OXYGEN TOXICITY

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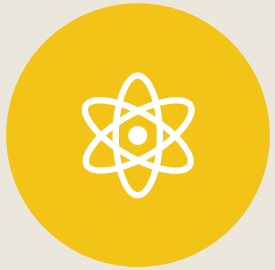
OBJECTIVES

- Why is oxygen toxicity such a big deal?
- Pathophysiology of oxygen toxicity
- Clinical manifestation
- Treatment options
- Differential diagnoses
- Prognoses

Why is Oxygen Toxicity Such A Big Deal?

- Oxygen is a drug
- Written order from a MD is needed
- Two groups of oxygen toxicity;
  - *Patient is exposed to very high concentrations of oxygen for a short duration*
  - *Patient is exposed to lower concentrations of oxygen but for a longer duration*
- Acute toxicity manifests generally with central nervous system (CNS) effects
- Chronic toxicity has mainly pulmonary effects.
- Severe cases of oxygen toxicity can lead to cell damage and death

INTRODUCTION

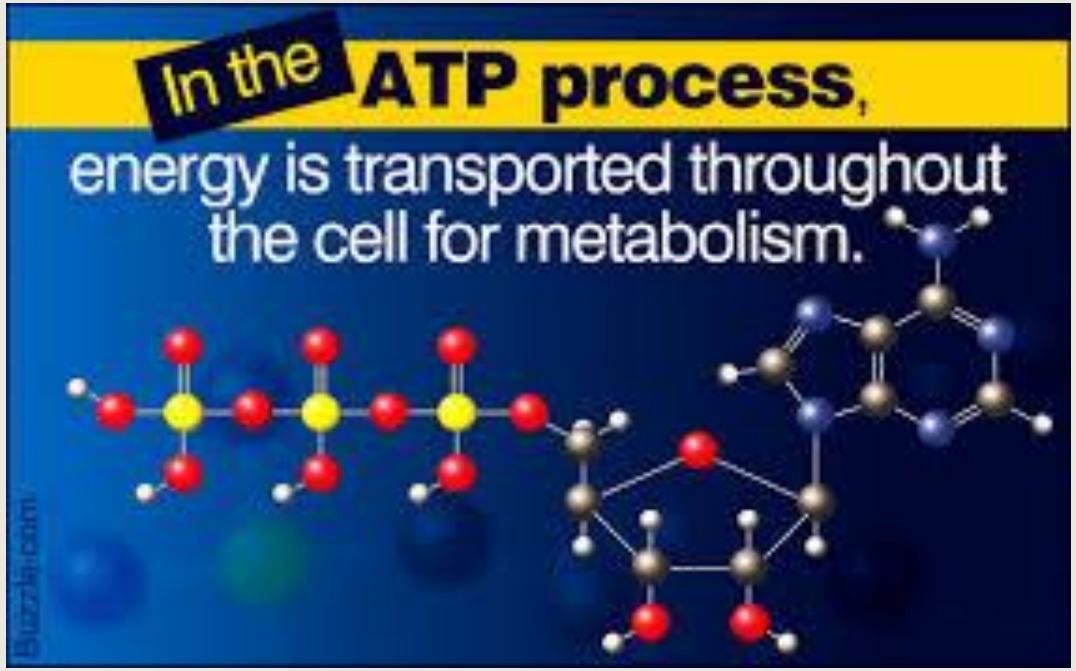


Oxygen is a chemical *element with symbol O and atomic number 8.*

By mass, oxygen is the *third-most abundant* element in the universe, after hydrogen and helium, comprising *about 21%* of atmospheric air.

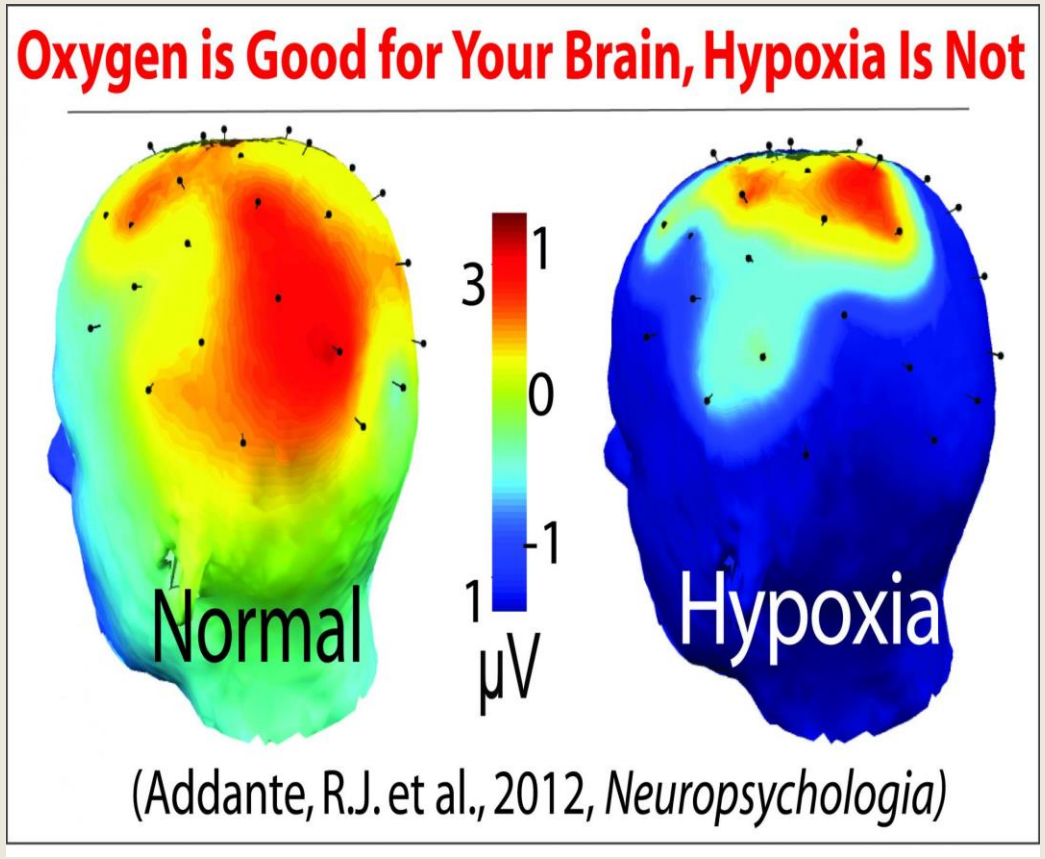
OXYGEN IS A DRUG AND IS PRESCRIBED!!

Oxygen therapy is the administration of O2 at a *concentration greater than a room air(21%)* with a goal of treating/preventing symptoms and manifestations of *hypoxia*.



Why do we need oxygen?

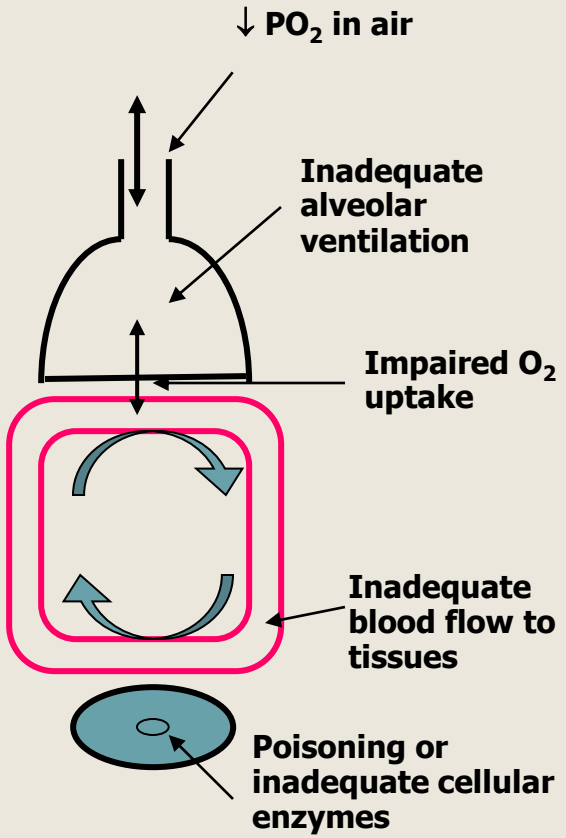
- The *aerobic metabolic* system functions using the *Krebs Cycle*
- Complex series of chemical reactions that use oxygen to *convert* nutrients (*carbohydrates*, *fats*, and *protein*) to *carbon dioxide* and adenosine triphosphate (*ATP*), an energy-rich compound.



INDICATIONS

- The main indication of O2 therapy is the treatment and prevention of Hypoxia.
- The brain loves Oxygen
- Between 30-180 seconds of oxygen deprivation, you may lose consciousness.
- At the one-minute mark, brain cells begin dying.
- At three minutes, neurons suffer more extensive damage, and lasting brain damage becomes more likely.
- At five minutes, death becomes imminent.
- At 10 minutes, even if the brain remains alive, a coma and lasting brain damage are almost inevitable.
- At 15 minutes, survival becomes nearly impossible.

CAUSES OF HYPOXIA



- Reduced partial pressure of oxygen in air.
- Inadequate alveolar ventilation.
- Impaired pulmonary uptake.

SIGNS OF HYPOXIA

Dyspnea .

Tachypnea.

Severe hypoxemia (decreased oxygen concentration in the blood)

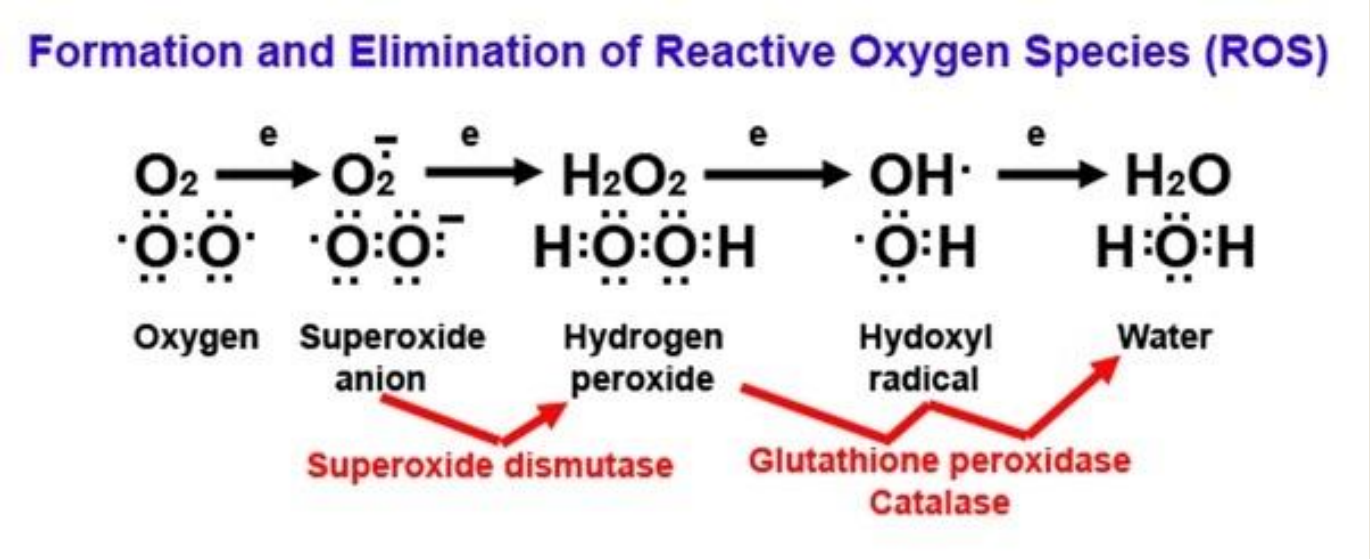
Pulmonary hypertension.

Cyanosis.

Normal Arterial Blood Gas

Value	Normal Range	Significance
pH	7.35 – 7.45	Reflects hydrogen ion concentration • <7.35 = **acidosis** • > 7.45 = **alkalosis**
$PaCO_2$	35 to 45 mmHg	Partial pressure of CO_2 in arterial blood • < 35 mmHg = **hypocapnia** **apnia**
PaO_2	80 – 100 mmHg	Partial pressure of O_2 arterial blood • < 80 mmHg = **hypo emia**
HCO_3^-	22 to 26 mEq/L	Bicarbonate concentration in plasma

MECHANISM OF OXYGEN TOXICITY



- Usually Reactive Oxygen Species (ROS) are *produced during normal physiological processes* like Electron Transport Chain(ETC),etc.
- The most produced ROS are:
- *Superoxide anion (O2-)*
- *Hydroxyl radical (OH•)*
- *Hydrogen peroxide (H2O2)*
- *Hypochlorous acid (HOCl)*

The Role of Anti-Oxidants

Under normal circumstances the ***body is able to handle*** the ROS produced using ***anti oxidants*** but can be ***overwhelmed*** incase of ***excessive production*** of ROS,hence toxic effects of O2.

Glutathione is the mother of all anti oxidants.

Others Anti-oxidants are ***catalase***,***superoxide dismutase***,***vitamin C,E***.

Etiology

Extended exposure can cause oxidative damage to cell membranes leading to the collapse of the alveoli in the lungs

Pulmonary effects can present as early as within 24 hours of breathing pure oxygen.

Symptoms of Oxygen Toxicity

Symptoms include pleuritic chest pain, substernal heaviness, coughing, and dyspnea secondary to tracheobronchitis and absorptive atelectasis which can lead to pulmonary edema.

Pulmonary symptoms typically abate 4 hours after cessation of exposure

CNS effects manifest with a multitude of potential symptoms including twitching of perioral and small muscles of the hand is a consistent feature.

If exposure to oxygen pressures is sustained tinnitus, dysphoria, nausea, and generalized convulsions can develop.

CNS toxicity is expedited by factors such as raised PCO_2, stress, fatigue and cold

Epidemiology

CNS symptoms secondary to oxygen toxicity is 2% with a seizure rate of 0.6%.

Oxygen toxicity to the CNS is known as the **Bert Effect**.

Pulmonary toxicity is referred to as the **Smith Effect**.

Incidence of displaying pulmonary symptoms with oxygen toxicity is 5%.

Preterm newborns are at risk for bronchopulmonary dysplasia with prolonged exposure to high concentrations of oxygen.

Chemotherapeutic agent **bleomycin** also increase the risk of oxygen toxicity

Pathophysiology

Oxygen-derived free radicals are the cause of oxygen toxicity.

Free radicals are generated due to the mitochondrial oxidoreductive processes and Phagocytes during the bacterial killing.

Free radicals create lipid peroxidations, especially in the cell membranes, subdue nucleic acids and protein synthesis, and mollify cellular enzymes.

Damages the pulmonary epithelium, inactivate the surfactant, form intra-alveolar edema, interstitial thickening, fibrosis, and ultimately lead to pulmonary atelectasis

Histopathology

Oxygen toxicity stimulates the development of histological changes in the lung. Pulmonary edema, congestion, intra-alveolar hemorrhage, and pulmonary injury

Surfactant interruption and epithelial injury initiate the expression of cytokines that activate inflammatory cells.

The heightened release of oxygen free radicals modifies normal endothelial function.

Microscopic examination display the alveoli in the lung filled with smooth to slight floccular pink material characteristic of pulmonary edema and congestion.

The capillaries in the alveolar walls are congested with many red blood cells.

Toxicokinetics

100% oxygen can be tolerated at sea level for about 24-48 hours without any severe tissue damage

Lengthy exposures produce definite tissue injury

Most patients' symptoms subside 4 hours after cessation of exposure

History and Physical

Symptoms may include disorientation, breathing problems, and visual changes such as myopia and cataract formation.

Central nervous system signs and symptoms:

Headache, Irritability and anxiety, Dizziness, Disorientation

Hyperventilation, Hiccups, Cold shivering, Fatigue

Tingling in the limbs, Visual changes such as blurring and tunnel vision ,Tinnitus and Hearing disturbances, Nausea, Twitching

Evaluation

Patients at risk for pulmonary oxygen toxicity should be monitored for oxygen saturation and elevated work of breathing.

Evaluated by pulmonary function testing and chest x-ray for acute respiratory distress syndrome (ARDS).

Eye exams assessing acuity and looking for lens opacification.

CNS toxicity manifests as tachycardia and diaphoresis.

Aborting a hyperbaric exposure can prevent seizure occurrence

Treatment / Management

- Managed by reducing the exposure to increased oxygen levels
- Manage O2 levels that alleviates tissue hypoxia is optimal in patients with ARDS and hypoxic neonates.
- Oxygen-induced seizures are self-limited and do not increase susceptibility to epilepsy.
- There is concern that oxygen-induced seizures could lead to damage but are felt to be benignant and like febrile seizures in children.
- Hyperbaric oxygen treatments, those at high risk may benefit from:
  - *anti-epileptic therapy*
  - *prolonged exposure*
  - *limited treatment pressure*
- Protocols for the avoidance of hyperoxia exist in fields where oxygen is breathed at higher-than-normal partial pressures.

Differential Diagnosis

Several conditions can be mistaken for oxygen toxicity.

Typically diagnosis is made clinically and can be confirmed with PaO2 (arterial oxygen levels).

The following conditions must be ruled out when clinically evaluating for oxygen toxicity

Carbon dioxide narcosis, Carbon monoxide poisoning, Hyperventilation, Toxin ingestion, Cerebrovascular event, Migraine, Seizure disorder, Infection, Multiple sclerosis, Hypoglycemia

Treatment Planning

Deliver Oxygen concentrations that alleviate symptoms

Oxygen toxicity can be influenced by a variety of conditions, procedures and drugs

Antioxidant enzymes, such as superoxide dismutase has been tried successfully

May lead to the progression of tolerance to subsequent hyperoxic exposure

Exogenous antioxidants, notably vitamin E and C have been found to lower the prevalence of retrolental fibroplasia in premature infants on hyperoxic therapy

Prognosis

- Adults,
  - *Studies show that with the removal of the inciting agent no long-term neurological damage occurs*
  - *Damage due to oxygen-induced pulmonary toxicity is reversible in most adults.*
- Infants,
  - *Those who have survived following an incidence of bronchopulmonary dysplasia will ultimately recover near-normal lung function*
  - *Likely to be more vulnerable to respiratory infections for the rest of their lives*
- Retinopathy of prematurity (ROP) in infants frequently reverses without intervention.
  - *When the disease has advanced to the stages requiring surgery, the results are generally good for the treatment of stage 3 ROP.*

Complications

Oxygen toxicity can cause a variety of complications affecting multiple organ systems.

CNS complications primarily include tonic-clonic convulsions and amnesia.

Pulmonary complications range from mild tracheobronchitis and absorptive atelectasis to diffuse alveolar damage that is indistinguishable from ARDS.

Ocular complications consist of reversible myopia, delayed cataract formation, and in children, retrolental fibrosis

Chronic obstructive pulmonary disease (COPD), status asthmaticus, poliomyelitis, or myasthenia gravis and in those with central respiratory depression from narcotic poisoning

Oxygen toxicity can cause carbon dioxide narcosis secondary to a loss in the hypoxemic drive and decrease in ventilation.

Managing patients on ventilators

According to the oxygen–hemoglobin dissociation curve, the goal of oxygen titration is to achieve a Pa_{02} in the range of 60–65 mm Hg, with Sa_{02} approximately 90%.

Critically ill patients often tolerate lower Pa_{02} levels (“permissive hypoxemia”)

Randomized multicenter study compared a conservative oxygenation strategy for mechanically ventilated patients

- Randomized, controlled, unblinded, international multicenter study compared oxygenation delivery strategy
  - *Sp_{02} 88–92% versus Sp_{02} > 96%*
  - *357 mechanically ventilated patients for an expected duration of more than 2 days*
  - *104 patients were enrolled.*
- They comparing low oxygen levels (88-92%) versus higher levels (>96%)
- Development of multiple organ dysfunction, worsening lung injury, and other adverse clinical outcomes were similar in two groups.

Summary

- Oxygen is safe if used correctly
- Understand the CNS and Pulmonary effects of Oxygen Toxicity
- Know how to manage your patients with Permissive Hypoxemia

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