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Review Article

The Evaluation of Oxygen Need

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Abstract

Physiologic responses to oxygen deprivation may be seen in various body systems when oxygen supply is diminished, perfusion of oxygen is depleted, or there is not enough circulating supply for the demand required. The Body systems that demonstrate symptoms when deprived of oxygen include the Respiratory or Pulmonary system, the Cardiovascular system (include the heart and vascular supply of blood *via* arteries and veins), the Neuro-Muscular systems (including the brain, nervous system, and muscles), the renal system and body fluids, the regulation of acid-base balance, and the gastrointestinal system [1]. A synthesis of physiological signs and symptoms demonstrated through various body organs as sources or contributing factors related to hypoxia or prolonged hypoxemia presented as a guide for evaluating oxygen need. There are many symptoms notable for oxygen deprivation and the symptoms may be subtle and occur over long periods of time or they may have a very acute or abrupt disruption of circulation or blood flow that is of immediate concern and life threatening. This article will discuss the physiology and symptomatology of oxygen deprivation.

Keywords: Hypoxia; Hypoxemia; Anemia; Iron Deficiency Anemia; Altitude sickness; Hypercarbia; Tissue hypoxia; Pulse Oximetry

Introduction

Oxygen is necessary for your brain, liver, heart, lungs, and other vital organs to survive. Low oxygen levels contribute to hypoxemia (low oxygen in the blood) and low oxygen in the tissue contributes to hypoxia [1]. Room air at sea level provides 20.9 % or 21% oxygen of dry air. This is considered the normal room air level for all levels while higher elevations or higher altitude has a lower oxygen supply in the air (Table 1) based on altitude above sea level [2]. The World health Organization (WHO) defines anemia for adult men as a hemoglobin (Hgb) level less than 13 g/dL and a hemoglobin of less than 12 g/dL in adult women [3].

Background

Sarkar et al. [4] discuss the role of red blood cells carrying oxygen, the blood supply then circulates the oxygen throughout the body, and the various conditions that may be altered as a result of poor perfusion, and the impact on the partial pressure of oxygen and the various mechanisms and differing features of hypoxemia in humans. Anemia is a condition that contributes to low blood supply. Low circulating blood supply or anemia contributes to the progression or deterioration of many conditions. A person would have bloodwork, or specific labs drawn to determine if there is anemia. Oxygen saturation is described as the amount of oxygen circulating in the blood at any given moment as captured on a pulse oximeter.

Measurement Devices

The pulse oximeter is a small probe or device that registers the amount of oxygen through the skin [5]. This device usually clips or is attached to a finger to register the current amount of circulating oxygen saturation supplied in the blood. A saturation of 90% on roomair is the minimum required to prevent symptoms of hypoxia from developing. A typical healthy person will have 94% to 100% blood oxygen saturation levels at any given time. For patients with known lung or heart disease the blood oxygen saturation would need to be at 90% or higher for adequate oxygen to perform daily activities.

Risk Factors

People at higher risk for anemia are menstruating women [prolonged duration of bleeding or very heavy menses in women], those with malnutrition, active forms of cancer, chronic kidney disease, anemia of chronic disease, various chronic lung conditions and chronic lung diseases, forms of sleep apnea, liver diseases (NASH or Alcoholic), obesity hypoventilation syndrome, chronic heart diseases, those with restrictive lung diseases such as stroke victims, or other neuro-musculoskeletal paralysis conditions are more prone to a variety of chronic inflammatory conditions or acute on chronic conditions which contributes to a higher risk for low blood oxygen saturations [1,4]. Khan et al. discuss their research and propose unexplained hemoglobin (Hgb) less than 13 and 12 g/dl in adults may suggest evidence more likely due to a chronic inflammatory process involving inflammatory markers such as interleukins (IL) 6, 12, and C-reactive protein [6]. Their study was evaluating the elderly with obstructive sleep apnea (OSA) and were hypothesizing that hypoxic stimulation of erythropoiesis may obscure anemia of aging for those 65 and older.

Impacting Conditions

A person may have a reading of 98% at sea level; it may decrease to 95% at 5,000 ft. and further to 90% at 10,000 ft. At altitude above 10,000 ft., a person may fail to adjust to the low level of oxygen and his SpO2 may drop below 80% resulting in hypoxic conditions [5]. People with high risk behaviors, such as smoking/ vaping/ huffing or inhalation of toxic chemicals (oil & gas)/ drugs for recreational use, or whose who may have hobbies that may increase exposure for lung injury risk such as aerosolized painting, or air brushing artwork, various forms of restoration art/ remodeling work), or those who may be employed in environments that contribute to poor air quality or increased risk for exposure to particulate matter such as pesticides/ herbicides, asbestos, dust, powder, mill work, farming, painting, mining, or other factory work may contribute to a higher risk for lung injury may develop low blood oxygen saturations level problems or hypoxia over time.

Biomedical engineers at Baylor University used computer modeling to test out three different scenarios to determine the theory for silent hypoxemia. Herrmann, et al. [7] conducted their research to help explain how and why the lungs stop providing oxygen to the bloodstream. Their research revealed silent hypoxia is likely due to a combination of biological mechanisms that may occur simultaneously in the lungs of COVID-19 patients. Herrmann et al. [7] used a mathematical model to determine possible explanations for the severe hypoxemia observed in patients with early-stage COVID-19 patient population. Their research suggested three plausible contributing factors: (1) extensive perfusion defect, (2) perfusion defect combined with ventilation-perfusion mismatching in the noninjured lung, or (3) hyperperfusion of the small, injured fraction. The result of hyperperfusion within a small amount of injured lung were examined further with three mechanisms considered: (1) alterations to hypoxic pulmonary vasoconstriction, (2) thrombosismediated perfusion defects, and (3) ventilation-perfusion mismatching in the noninjured lung [7].

Comorbid Diseases

Inflammatory conditions my contribute to the explanation as to why patients with comorbidities such as metabolic syndrome and diabetes are more prone to severe and critical phases of COVID-19 may heighten the baseline inflammatory state in patients with preexisting compromised metabolic health [8]. The associations between endothelial dysfunction, hypoxia, and thrombus formation are well established in the septic microvasculature, and hypoxia may be both a consequence and cause of microthrombosis due to the positive feedback loop between thrombus formation and inflammation [9]. Cells experience sustained periods of hypoxia in diseased tissues, such as malignant tumors, atherosclerotic plaques, and arthritic joints. The heart can fail from overwork, or insufficient oxygen which may cause cell death and tissue damage in the heart and other vital organs. A virus, such as covid-19, may infect and damage the heart's muscle tissue directly, just as other viruses may also contribute to infections, including some strains of the flu. The identification of hypoxia-responsive transcription factors, target genes, or signaling responses that control thrombus formation could represent an important step towards the development of novel and safe prophylactic therapies that reduce thrombosis. Hypoxia-responsive signaling pathways can also regulate thrombogenesis indirectly through the induction of pro-inflammatory mediators such as tumor necrosis factor (TNF) α and interleukin (IL) 1. Hypoxia also stimulates an expression and/ or phosphorylation of various proteins in the nuclear factor-κB (NF-κB) signaling pathway as well [10]. A cytokine storm, is an immune system response causes inflammation that can overwhelm the body, destroying healthy tissue and damaging organs such as the kidneys, liver and heart. This inflammatory response is a normal defensive event that is exaggerated and leaves someone vulnerable to a cytokine storm. Severe inflammatory conditions such as COVID-19, is viral inflammatory disease, that directly affects endothelial cells, which form the lining of the blood vessels. When attacked by a virus, the body undergoes stress and releases a surge of chemicals called catecholamines, which can stun the heart. A viral infection may cause cardiomyopathy, a disorder affecting the heart muscle that impacts the heart's ability to pump blood effectively [11]. In a 2022 study conducted by Hall, et al. long COVID was linked to having a reduced oxygen uptake in the brain [12]. The researchers say the findings demonstrate a significant as a lack of sufficient oxygen supply may be one of the mechanisms that contributes to reported brain fog, cognitive problems, and an increased risk of depression and anxiety for those persons who are experiencing long COVID.

Symptomatology

Classic medical textbooks describe the basic physiology of cells, cell membrane, tissues, nerve, muscles, and organs [1]. Physiologic responses to oxygen deprivation may be seen in various body systems when oxygen supply is diminished, perfusion of oxygen is depleted, or there is not enough circulating supply for the demand required. The Body systems that demonstrate symptoms when deprived of oxygen include the Respiratory or Pulmonary system, the Cardiovascular system (include the heart and vascular supply of blood *via* arteries and veins), the Neuro-Muscular systems (including the brain, nervous system, and muscles), the renal system and body fluids, the regulation of acid-base balance, and the gastrointestinal system [1]. There are many different mechanisms in play to balance the body systems and these may display overt system responses when there is a loss of supply or an interruption in the ability of the organs to function. There is a regulation of oxygen and carbon dioxide concentrations in the extracellular fluid. Hemoglobin is present in all red blood cells and is necessary for oxygen regulation [1]. Symptoms of demonstrated low oxygenation may include either a fast heart rate (tachycardia), or a very slow heart rate (bradycardia), a rapid respiratory effort (tachypnea) with evidence of work of breathing [nasal flaring, grunting, deep sighing, increased cough accessory muscle use (ribs and abdomen)] and shortness of breath as well as demonstrated tissue mottling or cyanosis (lips, nailbeds) and coolness with skin moisture may be visible [1]. When the cardiac system is demonstrating oxygen deprivation, there may be tissue ischemia of the heart itself as demonstrated by chest pain, EKG changes like cardiac straining or a progression towards a myocardial infarction may be noted if there is a reduced or complete loss of supply to an area of the heart due to a blockage. A narrowing pulse pressure signifies a drop in cardiac output and this circumstance may interfere with the ability to complete more strenuous activities that require a higher cardiac demand. The renal system is responsible for managing the fluid balance along with the lymphatic system. When tissue hypoxia persists, there may not be nutrients getting to the vital organs and thus there may be edema or swelling of extremities or even fluid displacing into the abdomen or third-spacing as a result of limited ability to circulate the supply due to increased cardiac demand. Activity intolerance ensues along with poor appetite, nausea, and diarrhea if the renal system is not able to maintain adequate oxygenation to filter the blood. The renal system would demonstrate low urine production or output, concentrated urine, odorous urine, and a larger amount of sediment in the urine because of low oxygen supply perfusing the kidneys. Additional gastrointestinal system oxygen deprivation may include abdominal cramping, belching, abdominal ascites, sacral edema, heartburn, acid reflux, increased abdominal girth related to poor oxygenation of the vital organs necessary to digest food. The neuro-muscular systems may show symptoms for muscle cramping, muscle twitching or muscles spasms, extremity weakness, leg heaviness, numbness, and tingling. There may be headaches, blurred vision, dizziness, agitation, anxiety, drowsiness, fatigue, impaired vision (double vision, blurred vision), forgetfulness, impaired judgement, and confusion when the neurological system is displaying symptoms related to poor oxygenation or depleted oxygen supply [1].

HYPOXICO ALTITUDE TRAINING SYSTEMS

Hypoxico, Inc.
Altitude Training Systems

HYPOXICO ALTITUDE TO OXYGEN CHART

Altitude (Feet)	Altitude (Meters)	O2 Monitor Reading	Effective Oxygen Percentage	Similar Location
Sea Level	Sea Level	20.90%	20.90%	Hypoxico HQ - New York, NY
1,000'	304m	20.10%	20.10%	Tbilisi, Georgia (1,479' - 451m)
2,000'	609m	19.40%	19.40%	Canberra, Australia (1,984' - 605m)
3,000'	914m	18.60%	18.60%	Chamonix, France (3,264' - 995m)
4,000'	1219m	17.90%	17.90%	Salt Lake City, UT (4,226' - 1288m)
5,000'	1524m	17.30%	17.30%	Boulder, CO (5,430' - 1655m)
6,000'	1828m	16.60%	16.60%	Stanley, ID (6,253' - 1906m)
7,000'	2133m	16%	16%	Flagstaff, AZ (6,910' - 2106m)
8,000'	2438m	15.40%	15.40%	Aspen, CO (7,907' - 2410m)
9,000'	2743m	14.80%	14.80%	Bogata, Columbia (8,660' - 2640m)
10,000'	3048m	14.30%	14.30%	Leadville, CO (10,200' - 3109m)
11,000'	3352m	13.70%	13.70%	Cusco, Peru (11,152' - 3399m)
12,000'	3657m	13.20%	13.20%	La Paz, Bolivia (11,942' - 3640m)
13,000'	3962m	12.70%	12.70%	Yabuk Camp, Sikkim, India (12,467' - 3800m)
14,000'	4267m	12.30%	12.30%	Pikes Peak, CO (14,115' - 4302m)
15,000'	4572m	11.80%	11.80%	Mount Rainier, WA (14,411' - 4392m)
16,000'	4876m	11.40%	11.40%	Mount Blanc (15,777' - 4808m)
17,000'	5181m	11%	11%	Everest Base Camp (16,900 ft. - 5150m)
18,000'	5486m	10.50%	10.50%	Mount Elbrus (18,510' - 5642m)
19,000'	5791m	10.10%	10.10%	Mt. Kilimanjaro (19,341' - 5895m)
20,000'	6096m	9.70%	9.70%	Mt. Denali (20,310' - 6190m)
21,000'	6400m	9.40%	9.40%	Hypoxico Home Generator Max
22,000'	6705m	9%	9%	Ama Dablam (22,349' - 6812m)
23,000'	7010m	8.70%	8.70%	Aconcagua (22,841' - 6960m)
24,000'	7315m	8.40%	8.40%	K12, Pakistan (24,370' - 7428m)
25,000'	7620m	8.10%	8.10%	Chomo Lonzo, Himalayas (25,604' - 7804m)
26,000'	7924m	7.80%	7.80%	Annapurna (26,545' - 8091m)
27,000'	8229m	7.50%	7.50%	Cho Oyu (26,864 ft. - 8188m)
28,000'	8534m	7.20%	7.20%	K2 (28,251 ft. - 8611m)
29,000'	8839m	6.90%	6.90%	Mt. Everest (29,029 ft. - 8848m)
30,000'	9144m	6.30%	6.30%	Hypoxico K2 High Flow Max

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Table 1: Hypoxico Altitude to Oxygen Chart.

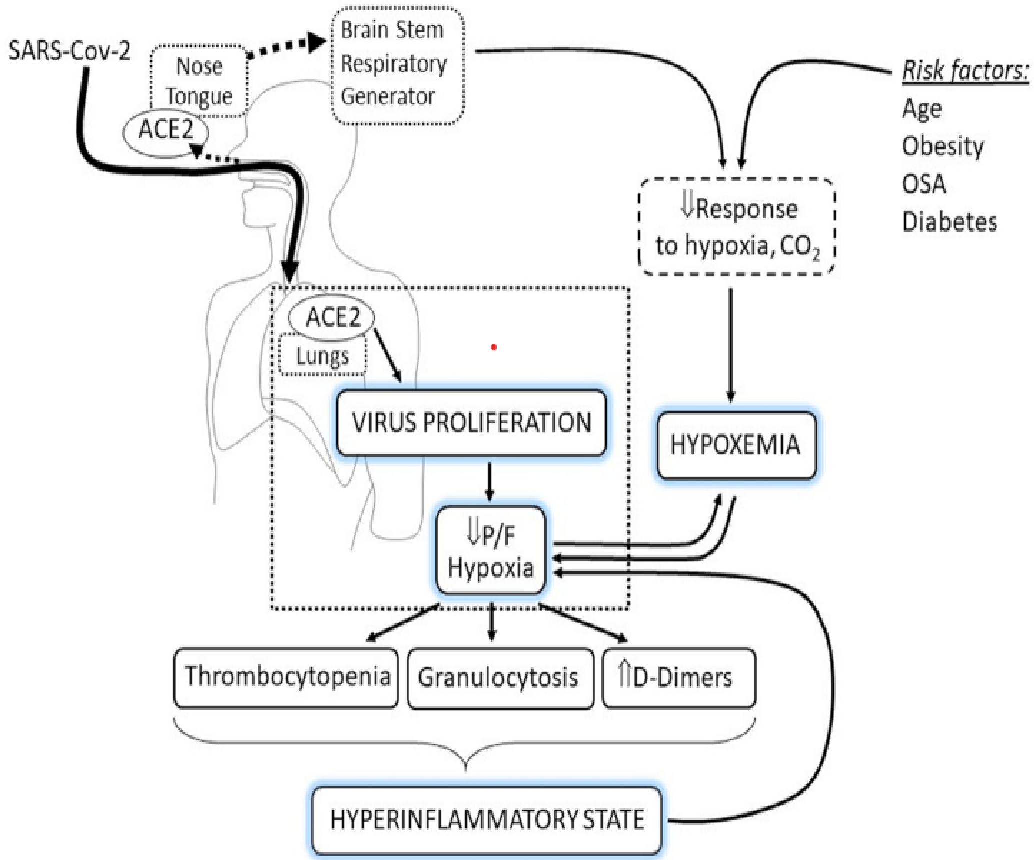

Figure 1: Role of Hypoxemia and COVID-19.

Scheme indicating the central role of hypoxia in the development of severe/critical stage (phase) of COVID-19. P/F, the ratio of arterial oxygen partial pressure (PaO2) to fractional inspired oxygen (FiO2), is the main determinant of hypoxemia and lung tissues hypoxia [8].

Symptoms of Oxygen Deprivation

Cardiovascular	Respiratory	Gastrointestinal	Renal/ Body Fluids	Neuro-Muscular
• Tachycardia • Bradycardia • Irregular HR • Dysrhythmia • Palpitations • Chest retractions • Hypertension • Orthostatic BP • Positive tilt • Delayed pulses • Widen pulse pressure • Ashen color • Mottling • Cool skin • Cyanosis • Pale digits • Sweating/ perspiration • Capillary refill >3 seconds • Activity intolerance • Changes in ability to do Activities of daily living (ADLs) • Fatigability • edema	• Tachypnea (RR > 30 per min) • Cyanosis (Mouth, lips, nailbeds) • Clubbing • Shortness of breath • Dyspnea • Periods of apnea • Work of breathing • Nasal flaring • Tracheal tugging • Grunting • Coughing • Noisy breathing • Conversational dyspnea • Deep sighing • Asymmetrical chest movement • Accessory muscle use: face, neck, back, chest, intercostals, diaphragm, abdomen • Paradoxical breathing of abdomen/chest • Positioning to comfort for breathing • Recovery breathing positions • Pleural effusions	• Poor appetite • Nausea • Vomiting • Abdominal cramping • Bloating • Fullness • Acid Reflux • Heartburn • Hiccoughs • Belching • Diarrhea • Constipation • Abdominal distention • Abdominal ascites • Sacral edema • Increased abdominal girth	• Low urine output • Concentrated urine • Odorous urine • Large urinary sediment • Generalized swelling • Generalized edema • Sacral edema • Abdominal ascites • Lymphedema	• Anxiety • Agitation • Headaches • Blurred vision • Double vision • Dizziness • Forgetfulness • Impaired judgement • Confusion • Drowsiness • Weakness • Leg cramps • Muscle twitching • Numbness • Tingling **Low Blood Glucose may alter the neurological signs and symptoms and conditions such as diabetes may need to be evaluated.

Table 2: Synthesis of physiological signs of oxygen deprivation; Source: Guyton&Hall, 2000.

Discussion

A synthesis of physiological signs and symptoms of oxygen deprivation or hypoxemia may be demonstrated through various body organs as sources or contributing factors related to poor oxygenation, hypoxia, or prolonged hypoxemia presented as a guide for skilled healthcare staff to determine when to set-up oxygen in an outpatient setting [13]. A retrospective investigational study [13] was conducted to determine the percentage of homecare patients using oxygen therapy prior to homecare services. After the introduction of education and use of an evaluating oxygen guide was distributed the use of oxygen was evaluated for safety, utilization of oxygen, and to determine if there were any additional adverse events reported such as falls and if there was any impact on re-hospitalization rates for oxygen patients. The study identified 5% of the patients had oxygen prior to the study and there was an implementation rate of 3-8% per month for oxygen initiation after a six-month training and introduction of oxygen guide with 80% initiation rate identified amongst the homecare skilled clinical staff. There was an identified 92% benefit seen for the identification of hypoxia and subsequent oxygen need [13].

There are many symptoms notable for oxygen deprivation and the symptoms may be subtle and occur over long periods of time or they may have a very acute or abrupt disruption of circulation or blood flow that is of immediate concern and life threatening. The long-standing limitations without adequate oxygen supply results in debilitating effects as one may be unaware of the harmful long-term effects of oxygen deprivation over longer periods of time leading to more permanent damage of the tissues and vital organs often cascading into a cycle towards premature death. The importance of identifying variations for anemia, iron deficiency anemia (IDA), forms of iron deficiency, and other conditions such as chronic obstructive lung disease (COPD), obstructive sleep apnea (OSA), congestive heart failure (CHF), during clinical presentation are important to recognize and capture as progressive syndromes of oxygen deprivation, hypoxia, and hypoxemia in the end. When assessing an individual for red flags in their history and clinical exam, particularly when covid peaked, demonstrated the importance of an astute clinician in recognizing patterns of ischemia, or thrombosis.

Evans et al. [14] presented a table displaying the red flags in the history and clinical examination. The red flag in the history may include persistent breathlessness on exertion, rapid deterioration of breathing, several impairments in their ability to walk or exert themselves, coughing up blood, and a significant history of smoking, asthma, COPD, or recurrent bronchitis, prior episodes of pneumonia. The clinical exam may demonstrate exertional desaturations of oxygen via pulse oximeter, altered respiratory patterns 9 very fast or very slow), signs of pulmonary embolism, signs of cardiac strain, signs of deep vein thrombosis, an unstable cardiac rhythm, marked asymmetrical breath sounds, and persistent true stridor on inspiration are worthy of emergent attention. The differential diagnoses for these various symptoms and conditions of physical exam may include heart failure, cardiomyopathy, pericarditis, myositis, pulmonary embolism, arrythmia, pulmonary hypertension, pulmonary fibrosis, pleural effusion, pneumothorax, lung cancer, laryngeal obstruction, coronavirus (covid-19), or severe acute respiratory syndrome (SARS) or other severe respiratory disease conditions in their acute phase of illness may be considered [14]. The clinician is ultimately in the best position to recognize patterns of disease and to understand the urgency of the condition as it is presented. Please see Table 3 for the comparison of linked symptoms to covid-19 versus those identified in the non-covid cases.

History	Clinical examination	Differential diagnosis
Red flags		
• Persistent, progressive breathlessness on exertion (and eventually at rest) • Rapid deterioration • Severe impairment (eg, too breathless to walk) • Breathlessness with haemoptysis • Significant smoking history in context of above	• Unexplained hypoxia or exertional desaturation • Altered mental status • Persistent tachycardia • Hypotension • Signs of deep vein thrombosis • Signs of cardiac strain (eg, heave, neck vein distension, additional heart sound, unexplained murmurs) · • Unstable cardiac arrhythmia • Marked asymmetry in breath sounds • True stridor (inspiratory, persistent)	Identify or exclude serious conditions (due to covid-19 or other pathology) such as heart failure, arrhythmia, coronary artery disease, pulmonary emboli, pulmonary hypertension, pulmonary fibrosis, myocarditis/pericarditis, lung cancer, pleural effusion, pneumothorax or lung collapse, laryngeal obstruction
Linked to previous covid-19		
Breathlessness persisting after 4 weeks with ongoing trajectory of improvement	Elevated respiratory rate, hypoxia, generalised or focal crackles	Resolving covid pneumonitis (seen especially in patients hospitalised with acute covid-19)
Excessive awareness of breathing, pressure or tightness, air hunger	Thoracic breathing, sighing, yawning, mouth breathing, irregular breathing	Long covid and breathing pattern disorder (box 2)
Persistent or intermittent breathlessness with other symptoms (eg, fatigue, brain fog, joint pains)	Variable; there may be few or no abnormal findings	Long covid and investigate breathlessness in context of other symptoms. Breathing pattern disorder can occur in isolation or alongside multiple symptoms
Breathlessness with palpitations or fast heart rate, especially on standing	Sustained increase in heart rate on standing of 30 bpm or to >120 bpm, absence of hypotension	Long covid with dysautonomia or postural orthostatic tachycardia syndrome (covered in previous article in this series[29])
Breathlessness and loss of voice with talking	Audible noisy breathing and wheeze (often variable)	Intermittent laryngeal obstruction or vocal cord dysfunction. Important to distinguish from true stridor, which requires urgent ENT referral
Exertional breathlessness may not be progressive	Variable; can be normal or have bilateral inspiratory crackles	Covid related interstitial lung disease or pulmonary fibrosis
Non-covid causes		
Intermittent breathlessness with familial or atopic history, nocturnal pattern, triggers	Variable; can be normal. Widespread wheezing, accessory muscle use, decreased breath sounds, pulsus paradoxus	Asthma: exclude acute severe or life threatening asthma
Persistent breathlessness with exacerbations, particularly in winter months	Variable; can be normal. Widespread wheezing, accessory muscle use, decreased breath sounds, pulsus paradoxus	Exacerbation of chronic obstructive pulmonary disease
Breathlessness, acutely unwell and deteriorating	Fever, crackles, bronchial breathing	Pneumonia
Sudden or progressive breathlessness and worsening exercise tolerance over days or weeks	Localised, decreased, or absent breath sounds	Pneumothorax (commonly starts with pain), pleural effusion, lung or lobar collapse
Progressive breathlessness and worsening exercise tolerance over weeks or months	Variable; can be normal. Fine end-inspiratory basal crackles Elevated JVP, 3rd or 4th heart sound, peripheral oedema Ejection systolic murmur over right carotid area	Interstitial lung disease or pulmonary fibrosis Heart failure (consider underlying coronary heart disease) Aortic stenosis

bpm = beats per minute. ENT = ear, nose, and throat. JVP = jugular venous pulse.

Table 3: Assessment & differential diagnosis of the patient with persistent breathlessness after covid-19.

Conclusion

As we delve into the various contributing conditions and see the relationship to the importance of oxygen, we see the dynamics of the snowballing effects for body stems. There are far too many risk factors for worsening conditions when anemia, iron deficiency and other manageable conditions are identified. Nutritional awareness and longstanding prevention of disease is a standard of care. Evidence based medicine needs to maintain healthy living and prevention in the forefront of care. Education of individuals as to cause and effect and consequences may alter health for the future. Individuals armed with proper education of body stems and the importance of oxygen may reduce long-term risk and alter behaviors such as smoking or non-compliance with sleep devices used for sleep apnea, maintaining a healthy diet, and understanding the importance of iron rich foods. The future in healthcare may start with the patient.

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