



## A Review - Oxygen Therapy is Booster Dose in Medical Sciences for Various Diseases.

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### ABSTRACT

To understand the importance of oxygen as a medical gas in Allopathy, Ayurveda, Naturopathy and Yoga. To appreciate why under-supply or excess-supply of oxygen is hazardous. To understand the dangers involved in using oxygen cylinders at home and benefits of Oxygen Supply through Yoga and Exercise.

**Keywords:** Oxygen therapy, oxygen treatment, COVID-19

### Introduction

Oxygen is a colourless and odourless gas and first recognized by Joseph Priestley in 1771. It has been used in our clinical practice for more than 200 years. It is essential for the functioning and survival of all body tissues and lack of oxygen for a few minutes can be fatal. It must be considered as a pharmacological agent with indications, benefits and side effects like any other drugs. Oxygen therapy is a treatment that provides the patient with extra oxygen (>21%). It is widely used in prehospital and hospital environments as well as domiciliary or long-term oxygen therapy. This short article includes oxygen manufacture and storage, practical uses of oxygen therapy, oxygen delivering devices, how to prescribe oxygen and risks of oxygen treatment.

We need oxygen for the cells in our body to work. The air we breathe contains about 21% oxygen, which is plenty for people with healthy lungs and many with lung disease. However, if you have bad enough lung disease, you may not be able to get enough oxygen from your lungs into your blood. Hence, if your oxygen level is low, your healthcare provider will recommend supplemental oxygen. Sometimes you only

need extra oxygen in special situations. For example, you may need oxygen at very high altitudes (like in the mountains or in an airplane) even if you do not at sea level.

Governments across the world attended medical emergencies triggered by the COVID-19 pandemic. Like several other countries, India, the second-most populous country, battled for optimal usage of medical infrastructures, such as hospital beds, medical oxygen,

and others [1]. This pandemic required different kinds of facility to handle patients from distance [2] while prediction of lockdown period also had importance as discussed [3]. Apart from its industrial usage, oxygen is used for various medical purposes - from general medicine administration to medical assistance and emergency procedures. Oxygen is a critical element for human life existence, and because of its natural availability through the air, it is sometimes forgotten to be a life-saving essential medicine. The timely availability of medical oxygen is a decider of life and death for the patient. Hospitals are always giving priority over the rest regarding the continuous availability of medical oxygen. Medical

Oxygen is a critical ingredient in treating certain critical health conditions such as pneumonia, malaria, sepsis, and meningitis. Children and mothers are often administered medical oxygen to ease breathing when their lives are at risk during medical treatment. Its importance once grew more during the COVID-19 pandemic because of its close association with the respiratory system [4]. High-flow nasal oxygen is found to be a safe and efficient treatment for COVID-19 patients who are not in an ICU [5]. The WHO says that 15 percent of COVID-19 patients require medical oxygen because of breathing difficulties [6]. Silent hypoxia patients do not show any evident respiratory distress but experience sudden dangerously low oxygen levels [7]. NIH recommends high-flow nasal cannula (HFNC) oxygen over non-invasive positive pressure ventilation (NIPPV) [8]. Some critically ill patients even require a ventilator. However, the available number of ventilators is too low. This forced medical equipment manufacturers to quickly go into production mode. COVID-19 clearly exposed a major weakness in the health systems – that of medical oxygen production and delivery [9]. Despite administrations trying to do their best to supply medical oxygen, demand overtook the supply, making its availability inadequate during the pandemic times. Some modern methods, such as onsite medical oxygen production using oxygen generators, are experimented. Such setup enables continuous, reliable, and cost effective supply for mobile and static medicine. They are specially designed and developed to supply oxygen in medical facilities following strict quality guidelines. These generators meet global quality standards and provide purity of 93 to 95 percent. Thanks to Industry 4.0 standards, remote monitoring, and operation of the medical oxygen generation systems can be done from a computer.

Work-station, tablet, or smartphone from anywhere in the world [10]. Smart factories can help in optimizing the compressor room practices at the manufacturing unit [9]. Hospitals procure medical oxygen through cylinders that fill it at industrial gas plants.

The cylinders are installed in the hospital basement or at proximity and piped to the patient's bed. The patients are charged based on consumption. Typically, a \$40–\$60 would be charged for a severe pneumonia child who spends 3–4 days and consumes 4,000 to 8,000 cubic liters of oxygen. The challenge for medical and health administration is to increase the supply of medical oxygen while reducing cost so that it is accessible where it is needed most, free at the point of use. This demands increased investment and commitment to put oxygen infrastructure at the centre of universal health coverage strategies [4]. Most of the COVID beds in hospitals worldwide faced a sudden demand for piped oxygen supply forcing hospital administrations to spend more to supply copper piped oxygen connected to a cylinder bank.

Oxygen is one of the commonest therapeutic interventions in health care worldwide. Yet, despite the widespread use, problems regarding prescription and administration exist, 1–7 resulting in a significant burden for patients, carers and health care resources. Poor practice regarding oxygen therapy, such as inadequate assessment and poor follow-up, has been uncovered in the United Kingdom.<sup>7</sup> This led to major changes in prescription and provision of domiciliary oxygen therapy, principally the provision of clinical standards for initial assessment and subsequent patient management.<sup>8</sup> Despite implementation of these changes, problems continue.<sup>9,10</sup> It is unclear what factors contribute to persisting poor practice; the problem may stem from a belief that oxygen alleviates breathlessness,<sup>11</sup> but there is no evidence supporting this claim.

Oxygen in both acute and chronic settings has been recognized as a major area for improvement in the United Kingdom,<sup>12</sup> but in order to address these recommendations there is a need to identify reasons for enduring poor practices. The review question, 'how do respiratory patients perceive oxygen therapy?', is orientated towards respiratory patients' perceptions rather than efficacy of the intervention. The literature is therefore dominated by qualitative research as these

voices are brought to the fore. Relevant quantitative data were also evident and so directed the review to one of an integrative approach. Integration and synthesis of both qualitative and quantitative research, although complex and challenging, have the potential to enhance holistic understanding of the topic being investigated and therefore increases relevance.<sup>13</sup> The specific review question appears elusive in published literature, and it became apparent that extrapolation from studies with a wider focus was necessary. This directed the decision to utilize an interpretative, rather than aggregative, approach and informed the selection of a critical interpretive synthesis method.

The aim of this review was to explore respiratory patients' beliefs and perceptions of oxygen therapy

in order to highlight and provide a platform for further investigation.

### Search strategy

A systematic approach to searching, locating and retrieving relevant literature was adopted (Centre for Reviews and Dissemination (CRD), 2009). Medline (1950–2014), Cinahl (1981–2014), Embase (1980–2014), British Nursing Index (1985–2014) and Psych Info (1806–2014) and searched via EvidenceSearch ([www.evidence.nhs.uk](http://www.evidence.nhs.uk)) using key words oxygen therapy, chronic respiratory disease, COPD, interstitial lung disease. No date or publication type restrictions were applied.

Oxygen is an invincible and inevitable gas used in diversified industrial applications such as welding, cutting, brazing, and other metal fabrication activities, and in medical and healthcare applications. Oxygen gas is compressed and filled in a high-pressure cylinder to make it easy to transport. The medical use and benefits that accrue from the usage of oxygen are innumerable. However, it requires safe handling by qualified and trained personnel failing which the lives of various stakeholders, including that of the patient's health condition could be in danger. Overdosage, or over-usage of oxygen, can put the patient into a coma while insufficient

levels could lead to breathlessness. Several researchers questioned the benefits that accrue from the clinical settings at which medical oxygen is routinely used. [1] The care and caution of dealing with oxygen begin from the stage of filling it to the cylinders, and later through the transportation till the final step of fixing of equipment and end-patient delivery. Failures in safe handling can lead to an accidental blast that can claim human lives. [2]

The air we breathe contains about 21% oxygen. Without oxygen we would die in a matter of minutes **1**. Many people at work and sometimes at home use oxygen gas in cylinders. It is widely used in welding, people who work in deep sea diving, for food preservation, in steel works and for medical purpose etc. Greensmith **2** has observed that hyperbaric oxygen therapy potentially can provide enhanced oxygen delivery to peripheral tissues affected by vascular disruption, cytogenic and vasogenic edema and cellular hypoxia caused by extremity trauma. After appropriate resuscitation, macrovascular repair, and fracture stabilization, adjunctive hyperbaric oxygen therapy can enhance tissue oxygen content. In growing edge of industrial and medical advancements, increased use of compressed gases like oxygen, nitrogen, carbon dioxide, helium, argon, krypton, acetylene etc is the need of an hour. In spite of being vital to the human life, oxygen can be most dangerous to snatch a soul from body if not handled with caution. Few lay press news items such as three people were killed and one injured after an oxygen cylinder blast at their job site **3**, and two people died and one sustained serious burns after cylinder blast **4** while filling gas are not uncommon. Gases in their compressed state, and particularly compressed air, are almost indispensable to modern industry can cause disastrous effect in absence of proper handling, storage and transport. Precautions taken during handling, storage and transport can save damages to both human beings and inanimate things of terrorist activities rather than conventional wars, civil tragedies are usually industrial, as in individual incidents in

mines and quarries or on a larger scale, such as the denotation of chemical stores, ships and factories<sup>6</sup>. Injuries due to an explosion are primary blast injury (this is the result of sudden change in the environmental pressure changes resulting from blast waves), secondary blast injuries (fragments and other missiles cause these injuries), tertiary blast injuries (include acceleration and deceleration injuries caused by the victim's body impacting against stationary objects or injuries caused by collapse of structures and buildings) and thermal and/or chemical injuries<sup>7</sup>. The specific injury produced in lungs by the blast is known as blast lung, which is grossly characterized as sub pleural patchy haemorrhage, often in the line of the ribs, intrapulmonary haemorrhage and bullae at the lung margins<sup>6</sup>

## II. Oxygen Manufacture and Storage

99% or 99.5% pure oxygen is regarded as medical grade oxygen. It is manufactured by fractional distillation of liquefied air based on different boiling points of gases contained in the atmospheric air. After oxygen is manufactured, it can be stored as follows:

### (i) Vacuum insulated evaporator (VIE):

When the gas becomes liquid form, it occupies a much smaller volume. Therefore, a large amount of oxygen can be stored in the form of liquid. A VIE is a container designed to store liquid oxygen.<sup>2</sup> The VIE system is used in large hospitals which have a pipeline system. It is the most economical way to store and supply oxygen.<sup>4</sup>

### (ii) Oxygen cylinders:

Oxygen can be stored under pressure in cylinders. Oxygen cylinders are made of molybdenum steel and manufactured in different sizes (Table I). Size E cylinder is usually attached to the anaesthetic machine.<sup>4</sup> They are color-coded as black body and white shoulder in UK<sup>1</sup> (Figure 1).

Oxygen can also be produced by oxygen concentrator. It is a device which extracts oxygen from atmospheric air by using zeolite molecular sieve. Small or large concentrators

are available to supply a single patient or for pipeline system.

## II. Uses of Oxygen Therapy in Various Disease

### (i) Hypoxia:

Hypoxia is a deficiency of oxygen at the tissue level. Hypoxaemia is deficiency of oxygen in arterial blood ( $\text{PaO}_2 < 60 \text{ mmHg}$ ). Hypoxia can be divided into 4 types:<sup>2</sup>

#### (ii) Hypoxic hypoxia

In this type of hypoxia, oxygen tension of arterial blood is reduced, eg. altitude, equipment error, drug overdose, asthma.

#### (iii) Anaemic hypoxia:

In this type of hypoxia, arterial oxygen tension is normal. However, amount of Hb available to carry oxygen or Hb function is reduced, eg. anaemia, carboxyhemoglobinemia, methemoglobinemia.

#### (iv) Ischaemic hypoxia:

In this category, arterial oxygen tension and Hb concentration are normal. Blood flow to the tissues is reduced and oxygen cannot be delivered to the tissues, eg. congestive heart failure, dehydration.

#### (v) Histotoxic hypoxia:

Above all factors are normal in this type, however a toxic agent prevents the cells from using oxygen although oxygen is delivered to the tissues, eg. cyanide toxicity.

### (ii) Pre-oxygenation:

If the patient is breathing room air, the oxygen store in functional residual capacity (FRC) is approximately 450 ml and it can be increased to 3000 ml with breathing 100% oxygen. As a result, there will be a rapid fall in oxygen saturation during apnoea (e.g. following induction of anaesthesia) if breathing room air. Pre-oxygenation means breathing 100% Oxygen for three to five minutes through an anaesthetic circuit with a face mask firmly applied to the face. This will replace the nitrogen in the FRC with oxygen and also referred to as denitrogenation. The extra oxygen in the FRC can provide an essential

store of oxygen for period of apnoea after induction. It is particularly essential for rapid sequence induction and difficult intubation.<sup>5</sup>

### **(iii) Postoperative oxygen:**

Additional oxygen should be given to all patients for the first 10 min after general anaesthesia, as a result of hypoxaemia during the early recovery period. Postoperative hypoventilation is common due to the residual effect of anaesthesia, opioid analgesia, pain or airway obstruction. Prolonged oxygen therapy is required after operation in certain conditions such as hypotension, ischaemic heart disease, anaemia, obesity and shivering.<sup>1</sup>

### **(iv) Hyperbaric oxygen therapy:**

Hyperbaric oxygen therapy means the patient is exposed to oxygen tension exceeding ambient barometric pressure. It is indicated in decompression sickness, gas embolism, gas gangrene and carbon monoxide poisoning.<sup>3</sup>

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## **IV. Oxygen Delivering Devices**

There are two main types of oxygen delivering devices; fixed and variable performance devices.<sup>2</sup>

### **(i) Fixed performance devices:**

By using fixed performance devices, patient receives a constant inspired oxygen concentration (FiO<sub>2</sub>) and it does not depend on patient's ventilation. It is regarded as patient independent devices. Examples of fixed performance devices are:

(a) High air flow oxygen enrichment devices (HAFOE devices) eg. Ventimask

(b) Head boxes for neonates

#### **(a) HAFOE devices eg. Ventimask:**

Ventimasks are colour coded (Figure 2) and it states the flow of oxygen in litres per minute required to deliver a specific inspired oxygen concentration. Holes on the Venturi device allow entrainment of room air by the Venturi principle. These holes also flush expired gas. Advantages of using Ventimask include very precise measurement of delivered oxygen and no rebreathing. However, the mask is hot and may irritate the skin.

Components of Ventimask<sup>4</sup>

- Body of the mask with holes
- Color-coded venturi device
- Corrugated tubing
- Adjustable head strap

#### **(b) Head box for neonates (Oxygen hood):**

It is ideal for relatively short-term oxygen therapy for newborns and inactive infants. It covers only the head and oxygen is delivered into the box with 10-15 L/min to flush CO<sub>2</sub> (minimum flow 7L/min).<sup>3</sup>

### **(ii) Variable performance devices:**

By using variable performance devices, the oxygen concentration delivered depends on patient minute ventilation, peak inspiratory flow rate and oxygen flow rate.<sup>2</sup> It is regarded as patient dependent devices.

Examples of variable performance devices are:

- (a) Nasal cannula
- (b) Simple face mask
- (c) Mask with O2 reservoir

**(a) Nasal cannula:**

It is ideal for long term oxygen therapy. It does not increase dead space and there is no rebreathing. Flow rate of 2-4

L/min is recommended as higher flow rate (>5L/min) can result in discomfort of the patient.<sup>3</sup>Advantages and

disadvantages of nasal cannula can be seen in Table II.

Components<sup>4</sup> (Figure 3)

- Adjustable head strap
- Two prongs
- Plastic oxygen tubing

**Advantages**

1. Easy to use
2. Low-flow oxygen administration
3. Less restrictive than face mask
4. No increase in dead space
5. More tolerable than oxygen mask
6. Allow speech and eating/drinking

**Disadvantages**

1. Drying and irritation of nasal mucosa
2. Chance of nasal bleeding
3. Sores around the external nares in long-term

**(b) Simple face mask:**

It is made of transparent plastic. Body of the mask serves as a reservoir for both oxygen and expired CO<sub>2</sub>. It has a small dead space and can result in a small amount of rebreathing. Dead space depends on oxygen flow and patient’s minute ventilation. Various sizes are available from paediatric to adult. It is indicated for patients who require higher levels of oxygen than cannulas eg. during medical transport, postanaesthesia care unit and emergency department.<sup>3</sup> Components<sup>4</sup> (Figure 4)

- Body
- Vent holes
- Elastic band

**Disadvantages of using simple face mask**

- Patient complains of feeling of suffocation and poorly tolerated.
- Speech is muffled, eating and drinking are difficult.

**Table 1: Shows flow rates and approximate oxygen concentration delivered.<sup>3,6</sup>**

Type	Oxygen Flow (L/min.)	Oxygen Contraction (%)
Nasal Cannulae	1	21-24
	2	23-28
	3	27-34
	4	31-38
Simple Face Mask	5-6	30-45
	7-8	40-65
Mask with oxygen reservoir (rebreathing system)	10-15	70-80
Mask with oxygen reservoir (Non rebreathing system)	10-15	95-100

**Table 2: Cylinder sizes common in health facilities**

Cylinder size	D	E	F	G	J
Nominal content/oxygen capacity (L)	340	680	1360	3400	6800
Water capacity (L)	2.3	4.7	9.4	23.6	47.2
Dimensions (height × diameter) (mm)	535 × 102	865 × 102	930 × 140	1320 × 178	1520 × 229
Approximate full weight (kg)	3.9	6.5	17	39	78
Valve outlet connection (and specification)	Pin index (ISO 407)	Pin index (ISO 407)	Bullnose (BS 341)	Bullnose (BS 341)	Pin index side spindle (ISO 407)
Nominal service pressure (kPa/bar/psi)	13 700 kPa (137 bar/1987 psi)	13 700 kPa (137 bar/1987 psi)	13 700 kPa (137 bar/1987 psi)	13 700 kPa (137 bar/1987 psi)	13 700 kPa (137 bar/1987 psi)
Health facility use	Emergency and ambulance transport	Emergency and ambulance transport	Stand-alone	Stand-alone	Manifold connection and stand-alone

**(c) Mask with O2 reservoir:**

It is a standard face mask with addition of reservoir bag to increase the capacity of O2 reservoir by 600 ml. There are two types of mask with O2 reservoir; rebreathing system where there is no valve and gas can be exhaled in the initial phase of expiration returns to the reservoir bag and non-rebreathing systems where one-way valve is incorporated to prevent any exhaled gas from returning to the reservoir bag.<sup>6</sup>

**How to Prescribe Oxygen**

**(a) Uncontrolled oxygen therapy:**

Oxygen is commonly prescribed freely to patients with cardiac or respiratory arrest, respiratory distress, asthma,

hypotension or other critical conditions by using variable oxygen administration devices.

**(b) Controlled oxygen therapy:**

The oxygen concentration is prescribed using a HAFOE device in a small group of patients with chronic obstructive pulmonary disease (COPD). In those type of patients, CO2 level is chronically raised and they depend on hypoxia to stimulate their respiration (hypoxic respiratory drive). High concentration O2 can reduce respiration and cause respiratory depression. O2 concentration should be started with 24-28% aiming to achieve PaO2 >50 mmHg or SpO2 85- 90%.<sup>2</sup>

**Complications of Oxygen Treatment**

There are both respiratory and non-respiratory toxicity due to the effects of oxygen therapy. It depends on patient susceptibility, FiO2 and duration of therapy.<sup>3</sup>

**(i) Fire hazard:**

Oxygen supports combustion of other fuels.

**(ii) Absorption atelectasis:**

High concentrations of oxygen can cause atelectasis especially in dependant areas of the lungs.<sup>2</sup>When oxygen is the only

gas being given, it is rapidly and completely absorbed from the alveoli and results in collapse (absorption atelectasis).<sup>5</sup>Nitrogen present in the air is absorbed more slowly and prevents the alveolus from collapsing.

**(iii) Retinopathy of prematurity (ROP):**

It is a neovascular retinal disorder and formerly termed retrolental fibroplasia. It is caused by vascular proliferation followed by fibrosis and retinal detachment leads to blindness. The low birth weight, very premature infant is at risk.<sup>2</sup>It is resolved in 80% of cases without visual loss. PaO2 of 50-80 mmHg is recommended in premature infants receiving

oxygen.<sup>3</sup>

**(iv) Pulmonary toxicity:**

Patients exposed to high oxygen levels for a prolonged period of time have lung damage. It depends on FiO<sub>2</sub> and duration of exposure. It is due to intracellular generation of reactive O<sub>2</sub> metabolites (free radicals) such as superoxide and activated hydroxyl ions, singlet O<sub>2</sub> and hydrogen peroxide, which can damage alveolar-capillary membrane. Pulmonary capillary permeability increases and leading to edema, thickened membranes and finally to pulmonary fibrosis.<sup>3</sup> Pulmonary fibrosis may occur after exposure to high concentration of oxygen for a week.<sup>1</sup>

**(v) Depression of ventilation:**

It is seen in COPD patients with chronic CO<sub>2</sub> retention who have hypoxic respiratory drive to breath. Increased arterial tension to normal can lose the hypercapnoeic stimulus to maintain ventilation resulting in hypoventilation in this patient.<sup>3</sup>

**(vi) Hyperbaric oxygen toxicity:**

Prolonged exposure of hyperbaric O<sub>2</sub> therapy can lead to pulmonary, optic and central nervous system toxicity. Symptoms of pulmonary toxicity include retrosternal burning, cough and chest tightness. It can cause narrowing of the visual fields and myopia in adults. Signs and symptoms of central nervous system toxicity include behaviour changes, nausea, vertigo, facial twitching and tonic-clonic seizures.<sup>1</sup>

**Conclusion**

Oxygen is essential for all vital organs in our body and widely used in all medical specialities. It is the first drug to be given in any crisis condition. Different types of oxygen delivering systems are available and necessary to choose depending on condition of individual patients. As each drug has its own adverse effect, oxygen therapy also has some risks. However in any crisis condition, it is the lifesaving drug, therefore should never prevent oxygen since lifesaving is

Our first priority. Oxygen cylinders come in many different sizes. Cylinder sizes for medical gases are named alphabetically, unlike industrial cylinders which are numbered. Table 3.2

summarizes the key features of cylinder sizes commonly used in health care facilities. Unlike liquids, gases can be compressed, and doing so increases their density. That is why a gas cylinder of 47 L volume under pressure can contain gas that expands to 6800 L of volume when released into normal atmospheric pressure.

Cylinders are fitted with customized valves (either pin index or bullnose type) that are opened with valve keys, and with valve guards for safety. The Pin Index Safety System (PISS) is designed to ensure the correct gas is connected to the regulator or other equipment. The arrangement of the pins is unique for each gas, and the positions of the holes on the cylinder valve must correspond with the pins to prevent the use of the wrong gas.

Some cylinders have built-in, integral pressure regulators, which do not require a separate pressure regulator to be fitted to the cylinder valve before use.

**References**

1. Suzanne C. Lareau RN, MS, Bonnie Fahy RN, MN; Oxygen Therapy; Am J. Respir. Crit. Care. Med. Vol 171, P1-P2, 2005.
2. G. Kapoor, S. Hauck, A. Sriram, J. Joshi, E. Schueller, I. Frost, A. Nandi, State-wise
3. estimates of current hospital beds, intensive care unit (ICU) beds and ventilators in India: are we prepared for a surge in COVID-19 hospitalizations?, Center Disease Dyn Econ. Policy (2020), <https://doi.org/10.1101/2020.06.16.20132787>.
4. G. Arora, A.K. Maurya, N. Kumar, A.K. Mishra, Application of big data generated by IoT environment for HealthCare using Voice Recognition, Int. J. Res. Eng. IT Social Sci. 08 (11) (November 2018) 132–136.
5. P. Wadhwa, Aishwarya, A. Tripathi, P. Singh, M. Diwakar, N. Kumar, Predicting
6. the time period of extension of lockdown due to increase in Rate of COVID-19 cases in India using machine learning, Mater. Today: Proc. Elsevier (2020).
7. K. Watkins, Oxygen for all, during COVID-19 (coronavirus) and beyond, 2020, May 26. Retrieved from



- <https://blogs.worldbank.org/health/oxygen-all-during-covid-19-coronavirus-and-beyond>.
8. T. Guy, A. Créac'hacdec, C. Ricordel, A. Salé, B. Arnouat, J.-L. Bizec, M. Langelot, C. Lineau, D. Marquette, F. Martin, M. Lederlin, S. Jouneau, High-flow nasal oxygen: a safe, efficient treatment for COVID-19 patients not in an ICU, *Eur. Respir. J.* 56 (5) (2020) 2001154, <https://doi.org/10.1183/1399-3003.01154-2020>. Shareable1.
  9. WHO, Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected. Interim guidance, 2020, March 13. Retrieved from <https://www.who.int/docs/default-source/coronaviruse/clinicalmanagement-of-novel-cov.pdf>
  10. IANS, Why some Covid-19 patients with low oxygen level breathe well. ET
  11. Healthworld, 2020, July 4. Retrieved from <https://health.economictimes.indiatimes.com/news/diagnostics/why-some-covid-19-patients-with-low-oxygen-level-breathe-well/76785165>
  12. NIH, Oxygenation and Ventilation, 2020, July 17. Retrieved from <https://www.covid19treatmentguidelines.nih.gov/critical-care/oxygenation-and-ventilation/> T. Anderson, COVID 19 and the oxygen bottleneck, *Bull. World Health Organ.* 98 (2020) 586–587, <https://doi.org/10.2471/BLT.20.020920>.
  13. Inmatec, Medical Oxygen, 2020. Retrieved from <https://www.inmatec.de/en/medical-oxygen.html> Carol Ann Kelly and Michelle Maden, How do respiratory patients perceive oxygen therapy? A critical interpretative synthesis of the literature; *Chronic Respiratory Disease* 2014, Vol. 11(4) 209–228
  14. Sjoberg, F., & Singer, M. (2013). The medical use of oxygen: a time for critical reappraisal. *Journal of Internal Medicine*. doi:<https://doi.org/10.1111/joim.12139> [2]
  - Gupta, S., & Jani, C. (2009, March). Oxygen Cylinders: "life" or "death"? *African Health Sciences*, 9(1), 57-60.
  15. Take care with oxygen (fire and explosion hazards in the use of oxygen). Published by Health and Safety Executives (rev 2), reprinted 02/2008. Available at: <http://www.hse.gov.uk/pubns/hse8.pdf>.
  16. Greensmith JE. Hyperbaric oxygen therapy in extremity trauma. *J Am Acad Orthop Surg*, 2004; 12(6): 376-384.
  17. The Tribune News Services, Chandigarh, India, Jalandhar edition, July 22, 2008. The Times of India, Bangalore edition, November 15, 2008.
  18. Rani M, Gupta A, Dikshit PC, Aggrawl A, Sethi P, and Dhanikar V. Accidental Death Resulting from Acetylene Cylinder Impact. *Am J Forensic Med Pathol*, 2005; 26(2):170-173.
  19. Knight B. Death from Explosion. *Forensic Pathology*. 2<sup>nd</sup> edition, Arnold publisher, London, 1996; pp 270-273.
  20. Dogra TD and Rudra A. Blast Injuries. *Lyon's Medical Jurisprudence & Toxicology*, 11th edition, Delhi Law House, 2005; pp 949-953.
  21. Alan RA, Iain KM, Jonathan PT. *Textbook of anaesthesia*. 6th edition, 2013.
  22. Andrei MV, Sara H. Acute Oxygen treatment. *Update in anaesthesia* 12, 2000.
  23. Edward M, Maged SM, Michael JM. *Clinical anaesthesiology*. 4th edition, 2005.
  24. Baha A, Simon S. *Essentials of anaesthetic equipment*. 1995.
  25. Rob L, Henry B. The physiology of oxygen delivery. *Update in anaesthesia* 10, 1999.
  26. Advanced life support training manual. Ministry of health, Malaysia. 2012.