



# This Week in the Journal

October 3, 2002

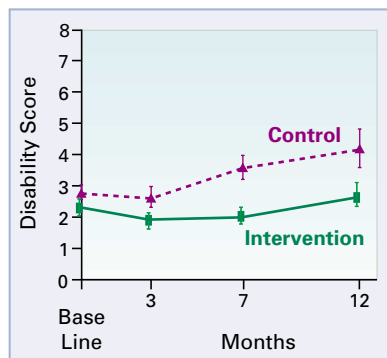
*“Our results support the use of hyperbaric oxygen in patients with acute carbon monoxide poisoning.”*

## Hyperbaric Oxygen for Acute Carbon Monoxide Poisoning

Cognitive sequelae often occur after acute carbon monoxide poisoning. This double-blind, randomized trial assigned subjects either to three sessions in a hyperbaric-oxygen chamber or to one normobaric-oxygen treatment plus two sessions of exposure to normobaric room air, all administered within 24 hours after the end of exposure to carbon monoxide. Cognitive sequelae six weeks later were less frequent among persons who received hyperbaric-oxygen therapy (25.0 percent) than among those who received normobaric-oxygen treatment (46.1 percent,  $P=0.007$ ). Differences were sustained 12 months after the episode of acute carbon monoxide poisoning.

*Hyperbaric-oxygen treatments within 24 hours after acute carbon monoxide poisoning should be the standard of care.*

see page 1057 (Perspective, page 1054; editorial, page 1105)



## Prevention of Functional Decline in Frail, Elderly Persons

This randomized, controlled trial assessed the efficacy of a home-based program to prevent functional decline among 188 frail, elderly persons. The program, which involved physical therapy and focused on improving underlying impairments in physical abilities, was more effective than an educational program in slowing the progression of disability with respect to activities of daily living.

*A home-based intervention targeted to impairments in physical abilities may reduce the progression of disability in frail, elderly patients, but it remains unclear whether it can ultimately reduce the need for nursing home care in this population.*

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## PERSPECTIVE

## Carbon Monoxide Poisoning

Carbon monoxide poisoning is the most common type of accidental poisoning in the United States, accounting for thousands of emergency department visits and some 800 deaths annually. Carbon monoxide, an insidious by-product of incomplete hydrocarbon combustion, is generated in toxic amounts by internal-combustion engines, fossil-fuel furnaces, and fires. Carbon monoxide emissions from modern automobiles, though controlled by regulatory standards, are still highly toxic in poorly ventilated spaces. A stable gas at physiologic temperatures, carbon monoxide diffuses rapidly across the alveolar cap-

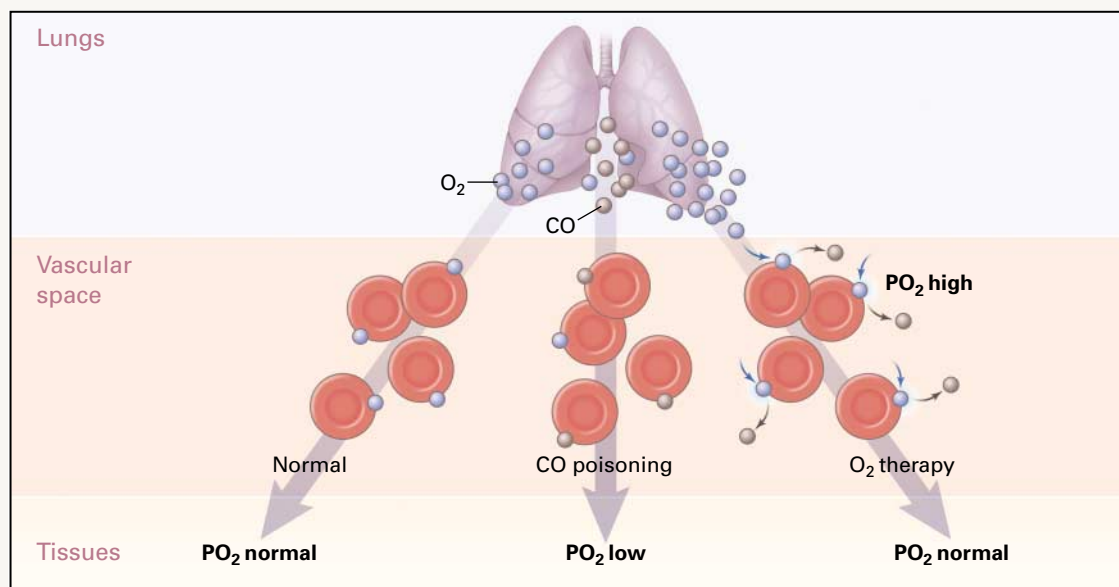
illary membrane and binds tightly to iron centers in hemoglobin and other hemoproteins.

Claude Bernard first proposed in 1865 that toxic effects of carbon monoxide resulted from the formation of carboxyhemoglobin. Carboxyhemoglobin decreases the blood oxygen content and hinders the allosteric release of oxygen from hemoglobin to tissues. In patients with severe poisoning, carboxyhemoglobin compromises the delivery of oxygen to tissue and leads to tissue hypoxia and its immediate functional implications, especially for organs with high oxygen demands such as the brain and the heart.

Although an elevated carboxyhemoglobin level is a diagnostic sine qua non of poisoning, it does not predict the severity of clinical signs and symptoms, particularly those affecting the brain. This poor correlation between carboxyhemoglobin

levels and neurologic presentation, which has long been recognized, is related to unmeasured tissue uptake of carbon monoxide, which increases during hypoxia because of competition between carbon monoxide and oxygen at the oxygen-binding sites on hemoproteins (see Figure). After cellular uptake of carbon monoxide, nonhypoxic mechanisms, including reoxygenation injury, contribute to pathogenesis.

The most common signs and symptoms of carbon monoxide poisoning are nonspecific and include headache, dizziness, and confusion. A high index of suspicion is needed to make the diagnosis, particularly when the means of exposure is not evident. The diagnosis is confirmed by measurement of blood carboxyhemoglobin. Indeed, it has been estimated that more than 5 percent of patients in emergency departments who present with influenza-like illnesses during the winter have occult



## The Pathogenesis of Carbon Monoxide Poisoning.

Carbon monoxide and hemoglobin form carboxyhemoglobin, displacing oxygen and leading to tissue hypoxia. As the partial pressure of oxygen (PO<sub>2</sub>) in tissue falls, the amount of carbon monoxide entering the tissues and binding to cell hemoproteins, such as myoglobin and cytochrome oxidase, increases, interfering with their function. After the exposure and during treatment with oxygen, a higher partial pressure of oxygen in the lung and vascular space causes the carboxyhemoglobin level to decrease faster than the level of carbon monoxide bound in tissues, where the partial pressure of oxygen is lower. Thus, the carboxyhemoglobin level may not correlate with the clinical presentation of the patient.



### Brief Report: *Salmonella* Sepsis after a Platelet Transfusion

Two patients had salmonella sepsis after receiving platelet transfusions, and the source of the infection was traced to the pet snake of the platelet donor. The donor was asymptomatic, but *Salmonella enterica* serotype enteritidis was cultured from his pet boa constrictor. The isolate was identical to the isolates from the two patients with sepsis.

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carbon monoxide poisoning. The normal carboxyhemoglobin level is 1 to 3 percent, a result of endogenous carbon monoxide production by heme catabolism and low-level environmental carbon monoxide exposure. Cigarette smokers increase their carboxyhemoglobin level by an average of 5 percent per pack smoked per day, and otherwise healthy smokers tolerate carboxyhemoglobin levels of 10 percent without having symptoms. Overt signs of toxic effects usually appear at carboxyhemoglobin levels of 15 to 20 percent, and a level of 25 percent is an index of severe poisoning, which may lead to sudden loss of consciousness.

Serious consequences occur in half of victims of severe carbon monoxide poisoning and fall into two major categories: acute cardiac or neurologic injuries and late effects. A delayed neurologic syndrome, typified by memory loss and other, sometimes subtle, cognitive deficits occurs in approximately 15 percent of severely poisoned patients after an interval of 2 to 28 days. Age and loss of consciousness have been identified as independent risk factors. The delayed neurologic syndrome naturally tends to improve gradually, and many patients have normal functional status a year after poisoning, but all require careful follow-up for residual neuropsychological effects.

The cornerstone of treatment for carbon monoxide poisoning is supplemental oxygen, which hastens the dissociation of carbon

monoxide from hemoproteins in direct relation to the partial pressure of oxygen. Hyperbaric oxygen at a pressure of 2.5 to 3.0 atmospheres absolute, with which an arterial partial pressure of oxygen above 1800 mm Hg can be achieved, greatly facilitates carboxyhemoglobin dissociation as compared with normobaric oxygen at sea level. In experimentally induced carbon monoxide poisoning, hyperbaric oxygen also benefits the brain more than normobaric oxygen does, by improving energy metabolism, preventing lipid peroxidation, and decreasing neutrophil adherence.

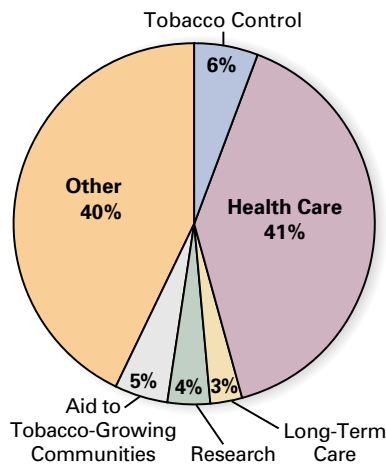
Whether to use hyperbaric oxygen clinically and, if so, when to use it are matters that have been debated since it emerged as a treatment for carbon monoxide poisoning in 1960. Practice guidelines were developed on the basis of clinical experience and inferences of efficacy in uncontrolled studies. Results of past controlled trials comparing hyperbaric-oxygen and normobaric-oxygen therapy have been inconclusive because of methodologic difficulties. However, in this issue of the *Journal*, Weaver et al. (pages 1057–1067) clearly demonstrate, in a carefully designed, double-blind, randomized trial involving 152 patients, that hyperbaric-oxygen therapy at 3 atmospheres absolute is superior to normobaric-oxygen therapy in reducing the incidence of cognitive dysfunction at 6 weeks and 12 months after acute carbon monoxide poisoning.

These findings strengthen the ra-

tionale for hyperbaric-oxygen therapy in patients with acute carbon monoxide poisoning, but important clinical issues remain. First, we need better predictive tests or criteria for determining the risk of delayed and permanent effects of carbon monoxide poisoning. Second, practical questions remain concerning optimal hyperbaric-oxygen regimens — for example, the optimal number of treatments and the maximal delay after which hyperbaric oxygen is no longer useful. Most trials have enrolled patients as soon as possible after poisoning, yet Weaver et al. leave open the question of whether some patients benefit from hyperbaric oxygen after the often-quoted therapeutic window of 6 to 12 hours. A third unresolved issue is that of mild carbon monoxide poisoning: how should patients who do not need hyperbaric-oxygen therapy be treated? Many practitioners recommend six hours of 100 percent normobaric oxygen delivered by face mask, although the efficacy of this treatment has not been validated. Finally, it must be emphasized that neither hyperbaric oxygen nor any other therapy can be expected to prevent cognitive deficits due to cell death sustained during the episode of poisoning. Therefore, prevention remains a vital public health issue.

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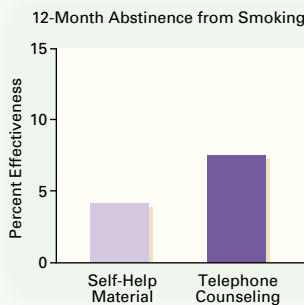


### Special Article: State Expenditures for Tobacco-Control Programs

One of the goals of the legal settlement between the tobacco industry and the states was to promote public health. In this study, the authors examined state spending on tobacco-control programs. In 2001 the average state received \$164 million from the tobacco settlement but allocated only 6 percent of these funds to tobacco-control programs. Only six states exceeded the minimal level of funding for tobacco-control programs recommended by the Centers for Disease Control and Prevention. Program funding was not higher in states with more tobacco-related health problems.

*States are directing only a small percentage of tobacco-settlement funds to tobacco-control programs. These findings suggest that the tobacco settlement represents an unrealized opportunity to reduce morbidity and mortality from smoking.*

see page 1080 (editorial, page 1106)



### Special Article: Real-World Effectiveness of a Telephone Quitline for Smokers

Telephone counseling for smoking cessation has been effective in clinical trials, and many states have established “quitlines.” This randomized study of 3282 smokers was designed to evaluate the real-world effectiveness of the California Smokers’ Helpline. Smokers who were randomly assigned to counseling received up to seven counseling sessions that focused on motivation, self-efficacy, social support, planning for quitting, and relapse prevention. At 12 months of follow-up, smoking-cessation rates were somewhat higher for subjects who received telephone counseling than for those who received only self-help materials (7.5 percent vs. 4.1 percent).

*Most smokers who called the quitline continued to smoke; however, telephone counseling was effective in helping some smokers to quit. This study did not evaluate the costs of the program. Given the enormous suffering and costs associated with smoking, the benefit achieved by the quitline is likely to outweigh the cost of this low-intensity intervention.*

see page 1087 (editorial, page 1106)

*“Clinicians should generally be able to provide effective relief of pain in infants and children with a wide margin of safety.”*

### Drug Therapy: Analgesics for the Treatment of Pain in Children

The treatment of pain in infants and children has often been insufficient, owing to lack of information and understanding of how to use analgesic agents in the very young. This review discusses the development of nociception; the differences in metabolism of analgesics among infants, children, and adults; and agents that can be used for pain control in a variety of settings.

*Infants and children can receive analgesia and anesthesia safely, provided proper age-related adjustments are made in clinical practice and dosage.*

see page 1094