Carbon monoxide poisoning: an ancient and frequent cause of accidental death

Carbon monoxide poisoning is both an ancient and current cause of inadvertent (accidental) death and more recently has emerged as a cause of suicide worldwide. This article describes the pathophysiology and epidemiology of this most toxic and frequently occult poison.

When carbon-containing fuels are burnt in a lack of oxygen, they produce the highly poisonous gas carbon monoxide. Many appliances and internal combustion engines are capable of producing lethal quantities of this gas, but perhaps the most easily overlooked source is the portable barbecue. The association of barbecuing with leisurely summer activities, camping and outdoor events tends to obscure our appreciation of the commonest cause of accidental poisoning worldwide (Thom, 2002). Inadvertent death from poisoning by carbon monoxide is one of the most ancient to be described (Chiew and Buckley, 2014). The death of the Roman emperor Flavius Jovianus Augustus in 364AD is thought likely to have occurred as a result of carbon monoxide poisoning (Lascaratos and Marketos, 1998). While on campaign he had asked for a brazier of charcoal to heat his tent and was found dead the following morning. This article describes the pathology and epidemiology of this condition in the UK, with reference to several new developments in determining prognosis and therapy.

Pathophysiology and symptoms of carbon monoxide poisoning

Carbon monoxide is odourless, tasteless and colourless and, in enclosed spaces, can be very rapidly fatal. It binds to haemoglobin with an affinity >200 times that of oxygen. The surprisingly avid affinity of haemoglobin for carbon monoxide is explained by the need to scavenge the small amounts of this highly toxic substance produced naturally by the enzyme haem oxygenase during the conversion of protoporphyrin into bilirubin (Torrance, 1996).

A reduced capacity for haemoglobin to carry oxygen will mean that tissues and vital organs, including the brain and heart, will become hypoxic. Carbon monoxide also binds to mitochondrial cytochrome oxidase (analogous to the actions of cyanide) and interferes with other ferroproteins, including myoglobin (Miro et al, 1998; Walker and Hay, 1999). Further harmful effects are produced by a combination of oxidative stress, neutrophil degranulation, free radical production, inflammatory reactions and cellular apoptosis (Thom, 2009; Chiew and Buckley, 2014).

The first symptoms of carbon monoxide toxicity occur at carboxyhaemoglobin concentrations of greater than 15% (the background level in non-smokers is around 0.7–1.5%) (Coburn et al, 1963). Symptoms of carbon monoxide intoxication include headache, drowsiness, dizziness, chest pains, nausea and vomiting. These symptoms can be easily misinterpreted as less sinister maladies, including flu or food poisoning. The danger lies in patients being reassured and then returning to their original toxic environment. At higher percentage levels of carboxyhaemoglobin (30–40%), poisoning causes collapse, while at 50–60% loss of consciousness will ensue. Death occurs within 2 hours at carboxyhaemoglobin levels of 60–70% and within minutes at 90–100% (Leigh-Smith, 2004). In survivors of carbon monoxide poisoning, sequelae include severe neurological and cardiac damage which in many cases have a delayed onset (Thom et al, 1995; Weaver, 2009). Neurological dysfunction is likely to occur through lipid peroxidation and subsequent delayed reversible demyelination of brain white matter (Gorman et al, 2003). Serious neurological sequelae have been related to serum levels of the biomarker S100β, a structural protein component of astroglial cells released in response to hypoxic brain damage as a result of carbon monoxide poisoning (Yardan et al, 2011; Akelma et al, 2013). Further indicators of a poor prognosis include prolonged unconsciousness and elevations in levels of troponin as a result of myocardial damage (Henry et al, 2006).

Accidental and deliberate deaths from carbon monoxide

In the UK, deaths are more commonly accidental, although carbon monoxide has long been recognized as a means of deliberate suicide by inhaling motor vehicle exhaust fumes (Close et al, 2007). Between 1998 and 2007, 45% of hospital admissions for carbon monoxide poisoning in England were accidental and 42.5% were deliberate. In both scenarios men predominate (Close et

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al, 2007). In the remaining 12.5% of cases, the cause was unknown. These statistics are similar to those published by the Carbon Monoxide and Gas Safety Society (2014) who list the names and circumstances of around 647 accidental carbon monoxide deaths since 1995. This equates to almost 36 deaths/year. Within this list are eight deaths caused by use of portable barbecues, of which four occurred inside tents, two in apartments and one each in a camper van and wood cabin.

Official figures from the Department of Health indicate that 40–50 people die of accidental carbon monoxide poisoning per year in the UK (*Figure 1*), approximately 200 are hospitalized and 4000 attend accident and emergency departments (Department of Health, 2011). At the authors' district general hospital, there have been 19 cases of carbon monoxide poisoning over the last 10 years, of which 12 (63%) were accidental and seven (37%) were intentional. No cases proved fatal.

While unusual in the UK (Brooks-Lim and Sadler, 2009), deliberate suicide through the burning of charcoal has gained popularity in some south east Asian countries as a means of deliberate self-poisoning. In Japan, the prevalence of charcoal burning in relation to suicide has been described as an epidemic (Yoshioka et al, 2014). This trend follows the publicized death of a young woman in Hong Kong and the attraction of an effective and relatively painless method of committing suicide (Liu et al, 2007).

In industrialized countries carbon monoxide poisoning accounts for more than 50% of fatal poisonings, although exactly how many are accidental is difficult to calculate (Omaye, 2002). The United States report between 1000 and 2000 accidental deaths per year as a result of carbon monoxide poisoning (Centers for Disease Control and Prevention, 2007). Many different scenarios are responsible (Hampson, 1998), but deaths are largely the result of domestic heating appliance dysfunction. Other occurrences include falling asleep in stationary motor vehicles while the engine is running, in many cases associated with intoxication from alcohol or drug use. Between 1979 and 1988 there were a total of 30 244 deaths in the United States from carbon monoxide poisoning that were deemed to be unintentional (Cobb and Etzel, 1991). In less industrialized countries, where numbers are available, the mortality is far higher (Song, 1985). As an example a South Korean study reported 1950 people poisoned by carbon monoxide with 254 deaths from 2001–2003 (Song et al, 2009).

While inadvertent deaths from carbon monoxide poisoning are 'accidental', many deaths from fixed appliance dysfunction could be prevented by the use of carbon monoxide detection meters. One of the most overlooked sources of carbon monoxide are portable barbecues. These are widely available and can be purchased as a disposable unit for less than £4 (*Figure 2*). They are easily transported and may be used in many inappropriate environments (Lyness and Crane, 2011). A sudden deterioration in weather conditions, when a barbecue is already alight and cooking food, can result in it being moved into a shed, tent, caravan, garage or other poorly ventilated space. If this area is occupied, individuals can quickly fall ill as a result of a build up of carbon monoxide. Charcoal, coke, gas, petroleum or wood-burning patio heaters and combined heating and cooking devices (i.e. hibachi and chimenea) require similar caution in poorly ventilated spaces. Similarly, such cooking appliances are often carried or wheeled 'inside' to provide warmth if the weather becomes colder in the evening or through the night, with simi-

Figure 1. Total numbers of deaths from accidental poisoning by carbon monoxide for England, Wales and Scotland 2001–11. From Department of Health (2011).

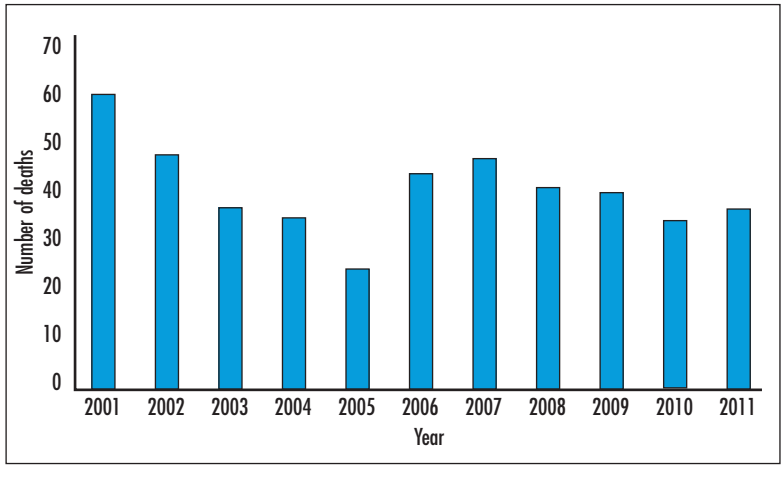

Figure 2. Portable barbecue. Notice the carbon monoxide warning and indications that charcoal should not be not be burnt within homes, vehicles or tents.

larly dangerous consequences. Camping stoves in tents, cabins and snow caves carry similar risks when used either for cooking food or heating.

Therapies for carbon monoxide poisoning

Poisoning by carbon monoxide is suspected from symptoms and likely circumstances (environment, clustering of cases, appliances found at the scene) with confirmation provided by blood gas analysis or through use of a carbon monoxide-oximeter to determine carboxyhaemoglobin levels. Treatment involves removing the patient from the source and providing oxygen or hyperbaric oxygen. The half life of carboxyhaemoglobin in carbon monoxide-poisoned patients in fresh air (around 21% oxygen) is around 4–5 hours – treated with 100% oxygen at atmospheric pressure it is reduced to 74±25 minutes and in hyperbaric chambers (at 2 atm) to around 23 minutes (Weaver et al, 2000). The frequent delay in obtaining hyperbaric oxygen services also has to be factored into the benefits of arranging this therapy. While the role of hyperbaric oxygen in acute cases of severe carbon monoxide poisoning (coma, seizures and cardiac dysfunction) is controversial (Henry, 2005), the main drive for its continued use is a perceived benefit in preventing delayed neurocognitive and psychiatric complications (Buras and Garcia-Covarrubias, 2008). A Cochrane database review (Buckley et al, 2011) and current National Institute for Health and Care Excellence (2013) guidelines both cast doubt on the benefits of hyperbaric oxygen.

Novel therapies to treat carbon monoxide poisoning

Erythropoietin, originally identified in relation to erythropoiesis, is also produced within the CNS and has a neuroprotective role in reducing reperfusion injuries (Pang et al, 2013). Following successful animal studies, erythropoietin was used in a placebo controlled trial of 103 patients poisoned by carbon monoxide. Patients in the erythropoietin group showed more rapid reductions in levels of the neuro-biomarker S100β, and had better stroke scores. Delayed neurological sequelae at 30 days post exposure were also significantly lower in the erythropoietin group (12%) compared to those in the placebo arm (30%) (Pang et al, 2013). This study demonstrated that erythropoietin may improve neurological outcomes and that the biomarker S100β might be a useful indicator for assessing response to therapy.

A wide range of other therapies have been used in animal models with some success, including hydrogen-rich saline, nimodipine, granulocyte-stimulating factor, fructose diphosphate and hyperoxygenated solutions (Chiew and Buckley, 2014).w

Conclusions

This most ancient cause of poisoning remains a serious health threat in many countries in the 21st century. Rapid administration of oxygen is the most established and effective method to treat this condition with some doubt cast on the future role for hyperbaric oxygen therapy. Physicians should always consider this often occult explanation for symptoms that may mimic many less sinister conditions. This threat to human life remains an issue and is nowhere better illustrated than by the innocuous, but potentially lethal, portable barbecue. **BJHM**

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KEY POINTS

- Carbon monoxide poisoning remains one of the world's most common causes of morbidity and mortality.
- All carbon-containing fuels can produce carbon monoxide when burnt in a relative absence of oxygen.
- Smouldering barbecues continue to produce carbon monoxide.
- Biomarkers, including troponin and S100β, are useful indicators of cardiac and cerebral damage and are of prognostic significance.
- The continued use of hyperbaric oxygen is controversial.
- Carbon monoxide detection meters should be installed near fixed combustion appliances.

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