

Chapter 63

Carbon Monoxide Poisoning

Joshua Rucker and Joseph Fisher

KEY POINTS

- Carbon monoxide poisoning is the most common cause of poisoning morbidity and mortality in the world.
- Nonspecific symptoms frequently lead to misdiagnosis.
- The central nervous and cardiovascular systems are the most frequently affected.
- All patients should be treated with 100% oxygen.
- Severely poisoned patients should be considered for hyperbaric oxygen

Carbon monoxide (CO) is a colorless, odorless gas produced from the incomplete combustion of carbonaceous compounds. CO inhalation is the most common cause of poisoning in the industrialized world. Severe CO poisoning can cause multiorgan dysfunction and frequently necessitating admission to intensive care units.

EPIDEMIOLOGY, RISK FACTORS, AND PATHOGENESIS

In the United States, CO poisoning accounts for 40,000 to 70,000 emergency visits and between 3500 and 4000 deaths annually. The most common causes of severe CO poisoning are prolonged intentional or unintentional exposure to motor vehicle exhaust; indoor burning of wood, kerosene, or coal with inadequate ventilation; and combustion of fossil fuels in pipelines or containers. Risk factors for CO poisoning include cold climate, the presence of an indoor gas heater, and cohabitants with influenza-like symptoms.

CO Kinetics

CO is inhaled into the lung and then diffuses into the blood, where it mostly binds to hemoglobin to form carboxyhemoglobin (COHb). (A small amount of CO remains dissolved in blood in equilibrium with that bound to hemoglobin.) The rate of uptake of CO into the blood is increased by higher ambient CO partial pressure and increased minute ventilation. The rise in COHb is also affected by the total body hemoglobin content. For a given rate of uptake of CO into the blood, anemic patients and those with reduced circulatory volumes (e.g., females and bleeding patients) will have a faster rise in COHb levels than large patients with high hemoglobin concentrations.

After absorbing into the blood, up to 15% of the CO will slowly diffuse into the tissues, where it is primarily bound to

myoglobin and cytochrome oxidases. This intracellular binding is facilitated by conditions of hypoxia and hypotension. It can take several hours for equilibrium to be attained between the inhaled concentration and that in the blood and between the blood and the tissues. Removal of the victim from the elevated CO environment before equilibrium is established will limit the rise in COHb. Rapid elimination of COHb by early, vigorous treatment can help prevent the absorption of CO into the tissues and the resulting cellular toxicity.

CO is almost exclusively eliminated via the lungs. The rate of elimination varies with the partial pressure of oxygen (O₂) and minute ventilation (Fig. 63.1). The half-time of CO elimination when breathing room air ranges from 240 to 300 minutes. Breathing 100% O₂ reduces the half-time to 40 to 80 minutes. By raising the partial pressure of O₂ by two or three times, treatment with hyperbaric O₂ (HBO₂) reduces the half-time even further to 20 to 40 minutes. Although hyperventilation will accelerate the elimination of CO, the concomitant reduction in the partial pressure of arterial carbon dioxide will reduce the blood flow to the brain and the heart. As such, hyperventilation without measures to prevent hypocapnia may be deleterious and is not recommended treatment for CO poisoning.

PATHOPHYSIOLOGY

CO has several pathophysiologic mechanisms; the importance of each remains unclear (Fig. 63.2). CO has long been known to bind tightly to hemoglobin with 240 times the affinity of oxygen. Not only does CO decrease blood O₂ content by preventing the binding of hemoglobin to O₂ but it also decreases oxygen delivery at the tissues by shifting the oxyhemoglobin dissociation curve to the left (Fig. 63.3). Hence, much of the cellular damage caused by CO is secondary to hypoxia. However, CO is also likely a direct cellular toxin. Intracellular CO can interfere with cellular respiration and when combined with hypotension can initiate a series of events resulting in ischemia-reperfusion injury. Other postulated mechanisms of direct cellular toxicity include nitric oxide-mediated tissue injury, promotion of brain lipid peroxidation, hastening apoptosis, and interference with intracellular oxygen transport.

CLINICAL FEATURES

The symptoms of CO poisoning are nonspecific, frequently leading to misdiagnosis (Table 63.1). CO can affect multiple organ systems, but the central nervous system and cardiovascular

1

2

1

Section 10

Other Critical Care Problems

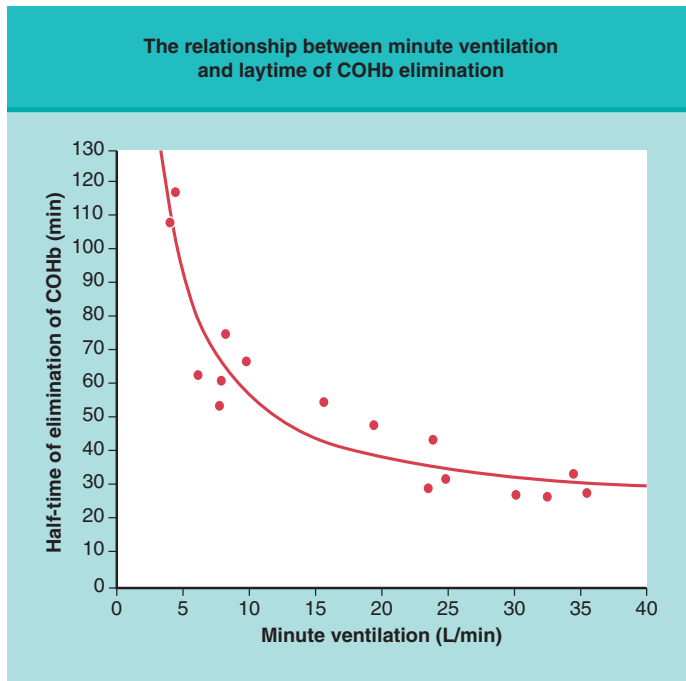


Figure 63.1. The relationship between minute ventilation and half-time of COHb elimination. (Adapted from Takeuchi A, Vesley A, Rucker J, et al: A simple “new” method to accelerate clearance of carbon monoxide. *Am J Respir Crit Care Med* 2000;161:1816–1819).

Table 63.1 Clinical Manifestations of CO Poisoning			
Severity	Central Nervous System	Cardiovascular System	Other
Mild	Headache Dizziness		Nausea/vomiting
Moderate	Confusion Weakness Blurred vision Ataxia	Chest pain Tachycardia	Tachypnea Dyspnea Myonecrosis
Severe	Disorientation Seizures Coma Stroke	Palpitations Dysrhythmias Hypotension Myocardial ischemia	Pulmonary edema Renal failure

system are the most severely affected due to their high oxygen requirements.

Central Nervous System Effects

Headache is the earliest and most common symptom of CO poisoning. Other common neurological symptoms include dizziness, lightheadedness, weakness, and confusion. Severely poisoned patients can have a decreased level of consciousness progressing to coma, seizures, and acute stroke. Brain computed tomography and magnetic resonance imaging of severely poisoned patients may reveal low density of the white matter and necrosis of the basal ganglia and cerebral gyri.

Cardiovascular Effects

Patients with CO poisoning may present with symptoms and electrocardiographic changes consistent with myocardial ischemia or infarction, especially if they have underlying coronary artery disease. Cardiac troponin isoenzymes are often elevated even in the absence of electrocardiograph (ECG) changes. Supraventricular dysrhythmias and intraventricular conduction delay have also been observed. Early mortality in severely poisoned patients is often due to hypoxia-induced ventricular dysrhythmias.

Respiratory Effects

CO-induced hypoxia can result in a compensatory respiratory alkalosis that in severe cases is further fueled by the ventilatory response to lactic acidosis. Twenty percent to 30% of intubated CO-poisoned patients develop pulmonary edema presumably due to left ventricular failure because CO appears to have no direct pulmonary toxicity. Victims of smoke inhalation may develop airway compromise and/or acute lung injury independent of CO poisoning.

Renal Effects

Severely poisoned patients infrequently develop acute renal failure secondary to nontraumatic rhabdomyolysis. Although CO may have some direct toxicity to the renal tubules, nearly all reported cases of acute renal failure in CO poisoning have been accompanied by muscle necrosis.

Dermatologic Effects

Cutaneous blisters are common in severe CO poisoning, likely secondary to pressure necrosis. The “classic” finding of “cherry-red skin” is a rare and usually postmortem observation likely due to the combination of CO-induced vasodilatation and tissue ischemia.

Delayed Neurologic Syndrome

Many patients with CO poisoning present with acute neurologic deficits; however, 1% to 10% of victims of CO poisoning will develop new neurologic symptoms after a lucid period of 2 to 40 days, described as delayed neurologic syndrome (DNS). These symptoms classically consist of mental deterioration (dementia, personality change, and primitive reflexes), urinary incontinence, and gait disturbance but can include a myriad of neurologic symptoms, such as parkinsonism, amnesia, mutism, psychosis, paralysis, tremor, peripheral neuropathy, and flaccid paralysis. The likelihood of DNS increases with severity of poisoning and the patient’s age. Although up to 75% of patients with DNS will fully or partially recover, many victims of CO poisoning suffer permanent changes in personality, affect, and cognition.

DIAGNOSIS

CO poisoning is an often overlooked diagnosis because not only are the symptoms and signs nonspecific but also initial investigations can be misleading. Despite the decreased O₂ carrying capacity of CO-poisoned patients, pulse oximetry and arterial blood gases will fail to reveal CO-induced hypoxia because the 660 and 940 nm diodes used in most pulse oximeters cannot differentiate COHb from oxyhemoglobin and the O₂ electrodes

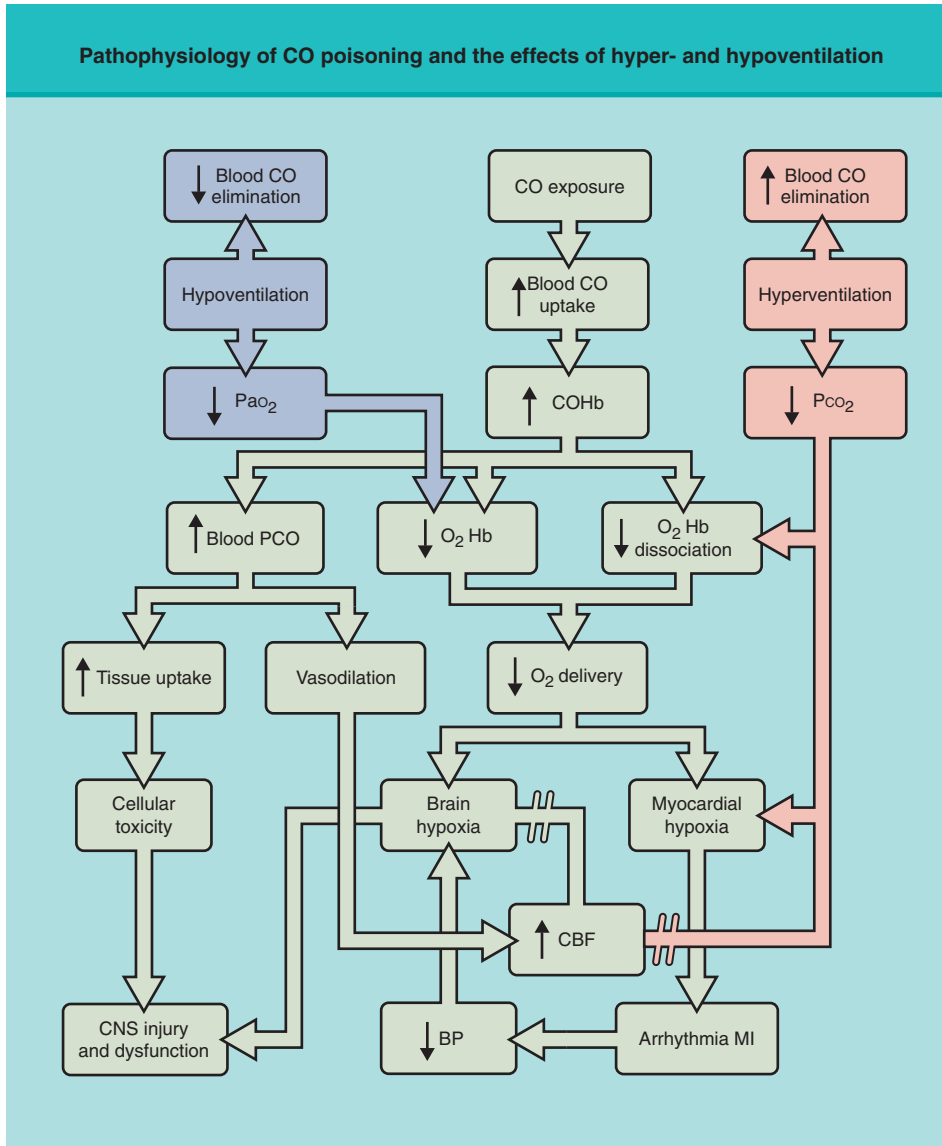


Figure 63.2. Pathophysiology of CO poisoning and the effects of hyper- and hypoventilation. The multiple effects of CO poisoning ultimately result in CNS injury. indicates an inhibitory effect.

in blood gas analyzers respond only to the partial pressure of O_2 in plasma, which is often normal. The definitive diagnosis of CO poisoning can be made by measuring elevated levels of COHb in either arterial or venous blood with a CO oximeter. Normal COHb levels are less than 3% (up to 10% in a recent smoker). The COHb level on presentation will depend on multiple factors related to the time course of exposure, rescue, and treatment and therefore may not correlate with the severity of symptoms. In some cases, the initial COHb level may even be normal and the diagnosis must be made on clinical grounds alone. Since cyanides can be produced during fires, victims of smoke inhalation should also be tested for cyanide poisoning.

TREATMENT

The prehospital management of CO poisoning is rapid removal of the patient from the CO environment and treatment with 100% O_2 . Hyperoxia will both accelerate the elimination of CO and provide a modest increase in blood O_2 content. Since max-

imizing arterial PO_2 is crucial, we recommend spontaneously breathing patients be treated with 100% O_2 via a tight-fitting self-inflating bag-valve-mask system. (Commonly available O_2 masks often provide far less than 100% O_2 because of obligatory entrainment of air from the side holes in the masks and because of leaks between the mask and the face.) If intubation is indicated, then ventilation should continue with 100% O_2 . Intravenous access should be secured, and the patient should be monitored for dysrhythmias.

Upon arrival in the emergency room, vital signs, including neurovitals, cardiac rhythm, and urine output, should be monitored. Initial investigations should include an ECG, chest X-ray, complete blood count, electrolytes, blood glucose, creatinine, urinalysis including urine myoglobin, cardiac enzymes, creatinine kinase, arterial blood gas, and serial carboxyhemoglobin levels. Treatment should continue with 100% O_2 and supportive measures to maintain adequate blood pressure and urine output. Standard ACLS protocols should be followed for the treatment of serious dysrhythmias. Moderate academia can be

Section 10

Other Critical Care Problems

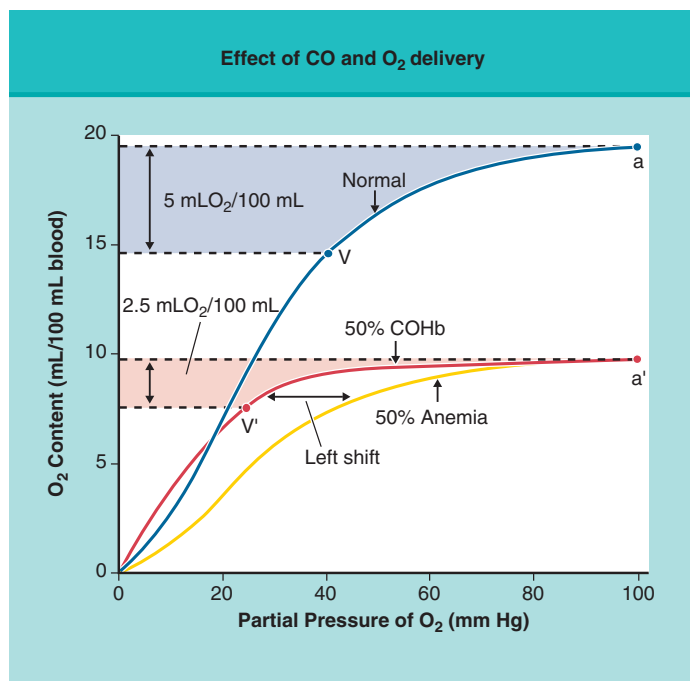


Figure 63.3. Effect of CO on O₂ delivery. The normal oxyhemoglobin dissociation curve and curves for 50% anemia and 50% carboxyhemoglobinemia are illustrated. The delivery of 5 mL/100 mL of blood delivered requires a decrease in the partial pressure of O₂ of approximately 60 mm Hg (from point a to point V on the normal curve). In the presence of 50% COHb, a delivery of only 2.5 mL/100 mL of blood delivered requires a decrease of 75 mm Hg (from point a' to point V'). (Modified from Bartlett, 1973.)

5

tolerated since its effects on the oxyhemoglobin dissociation curve will improve O₂ unloading at the tissues. In contrast, even mild respiratory acidosis (i.e., PCO₂ = 50) may warrant mechanical ventilation to maximize oxygenation and accelerate COHb elimination. Given the deleterious effects of hyperglycemia on brain injury, euglycemia should be maintained with an insulin infusion if necessary. In cases of unintentional CO poisoning, it is important for the treating physician to ensure that the patient's cohabitants are alerted and evacuated.

Hyperbaric Oxygen

Hyperbaric oxygen therapy has long been considered standard therapy for CO poisoning. In addition to accelerating CO elimination, HBO₂ may also reverse some of the direct cellular toxicity of CO, such as lipid peroxidation. The major risks of HBO₂ are barotraumas and O₂ toxicity, and the overall complication rate is approximately 2% or 3%. Although there has long been strong basic science research and numerous observational studies in support of HBO₂ therapy, only recently have large, well-designed randomized controlled trials investigated the efficacy of HBO₂ for CO poisoning.

Scheinkestel and colleagues (1999) randomized 191 CO-poisoned patients to be treated with either daily HBO₂ and intervening high-flow normobaric O₂ or only high-flow normobaric O₂ for 3 to 6 days. They found that patients treated with HBO₂

4

fared no better on neuropsychological tests following treatment or 1 month later. However, a high proportion (69%) of their patients had attempted suicide and half had ingested alcohol or drugs, which may have confounded their results. Furthermore, both the HBO₂ and the normobaric O₂ protocols did not conform to standard clinical practice, making it difficult to draw clinically relevant conclusions.

Weaver and associates (2002) randomized 152 acutely CO-poisoned patients to treatment with three sessions of either HBO₂ or normobaric O₂. At 6 weeks postpoisoning, cognitive sequelae were less frequent in the HBO₂ group (25 vs 46%). However, patients randomized to normobaric O₂ in this study received only 4 to 10 hours of 100% O₂ compared to 3 days in Scheinkestel and colleagues's (1999) study, which may partially explain the difference in results.

Given the lack of consistency in the literature, it is not surprising that there are no universally accepted criteria for the treatment of CO poisoning with HBO₂ therapy. Based on expert opinion from senior members of the Undersea and Hyperbaric Medicine Society, patients with transient or persistent unconsciousness, neurologic or cardiovascular dysfunction, or severe acidosis should be treated with at least one session of HBO₂ at 2.5 to 3.0 atm if it can be provided within 24 hours of CO exposure. Patients with persistent neurologic symptoms can be considered for additional HBO₂ treatment. Regardless of whether a patient receives HBO₂, he or she should be treated with 6 to 12 hours of 100% normobaric O₂.

Many victims of CO poisoning are initially treated at hospitals without hyperbaric facilities, and often a decision must be made as to whether the patient should be transferred for HBO₂ treatment. Patients who are most likely to benefit from transport to a HBO₂ facility include those who can be transported a short distance by ground, will receive treatment within 6 hours of poisoning, and are at high risk for neurologic sequelae (i.e., history of neurologic dysfunction, cerebellar signs, loss of consciousness, and/or COHb >25%).

Management of the CO-poisoned pregnant patient

CO poisoning poses significant risk to the fetus of a pregnant patient. Maternal CO poisoning (even minor exposures, without loss of consciousness) can result in fetal death, cerebral palsy, limb and cranial deformities, and a variety of mental disabilities. Animal studies in sheep have shown that fetal CO uptake is delayed for 2 or 3 hours. Nevertheless, extrication of the mother does not necessarily eliminate the risk to the fetus. Due to the greater affinity of fetal hemoglobin for CO compared to maternal hemoglobin, the fetus may continue to absorb CO from the maternal blood even as the maternal COHb is falling, and the fetus may eventually develop COHb levels exceeding maternal levels (Fig. 63.4).

Given the high morbidity and mortality of CO poisoning on the fetus, rapid treatment with HBO₂ therapy is generally recommended. It has been suggested that HBO₂ therapy may pose a risk of induction of labor or birth defects; however, several case series have demonstrated that HBO₂ therapy per se does not have significant adverse effects on the mother or fetus. Therefore, pregnant women who meet criteria should receive HBO₂ therapy, and since fetal COHb may rise significantly above maternal COHb, strong consideration should be given to treating even mildly poisoned, asymptomatic pregnant patients.

3

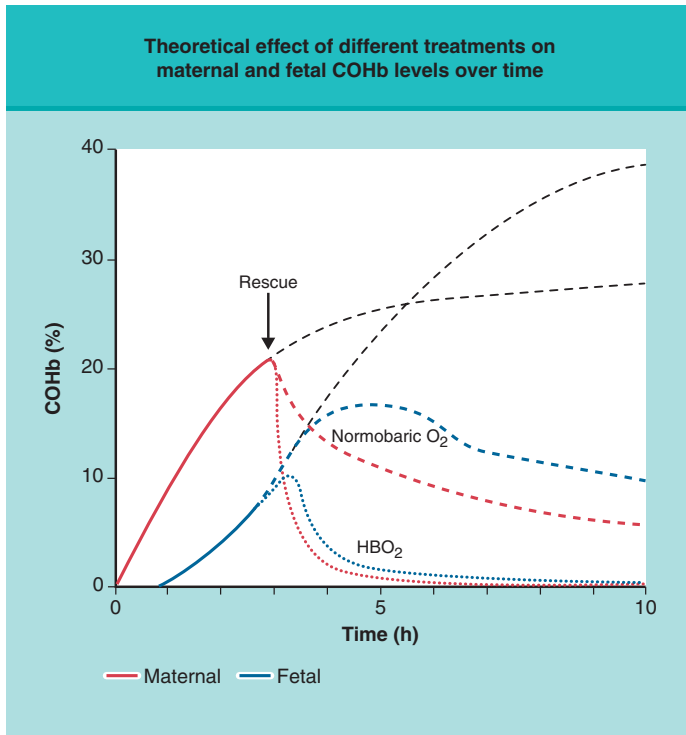


Figure 63.4. The theoretical effect of different treatments on maternal and fetal COHb levels over time. Although fetal CO uptake is delayed, fetal COHb levels will eventually far exceed maternal levels if the mother is not rescued from the CO environment. If the mother is rescued and treated with normobaric O₂, the prolonged CO elimination allows fetal levels to continue to rise; however, rapid elimination of CO with HBO₂ may prevent the delayed increase in fetal COHb. (Partially based on data from Longo LD: The biological effects of carbon monoxide on the pregnant woman, fetus, and newborn infant. *Am J Obstet Gynecol* 1977;129:69–103.)

REFERENCES

- Scheinkestel CD, Bailey M, Myles PS, et al: Hyperbaric or normobaric oxygen for acute carbon monoxide poisoning: A randomized controlled clinical trial. *Med J Aust* 1999;170:203–210.
- Weaver LK, Hopkins RO, Chan KJ, et al: Hyperbaric oxygen for acute carbon monoxide poisoning. *N Engl J Med* 2002;347(14):1057–1067.

SUGGESTED READING

- Cobb N, Etzel RA: Unintentional carbon monoxide-related deaths in the United States, 1979 through. *JAMA* 1991;266(5):659–663.
- Elkharrat D, Raphael JC, Korach JM, et al: Acute carbon monoxide intoxication and hyperbaric oxygen in pregnancy. *Intensive Care Med* 1991;17:289–292.
- Hampson NB: Emergency department visits for carbon monoxide poisoning in the Pacific Northwest. *J Emerg Med* 1998;16(5):695–698.
- Hampson NB, Mathieu D, Piantadosi CA, et al: Carbon monoxide poisoning: Interpretation of randomized clinical trials and unresolved treatment issues. *Undersea Hyper Med* 2001;28(3):157–164.
- Longo LD: The biological effects of carbon monoxide on the pregnant woman, fetus, and newborn infant. *Am J Obstet Gynecol* 1977; 129:69–103.
- Thom SR, Weaver LK. Carbon monoxide poisoning. In Feldmeier J (ed): *Hyperbaric Oxygen 2003: Indications and Results*. Kensington, UK, Undersea and Hyperbaric Medical Society, 2003, pp 11–17.
- Tomaszewski C. Carbon monoxide. In Goldfrank L, Flomenbaum N, Lewin N, et al (eds): *Goldfrank's Toxicologic Emergencies* 7th ed. New York, McGraw-Hill, 2002, pp 1478–1491.

AUTHOR QUERY FORM

Dear Author:

During the preparation of your manuscript for publication, the questions listed below have arisen. Please attend to these matters and return this form with your proof.

Many thanks for your assistance.

Query References	Query	Remarks
1	AU: OK as edited?	
2	AU: OK as edited?	
3	AU: OK as edited?	
4	AU: Pls provide year.	
5	AU: Pls provide complete ref.	