Carbon monoxide poisoning

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The deadly effect of carbon monoxide was known as long ago as Greek and Roman times, when the gas was used for executions[1]. In 1857 Claude Bernard postulated that its noxious effect was caused by reversible displacement of oxygen from haemoglobin to form carboxyhaemoglobin[2]. In 1926 it became apparent that hypoxia was caused not only by deficient oxygen transport but also by poor tissue uptake. Warberg used yeast cultures to show that cellular uptake of oxygen was inhibited by exposure to a large amount of carbon monoxide[3].

Carbon monoxide is known as the silent killer since it has no colour or smell. Each year in Britain about 50 people die and 200 are severely injured by carbon monoxide poisoning[4]. Some poisonings are caused by self-harm but most are accidental[5]. It is the commonest cause of accidental poisoning and, according to one estimate, as many as 25 000 people in the UK have symptoms due to faulty gas appliances[4]. In the 1960s and 1970s the conversion from coal gas to carbon-monoxide-free natural gas caused a dramatic reduction in poisoning[6]. In this review I discuss modern approaches to management and prevention.

SOURCES

Carbon monoxide is produced endogenously in small amounts as a byproduct of haem catabolism. Together with nitric oxide it affects cellular function and acts as a neurotransmitter[1]. Environmental carbon monoxide is produced by incomplete combustion of any carbon-containing fuel (coal, petroleum, peat, natural gas). In Britain most accidents arise through central heating faults[7]. By contrast, in the USA most deaths are caused by inhalation of exhaust fumes[8]. In the United Kingdom car exhaust emissions of carbon monoxide have been reduced by catalytic convertors in all new cars. Surprisingly, when deaths occur in garages there have usually been open doors and windows[9]. There are even reports of poisoning occurring from carbon monoxide inhalation in the open air[10]. Methylene chloride (paint stripper) fume inhalation is a rare cause of poisoning. In the liver it is converted to carbon monoxide[11].

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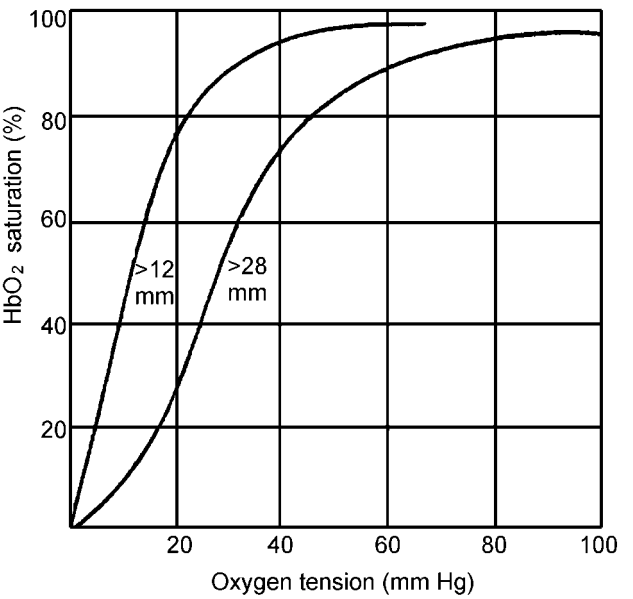

Figure 1 **Carbon monoxide shifts the oxygen-haemoglobin saturation curve to the left and changes it to a more hyperbolic shape.** Less oxygen is available for the tissues. Shown is the oxygen diffusion gradient difference at 50% saturation

PATHOPHYSIOLOGY

Carbon monoxide has 210 times greater affinity for haemoglobin than oxygen[1]. A small environmental concentration will thus cause toxic levels of carboxyhaemoglobin. After the carbon monoxide has selectively bound to haemoglobin the oxygen-haemoglobin dissociation curve of the remaining oxyhaemoglobin shifts to the left, reducing oxygen release (Figure 1). The affinity of carbon monoxide for myoglobin is even greater than for haemoglobin[1]. Binding to cardiac myoglobin causes myocardial depression, hypotension and arrhythmias. Cardiac decompensation results in further tissue hypoxia and is ultimately the cause of death[12].

Cellular uptake of oxygen is blocked by binding of carbon monoxide with mitochondrial cytochrome aa_3. The hypoxia precipitates endothelial cell and platelet release of nitric acid, which forms the free radical peroxynitrate. In the brain this causes further mitochondrial dysfunction, capillary leakage, leukocyte sequestration and apoptosis[13]. The pathological changes occur mainly during the recovery (reperfusion) phase when lipid peroxidation (degradation of unsaturated fatty acids) occurs. The net result is

reversible demyelination in the brain[11,14]. Such changes are clearly evident on magnetic resonance imaging[15]. Carbon monoxide has a predilection for 'watershed' areas of the brain where there is a meagre blood supply[16]. The basal ganglia, with their high oxygen consumption, are most often affected[1]. Other commonly affected areas are the cerebral white matter, hippocampus and cerebellum.

CLINICAL SIGNS AND DIAGNOSIS

The signs of carbon monoxide poisoning vary with concentration and length of exposure. Subtle cardiovascular or neurobehavioural effects occur at low concentrations[12]. Lengthy exposure or acute exposure to high concentrations often causes coma and death. The onset of chronic poisoning is usually insidious and easily mistaken for 'flu, depression, food poisoning or in children gastroenteritis[11,12]. Other family members may have a similar illness.

The most common symptoms are headache, nausea and vomiting, dizziness, lethargy and a feeling of weakness. Infants may be irritable and feed poorly. Neurological signs include confusion, disorientation, visual disturbance, syncope and seizures[14,16,17]. In acute poisoning, common abnormalities of posture and tone are cogwheel rigidity, opisthotonus and flaccidity or spasticity. Adults with coronary heart disease may experience angina, arrhythmias and myocardial infarction[14]. Retinal haemorrhages and the classic cherry red skin colour are seldom seen. Other organs such as the kidney, liver and pancreas are rarely affected[12]. A rise in creatine phosphokinase follows muscle necrosis. Hypoxaemia causes lactic acidaemia.

Carbon monoxide poisoning is diagnosed by measuring carboxyhaemoglobin in a heparinized blood sample (arterial or venous)[18]. Symptoms usually begin when the concentration rises above 10%[12,16]. There is a poor correlation between the blood level and the clinical condition. Symptoms reflect the dissolved concentration, which may be low in the face of a high carboxyhaemoglobin[14]. In general, levels below 40% are not associated with coma or death. In a normal non-smoker the average is about 1%, rising to 15% in a heavy smoker[12]. Levels of 5% are found in haemolytic anaemias and pregnancy[16]. Pulse oximeters are not suitable for the diagnosis of carbon monoxide poisoning. The wavelength of most cannot distinguish between oxyhaemoglobin and carboxyhaemoglobin[19]. A carbon monoxide breathalyser is a simple bedside screening test but its practical value is limited by numerous confounders such as smoking and alcohol[20,21].

The fetus is particularly vulnerable to carbon monoxide poisoning. Fetal haemoglobin shifts the oxygen-haemoglobin dissociation curve to the left. Chronic exposure to carbon monoxide in pregnancy causes growth retardation, fetal distress and death. Survivors may have developmental disorders and brain damage[12,22]. The risk is compounded by smoking in pregnancy. In the first months of infancy, while fetal haemoglobin remains raised, the risk is greater. People with sickle cell anaemia and thalassaemia who have a raised fetal haemoglobin are likewise at excess risk[16].

TREATMENT AND PROGNOSIS

The mainstay of treatment is 100% oxygen administration until the carboxyhaemoglobin level is normal. On this regimen the half-life of carboxyhaemoglobin is 74 minutes (compared with 320 minutes breathing air)[16,23]. Lactic acidosis facilitates tissue oxygen diffusion and should not be corrected unless extreme ($pH < 7.15$). When the patient is stable enough to be transported, hyperbaric oxygen should be considered. This treatment is safe and well tolerated, the main complication being ear barotrauma[24]. The decision about hyperbaric oxygen will often depend on ease of access to a hyperbaric facility. In Britain the average time from exposure to hyperbaric oxygen treatment is 9 hours[7]. The time-frame within which hyperbaric oxygen is most effective is not known. In one large retrospective study it was not effective if started after 6 hours[25].

In 1895, Haldane demonstrated that a mouse could be kept alive by exposure to hyperbaric oxygen at the same time as carbon monoxide. This seminal experiment proved that enough oxygen for survival could be transported in solution when transport by haemoglobin was severely impaired[26]. Haldane set the scene for the subsequent use of hyperbaric oxygen treatment of human patients.

Hyperbaric oxygen has many benefits. The half-life of carboxyhaemoglobin at 3 ATA (absolute atmospheres) of oxygen is only 23 minutes[27]. Other benefits are improved mitochondrial function, impairment of platelet adhesion in the capillaries and inhibition of lipid peroxidation[12]. But contrary to expectation, clinical trials of hyperbaric oxygen have given conflicting results. A recent Cochrane review of three major randomized controlled trials concluded that there is as yet no evidence of neurological benefit at one month[28]. Ongoing trials will soon provide further information[28]. In the absence of firm evidence most centres continue using hyperbaric oxygen if the carboxyhaemoglobin is above 25–30%. Myocardial ischaemia and neurological signs, especially coma, are treated with hyperbaric oxygen irrespective of the concentration. There is general agreement that prolonged hyperbaric oxygen is the treatment of choice in pregnancy. This is because fetal carboxyhaemoglobin is higher and clearance slower than in the mother[22].

Carbon monoxide poisoning is unique in that neuropsychiatric signs can appear insidiously weeks after

the patient appears to have recovered. These signs, which are most common in the elderly, occur within a month in 10–30%[12]. Some of the frank neurological signs such as parkinsonism are easily detected. Personality, cognitive and memory changes are not readily apparent and can be missed unless specifically targeted. Children may present with behaviour or education problems[11]. Most neuropsychiatric signs resolve within a year[29]. In one study, review at 3 years revealed persistent signs in 11%[30]. There is no means of predicting recovery. However, patients with permanent signs are likely to have presented in coma[29,31].

PREVENTION

Public education about the danger of carbon monoxide, with emphasis on safety in the home and workplace, is the key to effective prevention. Professional education targeted at community workers is also needed. This could be achieved through a media campaign when risk is greatest, during the winter. Because of the high incidence of gas-related poisoning, there is a role for the gas industry in public education. Close liaison between public health physicians and leaders of the building, gas and home heating industries is a prerequisite for an effective prevention strategy. Such collaboration ensures safety through proper standards for home ventilation, central heating installation and maintenance. Cheap battery-operated carbon monoxide detectors are now widely available. They should be installed in new homes and in buildings such as garages where workers are at risk from exhaust fumes. In old properties, particularly where there is solid fuel heating, carbon monoxide detectors should be located in sleeping areas. In Britain only BSI standard detectors should be installed. In the USA, where detectors are mandatory in some cities, their value in preventing home poisoning has been well demonstrated[32].

REFERENCES

1 Ganong WF. *Review of Medical Physiology*. Norwalk Ct: Appleton & Lange, 1995

2 Bernard C. *Le Cons Sur les Effets des Substances Toxiques et Médicamenteuses*. Paris: Bailliere, 1857

3 Warburg O. Über die Wirkung des Kohlenoxyds auf den Stoffwechsel der Hefe. *Biochem Z* 1926;**177**:471

4 Walker E, Hay A. Carbon monoxide poisoning is still an under recognised problem. *BMJ* 1999;**319**:1082–3

5 Guy KM, Pimlott JK, Rogers M, Cross M. The new CO and smoke inhalation advisory service in the UK. Treatment of poisoning. *Indoor Built Environment* 1999;**8**:199–202

6 Anonymous. Carbon monoxide, an old enemy forgot. *Lancet* 1981; **ii**:75–6

7 Hamilton-Farrel MR. British Hyperbaric Association carbon monoxide database, 1993–96. *J Accid Emerg Med* 1999;**16**:98–103

8 Cobb N, Etzel RA. Unintentional carbon monoxide-related deaths in the United States, 1979–1988. *JAMA* 1991;**266**:659–63

9 Baron RC, Backer RC, Sopher IM. Unintentional deaths from carbon monoxide in motor vehicle exhaust: West Virginia. *Am J Publ Health* 1989;**29**:328–30

10 Easley RB. Open air carbon monoxide poisoning in a child swimming behind a boat. *South Med J* 2000;**93**:430–32

11 Tomaszewski C. Carbon monoxide poisoning. Early awareness and intervention can save lives. *Postgrad Med* 1999;**105**:39–52

12 Raub JA, Mathieu-Nolf M, Hampson NB, Thom SR. Carbon monoxide poisoning – a public health perspective. *Toxicology* 2000; **145**:1–14

13 Thom SR, Fisher D, Xu YA, Notarfrancesco K, Ischiropoulos H. Adaptive responses and apoptosis in endothelial cells exposed to carbon monoxide. *Proc Natl Acad Sci USA* 2000;**97**:1305–10

14 Ernst A, Zibrak JD. Carbon monoxide poisoning. *N Engl J Med* 1998; **339**:1603–8

15 Chang KH, Han MH, Kim HS, Wie BA, Han MC. Delayed encephalopathy after acute carbon monoxide intoxication: MR imaging features and distribution of cerebral white matter lesions. *Radiology* 1992;**184**:117–22

16 Department of Health, London. *Carbon Monoxide: the Forgotten Killer*. Letter from the Chief Medical Officer, PL/CMO/98/5. London: DoH, 1998

17 Rudge FW. Carbon monoxide poisoning in infants: treatment with hyperbaric oxygen. *South Med J* 1993;**334**:7

18 Touger M, Gallagher EJ, Tyrrel J. Relationship between venous and arterial carboxy-haemoglobin levels in patients with suspected carbon monoxide poisoning. *Ann Emerg Med* 1995;**25**:481–3

19 Hampson NB. Pulse oximetry in severe carbon monoxide poisoning. *Chest* 1998;**114**:1036–41

20 Turnbull TL, Hart RG, Strange GR, *et al*. Emergency department screening for unsuspected carbon monoxide exposure. *Ann Emerg Med* 1988;**17**:478–83

21 Shenoi R, Stewart G, Rosenberg N. Screening for carbon monoxide in children. *Pediatr Emerg Care* 1998;**14**:399–402

22 Aubard Y, Magne I. Carbon monoxide poisoning in pregnancy. *Br J Obstet Gynaecol* 2000;**107**:833–8

23 Weaver LK, Howe S, Hopkins R, Chan KJ. Carboxy hemoglobin half-life in carbon monoxide-poisoned patients treated with 100% oxygen at atmospheric pressure. *Chest* 2000;**117**:801–8

24 Liebelt EL. Hyperbaric oxygen therapy in childhood carbon monoxide poisoning. *Curr Opin Pediatr* 1999;**11**:259–64

25 Goulon M, Barios A, Rapin M. Carbon monoxide poisoning and acute anoxia due to breathing coal gas and hydrocarbons. *Ann Med Interne* (Paris) 1969;**120**:335–49

26 Haldane JS. The relation of carbonic oxide to oxygen tension. *J Physiol (Lond)* 1895;**18**:201–7

27 Myers RA, Snyder SK, Emhoff TA. Subacute sequelae of carbon monoxide poisoning. *Ann Emerg Med* **14**:1163–7

28 Juurlink DN, Stanbrook MB, McGuigan MA. Hyperbaric oxygen for carbon monoxide poisoning. *Cochrane Database Syst Rev* 2000;**2**: CD00204

29 Choi IS. Delayed neurologic sequelae in carbon monoxide intoxication. *Arch Neurol* 1983;**40**:433–5

30 Smith JS, Brandon S. Morbidity from acute carbon monoxide poisoning at three-year follow-up. *BMJ* 1973;**1**:318–21

31 Raphael JC, Elkharrat D, Jars-Guincestre MC *et al*. Trial of normobaric and hyperbaric oxygen for acute carbon-monoxide intoxication. *Lancet* 1989;**ii**:414–19

32 Leikin JB, Clifton JC, Hanashiro PK. Carbon monoxide poisoning. *N Engl J Med* 1999;**340**:1290