RS MODULE
PHYSIOLOGY (LECTURE 9)

Hypoxia and Cyanosis

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Hypoxia

Hypoxia

Decreased oxygen supply to tissues (O_2 deficiency at tissue level).

Hypoxaemia

Decreased oxygen tension in blood (O_2 deficiency in the blood).

Types of Hypoxia

1. **Hypoxic hypoxia.**
2. **Anaemic hypoxia.**
3. **Stagnant hypoxia.**
4. **Histotoxic hypoxia.**

I. Hypoxic hypoxia

It means decreased oxygen supply to tissues secondary to **defective oxygenation** of blood in the lungs (i.e. **hypoxaemia).**

Causes:

1. Breathing air containing less oxygen:

- At the sea level in closed **badly ventilated spaces**.
- At **high altitudes** due to low oxygen tension.

2. All factors interfering with ventilation:

- **Air way obstruction** by a foreign body or bronchial asthma.
- **Paralysis of respiratory muscles** e.g. poliomyelitis.
- **Chest wall injury or deformities** as in rickets.
- The **presence of air** (i.e. pneumothorax) or fluid (i.e. hydrothorax, pyothorax, or haemothorax) in the **pleural cavity.**

3. Respiratory centre depression e.g. morphine toxicity.

4. Decreased lung perfusion e.g. thrombosis of pulmonary artery.

5. All factors interfering with pulmonary gas exchange (i.e. **diffusion**):

- **Pulmonary edema**
- **Lung (pulmonary) fibrosis** (↑ thickness of pulmonary membrane).
- **Emphysema** (↓ surface of pulmonary membrane).

6. Right to left shunt as blood **bypasses** the lungs as in atrial septal and ventricular septal defects.

Blood Changes of hypoxic hypoxia:

Parameter	Arterial	Venous
O_2 tension	Decreased	Decreased
O_2 content	Decreased	Decreased

II. Anaemic hypoxia

It **means** decreased oxygen supply to the tissues **secondary to decreased haemoglobin** (Hb) content of blood or **impaired haemoglobin function.**

Causes:

- Decreased Hb content as in **all types of anaemia**.
- Impaired Hb function (i.e. **abnormal Hb**); where Hb content is normal but Hb is unable to carry oxygen.
- **Examples of abnormal Hb**
  - **Methemoglobin.**
  - **Sulphhemoglobin.**
  - **Carboxyhaemoglobin**

Examples of abnormal Hb:

A. Methemoglobinaemia:

- The normal ferrous iron of Hb (ferrous protoporphyrin) is oxidised to ferric by nitrites or chlorates and hence, cannot give its oxygen to tissues.

B. Sulphhemoglobin:

Excessive fermentation and putrefaction of food in the gut as in intestinal obstruction → formation of hydrogen sulphide (H_2S) → absorbed and reacts with Hb to form sulphhaemoglobin which is **unable** to carry oxygen.

C. Carboxyhaemoglobin: (in Carbon Monoxide; CO Poisoning)

- CO combines with haemoglobin to form carboxyhaemoglobin at the same site of oxygen thus preventing oxygen carriage. It is **dangerous** because:

a) The affinity of Hb for CO is **210** times that for oxygen.

b) Carboxyhaemoglobin formed shifts the oxygen dissociation curve of the remaining oxyhaemoglobin to the **left** i.e. it **hardly gives** its oxygen to the tissues

Blood Changes of anaemic hypoxia

Parameter	Arterial	Venous
Oxygen tension	Normal	Decreased
Oxygen content	Decreased	Decreased

III. Stagnant hypoxia

Definition: Decreased oxygen supply to the tissues secondary to marked **decrease** of **blood flow** **(blood stagnation)** to the tissues.

Causes:

- **Generalized**: as in congestive **heart failure** or increased blood viscosity.
- **Localized**: as in **obstruction** of arterial blood supply to a limb by;
  - Vasospasm as in Raynaud's disease.
  - Thrombosis or embolism.

Blood Changes of stagnant hypoxia

Parameter	Arterial	Venous
Oxygen tension	Normal	Decreased
Oxygen content	Normal	Decreased

IV. Histotoxic hypoxia

Definition: decreased oxygen supply to the tissues due to **inability** of the tissues to **utilize** and so to **extract** oxygen from arterial blood secondary to **defect** in **oxidative enzymes** (e.g. dehydrogenase and cytochrome oxidase).

Causes:

- **Cyanide poisoning**: Cytochrome oxidase is blocked by cyanides
- **Alcohol intoxication**: Alcohol blocks the dehydrogenase enzyme.

Blood Changes of histotoxic hypoxia

Parameter	Arterial	Venous
Oxygen tension	Normal	Increased
Oxygen content	Normal	Increased

Cyanosis

Definition:

Bluish discoloration of skin and mucous membranes **due to increased** concentration of **reduced haemoglobin more** than **5 gm %** *the threshold for cyanosis*) in the **capillary blood**.

In a normal healthy individual, the following occurs:

- **Arterial blood haemoglobin** is **97 %** saturated with O_2 and **3 % only** are unsaturated i.e. arterial blood reduced haemoglobin concentration = **15 x 3/100 = 0.45 gm % … (A)**
- **Venous blood haemoglobin** is 70% saturated with O_2 and **30 %** unsaturated with O_2 i.e.
- Venous blood reduced haemoglobin concentration =

15 x 30/100 = 4.5 gm % …. (B)

Mean Capillary blood reduced haemoglobin concentration =

(A+B)/2 = (0.45 + 4.5)/2 = 4.95 = ~ 2.5 gm %

So, under **normal conditions**, no cyanosis occurs **since** the amount of reduced haemoglobin in the capillary blood (**2.5 gm *%)*** is **far below** the threshold of cyanosis (**5 gm *%).***

Causes of cyanosis

- **All causes of hypoxic hypoxia.**
- **All causes of stagnant hypoxia.**
- **Asphyxia.**

Types of cyanosis

A. Central Cyanosis:

- As in hypoxic hypoxia.
- It is **due to** defective oxygenation of blood in the lungs.

A. Peripheral Cyanosis:

- As in stagnant hypoxia.
- It is **due to** excessive uptake of oxygen by the tissues **especially** when the rate of blood flow is decreased.


A
B
A
B

Types of hypoxia not associated with cyanosis

- **Histotoxic hypoxia:** Because;

Both arterial and venous blood haemoglobin are **highly saturated** with O_2 so, capillary reduced haemoglobin concentration is **far below** the threshold for cyanosis.

- **Anaemic hypoxia: because;**

- Haemoglobin content is **reduced.**

Effects of Hypoxia:

- The effects of hypoxia **depend on** the **onset** sudden acute or gradual chronic and the **alveolar P_{O2} level**;
- Acute severe hypoxia is **fatal** within 5 minutes due to **direct** respiratory centre depression.
- **e.g.** When the pressure in the aeroplane cabin is **suddenly** lost while flying at (30.000 feet) as the alveolar Po_2 suddenly **drops** to **20 mm Hg.**

Acute mountain sickness:

A condition that occurs in individuals when ascend to high altitudes (20.000 feet) (**alveolar P_{O2} < 40 mmHg**).

Symptoms: headache, fatigue, irritability, insomnia, dyspnea, palpitation, anorexia, nausea and vomiting

Cause: Cerebral edema which occurs secondary to VD of cerebral blood vessels as a result of low arterial Po_2

Mechanism:

- Cerebral Oedema due to O_2 lack → cerebral arteriolar vasodilatation → ↑ cerebral capillary pressure → brain oedema → excitation of brain centres.

Pulmonary Oedema:

Mechanism:

- O_2 lack → pulmonary arteriolar **vasoconstriction** → ↑ pulmonary blood pressure (i.e. pulmonary hypertension) → ↑ pulmonary capillary pressure → **↑ capillary permeability** → **pulmonary oedema**.

Acclimatization

The adaptive mechanisms that occur in high altitudes (10.000 feet) (on prolonged exposure to low O_2 pressures, **alveolar Po_2 <u>decreases</u>** to **60 mm Hg) (chronic mountain sickness)**.

Acclimatization Mechanisms:

Compensatory mechanisms involved in acclimatization aim at increasing O_2 delivery to tissues.

They include the following:

1. Respiratory effects:

Alveolar Po_2 **decreases** to 60 mm Hg **resulting in;**

Hyperventilation (↑ rate and ↑ depth of breathing) **due to** stimulation of the respiratory centre through the **peripheral chemoreceptors .**

Hyperventilation → ↓blood CO_2 → **alkalosis** which can be **corrected** by increased bicarbonate secretion in urine.

2. Increase of the blood O_2-carrying capacity

This occurs as a result of erythropoiesis under effect of erythropoietin hormone (which is secreted by kidney in response to hypoxia). The RBCs count increases (**physiological polycythaemia**).

3. Circulatory changes:

Peripheral chemoreceptors stimulate the vasomotor centre resulting in **tachycardia** and **increase** of both **cardiac output and arterial blood pressure**. In addition, **peripheral VD** also occur under effect of hypoxia to increase oxygen supply to tissues.

4. Increase of O_2 liberation at the tissues

This is produced through stimulation of **2,3 DPG** synthesis in RBCs at high altitudes which facilitates O_2 liberation from HbO_2 by shifting O_2-Hb dissociation curve to the right.

↑ 2,3-DPG in RBCs → shift of O_2 dissociation curve to the **right and antagonizes the effect of alkalosis**.

5. Cellular compensatory changes

In response to low arterial Po_2, all the following increase in cells:

- The mitochondria.
- The myoglobin content in skeletal muscles.
- The oxidative enzymes (especially cytochrome oxidase enzyme)


THANK YOU