

be an acid mucopolysaccharide.

The thiazide story, like the universe, is still unfolding. There are still wide gaps in our knowledge concerning many aspects of the use of thiazide agents. To give only a few examples, more needs to be known about the correlation between biochemical response and therapeutic efficacy, the significance of little-known thiazide effects such as magnesium and zinc deficiency has yet to be determined, and the failure of the drug in a small proportion of treated patients must still be explained. However, the point has surely been reached at which it can be stated unequivocally that hydrochlorothiazide is highly effective in preventing calcium stones and merits serious consideration for a prominent role in the modern management of this disorder. It is hoped that in the not too distant future, experts in this field will come to some consensus concerning the relative merits of this agent with respect to others such as orthophosphates and cellulose phosphate, which are also in current use,

so that the medical profession will be able to apply these new developments more effectively in the management of their patients.

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## Carbon monoxide in the modern society

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Despite the technologic advances in this century carbon monoxide remains a common cause of fatal poisoning,<sup>1</sup> and our technology may increase the risks.<sup>2</sup>

Carbon monoxide is an asphyxiant gas that diffuses readily in the air and is insidious because it has neither colour nor odour. Although other products of incomplete combustion may produce an odour or unpleasant fumes, these often provide insufficient warning to the individual at risk. Carbon monoxide diffuses across the alveolar membrane and binds to hemoglobin. Since hemoglobin has 200 to 300 times more affinity for carbon monoxide than for oxygen, the oxyhemoglobin dissociation curve is shifted to the left and the tissue oxygen tension must decrease before the remaining oxyhemoglobin can give up its oxygen.<sup>3</sup> Although it has been suggested that carbon monoxide may have some adverse toxic effects of its own,<sup>4</sup> the pathologic effects of carbon monoxide appear to be due to hypoxia from the reduced oxygen-

carrying capacity of the blood.<sup>5</sup>

The "background" carbon monoxide in our blood may come in small part from the endogenous metabolism of heme, but most comes from exogenous production. Maugh<sup>6</sup> has argued that the amount of carbon monoxide produced by the processes of plant growth and death dwarf man's production on a global basis, but nevertheless there has been increasing concern in recent years about the large amounts produced by household fuels and automobile exhaust.

The current energy crisis has led to repeated requests that people reduce their fuel consumption. We have been advised, for example, to make our houses airtight so that heat is preserved. In following this advice many people have substantially reduced the ventilation in their homes. At the same time, many have resorted to using fireplaces for heat to reduce fuel costs. This can prove to be hazardous because the airtight home does not allow adequate air

flow to the fireplace, and backdraught may bring some of the products of combustion into the room. If combustion is incomplete owing to poor oxygenation, the build-up of carbon monoxide in an airtight room can reach dangerous concentrations. The danger may be compounded by the use of inappropriate fuels such as charcoal briquettes, which generate large amounts of carbon monoxide if ventilation is poor.

In recent years much attention has been given to the large amounts of carbon monoxide produced by automobiles; it is estimated that in New York City automobile traffic alone produces 3.7 million kilograms of carbon monoxide daily.<sup>7</sup> High concentrations of carbon monoxide along city streets and freeways have caused concern for the safety of automobile drivers.

Most cases of acute carbon monoxide poisoning probably are not recognized, and the nonspecific symptoms of headache, fatigue, irritability, dizziness, paresthesia and disturb-

ances of consciousness are explained away in some other fashion. Persons who recover from carbon monoxide poisoning often have few sequelae, but a neurologic deficit may result, as it may from any long-term hypoxic event. It is estimated that approximately 150 Canadians and 600 Americans die each year from carbon monoxide poisoning. There are probably other deaths due to carbon monoxide that are not diagnosed correctly. Most of these deaths result from automobile exhaust fumes in closed garages or from cars parked with the engine running. Other deaths involve improperly operated heaters, usually with insufficient air flow or poor ventilation resulting from poor burner design, blocked air entries or backdraughting due to negative pressure or airtightness.

Probably the heaviest nonindustrial exposure occurs in individual smokers: a heavy smoker may have a carbon monoxide blood value of 5%, a person smoking up to three packs of cigarettes per day may have values of up to 9%, and a heavy smoker of cigars may have values as high as 20%.<sup>2</sup> Smoking adds to the background concentration of carbon monoxide in our blood that is already causing concern. Background carbon monoxide concentrations are of particular concern in areas such as Calgary<sup>7</sup> that have high-density automobile traffic, weather inversions, high altitude and cold weather.

Many deaths have been reported from use of hibachis or barbecues indoors. Wilson, Rich and Messman<sup>8</sup> reported five deaths over a 14-month period in Utah from the burning of charcoal briquettes inside a Volkswagen bus, a trailer, a station wagon and a potato cellar. They also had information on five other deaths from the use of charcoal briquettes in enclosed, poorly ventilated spaces. More recently, the hazard created by people using their barbecues in indoor fireplaces because of poor weather outside has been recognized. If the room is poorly ventilated high concentrations of carbon monoxide accumulate rapidly.

The build-up of carbon monoxide in ice-skating rinks due to ice resurfacing machines is another common problem. In Seattle 15 children became ill after skating at an enclosed rink.<sup>9</sup> Because they had nausea and

vomiting, food poisoning was suspected initially. After many patrons noted gassy odours, the propane-fueled ice resurfacing machine was examined and was found to produce high concentrations of carbon monoxide. The problem was compounded because children have higher rates of metabolism and of uptake of carbon monoxide, and the activity of skating increases their respiratory volume. A survey of other rinks in the Seattle area showed that this was a common problem. A program was instituted to educate rink owners and to encourage them to purchase carbon monoxide detectors. Improvement occurred in these rinks when the machines were run less frequently and for shorter periods, and when the rinks were better ventilated. The use of catalytic mufflers was recommended. A more dramatic episode was reported by Saslow and Clark<sup>10</sup> after 171 patrons in a sports arena manifested dizziness, nausea, tinnitus, disorientation, numbness of the feet and hands, blurred vision, vomiting and, in some cases, loss of consciousness. The source of the gas was traced to a broken exhaust pipe on a natural gas engine used in the ventilation system of the sports arena.

Although most cases of carbon monoxide poisoning result from incomplete combustion of carbonaceous fuels, an unusual source of carbon monoxide was described recently by Stewart and Hake.<sup>11</sup> Paint strippers, whose basic ingredient is methylene chloride, were noted to produce high concentrations of carbon monoxide in poorly ventilated rooms.<sup>11</sup>

Recently I saw a case of acute carbon monoxide poisoning in a high-school student who was working over a chafing dish heated by three cans of Sterno (manufactured by Colgate-Palmolive). The chafing dish was surrounded by aluminum foil except for one opening, where the food server stood. We obtained values of 1000 to 3000 parts per million (ppm) of carbon monoxide around this apparatus and values of 750 to 1000 ppm at the level of the food server's face. Her episode of unconsciousness was initially attributed to epilepsy. On investigating the case I found that all the girls who served at this table had had symptoms of carbon monoxide poisoning. Fortunately the

# <sup>N</sup> Empracet-30

## Acetaminophen + Codeine Analgesic-Antipyretic-Antitussive

**Indications:** To provide enhanced analgesia in a wide variety of conditions requiring the control of moderate to severe acute or chronic pain, especially when other analgesics are insufficient; also as a non-salicylate analgesic-antipyretic-antitussive in acute cold and in other acute respiratory diseases.

**Adverse Effects:** When used as directed, acetaminophen is virtually free of severe toxicity or side effects. The incidence of gastrointestinal upset is less than after salicylate administration. If a rare sensitivity reaction occurs, discontinue the drug. Hypersensitivity to acetaminophen is usually manifested by a rash or urticaria. Acetaminophen poisoning can result in severe hepatic damage. Phenobarbital increases the activity of microsomal enzymes which produce a toxic metabolite and therefore acetaminophen's hepatotoxicity is enhanced. Thus, concomitant ingestion of phenobarbital may increase the likelihood of liver necrosis in acetaminophen overdose.

**Overdose:** The literature has reported that some adults who have ingested doses in excess of 10 g should be closely monitored until it is ascertained that there is no hepatotoxicity.

**Symptoms:** Nausea, vomiting and upper abdominal pain. Initially, CNS stimulation may be noted followed by somnolence, lethargy, or stupor. In the most severe cases a 24 hour latent period may be followed by drowsiness progressing to coma due to hepatic necrosis; in these cases death may occur 2 to 4 days following ingestion. The chief biochemical changes noted in the blood are gross elevation of liver enzymes, some elevation of bilirubin level, prolongation of prothrombin time and possibly hypoglycemia or hyperglycemia. The codeine phosphate in sufficient overdosage produces narcosis, sometimes preceded by a feeling of exhilaration and followed by convulsions. Nausea and vomiting are usually prominent symptoms. The pupils are contracted and the pulse rate is usually increased. Cardiorespiratory depression accompanied by cyanosis occurs, followed by a fall in body temperature, circulatory collapse, coma, and death.

**Treatment:** When the possibility of an overdosage exists (approx. 10 g of acetaminophen) treatment should be immediate. Although no specific treatment has been developed or accepted, ipecac—or apomorphine-induced emesis followed by 50 g of activated charcoal given orally to decrease absorption of the drug, is the best available treatment. If this is not quickly available, administer the universal antidote. Since there is no specific antidote, treatment is primarily supportive. Once overdosage with acetaminophen is established, liver studies should be carried out and followed carefully for a period of 7 days. The possibility of liver damage may be suspected by the presence of a leukocytosis in conjunction with a low erythrocyte sedimentation rate. CNS stimulation may be controlled by cautious use of an intermediate-acting barbiturate such as sodium butabarbital. If signs of codeine overdosage are present a specific antagonist such as nalorphine or levallorphan should be administered immediately. In the unconscious patient, give nalorphine in i.v. doses of 5 to 10 mg to adults or 1 to 2 mg to children, depending on the severity of narcosis and respiratory depression. Levallorphan is given in doses one-tenth that of nalorphine. Maintain a patent airway through the use of an oropharyngeal airway or endotracheal tube, oxygen should be administered, and respiration should be assisted by artificial respiration. Circulatory collapse and shock may be counteracted by use of dextran, plasma, or concentrated albumin and vasopressor drugs, e.g. norepinephrine. Short-acting barbiturates, e.g. thiopental, may be used cautiously to control convulsions. Avoid the use of analeptic drugs.

**Dosage:** 1 to 2 tablets every 6 hours as required.

**Supplied:** Each round peach coloured tablet contains acetaminophen 300 mg and 30 mg of codeine phosphate. In bottles of 100.

Code Number Wellcome K98

Additional prescribing information available on request.



\*Trade Mark

C-6002

dining room was well ventilated and the university students were exposed to values of only 50 to 70 ppm while they were eating. (This case is reported in greater detail in this issue of the Journal, beginning on page 800).

Gilbert and Glaser<sup>12</sup> described a remarkable case in which the signs and symptoms of carbon monoxide poisoning were also thought to be due to epilepsy. The man had had repeated episodes of unconsciousness and personality change over a 4-year period due to carbon monoxide poisoning at his place of work.

As we become more aware of the risks of acute carbon monoxide poisoning, questions are being raised about the possible effects of low exposures over a long period. The relation of such exposure to vascular disease, atherosclerosis, myocardial infarction and recurrent angina pectoris is being assessed.<sup>13-15</sup> Uncertainty about the effects of long-term exposure to low concentrations of carbon monoxide has given rise to doubts about safety standards. In the past 50 ppm of carbon monoxide for 8 hours was the maximum allowable concentration. The United States Environmental Protection Agency has recommended 35 ppm for 1 hour or 9 ppm for 8 hours.<sup>16</sup> The objective of Environment Canada for quality of ambient air is an average concentration of 0 to 6 mg/m<sup>3</sup> over 8 hours or 0 to 15 mg/m<sup>3</sup> over 1 hour. Acceptable average concentrations are 6 to 15 mg/m<sup>3</sup> over 8 hours or 15 to 32 mg/m<sup>3</sup> over 1 hour. An acceptable occupational concentration is an average of 55 mg/m<sup>3</sup> over 8 hours or 440 mg/m<sup>3</sup> during an exposure of less than 15 minutes.

At a time when homes are being made airtight and when cheaper methods of heating are being sought, it is important that the public be made aware of the dangers of carbon monoxide poisoning. There should be wide public recognition of the fact that the burning of any fuel, whether in a fireplace or by a motor, requires adequate oxygenation and ventilation. Incomplete burning of any fuel will produce carbon monoxide.

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# Beconase<sup>®</sup> (beclomethasone dipropionate) Nasal Spray

## Prescribing information

**Indications and clinical uses** Beconase is indicated for the treatment of perennial and seasonal allergic rhinitis unresponsive to conventional treatment.

**Contraindications** Active or quiescent tuberculosis or untreated fungal, bacterial and viral infections. Children under six years of age.

**Warnings** In patients previously on high doses of systemic steroids, transfer to Beconase may cause withdrawal symptoms such as tiredness, aches and pains, and depression. In severe cases adrenal insufficiency may occur, necessitating the temporary resumption of systemic steroids. The safety of Beconase in pregnancy has not been established. If used, the expected benefits should be weighed against the potential hazard to the fetus, particularly during the first trimester of pregnancy.

**Precautions** The replacement of a systemic steroid with Beconase has to be gradual and carefully supervised by the physician. The guidelines under "Administration" should be followed in all such cases. Unnecessary administration of drugs during pregnancy is undesirable. Corticosteroids may mask some signs of infection and new infections may appear. A decreased resistance to localized infection has been observed during corticosteroid therapy. During long-term therapy, pituitary-adrenal function and hematological status should be periodically assessed. Fluorocarbon propellants may be hazardous if they are deliberately abused. Inhalation of high concentrations of aerosol sprays has brought about cardiovascular toxic effects, and even death, especially under conditions of hypoxia. However, evidence attests to the relative safety of aerosols when used intranasally and with adequate ventilation. There is an enhanced effect of corticosteroids on patients with hypothyroidism and in those with cirrhosis. Acetylsalicylic acid should be used cautiously in conjunction with corticosteroids in hypoprotrombinemia. Patients should be advised to inform subsequent physicians of the prior use of corticosteroids. During Beconase therapy, the possibility of atrophic rhinitis and/or pharyngeal candidiasis should be kept in mind.

**Adverse reactions** No major side effects attributable to Beconase have been reported. Occasional sneezing attacks have followed immediately after the use of the intranasal aerosol. A few patients have complained of burning sensation and irritation in the nose after Beconase nasal inhalation. When patients are transferred to Beconase from a systemic steroid, allergic conditions such as asthma or eczema may be unmasked.

**Dosage and administration** The usual dosage for patients of all ages who received no previous systemic steroid is one application (50 mcg of beclomethasone dipropionate) into each nostril three to four times daily. Maximum daily dose should not exceed twenty applications in adults and ten applications in children. If Beclomethasone is used concurrently, the maximum dose of each aerosol is ten applications in adults and five applications in children. Beconase should not be used under six years of age. Since the effect of Beconase depends on its regular use, patients must be instructed to take the nasal inhalations at regular intervals and not, as with other nasal sprays, as they feel necessary. They should also be instructed in the correct method, which is to blow the nose, then insert the nozzle firmly into the nostril, compress the opposite nostril and actuate the aerosol while inspiring through the nose, with the mouth closed. In the presence of excessive nasal mucus secretion or edema of the nasal mucosa, the drug may fail to reach the site of action. In such cases it is advisable to use a nasal vasoconstrictor for two or three days prior to Beconase. Careful attention must be given to patients previously treated for prolonged periods with systemic corticosteroids when transferred to Beconase. Initially, Beconase and the systemic corticosteroid must be given concomitantly, while the dose of the latter is gradually decreased. The usual rate of withdrawal of the systemic steroid is the equivalent of 2.5 mg of prednisone every four days if the patient is under close supervision. If continuous supervision is not feasible, the withdrawal of the systemic steroid should be slower, approximately 2.5 mg of prednisone (or equivalent) every ten days. If withdrawal symptoms appear, the previous dose of the systemic steroid should be resumed for a week before further decrease is attempted. **Dosage form** Beconase is a metered-dose aerosol, delivering 50 micrograms of beclomethasone dipropionate with each depression of the valve. There are two hundred doses in a container. Official product monograph on request.

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