Oxygen toxicity and it's mechanism

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Outline

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- Protective mechanisms
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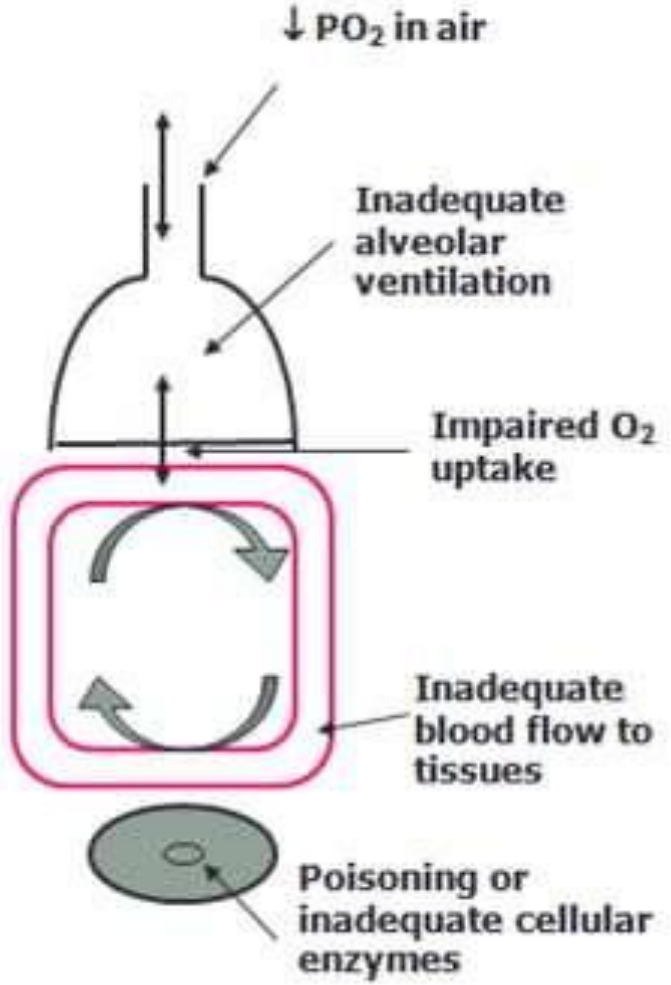
Introduction

- 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.
- aerobic metabolic system functions using the Krebs Cycle, a complex series of chemical reactions that use oxygen to convert nutrients to CO2 and ATP, an energy-rich compound.
- A double edge sword !
- A friend or a foe ?

Indication

- The main indication of O2 therapy is treatment/prevention of Hypoxia



Definition

- Oxygen toxicity is a condition resulting from the harmful effects of breathing molecular oxygen (O_2) at increased partial pressure.
- Effect of hyperoxia
- Mostly associated with long term oxygen therapy or hyperbaric oxygen therapy
- Like any other medication also has its side effects

High risk groups

- **Long term ventilation with high Fi02**
- those on high concentrations of supplemental oxygen for long duration (100% oxygen for >8-12 hrs)
- Infants and neonates getting 100% Oxygen for >2-3 hrs.
- Premature babies
- patients on mechanical ventilation with exposure to levels of > 50%
- exposed to chemicals that increase risk for O2 toxicity like chemotherapeutic agent bleomycin
- undergoing hyperbaric oxygen therapy.
- underwater divers

Factors on which toxicity depends

- Pressure
  - Normobaric hypoxia
  - Hyperbaric hypoxia
- Time of exposure
  - Fio2 > 60% longer than 36 hrs
  - Fio2>80%longer than 24 hrs
  - Fio2>100%longer than 12hrs
- Oxygen concentration

Mechanism

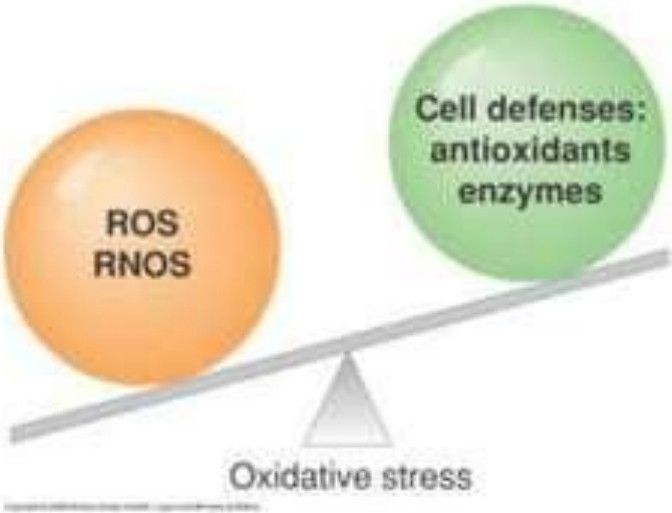
- Partial reduction of oxygen by one or two electrons to form reactive oxygen species,
- most commonly produced ROS are:

-Superoxide anion (O_2^-)

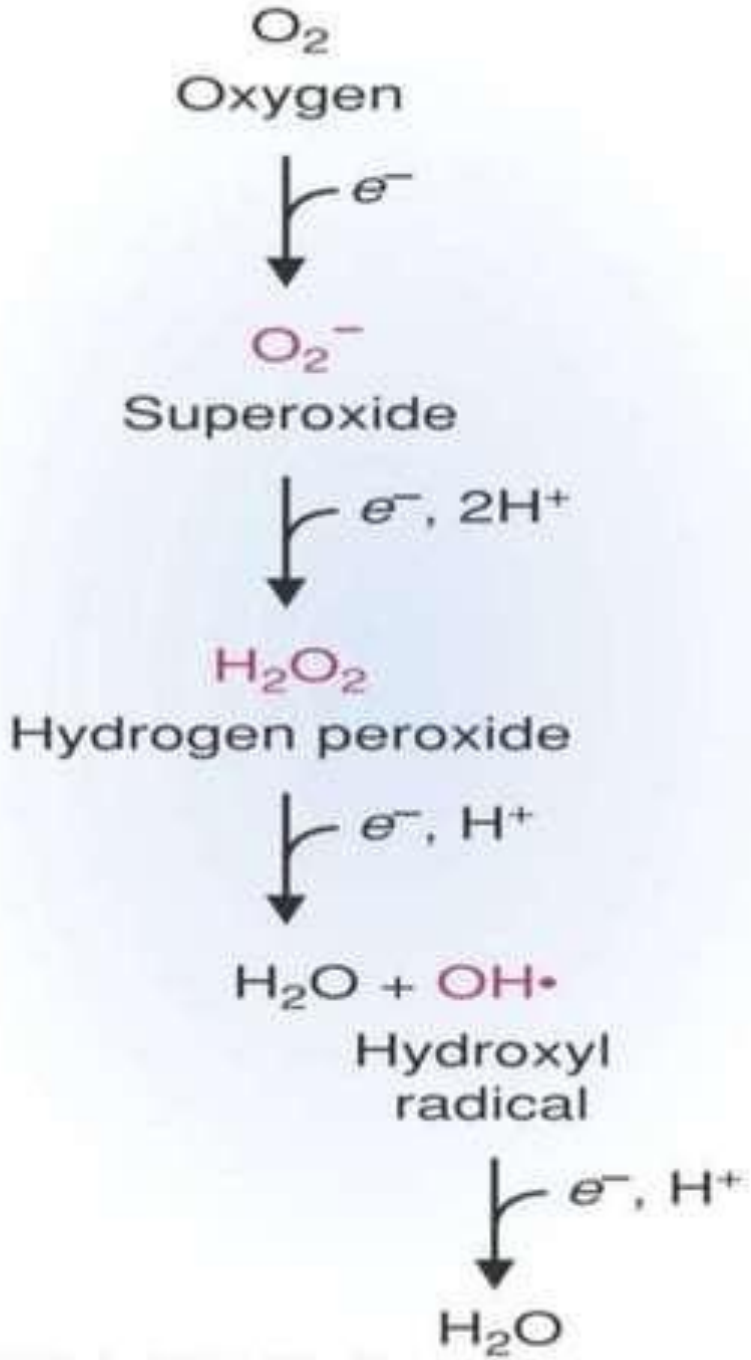
-Hydroxyl radical (OH•)

-Hydrogen peroxide (H_2O_2)

-Hypochlorous acid (HOCl)



ELECTRON TRANSPORT CHAIN



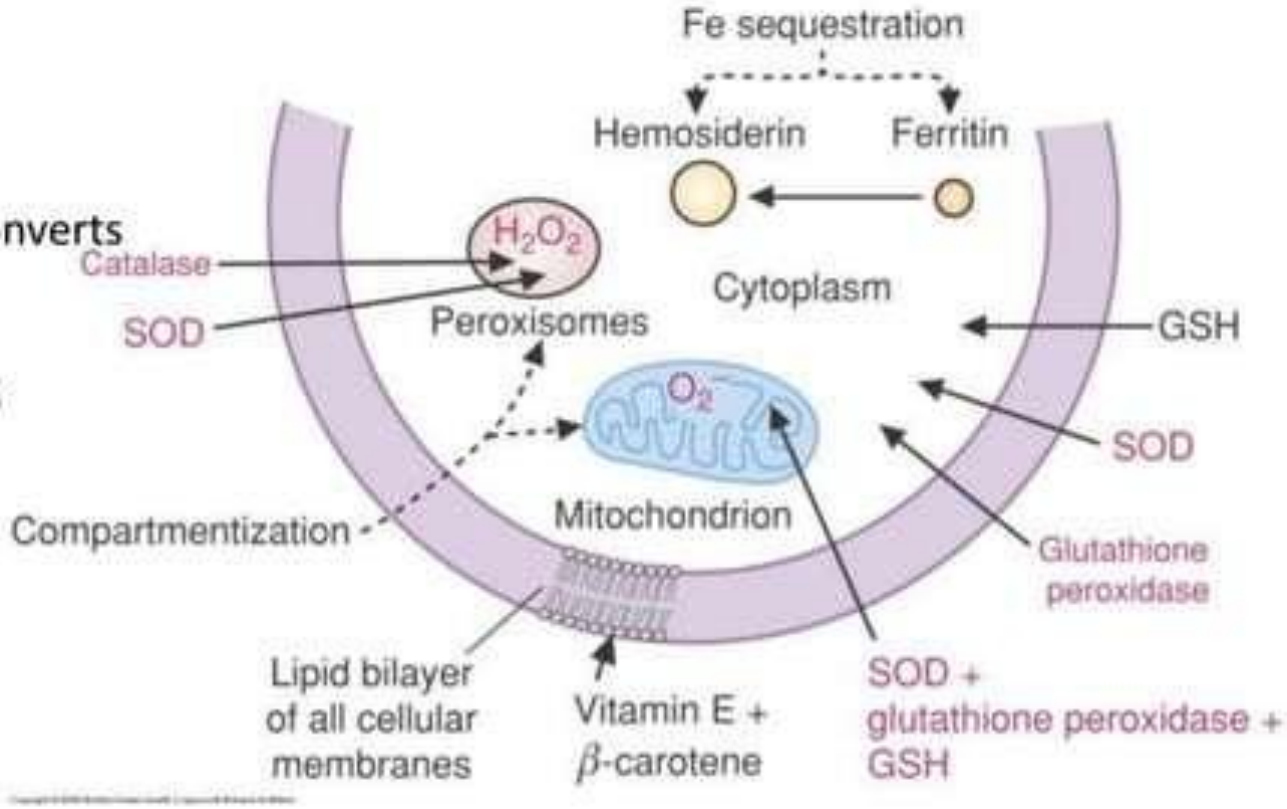
Protective factors

- 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 → toxic effects of O2.
- Glutathione is most effective anti oxidants.
- Others : catalase,superoxide dismutase, vitamin C& E

Protective mechanisms of the body

- ❑Antioxidant scavenging enzymes (red).
- ❑Nonenzymatic antioxidants (free radical scavengers).
- ❑Compartmentalization.
- ❑Repair of damaged components.
- ❑Metal sequestration.

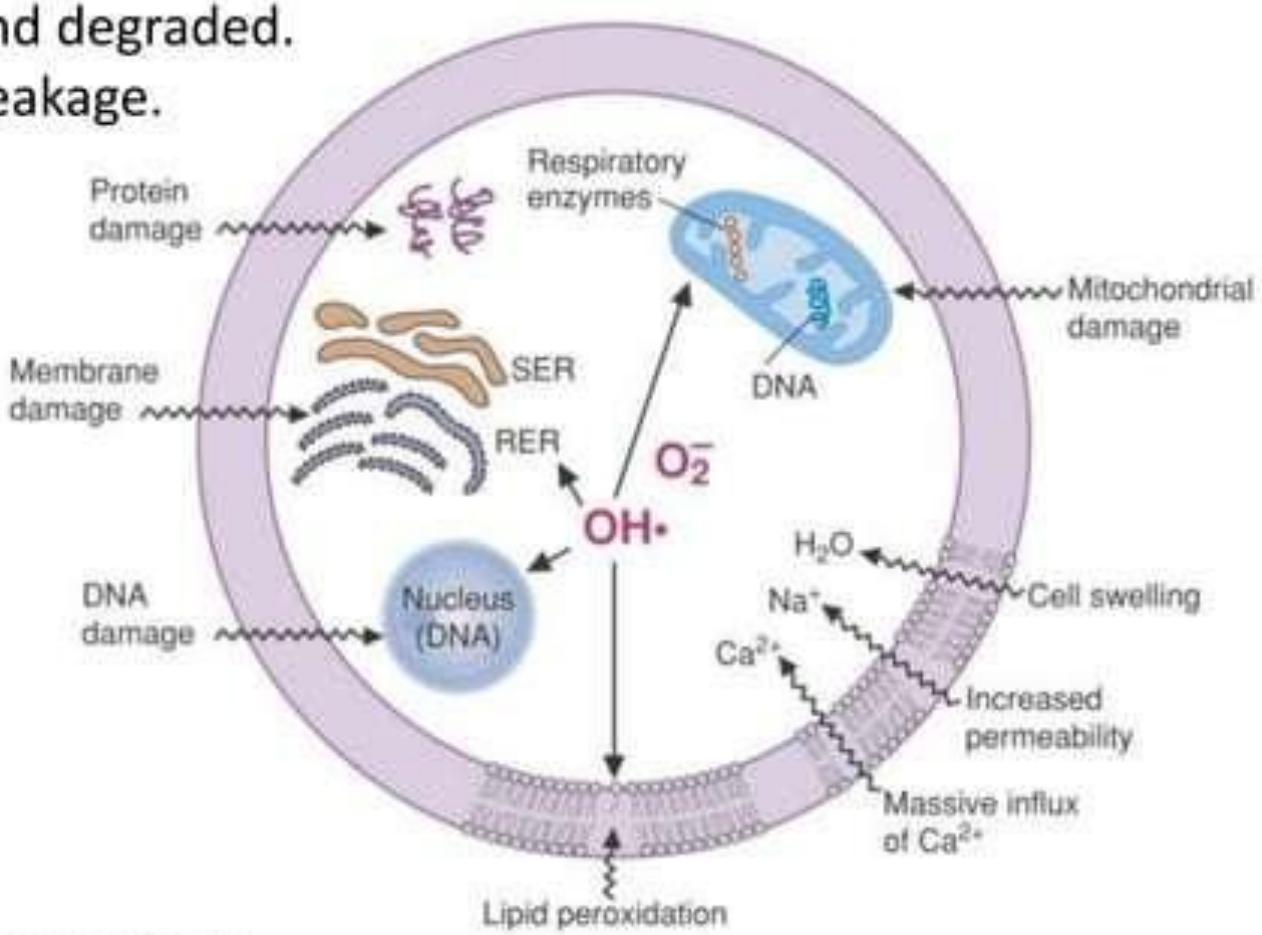
SOD = superoxide dismutase converts O2- to H2O2
GSH = glutathione
Catalase=reduces H2O2 to H2O

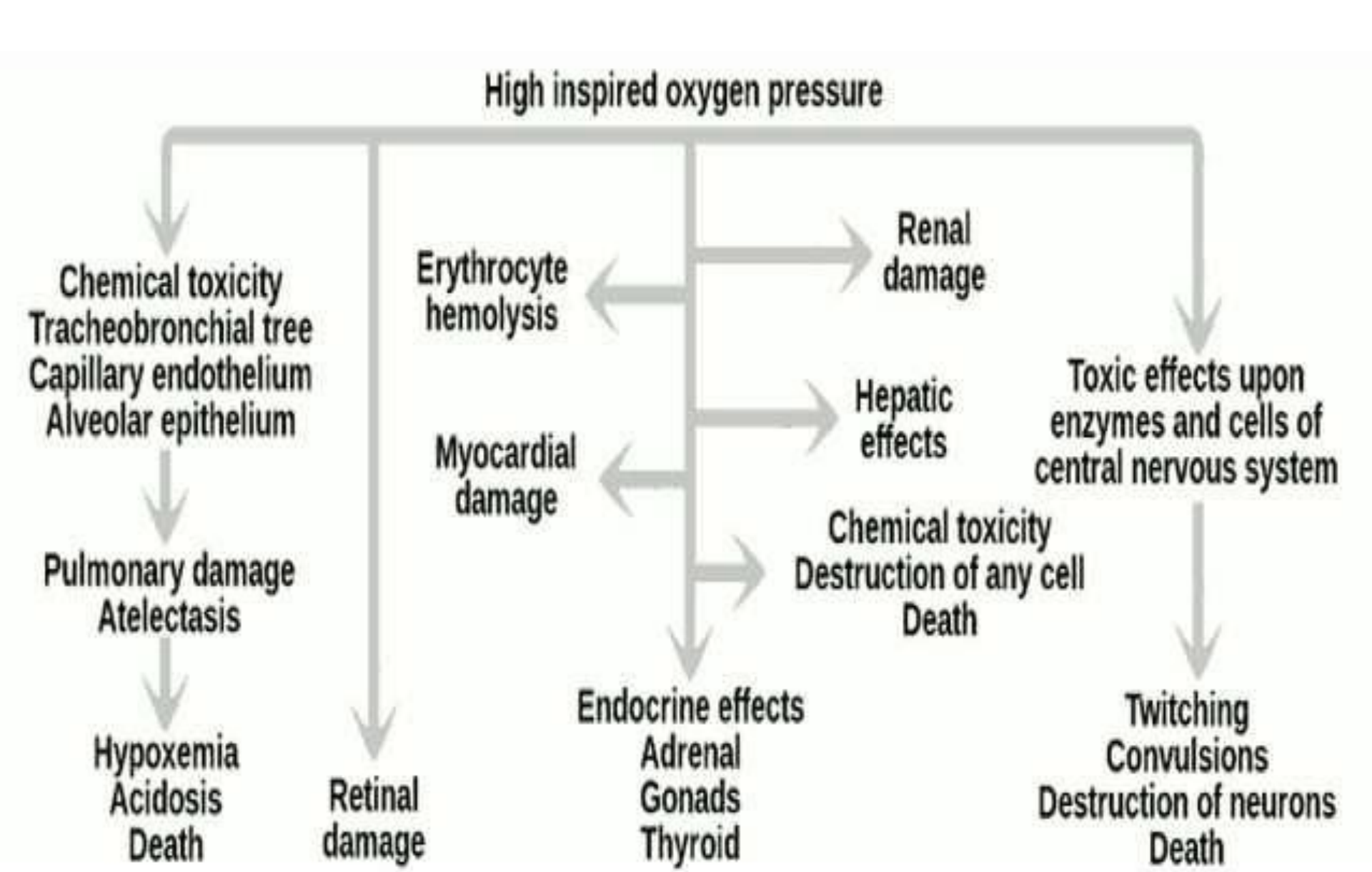


Harmful effects of these radicals…

Oxygen radicals react with cell components:

- Lipid peroxidation of membranes.
- Increased permeability → influx Ca^{2+} → mitochondrial damage.
- Proteins oxidized and degraded.
- DNA oxidized → breakage.





Systemic effects of oxygen toxicity

Complications of oxygen toxicity

- carbon dioxide narcosis
  - in patients with lung ailments such as COPD, Status asthmaticus, weak respiratory muscles or with central respiratory depression
  - Raised intracranial tension; clinically manifesting by sweating, twitchings, drowsiness, convulsions, papilloedema and coma

CNS effects

- Paul Bert effect
  - first described by Paul Bert in 1878
  - showed that oxygen was toxic to insects, fungi, germinating seeds, birds & other animals
- initially visual changes (tunnel vision), tinnitus, nausea, twitching (especially of the face), behavioral changes (irritability, anxiety, confusion), and dizziness.
- Convulsions : tonic-clonic type
- Unconsciousness

Respiratory effects

- Lorrain Smith effect
  - first described by J. Lorrain Smith in 1899
  - discovered in experiments in mice and birds that 0.43 bar (43 kPa) had no effect but 0.75 bar (75 kPa) of oxygen was a pulmonary irritant
- Reduction in the vital capacity of the patient is an indicator to monitor pulmonary toxicity
- Dyspnea
- Absorption atelectasis
  - presence of significant partial pressures of inert gases, typically nitrogen, will prevent this effect

Pulmonary efects

- ARDS :
  - diffuse alveolar damage
  - bubbling rales, fever, and hyperemia of the nasal mucosa
  - Pulmonary function measurements are reduced, X-ray changes
- Tracheobronchitis : mild tickle on inhalation and progresses to frequent coughing
- Bronchopulmonary dysplasia in neonates

Ocular effects

- Myopia
- Cataract
- Retinal detachments
- Retrolental fibroplasia/retinopathy of prematurity (ROP)
  - observed via an ophthalmoscope as a demarcation between the vascularised and non-vascularised regions of an infant's retina

Hyperbaric oxygen

- Delivering Oxygen at above 1 atm.
- In special hyperbaric chambers
- In decompression sickness and severe carbon monoxide poisonings
- Uncommon uses : Ischemia, cyanide poisonings, infections
- CNS and pulmonary symptoms manifest above 2 atm
- Pressure >2.8 atm with 100% O2 and >6atm with air is not advisable
- One therapy should be <2 hours and total duration should not exceed >5 hrs.

Hyperbaric oxygen toxicity

- Pulmonary : ARDS
- CNS : seizures preceded by facial numbness, twitching, unpleasant olfactory and gustatory sensation
- Eye : myopia, nuclear cataract, Retrolental fibroplasia
- Abnormal RBC morphology
- Avascular necrosis of bone/ dysbaric osteonecrosis
- Ear : Serous Otitis media
- Barotrauma

Differential diagnosis

- If epilepsy or hypoglycemia is ruled out , a seizure occurring in the setting of breathing oxygen at partial pressures > 1.4 bar (140 kPa) suggests a diagnosis

- If ECHO rules out CHD or PAH then in an infant who received O2 for long term whose breathing does not improve with time, blood tests and x-rays may be used to confirm BPD.

Differential diagnosis

- Diagnosis of ROP in infants ia made by the clinical setting of Prematurity, LBW and a history of oxygen exposure

Management

- Seizures
  - removing the mask from the patient
  - dropping the partial pressure of oxygen inspired below 0.6 bar
  - Manage in the line of status epilepticus
- Bronchopulmonary dysplasia or ARDS
  - lowering the fraction of oxygen administered
  - reduction in the periods of exposure
  - an increase in the break periods where normal air is supplied.
  - bronchodilators and pulmonary surfactants

Management

- BPD CONTD…
  - Where supplemental oxygen is required for treatment of another disease (particularly in infants), a ventilator may be needed to ensure that the lung tissue remains inflated.
- ROP
  - may regress spontaneously
  - cryosurgery and laser surgery have been shown to reduce the risk of blindness
- Retinal detachment
  - scleral buckling and vitrectomy surgery

Prevention

- FiO2 should be <60% in patients in mechanical ventilator
- ROP
  - monitoring of blood oxygen levels in premature infants receiving oxygen to balance hypoxia and ROP
  - preventable by screening
  - Current guidelines require that all babies of less than 32 weeks gestational age or having a birth weight less than 1.5 kg should be screened for ROP at least every 2 weeks

Prevention

- BPD
  - reversible in the early stages
  - break periods on lower pressures of oxygen
- Exogenous antioxidants especially vitamin E and C may be used prophylactically in high risk infants
- In divers
  - taught to calculate a maximum operating depth for oxygen-rich breathing gases
- H/O fever or seizure : relative contraindication to hyperbaric oxygen treatment

Take home message

- As the management of the toxicity is purely supportive, prevention and monitoring for early recognition is of great importance
- O2 therapy should be used only if there are confirmed indications.
- Causative problem of Hypoxia should be identified and intervened appropriately-giving O2 alone is not a solution.
- Use of appropriate Pulse oximeter size to age.
- Close monitoring of the pts on O2 therapy(i.e O2 saturation level)

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THANK YOU