Carbon dioxide (CO2): Normal Physiology; Hazards and Risks

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CO2 in normal physiology:

In humans, carbon dioxide (CO2) is produced in cells as a byproduct of metabolism.[2] Then it circulates through the bloodstream, mostly within red blood cells, to be exhaled from the lungs as CO2 and excreted from kidneys as bicarbonate (HCO3-).

CO2 levels:[3]

- play a major role in regulating blood and tissue pH (acid-base balance),
- largely determine respiratory drive (rate and depth of breathing), and
- influence oxygen attachment to hemoglobin

Internal physiologic processes tightly regulate CO2 levels in the blood; abnormally high concentrations cause a variety of signs and symptoms. (See CO2 toxicity below.)

Maintaining blood pH within a narrow range is essential for normal functioning of virtually all organs and physiologic systems. CO2 plays a central role via these reactions:

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow HCO_3^- + H^+$$

where H2O is water, H2CO3 is carbonic acid; HCO3- is bicarbonate; H+ is hydrogen ion.

As shown, these reactions occur in both directions so that, in the lungs, bicarbonate and carbonic acid liberate CO2, which is exhaled. The kidneys also play an important role in maintaining normal pH by regulating levels of HCO3-.

Humans and virtually every living organism (plants and animals) have evolved to produce an enzyme, carbonic anhydrase,[4] which dramatically increases the speed of the first part of the above reaction, ($CO_2 + H_2O \leftrightarrow H_2CO_3$), making this an ideal system for very rapidly fine-tuning the regulation of CO2 levels and blood pH through changes in the rate and depth of respiration.

CO2 also reacts with water to form carbonic acid in a CO2 pipeline, even in the absence of carbonic anhydrase, albeit much more slowly. Carbonic acid is highly corrosive to carbon steel.

The main drivers of respiratory rate and depth are normally bloodstream CO2 levels and associated pH changes. These are maintained within healthy limits by chemoreceptors located in the medulla at the base of the brain (central chemoreceptors) and in the aorta and carotid arteries (peripheral chemoreceptors). Brain

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[2] *Krebs Cycle.* Redwood City, Calif.: Course Hero, Inc., undated; https://bit.ly/3NfXhzh

[3] G.J. Arthurs and M. Sudhakar, "Carbon dioxide transport," *Continuing Education in Anaesthesia Critical Care & Pain* Vol. 5, No. 6 (Dec. 2005), pgs. 207-210; https://bit.ly/37V9qto

[4] At least seven families of carbonic anhydrase enzymes have been identified, coded by distinct gene families, and at least one family is present in virtually every living organism. See Rossana Occhipinti and Walter F. Boron, "Role of Carbonic Anhydrases and Inhibitors in Acid-Base Physiology: Insights from Mathematical Modeling," *International Journal of Molecular Sciences* Vol. 20 (2019), 30 pgs. http://bit.ly/3JEk2us

receptors detect changes in the CO2 and pH, aorta receptors detect changes in CO2 and oxygen, and carotid receptors detect changes in all three. Respiratory rate and depth increase primarily in response to an increase in CO2/decrease in pH to reduce CO2 and maintain pH within normal limits.

CO2—an asphyxiant and toxicant:

CO2 is colorless, odorless, non-flammable, and heavier than air. As a gas in air, concentrations will be higher near the floor or ground. It can be compressed at high pressures into a liquid or frozen at very low temperatures into a solid (dry ice).

CO2 is classified as a hazardous substance by the Occupational Safety and Health Administration (OSHA) and National Institute for Occupational Safety and Health (NIOSH)[5]

Workplace exposure limits:

> OSHA: Airborne permissible exposure limit (PEL) is 5000 ppm (0.5%) averaged over 8 hrs.
>
> NIOSH: Recommended airborne exposure limit (REL) is 5000 ppm averaged over 10 hrs. and not to exceed 30,000 ppm (3%) over any 15 min. period.

Ambient air contains about 0.04% (400 ppm) CO2, 20% O2, 79% nitrogen, and small amounts of other gases.

This air level of CO2 has no direct adverse health effects in humans. As a potent greenhouse gas, however, this steadily-increasing atmospheric concentration is a major driver of climate change, which has wide-ranging direct and indirect health impacts globally.

Inhalation exposures to concentrations of CO2 higher than OSHA and NIOSH exposure limits are hazardous in two ways, both of which contribute to signs and symptoms (see table below):

1) Gaseous CO2 is heavier than air and when released in concentrated amounts it flows downhill, collects in low-lying areas—indoors or outdoors—or confined, poorly-ventilated spaces such as basements, storage tanks, dry-ice refrigeration systems, fermentation areas, or mines. It displaces ambient air so that oxygen levels can fall to dangerously low levels. For that reason, CO2 is well-known as an asphyxiant.
2) CO2 also has toxic properties in addition to causing oxygen-deprivation. Inhalation of high concentrations of CO2 can sharply lower the pH of blood and tissues (acidosis) causing acute effects on the respiratory, cardiovascular, and central nervous systems.

The response to excessive CO2 inhalation varies even among healthy individuals[6] so that the timing of onset of signs and symptoms of toxicity can vary from one person to another. This may be due to underlying health status, age, or variability in chemoreceptor sensitivity and respiratory response to acute CO2 exposures.

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[5] "Carbon Dioxide," in *NIOSH Pocket Guide to Chemical Hazards* (Atlanta, Georgia: Centers for Disease Control and Prevention, Oct. 30, 2019); https://bit.ly/3tyCGON

[6] Matthew Gill and others, "Effects of elevated oxygen and carbon dioxide partial pressures on respiratory function and cognitive performance," *Journal of Applied Physiology* Vol. 117, No. 4 (Aug. 15, 2014), pgs. 406-412; https://bit.ly/3qw4HEL

Symptoms depend in large part on the concentration of inhaled CO2 and the length of time a person is exposed. Since CO2 is odorless and does not cause irritation, unlike some other gases, it gives no warning and people may be unaware of excessive exposures until they experience troubling, dangerous symptoms.

CO2 toxicity[7]

CO2 Concentration	Health Effect	Timing
2% (20,000 ppm)	Respiratory center stimulated causing increases in breathing (tidal) volume.	Rapid
4% (40,000 ppm)	Increase in breathing rate becomes distressing; development of respiratory acidosis.	Immediately dangerous to life and health (IDLH) [NIOSH] *
5-10%	Dimmed sight, sweating, tremor, increased heart rate and blood pressure; can > unconsciousness.**	Within a few minutes.
more than 10%	Can cause convulsions; coma (less than a minute)	Death within 10 minutes
20-30%	Loss of consciousness; death	Within one minute

* NIOSH considers this level to be immediately dangerous to life and health because it can cause confusion and impair ability to respond and get to safety. Signs and symptoms resulting from low to moderate exposures are generally reversible when a person is removed from a high CO2 environment.

** Symptoms are due to a combination of lower oxygen levels and CO2 toxicity.[8]

[7] Wouter ter Burg and Peter M.J. Bos, *Evaluation of the acute toxicity of CO2.* (Bilthoven, The Netherlands: National Institute for Public Health and the Environment [RIVM], July, 2009); https://bit.ly/3txCj76. And: Kris Permentier and others, "Carbon dioxide poisoning: a literature review of an often forgotten cause of intoxication in the emergency department," *International Journal of Emergency Medicine* Vol. 10, No. 14 (2017), 4 pgs.; https://bit.ly/3umxqNv. And: Food Safety and Inspection Service Environmental, Safety and Health Group, *Carbon Dioxide Health Hazard Information Sheet [ESGH-Health-02.00]* (Washington, D.C.: U.S. Department of Agriculture, no date; retrieved Mar. 23, 2022.); https://bit.ly/2VCrjqC And: "Carbon Dioxide," in *NIOSH Pocket Guide to Chemical Hazards* (Atlanta, Georgia: Centers for Disease Control and Prevention, Oct. 30, 2019); https://bit.ly/3tyCGON

[8] Richard E. Fairfax, "Clarification of OSHA's requirement for breathing air to have at least 19.5 percent oxygen content" in correspondence to William Costello April 2, 2007. Washington, D.C.: Occupational Safety and Health Administration, United States Department of Labor, April 2, 2007; https://bit.ly/3IsWoQo.