Oxygen:
The good, the bad & the ugly

VTAS 2011
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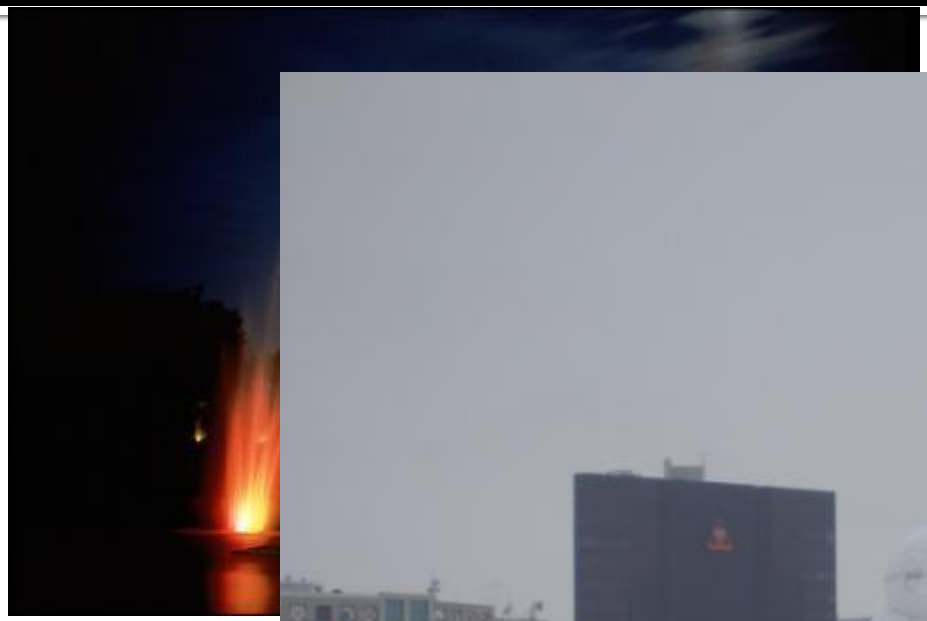
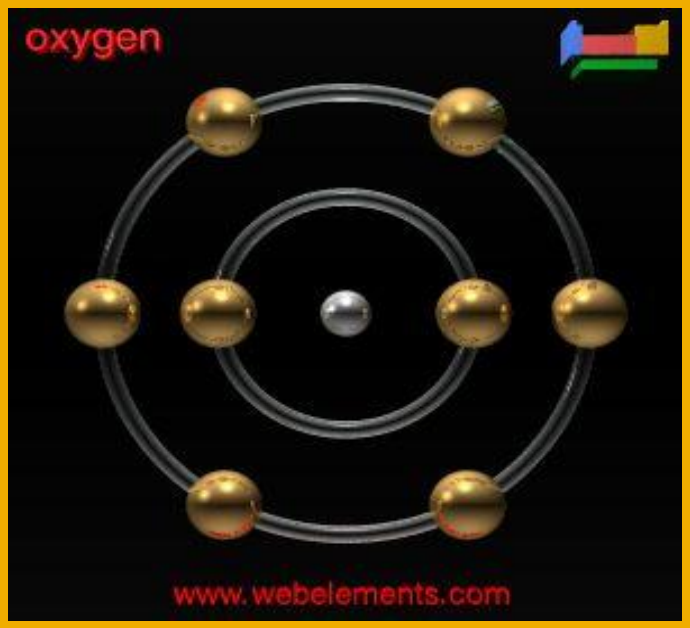
Greetings from Winnipeg!



Outline

- The tale of Dr Jekyll & Mr Hyde
- Oxygen – the gas
- Oxygen – toxicity
- Protection
- Safe oxygen practices

A primer on oxygen: A Jekyll & Hyde gas



The tale:

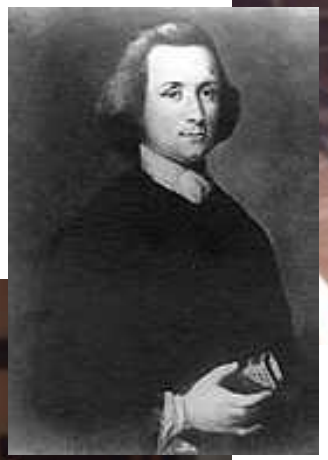
- **Dr. Henry Jekyll:** The good guy
  - A prominent doctor, tall and handsome. He is described as well respected and proper. The doctor belief that within each human being there exists two countering forces, good and evil, leads to his experiments that try to separate the two. This, however, was not done merely for scientific reasons, but also because he enjoyed escaping the confines of the respectable guise of Dr. Jekyll.

The tale:

- **Edward Hyde:** The bad guy
  - A small, deformed, disgusting man that is devoid of an apparent profession. He is often compared to animals, implying that he is not a fully evolved human being. Despite these horrific descriptions, Hyde is generally civilized in his interactions with others. Dr. Jekyll describes Hyde as "pure evil," and he menaces society at night.

The discovery of oxygen-1

- Priestly (1774)



Other accomplishments:

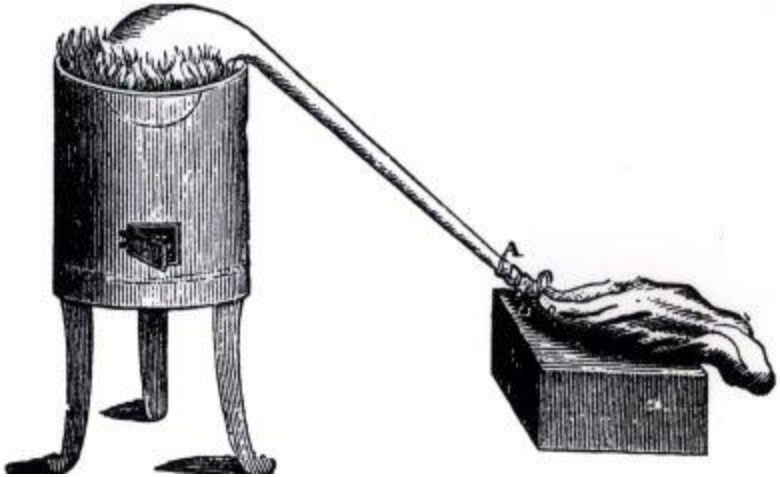
-carbonated water

-eraser

-Unitarianism

The discovery of oxygen-2

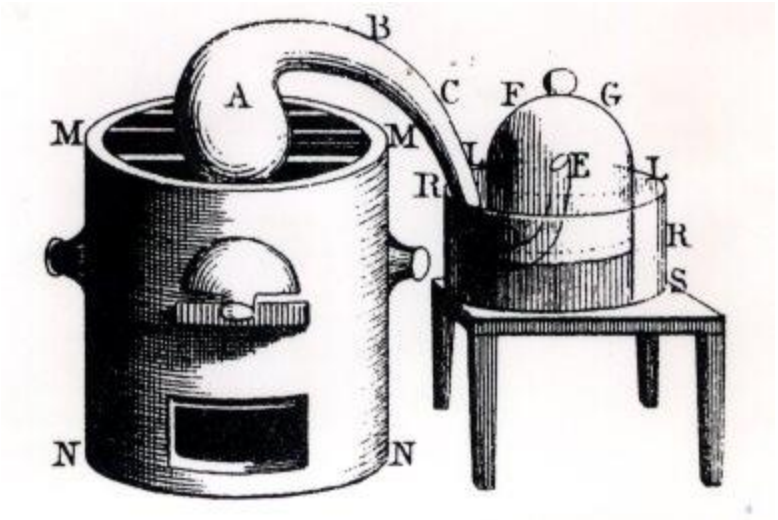
- Scheele (1772 -publication 1777)
  - First to report the action of light on silver salts which lead to modern photography
  - Discovered numerous elements



Died young from exposure to his experiments – tasting mercury!

The discovery of oxygen-3

- Lavoisier (1774)
- "founder of modern chemistry"
- "metric system"
- "plaster of Paris"



Little known fact – guillotined during French Revolution

Oxygen: the gas

- O_2 is technically "dioxygen"
- 99% of atmospheric O_2 is oxygen-16, 0.04% oxygen-17 and 0.2% oxygen-18
- Toxic, mutagenic
- Fire risk

Adaptation to an oxygen environment

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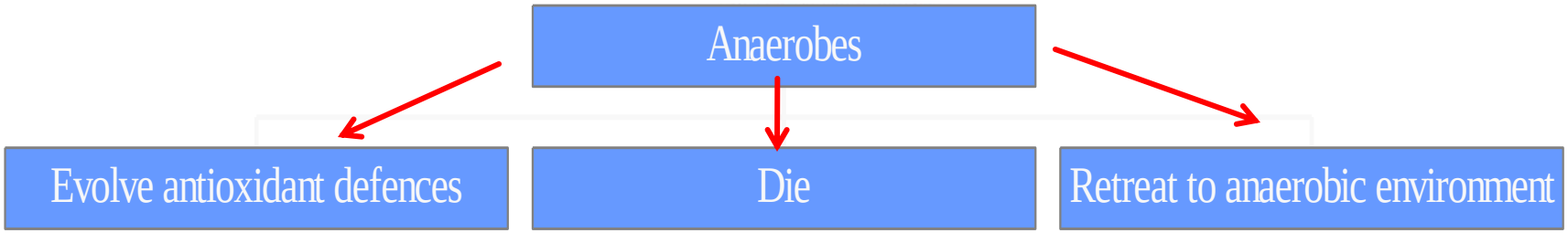


* oxygen stress

The role of oxygen in the human body

- Tissue respiration
  - Aerobic metabolism
  - 20 x more fuel
  - Mitochondria
  - Electron transfer
  - Process 'oxidative phosphorylation'

Effect of hypoxia/absence of oxygen

- Dyspnea/tachypnea/hypoventilation
- CVS: arrhythmias
- CNS: stupor, coma
- GI disturbances

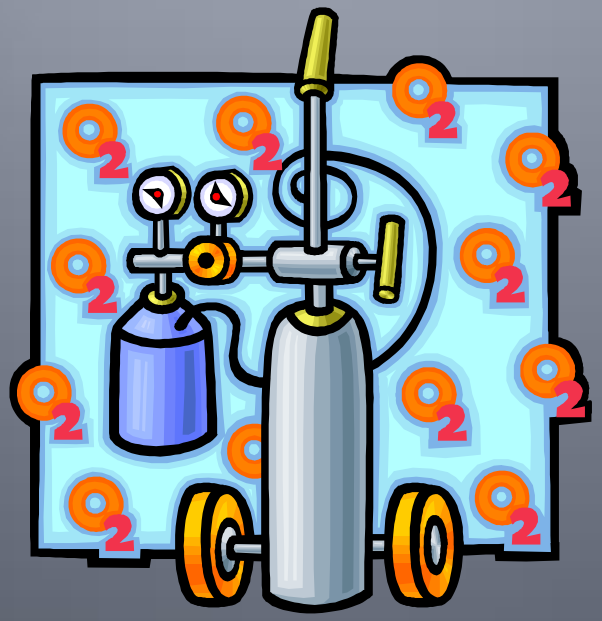
- Cyanosis is an unreliable indicator of oxygen status

Conclusion:
Oxygen is a Dr. Jekyll gas

- Oxygen provides fuel for energy
- Oxygen allows for multicellular organisms
- Oxygen is abundant

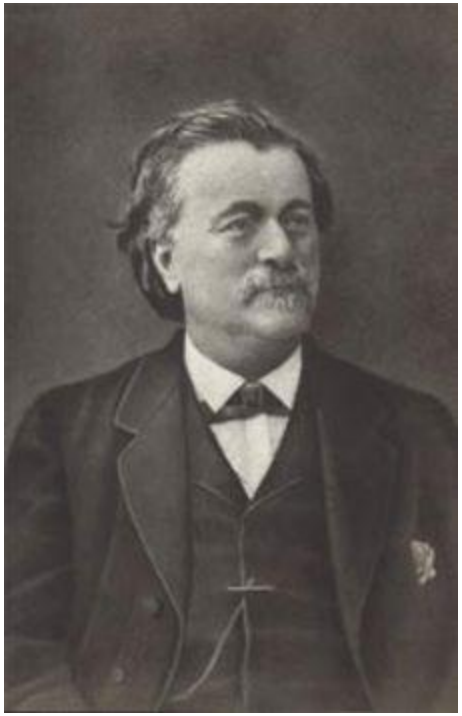
- Oxygen is good!!!

Danger ahead?



Dangers of oxygen therapy

- Fire
  - Combustion
- Pulmonary oxygen toxicity
  - ARDS
- Paul-Bert effect
  - CNS dysfunction



Oxygen is a toxic gas

- Priestly not only discovered oxygen but was the 1st to propose that it was toxic (c. 1774)
- Bert (100 yrs later) described "poisoning by oxygen" in animal experiments
- 1899, Smith demonstrated that oxygen damaged lungs

How is oxygen toxic?

- Initially thought that O_2 directly inhibited cellular enzymes
- Now know that O_2 toxicity is due to oxygen radicals which inactivate/inhibit enzymes

Studies on O_2 toxicity

- O_2 1.0 ATA: pulmonary symptoms within 12 hrs
- Substernal irritation, cough
- Increased A-a gradient, ↓ lung volumes and DLCO
- Lower limits of "safe" exposure not known but FiO_2 0.55 appears "safe" over 7 days and 0.40 over 40 days

Oxygen toxicity by oxygen therapy

High inspired O_2 concentrations

Pulmonary toxicity

↓

Tracheobronchitis

Epithelial damage

Endothelial damage

↓

Pulmonary edema

↓

Hypoxemia

Eye toxicity

↓

Retinal damage

CNS toxicity

↓

↓ Seizure threshold

↓

Convulsions

↓

Neuronal damage

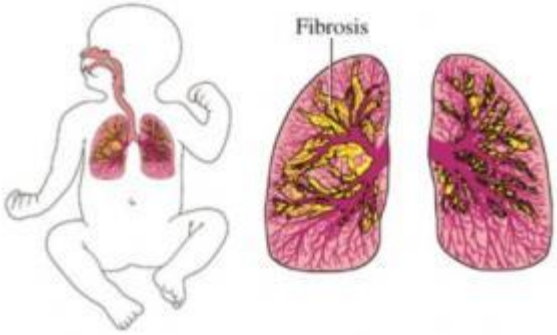
Death

Four clinical syndromes of pulmonary oxygen toxicity

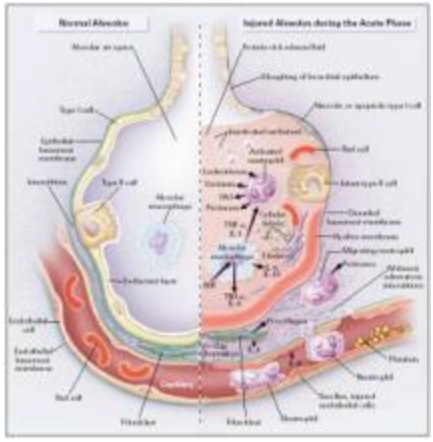
Absorption atelectasis

Tracheobronchitis

Bronchopulmonary dysplasia

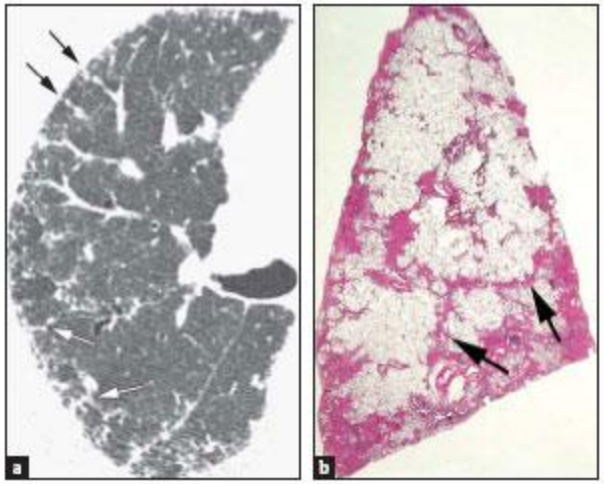


ARDS

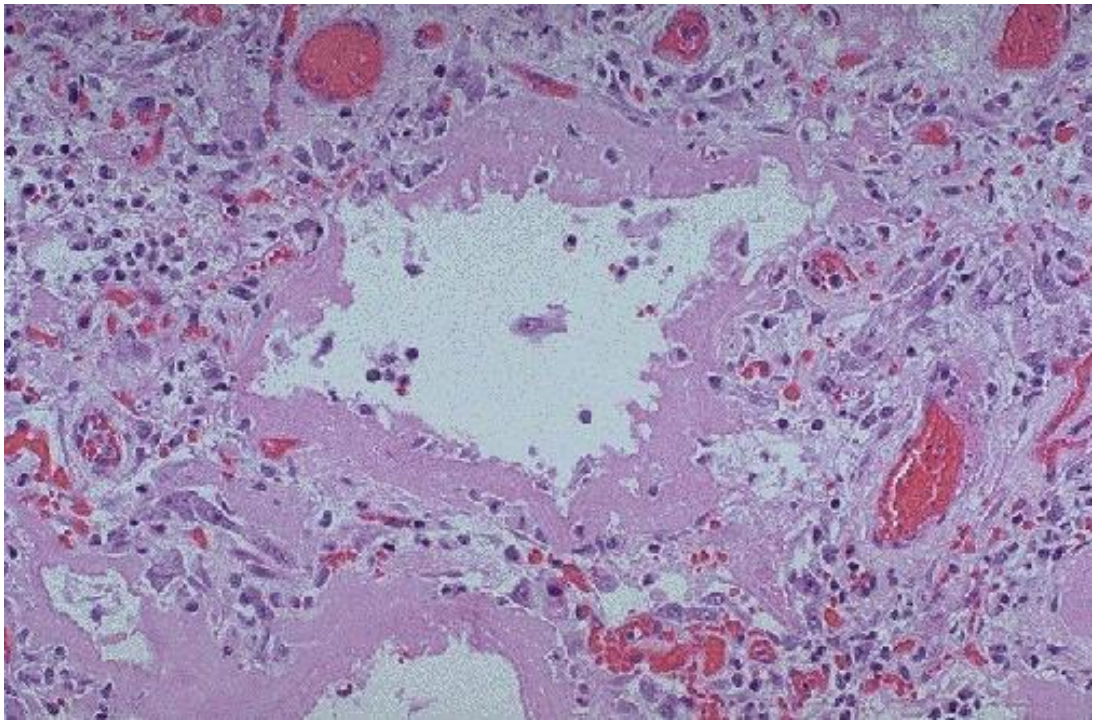


Pathology of oxygen toxicity

- Injury
- Inflammation
- Hyaline membrane formation
- Repair
  - Proliferation
  - Fibrosis



Pathology of oxygen toxicity



Oxygen is a toxic gas

What is it about oxygen that makes it so toxic?

The answer is in the chemistry of free radicals

Oxygen free radicals…

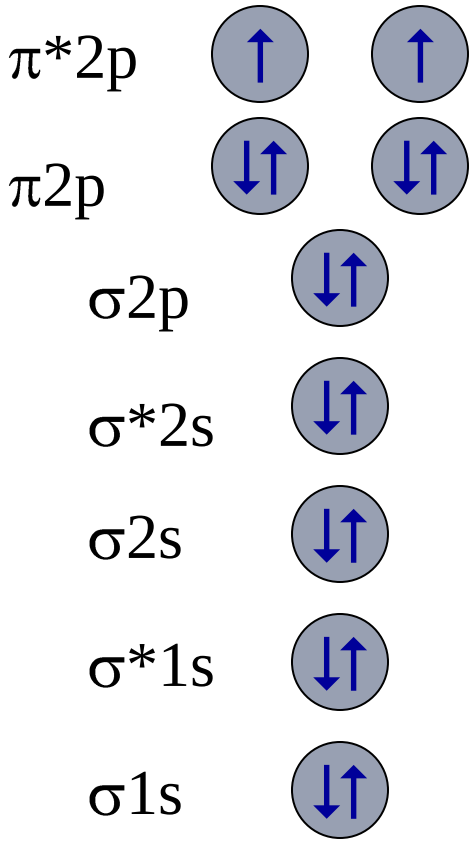
Oxygen free radicals

A discussion of free radicals (or what you really need to know)

A free radical is any species that is capable of independent existence that has ≥ 1 unpaired electrons

Oxygen is a free radical

Ground state O_2



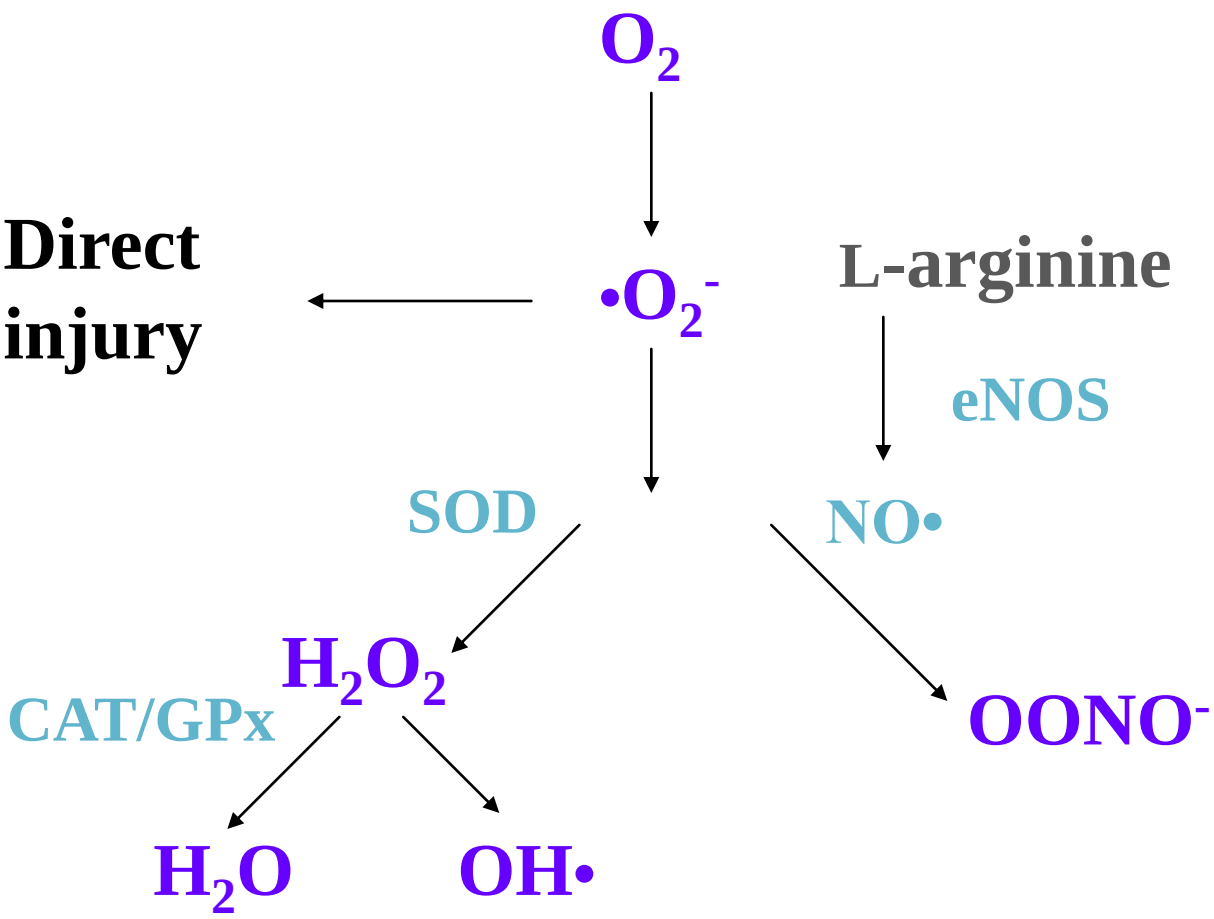
Superoxide theory of oxygen toxicity

Oxygen toxicity is due to an overproduction of superoxide

Where is it produced?

Enzymatic reactions
Auto-oxidation
Haem proteins
Mitochondria (electron transport)
Bacteria
Endoplasmic reticulum
Nucleus

The reactions of superoxide



Oxidative stress in lung injury

- **Important pathway in multiple clinical conditions**
  - Hyperoxia, inflammation, ischemia/reperfusion
  - Damage lipids, proteins, DNA
  - Adaptation to further oxidative stress
- **Mediated by reactive oxygen species (ROS)**
  - Normal byproduct of metabolism
  - Injury when ROS exceed antioxidant capabilities

Conclusion:
Oxygen is a Mr. Hyde gas

- Oxygen is a pollutant
- Oxygen is lethal to living cells
- Oxygen is a fire hazard

- Oxygen is bad!!!

Defending against oxygen toxicity

Antioxidants: Protection

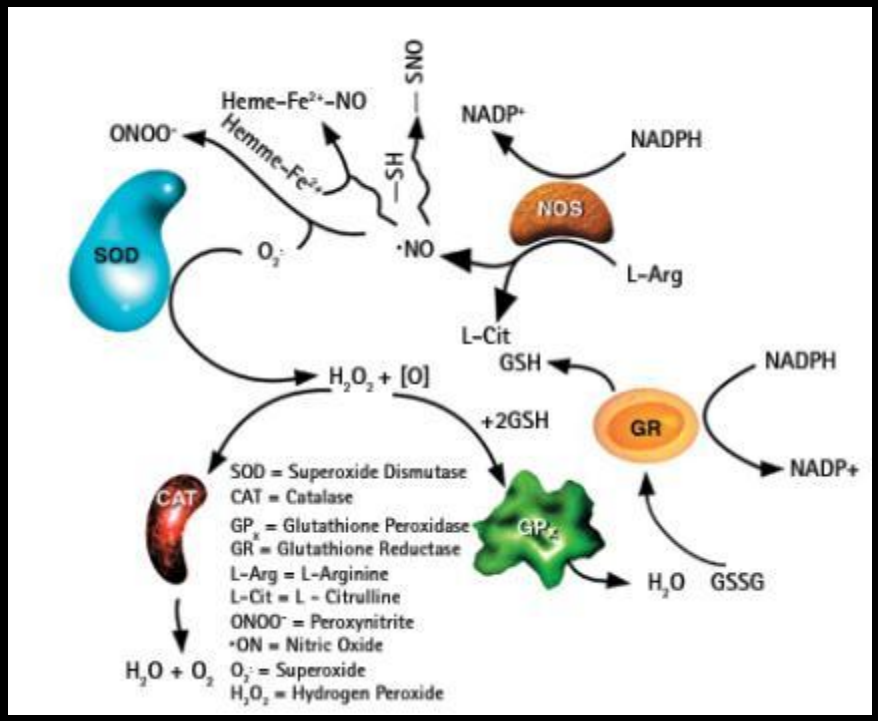
Non-enzymatic

- Synthesized LMW agents
  - Bilirubin
  - Melatonin
  - Coenzyme Q
  - Uric acid
- Dietary LMW agents
  - Ascorbic acid
  - α- tocopherol

Enzymatic

- Superoxide dismutases
- Catalases
- Glutathione peroxidases
- Other peroxidases
  - Cytochrome c peroxidase
  - NADH peroxidase
  - Horseradish peroxidase

Antioxidant protection



So how do we protect our patients from oxygen toxicity?

Safe oxygen practices

Safe prescribing practices!

Checklist for safe prescribing of oxygen

- How can inadequate tissue oxygenation be recognised?
- When is acute oxygen therapy appropriate and at what dose?
- Is outcome of disease improved?
- How is oxygen best delivered and is humidification necessary?
- What are the dangers of oxygen treatment?
- What assessment and monitoring are necessary?
- When should oxygen therapy be stopped?

What about resuscitation??

There is NO need to maintain high SpO2!!

Did we cover it all???

- The tale of Dr Jekyll & Mr Hyde √
- Oxygen – the gas √
- Oxygen – toxicity √
- Protection √
- Safe oxygen practices √

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