



A Concise Review on Hypoxia and Ischemia

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Abstract: Hypoxia and ischemia are critical conditions characterized by insufficient oxygen supply to tissues. Hypoxia occurs when oxygen delivery falls below the tissue demand, while ischemia refers to inadequate blood flow leading to oxygen deprivation. Both conditions disrupt cellular metabolism, triggering a cascade of cellular and molecular responses. In hypoxia, cells activate adaptive mechanisms such as hypoxia-inducible factors (HIFs) to enhance oxygen delivery and maintain cellular homeostasis. However, prolonged hypoxia can lead to tissue damage and organ dysfunction. Ischemia exacerbates hypoxia by restricting blood flow, depriving tissues of oxygen and essential nutrients. Without timely intervention, ischemic tissues undergo irreversible damage, culminating in necrosis or apoptosis. Understanding the underlying mechanisms of hypoxia and ischemia is crucial for developing effective therapeutic strategies. Current treatments focus on restoring oxygen supply, improving blood flow, and mitigating tissue damage. These may include oxygen therapy, reperfusion techniques, and pharmacological interventions targeting cellular pathways involved in hypoxia and ischemia. In summary, hypoxia and ischemia represent significant challenges in clinical practice, necessitating ongoing research to unravel their complexities and develop targeted therapies to mitigate their detrimental effects on human health.

IndexTerms - Hypoxia, Types of Hypoxia, Hyperbaric Oxygen Therapy, Ischemia, Types of ischemia.

I. INTRODUCTION

Hypoxia and ischemia are two closely related conditions characterized by insufficient oxygen supply to tissues, with significant implications for human health. While both involve oxygen deprivation, they differ in their underlying mechanisms and clinical manifestations. Understanding these conditions is crucial for diagnosing and managing various diseases and injuries effectively.

Hypoxia occurs when there is an inadequate supply of oxygen to tissues relative to their metabolic demand. This can result from various factors, including respiratory disorders, cardiovascular diseases, high altitudes, or exposure to environmental toxins. Cellular responses to hypoxia include activation of hypoxia-inducible factors (HIFs), which regulate gene expression to promote oxygen delivery and cellular adaptation. However, prolonged or severe hypoxia can lead to tissue damage, organ dysfunction, and potentially life-threatening complications.

Ischemia, on the other hand, refers to a reduction or cessation of blood flow to tissues, leading to oxygen deprivation and nutrient depletion. Common causes of ischemia include arterial blockages, thrombosis, embolism, or vasoconstriction. Ischemic conditions can affect various organs, such as the heart, brain, limbs, and intestines, resulting in tissue damage, organ dysfunction, and clinical symptoms ranging from chest pain and stroke to peripheral artery disease and mesenteric ischemia.

While hypoxia and ischemia are distinct conditions, they often occur together and can exacerbate each other's effects. Ischemia leads to hypoxia by restricting oxygen delivery, while hypoxia can exacerbate ischemia by impairing cellular metabolism and promoting tissue damage. The interplay between hypoxia and ischemia underlies the pathophysiology of numerous diseases, including stroke, myocardial infarction, and peripheral vascular disease. ^[1]

II. HYPOXIA

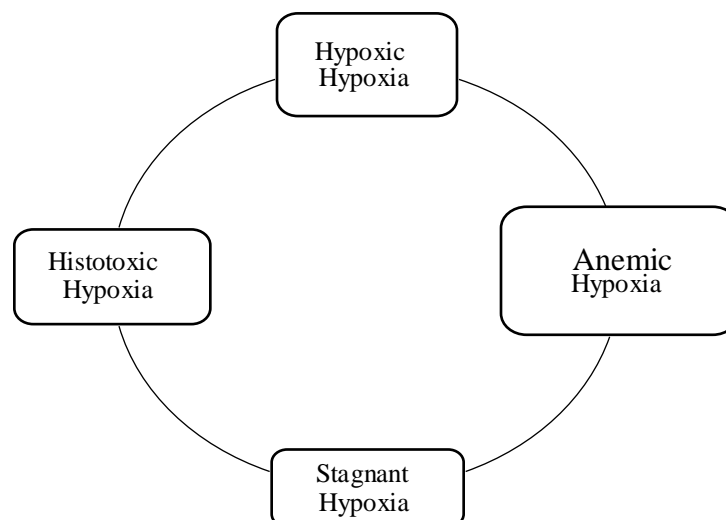
When the body, or a portion of it, does not receive enough oxygen at the tissue level, it is said to be hypoxia. The situation is known as anoxia in its most severe form, when oxygen is completely absent. When our blood doesn't supply our tissues with enough oxygen to meet their needs, it can lead to hypoxia, or low oxygen in the tissues. This situation is known as hypoxemia. Both issues are sometimes referred to as hypoxia. Even yet, they could differ from person to person.

The most common symptoms of Hypoxia are:

Variations in your skin tone, from blue to reddish-pink, confusion cough, Inability to breathe, rapid breathing, increased heart rate, and slow heart rate Exhaling and Sweating.

Common Causes: high altitude. low amount of haemoglobin, Low tissue perfusion, Low oxygen carrying capacity, and Reduced oxygen supply to a region inadequate airflow, reduced oxygen diffusion. ^[1]

III. TYPES OF HYPOXIA



III.A. Hypoxic hypoxia:

The most prevalent type of hypoxia, which is indicated by pulmonary capillaries with lower oxygen tension. Hypoxic hypoxia is characterized by low oxygen pressure in inhaled air, impaired lung ventilation, or widespread disease processes in the respiratory system that result in obstruction of the alveoli and capillaries. Hypoxemia results from red blood cells' haemoglobin not being able to fully saturate with oxygen due to decreased oxygen tension in pulmonary capillaries.

Causes of Hypoxic hypoxia:

1. Low partial pressure of oxygen in the inhaled air.
2. Decreased pulmonary ventilation due to respiratory disorder.
3. Inadequate oxygenation of blood due to respiratory disorders. ^[2]

III.B. Anemic hypoxia:

As anemic hypoxia is a condition that happens when the blood's capacity to carry oxygen declines, blood is especially linked to this problem. This suggests that there are less oxygen-binding sites or haemoglobin molecules accessible to bind oxygen. True anaemia or a reduced haematocrit is the most typical example. Reduced hemoglobin concentration in red blood cells (RBCs) results in a decrease in the blood's ability to carry oxygen.

Causes of Anemic hypoxia:

1. Decreased number of red blood cells.
2. Formation of altered haemoglobin
3. Combination of haemoglobin with gases other than O₂ and CO₂. ^[3]

III.C. Stagnant hypoxia:

As the name suggests, stagnant hypoxia describes conditions where blood flow is abnormally low, such as in shock, syncope, or other "low-flow" states. Hypoperfusion, or reduced blood flow, is the main obstacle to oxygen delivery; as a result, the cardiovascular system is the source of the issue. Another name for it is ischaemic hypoxia.

Causes of Stagnant hypoxia:

1. Surgical stroke.
2. Haemorrhage.
3. Congestive cardiac failure. ^[4]

III.D. Histotoxic hypoxia:

The term "histotoxic hypoxia" describes a decrease in the mitochondria's ability to produce ATP as a result of an error in the cell's use of oxygen. A case of histotoxic hypoxia is poisoning with cyanide. Since the presence of cyanide blocks the reaction of oxygen with cytochrome c oxidase, there is a significant decrease in tissue oxygen consumption.

Causes of Stagnant hypoxia:

1. Cyanide poisoning.^[5]

IV. HYPOXIA-INDUCIBLE FACTOR (HIF_s)

Hypoxia-inducible factors (HIF_s) are transcription factors that respond to decreases in available oxygen in the cellular environment, or hypoxia.^{[6][7]} They also respond to instances of pseudohypoxia, such as thiamine deficiency.^{[8][9]} Both hypoxia and pseudohypoxia leads to impairment of adenosine triphosphate (ATP) production by the mitochondria.

V. HYPERBARIC OXYGEN THERAPY

An alternative form of oxygen therapy is called hyperbaric oxygen therapy (HBOT). It is inhaling oxygen through a tube or pressurized chamber. This makes it possible for your lungs to absorb up to three times as much oxygen as they would if you were inhaling regular air pressure. Your blood carries the excess oxygen to your organs and bodily tissues. HBOT is used to treat infections, burns, and some very acute wounds. In addition, it addresses hypoxia of various kinds, decompression sickness in divers, air or gas embolisms (bubbles of air in the blood), and carbon monoxide poisoning.^[10]

Table 1: Role of Hyperbaric oxygen therapy in hypoxia

Types of hypoxia	Role of Hyperbaric oxygen therapy
Hypoxic hypoxia	Oxygen therapy is 100% effective except when it is due to venous-to-arterial shunts, because the deoxygenated venous blood by-passes the lungs and remain deoxygenated.
Anemic hypoxia	Oxygen therapy is of very limited value; because O ₂ transport by the haemoglobin is not increased. Administration of O ₂ only increases the dissolved O ₂ in the arterial blood. This small amount of O ₂ can be the difference between the life and death.
Stagnant or ischemic hypoxia	Oxygen therapy is of very limited value; because O ₂ cannot be carried to the tissues.
Histotoxic hypoxia	Oxygen therapy is of very limited value; because O ₂ cannot be carried to the tissues.

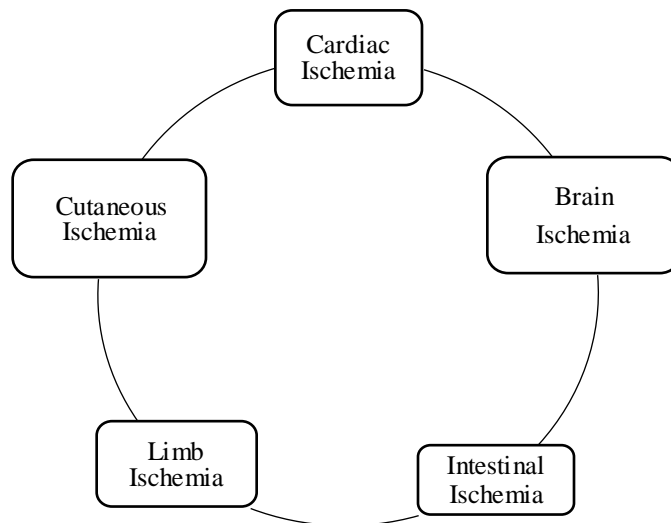
VI. ISCHEMIA

Ischemia means a "reduced blood supply". A waxy material known as plaque (plak) accumulates inside blood vessels and obstructs normal blood flow, causing ischemic heart disease (IHD). Atherosclerosis is the term for the condition that occurs when plaque accumulates in the arteries (ATH-er-o-skler-O-sis). Any artery in the body, including those in the heart, brain, arms, legs, pelvis, and kidneys, can develop atherosclerosis. Consequently, depending on which arteries are impacted, distinct disorders may manifest. The term "ischemic vascular disease" (IVD) refers to a collection of conditions brought on by plaque accumulation.

The most common symptoms of ischemia are:

1. May be caused by inadequate cardiac output but not all tissues are equally affected because of redistribution of available blood.
2. Obstruction of arterial flow and extensive venous and capillary damage.^[11]

VII. TYPES OF ISCHEMIA



VII.A. Brain Ischemia:

An established and frequent cause of permanent brain injury is cerebral ischemia, which results from a significant decrease in cerebral blood flow. The finding that brain cells are more resistant to ischemia than was previously believed based on clinical experience has sparked a great deal of research aimed at identifying the variables causing irreversible ischemia-induced cell damage. As of right now, the results of these studies suggest that the final survival of nerve cells may be particularly dependent on cellular acidosis and biochemical disruptions brought on by aberrant intracellular ion homeostasis. This review looks at the molecular processes that ischemia starts and how they might affect brain cells' ability to survive in the end.

Symptoms:

1. Weakness in one arm or leg.
2. Weakness in one entire side of the body.
3. Dizziness, vertigo, double vision.^[12]

VII.B. Cardiac Ischemia:

The condition known as cardiac ischemia or myocardial ischemia decreases the heart muscle's capacity to pump blood. An acute, significant blockage of an artery in the heart may cause a heart attack. In addition, myocardial ischemia may result in dangerously irregular cardiac beats. Increasing the blood supply to the heart muscle is the goal of treatment for myocardial ischemia. Medication, bypass surgery, or an angioplasty to clear clogged arteries are possible forms of treatment. It is crucial to adopt heart-healthy lifestyle choices for managing and preventing myocardial ischemia.

Symptoms:

1. Nausea and vomiting.
2. A fast heartbeat
3. Shortness of breath when you are physically active.^[13]

VII.C. Intestinal Ischemia:

The condition known as cardiac ischemia or myocardial ischemia decreases the heart muscle's capacity to pump blood. An acute, significant blockage of an artery in the heart may cause a heart attack. In addition, myocardial ischemia may result in dangerously irregular cardiac beats. Increasing the blood supply to the heart muscle is the goal of treatment for myocardial ischemia. Medication, bypass surgery, or an angioplasty to clear clogged arteries are possible forms of treatment. It is crucial to adopt heart-healthy lifestyle choices for managing and preventing myocardial ischemia. A range of disorders known as intestinal ischemia are caused by a decrease in blood flow to the intestines. Ischemia can result from low blood pressure, which reduces total blood flow, or from a wholly or partially blocked blood vessel, generally an artery. Your large intestine (colon), small intestine, or both may be affected by intestinal ischemia. Your digestive system's cells aren't getting enough oxygen because of the reduced blood flow. A dangerous illness called intestinal ischemia can hurt and impair the normal function of your intestines. Loss of blood supply to the intestines in extreme circumstances can harm intestinal tissue and even cause death. There are therapies for ischemia of the intestine. It is critical to identify the early symptoms and seek medical attention as soon as possible to increase the likelihood of recovery.

Symptoms:

1. Sudden belly (abdominal) pain that may be mild, moderate or severe.
2. An urgent need to have a bowel movement.
3. Blood in stool.^[14]

VII.D. Limb Ischemia:

A sudden stoppage of blood supply to a limb within 14 days of the onset of symptoms is known as limb ischemia. It is not to be confused with critical limb ischemia (CLD), a more chronic (lasting more than 14 days) illness. The terminal stage of peripheral vascular disease, known as CLD, is characterized by residual collateral circulation, or alternative circulation pathways, which provide some, but insufficient, blood flow to the extremities' distal regions. A persistently ischemic limb is usually warm and pink

because of a well-developed collateral artery network; unlike acute limb ischemia, which can cause limb loss, it usually does not require emergency care.

Symptoms:

1. Pallor (pale appearance of the limb).
2. Paresthesias (abnormal sensation in the limb).
3. Perishingly cold. ^[15]

VII.E. Cutaneous Ischemia:

Skin discoloration that is uneven, patchy, or mottled may be caused by reduced blood flow to the skin's layers. Treatment of cutaneous ischemia depends on the underlying cause. It may involve medications to improve blood flow, interventions to remove obstructions in blood vessels, wound care, and lifestyle changes to reduce risk factors such as smoking or poor diet. In severe cases, surgical procedures like vascular bypass or angioplasty may be necessary to restore adequate blood flow to the affected area. Early diagnosis and management are essential to prevent complications and promote healing. If you suspect you have cutaneous ischemia or any related symptoms, it's crucial to consult a healthcare professional for proper evaluation and treatment.

Symptoms:

1. Pale or bluish discoloration of the skin in the affected area.
2. Coldness or numbness.
3. Pain or discomfort, especially during movement or pressure on the affected area. ^[13]

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