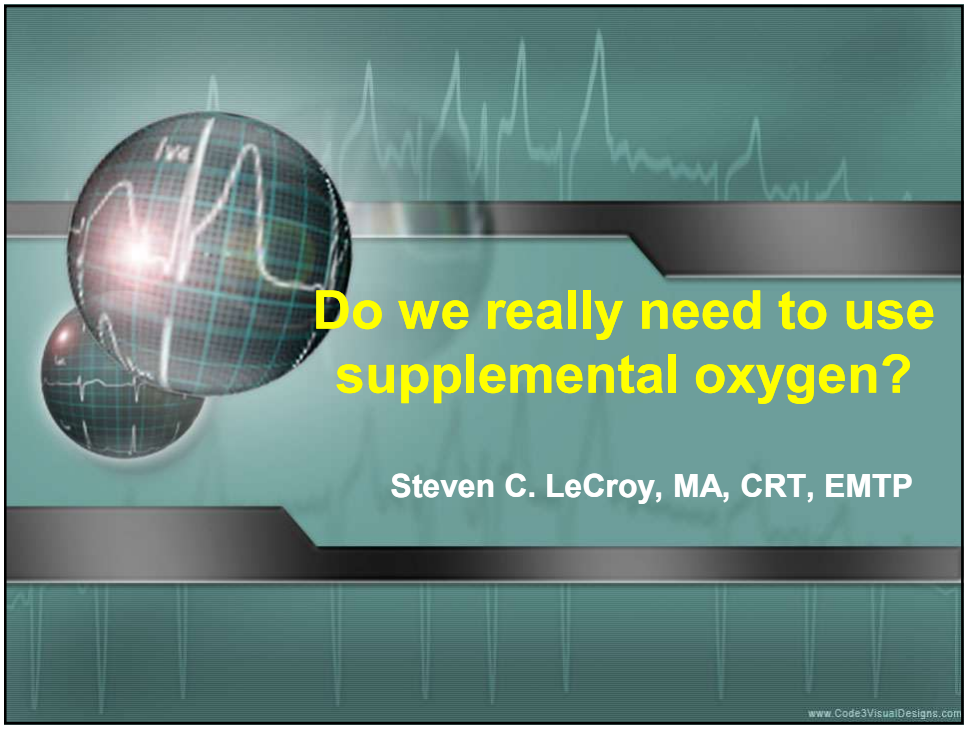

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Conflict of Interest Disclosure
Steven C. LeCroy

I disclose the following financial relationships with a commercial entity that produces healthcare-related products or services relevant to the content I am presenting:

Company	Relationship	Content Area
Mercury Medical	Director of Clinical Support	Respiratory

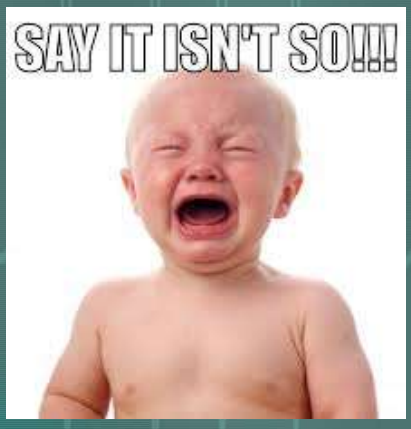
2

Questions to think about

- Do we really need to administer supplemental oxygen?
- Are there medical conditions where supplemental oxygen is harmful?
- Are there traumatic conditions where supplemental oxygen is harmful?

3

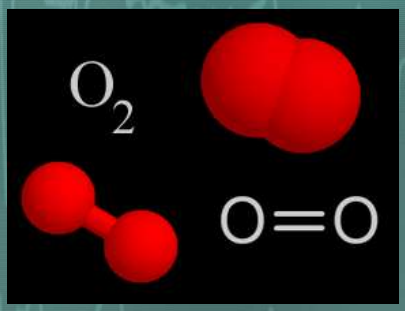
Chemistry Warning



4

Oxygen

- Oxygen:
  - Atomic weight = 15.9994 g^{-1}
  - Colorless
  - Tasteless
  - Third most abundant element in the Universe.
  - Present in Earth's atmosphere at 20.95%.



Money is like oxygen, it is only important if you don't have any.

5

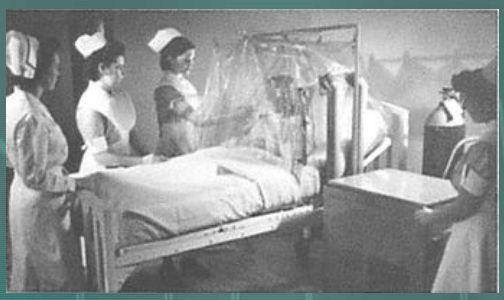
Oxygen

- Oxygen is essential for animal life.

6

Oxygen

- First recorded use of oxygen to treat patients was in 1885



7

Oxygen

What do we know now that we didn't know then?

8

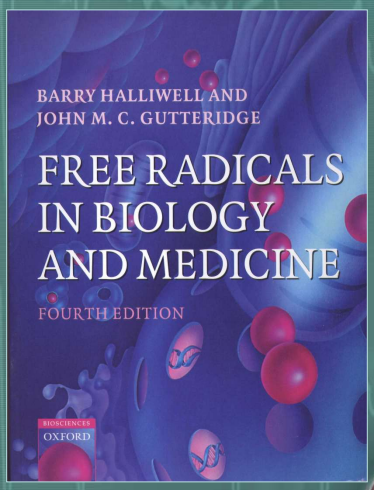
Oxygen

- In 1977 (Respiratory School) there was very little information on oxygen and it's effect on patients. Oxygen was good, more oxygen was better.

9

Oxygen

- Now, there are shelves of textbooks on the subject.



10

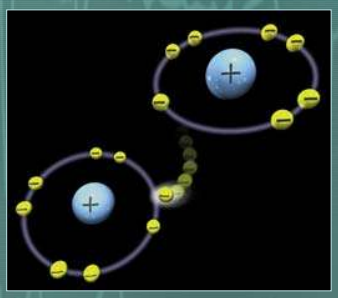
Oxygen

- We are learning that oxygen is a double edge sword.
- It can be beneficial.
- It can be harmful.

11

The Chemistry of Oxygen

- *Free Radicals:*
  - An atom or group of atoms that has at least one unpaired electron and is therefore unstable and highly reactive. In animal tissues, free radicals can damage cells and are believed to accelerate the progression of cancer, cardiovascular disease, and age-related diseases.
    - American Heritage Dictionary



12

The Chemistry of Oxygen

- An excess of free-radicals damages cells and is called oxidative stress.

13

The Chemistry of Oxygen

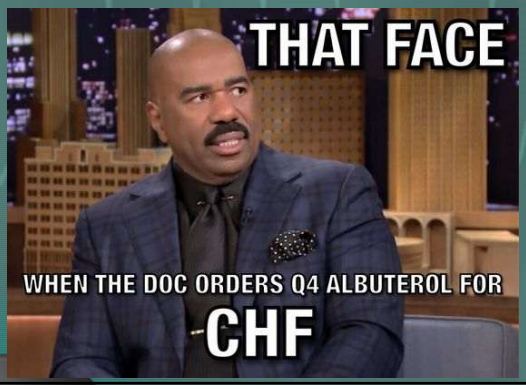
Diseases associated with free-radicals:

- Arthritis
- Cancer
- Atherosclerosis
- Parkinson's disease
- Alzheimer's disease
- Diabetes
- ALS
- Neonatal diseases:
  - Intraventricular hemorrhage
  - Periventricular leukomalacia
  - Chronic lung disease / bronchopulmonary dysplasia
  - Retinopathy of prematurity.
  - Necrotizing enterocolitis.

14

The Chemistry of Oxygen

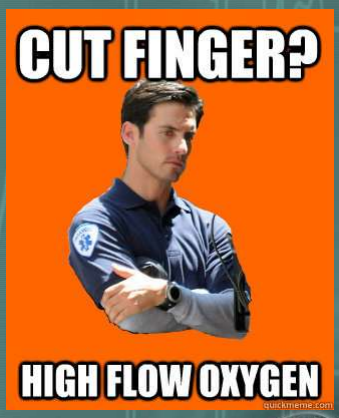
- So, what does all this mean to me as a clinician?



15

The Chemistry of Oxygen

- Oxidative stress occurs primarily during reperfusion—not during hypoxia.
- Flooding previously ischemic cells with oxygen during reperfusion worsens oxidative stress.



16

17

Reperfusion Injury

- Reperfusion injury occurs when oxygen is reintroduced to ischemic tissues.
- Organs most affected:
  - Heart
  - Kidney
  - Liver
  - Lung
  - Intestine

18

Reperfusion Injury

- When tissues are reperfused with oxygen, reactive oxygen species (ROS) are produced.

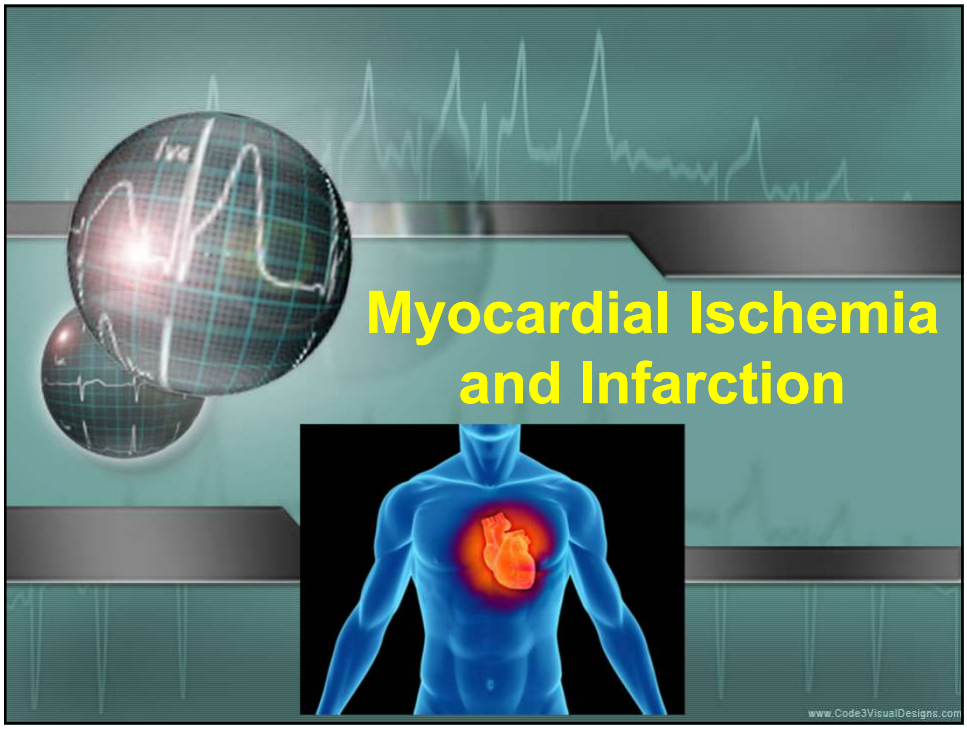
Reactive oxygen species (ROS) are highly reactive ions and “free radicals” (chemicals containing atoms with an unpaired electron in its outer orbit) involving oxygen molecules.

19

Reperfusion Injury

- Reperfusion injury is particularly problematic in:
  - Stroke
  - Acute coronary syndrome
  - Trauma
  - Carbon monoxide poisoning
  - Cyanide poisoning

20



21

Historical Overview

- Oxygen relieved pain during episodes of angina pectoris
- Steele C. Severe angina pectoris relieved by oxygen inhalations
  BMJ 1900, 2:1568.
- Hypoxia of the myocardium described as the cause of angina
- Keefer CS, Resnik WH. Angina pectoris: a syndrome caused by anoxemia of the myocardium. Arch Intern Med 1928, 41:769-807.

22

What Do We Know and Sometimes Forget - Published in 1950

- 100% oxygen either pronounced or prolonged
- electrocardiographic changes
- Failed to prevent the onset of anginal pain
- Failed to influence the duration of pain

Russek HI, Regan FD, Naegele CF. One hundred percent oxygen in the treatment of acute myocardial infarction and severe angina pectoris. JAMA 1950, 144:373-375.

23

What Do We Know and Sometimes Forget Published in 1964

- Breathing high concentrations of oxygen for at least 30 minutes in the first 24 hours after MI
  - Decreased heart rate
  - Reduced cardiac output
  - Increased systemic vascular resistance
- High concentration – 85% to 90%

MacKenzie GJ, Flenley DC, Taylor SH, McDonald AH, Stanton HP, Donald KW. Circulatory and respiratory studies in myocardial infarction and cardiogenic shock. Lancet 1964, 2:825-832.

24

What Do We Know and Sometimes Forget Published in 1965

- Administration of 40% oxygen for 20 minutes
  - 17% decrease in cardiac output
  - 5% increase in arterial blood pressure

Thomas M, Malmcroma R, Shillingford J. Haemodynamic effects of oxygen in myocardial infarction. Brit Heart J 1965,27:401-407.

25

What Do We Know and Sometimes Forget Published in 1969

- Normal subjects
  - Hypoxia does not affect the availability of oxygen for myocardial
- metabolism until arterial oxygen saturation falls to as low as 50%
- Patients with coronary artery disease
  - Myocardial ischemia is not observed until oxygen saturation fell below 85%
  - Hyperoxia did not improve myocardial oxygen availability
  - Subset of patients with severe triple-vessel disease
- 6 minutes of high-flow oxygen reduced coronary blood flow sufficiently to induce myocardial ischemia

Neill WA. Effects of arterial hypoxemia and hyperoxia on oxygen availability for myocardial metabolism: patients with and without coronary artery disease. Am J Cardiol 1969, 24:166-171.

Bourassa MG, Campeau L, Bois MA, Rico O. The effects of inhalation of 100 percent oxygen on myocardial lactate metabolism in coronary heart disease. Am J Cardiol 1969, 24:172-177.

26

What Do We Know and Sometimes Forget Published in 2007

- Breathing 100% oxygen for 10 minutes
  - Increases vascular resistance in the left anterior descending artery
- by 23%
  - Diameter of the large conduit coronary arteries was not appreciably affected
  - Suggests vasoconstriction at the level of the myocardial
- microcirculation

McNulty PH, Robertson BJ, Tulli MA, Hess J, Harach LA, Scott S, Sinoway LI. Effect of hyperoxemia and vitamin C on coronary blood flow in patients with ischemic heart disease. J Appl Physiol 2007, 102:2040-2045

27

Effect of Hyperoxia on Myocardial Oxygenation and Function in Patients With Stable Multivessel Coronary Artery Disease

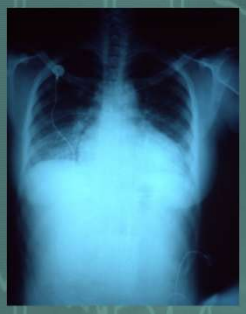
- Conclusions
- Patients with CAD and pre-existent myocardial injury who respond to hyperoxic challenge with strain abnormalities appear susceptible for hyperoxia-induced regional deoxygenation and deterioration of myocardial function.

DP Guensch, K Fischer, K Yamaji Effect of hyperoxia on myocardial oxygenation and function in patients with stable multivessel coronary artery disease. J Am Heart Assoc 9: e014730- 2020

28

Congestive Heart Failure (CHF)

- Patients with stable congestive heart failure
  - Administration of 100% oxygen for 20 minutes
    - Cardiac output decreased by 16%
    - Stroke volume decreased by 16%
    - Systemic vascular resistance increased



Haque WA, Boehmer J, Clemson BS, Leuenberger UA, Silber DH, Sinoway LI. Hemodynamic effects of supplemental oxygen in congestive heart failure. J Am Coll Cardiol 1996, 27:353-357.

29

STROKE

30

Stroke

- Reperfusion injury in stroke:
  - Free-radical release.
  - Neuronal breakdown (leading to more free-radicals).

31

Stroke

- "In 1994, the American Heart Association Stroke Council concluded that there were no data to support the routine use of supplemental oxygen in patients who had a stroke."
- "More recently, supplemental oxygen has been suggested to be potentially detrimental."

Panciolli AM, *et* al. Supplemental oxygen use in ischemic stroke patients: does utilization correspond to need for oxygen therapy. *Arch Intern Med*. 2002;162:49-52.

32

Stroke

- "In non-hypoxic patients with minor or moderate strokes, supplemental oxygen is of no clinical benefit."

Portier de la Morandiere KP, Walter D. Oxygen therapy in acute stroke. *Emergency Medicine Journal*. 2003;20:547-553

33

Stroke

- "Supplemental oxygen should not routinely be given to non-hypoxic stroke victims with minor to moderate strokes."
- "Further evidence is needed to give conclusive advice concerning oxygen supplementation for patients with severe strokes."

Ronning OM, Guldvog B. Should Stroke Victims Routinely Receive Supplemental Oxygen? A Quasi-Randomized Controlled Trial. *Stroke*. 1999;30:2033-2037.

34

Oxygen & Stroke

- No benefit in clinical performance scores or outcome
- Lower survival at 1 year in non-hypoxic patients with mild to moderate strokes
- Severe strokes and consequent hypoxemia trend towards increased mortality.

Padma MV, Bhasin A, Bhatia R, Garg A, Singh MB, Tripathi M, Prasad K. Normobaric oxygen therapy in acute ischemic stroke: a pilot study in Indian patients. *Ann Indian Acad Neurol* 2010, 13:284-288.

Ronning OM, Guldvog B: Should stroke victims routinely receive supplemental oxygen? A quasi-randomized controlled trial. *Stroke* 1999, 30:2033-2037.

35

NEONATES

36

Neonates

- The prevailing wisdom is that oxygen is harmful to most neonates.

37

Neonates

- Health hazards and morbidities associated with excess oxygen:
  - Aging
  - DNA damage
  - Cancer
  - Retinopathy of prematurity (ROP)
  - Bronchopulmonary dysplasia (BPD)

Sola A, Rogido MR, Deulofeut R. Oxygen as a neonatal health hazard: call for détente in clinical practice. *Acta Pediatrica*. 2007;96:801-812.

38

Neonates

- Consequences of neonatal resuscitation with supplemental oxygen:
  - Delayed onset of first cry and sustained respiratory effort.

39

Neonates

- 1,737 depressed neonates:
  - 881 resuscitated with room air
  - 856 resuscitated with 100% oxygen
- Mortality:
  - Room air resuscitation: 8.0%
  - 100% oxygen resuscitation: 13.0%
- Neonatal mortality reduced with room air resuscitation.

Davis PG, Tan A, O'Donnell CP, et al: Resuscitation of newborn infants with 100% oxygen or air: a systematic review and meta-analysis. *Lancet* 364:1329-1333, 2004

40

Neonates

- **Neonates resuscitated with room air had lower mortality in the first week of life (OR 0.70, 95% CI 0.50-0.98) and at 1 month and beyond (OR 0.63, 95% CI 0.42-0.94).**
- **Room air is superior to 100% oxygen for initial resuscitation.**

Rabi Y, Rabi D, Yee W: Room air resuscitation of the depressed newborn: a systematic review and meta-analysis. *Resuscitation* 72:353-363, 2007

41

Neonates

- Initiating resuscitation of preterm newborns with high oxygen (65% or greater) is not recommended (Class III: No Benefit, LOE B-R). B-R).

Part 13: Neonatal Resuscitation
2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care
Myra H. Wyckoff, Chair; Khalid Aziz; Marilyn B. Escobedo; Vishal S. Kapadia; John Kattwinkel; Jeffrey M. Perlman; Wendy M. Simon; Gary M. Weiner; Jeanette G. Zaichkin

42

Neonates

- It is reasonable to initiate resuscitation with air (21% oxygen at sea level).
- Resuscitation of preterm newborns of less than 35 weeks of gestation should be initiated with low oxygen (21% to 30%),

Part 13: Neonatal Resuscitation
2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care
Myra H. Wyckoff, Chair; Khalid Aziz; Marilyn B. Escobedo; Vishal S. Kapadia; John Kattwinkel; Jeffrey M. Perlman; Wendy M. Simon; Gary M. Weiner; Jeanette G. Zaichkin

43

Neonates

- Supplementary oxygen may be administered and titrated to achieve a preductal oxygen saturation approximating the interquartile range measured in healthy term infants after vaginal birth at sea level

Part 13: Neonatal Resuscitation
2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care
Myra H. Wyckoff, Chair; Khalid Aziz; Marilyn B. Escobedo; Vishal S. Kapadia; John Kattwinkel; Jeffrey M. Perlman; Wendy M. Simon; Gary M. Weiner; Jeanette G. Zaichkin

Targeted pre-ductal SpO2 after birth

• 1min	60-70%
• 2min	65-85%
• 3min	70-90%
• 4min	75-90%
• 5min	80-90%
• 10min	85-90%

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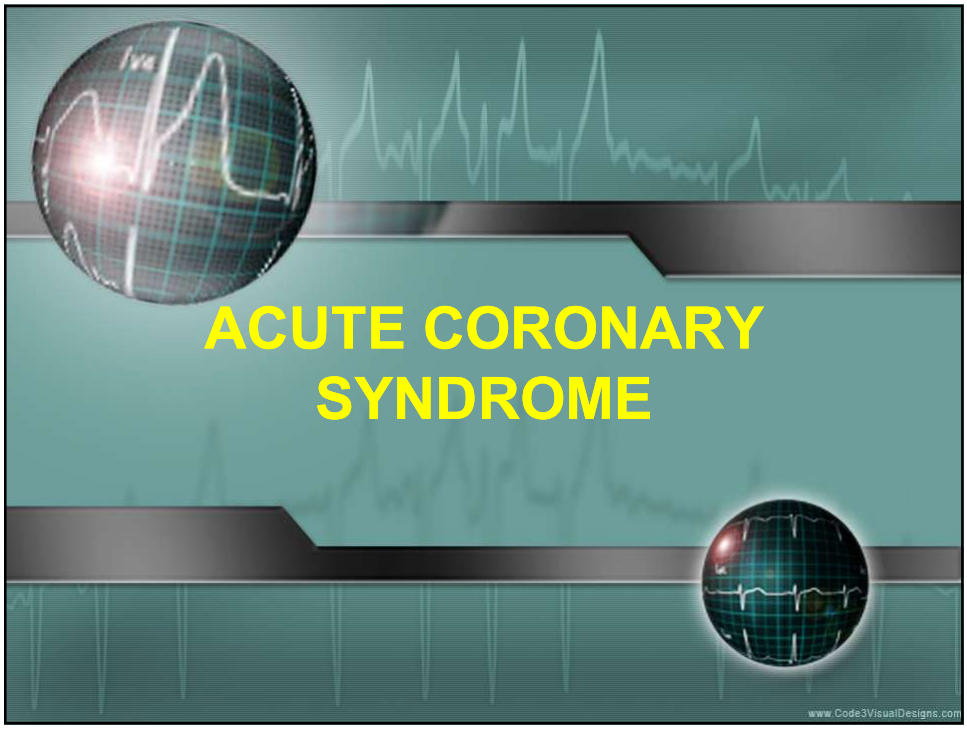

45

Acute Coronary Syndrome

- In patients with both acute coronary syndromes and stable coronary disease, oxygen administration may constrict the coronary vessels, lower myocardial oxygen delivery, and may actually worsen ischemia

.

Kones, R.,Oxygen therapy for acute myocardial infarction-then and now. A century of uncertainty. Am J Med. 2011 Nov;124(11):1000-5. doi: 10.1016/j.amjmed.2011.04.034

46

47

Post-Cardiac Arrest

- Post-cardiac arrest brain injury is a common cause of morbidity and mortality.
- Causes:
  - Limited tolerance of ischemia
  - Unique response to reperfusion

48

Post-Cardiac Arrest

- **Burst of ROS has been observed in cardiomyocytes in the first few minutes of reperfusion.**
- **Antioxidants and other cardioprotective measures diminish during the reperfusion burst.**

The oxidative burst, a rapid, transient, production of huge amounts of reactive oxygen species (ROS)

49

Post-Cardiac Arrest

- When resources are available to titrate the FiO_2 and to monitor oxyhemoglobin saturation, it is reasonable to decrease the FiO_2 when oxyhemoglobin saturation is 100%, provided the oxyhemoglobin saturation can be maintained at 94% or greater (Class IIa, LOE C-LD).

Part 8: Post–Cardiac Arrest Care
2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care
Clifton W. Callaway, Chair; Michael W. Donnino; Ericka L. Fink; Romergryko G. Geocadin; Eyal Golan; Karl B. Kern; Marion Leary; William J. Meurer; Mary Ann Peberdy; Trevonne M. Thompson; Janice L. Zimmerman

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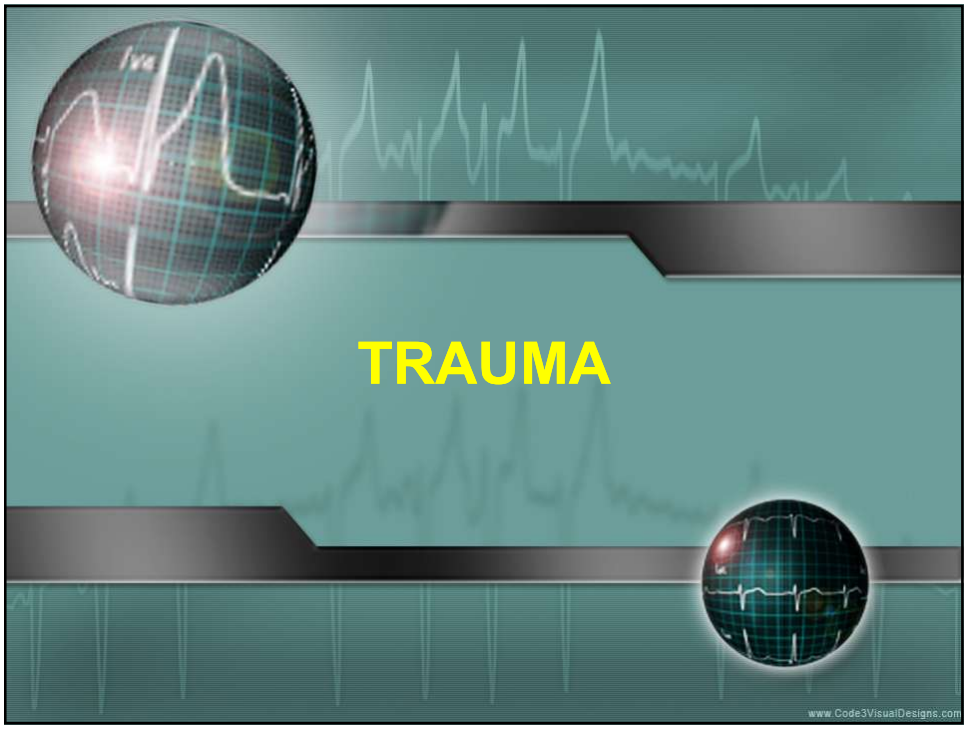


51

Trauma

- Charity Hospital (1/1/2000-9/30/2002):
- 5,549 trauma patients by EMS
  - 459 received assisted ventilation and excluded)
  - 5,090 remaining prehospital patients:
    - 2,203 (43.3%) received prehospital oxygen
    - 2,887 (56.7%) did not receive prehospital oxygen

52

Trauma

- **"Our analysis suggest that there is no survival benefit to the use of supplemental oxygen in the prehospital setting in traumatized patients who do not require mechanical ventilation or airway protection."**

Stockinger ZT, McSwain NE. Prehospital Supplemental Oxygen in Trauma Patients: Its Efficacy and Implications for Military Medical Care. *Mil Med*. 2004;169:609-612.

53

Sepsis

- Hyperoxia may impair oxygen deliver in sepsis
- Hyperoxia decreases whole-body oxygen consumption in critically ill patients
- Surviving Sepsis Campaign Guidelines Peripheral oxygen saturation should be maintained between 88% and 95% in patients with ARDS

Rossi P, Tauzin L, Weiss M, Rostain JC, Sainty JM, Boussuges A. Could hyperoxic ventilation impair oxygen delivery in septic patients? *Clin Physio Funct Imaging* 2007, 27:180-184.

Reinhart K, Bloos F, Konig F, Bredle D, Hanneman L. Reversible decrease of oxygen consumption by hyperoxia. *Chest* 1991, 99:690-694.

54

Sickle Cell Crisis

- Oxygen therapy has not been shown to affect the duration of pain crisis
- Oxygen has not been shown to be useful in patients with acute chest syndrome with normoxemia
- Oxygen should be administered only if hypoxemia is present

Rees DC, Olujohungbe AD, Parker NE, Stephens AD, Telfer P, Wright J; British Committee for Standards in Haematology General Haematology Task Force by the Sickle Cell Working Party. Guidelines for the management of the acute painful crisis in sickle cell disease. Br J Haematol 2003;120(5):744-752.

Zipursky A, Robieux IC, Brown EJ, Shaw D, O'Brodovich H, Kellner JD, et al. Oxygen therapy in sickle cell disease. Am J Pediatr Hematol Oncol 1992;14(2):222-228.

55

RECOMMENDATIONS FROM THE BRITISH THORACIC SOCIETY

56

British Thoracic Society

- **Do all breathless patients benefit from oxygen therapy?**
  - Amongst healthcare professionals there is a widespread belief that oxygen relieves breathlessness, yet there is no evidence that this is the case, providing that oxygen levels in the blood are normal (which is true in many serious illnesses, even if breathlessness is present). In fact, giving oxygen when blood saturation levels are normal will produce hyperoxia which may stimulate reflexes that actually reduce the blood flow to organs such as the heart and might therefore reduce the delivery of oxygen to these vital organs.

57

British Thoracic Society

- **Can the routine administration of high-dose oxygen to all sick patients have any harmful effects?**
  - Unnecessary oxygen therapy can hinder the efforts of healthcare professionals by delaying the recognition of patient deterioration due to the false reassurance that can be provided by a high oxygen saturation reading. Additionally, patients with some lung diseases, such as COPD, are sensitive to oxygen and an excess can have harmful consequences.

58

British Thoracic Society

- Oxygen is a treatment for hypoxemia, not breathlessness. (Oxygen has not been shown to have any effect on the sensation of breathlessness in non-hypoxemic patients.)

59

British Thoracic Society

- Generally, try to keep SpO_2 between 92-96%.
- Treat only documented hypoxemia unless patient critically ill.

60

Clinical Takeaways

- Avoid Routine Hyperoxia: Unless clinically indicated, avoid administering high concentrations of oxygen to critically ill patients.
- Monitor Oxygen Saturation: Use pulse oximetry to guide oxygen therapy and adjust as needed to maintain target saturation levels.
- Individualized Approach: Tailor oxygen therapy to the specific needs and conditions of each patient, considering factors such as underlying diseases and risk of hypercapnia.

61

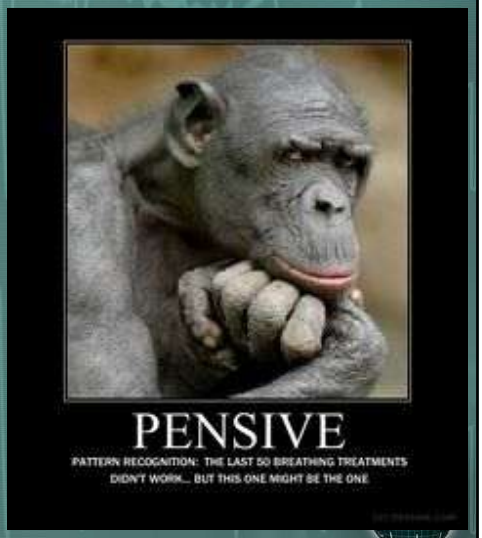
Take Home Message

- Oxygen should be treated like any other drug.
- It has benefits and risks.
- Empiric use is not a good practice.
- Use oximetry to guide care.

62

Take Home Message

- As this evolves, I suspect that the usage of oxygen will be curtailed.
- It is time to change from empiric therapy to focused therapy.



63

Summary

- MI – Avoid hyperoxemia
- CHF – Avoid hyperoxemia
- COPD – Avoid hyperoxemia (SpO2 88% - 92%)
- Pneumonia – Avoid hypoxemia
- Asthma – Avoid hyperoxemia
- Stroke – Avoid hyperoxemia
- Severe stroke – Avoid hypoxemia
- CPR – Avoid hyperoxemia
- Septic Shock – Avoid hyperoxemia
- Sickle Cell Crisis – No help unless hypoxemia present
- Hemorrhagic Shock – Avoid hypoxemia and hyperoxemia

64

Final Thoughts & Questions

Yeah, I'm really gonna jump on this STAT

Incentive spirometry order

65

Should a question arise in the future regarding the use of supplemental oxygen please contact me at the following:

Steve LeCroy, MA, CRT, EMTP
paraexp@aol.com
(727) 412-4153

66