OXYGEN DELIVERY IN HEALTH AND DISEASE

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MAYO CLINIC COLLEGE OF MEDICINE

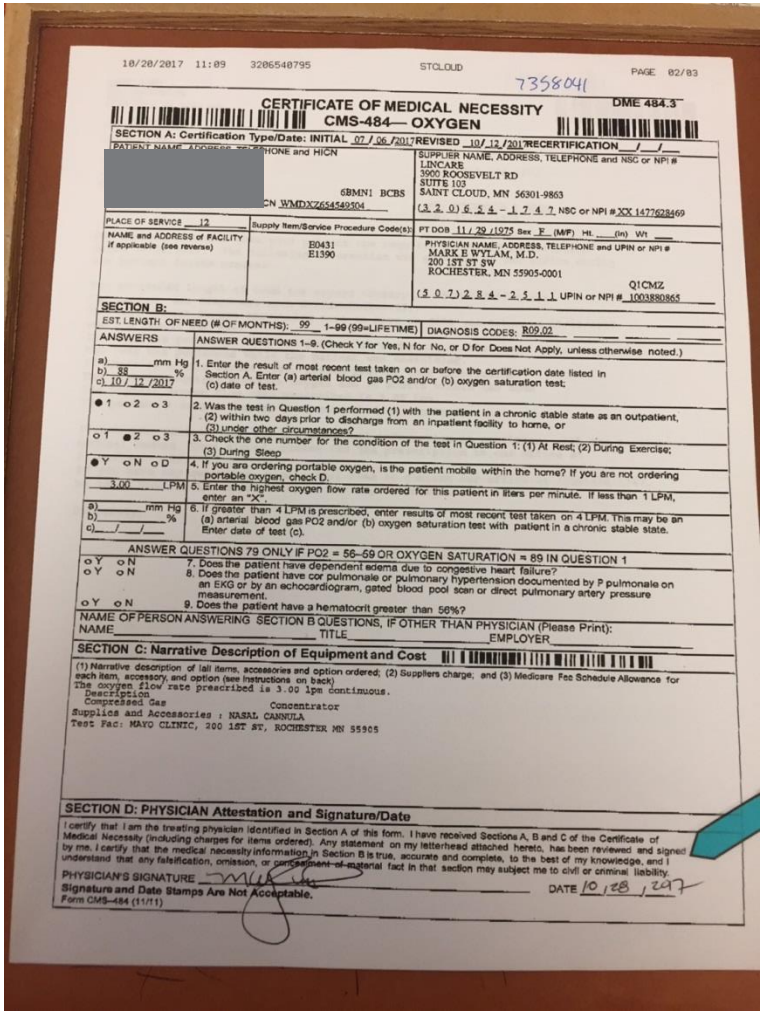
U.S. COST OF O_2 SERVICES

> 1 million people rely on Medicare for home-oxygen therapy.

- 2009 $2.9 billion/yr ($500 billion budget).

- Average cost (2006) $201.20/pt/month, ($55.81 for equipment and $145.39 for services).

WSJ June 16, 2009



10/20/2017 11:09 3206540795 STCLOUD PAGE 02/03

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CERTIFICATE OF MEDICAL NECESSITY DME 484.3
CMS-484— OXYGEN

SECTION A: Certification Type/Date: INITIAL 07/06/2017 REVISED 10/12/2017 RECERTIFICATION __/__/__

PATIENT NAME, ADDRESS, TELEPHONE and HICN
[redacted]
6BMN1 BCBS
CN WMDXZ654549504

SUPPLIER NAME, ADDRESS, TELEPHONE and NSC or NPI #
LINCARE
3900 ROOSEVELT RD
SUITE 103
SAINT CLOUD, MN 56301-9863
(320)654-1747 NSC or NPI # XX 1477628469

PLACE OF SERVICE 12

Supply Item/Service Procedure Code(s):

NAME and ADDRESS of FACILITY if applicable (see reverse)

E0431
E1390

PT DOB 11/29/1975 Sex F (M/F) Ht. ___(in) Wt. ___

PHYSICIAN NAME, ADDRESS, TELEPHONE and UPIN or NPI #
MARK E WYLAM, M.D.
200 1ST ST SW
ROCHESTER, MN 55905-0001
Q1CMZ
(507)284-2511 UPIN or NPI # 1003880865

SECTION B:

EST. LENGTH OF NEED (# OF MONTHS): 99 1–99 (99=LIFETIME) | DIAGNOSIS CODES: R09.02

ANSWERS	ANSWER QUESTIONS 1–9. (Check Y for Yes, N for No, or D for Does Not Apply, unless otherwise noted.)
a)_____mm Hg b) 88 % c) 10/12/2017	1. Enter the result of most recent test taken on or before the certification date listed in Section A. Enter (a) arterial blood gas PO2 and/or (b) oxygen saturation test; (c) date of test.
●1 ○2 ○3	2. Was the test in Question 1 performed (1) with the patient in a chronic stable state as an outpatient, (2) within two days prior to discharge from an inpatient facility to home, or (3) under other circumstances?
○1 ●2 ○3	3. Check the one number for the condition of the test in Question 1: (1) At Rest; (2) During Exercise; (3) During Sleep
●Y ○N ○D	4. If you are ordering portable oxygen, is the patient mobile within the home? If you are not ordering portable oxygen, check D.
3.00 LPM	5. Enter the highest oxygen flow rate ordered for this patient in liters per minute. If less than 1 LPM, enter an "X".
a)_____mm Hg b)_____% c)__/__/__	6. If greater than 4 LPM is prescribed, enter results of most recent test taken on 4 LPM. This may be an (a) arterial blood gas PO2 and/or (b) oxygen saturation test with patient in a chronic stable state. Enter date of test (c).

ANSWER QUESTIONS 7-9 ONLY IF PO2 = 56–59 OR OXYGEN SATURATION = 89 IN QUESTION 1

○Y ○N 7. Does the patient have dependent edema due to congestive heart failure?
○Y ○N 8. Does the patient have cor pulmonale or pulmonary hypertension documented by P pulmonale on an EKG or by an echocardiogram, gated blood pool scan or direct pulmonary artery pressure measurement.
○Y ○N 9. Does the patient have a hematocrit greater than 56%?

NAME OF PERSON ANSWERING SECTION B QUESTIONS, IF OTHER THAN PHYSICIAN (Please Print):
NAME_____ TITLE_____ EMPLOYER_____

SECTION C: Narrative Description of Equipment and Cost

(1) Narrative description of (all items, accessories and option ordered; (2) Suppliers charge; and (3) Medicare Fee Schedule Allowance for each item, accessory, and option (see instructions on back)
The oxygen flow rate prescribed is 3.00 lpm continuous.
Description
Compressed Gas Concentrator
Supplies and Accessories : NASAL CANNULA
Test Fac: MAYO CLINIC, 200 1ST ST, ROCHESTER MN 55905

SECTION D: PHYSICIAN Attestation and Signature/Date

I certify that I am the treating physician identified in Section A of this form. I have received Sections A, B and C of the Certificate of Medical Necessity (including charges for items ordered). Any statement on my letterhead attached hereto, has been reviewed and signed by me. I certify that the medical necessity information in Section B is true, accurate and complete, to the best of my knowledge, and I understand that any falsification, omission, or concealment of material fact in that section may subject me to civil or criminal liability.

PHYSICIAN'S SIGNATURE MWLK DATE 10/28/2017

Signature and Date Stamps Are Not Acceptable.

Form CMS-484 (11/11)

Group I Criteria
Rest PO2 < 55 mm Hg or the arterial oxygen saturation < 88%.

Sleep PO2 falls to 56-59 mg Hg or the arterial oxygen saturation is 89% for at least 5 minutes.

Exercise, the arterial PO2 < 55mm Hg or the arterial oxygen saturation is < 88

Recertification is required after the beneficiary has been receiving oxygen therapy for nine months.

A supplier who knowingly and willfully fails to include this information may be subject to a civil monetary penalty up to $1,000 for each form or document so distributed.

GUIDELINES TO OXYGEN USE

Prior to 2008 BTS guidelines

- 34% ambulance rides used O_2 (2million/yr)

- Poor O_2 prescription use

- Problems
  - O2 may worsen gas exchange (COPD)
  - O2 does no relieve dyspnea in non-hypoxemic pts
  - Minimal effectiveness in mildly hypoxemic COPD or advanced cancer patients.

GUIDELINES TO OXYGEN USE

BTS Guideline for Oxygen Use in Adults in Healthcare and Emergency Settings.

- “Oxygen is probably the commonest drug used in the care of patients who present with medical emergencies”

Thorax 72:i1-i90, 2017

Oxygen prescription for acutely hypoxaemic patients in hospital.

Thorax 72:i1-i90, 2017

THE O_2 AVAILABILITY GAP

25% health facilities sub-Saharan Africa never have O2.

Kenya 42% children prescribed O2 unable to get it.

Need steady power supply, transportation and health care training.

WHO lists O_2 as an essential medicine.

lymphatic circulation is regulated, allowing the skin to become nourished with active substances. This cellular revitalisation treatment consists of mixing pure Oxygen (hyperbaric) with an anti-ageing serum rich in active ingredients, by applying it under and on the epidermis by propulsion. Oxygen replenishes and moisturises the skin, and wrinkles are thus filled and smoothed. Concept Clinic offers its patients Oxygen treatment to reduce the appearance of wrinkles, giving a glow to the face.

Treatment and results

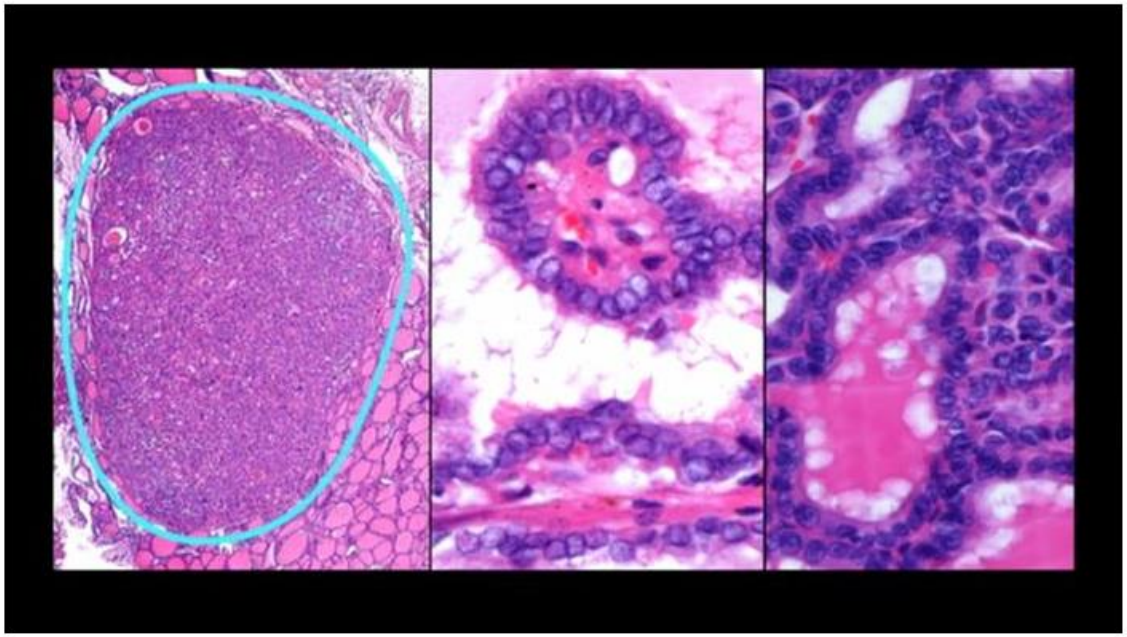
During your consultation, you will be attended to by one of our aesthetic experts, who will assess the condition of your skin and your expectations of Oxygen therapy. Oxygen treatment lasts between 20 to 30 minutes. During Oxygen therapy, we will apply a mixture of Oxygen and anti-ageing serum (hyaluronic acid, vitamins and antioxidants) to your skin. This Oxygen care may also be combined with other wrinkle treatments, and also forms an ideal complement to facial plastic surgery.

Alternatives to Oxygen therapy

SCIENCE

Swiss researchers claim boosting oxygen as their 'radical' new cancer treatment

Swiss researchers are testing how oxygen can be used to fight cancer. Their new approach goes against everything that's been common in cancer treatment until now - but it could be an effective tool.



Oxygen is at the center of research conducted by scientists at Zurich's university hospital. But instead of depriving tumors of oxygen - as you may expect - the researchers are upping the load.

They are using the chemical molecule ITPP (Inositol Trispyrophosphat).

The idea is that ITPP should normalize blood vessels changed by a tumor by increasing the oxygen flow to those vessels. Then, a patient would start on chemotherapy, says Pierre-Alain Clavien, the director of the study.

DUAL NATURE OF O_2 AND AEROBIC RESPIRATION

O_2 reduction to water by ETC is required for ADP → ATP.

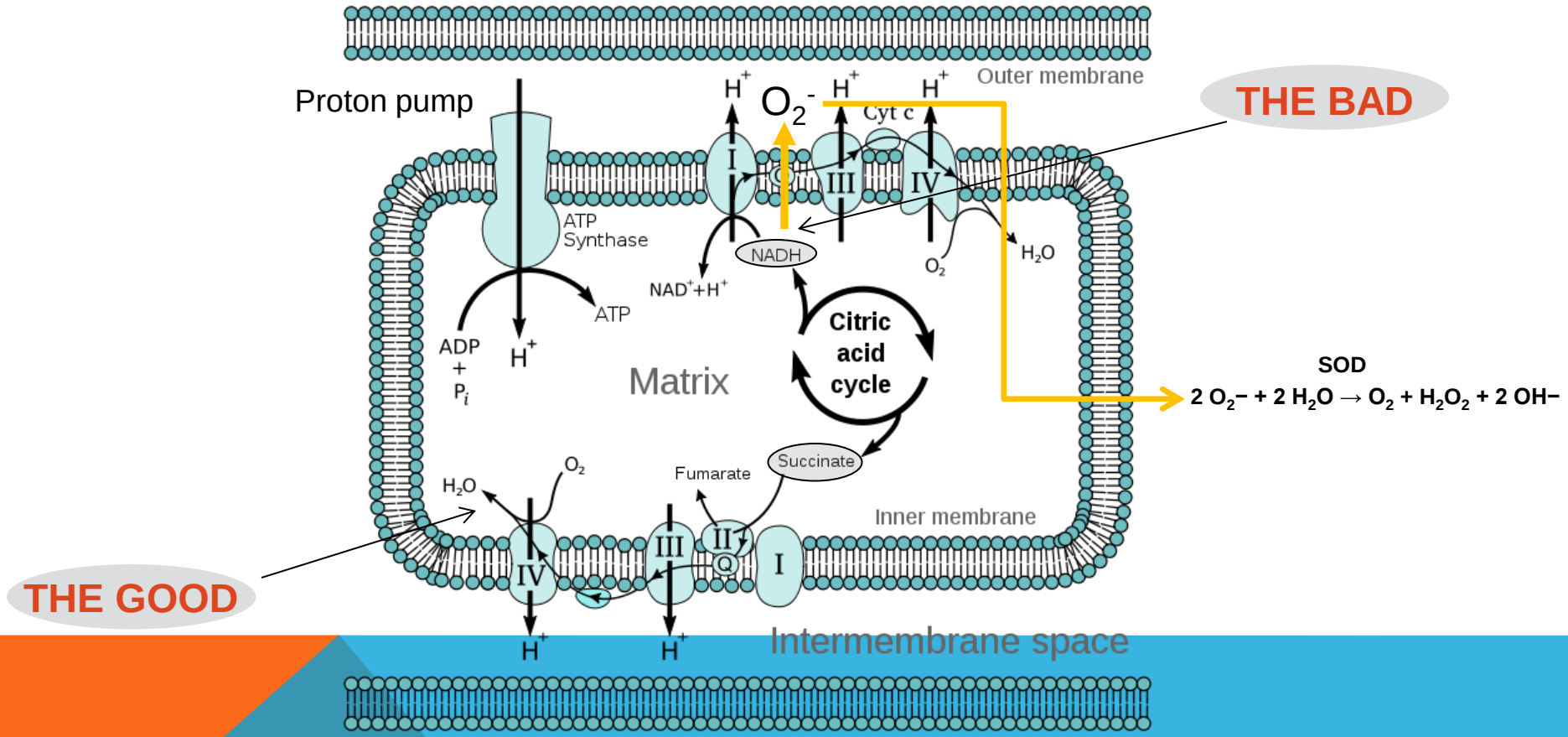
In normoxia (cell respiration not limited) small amounts of ROS are formed.

In cellular hypoxia = ETC inhibited. NADH → glycolytic pathways.

- depression of cellular metabolism.
- paradoxically further increases in ROS.

ETC = electron transport chain
ROS = reactive oxygen species

ELECTRON TRANSPORT CHAIN



In normoxia a small percentage of electrons are prematurely leaked to oxygen, resulting in the formation of the toxic free-radical superoxide (the one-electron **reduction** of dioxygen O_2).

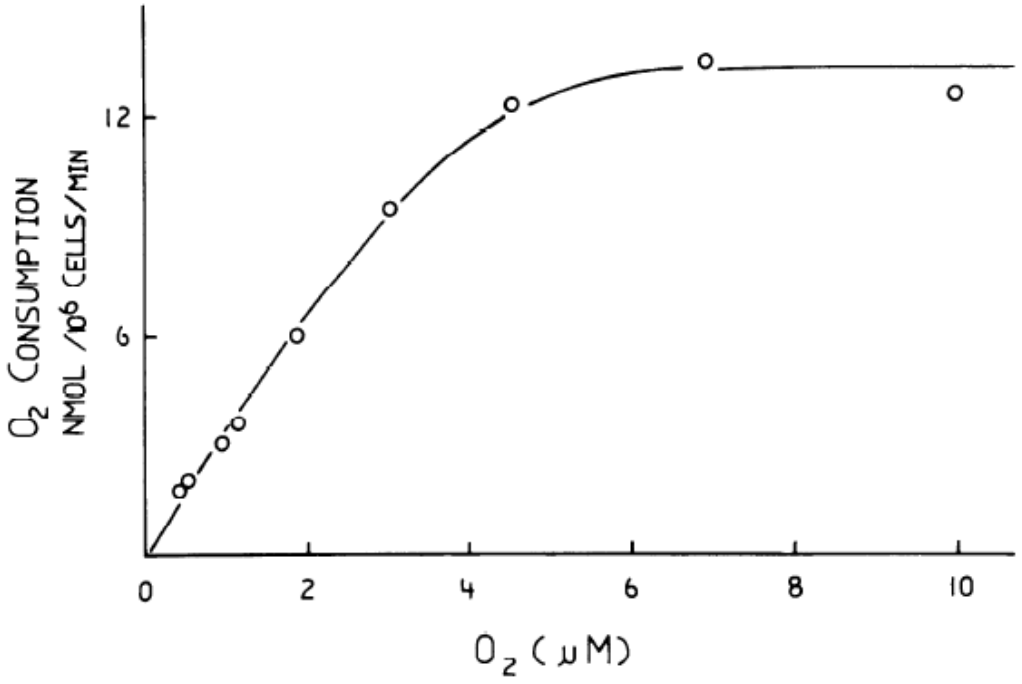
NORMOXIA, HYPOXIA, AND HYPEROXIA

Normoxia: oxygen required for normal energy production.

Hypoxia: imbalance in O_2 supply and demand, ETC inhibited, cells become energy deplete and glycolytic pathways become active.

Hyperoxia: excess production of ROS.

O_2: HOW MUCH DO CELLS NEED?

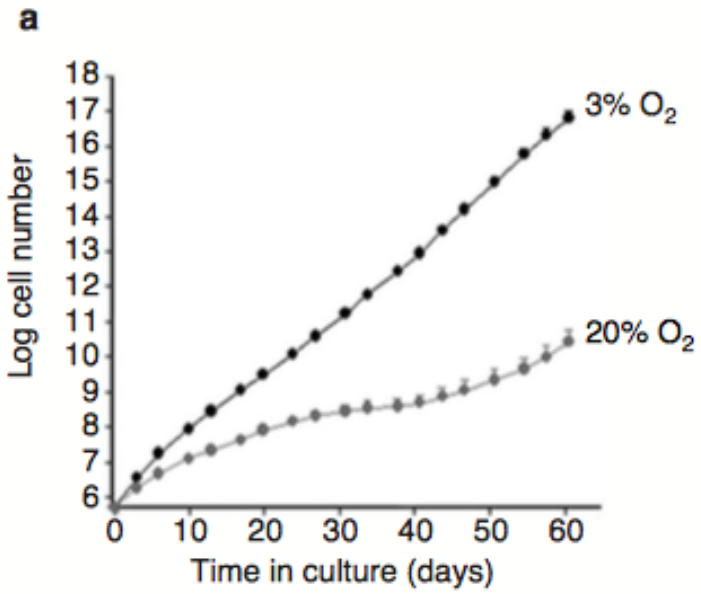


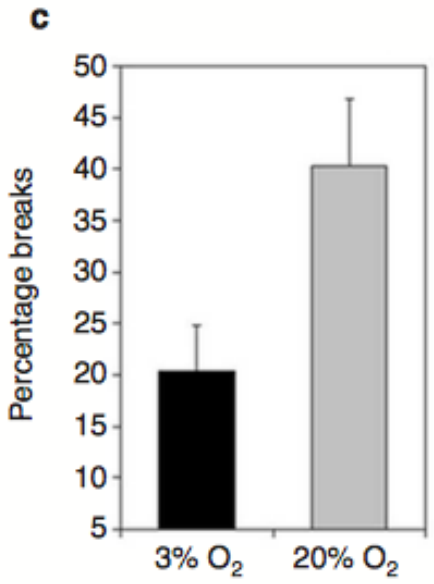
O_2 uptake in isolated hepatocytes cells decreases when O_2 tension is below a critical value of 1-10 torr.

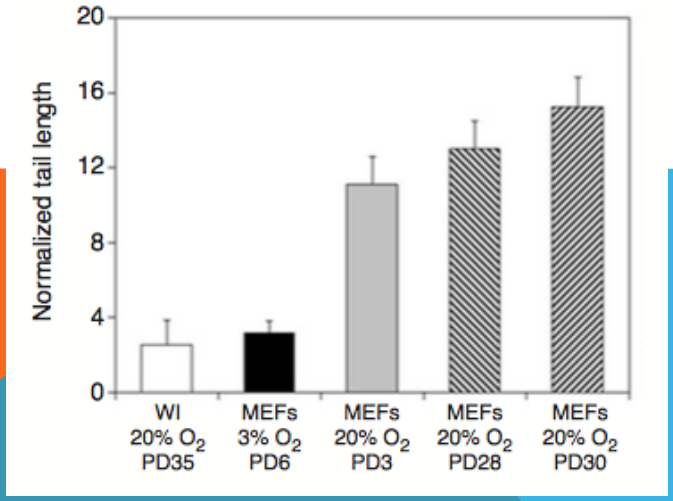
*K*m = 2.8 ± 0.9 μM; 1.55 Torr; 0.37 kPA

Dean Jones and Frances Kennedy
***AJP Cell* 243(5):C247-C253, 1982**

O_2: HOW MUCH IS TOO MUCH?







S. Parrinello et al.
Nature Cell Biol 5(8):741-747, 2003

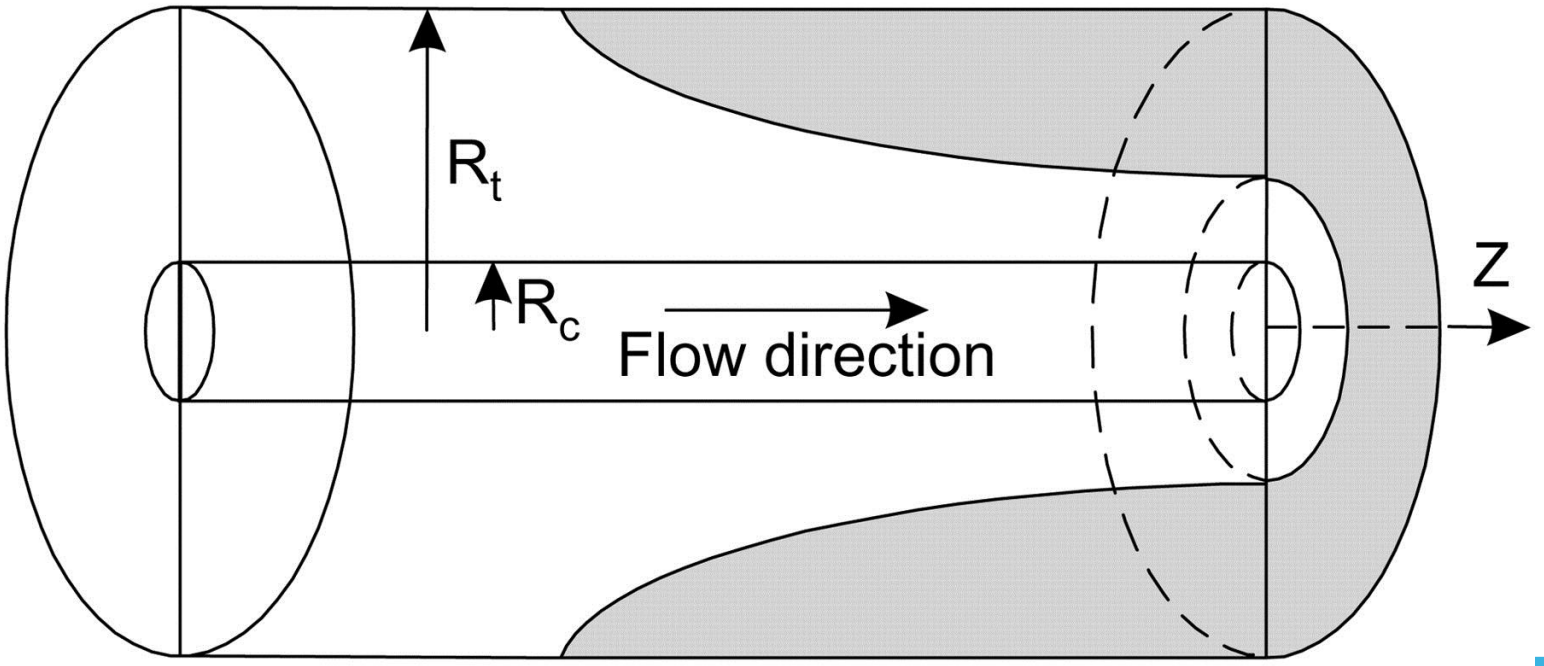
OXYGEN DELIVERY – ORGAN AND WHOLE ANIMAL

QO_2 = C.O. x arterial O_2 content

- arterial O_2 content = [HgB] and saturation (%)

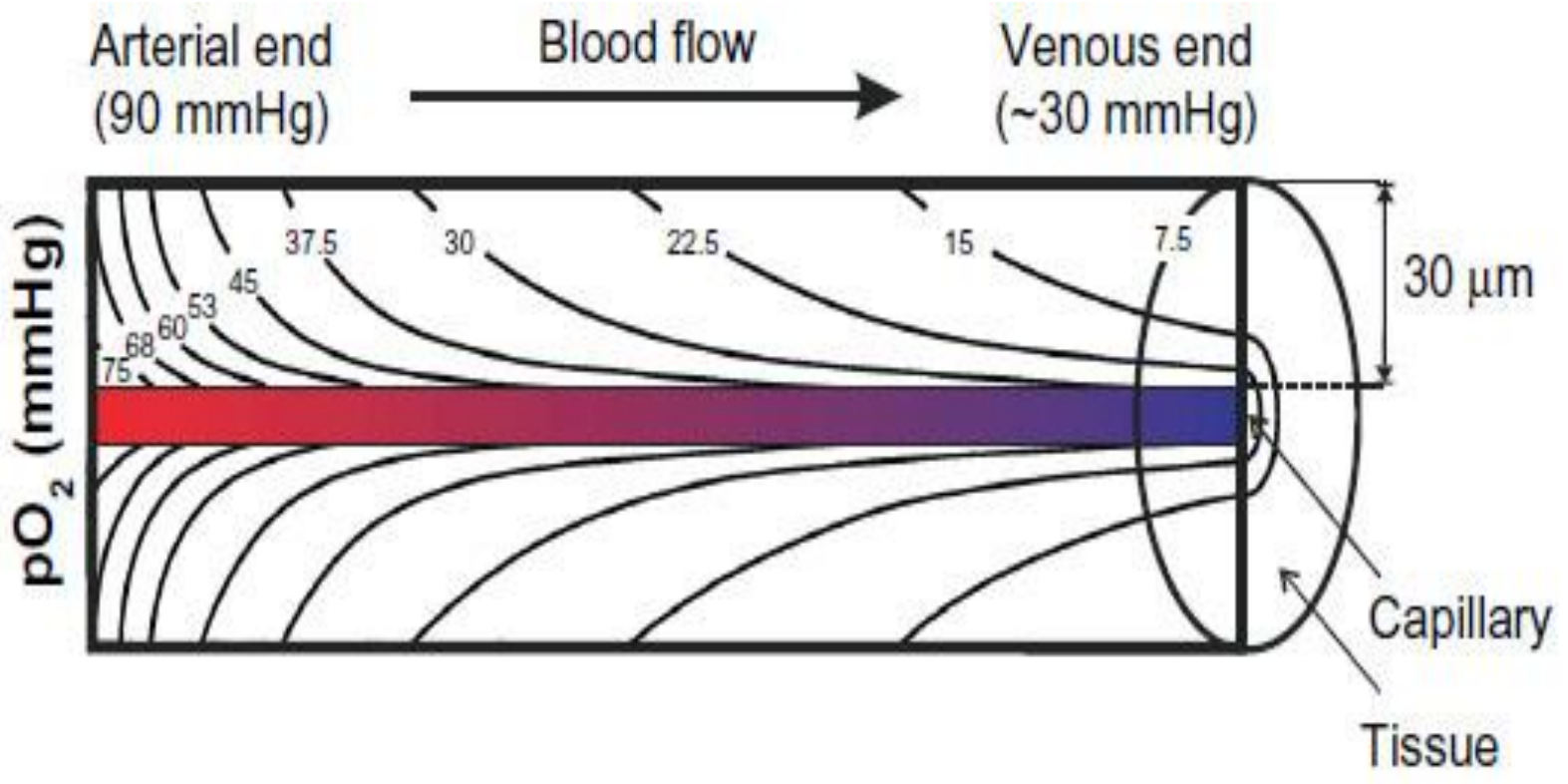
Stagnant hypoxia	reduced flow
Anemic hypoxia	reduced [HgB]
Hypoxic hypoxia	reduce HgB_{02sat}
Histotoxic hypoxia	directly impaired ETC

KROGH CYLINDER 1919



$$K\left[\frac{1}{r}\,\frac{d}{d}\left(r\,\frac{\mathrm{dP}}{dr}\right)\right] = M(P)$$

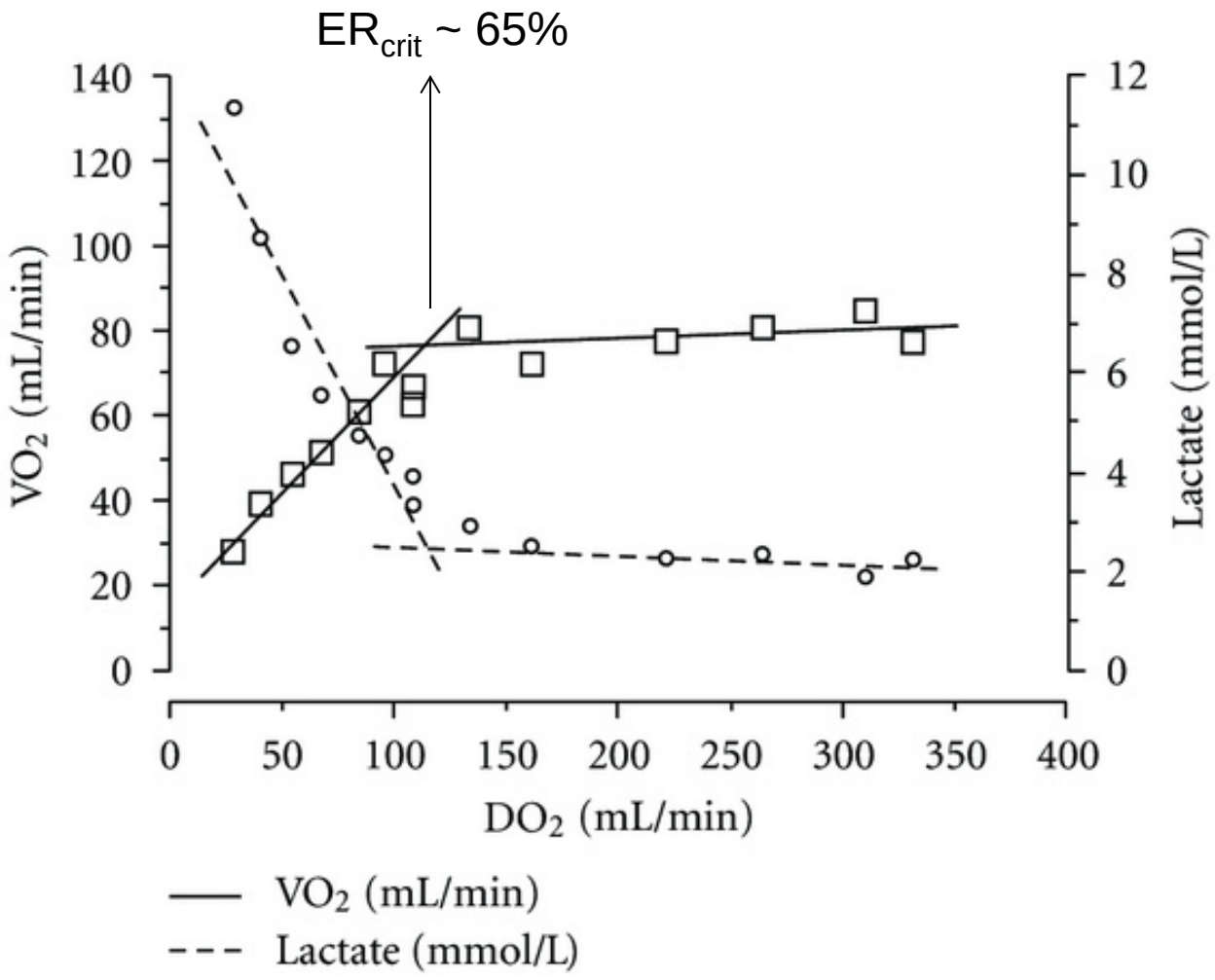
KROGH CYLINDER MODEL PREDICTS HYPOXIC HYPOXIA IS WORST



1920 Nobel Prize in Physiology or Medicine for the discovery of the mechanism of regulation of the capillaries in skeletal muscle

O_2 DELIVERY—

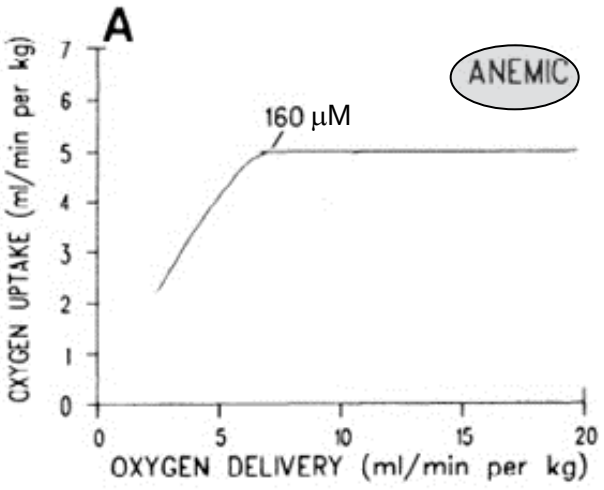
STAGNANT, ANEMIC HYPOXIA, AND HYPOXIC HYPOXIA



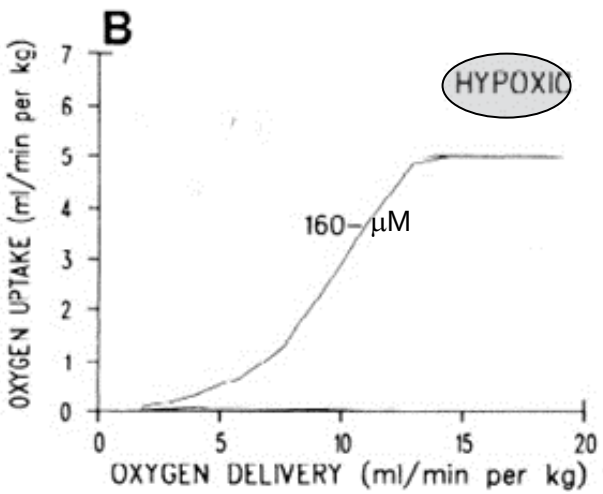
J.L Vincent et al.
Intensive Care Med 30:1990-1996, 2004

OXYGEN DELIVERY - GLOBAL

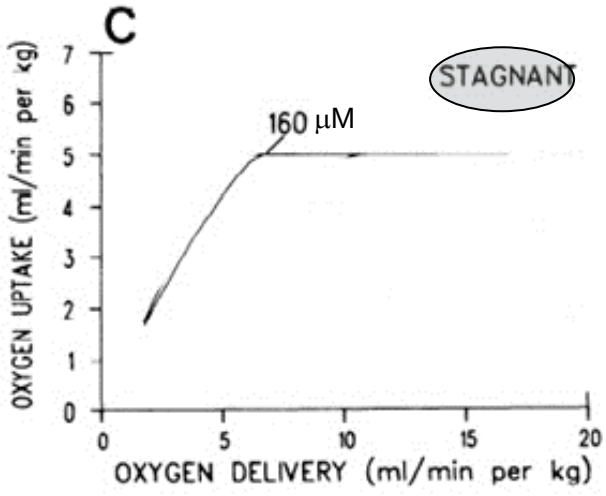
ER_{crit} ~ 71%



ER_{crit} ~ 39%



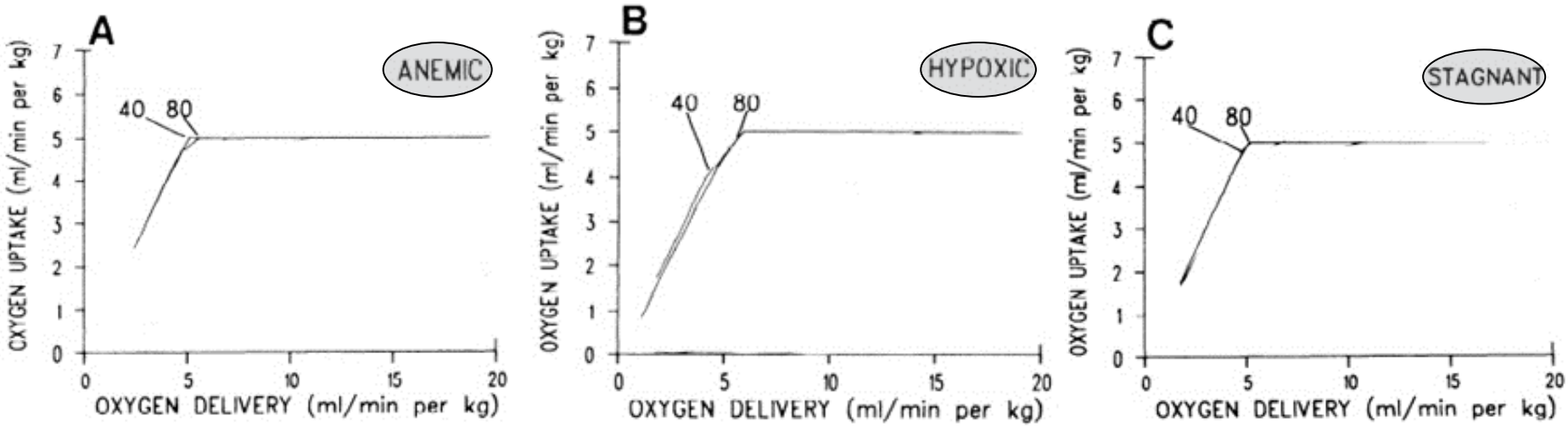
ER_{crit} ~ 71%



P.T. Schumaker and R.W. Samsel
J. Appl. Physiol 67(3):1234-1244, 1989

OXYGEN DELIVERY - GLOBAL

ER_{crit} ~ >90%



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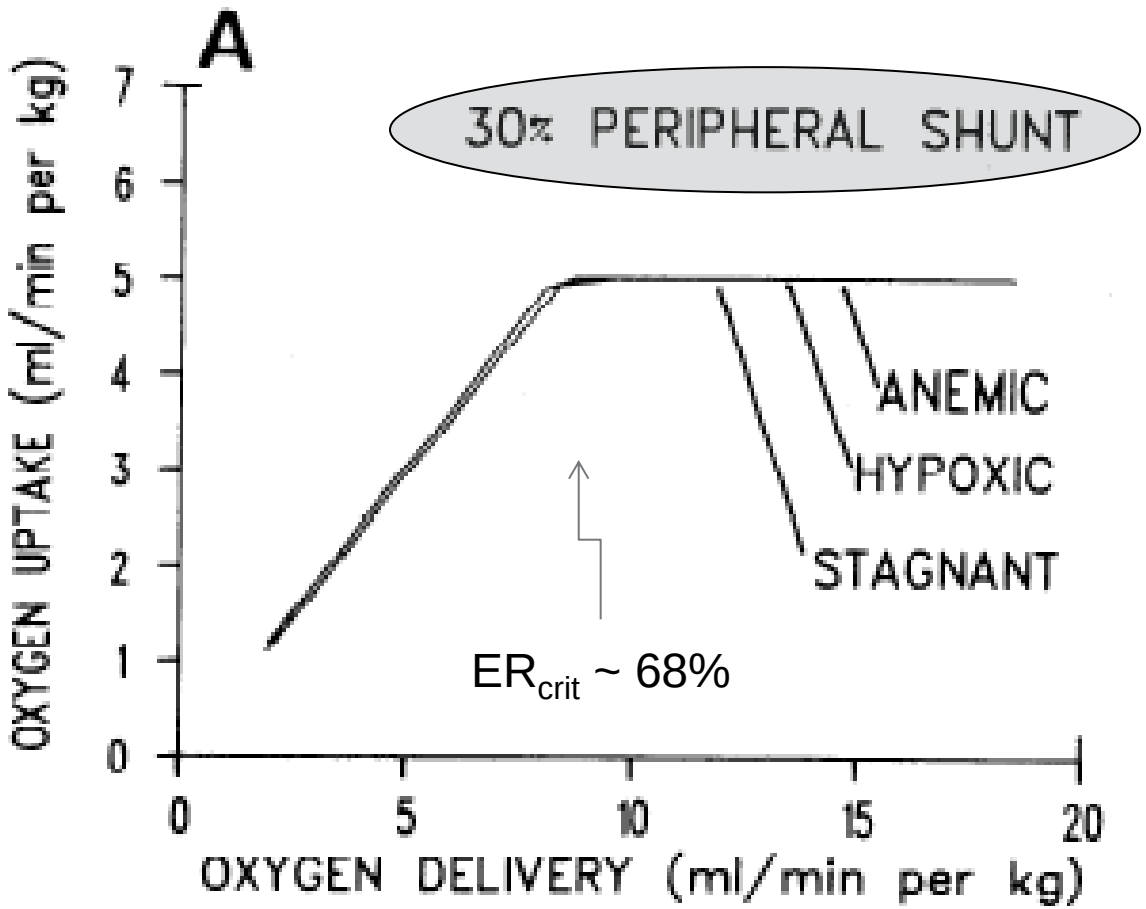
J. Appl. Physiol 67(3):1234-1244, 1989

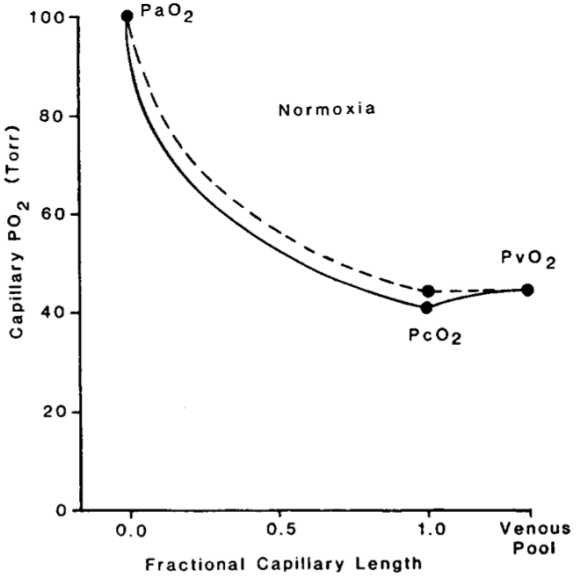
OXYGEN DELIVERY - GLOBAL

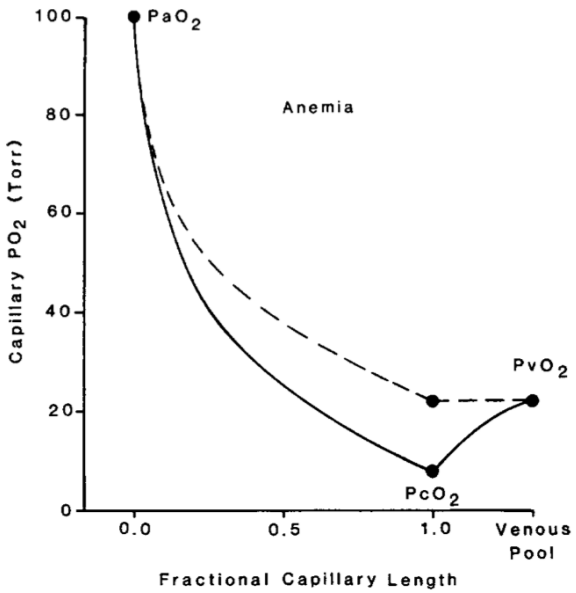


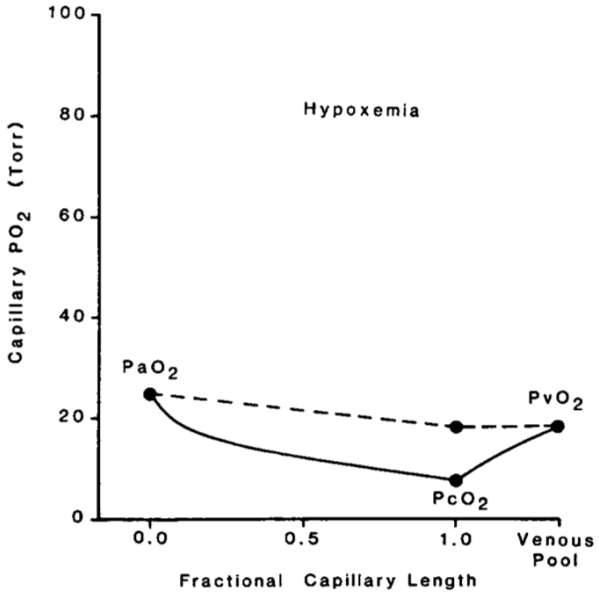
P.T. Schumaker and R.W. Samsel
J. Appl. Physiol 67(3):1234-1244, 1989

KINETICS OF RBC DEOXYGENATION

RELEASE KINETICS OF O2 FROM RBC IN ANEMIC AND HYPOXIC IS SIGNIFICANT







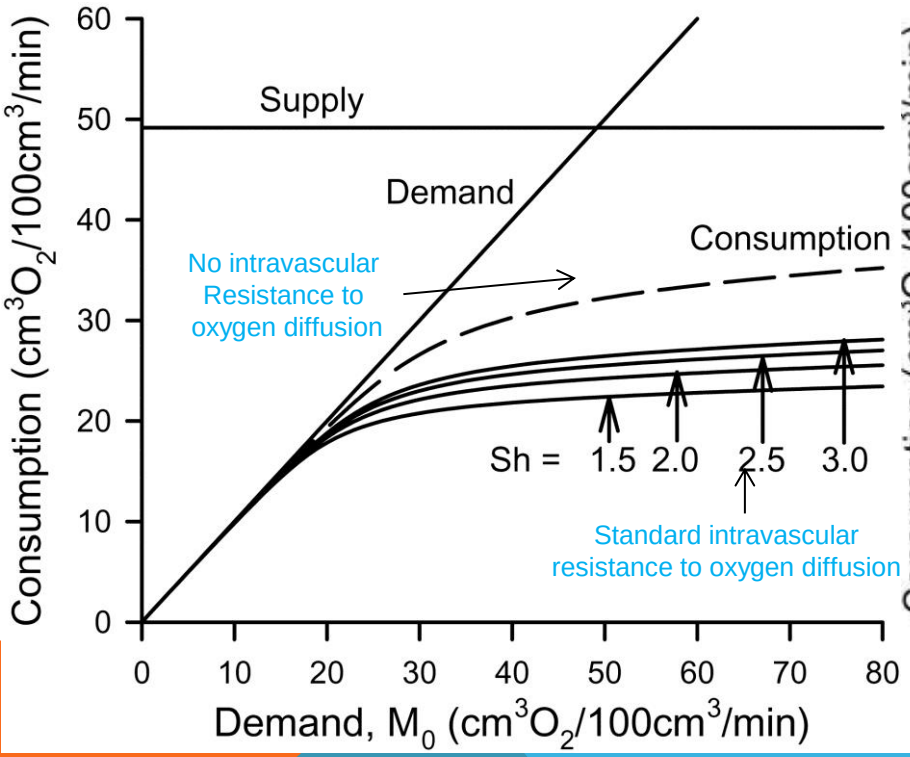
Instantaneous O2 Release from RBC

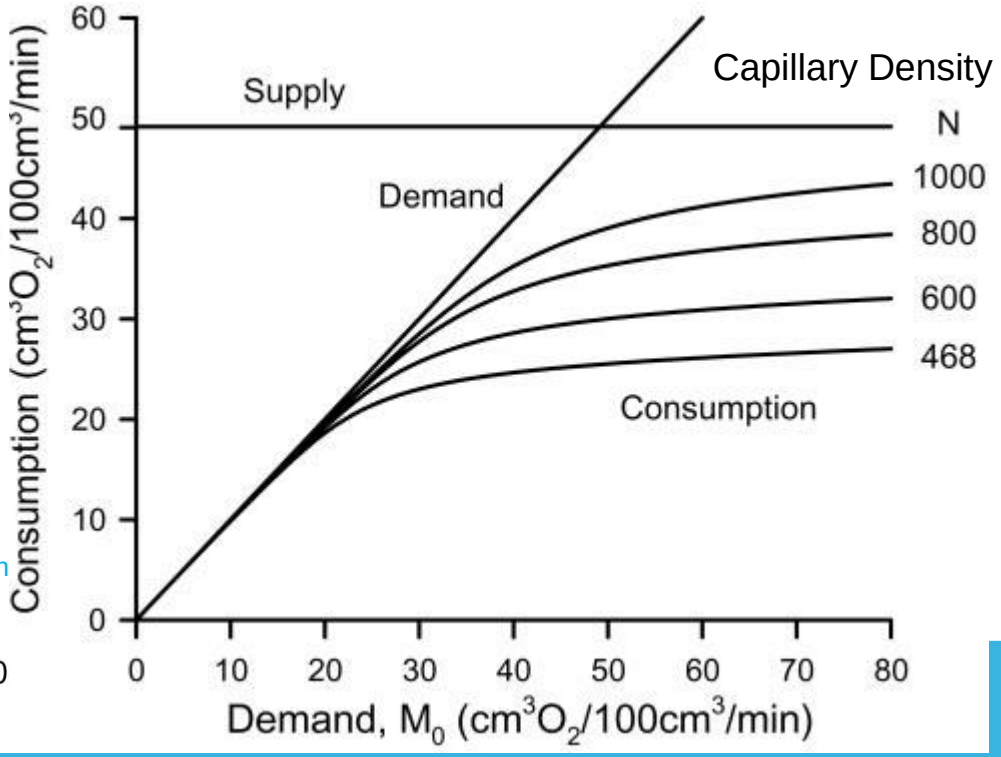
Time Dependent O2 Release from RBC

Guillermo Gutierrez
Resp Physio 63, 79-96, 1986

EFFECT OF DEMAND ON CONSUMPUTION:

THEORETIC EFFECTS OF EXERCISE





B. J. McGuire, and T. W. Secomb
J Appl Physiol 91:2255-2265, 2001

OXYGEN DELIVERY – LOCAL (MICROVASCULAR) "REVIEW OF LOCAL VARIABLES"

QO_2 = organ blood flow x arterial O_2 content

Complex 3D structure.

Small scale: RBC diameter approx. vessel size.

Heterogeneity in perfusion: local and systemic vasodilators and constrictors, microthrombi.

Dissociation and diffusion constants.

Effects of demand altering diffusion along the capillary.

THEORETICAL OR PRACTICAL

Exercise training:

- Reduces intravascular resistance to oxygen diffusion due to increased myoglobin content
- Increases mitochondrial density
- Increases capillary density
- Rightward shifts oxyhemoglobin dissociation curve.

J Appl Physiol 91: 2255–2265, 2001

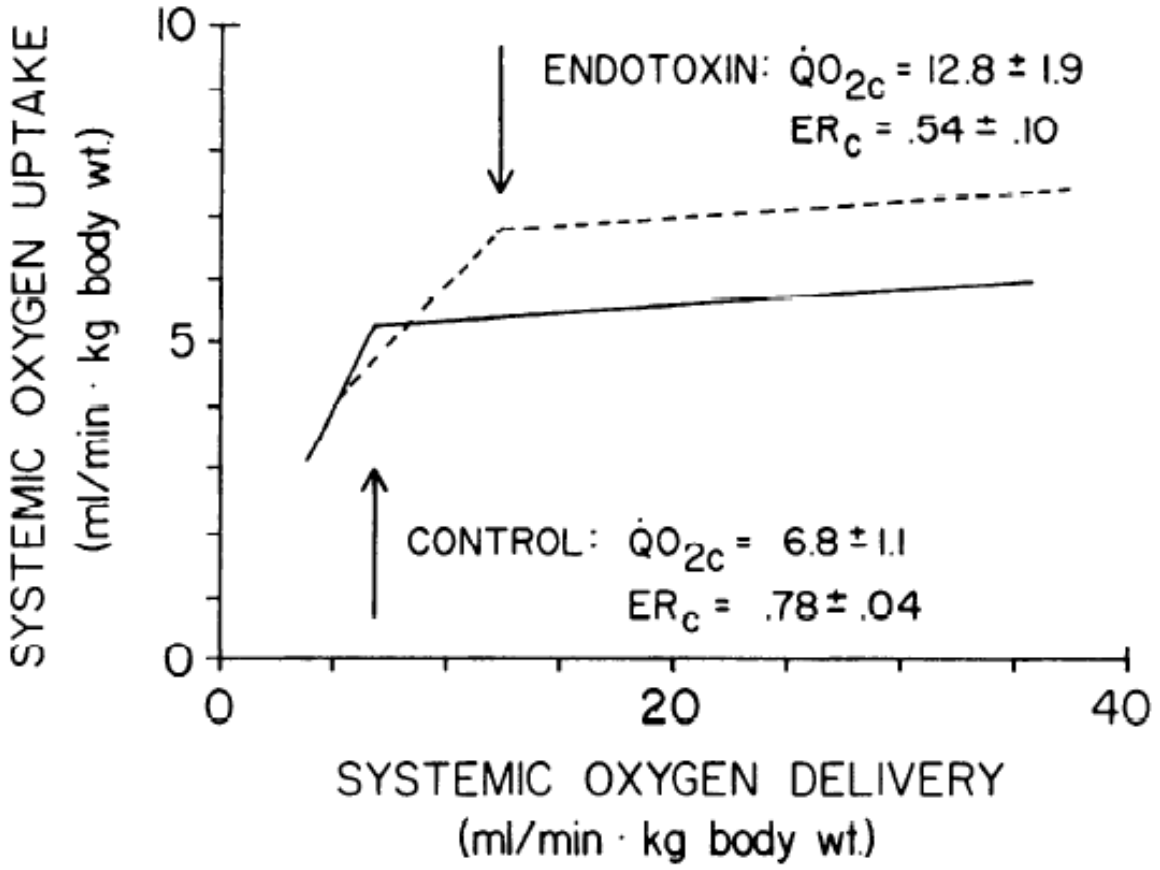
SEPSIS

COMPLEXITY OF OXYGEN DELIVERY

A SPECIAL FORM OF TISSUE HYPOXIA

EFFECT OF ENDOTOXEMIA ON O_2 EXTRACTION

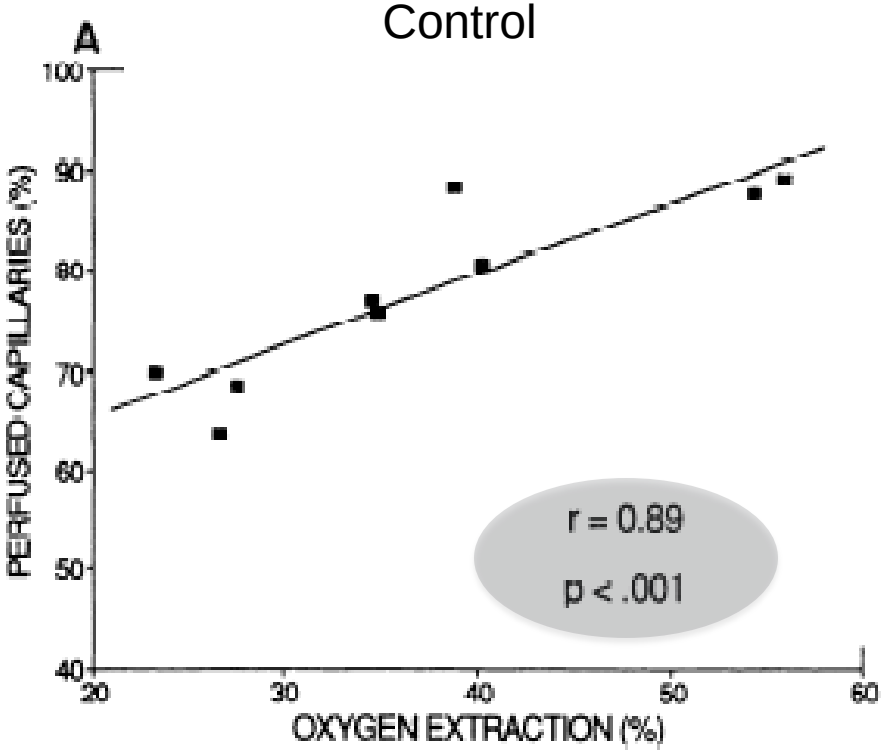
VO_2 ↑ 10% per 1°C



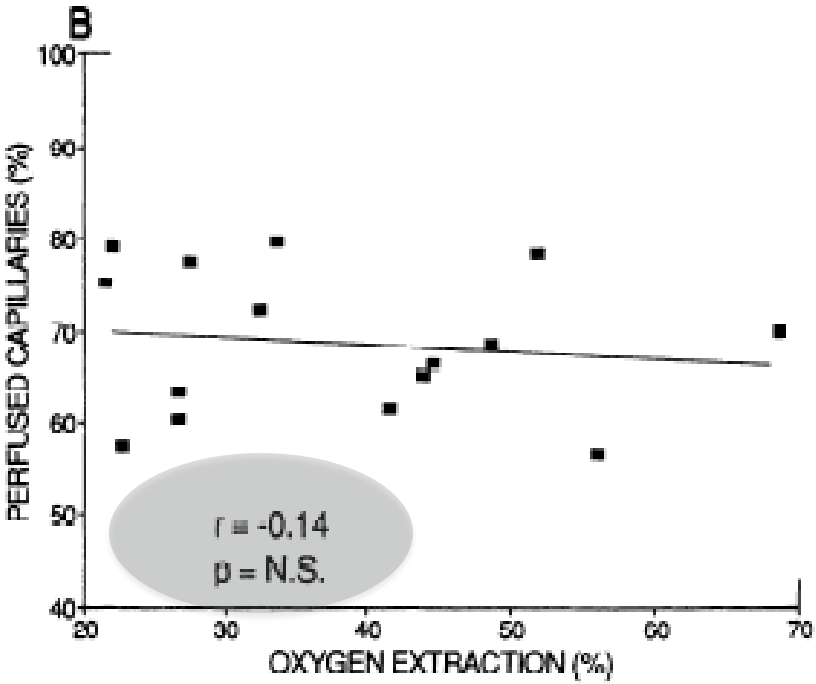
Nelson et al.
J Appl Physiol 64(6):2410-2419, 1988

EFFECT OF ENDOTOXEMIA ON O_2 EXTRACTION

Control



Endotoxin



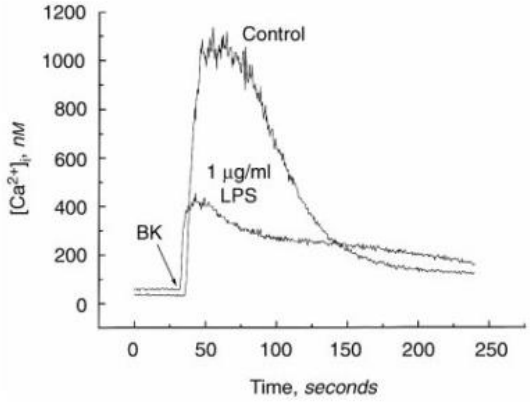
Drazenovic et al.
J. Appl. Physiol. 72(1):259-265, 1992

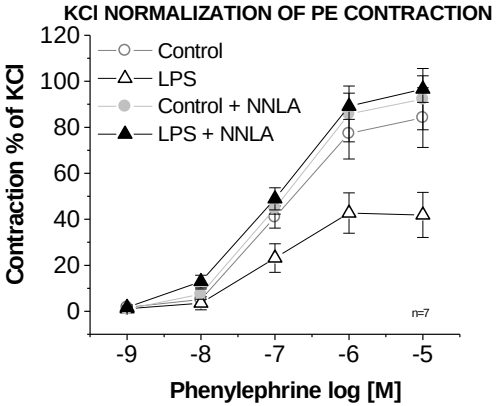
INTRINSIC VASCULAR EFFECTS OF ENDOTOXEMIA ON O_2 EXTRACTION

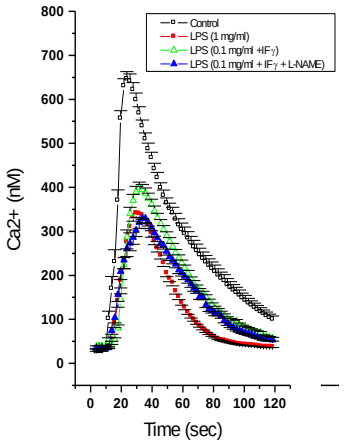
↓ Endothelial NOS

↑ Smooth Muscle NOS

Contractile Dysfunction







Reduced perfusion

GI, renal, brain

Over-perfusion

Muscle

Hypotension

*Essence: Microcirculation O_2 delivery mismatch in sepsis

Wylam et al.
Am Rev Respir Dis 148:1638-1645, 1991

ATTEMPTS TO IMPROVE BLOOD FLOW DISTRIBUTION IN SEPSIS

NOS inhibitors	Petros A, Lamb G, Leone A, Moncada S, Bennett D, Vallance P. Effects of a nitric oxide synthase inhibitor in humans with septic shock. *Cardiovasc. Res.* 28(1), 34–39 (1994).	fail to reduce mortality
	Lorente JA, Landin L, De Pablo R, Renes E, Liste D. L-arginine pathway in the sepsis syndrome. *Crit. Care Med.* 21(9), 1287–1295 (1993).	fail to reduce mortality
Methylene Blue	Kirov MY, Evgenov OV, Evgenov NV, et al. Infusion of methylene blue in human septic shock: a pilot, randomized, controlled study. Crit Care Med 2001; 29:1860-1867.	Survival 50% MB Survival 70% placebo
	Memis D, Karamanlioglu B, Yuksel M, et al. The influence of methylene blue infusion on cytokine levels during severe sepsis. Anaesth Intensive Care 2002; 30:755-762.	fail to reduce mortality
Vasoconstrictors	No clear consensus (NE, dopamine, vasopressin regarding the optimal or most effective vasopressor in patients in septic shock.	

SO WHAT TO DO IN SEPSIS?

EARLY GOAL DIRECTED THERAPY

This approach involves adjustments of:cardiac preload, afterload, and contractility to balance oxygen delivery with an increased oxygen demand.

It is a goal based approach to Acheive

CVP of 8-12 mmHg

Superior vena cava oxygen saturation (ScvO2) of > 70% OR mixed venous oxygen saturation (SvO2) of > 65%.

Mean arterial pressure of >/+ 65 mmHG.

Urine output of > 0.5 ml/kg/hr

Result: 15.9% absolute reduction in 28 day mortality rate.

NEJM 345(19):1368-77, 2001

SO WHAT TO DO IN SEPSIS?

LACTATE CLEARANCE VS. CENTRAL VENOUS OXYGEN SATURATION AS GOALS OF EARLY SEPSIS THERAPY A RANDOMIZED CLINICAL TRIAL

$$\frac{\text{Lactate } T_1 - \text{Lactate } T_2}{\text{Lactate } T_1}$$

Group 1: Seek CVP > 8 with fluid; MAP 65 with dopamine/NE; seek ScvO2 >70% with PRBCs or Dobutamine

Group 2: Same as Group 1, plus, seek lactate clearance of 10% (not knowing ScvO2) with PRBCs or Dobutamine

Hospital Mortality and Length of Stay

Variable	Lactate Clearance Group (n = 150)	$ScvO_2$ Group (n = 150)	Proportion Difference (95% Confidence Interval)	*P* Value[b]
In-hospital mortality, No. (%)[a] Intent to treat	25 (17)	34 (23)	6 (−3 to 15)	
Per protocol	25 (17)	33 (22)	5 (−3 to 14)	
Length of stay, mean (SD), d ICU	5.9 (8.46)	5.6 (7.39)		.75
Hospital	11.4 (10.89)	12.1 (11.68)		.60
Hospital complications Ventilator-free days, mean (SD)	9.3 (10.31)	9.9 (11.09)		.67
Multiple organ failure, No. (%)	37 (25)	33 (22)		.68
Care withdrawn, No. (%)	14 (9)	23 (15)		.15

JAMA 303(8): 739–746, 2010

SHOULD WE MONITIOR S_cVO_2 IN CRITICALLY ILL PATIENTS?

PROBLEMS

Correlation with S_vVO2 is only 0.75-0.81.

Does not reflect coronary sinus.

Ignores regional circulation sensitivity.

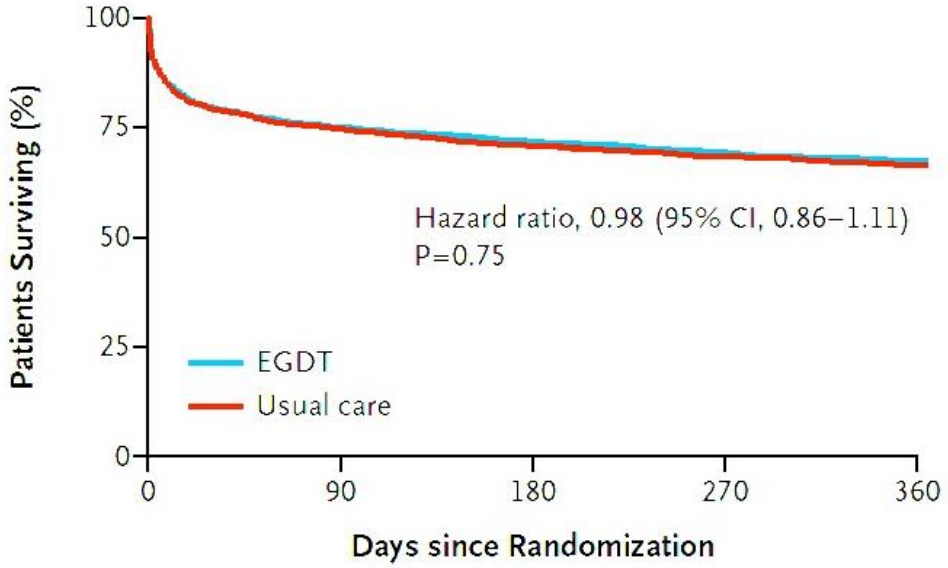
PROPONENTS

Rivers study showed lower mortality (46.5% to 30.5%) using $ScVO_2$ guided resuscitation.- Single center study.

NEJM 345:1368-1377, 2010

SHOULD WE MONITIOR $SCVO_2$ IN CRITICALLY ILL PATIENTS?- A PATIENT-LEVEL META-ANALYSIS

Resource use category	Statistic	ProCESS		ARISE		ProMISe	
		EGDT (N=439)	Usual resuscitation (N=456)	EGDT (N=793)	Usual resuscitation (N=798)	EGDT (N=625)	Usual resuscitation (N=626)
Interventions							
PreSep™ central venous oximetry catheter	N	391	19	705	3	545	2
	%	89%	4%	89%	0%	87%	0%
Standard CVC	N	72	246	109	494	48	316
	%	16%	54%	14%	62%	8%	50%



NEJM 376(23): 376;223234, 2017

ANEMIC HYPOXIA: AABB RED BLOOD CELL TRANSFUSION GUIDELINES

31 randomized clinical trials (RCTs), > 12, 500 pts.

2-tiered approach provides support for making more individualized transfusion decisions.

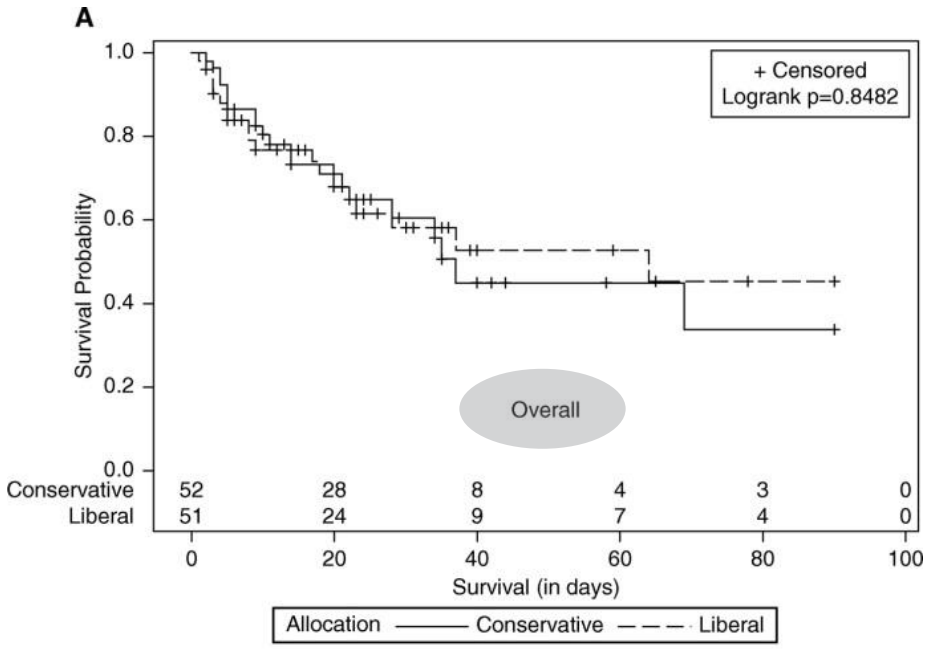
- Stable, adult inpatients hemoglobin concentration of less than 7 g/dL including those in the intensive care unit.
- Post-surgery patients or those with preexisting cardiac disease and hemoglobin concentration of less than 8 g/dL.

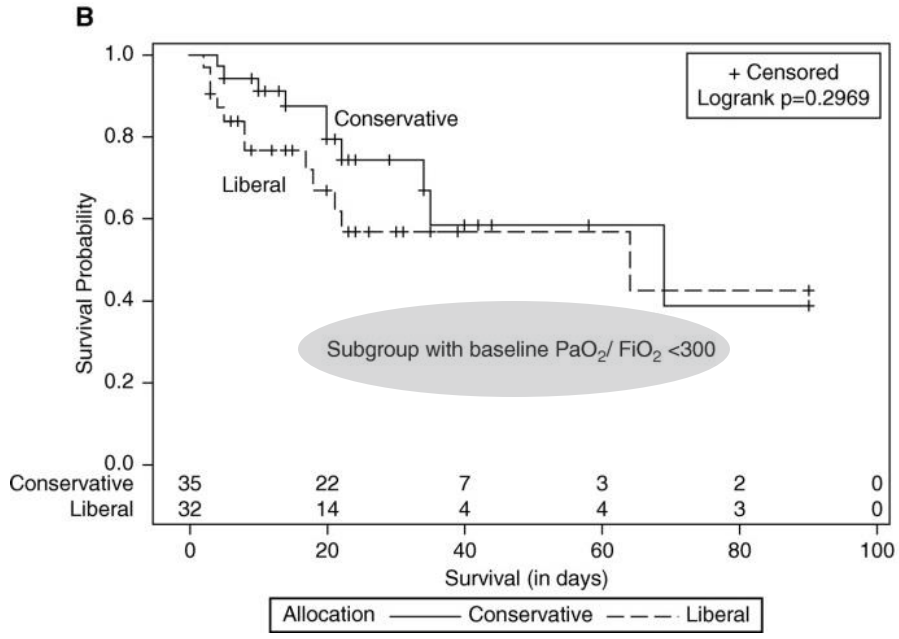
JAMA 316(19):1984-1985, 2016

What about Hypoxic hypoxia?

Inpatient and outpatient setting?

CONSERVATIVE VERSUS LIBERAL OXYGENATION TARGETS FOR MECHANICALLY VENTILATED PATIENTS





Conservative oxygenation strategy: target O_2 sat 88–92% (n = 52)

Liberal oxygenation strategy: target O_2 sat > or equal to 96% (n = 51).

AJRCCM (193)1:43-51, 2016

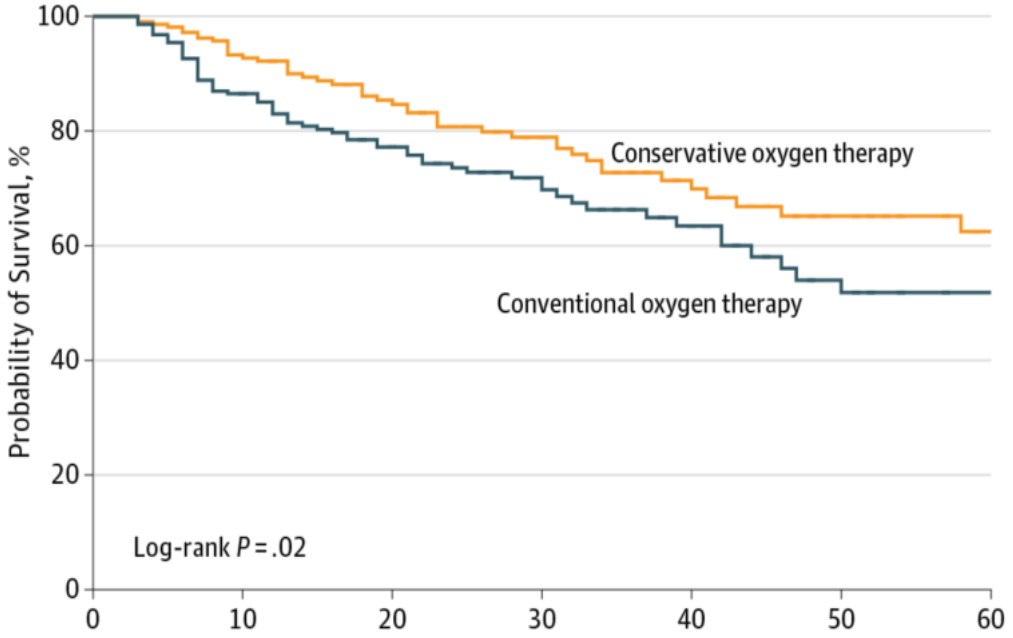
EFFECT OF CONSERVATIVE VS CONVENTIONAL OXYGEN THERAPY ON MORTALITY AMONG PATIENTS IN AN INTENSIVE CARE UNIT: THE OXYGEN-ICU RANDOMIZED CLINICAL TRIAL

480 patients randomly assigned

Conservative: O_2 to maintain Pao_2 70 - 100 mm Hg or Spo_2 94% -98%.

Conventional group: O_2 allowed Pao_2 values up to 150 mm Hg or Spo_2 97% -100% ().

Findings: Conservative: absolute risk reduction of mortality of 8.6% compared with conventional therapy.



Meaning: Among critically ill intensive care unit patients with a length of stay of 72 hours or longer, a conservative protocol for oxygen therapy may be beneficial.

JAMA 316(15):1583-1589, 2016

OXYGEN IN THE ICU TOO MUCH OF A GOOD THING?

What is a clinician to do?

The JAMA study is not a trial of permissive hypoxemia, which has been proposed but is as yet a completely unproven therapeutic strategy.

This trial involved targeting relative normoxia, avoiding both significant desaturations and exposure to supraphysiological $Pa0_2$.

Until the results of further trials : there appears to be little downside in the careful titration and monitoring of supplemental oxygen in the ICU to achieve physiologically normal levels of $Pa0_2$ while avoiding potentially dangerous hyperoxia.

SUPPLEMENTAL OXYGEN PROLONGS SURVIVAL FOR PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) AND RESTING HYPOXEMIA.

LANDMARK TRIALS

Continuous or Nocturnal Oxygen Therapy in Hypoxemic Chronic Obstructive Lung Disease: A Clinical Trial *Ann Intern Med*. 1980;93(3):391-398.

Long Term Domiciliary Oxygen Therapy in Chronic Hypoxic Cor Pulmonale Complicating Chronic Bronchitis and Emphysema.

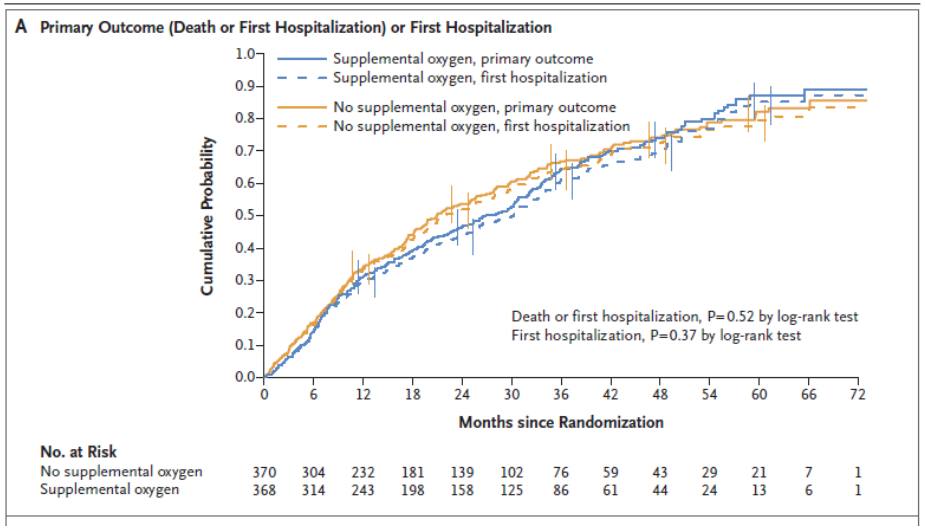
Lancet 8222 (1): 681-6, 1981

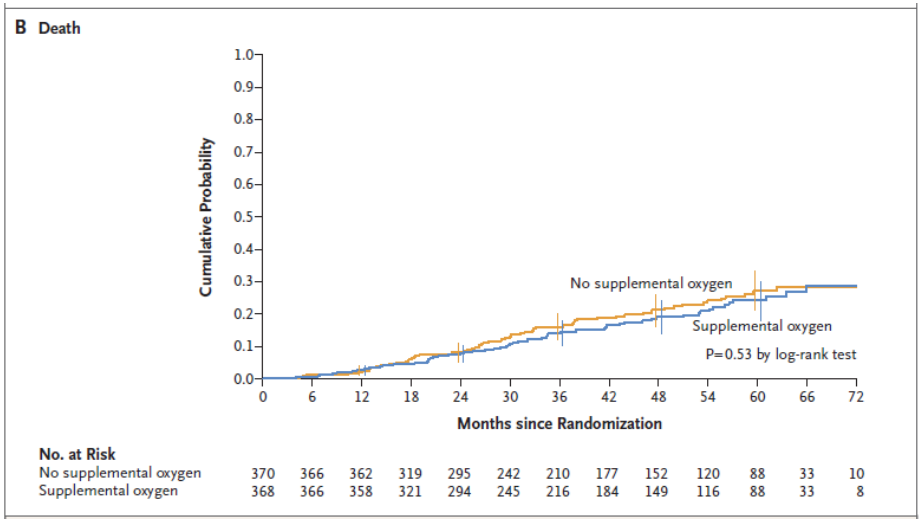
LONG-TERM OXYGEN TREATMENT TRIAL RESEARCH GROUP. A RANDOMIZED TRIAL OF LONG-TERM OXYGEN FOR COPD WITH MODERATE DESATURATION.

- Unblinded, multicenter, 738 patients, randomized, followed 1 to 6 years.
- Compared 24-hour supplemental oxygen to no such therapy.
- Stable COPD and moderate resting or exercise-induced desaturation (oxygen saturation, 89%-93%).

NEJM 375(17):1617-1627, 2016

LONG-TERM OXYGEN TREATMENT TRIAL RESEARCH GROUP. A RANDOMIZED TRIAL OF LONG-TERM OXYGEN FOR COPD WITH MODERATE DESATURATION.





No difference in time to death or first hospitalization for any cause.

No consistent benefit was found for secondary outcomes, including quality of life, depression, anxiety, lung function, or physical status.

Implications: Supplemental oxygen does not benefit patients with stable COPD and moderate resting or exercise-induced desaturation. Limiting use of supplemental oxygen to patients with COPD and severe desaturation will protect patients from supplemental oxygen–associated harms, lessen risk of tripping, and reduce costs.

NEJM 375(17):1617-1627, 2016

SUPPLEMENTAL O_2 IN INTERSTITIAL LUNG DISEASE: AN ART IN NEED OF SCIENCE

- Currently, the use of continuous supplemental O_2 for resting hypoxemia in ILD is extrapolated from studies in COPD patients published > 35 years ago.

- Advanced ILD frequently has a rapid and more severe exertional hypoxemia compared with those with COPD; suggesting that it is likely inappropriate to extrapolate COPD data to ILD.

- There are no high-quality studies evaluating the use of supplemental oxygen in patients with ILD who desaturate only with exertion.

Annals ATS 14(9):1373-1377, 2017

SUPPLEMENTAL O_2 IN INTERSTITIAL LUNG DISEASE: AN ART IN NEED OF SCIENCE

- Observational study (133 pts) with IPF + mild exertional hypoxemia reported no mortality benefit of supplemental oxygen. *Am J Respir Crit Care Med* 2000;161:1172–1178.
- Several studies in ILD demonstrate that breathing supplemental O_2 or hyperoxia during exercise improves endurance time, walk distance, dyspnea, maximal oxygen uptake, and maximal workload. *Eur Respir J* 2012;40:269–270.

  BUT these studies are small sample sizes, retrospective, lack blinding with sham oxygen, and have been inconsistent regarding confounders, such as disease severity or pulmonary hypertension.

- Double-blind, placebo-controlled crossover study (20 pts) with IPF + exertional desaturation found 4 L/min of nasal prong O_2 did not improve 6-min. walk distance compared with breathing room air. *Respir Med* 2013;107:1241–1246.

SUPPLEMENTAL O_2 IN INTERSTITIAL LUNG DISEASE: BEST RECOMMENDATIONS

ATS/ERS: Resting oxygen saturation less than 88% should be treated with supplemental oxygen.

Specific criteria for patients with isolated exertional hypoxemia were not provided

BTS: comments that long-term oxygen therapy may survival in patients with ILD with chronic resting hypoxemia, and suggests that patients with ILD with severe breathlessness could be considered for palliative oxygen therapy. However, this guideline further states that ambulatory oxygen should not be routinely offered to patients without chronic hypoxemia at rest (grade B recommendation).

Am J Respir Crit Care Med 183:788–824, 2011

Thorax 70:i1–i43, 2015

OPTIMUM OXYGEN THERAPY PRETERM BABIES

- Retinal and brain vasculature and lung epithelium are affected by O_2-regulated vascular endothelial growth factor.

- Hyperoxia of preterm elicits:
- ROS
- doubles risk of **cerebral palsy**
- an important cause of **BPD**

Arch Dis Child Fetal Neonatal Ed 92(2): F143–F147, 2007

OPTIMUM OXYGEN THERAPY PRETERM BABIES

- Target fractional oxygen saturation was 80–90% with the lower alarm limit set to operate only if saturation fell below 70% (restrictive approach).

- ROP was 6.3% compared to 27.7% in the liberal O2 group.

Arch Dis Child 84:F106–F110, 2001

OPTIMUM OXYGEN THERAPY IN TERM BABIES: BEST RECOMMENDATIONS

Benefit of Oxygen Saturation Targeting (BOOST) Trial was published in 2003.

Trial oximeters were modified to keep the functional saturation in the range 91–94% or 95–98% depending on allocation at trial entry, while displaying a figure in the range 93–96%.

No evidence that the growth and developmental outcome of the oxygen-dependent preterm infant was improved by keeping their oxygen saturation in the high range.

N Engl J Med. 349(10):959-67, 2003

SO_2S: No Benefit of Routine Oxygen in Acute Stroke

Determination of the Role of Oxygen in Suspected Acute Myocardial Infarction (DETO2X-AMI)-Sweden

Trials 15: 99, 2014

NEJM 377:1240-1249, 2017

BARRIERS TO OXYGEN USE

Costly, not funded for all who may benefit.

Many populations have no funding for exertional O_2.

Burdensome, makes one look and feel old and infirm.

Confusion on flow rates

In some minimal symptom relief

Compliance is low in frail populations.

High flow is impractical and dangerous.

MULTIPLE OTHER POTENTIAL ROLES FOR O2 IN DISEASE

Exercise.

Pulmonary hypertension.

High altitude with lung disease.

Hyperbaric O2 for wounds, stroke.

Carbon monoxide.

SUMMARY

To be done.