= Carbon monoxide poisoning =

Carbon monoxide poisoning occurs after too much inhalation of carbon monoxide (CO) . Carbon monoxide is a toxic gas , but , being colorless , odorless , tasteless , and initially non @-@ irritating , it is very difficult for people to detect . Carbon monoxide is a product of incomplete combustion of organic matter due to insufficient oxygen supply to enable complete oxidation to carbon dioxide (CO2) . It is often produced in domestic or industrial settings by motor vehicles that run on gasoline , diesel , methane , or other carbon @-@ based fuels and from tools , gas heaters , and cooking equipment that are powered by carbon @-@ based fuels such as propane , butane and charcoal . Exposure at 100 ppm or greater can be dangerous to human health .

Symptoms of mild acute poisoning include lightheadedness , confusion , headache , vertigo , and flu @-@ like effects ; larger exposures can lead to significant toxicity of the central nervous system and heart , and death . After acute poisoning , long @-@ term sequelae often occur . Carbon monoxide can also have severe effects on the fetus of a pregnant woman . Chronic exposure to low levels of carbon monoxide can lead to depression , confusion , and memory loss . Carbon monoxide mainly causes adverse effects in humans by combining with hemoglobin to form carboxyhemoglobin (HbCO) in the blood . This prevents hemoglobin from carrying oxygen to the tissues , effectively reducing the oxygen @-@ carrying capacity of the blood , leading to hypoxia . Additionally , myoglobin and mitochondrial cytochrome oxidase are thought to be adversely affected . Carboxyhemoglobin can revert to hemoglobin , but the recovery takes time because the HbCO complex is fairly stable .

Treatment of poisoning largely consists of administering 100 % oxygen or providing hyperbaric oxygen therapy , although the optimum treatment remains controversial . Oxygen works as an antidote as it increases the removal of carbon monoxide from hemoglobin , in turn providing the body with normal levels of oxygen . The prevention of poisoning is a significant public health issue . Domestic carbon monoxide poisoning can be prevented by early detection with the use of household carbon monoxide detectors . Carbon monoxide poisoning is the most common type of fatal poisoning in many countries . Historically , it was also commonly used as a method to commit suicide , usually by deliberately inhaling the exhaust fumes of a running car engine . Modern automobiles , even with electronically controlled combustion and catalytic converters , can still produce levels of carbon monoxide which will kill if enclosed within a garage or if the tailpipe is obstructed (for example , by snow) and exhaust gas cannot escape normally . Carbon monoxide poisoning has also been speculated as a possible cause of apparent haunted houses ; symptoms such as delirium and hallucinations may have led people suffering poisoning to think they have seen ghosts or to believe their house is haunted .

= = Signs and symptoms = =

Carbon monoxide is not toxic to all forms of life . Its harmful effects are due to binding with hemoglobin so its danger to organisms that do not use this compound is doubtful . It thus has no effect on photosynthesising plants . It is easily absorbed through the lungs . Inhaling the gas can lead to hypoxic injury , nervous system damage , and even death . Different people and populations may have different carbon monoxide tolerance levels . On average , exposures at 100 ppm or greater is dangerous to human health . In the United States , the OSHA limits long @-@ term workplace exposure levels to less than 50 ppm averaged over an 8 @-@ hour period ; in addition , employees are to be removed from any confined space if an upper limit (" ceiling ") of 100 ppm is reached . Carbon monoxide exposure may lead to a significantly shorter life span due to heart damage . The carbon monoxide tolerance level for any person is altered by several factors , including activity level , rate of ventilation , a pre @-@ existing cerebral or cardiovascular disease , cardiac output , anemia , sickle cell disease and other hematological disorders , barometric pressure , and metabolic rate .

The acute effects produced by carbon monoxide in relation to ambient concentration in parts per million are listed below :

= = = Acute poisoning = = =

The main manifestations of carbon monoxide poisoning develop in the organ systems most dependent on oxygen use , the central nervous system and the heart . The initial symptoms of acute carbon monoxide poisoning include headache , nausea , malaise , and fatigue . These symptoms are often mistaken for a virus such as influenza or other illnesses such as food poisoning or gastroenteritis . Headache is the most common symptom of acute carbon monoxide poisoning ; it is often described as dull , frontal , and continuous . Increasing exposure produces cardiac abnormalities including fast heart rate , low blood pressure , and cardiac arrhythmia ; central nervous system symptoms include delirium , hallucinations , dizziness , unsteady gait , confusion , seizures , central nervous system depression , unconsciousness , respiratory arrest , and death . Less common symptoms of acute carbon monoxide poisoning include myocardial ischemia , atrial fibrillation , pneumonia , pulmonary edema , high blood sugar , lactic acidosis , muscle necrosis , acute kidney failure , skin lesions , and visual and auditory problems .

One of the major concerns following acute carbon monoxide poisoning is the severe delayed neurological manifestations that may occur . Problems may include difficulty with higher intellectual functions , short @-@ term memory loss , dementia , amnesia , psychosis , irritability , a strange gait , speech disturbances , Parkinson 's disease @-@ like syndromes , cortical blindness , and a depressed mood . Depression may occur in those who did not have pre @-@ existing depression . These delayed neurological sequelae may occur in up to 50 % of poisoned people after 2 to 40 days . It is difficult to predict who will develop delayed sequelae ; however , advanced age , loss of consciousness while poisoned , and initial neurological abnormalities may increase the chance of developing delayed symptoms .

One classic sign of carbon monoxide poisoning is more often seen in the dead rather than the living ? people have been described as looking red @-@ cheeked and healthy (see below) . However , since this " cherry @-@ red " appearance is common only in the deceased , and is unusual in living people , it is not considered a useful diagnostic sign in clinical medicine . In pathological (autopsy) examination the ruddy appearance of carbon monoxide poisoning is notable because unembalmed dead persons are normally bluish and pale , whereas dead carbon @-@ monoxide poisoned persons may simply appear unusually lifelike in coloration . The colorant effect of carbon monoxide in such postmortem circumstances is thus analogous to its use as a red colorant in the commercial meat @-@ packing industry .

= = = Chronic poisoning = = =

Chronic exposure to relatively low levels of carbon monoxide may cause persistent headaches , lightheadedness , depression , confusion , memory loss , nausea and vomiting . It is unknown whether low @-@ level chronic exposure may cause permanent neurological damage . Typically , upon removal from exposure to carbon monoxide , symptoms usually resolve themselves , unless there has been an episode of severe acute poisoning . However , one case noted permanent memory loss and learning problems after a 3 @-@ year exposure to relatively low levels of carbon monoxide from a faulty furnace . Chronic exposure may worsen cardiovascular symptoms in some people . Chronic carbon monoxide exposure might increase the risk of developing atherosclerosis . Long @-@ term exposures to carbon monoxide present the greatest risk to persons with coronary heart disease and in females who are pregnant .

= = Causes = =

Carbon monoxide is a product of combustion of organic matter under conditions of restricted oxygen supply , which prevents complete oxidation to carbon dioxide (CO_2) . Sources of carbon monoxide include cigarette smoke , house fires , faulty furnaces , heaters , wood @-@ burning stoves , internal combustion vehicle exhaust , electrical generators , propane @-@ fueled

equipment such as portable stoves , and gasoline @-@ powered tools such as leaf blowers , lawn mowers , high @-@ pressure washers , concrete cutting saws , power trowels , and welders . Exposure typically occurs when equipment is used in buildings or semi @-@ enclosed spaces .

Riding in pickup trucks has led to poisoning in children . Idling automobiles with the exhaust pipe blocked by snow has led to the poisoning of car occupants . Any perforation between the exhaust manifold and shroud can result in exhaust gases reaching the cabin . Generators and propulsion engines on boats , especially houseboats , has resulted in fatal carbon monoxide exposures .

Poisoning may also occur following the use of a self @-@ contained underwater breathing apparatus (SCUBA) due to faulty diving air compressors .

In caves carbon monoxide can build up in enclosed chambers due to the presence of decomposing organic matter . In coal mines incomplete combustion may occur during explosions resulting in the production of afterdamp . The gas is up to 3 % CO and may be fatal after just a single breath . Following an explosion in a colliery adjacent , interconnected , mines may become dangerous due to the afterdamp leaking from mine to mine . Such an incident followed the Trimdon Grange explosion which killed men in the Kelloe mine .

Another source of poisoning is exposure to the organic solvent dichloromethane , found in some paint strippers , as the metabolism of dichloromethane produces carbon monoxide .

= = Pathophysiology = =

The precise mechanisms by which the effects of carbon monoxide are induced upon bodily systems , are complex and not yet fully understood . Known mechanisms include carbon monoxide binding to hemoglobin , myoglobin and mitochondrial cytochrome oxidase and restricting oxygen supply , and carbon monoxide causing brain lipid peroxidation .

= = = Hemoglobin = = =

Carbon monoxide has a higher diffusion coefficient compared to oxygen and the only enzyme in the human body that produces carbon monoxide is heme oxygenase which is located in all cells and breaks down heme . Under normal conditions carbon monoxide levels in the plasma are approximately 0 mmHg because it has a higher diffusion coefficient and the body easily gets rid of any CO made . When CO is not ventilated it binds to hemoglobin , which is the principal oxygen @-@ carrying compound in blood ; this produces a compound known as carboxyhemoglobin . The traditional belief is that carbon monoxide toxicity arises from the formation of carboxyhemoglobin , which decreases the oxygen @-@ carrying capacity of the blood and inhibits the transport , delivery , and utilization of oxygen by the body . The affinity between hemoglobin and carbon monoxide is approximately 230 times stronger than the affinity between hemoglobin and oxygen so hemoglobin binds to carbon monoxide in preference to oxygen .

Hemoglobin is a tetramer with four oxygen binding sites . The binding of carbon monoxide at one of these sites increases the oxygen affinity of the remaining three sites , which causes the hemoglobin molecule to retain oxygen that would otherwise be delivered to the tissue . This situation is described as carbon monoxide shifting the oxygen dissociation curve to the left . Because of the increased affinity between hemoglobin and oxygen during carbon monoxide poisoning , little oxygen will actually be released in the tissues . This causes hypoxic tissue injury . Hemoglobin acquires a bright red color when converted into carboxyhemoglobin , so poisoned cadavers and even commercial meats treated with carbon monoxide acquire an unnatural reddish hue .

= = = Myoglobin = = =

Carbon monoxide also binds to the hemeprotein myoglobin . It has a high affinity for myoglobin , about 60 times greater than that of oxygen . Carbon monoxide bound to myoglobin may impair its ability to utilize oxygen . This causes reduced cardiac output and hypotension , which may result in brain ischemia . A delayed return of symptoms have been reported . This results following a

recurrence of increased carboxyhemoglobin levels ; this effect may be due to a late release of carbon monoxide from myoglobin , which subsequently binds to hemoglobin .

= = = Cytochrome oxidase = = =

Another mechanism involves effects on the mitochondrial respiratory enzyme chain that is responsible for effective tissue utilization of oxygen . Carbon monoxide binds to cytochrome oxidase with less affinity than oxygen , so it is possible that it requires significant intracellular hypoxia before binding . This binding interferes with aerobic metabolism and efficient adenosine triphosphate synthesis . Cells respond by switching to anaerobic metabolism , causing anoxia , lactic acidosis , and eventual cell death . The rate of dissociation between carbon monoxide and cytochrome oxidase is slow , causing a relatively prolonged impairment of oxidative metabolism .

= = = Central nervous system effects = = =

The mechanism that is thought to have a significant influence on delayed effects involves formed blood cells and chemical mediators , which cause brain lipid peroxidation (degradation of unsaturated fatty acids) . Carbon monoxide causes endothelial cell and platelet release of nitric oxide , and the formation of oxygen free radicals including peroxynitrite . In the brain this causes further mitochondrial dysfunction , capillary leakage , leukocyte sequestration , and apoptosis . The result of these effects is lipid peroxidation , which causes delayed reversible demyelinization of white matter in the central nervous system known as Grinker myelinopathy , which can lead to edema and necrosis within the brain . This brain damage occurs mainly during the recovery period . This may result in cognitive defects , especially affecting memory and learning , and movement disorders . These disorders are typically related to damage to the cerebral white matter and basal ganglia . Hallmark pathological changes following poisoning are bilateral necrosis of the white matter , globus pallidus , cerebellum , hippocampus and the cerebral cortex .

= = = Pregnancy = = =

Carbon monoxide poisoning in pregnant women may cause severe adverse fetal effects . Poisoning causes fetal tissue hypoxia by decreasing the release of maternal oxygen to the fetus . Carbon monoxide also crosses the placenta and combines with fetal hemoglobin , causing more direct fetal tissue hypoxia . Additionally , fetal hemoglobin has a 10 to 15 % higher affinity for carbon monoxide than adult hemoglobin , causing more severe poisoning in the fetus than in the adult . Elimination of carbon monoxide is slower in the fetus , leading to an accumulation of the toxic chemical . The level of fetal morbidity and mortality in acute carbon monoxide poisoning is significant , so despite mild maternal poisoning or following maternal recovery , severe fetal poisoning or death may still occur .

= = Diagnosis = =

As many symptoms of carbon monoxide poisoning also occur with many other types of poisonings and infections (such as the flu) , the diagnosis is often difficult . A history of potential carbon monoxide exposure , such as being exposed to a residential fire , may suggest poisoning , but the diagnosis is confirmed by measuring the levels of carbon monoxide in the blood . This can be determined by measuring the amount of carboxyhemoglobin compared to the amount of hemoglobin in the blood .

As people may continue to experience significant symptoms of CO poisoning long after their blood carboxyhemoglobin concentration has returned to normal , presenting to examination with a normal carboxyhemoglobin level (which may happen in late states of poisoning) does not rule out poisoning .

A CO @-@ oximeter is used to determine carboxyhemoglobin levels . Pulse CO @-@ oximeters estimate carboxyhemoglobin with a non @-@ invasive finger clip similar to a pulse oximeter . These

devices function by passing various wavelengths of light through the fingertip and measuring the light absorption of the different types of hemoglobin in the capillaries .

The use of a regular pulse oximeter is not effective in the diagnosis of carbon monoxide poisoning as people suffering from carbon monoxide poisoning may have a normal oxygen saturation level on a pulse oximeter . This is due to the carboxyhemoglobin being misrepresented as oxyhemoglobin .

Breath CO monitoring offers a viable alternative to pulse CO @-@ oximetry . Carboxyhemoglobin levels have been shown to have a strong correlation with breath CO concentration . However , many of these devices require the user to inhale deeply and hold their breath to allow the CO in the blood to escape into the lung before the measurement can be made . As this is not possible in a nonresponsive patient , these devices are not appropriate for use in on @-@ scene emergency care detection of CO poisoning .

= = = Detection in biological specimens = = =

Carbon monoxide may be quantitated in blood using spectrophotometric methods or chromatographic techniques in order to confirm a diagnosis of poisoning in a person or to assist in the forensic investigation of a case of fatal exposure . Carboxyhemoglobin blood saturations may range up to 8 ? 10 % in heavy smokers or persons extensively exposed to automotive exhaust gases . In symptomatic poisoned people they are often in the 10 ? 30 % range , while persons who succumb may have postmortem blood levels of 30 ? 90 % .

The ratio of carboxyhemoglobin to hemoglobin molecules in an average person may be up to 5 % , although cigarette smokers who smoke two packs / day may have levels up to 9 % .

= = = Differential diagnosis = = =

There are many conditions to be considered in the differential diagnosis of carbon monoxide poisoning . The earliest symptoms , especially from low level exposures , are often non @-@ specific and readily confused with other illnesses , typically flu @-@ like viral syndromes , depression , chronic fatigue syndrome , chest pain , and migraine or other headaches . Carbon monoxide has been called a " great mimicker " due to the presentation of poisoning being diverse and nonspecific . Other conditions included in the differential diagnosis include acute respiratory distress syndrome , altitude sickness , lactic acidosis , diabetic ketoacidosis , meningitis , methemoglobinemia , or opioid or toxic alcohol poisoning .

= = Prevention = =

= = = Detectors = = =

Prevention remains a vital public health issue , requiring public education on the safe operation of appliances , heaters , fireplaces , and internal @-@ combustion engines , as well as increased emphasis on the installation of carbon monoxide detectors . Carbon monoxide is tasteless and odourless so can not be detected by smell .

The United States Consumer Product Safety Commission has stated , " carbon monoxide detectors are as important to home safety as smoke detectors are , " and recommends each home have at least one carbon monoxide detector , and preferably one on each level of the building . These devices , which are relatively inexpensive and widely available , are either battery- or AC @-@ powered , with or without battery backup . In buildings , carbon monoxide detectors are usually installed around heaters and other equipment . If a relatively high level of carbon monoxide is detected , the device sounds an alarm , giving people the chance to evacuate and ventilate the building . Unlike smoke detectors , carbon monoxide detectors do not need to be placed near ceiling level .

The use of carbon monoxide detectors has been standardized in many areas . In the USA , NFPA

720 @-@ 2009 , the carbon monoxide detector guidelines published by the National Fire Protection Association , mandates the placement of carbon monoxide detectors / alarms on every level of the residence , including the basement , in addition to outside sleeping areas . In new homes , AC @-@ powered detectors must have battery backup and be interconnected to ensure early warning of occupants at all levels . NFPA 720 @-@ 2009 is the first national carbon monoxide standard to address devices in non @-@ residential buildings . These guidelines , which now pertain to schools , healthcare centers , nursing homes and other non @-@ residential buildings , include three main points :

1 . A secondary power supply (battery backup) must operate all carbon monoxide notification appliances for at least 12 hours ,

2 . Detectors must be on the ceiling in the same room as permanently installed fuel @-@ burning appliances , and

3 . Detectors must be located on every habitable level and in every HVAC zone of the building .

Gas organizations will often recommend to get gas appliances serviced at least once a year .

= = = Legal requirements = = =

The NFPA standard is not necessarily enforced by law . As of April 2006 , the U.S. state of Massachusetts requires detectors to be present in all residences with potential CO sources , regardless of building age and whether they are owner @-@ occupied or rented . This is enforced by municipal inspectors , and was inspired by the death of 7 @-@ year @-@ old Nicole Garofalo in 2005 due to snow blocking a home heating vent . Other jurisdictions may have no requirement or only mandate detectors for new construction or at time of sale .

Despite similar deaths in vehicles with clogged exhaust pipes (for example in the Northeastern United States blizzard of 1978 and February 2013 nor 'easter) and the commercial availability of the equipment , there is no legal requirement for automotive CO detectors .

= = = World Health Organization recommendations = = =

The following guideline values (ppm values rounded) and periods of time @-@ weighted average exposures have been determined in such a way that the carboxyhaemoglobin (COHb) level of 2 @.@ 5 % is not exceeded , even when a normal subject engages in light or moderate exercise :

100 mg / m3 (87 ppm) for 15 min

60 mg / m3 (52 ppm) for 30 min

30 mg / m3 (26 ppm) for 1 h

10 mg / m3 (9 ppm) for 8 h

For indoor air quality 7 mg / m3 (6 ppm) for 24 h (so as not to exceed 2 % COHb for chronic exposure)

= = Treatment = =

Initial treatment for carbon monoxide poisoning is to immediately remove the person from the exposure without endangering further people . Those who are unconscious may require CPR on site . Administering oxygen via non @-@ rebreather mask shortens the half life of carbon monoxide from 320 minutes to 80 minutes on normal air . Oxygen hastens the dissociation of carbon monoxide from carboxyhemoglobin , thus turning it back into hemoglobin . Due to the possible severe effects in the fetus , pregnant women are treated with oxygen for longer periods of time than non @-@ pregnant people .

= = = Hyperbaric oxygen = = =

Hyperbaric oxygen is also used in the treatment of carbon monoxide poisoning , as it may hasten dissociation of CO from carboxyhemoglobin and cytochrome oxidase to a greater extent than normal

oxygen . Hyperbaric oxygen at three times atmospheric pressure reduces the half life of carbon monoxide to 23 (~ 80 / 3 minutes) minutes , compared to 80 minutes for regular oxygen . It may also enhance oxygen transport to the tissues by plasma , partially bypassing the normal transfer through hemoglobin . However , it is controversial whether hyperbaric oxygen actually offers any extra benefits over normal high flow oxygen , in terms of increased survival or improved long @-@ term outcomes . There have been randomized controlled trials in which the two treatment options have been compared ; of the six performed , four found hyperbaric oxygen improved outcome and two found no benefit for hyperbaric oxygen . Some of these trials have been criticized for apparent flaws in their implementation . A review of all the literature on carbon monoxide poisoning treatment concluded that the role of hyperbaric oxygen is unclear and the available evidence neither confirms nor denies a medically meaningful benefit . The authors suggested a large , well designed , externally audited , multicentre trial to compare normal oxygen with hyperbaric oxygen .

= = = Other = = =

Further treatment for other complications such as seizure , hypotension , cardiac abnormalities , pulmonary edema , and acidosis may be required . Increased muscle activity and seizures should be treated with dantrolene or diazepam ; diazepam should only be given with appropriate respiratory support . Hypotension requires treatment with intravenous fluids ; vasopressors may be required to treat myocardial depression . Cardiac dysrhythmias are treated with standard advanced cardiac life support protocols . If severe , metabolic acidosis is treated with sodium bicarbonate . Treatment with sodium bicarbonate is controversial as acidosis may increase tissue oxygen availability . Treatment of acidosis may only need to consist of oxygen therapy . The delayed development of neuropsychiatric impairment is one of the most serious complications of carbon monoxide poisoning . Brain damage is confirmed following MRI or CAT scans . Extensive follow up and supportive treatment is often required for delayed neurological damage . Outcomes are often difficult to predict following poisoning , especially people who have symptoms of cardiac arrest , coma , metabolic acidosis , or have high carboxyhemoglobin levels . One study reported that approximately 30 % of people with severe carbon monoxide poisoning will have a fatal outcome . It has been reported that electroconvulsive therapy (ECT) may increase the likelihood of delayed neuropsychiatric sequelae (DNS) after carbon monoxide (CO) poisoning .

= = Epidemiology = =

The true number of incidents of carbon monoxide poisoning is unknown , since many non @-@ lethal exposures go undetected . From the available data , carbon monoxide poisoning is the most common cause of injury and death due to poisoning worldwide . Poisoning is typically more common during the winter months . This is due to increased domestic use of gas furnaces , gas or kerosene space heaters , and kitchen stoves during the winter months , which if faulty and / or used without adequate ventilation , may produce excessive carbon monoxide . Carbon monoxide detection and poisoning also increases during power outages .

It has been estimated that more than 40 @,@ 000 people per year seek medical attention for carbon monoxide poisoning in the United States . 95 % of carbon monoxide poisoning deaths in the United States are due to gas space heaters . In many industrialized countries carbon monoxide is the cause of more than 50 % of fatal poisonings . In the United States , approximately 200 people die each year from carbon monoxide poisoning associated with home fuel @-@ burning heating equipment . Carbon monoxide poisoning contributes to the approximately 5613 smoke inhalation deaths each year in the United States . The CDC reports , " Each year , more than 500 Americans die from unintentional carbon monoxide poisoning , and more than 2 @,@ 000 commit suicide by intentionally poisoning themselves . " For the 10 @-@ year period from 1979 to 1988 , 56 @,@ 133 deaths from carbon monoxide poisoning occurred in the United States , with 25 @,@ 889 of those being suicides , leaving 30 @,@ 244 unintentional deaths . A report from New Zealand showed that 206 people died from carbon monoxide poisoning in the years of 2001 and 2002 . In total carbon

monoxide poisoning was responsible for 43 @.@ 9 % of deaths by poisoning in that country . In South Korea , 1 @,@ 950 people had been poisoned by carbon monoxide with 254 deaths from 2001 through 2003 . A report from Jerusalem showed 3 @.@ 53 per 100 @,@ 000 people were poisoned annually from 2001 through 2006 . In Hubei , China , 218 deaths from poisoning were reported over a 10 @-@ year period with 16 @.@ 5 % being from carbon monoxide exposure .

= = Society and culture = =

As part of the Holocaust during World War II , German Nazis used gas vans at Chelmno camp and elsewhere to kill an estimated over 700 @,@ 000 prisoners by carbon monoxide poisoning . This method was also used in the gas chambers of several death camps such as Treblinka , Sobibor and Belzec . Gassing with carbon monoxide started in action T4 , the euthanasia programme developed by the Nazis in Germany to murder the mentally ill and disabled people before the war started in earnest . Many key personnel were recruited to murder much larger numbers of people in the gas vans and the special gas chambers used in the death camps such as Treblinka . Exhaust fumes from tank engines for example , were used to supply the gas to the chambers .

= = Research = =

Carbon monoxide is produced naturally by the body as a byproduct of converting protoporphyrin into bilirubin . This carbon monoxide also combines with hemoglobin to make carboxyhemoglobin , but not at toxic levels .

Small amounts of CO are beneficial and enzymes exist that produce it at times of oxidative stress . Drugs are being developed to introduce small amounts of CO during certain kinds of surgery , these drugs are called Carbon monoxide @-@ releasing molecules .