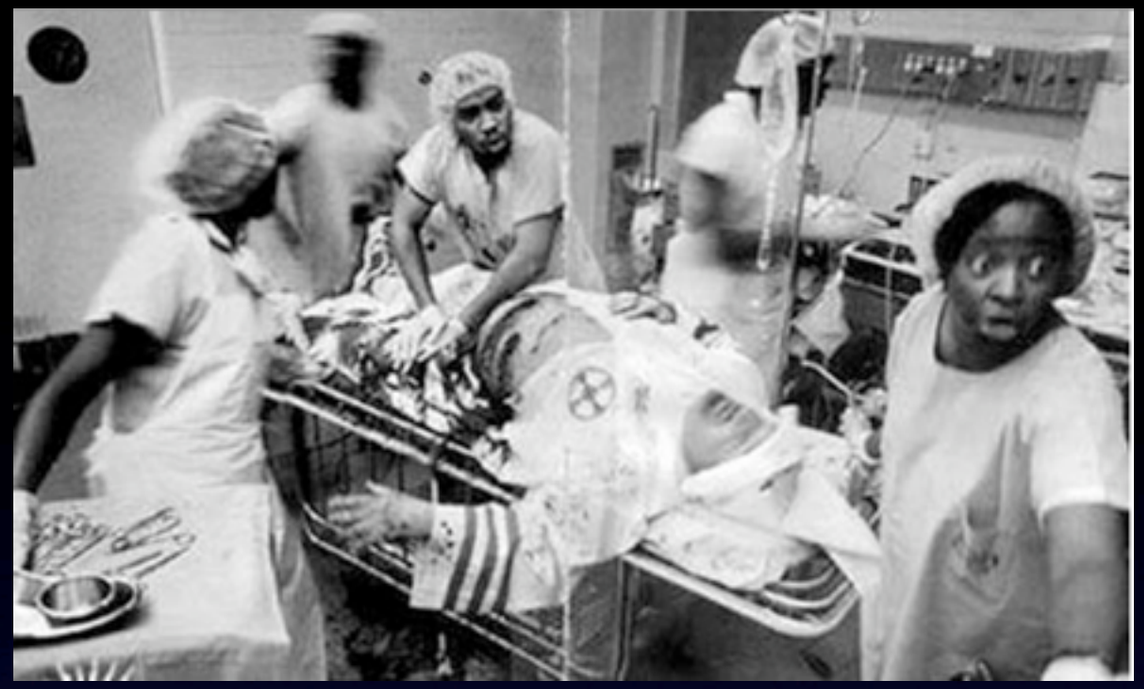
Summary of todays lecture

- Hb - the Transporter
- Hb - the Flow Regulator

Hb - the Transporter

Body needs ~ 250 ml oxygen / min

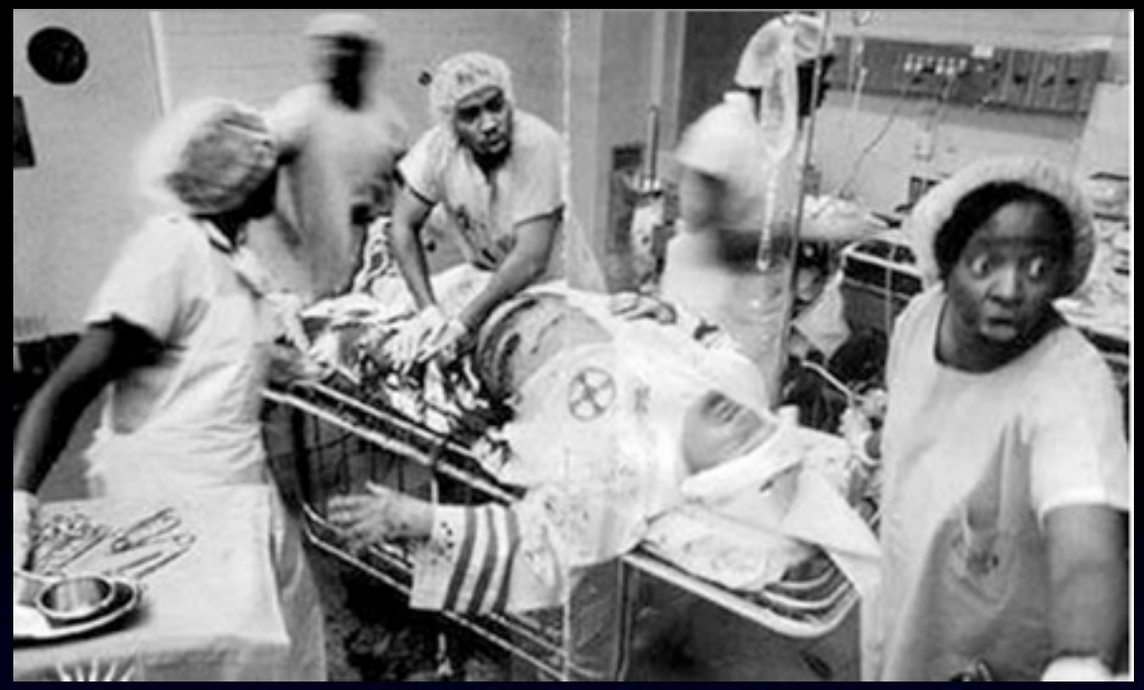
1000 ml O2 delivered



Cardiac output x Hb x % Sat O2

5l 7.5 gm 100 %

500 O2 ml/min delivered



Cardiac output x Hb x % Sat O2

5l 7.5 gm 100 %

2.5 l 7.5 gm 100 %

250 O2 ml/min delivered

Cardiac output x Hb x % Sat O2

- If one variable is halved, the oxygen delivery is reduced to 1/2
- If two variables is halved, the oxygen delivery is reduced to 1/4
- If three variables is halved, the oxygen delivery is reduced to 1/8

= 125 ml/min O2 delivered

When assessing a patient, consider the three factors **together!**

Just how important is Hb for O2 transport ?

"One if the important discoveries, I believe ... is the realization that anemia is well tolerated ... "

providing blood volume is maintained.

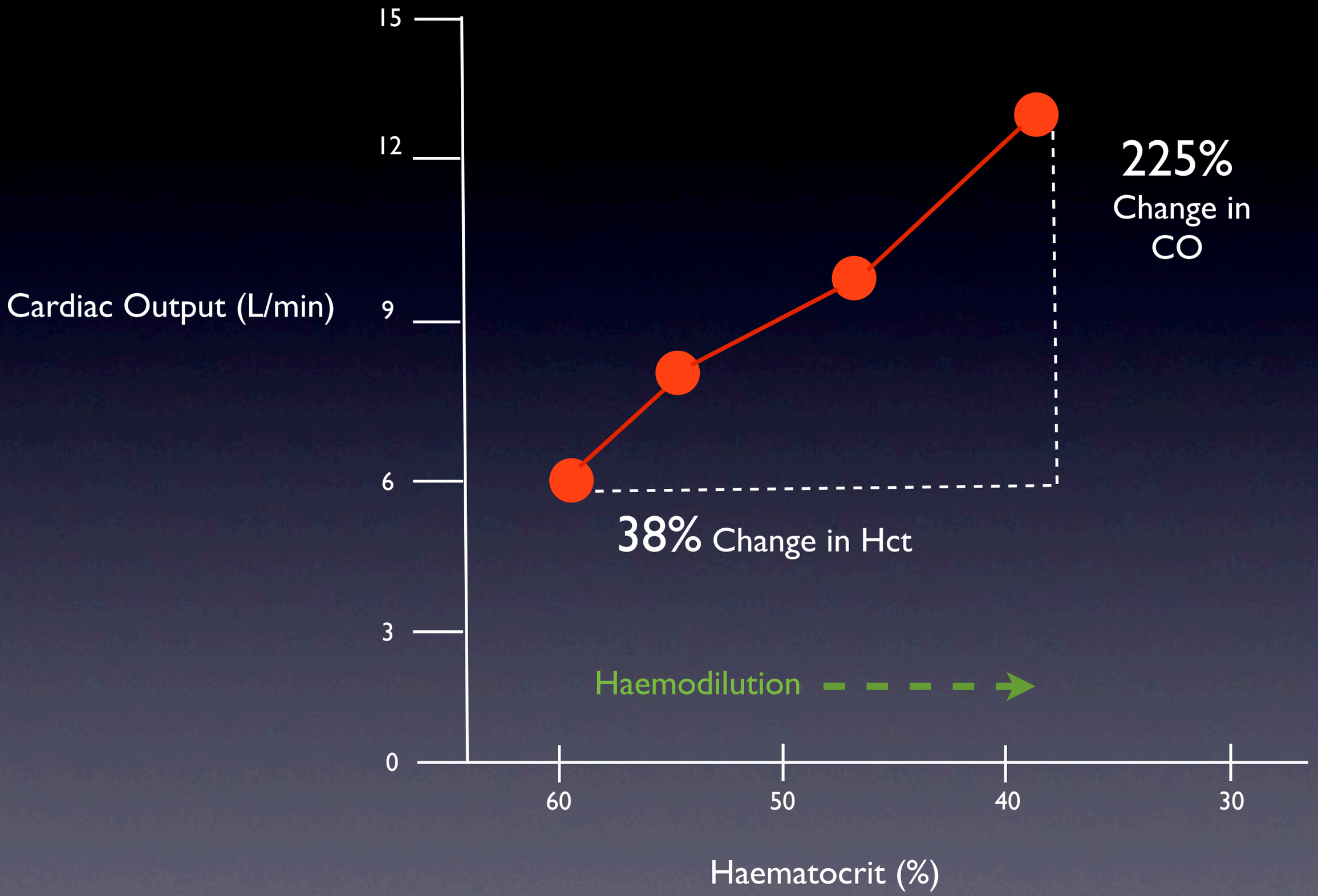
Daniel Ullyot, M.D.
Past President American College of Cardiology

Just how important is Hb for O2 transport ?

With anaemia, V02 remains constant because of compensatory increase in:

- **cardiac output**
- peripheral **02 extraction**

Drop in Hb is compensated for by an increase in cardiac output .....think of Ketchup!

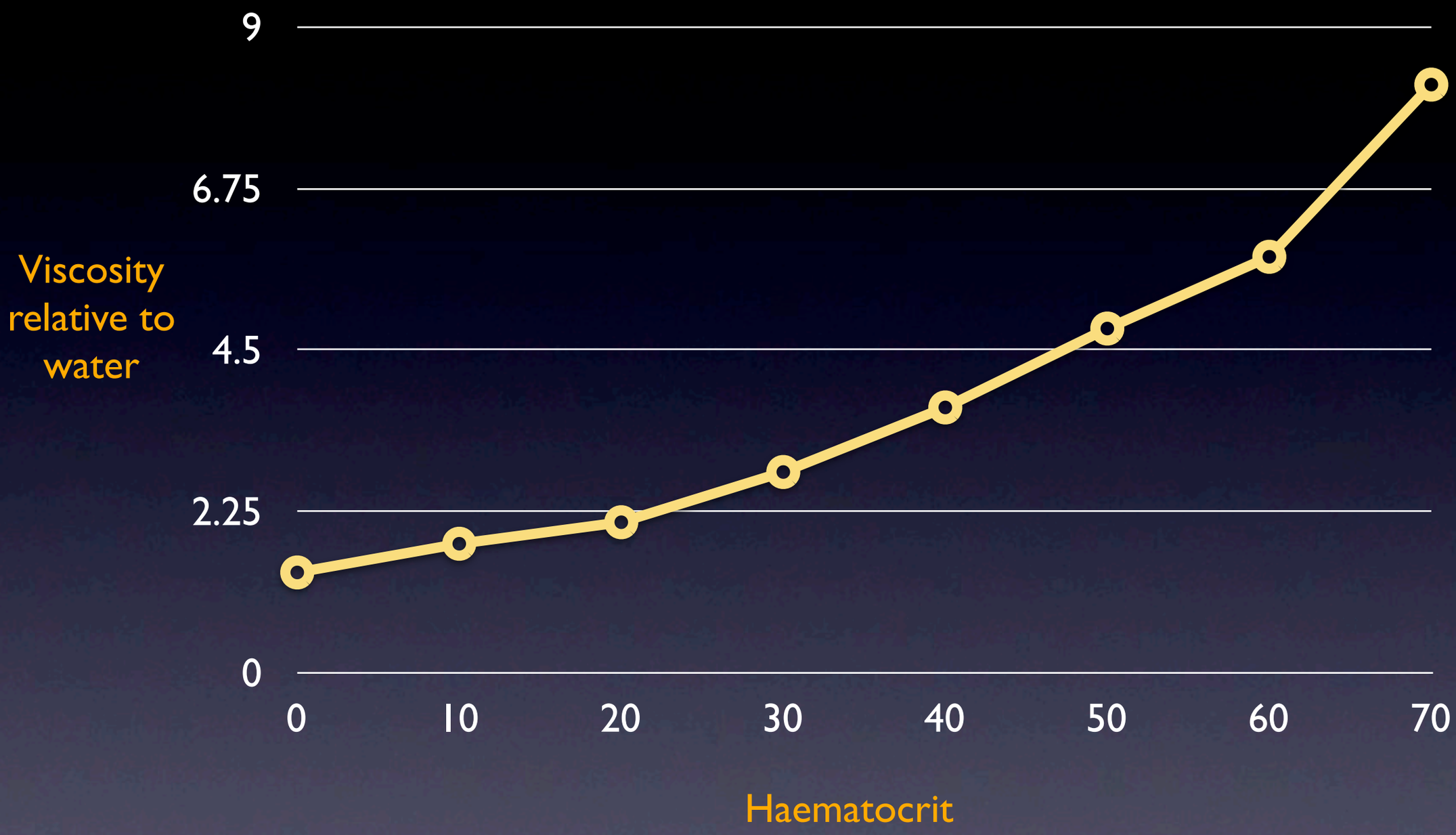


Surg Gynecol Obstet; 1980, 150:139

Why is this so? .....because of **shear thinning**

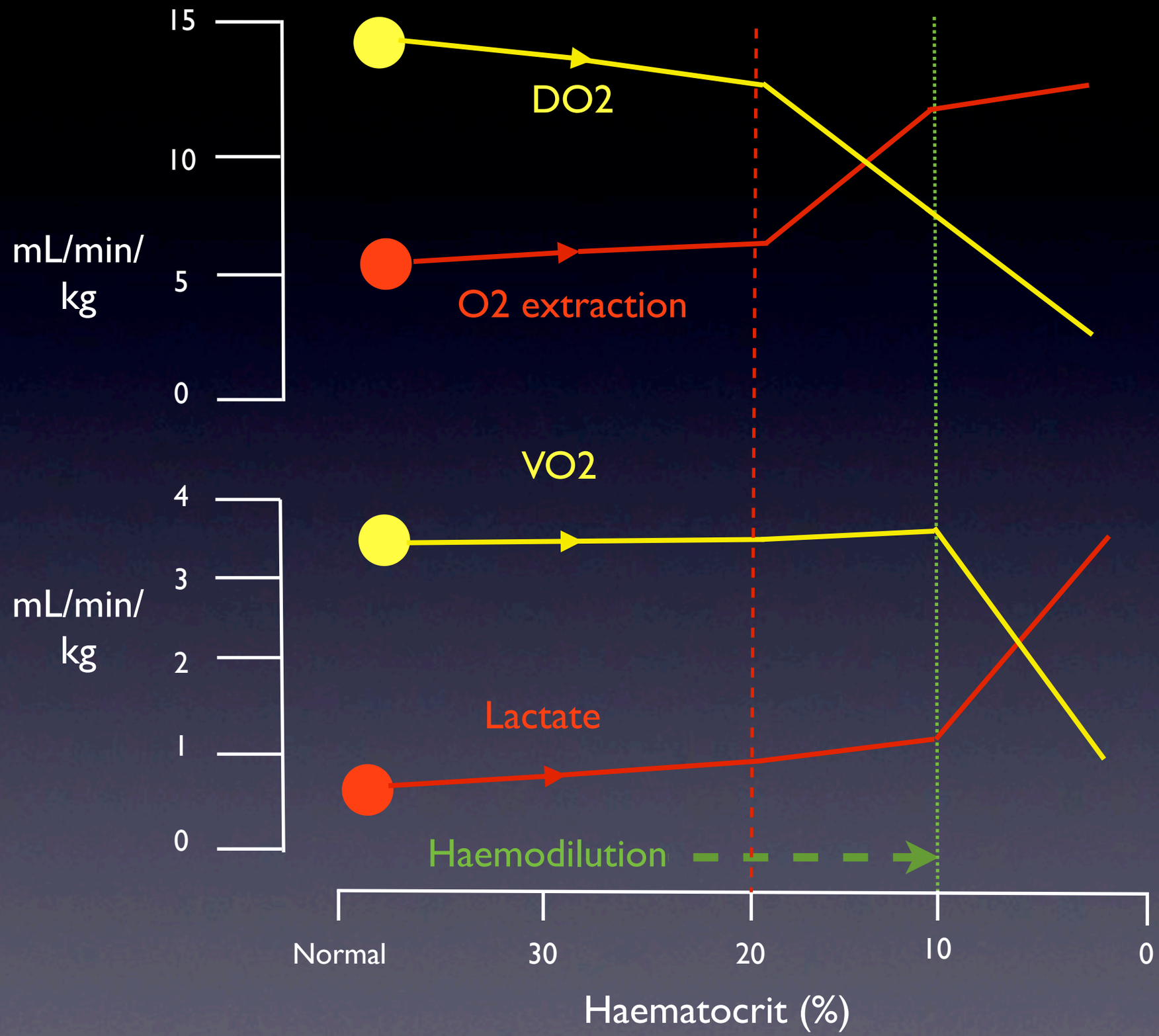
- In a Newtonian fluid, the **viscosity** is **constant** (ex. water).
- **Blood** is a **non-Newtonian** fluid (ex. ketchup, shampoo, non-drip paint, etc)
- Viscosity ("gooiness") varies **inversely** with a change in flow
- Important because the velocity of flow will increase in small vessels --> lowering of viscosity
- Haematocrit is the **most important factor** determining blood viscosity.

Blood viscosity as a function of Hct



Documenta Geigy Scientific Tables. 7th Ed. Basel:Documenta Geigy, 1966:557-558

Influence of anaemia on VO2



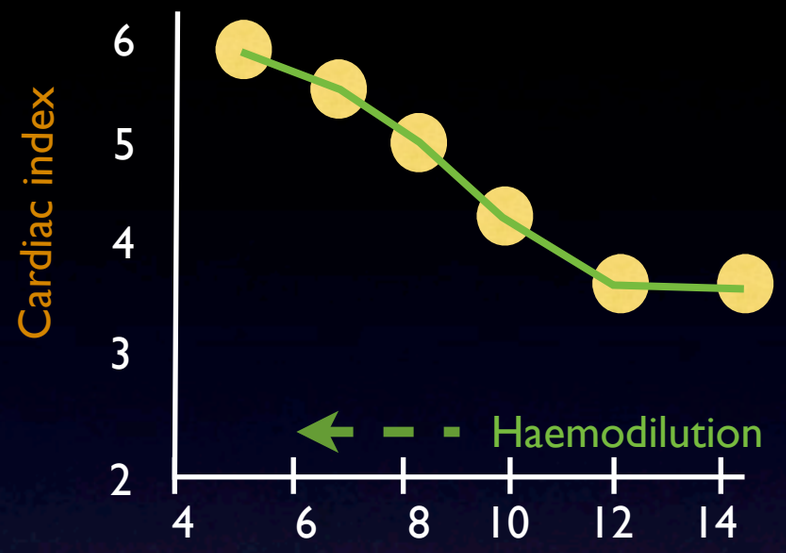
J Surg Res 1987; 42 : 629-634

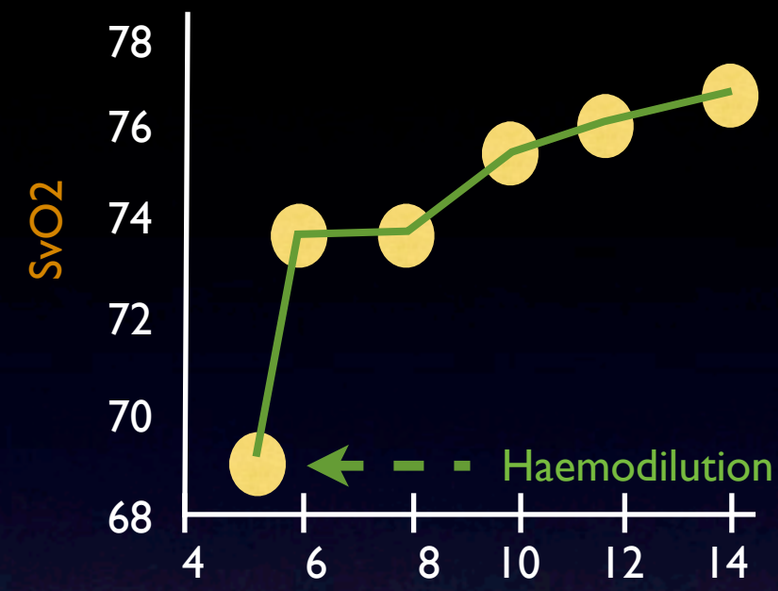
So how low can you go?

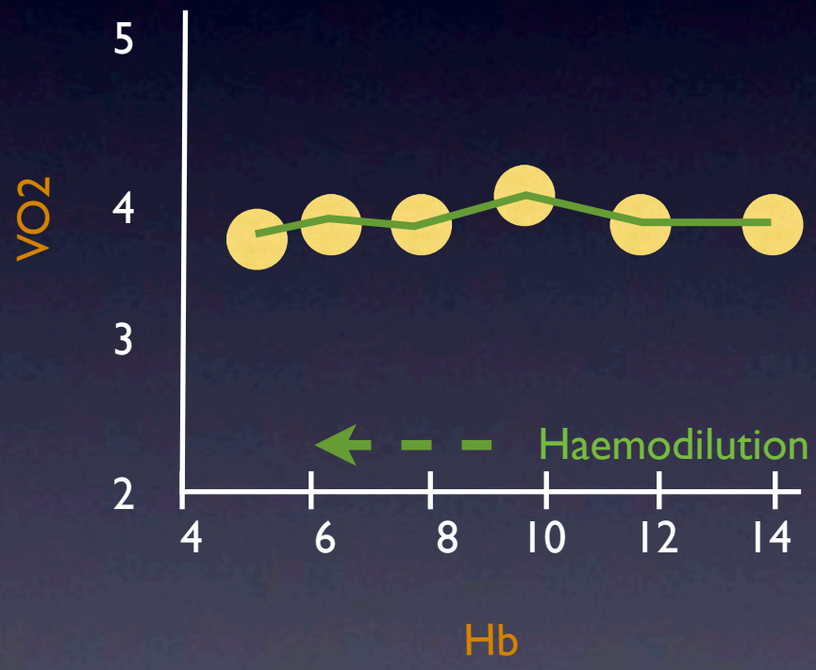
- 32 healthy patients haemodiluted to 5 Hb g/L
- Measured CV parameters, ECG, arterial, and mixed venous O2 content, oxyHb saturation and blood lactate.
- "Critical" oxygen delivery (DO2) was assessed by VO2, blood lactate and ST segment changes on ECG

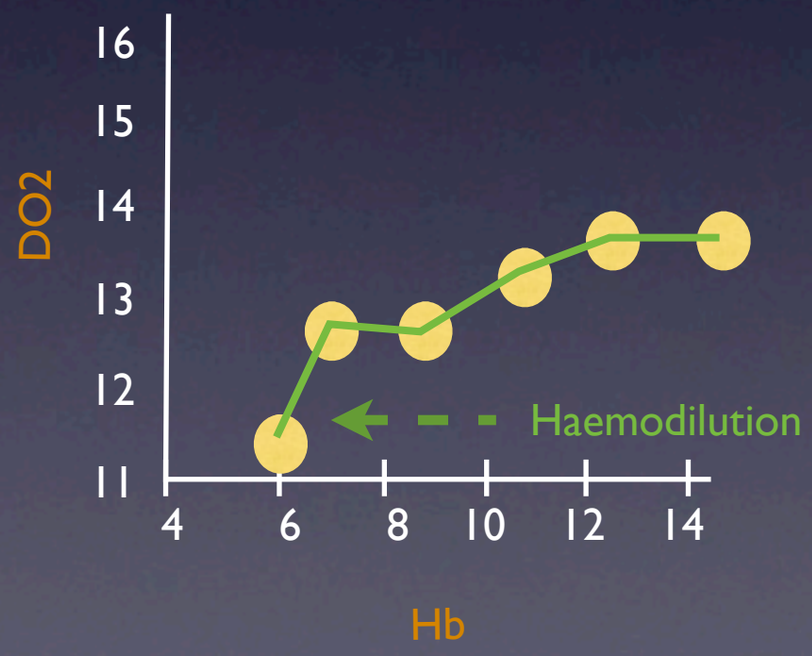
JAMA. 1998;279(3):217-221

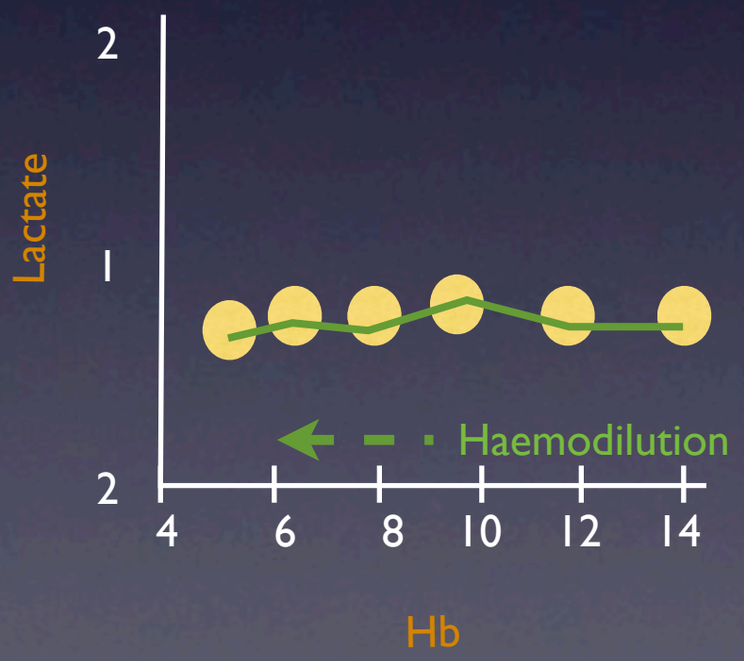
So how low can you go?











JAMA. 1998;279(3):217-221

So how low can you go?

- With a Hb of **5** gm/dL :
  - Decreased SVR and oxygen delivery
  - Increased HR, stroke volume, cardiac output and O2 extraction
- No evidence of inadequate oxygenation
  - VO2 did not change
  - Blood lactate did not change
  - No significant change in ST segment

JAMA. 1998;279(3):217-221

Pushing it to the limit !

Recent case report

<u>Normovolaemic</u> patient with a Hb of **<u>0.7 gm/dL</u>** !!!

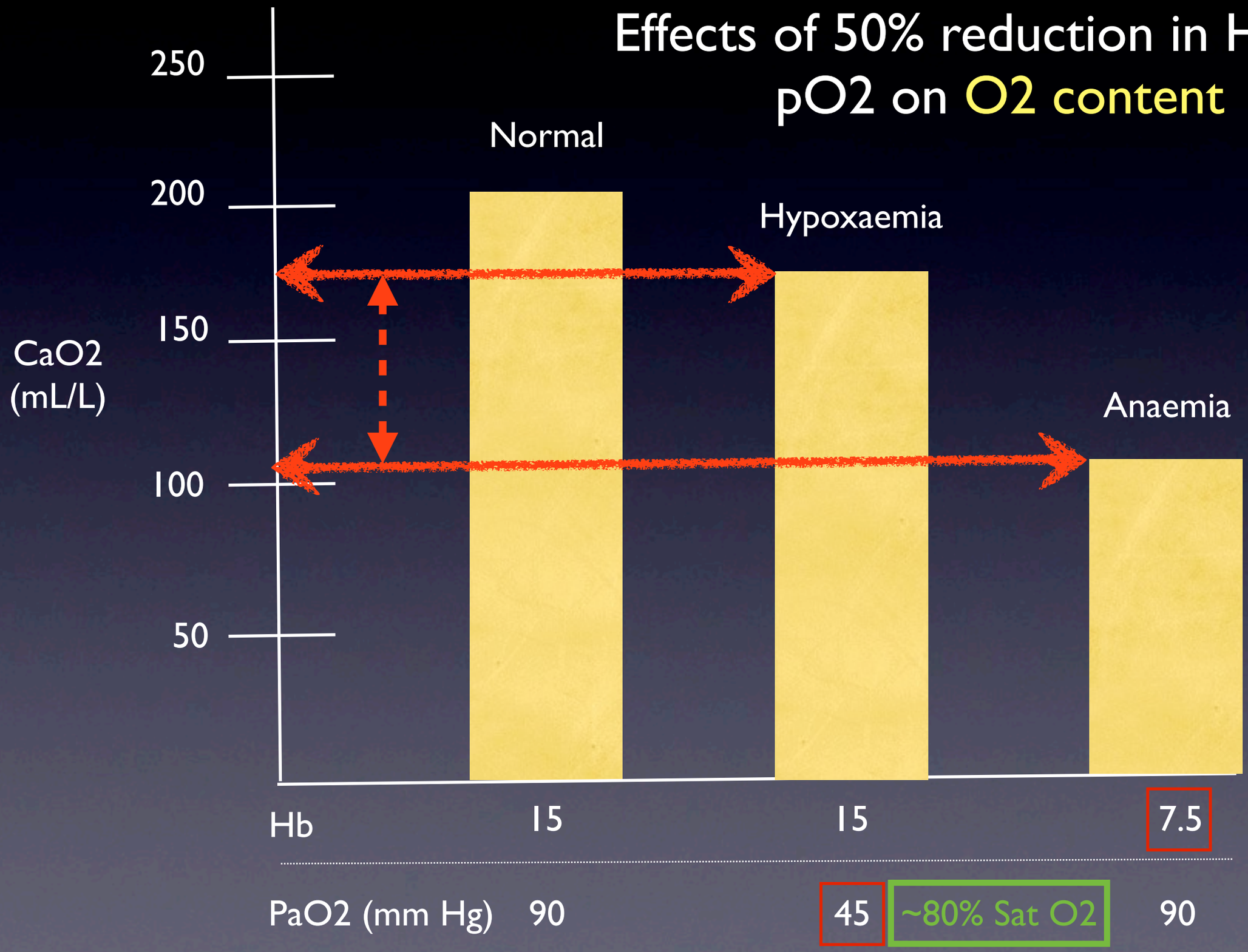
NB. breathing 100 % 02 (dissolved 02 ~ 3gm Hb/dL)

Anesthesia-Analgesia November 2010 • Volume 111 • Number 5

How does anaemia influence O2 content compared with hypoxaemia ?

Hct or O2 Saturation ?

Effects of 50% reduction in Hb and pO2 on O2 content



When do you transfuse?

- 1942 - Transfused when < 10 Hb g/L
- 1999 - Hébert showed that Hb 7 g/L was safe in ICU patients (? if unstable angina)
- But is this logical?

THE Sun

EXCLUSIVE

Jehovah dad 'died' in hospital

By NICK PARKER

Published: 07 Jun 2008

THE horrifically-injured Jehovah's Witness being denied a life-saving blood transfusion technically died in hospital, it was revealed last night.

John , 57, had to be resuscitated by medics when his heart stopped after he was mown down at 60mph by a suspected drunk driver.

But his wife Sheila, who is also a Witness, was last night **STILL** refusing to allow doctors to give him blood because it is banned by their faith.

The Sun told yesterday how the family is in turmoil, because the couple's two sons do not share their beliefs.

Family turmoil ... The Sun story

Sources revealed yesterday that John, of Southall, West London, lost half his blood and may lose his mangled left arm – if he survives at all.

He has internal injuries but surgeons cannot operate because he would need replacement blood.

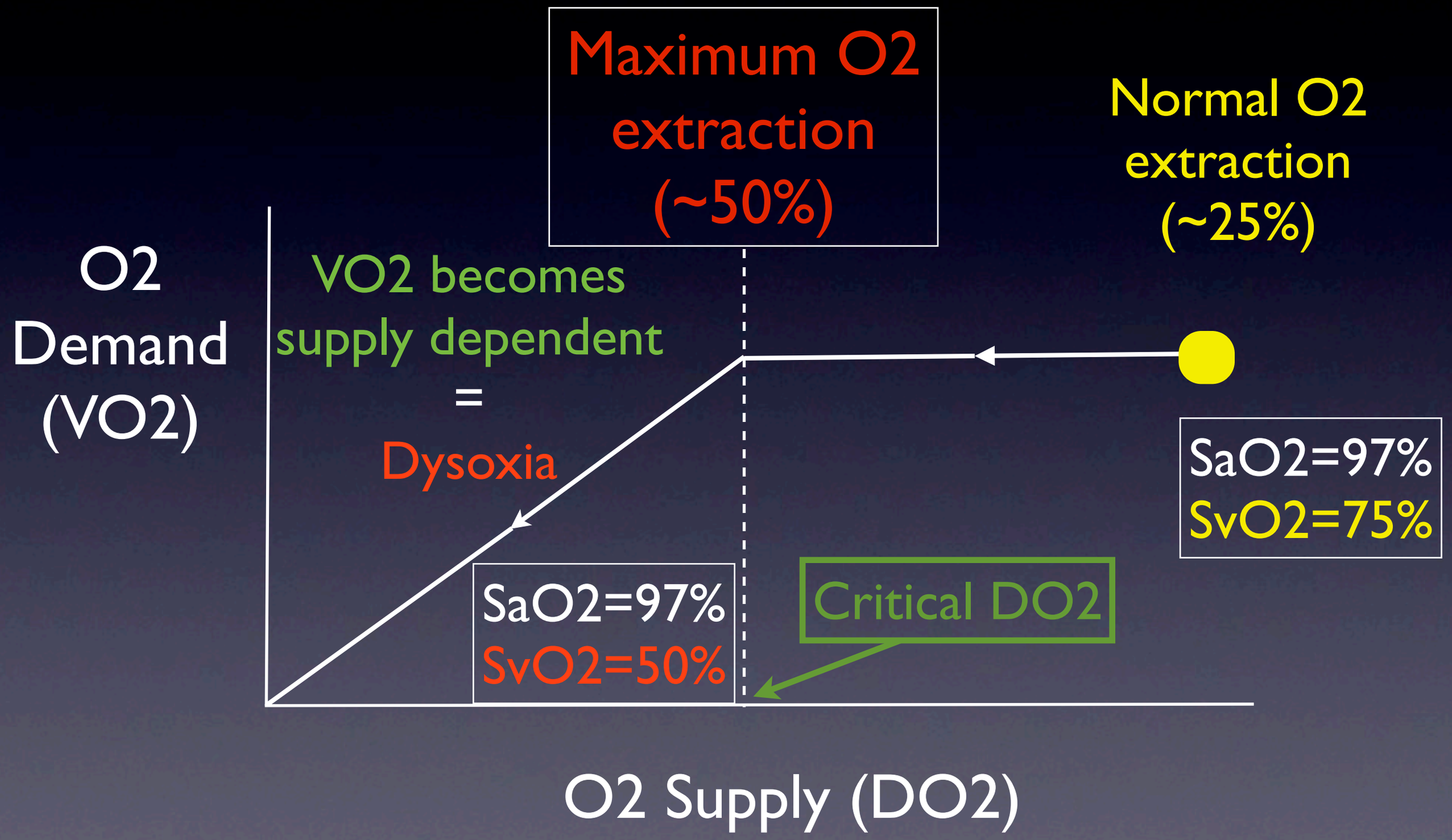
Sons Jonathan, 36, and Tom, 29, are respecting their mother's wishes.

They joined her in a heartbreaking vigil at council worker John's bedside at Ealing Hospital, West London.

Compensation - 2 Phases

- Phase 1 - The *"Big 3"* compensate each other
  - Cardiac Output
  - Hb
  - O2 Saturation
- Phase 2 - *Oxygen Extraction*
  - If O2 delivery decreases, O2 extraction increases

So, <u>Oxygen extraction</u> may be a more logical transfusion trigger ?

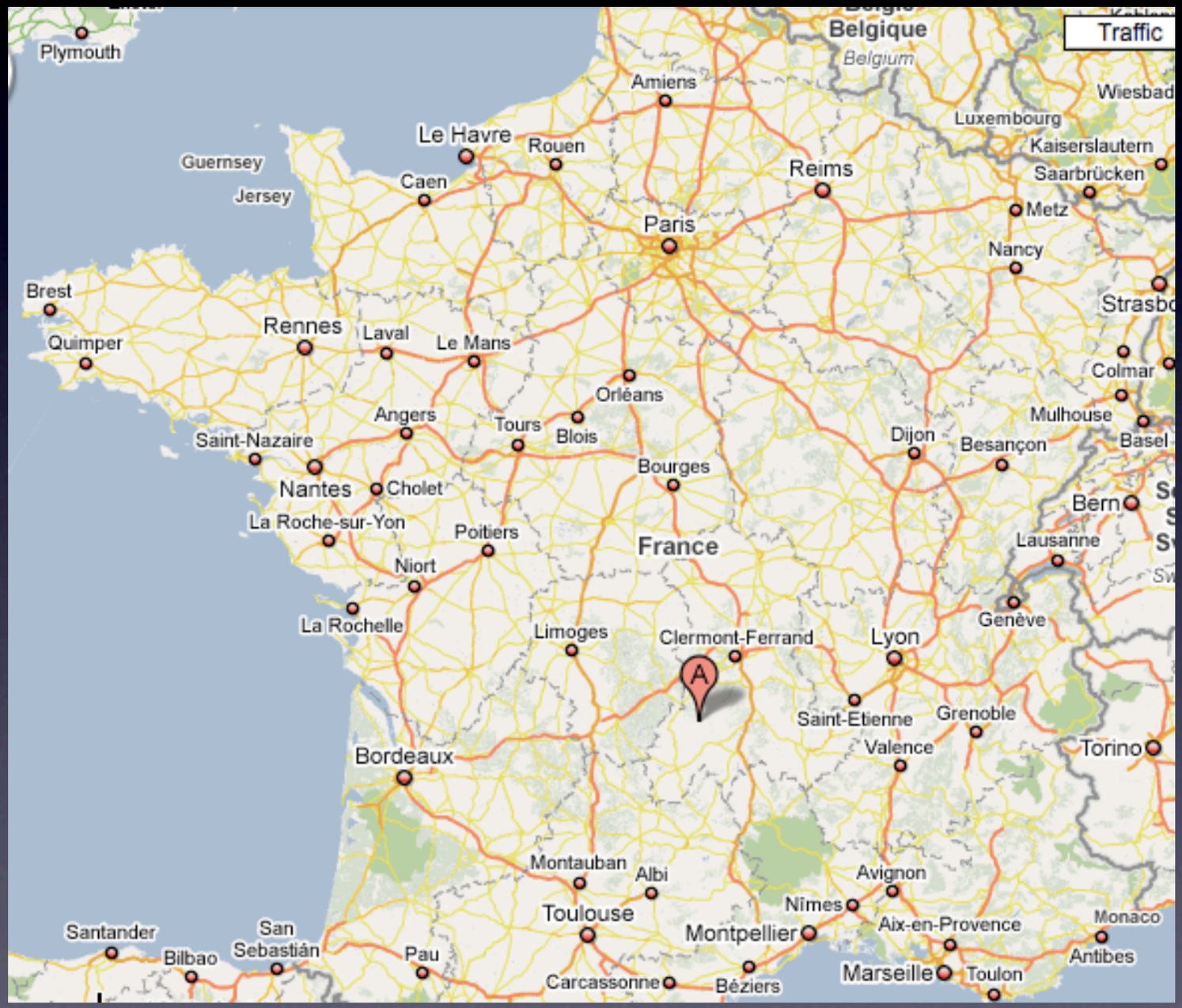


When someone bleeds,
blood improves tissue oxygenation.....
right?

Maybe...

- Hb - the Transporter
- Hb - the Flow Regulator

Level I Trauma in the Massif Central



Clinical Case

- RTA
- 50 yr old something male
- Positive peritoneal lavage
- Multiple severe, abdominal injuries
- 19 units of <u>fresh</u>, whole blood in glass bottles !

Produced a warm, well perfused patient!

The Use of Fresh Whole Blood in Massive Transfusion

- 1667 - Dr J.B. Denis transfused warm, whole lamb's blood, the "gentleness" would cure patient's maddening illness
- 1914 (WWI)-citrate storage allowed blood collection

Nothing mentioned about RBCs ability to deliver O2 to microvascular tissue beds!

- WWII - Stored whole blood was primarily used
- >1945-1980's - Logistics of sending massive quantities of blood to troops led to fractionation
- Current licensing requirements for stored RBCs same as in 1940's ....i.e., require 70% of transfused RBC membranes to be intact at 24 hrs...that's it!

J Trauma. 2006;60:S59–S69.

The Use of Fresh Whole Blood in Massive Transfusion

"There is, in the military surgical community, a strong perception that **fresh whole** blood is a better resuscitation product for the severely injured patient than component products."

"studies of stored RBCs that directly measure oxygen consumption for subjects in oxygen debt or shock or evaluate microvascular circulation indicate that oxygen consumption and **microvascular flow** remains the same or **decreases** after RBC transfusion"

But Why ?

J Trauma. 2006;60:S59 –S69

Could it be....

1 Unit RBCs
1 Unit Platelets
1 Unit FFP

660 mL plasma
Hct 29%
88,000 platelets
65% coagulation factor activity

Vs.

1 Unit **fresh**, whole blood

500 mL plasma
Hct 45%
150-350,000 platelets
86% coagulation factor activity

OR....

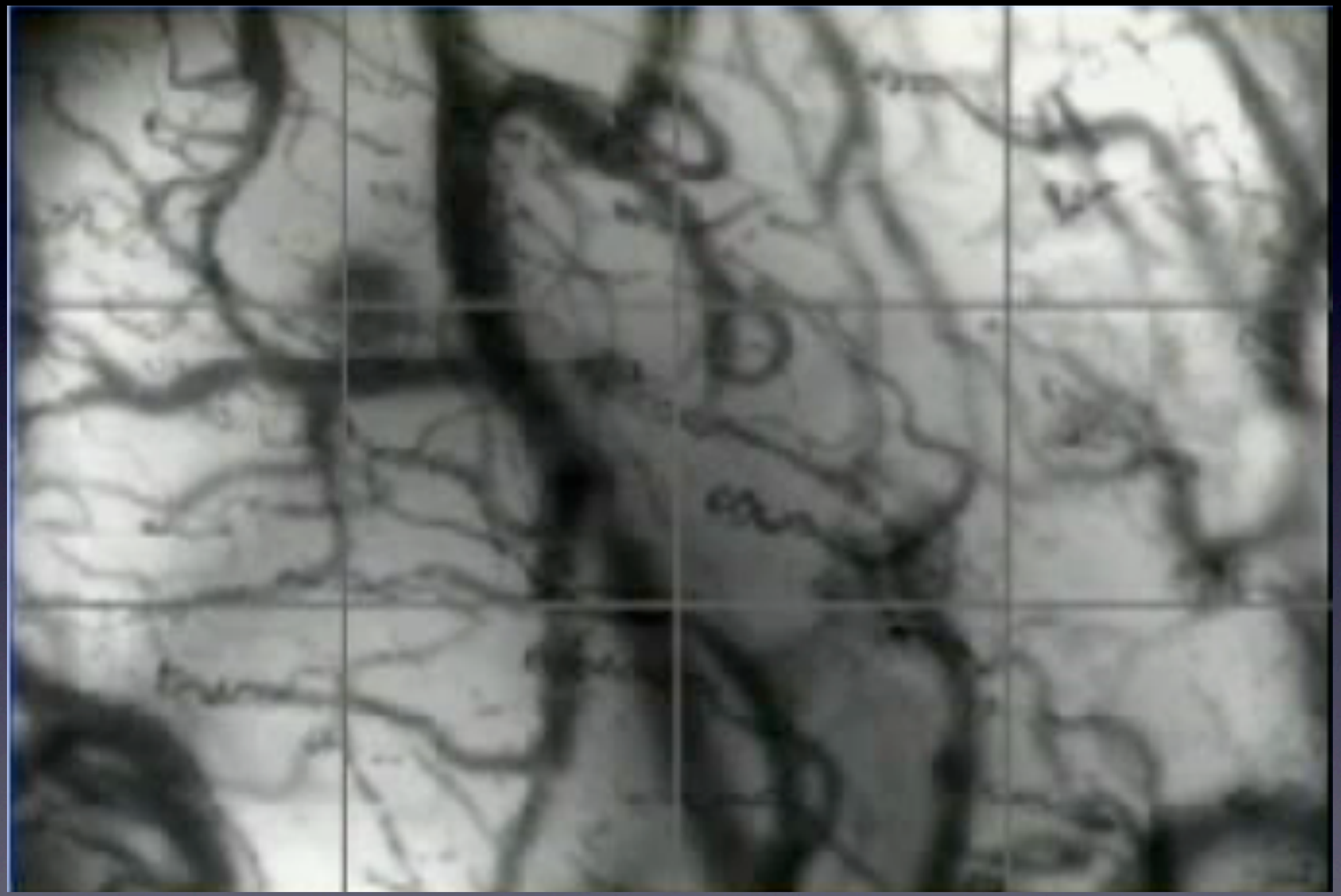
J Trauma. 2006;60:S59 –S69

Or, could it be....something else ?

- Visualise micro-vasculature with SDF spectroscopy

Vox Sang. 2007 Jul;93(1):12-8

Normal microcirculation viewed by SDF spectroscopy



Or, could it be....something else ?

- Visualise micro-vasculature with SDF spectroscopy
- Severe anaemia - Hb 4-5
- Microcirculation wide open - reasonable tissue pO2
- Transfused with banked blood to Hb 9.0

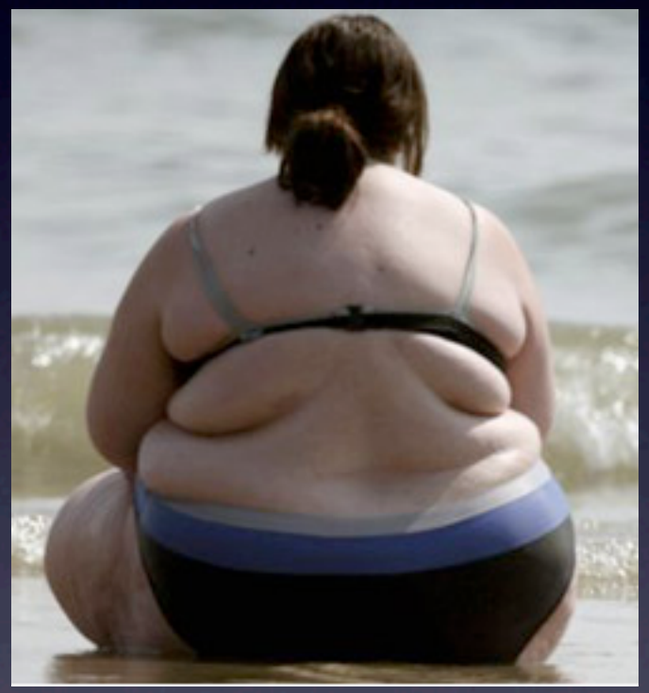
- Global hemodynamic indices .... better
- Microcirculation .....**worse**, with central shunting
- Drop in tissue pO2 !

Vox Sang. 2007 Jul;93(1):12-8

So what's going on....?

We store fuel, so if 02 is so vital, why do we not have oxygen stores?

What does a car manufacturer have to do with all this?



TOYOTA

Because...

...02 is toxic !

So **limiting** O2 concentration in the vicinity of cells may be protective!

BMJ

Effect of high flow oxygen on mortality in chronic obstructive pulmonary disease patients in prehospital setting: randomised controlled trial

BMJ 2010;341:c5462 doi:10.1136/bmj.c5462

Stroke

Should Stroke Victims Routinely Receive Supplemental Oxygen?

Stroke. 1999;30:2033-2037

THE LANCET

Oxygen therapy for acute myocardial infarction.

Cochrane Database Syst Rev. 2010 Jun 16;(6):CD007160.

Resuscitation of newborn infants: from oxygen to room air

The Lancet, Early Online Publication, 20 July 2010

JAMA®

Association Between Arterial Hyperoxia Following Resuscitation From Cardiac Arrest and In-Hospital Mortality

Vol. 303 No. 21, June 2, 2010

The bodies version of Toyota's "just in time" method?

- O2 is v. toxic to tissues
- Hb is the main local **controller** of O2

1. OxyHb curve
   - "controls local delivery" - amount of O2 released at "hot, acid" tissues
2. Hb controls **flow** of micro-circulation "**coupling**" it to metabolic needs

Red blood cells are the O2 sensors and controllers

- Fresh blood increases functional capillary density
- Stored blood decreased functional capillary density and tissue oxygenation

RBCs physiological role is to carefully match regional flow to metabolic demand

Surgery , Volume 141 , Issue 5 , Pages 630 - 639, May 2007

RBCs carefully match regional flow to metabolic demand .... but how?

Only recently discovered !

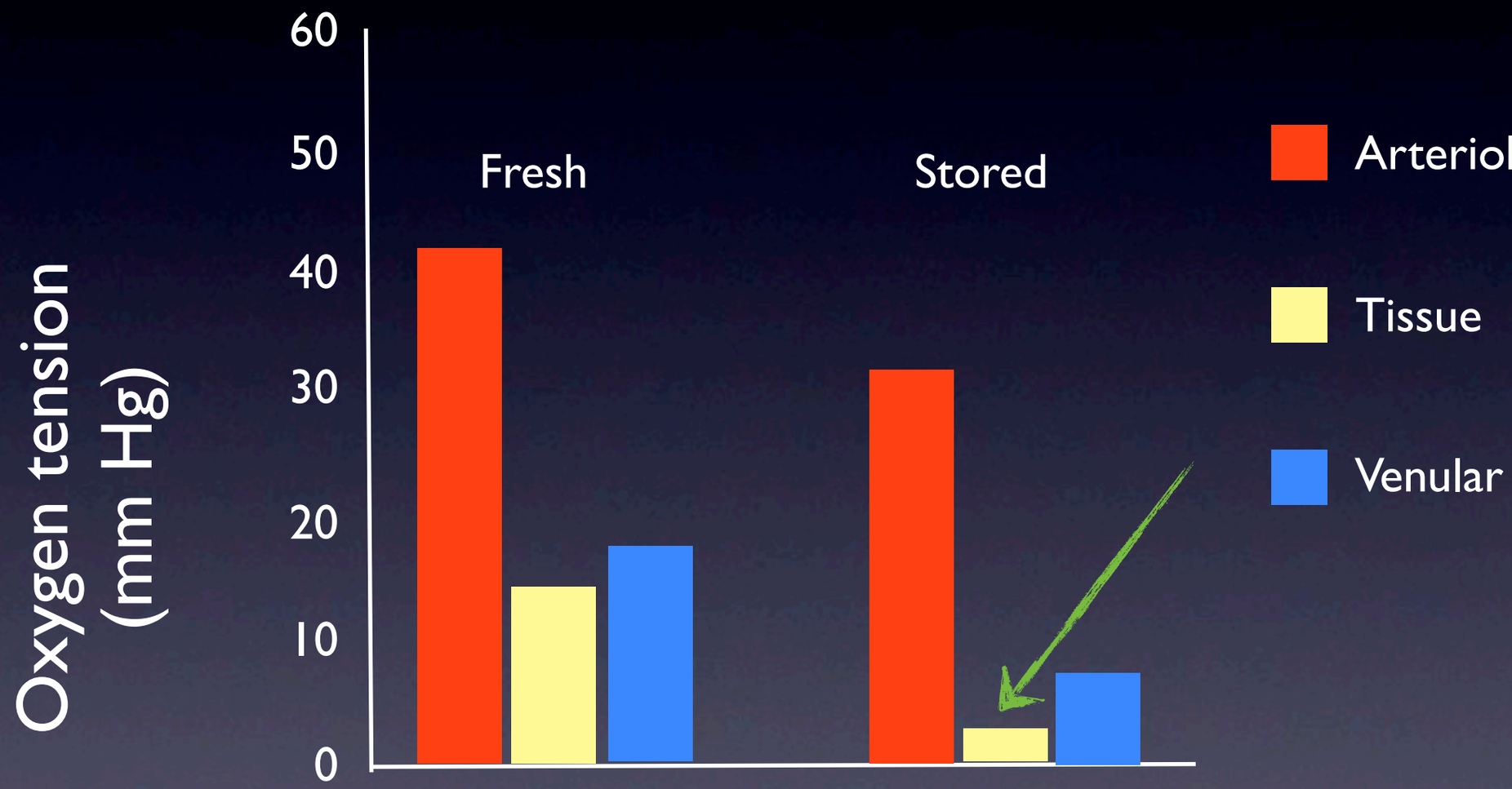
SNO-Hb - formed in RBC in proportion to

local hypoxia ⇢ local vasodilation

Surgery , Volume 141 , Issue 5 , Pages 630 - 639 May 2007

So how good are stored RBCs at delivering oxygen to the tissues?

MICROVASCULAR PERFUSION WITH STORED RBCs



Evolution of adverse changes in stored RBCs

- Storage increases O2 affinity by decreases in 2,3, DPG altering O2 content release at tissues
- But O2 delivery is deficient before decline in 2,3, DPG
- Storage effects RBC's O2-dependent **vasoregulatory function**
- **SNO-Hb** is the vasodilator through which desaturated Hb-O2 is **coupled** to regional increases in blood flow

PNAS , October 23, 2007 ; vol. 104 ; no. 43

Evolution of adverse changes in stored RBCs - S-nitrosohemoglobin (SNO) deficiency

- 500 ml blood drawn and stored from 15 healthy volunteers
- RBC SNO-Hb decreased rapidly by **3 hrs**
- In parallel, vasodilation by stored RBCs was depressed

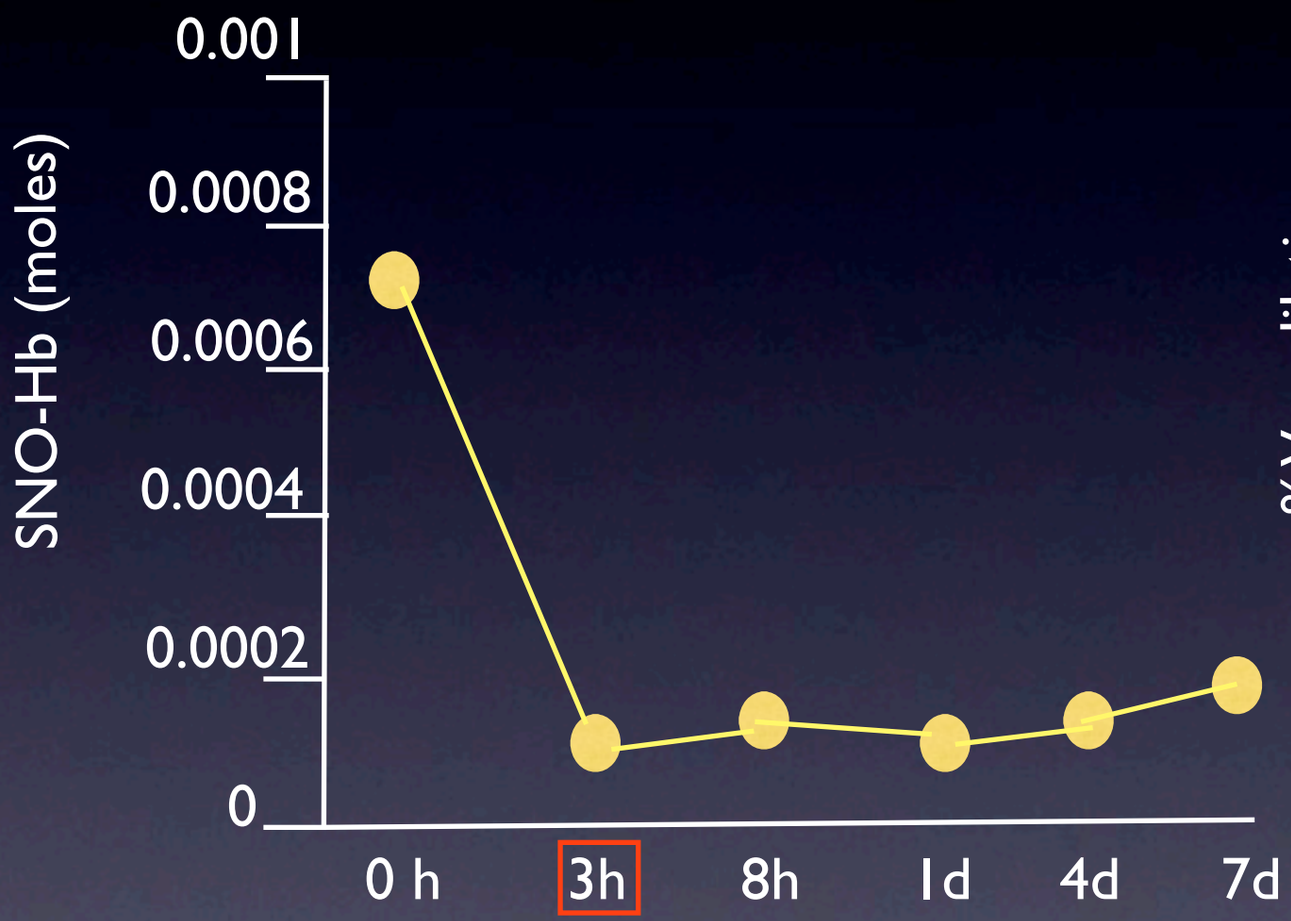
PNAS , October 23, 2007 ; vol. 104 ; no. 43

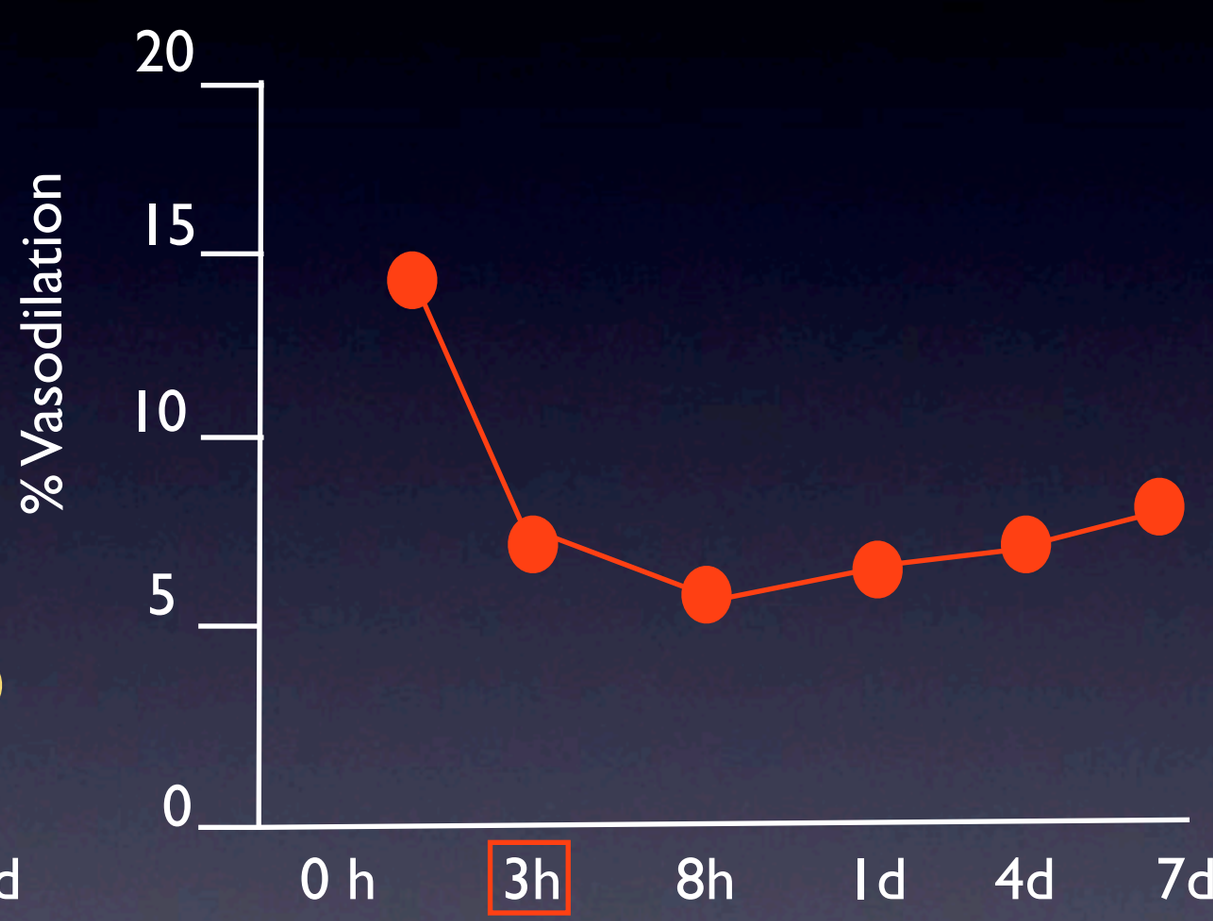
Evolution of adverse changes in stored RBCs
- Other “classical” causes

Also, slow and progressive (over 42 days) :

- ❖Decrease in deformability of RBCs
- ❖Decrease 2,3 DPG ⇢ decreased O2 release at tissues

Evolution of adverse changes in stored RBCs
- S-nitrosohemoglobin (SNO) deficiency

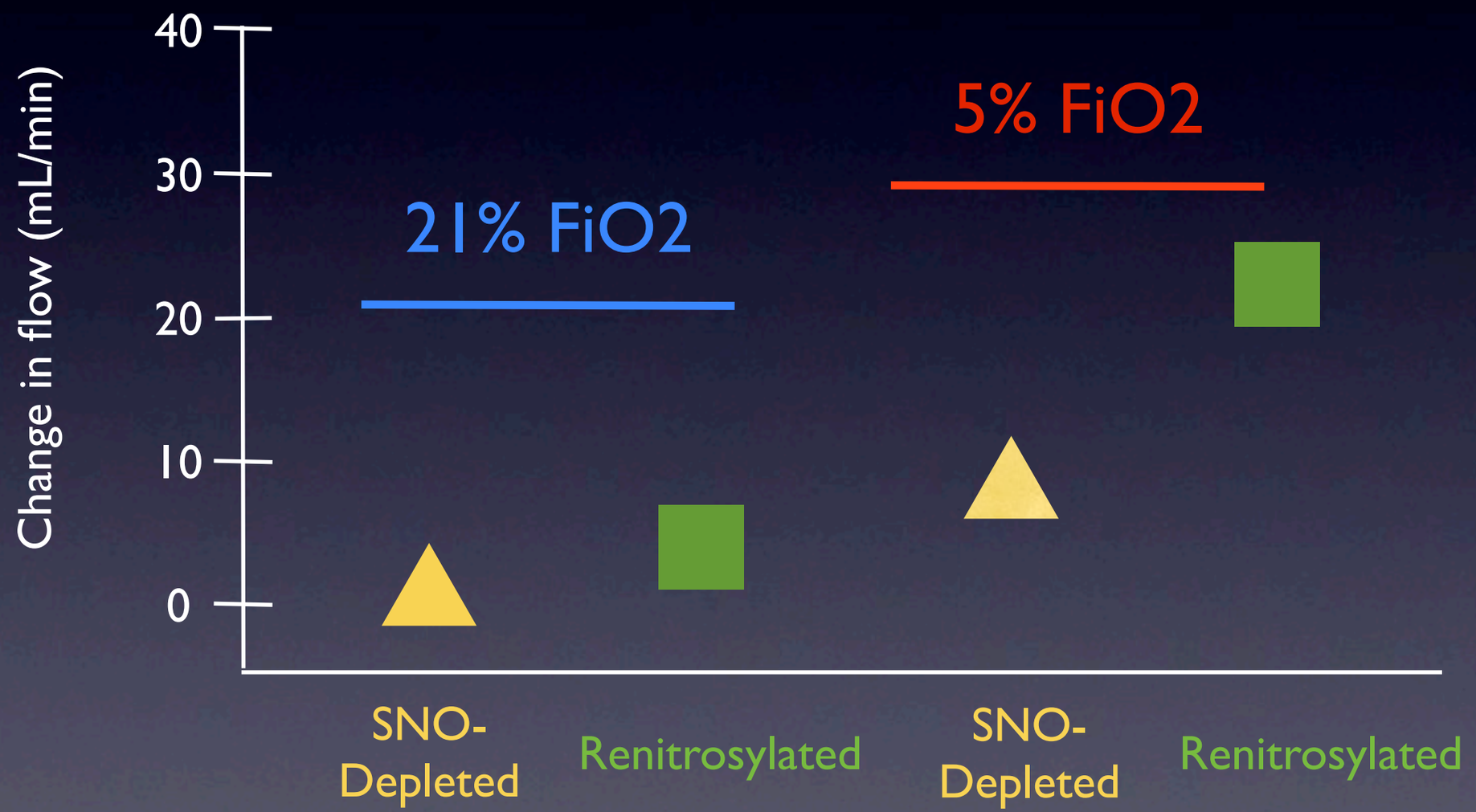




PNAS , October 23, 2007 ; vol. 104 ; no. 43

The future of transfusion?

Changes in canine coronary artery blood flow



Proceedings of National Academy Science; Oct 23, 2007; vol 104, No 43

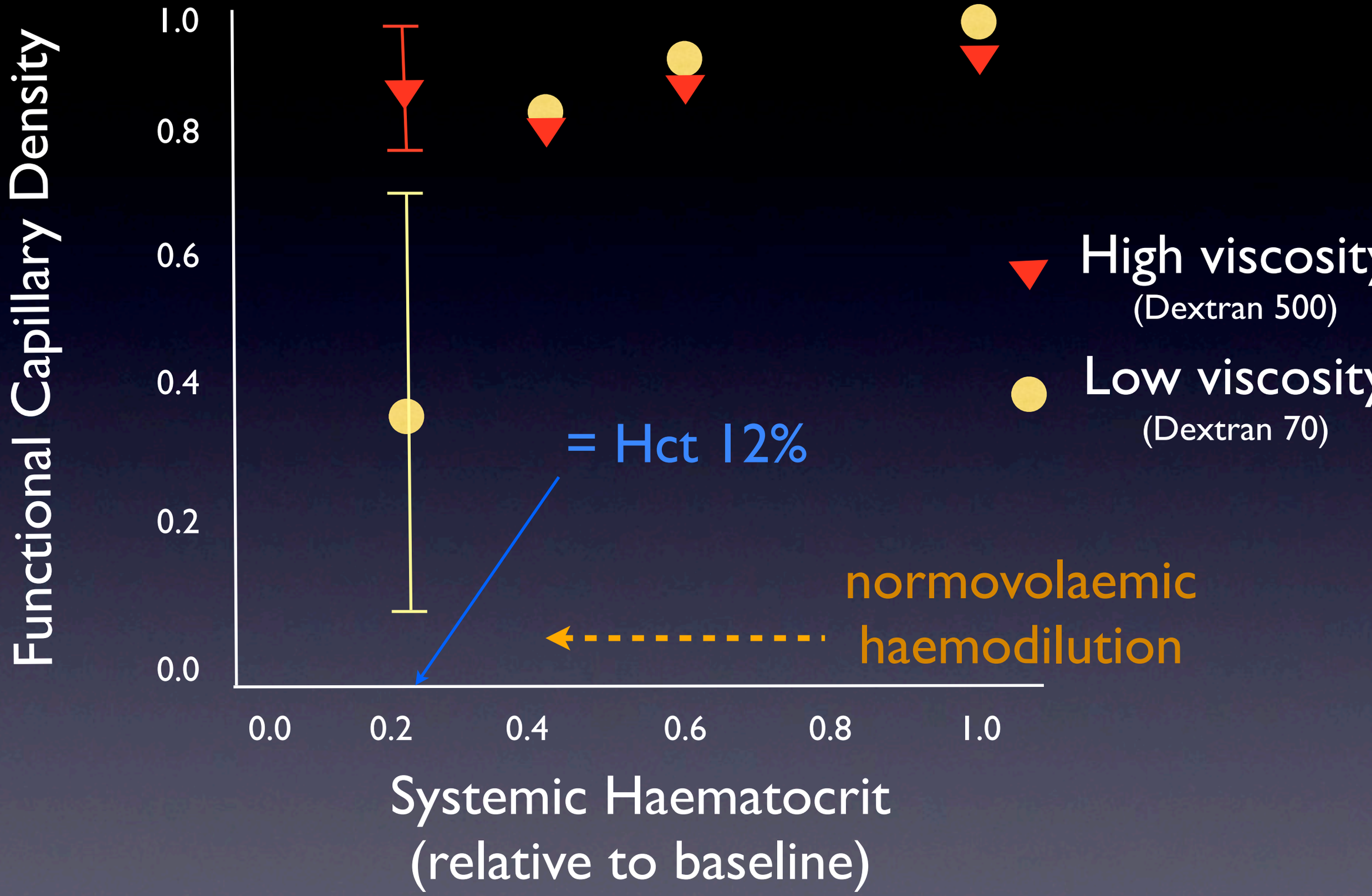
RBCs carefully match <u>regional flow</u> to metabolic demand .

Also by :

- ❖**<u>Viscosity</u>** increases shear stress ⇢ "viscous drag"

⇢ triggering mechanoreceptors and releasing endothelial NO/prostacyclin

Viscosity helps keeps the capillaries open!



275:2170-2180, 1998. *Am J Physiol Heart Circ Physiol*

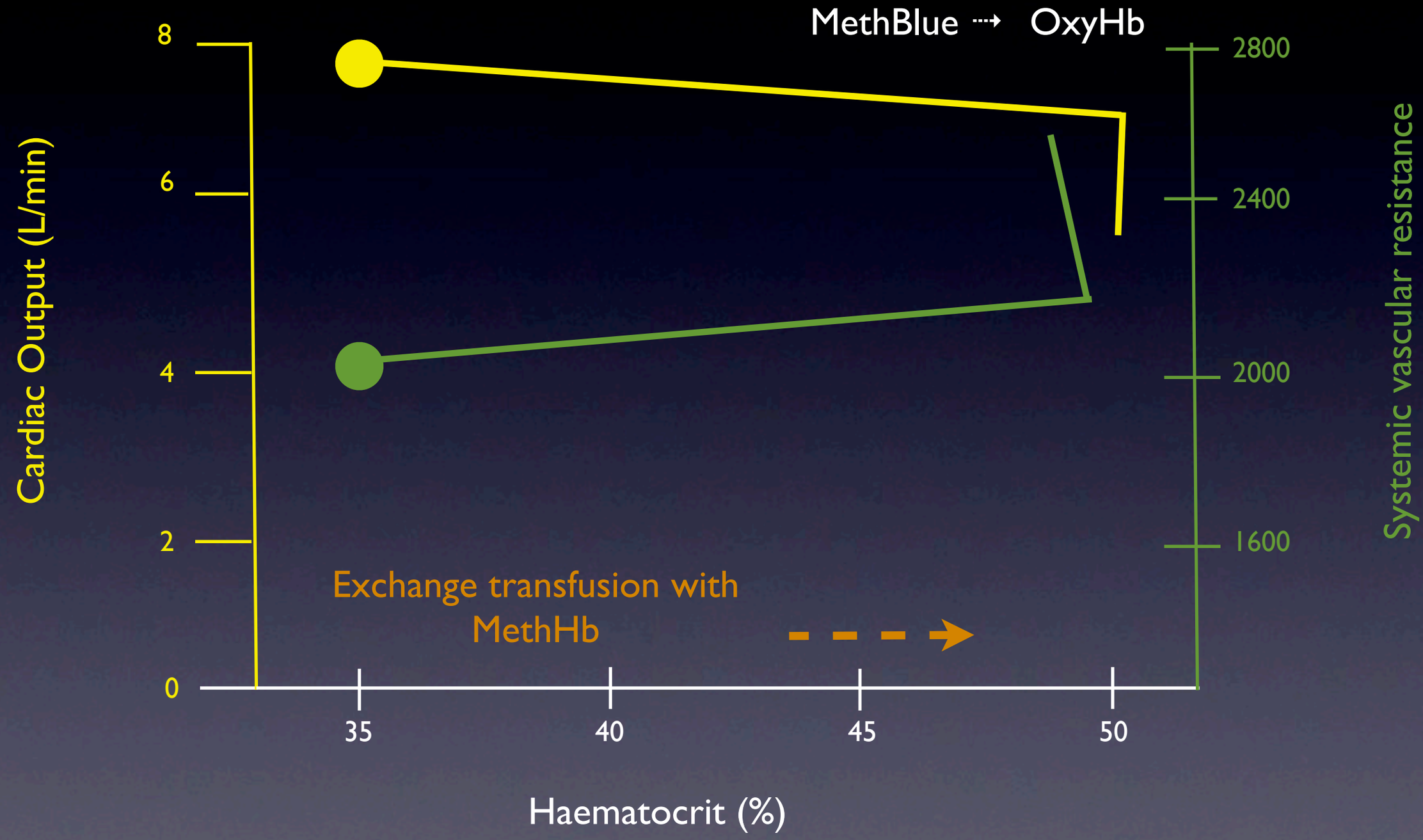
What's most important in flow control, viscosity or O2 content ?

- Dogs underwent exchange transfusion with methHb, with an increase in Hct and viscosity
- No fall in exercise C.O. nor rise in TPR
- Methylene blue administered converting metHb to oxyHb, thus increasing O2 content with no change in Hct nor viscosity
- Significant decrease in exercise C.O. and TPR.

"Thus, in this hematocrit range, systemic vascular resistance and cardiac output are actively regulated according to tissue oxygen demand."

Am J Physiol Heart Circ Physiol 289: H1821–H1825, 2005

Viscosity or O2 content ?



Am J Physiol Heart Circ Physiol 289: H1821–H1825, 2005

NO in high places - Tibet

- Tibetans had more than double the forearm blood flow of low-altitude residents
- Tibetans greater than sea level oxygen delivery to tissues
- Tibetans had >10-fold-higher circulating concentrations of bioactive NO products
- These findings shift attention from the traditional focus on pulmonary and hematological systems to vascular factors

Artificial Hb solutions good at carrying O2

BUT

causes vasoconstriction and hypertension

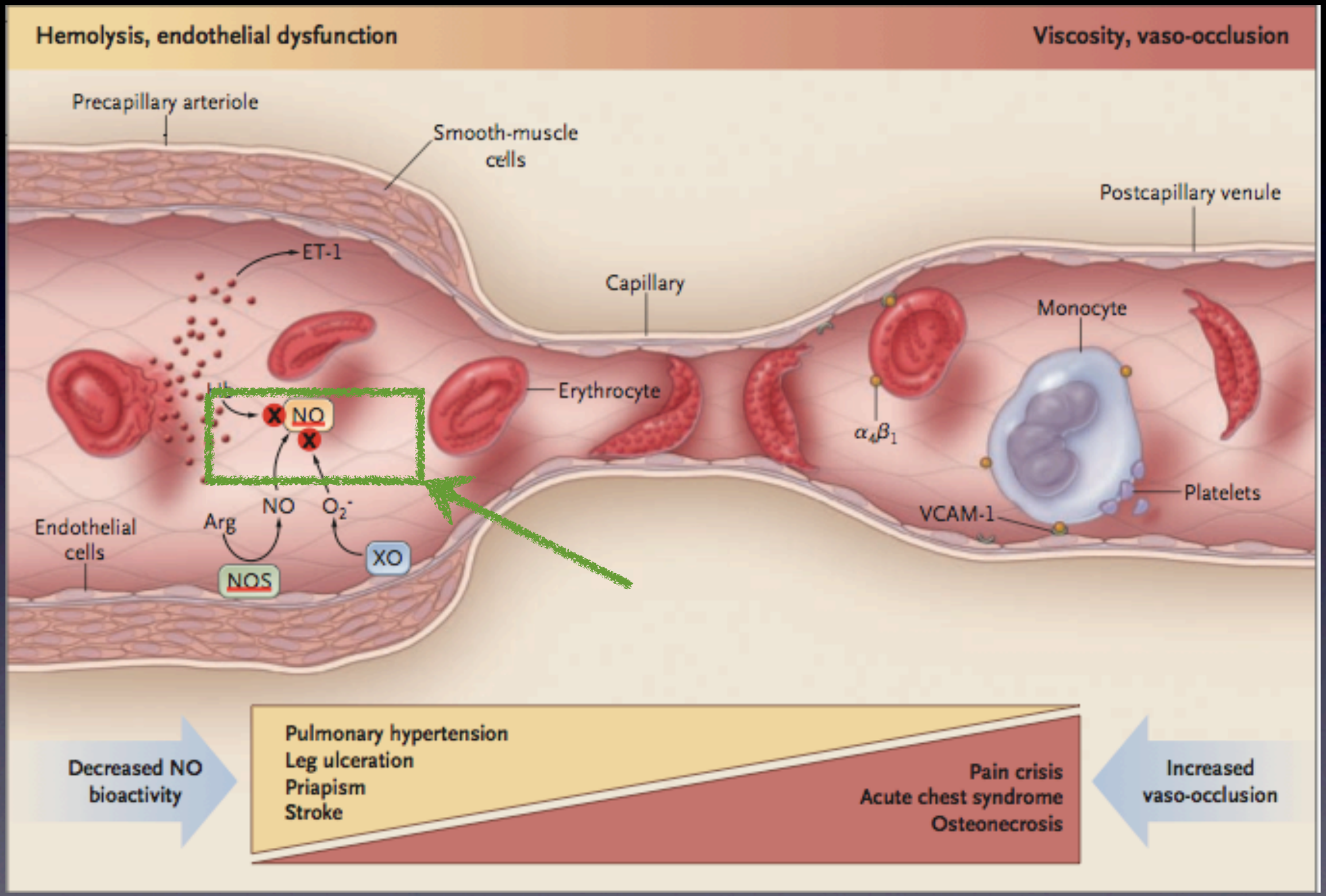
because...

free Hb also “sponges up” NO

If inside the cell it is vital

outside the cell it is toxic!

Haemolysis and effect on NO



N Engl J Med 2008;359:2254-65.

Recap

- Anaemia is well tolerated as long as blood volume is maintained!
- RBC is the hypoxic sensor, coupling local flow to metabolic need
- Improved global parameters do not necessarily mean micro-circulatory improvement

To download this lecture and for further reading:

http://web.me.com/johnvogel2

Questions ?