to their houses—built of porous materials—became blocked, venting fumes from a gas boiler into both homes.[11] All five deaths would almost certainly have been prevented by a domestic carbon monoxide alarm. More modern house design brings its own problems, however. In a well insulated home the negative pressure created by a bathroom extractor fan can be enough to cause retrograde flow in an otherwise normal chimney. Most people think of engine exhaust as a means of deliberate self poisoning, but in Quebec it is the commonest cause of unintentional carbon monoxide deaths, when engines are left running in enclosed spaces, for warmth or when being repaired.

Numbers of cases sublethal exposure to carbon monoxide in Britain are traditionally quoted as 200 a year, but up 250 000 gas appliances are condemned annually. Even assuming that as few as 10% of these appliances were giving off significant amounts of carbon monoxide, and discounting exposure from other domestic sources, this suggests that as many as 25 000 people every year may be exposed to the effects of carbon monoxide within the home. Whatever the actual number, the overwhelming majority of cases go unrecognised, unreported, and untreated. Chronic carbon monoxide exposure is misdiagnosed. A survey carried out by the charity Carbon Monoxide Support showed that in only one case out of 77 was exposure correctly identified on the basis of symptoms alone.[12]

The early symptoms of carbon monoxide poisoning are usually said to be flu like, which, though arguably true, also encourages the wrong diagnosis. As a result a doctor's most likely response when faced with more than one member of a household exhibiting similar symptoms is to think of a vague microbial cause (a diagnosis never tested) when in reality a far more prosaic cause may exist. Symptoms may initially be mild, often include gastrointestinal upset more in children, and usually bear a temporal relation to occupancy of a particular building or room. Classically, several family members (including pets) are affected. Testing for carboxyhaemoglobin is straightforward and will pick up exposure in its early stages. Oximetry on a sample of blood has long been the only useful immediate investigation, but breath meters, originally developed as smoking cessation aids, are now available.[13] Most of the time no one thinks to do the test.

Perhaps the most tragic consequence of a missed diagnosis is that patients may be discharged to the very environment that is poisoning them. When deaths are investigated it is not uncommon to find that the victim—sometimes even several members of the same family—had visited a doctor with symptoms of carbon monoxide toxicity in the days before death. With a simple, non-invasive testing device the chances of such tragedies could be dramatically lessened. But to achieve this we must also see increased awareness of the problem, among both patients and their doctors.

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Hyperbaric oxygen in carbon monoxide poisoning

Conflicting evidence that it works

There is little dispute that carbon monoxide poisoning is common: in the United States it produces an estimated 40 000 emergency department visits each year,[1] and the accompanying editorial outlines the difficulties in diagnosing poisoning caused by this "silent killer." There is disagreement, however, about how best to treat carbon monoxide poisoning, and in particular about the role of hyperbaric oxygen.

Carbon monoxide is produced endogenously in small amounts and as a byproduct of incomplete combustion. It is colourless, odourless, and undetectable by human senses. It binds to haemoglobin, displacing oxygen; causes a leftward shift of the oxyhaemoglobin dissociation curve; binds to many intracellular proteins; and may interfere with ATP production at the cytochrome level.[2] It can also activate neutrophils pathologically, leading to a reperfusion injury manifested by lipid peroxidation.[3] Low levels of carbon monoxide produce evidence of oxidative stress.[4] Recently, apoptosis in brain tissue has been observed after carbon monoxide poisoning.[5]

Supplemental oxygen was found helpful in treating carbon monoxide poisoning in 1868,[6] and hyperbaric oxygen was first used for clinical poisoning in 1942.[7] The theoretical benefits of hyperbaric oxygen include a faster reduction in carboxyhaemoglobin levels, increased intracellular delivery of oxygen, and reduced neutrophil activation and adherence, thereby reducing

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lipid peroxidation.[8] Despite anecdotal reports on the beneficial effects of hyperbaric oxygen for acute carbon monoxide poisoning,[8] its role in such poisoning has been questioned.[9 10]

Four randomised clinical trials have studied the issue in humans. Raphael et al treated non-comatose acutely poisoned patients with hyperbaric or normobaric oxygen and found no difference in subjective outcome at one month.[11] In a small trial in conscious patients Ducasse observed that hyperbaric oxygen preserved vascular responsiveness to acetazolamide and that treated patients had better quantitative electroencephalograms than those treated with normobaric oxygen.[12] Thom et al randomised conscious poisoned patients to hyperbaric or normobaric oxygen and found no delayed neurological sequelae in those receiving hyperbaric oxygen.[13] Only limited inferences can be drawn from these trials, however, because of methodological problems, including lack of blinding,[11–13] possible ineffective hyperbaric oxygen dosing,[11] delays in giving hyperbaric oxygen,[11] inconsistent and incomplete follow up,[11 13] lack of functional (neuropsychological) outcome measures,[11 12] and failure to enrol unconscious patients.[11–13]

A recent Australian double blind randomised trial addresses some of these limitations.[10] Scheinkestel et al showed that hyperbaric oxygen did not improve cognitive outcome in acute carbon monoxide poisoning, including in severe poisoning; indeed, they found that it might worsen outcome, in that more of the severely poisoned patients in the hyperbaric oxygen group had a poor outcome at completion of treatment. Most of their 191 patients (73%) had severe poisoning and most had attempted suicide (76%). Concomitant depression and use of psychoactive drugs might have influenced the results. The delay before most patients received hyperbaric oxygen (about seven hours) might have reduced its effectiveness.[8] Scheinkestel et al used high concentrations of oxygen continuously in both groups for three days, and more in patients who remained abnormal at three days. This dose of normobaric oxygen is generally not used in carbon monoxide poisoning, so the controls might not have represent a true control group for testing whether hyperbaric oxygen improves or worsens outcome. Cluster randomisation was necessary for practical purposes, but this might have caused differences between the two arms of the trial. All patients were admitted to hospital, and Scheinkestel et al's report would have been strengthened if it had included detailed outcome information at hospital discharge. Also the study is weakened by the fact that one month follow up was low (46%).

Nevertheless, this study reminds us of how damaging carbon monoxide poisoning can be: hospital mortality was 3%, and neuropsychological sequelae were present in 71% of patients at hospital discharge, and 62% at one month. Even with hyperbaric oxygen, neuropsychological sequelae occur,[14] and without hyperbaric oxygen, including in severe carbon monoxide poisoning, a normal functional recovery is possible.[15] Unfortunately, no marker exists that will predict which patients will develop neurocognitive sequelae. In carbon monoxide poisoning treatment of many of the pathological processes that occur is probably time dependent, and if patients are not treated promptly with hyperbaric oxygen one can reason that hyperbaric oxygen might be ineffective. However, the time window for hyperbaric oxygen in human carbon monoxide poisoning is unknown. Thom has shown in rats that lipid peroxidation can be prevented if hyperbaric oxygen is used within 90 minutes of carbon monoxide exposure.[16]

Obviously, prevention of carbon monoxide poisoning remains paramount. Households with attached garages or with any flame source should have regular inspections of their furnaces as well as carbon monoxide alarms. Those people who do suffer acute carbon monoxide poisoning deserve, at the minimum, several hours of high concentrations of oxygen (preferably 100% oxygen) and follow up after the poisoning. And if cognitive and affective problems are detected after carbon monoxide poisoning these patients should be referred to neuropsychologists and occasionally psychiatrists. However, although both 100% normobaric oxygen and hyperbaric oxygen are accepted treatments for carbon monoxide poisoning, it remains unclear on present evidence whether hyperbaric oxygen offers a substantial advantage in clinical poisoning. For now clinicians must balance the costs and risks of transport of hyperbaric treatment against its theoretical benefits. We still need a well designed, multicentre, prospective, randomised controlled trial to answer the question of when, if at all, to refer patients with acute carbon monoxide poisoning.

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