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Search of Medical Literature for Indoor Carbon Monoxide Exposure

**T. Brennan
M. Ivanovich**

December 1995

**Prepared for the U.S. Department of Energy
under Contract DE-AC06-76RLO 1830**

**Pacific Northwest National Laboratory
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Richland, Washington 99352

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1.0 Introduction

This report documents a literature search on carbon monoxide. The search was limited to the medical and toxicological databases at the National Library of Medicine (MEDLARS). The databases searched were Medline, Toxline and TOXNET. Searches were performed using a variety of strategies. Combinations of the following keywords were used: carbon, monoxide, accidental, residential, occult, diagnosis, misdiagnosis, heating, furnace, and indoor. The literature was searched from 1966 to the present. Over 1000 references were identified and summarized using the following abbreviations: AU (Author), TI (Title), SI (Search Index), SO (Source), and AB (Abstract).

A review of the abstracts was used to eliminate references that did not pertain to health effects, indoor exposures, or measurement methods. Copies of a number of papers were ordered and additional documents were culled from the references listed at the end of the papers.

The major findings of the search are:

1. Acute and subacute carbon monoxide exposures result in a large number of symptoms affecting the brain, kidneys, respiratory system, retina, and motor functions.
2. Acute and subacute carbon monoxide (CO) poisonings have been misdiagnosed on many occasions.
3. Very few systematic investigations have been made into the frequency and consequences of carbon monoxide poisonings.

The results of the search have been divided into three major categories with a number of sub-categories. The three major topics of the papers are: exposure, health effects, and measurement. A brief overview of the sub-topics in these three major categories follows.

Exposure

Misdiagnosed exposures - a number of studies report that victims of CO exposures were diagnosed incorrectly (Sadovnikoff; Samuels 1992; Dolan 1987; Fisher 1982; Grace 1981; Hopkinson 1980; Kelley 1978). One study found that of 55 patients complaining of flu-like symptoms at an emergency room, 13 had carboxyhemoglobin (COHb) blood levels greater than 10%. None of these patients were diagnosed with subacute CO intoxication by emergency room physicians. Diagnoses included urinary tract infection, viral syndrome, active pulmonary tuberculosis, tension headache, bronchitis, drug-induced headache, gastritis, biliary colic and orthostatic hypotension secondary to diuretic use (Dolan 1987). Cases of CO poisoning have also been initially diagnosed as conversion disorder (Samuels 1992), and gastroenteritis (Hopkinson 1980).

Residential indoor exposure - The medical and toxicological literature contains a small number of papers concerning residential exposures. Several papers were found that related to homes with unvented combustion devices (Wang 1988; Stevenson 1985; Prescher, Jaeger 1982). Several

residential exposure papers are listed in the section under misdiagnosed exposures (Dolan 1987; Grace 1981; Hopkinson 1980; Kelley 1978). One of the reasons residential exposures are misdiagnosed appears to be lack of surrounding evidence that is present when the CO exposure is the result of fire, vehicle operation, or suicide. This topic is discussed in a paper in *Journal of Forensic Sciences* (Caplan 1986).

Non-residential indoor exposures - Non-residential CO exposures or indoor levels are reported for office buildings (Wallace 1983; hospitals [Allen 1982]; arenas [Lee 1994], CDC 1994; Levesque 1990; Kwok 1986, vehicles [Nowak 1993; Ott 1994; Koushki 1992; Flachsbart 1987; Poulton 1987; Iglewicz 1984; and occupational groups such as confined spaces workers [Sahli 1993], foundry workers [Koskela 1994], coke plant workers [Sroczynski 1993], blast furnace workers [Lewis 1992], carbon black manufacture workers [Gardiner 1992], charcoal meat grilling workers [Madani 1992], and warehouse workers [Ely 1995]).

Tobacco related exposures - A good deal of literature is available on CO exposures with tobacco smoke as the source.

Health Effects

A large number of health effects from carbon monoxide exposures are presented in the literature. The following list summarizes health effects reported in the literature. Note: 1 ppm CO = 1.1 $\mu\text{g}/\text{M}^3$.

- misdiagnosis - Victims of CO exposures have been misdiagnosed as a variety of afflictions (Dolan 1985).
- high altitude speeds the effects of CO poisoning, suggestions have been made to lower the guidelines for higher altitudes (Song 1993; Horvath 1988).
- prenatal exposure - severe CO exposure resulted in death or toxic effects (anatomical malformations, functional alterations) in the foetus (Norman 1990); no relationships between neighborhood CO exposure and low birth weight babies (Alderman 1987).
- hypoxia - low oxygen supply to tissue (Haab 1990; Di Cera 1989).
- retinal hemorrhages - acute and subacute CO poisoning causes retinal hemorrhages in many victims (Ferguson 1985).
- tumor treatment - CO exposure reduces the effectiveness of radiation therapy.
- CO is produced endogenously (internally) from heme catabolism and seems to modulate long-term potentiation, memory, and cognitive function (Marks 1994, 1991).
- transient hydrocephalus (increased fluid in the cranium) (Prabhu 1993).

- atherosclerosis in smokers is probably not from CO exposures (Smith 1993), except possibly in the case of greatly elevated cholesterol (Penney 1991).
- immune system impairment - low concentrations of CO in combination with low levels of psycho-emotional stress is associated with a decrease in T lymphocytes in all groups (Dueva 1992).
- cardiovascular disease
 - no effect on arrhythmia in patients with cardiac arrhythmias (Dahms 1993)
 - myocardial ischemia - low doses of CO affects the flow of blood to the heart muscle during exercise in patients who have coronary artery disease (Allred 1991).
- CO induced amnesia - CO appears responsible for acute and delayed amnesia (Hiramatsu 1992).
- renal failure - kidney failure from anoxia, rhabdomyolysis (Jha, Wolff 1994; Florkowski 1992).
- neurological effects (Jha 1994) - CO poisoning produces anomalies in the temporo-parieto-occipital areas, the watershed areas of the major cerebral arteries and the temporal cortex (Denays 1994); lesions in the lower basal ganglia (globus pallidus and internal capsule) (Jones 1994); cerebral white matter (Choi, Gotoh 1993). A case is reported where cerebral blood flow and glucose utilization is impaired one year after CO exposure is reported (Shimosegawa 1992) possibly resulting in lowered responsiveness to stimuli.
- ventilatory efficiency - a strong correlation is reported between flow-volume measured by spirometer and CO exposures (Lee 1994). The effect seems transient.
- physical work capacity is impaired (Sedov 1991).
- human operator performance - exposures of 10 minutes to 900 $\mu\text{g}/\text{M}^3$, raising COHb levels to 10%, resulted in significant decline of performance of 2-dimensional compensatory tracking tasks combined with mental arithmetic (Iastrebov 1987); 8% COHb (Benignus 1987); motor performance not influenced by COHb of 5% (Mihevic 1983).
- dichloromethane exposure elevates COHb (Manno 1992; Pankow 1989).

Tobacco related health effects - a good deal of literature is available on CO health effects that are linked to tobacco smoke.

Measurement

Several papers on CO or carboxyhemoglobin measurement were found and are listed.

2.0 Papers Relating to Exposure

2.1 Misdiagnosed Exposures

AU - Sadovnikoff N

AU - Varon J

AU - Sternbach GL

Carbon monoxide poisoning. An occult epidemic.

Pulmonary and Critical Care Medicine Section, Baylor College of Medicine, Houston.

Language: Eng

SO - Postgrad Med 1992 Sep 15;92(4):86-8, 92-6

Unique Identifier: 92409492

AB - Carbon monoxide (CO) poisoning is a significant health threat in the United States. Smoke inhalation from fires is the most common source. History of carbon monoxide exposure and elevated carboxyhemoglobin levels should alert physicians to the diagnosis of acute poisoning. When no history of exposure occurs, carbon monoxide poisoning must be considered when two or more patients are similarly or simultaneously sick. The diagnosis must be excluded by a directed history and physical examination. If suspicion remains, carboxyhemoglobin levels should be determined and oxygen therapy should be started empirically while laboratory results are pending. Prompt administration of hyperbaric oxygen may reduce the risk of death. If carbon monoxide poisoning is confirmed, the source must be identified and recommendations for correction or avoidance should be made.

AU - Samuels AH

AU - Vamos MJ

AU - Taikato MR

TI - Carbon monoxide, amnesia and hyperbaric oxygen therapy

Auckland Hospital, New Zealand.

Language: Eng

SO - Aust N Z J Psychiatry 1992 Jun;26(2):316-9

Unique Identifier: 92352436

AB- A case of carbon monoxide (CO) poisoning, initially misdiagnosed as conversion disorder, is presented. Cognitive deficits demonstrated at the time of psychiatric assessment were successfully reversed by hyperbaric oxygen therapy despite the 1-week delay. The clinical manifestations of carbon monoxide poisoning and the rationale for and timing of hyperbaric oxygen therapy are discussed. Emphasis is placed on the need for a high index of suspicion for carbon monoxide poisoning in the clinical situation of profound memory disturbance.

AU - Dolan MC
AU - Haltom TL
AU - Barrows GH
AU - Short CS
AU - Ferriell KM
TI - Carboxyhemoglobin levels in patients with flu-like symptoms

Language: Eng

SO - Ann Emerg Med 1987 Jul;16(7):782-6

Unique Identifier: 87239576

AB - Subacute carbon monoxide (CO) poisoning is commonly misdiagnosed as an influenza-like viral illness. During February 1985, all patients presenting to the triage nurse at University Hospital with flu-like symptoms, were asked to give blood samples for carboxyhemoglobin determination. Of those eligible, 10% or 55 patients with headache, dizziness, nausea, vomiting, diarrhea, weakness, general malaise, or shortness of breath were enrolled in the study. Carboxyhemoglobin levels ranged from 0 to 21%. Of this self-selected subgroup, 13 patients (23.6%) had carboxyhemoglobin levels greater than or equal to 10%. No statistically significant difference in carboxyhemoglobin levels was found between smokers and nonsmokers. More patients using wood heat had elevated carboxyhemoglobin levels than patients using any other form of heating (P less than 0.05). No patient with a carboxyhemoglobin level greater than or equal to 10% was diagnosed by emergency physicians as having subacute CO poisoning. Physicians must seek out the possibility of CO toxicity in patients with flu-like illness, particularly in inner-city populations during the heating months. Fundoscopy and COHb levels may be useful in selected cases to correctly diagnose patients and avoid a return to a hazardous environment with potentially fatal consequences.

AU - Leikin JB

AU - Vogel S

TI - Carbon monoxide levels in cardiac patients in an urban emergency department

SI - TOXBIB/86/130921

SO - Am J Emerg Med; Vol 4, ISS 2, 1986, P126-8

AB - Arterial carboxyhemoglobin (COHb) levels of patients, who presented to an emergency department with cardiopulmonary complaints, were determined. The purpose of the study was to see whether COHb levels of these patients indicated an acute risk factor in the severity of exacerbation of their cardiac disease. Factors known or thought to increase COHb levels (smoking and arrival by ambulance, for example) were correlated with COHb levels and final diagnoses of myocardial infarction, exacerbation of stable angina or congestive heart failure, asthma, and chronic obstructive pulmonary disease. Statistically significant increases in COHb were found in patients admitted to the intensive care unit and with proven myocardial infarction than were found in a control group. However, these differences could be accounted for by smoking alone or by instrumental margin of error and were not thought to be related to ambient urban carbon monoxide.

AU - Fisher J

TI - Occult carbon monoxide poisoning

SO - Arch Intern Med; Vol 142, July, 1982, P1270-1271

AU - Grace TW

AU - Platt FW

TI - Subacute Carbon Monoxide Poisoning - Another Great Imitator

SO - JAMA; Vol 246, No 15, 1981, P1698-1700

AB - The illnesses of two patients with characteristic symptoms of subacute carbon monoxide poisoning were initially misdiagnosed. This error resulted in the needless exposure of one patient and two relatives to a toxic environment. The cherry-red color of the skin commonly cited in the literature was absent in both patients. The carbon monoxide poisoning probably contributed to the myocardial infarction and pulmonary emboli seen in these patients. Vague flu-like illnesses should raise the suspicion of carbon monoxide poisoning.

AU - Hopkinson JM

AU - Pearce PJ

AU - Oliver JS

TI - Carbon monoxide poisoning mimicking gastroenteritis

SO - Brit Med Jour; July 1980

AB - A family of five was presented with symptoms of gastroenteritis that were subsequently attributed to carbon monoxide (CO) poisoning. Although CO poisoning may occasionally be confused with drunkenness, the fact that it mimics gastroenteritis is not so well recognized. This fact is drawn to the attention of practitioners who may be called on to treat patients within caravans or other confined quarters where a possible source of CO is present.

AU - Kelley JS

AU - Sophocleus GJ

TI - Retinal Hemorrhages in Subacute Carbon Monoxide Poisoning - Exposures in Homes with Blocked Furnace Flues

SO - JAMA; Vol 239, No 15, 1978

AB - Three incidences of carbon monoxide (CO) poisoning occurred owing to defective heating systems. Twelve persons were affected; of these, three lost their lives. Because the symptoms of carbon monoxide poisoning closely resemble flu and other common illnesses, correct diagnosis was not made as promptly as it might have been. Hemorrhages were found in the nerve fiber layer of the retina in all five of the patients who had been exposed for more than 12 hours. It is determined therefore, that complete examination of the patient should always include ophthalmoscopy, and the finding of retinal hemorrhages, in addition to nausea, headache, and dizziness, should alert the physician to the possibility of carbon monoxide poisoning.

2.2 Residential Indoor Exposure

AU - Wang JN

AU - Cao SR

AU - Li Z

AU - Zhang Y

AU - Li SM

TI - Human exposure to carbon monoxide and inhalable particulate in Beijing, China

SI - TOXBIB/90/027043

SO - Biomed Environ Sci; Vol 1, ISS 1, 1988, P5-12

AB - A total of 20 non-smoking volunteers were selected from the staff members of the Institute of Health according to their housing conditions. Carbon monoxide (CO) and particulate matter in the outdoor and indoor air and personal exposure were monitored simultaneously for 1 week in summer and 1 week in winter. At the same time some public areas, such as workplaces and shopping and traffic areas, were also monitored. The average outdoor concentration for CO was 1.5 ppm in summer and 3.9 ppm in winter; indoors it averaged 2.8 ppm in summer and 20.1 ppm in winter. Personal exposure fluctuated between these values. The level of COHb averaged 0.2% in summer and 1.9% in winter. The level of inhalable particles was higher in winter than in summer, but the difference was not as marked as that for CO. The activity diary showed that time spent at home was around 66% and that total indoor (home and workplace) time was over 90%. This statistic indicates the importance of studying indoor pollution and personal exposure.

AU - Caplan YH

AU - Thompson BC

AU - Levine B

AU - Masemore W

TI - Accidental poisonings involving carbon monoxide, heating systems, and confined spaces

Language: Eng

SO - J Forensic Sci 1986 Jan;31(1):117-21

Unique Identifier: 86113946

AB - Of 11 incidents of carbon monoxide (CO) intoxication, 16 fatalities are reported. All of the cases involved heating systems as either the source or the means of distributing the CO. Blood samples were analyzed for ethanol and CO. Elevated blood CO saturations were found in 14 of the 16, victims while none of the victims had a blood ethanol concentration greater than 0.10% (w/v).

AU - Stevenson KJ

TI - Measurements of carbon monoxide and nitrogen dioxide in British homes using unflued heating or cooking appliances

SI - TOXBIB/86/262483

SO - Tokai J Exp Clin Med; Vol 10, ISS 4, 1985, P295-301

AB - Measurements of carbon monoxide (CO) and nitrogen dioxide (NO₂) were made in three kitchens, two with gas cookers and one all-electric, and two living rooms, one heated by a portable butane heater and the other by a paraffin stove. The measurements were taken while the homes were in normal use and the occupants kept a diary of when specific appliances were used. Measurements of NO₂ were made simultaneously by chemiluminescence and by diffusion tubes. The accuracy of the diffusion tube measurements, relative to the chemiluminescent standard, was estimated as +/- 10% and the precision less than or equal to 300 ppb. hour. Results from diffusion tubes were used to indicate the distribution of NO₂ throughout other rooms in the house. At the all-electric house the CO and NO₂ concentrations were very similar to the expected outdoor levels. In all the other houses, NO₂ levels exceeded typical outdoor concentrations measured in central London. In the paraffin heated house and one gas cooking house, median CO concentrations exceeded these measured at the curbside of a very busy road in central London. The living room concentrations of NO₂ where the paraffin heater was in use were elevated for long periods. Analysis of the decay of pollutant concentration in one kitchen yielded an effective deposition velocity for NO₂ of $3 \times 10^{-5} \text{ m s}^{-1}$. The magnitude of the CO and NO₂ concentrations measured in this survey confirms that indoor air pollution should be taken into account when assessing overall public exposure to air pollution.

AU - Prescher KE

TI - Occurrence of carbon monoxide, carbon dioxide and nitrogen oxides during the use of gas stoves

SI - TOXBIB/83/248980

SO - Schriftenr Ver Wasser Boden Lufthyg; Vol 53, 1982, P191-8

AB - The concentrations of carbon monoxide (CO), carbon dioxide, nitrogen monoxide, and nitrogen dioxide arising from gas burning have been measured under experimental and field conditions. In the test room propane, butane, and town-gas have been burned, whereas in the apartments investigated only town-gas has been used. The most important influence on the concentration of the four substances arises from the changes in the burning conditions of the flame. Laboratory experiments have been carried out in the test room with open flames and with an aluminum block or a kettle on the flame. The following results have been obtained: (a) for CO, the lowest concentration is obtained with open flames irrespective of the type of gas burned; higher concentrations have been found with aluminum blocks, whereas the highest concentrations were associated with the use of kettles and pots, (b) the experimental conditions have only a small influence on the CO₂ concentration, (c) NO concentrations are influenced by the gas type and by the experimental conditions. Concentrations are low with kettles but high with open flames, (d) NO₂ concentrations are less influenced by the experimental conditions than are NO concentrations. The results of more than 1000 paired determinations of NO₂ in kitchen and other rooms are presented. The concentrations that have been measured using diffusion tubes according to Palmes which were exposed for 48 hours, were highest in kitchens of dwellings fully equipped with gas devices (heating, cooking, warming water). The mean value of the concentrations was about 50 µg/m³, whereas the mean for dwellings without any gas device has been found to be lower than 20 µg/m³.

AU - Boleij J

AU - Lebret E

AU - Smit J

AU - Brunekreef B

AU - Biersteker K

TI - Indoor air pollution by carbon monoxide and nitrogen oxides

SI - TOXBIB/83/248981

SO - Schriftenr Ver Wasser Boden Lufthyg; Vol 53, 1982, P199-208

AB - The results of an exploratory survey of indoor levels of carbon monoxide and nitrogen dioxide from gas-fired cooking and waterheating appliances in the Dutch cities of Arnhem and Enschede in the fall of 1980 are reported. Measurements were carried out electrochemically (Ecolyzer 2000) or with Draeger tubes in the case of CO and with Palmes diffusion tubes (5 to 8 days exposure) in the case of NO₂. For CO, in 18% (27%) of the homes visited the limit of 600 (300) ppm in the flue gases was exceeded, whereas the Dutch Installation Code Standard of 50 ppm CO in room air was exceeded in 17% of the homes. The arithmetic mean value of the NO₂ concentration in 286 homes was 118 µg/m³ with a range of 35 to 472 µg/m³. The corresponding figures for living rooms were 58 and 35 to 346 µg/m³, respectively. Outdoor NO₂ concentrations were 2 to 3 times lower than indoor concentrations.

AU - Jaeger RJ
TI - Carbon monoxide in houses and vehicles
SI - TOXBIB/82/092437
SO - Bull N Y Acad Med; Vol 57, ISS 10, 1981, P860-72

AU - Sterling TD
AU - Sterling E
TI - Carbon Monoxide Levels in Kitchens and Homes with Gas Cookers
SO - JAPCA; March 1979, Vol 29, No3, P238-241
AB - It has always been assumed that only a small amount of CO will be produced by a gas stove when the mixture of air and gas are well-adjusted and that small amount will be dissipated by the home's ventilation and by a combination of a fan and hood over the stove. However, preparation of meals may substantially increase CO. The immediate air supply may be progressively diminished when more than one burner is used and air supply may be partially cut off by vessels placed over the gas flame. The purpose of this investigation was to determine the amount of CO that may be expected to be produced during normal cooking. The experiment measured CO levels, using multiple burners with and without cooking vessels, and the rate of dissipation of the accumulated gas under various conditions of ventilation.

2.3 Non-Residential Indoor Exposures

AU - Nagda NL
AU - Koontz MD
TI - Microenvironmental and total exposures to carbon monoxide for three population subgroups
SI - TOXBIB/85/132226
SO - J Air Pollut Control Assoc; Vol 35, ISS 2, 1985, P134-7

AU - Wallace LA
TI - Carbon monoxide in air and breath of employees in an underground office
SI - TOXBIB/84/033632
SO - J Air Pollut Control Assoc; Vol 33, ISS 7, 1983, P678-82

AU - Allen RJ
AU - Wadden RA
TI - Analysis of indoor concentrations of carbon monoxide and ozone in an urban hospital
SI - TOXBIB/82/164656
SO - Environ Res; Vol 27, ISS 1, 1982, P136-49

AU - Burney RE
AU - Wu SC
AU - Nemiroff MJ
TI - Mass carbon monoxide poisoning: clinical effects and results of treatment in 184 victims.
Language: Eng
SO - Ann Emerg Med 1982 Aug;11(8):394-9
Unique Identifier: 82254755

AB - An epidemiologic and clinical investigation has been conducted of 184 persons exposed to toxic levels of carbon monoxide (CO) in a public high school. Exposure to 500 ppm of CO for periods up to 150 minutes resulted in carboxyhemoglobin (COHb) levels as high as 30% and symptomatic illness in 87% of persons exposed before the possibility of mass CO poisoning was recognized. Severity of symptoms was a reliable basis for triage of victims for immediate hospital treatment, and correlated both with duration of exposure and the length of time it took for victims to feel normal. Therapy consisting of oxygen delivered by mask achieved a half-life for COHb of 137 minutes in hospital-treated patients (compared to 320 minutes with no treatment), but did not fully reverse the symptoms of CO toxicity.

2.4 Arena Exposures

AU - Lee K

AU - Yanagisawa Y

AU - Spengler JD

AU - Nakai S

TI - Carbon monoxide and nitrogen dioxide exposures in indoor ice skating rinks

SI - TOXBIB/94/343656

SO - J Sports Sci; Vol 12, ISS 3, 1994, P279-83

AB - Exposures to carbon monoxide (CO) and nitrogen dioxide (NO₂) were determined in seven enclosed ice skating rinks and one outdoor rink. The uptake of CO was also determined by the difference in alveolar CO concentration of the non-smoking hockey players before and after games. Carbon monoxide concentrations in enclosed rinks ranged from 4 to 117 ppm and NO₂ concentrations from 342 to 2729 ppb for 2-hour hockey games. The CO uptakes were linearly related to the ambient CO concentrations. Alveolar CO of the hockey players increased on average by 0.53 ppm per 1 ppm CO exposure over 2 hours. Considering the CO and NO₂ levels currently measured in enclosed ice skating rinks, indoor air quality guidelines or standards should be established. It is recommended that 1-hour maximum allowable limits of 20 ppm CO and 250 ppb NO₂ be established.

TI - From the Centers for Disease Control and Prevention. Carbon monoxide levels during indoor sporting events--Cincinnati, 1992-1993.

SI - TOXBIB/94/125516

SO - JAMA; Vol 271, ISS 6, 1994, P419

TI - Carbon monoxide levels during indoor sporting events--Cincinnati, 1992-1993

SI - TOXBIB/94/104571

SO - MMWR Morb Mortal Wkly Rep; Vol 43, ISS 2, 1994, P21-3

AB - Carbon monoxide (CO) produced by internal combustion engines is an indoor health hazard. High CO levels can occur during indoor sporting events--such as tractor pulls--that involve vehicles modified to achieve high horsepower. In January and March 1992 and January 1993, the Cincinnati Health Department evaluated CO levels during tractor pulls, monster-truck jumps, and a mud race event held in an indoor arena with a seating capacity of approximately 16,000 persons. This report summarizes findings from the evaluations.

TI - Carbon monoxide levels in indoor tractor-pull events--Manitoba
SI - TOXBIB/91/003739
SO - Can Med Assoc J; Vol 143, ISS 7, 1990, P647-8

AU - Levesque B
AU - Dewailly E
AU - Lavoie R
AU - Prud'Homme D
AU - Allaire S

TI - Carbon monoxide in indoor ice skating rinks: evaluation of absorption by adult hockey players
SI - TOXBIB/90/225190

SO - Am J Public Health; Vol 80, ISS 5, 1990, P594-8

AB - Alveolar carbon monoxide (CO) levels of 122 male, adult hockey players active in recreational leagues of the Quebec City region (Canada) were evaluated, before and after 10 weekly 90-minute games in 10 different rinks. Exposure was determined by quantifying the average CO level in the rink during the games. Other variables documented included age, pulmonary function, aerobic capacity, and smoking status. Environmental concentrations varied from 1.6 to 131.5 parts per million (ppm). Absorption/exposure relationship was examined using a simple linear regression model. In low CO exposure levels, physical exercise lowered the alveolar CO concentration. However, for each 10 ppm of CO in the ambient air, the players had adsorbed enough CO to raise their carboxyhemoglobin (COHb) levels by 1%. This relationship was true for smokers and for non-smokers. An average environmental concentration of 20 ppm of CO for the duration of a hockey game (90 minutes) should be the reference limit not to be exceeded in indoor skating rinks.

AU - Turner WA
AU - Cohen MA
AU - Moore S
AU - Spengler JD
AU - Hackett PH

TI - Carbon monoxide exposure in mountaineers on Denali

SI - TOXBIB/88/292624

SO - Alaska Med; Vol 30, ISS 3, 1988, P85-90

TI - Carbon monoxide exposures at an ice skating rink--Colorado

SI - TOXBIB/86/257056

SO - MMWR Morb Mortal Wkly Rep; Vol 35, ISS 27, 1986, P435-6, 441

AU - Kwok PW

TI - Evaluation and control of carbon monoxide exposure in indoor skating arenas

SI - TOXBIB/84/026035

SO - Can J Public Health; Vol 74, ISS 4, 1983, P261-5

2.5 Exposure Models

AU - Joumard R

AU - Chiron M

AU - Vidon R

AU - Maurin M

AU - Rouzioux JM

TI - Mathematical models of the uptake of carbon monoxide on hemoglobin at low carbon monoxide levels

SI - TOXBIB/82/138665

SO - Environ Health Perspect; Vol 41, 1981, P277-89

AB - Coburn's differential equation for the uptake of carbon monoxide by hemoglobin and two particular types of solution of this equation were considered and the solutions verified for a group of healthy adults consisting of 73 nonsmoking pedestrians or car passengers exposed to low levels of carbon monoxide, as experienced in the city of Lyon. The CO levels at the breathing level and the walking speed of the subjects was continually measured, and the carboxyhemoglobin levels determined at the beginning and the end of each test journey. The values of all the other relevant parameters were also determined. The half-life of carboxyhemoglobin was studied as a function of the degree of activity, the age, the sex, and the height of the subjects. Finally, a mathematical model was set up to represent a periodic uptake of CO that made it possible to estimate the variations in the carboxy-hemoglobin level for any subject during a period of a day or a week without any need to know the initial level.

AU - Bernard TE

AU - Duker J

TI - Modeling carbon monoxide uptake during work

SI - TOXBIB/81/181052

SO - Am Ind Hyg Assoc J; Vol 42, ISS 5, 1981, P361-4

AB - Acute carbon monoxide poisoning is the result of a diminished capacity of the blood to transport oxygen and sustain a level of metabolic activity. The diminished capacity is expressed in terms of the carboxyhemoglobin (COHb) level in the blood, which is dependent upon the concentration of CO in the inhaled air. The rate of CO uptake or elimination is dependent upon the concentration of CO in the air, as well as pulmonary diffusion capacity and alveolar ventilation, which change with different metabolic rates. Coburn, Forster and Kane (CFK) developed a mathematical model to describe the uptake and elimination kinetics of CO in sedentary individuals. The CFK model was used in a mathematical simulation of CO uptake and elimination where the independent variables were inhaled CO concentration and metabolic rate. The metabolic rate was used to specify pulmonary diffusing capacity and alveolar ventilation. As the level of COHb increased, the metabolic rate was decreased to a level compatible with the impaired oxygen transport. A physical fatigue limit was also included. The theoretical model was used to simulate conditions beyond the range of exposures permissible under experimental laboratory conditions.

2.6 Occupational Exposures

AU - Ely EW

AU - Moorehead B

AU - Haponik EF

TI - Warehouse workers' headache: emergency evaluation and management of 30 patients with carbon monoxide poisoning.

Section on Pulmonary and Critical Care Medicine, Bowman Gray School of Medicine, Winston-Salem, North Carolina 27157-105

Language: Eng

SO - Am J Med 1995 Feb;98(2):145-55

Unique Identifier: 95150087

AB - BACKGROUND: CO is the leading cause of fatal toxic inhalation in the United States, but the medical literature contains few reports of mass exposures. Warehouse workers' headache (WWH) is an infrequently reported form of CO poisoning due to industrial exposure. METHODS: The section describes 30 persons who developed WWH after inhaling exhaust from a propane-fueled forklift, their emergency medical management at a small community hospital, and their long-term courses.

RESULTS: Workers with more direct exposures to vented exhaust had significantly higher expired CO levels ($21.1 \pm 0.7\%$ versus $8.4 \pm 4.8\%$, $P < 0.0001$) and higher acute symptom scores (9.0 ± 2.2 versus 4.7 ± 3.3 , $P = 0.01$) than persons with less direct exposures. Work location, expired CO levels, and acute symptom scores did not correlate with symptom scores 2 years after exposure. Workers experiencing acute difficulty concentrating or confusion had higher expired CO levels than persons with neither of these symptoms ($16.3 \pm 6.7\%$ versus $8.4 \pm 5.2\%$, $P = 0.005$) and developed higher chronic symptom scores (3.9 ± 3.0 versus 1.1 ± 1.5 , $P = 0.04$), suggesting that this subgroup may require closer follow-up for long-term complications. CONCLUSION: With earlier recognition of ongoing CO toxicity, this disaster would likely have been averted. Because CO exposures are more common than is often recognized, general internists must be familiar with the manifestations of CO toxicity, its timely evaluation, management, and prevention.

AU - Koskela RS

TI - Cardiovascular diseases among foundry workers exposed to carbon monoxide

SI - TOXBIB/95/099272

SO - Scand J Work Environ Health; Vol 20, ISS 4, 1994, P286-93

AB - OBJECTIVES: The study investigated long-term effects of CO exposure on foundry workers' morbidity and mortality from cardiovascular diseases. METHODS: The study population comprised a cohort of 2857 men hired in 1950-1972 by 20 Finnish foundries and also 931 men who were still active in 1972, exposed for at least 4.2 years, took part in a health examination in 1973; 653 of the 931 had also been members of the cohort. These groups were followed to the end of 1987. RESULTS: The age-standardized incidence density rate (ID/1000 person-years) for compensated medication for hypertension was 4.7 for the unexposed workers and 9.4 for those exposed (rate ratio [RR] 2.0, 95% confidence interval [95% CI] 1.28-2.92); for the iron foundry workers the rates were 4.7 and 9.9 (RR 2.1, 95% CI 1.24-3.38), respectively. During 1950-1987, 255 cardiovascular deaths were observed (284 expected according to national rates). The observed number of deaths due to ischemic heart disease was 183 (203 expected). The iron foundry workers' mortality rate for cardiovascular deaths was 99% of the national expected value. No remarkable differences were found between the CO-exposure categories. For the health-examination group, the age-standardized incidence rate for

compensated medication for hypertension was 9.1 for the unexposed nonsmokers and 21.4 for the exposed smokers (RR 2.3, 95% CI 0.97-6.35). The difference originated among the iron foundry workers, for whom the rates were 8.1 and 24.0 (RR 3.0, 95% CI 0.96-9.78), respectively. The age-standardized mortality rate (ID/1000 person-years) was 2.7 for nonsmokers with no or slight CO exposure and 9.2 for exposed smokers (95% CI 1.13-12.11). This difference was mainly caused by ischemic heart disease. CONCLUSIONS: The results indicate that CO exposure increases the risk of cardiovascular morbidity and mortality.

AU - Sroczynski J

AU - Kaminska-Galwas B

TI - Effect of working in a coke plant on levels of carbon monoxide hemoglobin in employed workers

SI - TOXBIB/93/390315

SO - Med Pr; Vol 44, ISS 2, 1993, P117-20

AB - Concentrations of carbon monoxide hemoglobin in blood of 48 furnace-room, and of 31 carbon derivatives department workers for many years exposed to carbon monoxide (divided into smokers and non-smokers) were assessed by spectrophotometry. CO levels were within the values provided in the corresponding standards for the occupational exposure; however, the risk existed of periodically exceeding the MAC values. It has been found that HbCO levels in the workers of the furnace room and of the carbon derivatives department were significantly higher than in the controls, both in the smoker and in the non-smoker group.

AU - Lewis S

AU - Mason C

AU - Srna J

TI - Carbon monoxide exposure in blast furnace workers

SI - TOXBIB/93/129697

SO - Aust J Public Health; Vol 16, ISS 3, 1992, P262-8

AB - This study investigated the occupational exposure to CO of a group of blast furnace workers from an integrated steelworks, compared to a control group having no significant occupational CO exposure from other areas in the same works. The study was undertaken in 1984 at Port Kembla, New South Wales. Carboxyhemoglobin (COHb) levels before and after an 8 hour work shift were measured in 98 male steelworkers: 52 from 2 CO-exposed iron blast furnaces and 46 controls from production areas in the same steelworks. The sample was stratified by smoking habits. Environmental air CO levels had been found to be consistently higher on one furnace than on the other. Absorption of CO from the working environment occurred in workers on the blast furnace with higher CO levels, regardless of smoking habits. On this blast furnace, some readings of COHb levels after a workshift in nonsmokers approached the proposed Australian occupational limit of 5% COHb saturation. Overall, workers with the highest occupational exposure who smoked most heavily had the highest absorption of CO over a work shift. Biological monitoring gives an accurate measure of individual worker dose of CO from all sources. Both environmental monitoring and biological monitoring need to be included as part of a program for controlling occupational CO exposure.

AU - Gardiner K
AU - Trethowan WN
AU - Harrington JM
AU - Calvert IA
AU - Glass DC

TI - Occupational exposure to carbon monoxide and sulphur dioxide during the manufacture of carbon black

SI - TOXBIB/93/073446

SO - Ann Occup Hyg; Vol 36, ISS 4, 1992, P363-72

AB - The manufacture of carbon black is known to generate carbon monoxide and sulphur dioxide in the production gas and its pyrolysis products respectively. Adverse health effects have been reported as associated with both contaminants (coronary heart disease with carbon monoxide and respiratory morbidity with sulphur dioxide). A major cross-sectional and longitudinal respiratory morbidity study is being conducted to assess the effects of exposure to carbon black on lung function, on chest X-rays, and on responses to a questionnaire. The questionnaire includes questions on respiratory and cardiovascular symptoms, so that information regarding confounding exposure is essential. The working population of 18 manufacturing plants in seven European countries was split into 13 job title numbers (1-13) which were then amalgamated into five job categories (A-E), with an appropriate (statistically) number of samples taken from each plant-job category. In total, 1322 carbon monoxide samples and 1301 sulphur dioxide samples were taken, using actively pumped long-term colorimetric tubes. In the majority of cases, more than half of the samples in each plant-job category were either zero or trace, thereby preventing the accurate estimation of the average exposure. The highest median carbon monoxide concentration was from the amalgamated data from all 18 plants in job number was 9 (furnace operators), the highest median sulphur dioxide concentration was only trace. The large number of zero and trace values also precluded the generation of current and retrospective exposure indices.

AU - Madani IM
AU - Khalfan S
AU - Khalfan H
AU - Jidah J
AU - Aladin MN

TI - Occupational exposure to carbon monoxide during charcoal meat grilling

SI - TOXBIB/92/279746

SO - Sci Total Environ; Vol 114, 1992, P141-7

AB - Charcoal meat grill workers are one of the many occupational groups that are subject to carbon monoxide exposure. This group has often been overlooked and not investigated. Carboxyhemoglobin (%COHb) levels in 100 male workers were assessed before work and after work on the same day. Carboxyhemoglobin levels increased significantly after work in both smoking and nonsmoking workers. The mean COHb levels for smoking workers before work was 3.8% and for nonsmokers was 2.4%; whereas after work, the mean COHb level for smokers increased to 8.1% and for nonsmokers to 6.2%. These elevated mean COHb levels exceed the 5% COHb level recommended by WHO and NIOSH. With respect to smokers only, 36 (81.8%) workers after work exceed 5%, whereas the nonsmokers, 29 (51.8%) of the workers exceed 5%. These results indicate that charcoal meat grilling workers are exposed to significant levels of carbon monoxide. Several control measures have been suggested to mitigate this exposure.

AU - Sahli BP

AU - Armstrong CW

TI - Confined space fatalities in Virginia

Division of Health Hazards Control, Virginia Department of Health, Richmond 23218.

Language: Eng

SO - J Occup Med; Vol 34, ISS 9, 1992, P910-7

Unique Identifier: TOXBIB/93/078055

AB - To better understand the frequency and characteristics of occupational confined space fatalities in Virginia, a number of documents were reviewed: death certificates, workers' compensation files, a Virginia Occupational Safety and Health Administration listing, and medical examiner records for all 50 fatalities (41 accidents) reported during 1979 to 1986. All fatalities were identified in medical examiner records (50), more than in any other source. The majority of decedents were male craftsmen, operators, or laborers less than 50 years old (mean 38). Drug screens of the 43 decedents tested were negative, with the exception of 2 cases where blood alcohol was detected (greater than or equal to 0.06%). Approximately 5% of at work civilian deaths (excluding plane, train, and motor vehicle fatalities) were confined-space related. Virginia resident death rates per million employees were highest for shipbuilding and repair facilities (23.2), local government (8.9), and manufacturing other than shipbuilding (5.4%). Multiple fatalities occurred in 4 (10%) of the accidents, with 3 involving 2 fatalities each, and 1 accident involving 7 fatalities. Three fatalities (6%) were rescuers. Among rescuers, 50 nonfatal injuries were known to have occurred in these accidents, 15 of co-workers, and 35 of community rescue personnel (firefighters and rescue squad members). Approximately half the accidents occurred during the fourth quarter of the year and on a Thursday or Friday, and about one third occurred at night. The leading accident type was atmospheric condition, most commonly oxygen deficiency (33%) or the presence of carbon monoxide (20%). In 6 (40%) of the 15 accidents involving atmospheric condition, the toxic gas or oxygen deficiency was absent in the confined space at the time of entry. (ABSTRACT TRUNCATED AT 250 WORDS)

AU - Anon

TI - Fatal Accident Circumstances and Epidemiology (FACE) Report: Carbon Monoxide Kills Three Volunteer Firefighters Inside Well in Pennsylvania, May 1, 1990

SO - Govt Reports Announcements & Index (GRA&I), Issue 16, 1992

Unique Identifier: NTIS/PB92-183987

AB - TD3: The deaths of three volunteer firefighters from carbon-monoxide (630080) inside a 33-foot deep water well were investigated. A total of four volunteer firefighters responded to a request from a local resident to remove the remains of a dead animal from a 33-foot deep well. The concrete well opening measured 18 inches by 22 inches; and the well shaft was about 5 by 7 feet. The firefighters attempted to pump the water out of the well using a 9-horsepower gasoline engine pump placed on a platform about 15 feet into the well. After turning on the engine, two firefighters on the platform began to suffer dizziness, and collapsed. The engine was turned off after 8 to 9 minutes. A total of 8 volunteer firefighters entered the well in rescue attempts over approximately 3 hours. Only two of these wore supplied air respirators. One of the first two firefighters to enter the well was rescued and revived; the second firefighter and two of the rescuers died. Of the firefighters, two died of carbon-monoxide inhalation and the third died of drowning, with loss of function due to carbon-monoxide inhalation. It is recommended that proper procedures for entering confined spaces be followed; that a respiratory protection program be designed to protect firefighters from respiratory hazards; and that volunteer firefighters be trained in the use and limitations of gasoline powered pumps and the hazards of carbon-monoxide in a confined area.

AU - Brotherhood JR

AU - Budd GM

AU - Jeffery SE

AU - Hendrie AL

AU - Beasley FA

AU - Costin BP

AU - Wu ZE

TI - Fire fighters' exposure to carbon monoxide during Australian bushfires

SI - TOXBIB/90/224839

SO - Am Ind Hyg Assoc J; Vol 51, ISS 4, 1990, P234-40

AB - Fatal entrapments of Australian bushfire fighters have led to suggestions that carbon monoxide (CO) poisoning could have contributed to these accidents by impairing the fire fighters' judgement. Carboxyhemoglobin saturation (COHb%) levels were assessed from alveolar CO levels in 24 fire fighters working with handtools and in 12 accompanying scientific observers, before and after fire fighting (duration 37-187 min) on 15 experimental bushfires. Carboxyhemoglobin levels increased on average by 0.7% per hour in the fire fighters and by 0.3% per hour in the observers. Nonsmoking fire fighters had lower COHb% after fires than the smokers had before fires. Estimates of environmental CO concentrations (including cigarette smoke) during the fires averaged 31 parts per million (ppm) for the smokers, 17 ppm for the nonsmoking crew members, and 11 ppm for the observers, none of whom smoked. The highest estimates of environmental CO arising solely from bushfire smoke were 40 to 50 ppm. Smokers were exposed to as much CO from their cigarettes as from bushfire smoke. Carboxyhemoglobin levels at the end of 8-hour fire fighting shifts, predicted from these levels of environmental CO, averaged about 5% (maximum 11%) in smokers and about 3% (maximum 7%) in nonsmokers. Acute levels of COHb% of this degree are not considered to have significant effects on health or performance. These results indicate that bushfire fighters are generally unlikely to experience hazardous levels of CO exposure.

AU - Trajkovic M

TI - Study of pulmonary ventilation function in workers exposed to carbon monoxide in the Svetozarevo cable factory

SI - TOXBIB/85/168533

SO - Srp Arh Celok Lek; Vol 112, ISS 9, 1984, P909-17

AU - Kowalska S

TI - State of the hearing and equilibrium organs in workers exposed to carbon monoxide

SI - TOXBIB/82/080033

SO - Med Pr; Vol 32, ISS 2, 1981, P145-51

AB - In 78 men occupationally exposed to carbon monoxide, audiometric and electronystagmographic examinations have been carried out. In 66.6% of cases, receptive hearing impairment has been found. Vestibular changes, found in 79.5% of the group concerned, are regarded as typical and frequent effects of CO exposure. The results confirm ototoxic effects of carbon monoxide.

2.7 Vehicle Exposures

AU - Ott W

AU - Switzer P

AU - Willits N

TI - Carbon monoxide exposures inside an automobile traveling on an urban arterial highway

SI - TOXBIB/95/006148

SO - Air Waste; Vol 44, ISS 8, 1994, P1010-8

AB - Carbon monoxide (CO) exposures were measured inside a motor vehicle during 88 standardized drives on a major urban arterial highway, El Camino Real (traffic volume of 30,500-45,000 vehicles per day), over a 13.5-month period. On each trip (lasting between 31 and 61 minutes), the test vehicle drove the same 5.9-mile segment of roadway in both directions, for a total of 11.8 miles, passing through 20 intersections with traffic lights (10 in each direction) in three California cities (Menlo Park, Palo Alto, and Los Altos). Earlier tests showed the test vehicle was free of CO intrusion. For the 88 trips, the mean CO concentration was 9.8 ppm, with a standard deviation of 5.8 ppm. Of nine covariates that were examined to explain the variability in the mean CO exposures observed on the 88 trips (ambient CO at two fixed stations, atmospheric stability, seasonal trend function, time of day, average surrounding vehicle count, trip duration, proportion of time stopped at lights, and instrument type), a fairly strong seasonal trend was found. A model consisting of only a single measure of traffic volume and a seasonal trend component had substantial predictive power ($R^2 = 0.68$); by contrast, the ambient CO levels, although partially correlated with average exposures, contributed comparatively little predictive power to the model. The CO exposures experienced while drivers waited at the red lights at an intersection ranged from 6.8 to 14.9 ppm and differed considerably from intersection to intersection. (ABSTRACT TRUNCATED AT 250 WORDS)

AU - Nowak R

AU - Sachs H

TI - Development of carbon monoxide and hydrocyanic acid in automobile fires and their forensic significance

SI - TOXBIB/93/174871

SO - Versicherungsmedizin; Vol 45, ISS 1, 1993, P20-2

AB - The presence of carbon monoxide and cyanide in the blood of traffic fire victims is reported. In addition, CO and HCN was measured in the fire gas occurring in car fire.

AU - Koushki PA

AU - al-Dhowalia KH

AU - Niaizi SA

TI - Vehicle occupant exposure to carbon monoxide

SI - TOXBIB/93/103681

SO - J Air Waste Manage Assoc; Vol 42, ISS 12, 1992, P1603-8

AB - This paper focuses on the auto commuting micro-environment and presents typical carbon monoxide (CO) concentrations to which auto commuters in central Riyadh, Saudi Arabia were exposed. Two test vehicles traveling over four main arterial roadways were monitored for inside and outside CO levels during 80 peak and off-peak hours extending over an 8-month period. The relative importance of several variables which explained the variability in CO concentrations inside autos was also assessed. It was found that during peak hours auto commuters were exposed to mean CO levels

that ranged from 30 to 40 ppm over trips that typically took between 25 to 40 minutes. The mean ratio of inside to outside CO levels was 0.84. Results of variance component analyses indicated the most important variables affecting CO concentrations inside autos were, in addition to the smoking of vehicle occupants, traffic volume, vehicle speed, time of day, and wind velocity. An increase in traffic volume from 1000 to 5000 vehicles per hour (vph) increased mean CO level exposure by 71%. An increase in vehicle speed from 14 to 55 km/hour reduced mean CO exposure by 36%. The number of traffic interruptions had a moderate effect on mean concentrations of CO inside vehicles.

AU - Flachsbar PG

AU - Mack GA

AU - Howes JE

AU - Rodes CE

TI - Carbon monoxide exposures of Washington commuters

SI - TOXBIB/88/171574

SO - JAPCA; Vol 37, ISS 2, 1987, P135-42

AU - Poulton TJ

TI - Medical helicopters: carbon monoxide risk?

SI - TOXBIB/87/156441

SO - Aviat Space Environ Med; Vol 58, ISS 2, 1987, P166-8

AB - Carbon monoxide exposure of medical personnel working beneath the turning rotor of a medical helicopter appeared to cause mild clinical illness. The carbon monoxide levels found in various locations beneath the rotor of a jet helicopter were measured under two different conditions. Carbon monoxide levels ranged from 8-76 ppm depending on location of sampling and speed of operation of the engine. This level of carbon monoxide is potentially a problem, as is the inhalation of jet fuel vapor, when working beneath the rotors of an operating helicopter.

AU - Iglewicz R

AU - Rosenman KD

AU - Iglewicz B

AU - O'Leary K

AU - Hockemeier R

TI - Elevated levels of carbon monoxide in the patient compartment of ambulances

SI - TOXBIB/84/176307

SO - Am J Public Health; Vol 74, ISS 5, 1984, P511-2

AB - A total of 690 New Jersey ambulances were monitored for carbon monoxide (CO); 27% had CO levels of 10 ppm or more greater than ambient air in the breathing zone of the patient. Of these ambulances, 29 had levels of at least 35 ppm greater than ambient air. Results indicate that a CO exposure problem exists in ambulances.

2.8 Tobacco Related Exposures

AU - Jarvik ME

AU - Tashkin DP

AU - Caskey NH

AU - McCarthy WJ

AU - Rosenblatt MR

TI - Mentholated cigarettes decrease puff volume of smoke and increase carbon monoxide absorption

SI - TOXBIB/95/062629

SO - Physiol Behav; Vol 56, ISS 3, 1994, P563-70

AB - The influence of mentholated vs. regular cigarettes on selected chemical and topographic parameters was measured in 20 smokers in a pulmonary function laboratory. Half the subjects were black and half were white; half were menthol and half regular smokers. All subjects smoked both types of cigarettes, one type on each of two days. Compared to regular cigarettes, mentholated cigarettes produced a significantly greater boost in carbon monoxide, measured as both blood carboxyhemoglobin and end-expired carbon monoxide, despite the fact that mentholated cigarettes decreased average and total cumulative puff volumes and increased mean puff flow rates of inhaled smoke. These chemical and topographic differences were independent of race. No significant differences in depth of inhalation of the smoke or in the amount of insoluble smoke particulates delivered to or retained in the respiratory tract were noted between the two types of cigarettes. Mentholation of cigarettes may decrease volume of smoke inhaled, but appears to increase exposure of smokers to toxic effects of carbon monoxide.

AU - Sajid KM

AU - Akhter M

AU - Malik GQ

TI - Carbon monoxide fractions in cigarette and hookah (hubble bubble) smoke

SI - TOXBIB/94/111276

SO - JPMA J Pak Med Assoc; Vol 43, ISS 9, 1993, P179-82

AB - The carbon monoxide (CO) fractions in hookah and cigarette smoke were studied, using a carbon monoxide micro smokerlyzer (model EC50, BEDFONT, U.K.). Mean carbon monoxide fractions (% by volume) of hookah smoke, using domestic charcoal were 0.38 +/- 0.07 (large hookah; unfiltered); 1.40 +/- 0.43 (small hookah; unfiltered); 0.34 +/- 0.06 (large hookah; filtered); 1.36 +/- 0.35 (small hookah; filtered) and 0.41 +/- 0.08 (cigarette smoke). The highest fractions were obtained with small size hookah and increase in size of hookah (i.e., volume of air in water base, fire bowl volume, pipe length, etc.) reduced the CO fraction significantly ($P < 0.001$). The fractions of cigarette lie between large and small hookah. The fractions vary slightly with different varieties of tobacco, e.g., CO fractions with Dera wala tobacco are significantly low ($P < 0.05$). Use of commercial charcoal gives significant rise in CO fractions ($P < 0.001$). Comparison of filtered and unfiltered smoke shows no significant difference in values. The conclusion is the CO hazard is as high with hookah smoking as with cigarette smoking.

AU - Tutt D

AU - Harris W

TI - Where there's smoke...carbon monoxide exposures in smoking and smoke-free workplaces

SI - TOXBIB/91/070950

SO - Community Health Stud; Vol 14, ISS 3, 1990, P297-302

AB - Comparisons of expired air carbon monoxide levels in non-smoking staff in six licensed clubs (a smoking workplace) were made with those of non-smoking staff of a large public hospital (a smoke-free workplace). A significant difference was found between clubs and hospital in levels of CO at end of the workday. The average concentration of club workers was 8.7 ppm (Hospital, 5.3 ppm). Approximately one third of these non-smokers in licensed clubs exceeded 10 ppm, putting them in the light smoker category according to the manufacturer of the monitoring equipment. Club workers increased their CO level during work time by four times the increase of hospital staff. This study suggests significant gains are to be made in reduction of intake of harmful passive-smoking products by removing tobacco smoke from workplaces.

AU - Weinhold LL

AU - Stitzer ML

TI - Effects of puff number and puff spacing on carbon monoxide exposure from commercial brand cigarettes

SI - TOXBIB/90/139178

SO - Pharmacol Biochem Behav; Vol 33, ISS 4, 1989, P853-8

AB - Six chronic smokers of mid- to high-carbon monoxide (CO) yield cigarettes smoked ultralow- (1.6 mg CO), low- (5.9 mg CO) and high- (14.3 mg CO) yield commercial cigarettes under controlled smoking conditions in which either puff number or puff spacing was manipulated. CO exposure (pre- to postsmoking increments) was directly related to the number of puffs taken for all cigarette yields. CO exposure from the high- and low-yield cigarettes was equivalent when the number of puffs taken from the low-yield cigarettes was increased by 50% (from 8 to 12 puffs). In contrast, CO exposure from ultralow-yield cigarettes was still marginally lower than exposure from high-yield cigarettes after a 4-fold increase in puff number (8 to 32 puffs). Puff spacing did not affect biological exposure to CO. The study showed the number of puffs taken during smoking can clearly affect biological exposure to CO, but that compensation for lowered yield using increased puffs is much more difficult when ultralow, as compared with low- or light-yield cigarettes.

AU - Weinhold LL

AU - Stitzer ML

AU - Yingling JE

TI - Carbon monoxide exposure from commercial brand cigarettes under controlled smoking conditions

SI - TOXBIB/89/297116

SO - Pharmacol Biochem Behav; Vol 31, ISS 1, 1988, P93-6

AB - Carbon monoxide (CO) exposure from ultralow-, low- and high-CO delivery commercial cigarettes was examined under controlled smoking conditions. Seven chronic smokers of mid- to high-CO delivery commercial cigarettes served in the experiment. CO level increases of 2.10, 5.76, and 7.38 ppm were obtained from ultralow-yield (1.6 mg CO delivery), low-yield (5.9 mg CO delivery) and high-yield (14.3 mg CO delivery) cigarettes, respectively. Subjects achieved significantly higher increases in CO levels from both low- and high-yield cigarettes than from ultralow-yield cigarettes, but increased levels of CO from low- and high-yield cigarettes were not different from each other. The data suggest that degree of CO absorption by the lungs during a short period of time may limit increases in CO levels obtained from high-yield cigarettes.

AU - Benowitz NL

AU - Jacob P 3d

AU - Yu L

AU - Talcott R

AU - Hall S

AU - Jones RT

TI - Reduced tar, nicotine, and carbon monoxide exposure while smoking ultralow-, but not low-yield cigarettes

SI - TOXBIB/86/254540

SO - JAMA; Vol 256, ISS 2, 1986, P241-6

AB - An unresolved public health issue is whether some modern cigarettes are less hazardous than others and whether patients who cannot stop smoking should be advised to switch to lower-yield cigarettes. Tar (estimated by urine mutagenicity), nicotine, and carbon monoxide exposure were studied in habitual smokers who switched from their usual brand to high- (15 mg of tar), low- (5 mg of tar), or ultralow-yield (1 mg of tar) cigarettes. No differences were found in exposure comparing high- or low-yield cigarettes, but tar and nicotine exposures were reduced by 49% and 56%, respectively, and carbon monoxide exposure was reduced by 36% when smoking ultralow-yield cigarettes. Similarly, in 248 subjects smoking their self-selected brand, nicotine intake (estimated by blood concentrations of its metabolite cotinine) was 40% lower in those who smoked ultralow, but no different in those smoking higher yields of cigarettes. Data indicate that ultralow-yield cigarettes do deliver substantial doses of tar, nicotine, and carbon monoxide, but that exposures are considerably less than for other cigarettes.

AU - Rickert WS

AU - Collishaw NE

AU - Bray DF

AU - Robinson JC

TI - Estimates of maximum or average cigarette tar, nicotine, and carbon monoxide yields can be obtained from yields under standard conditions (published erratum appears in Prev Med 1987 Mar;16[2]:290)

SI - TOXBIB/86/233151

SO - Prev Med; Vol 15, ISS 1, 1986, P82-91

AB - Average yields of tar, nicotine, and carbon monoxide per liter of smoke and per cigarette were determined for 10 brands of cigarettes smoked under 27 different conditions (one standard and 26 nonstandard). Per cigarette yields were highly variable across smoking conditions, due to differences in the total volume of smoke taken for analysis. The results of a simple linear regression analysis indicated that up to 95% of the variation in tar yield per cigarette could be explained by variations in the total volume of smoke produced per cigarette. Per liter yields for tar, nicotine, and carbon monoxide were almost constant over the conditions investigated. Because most smokers inhale less than this amount, yields per liter provide a rough estimate of the maximum amount to which a smoker might be exposed. Yields per liter, taken over all 26 conditions, are highly correlated with per cigarette yields under standard conditions. Consequently, values on one scale can be converted to the other, at least for the 10 brands investigated. The average conversion factor for tar, nicotine, and carbon monoxide is 2.5 when proceeding from milligrams per king-size cigarette under standard conditions to milligrams per liter. This relationship is true for both vented and nonvented cigarettes when ventilation holes are not blocked.

AU - Jarvis MJ

AU - Feyerabend C

AU - Saloojee Y

TI - Reduction of tar, nicotine and carbon monoxide intake in low tar smokers

SI - TOXBIB/86/225951

SO - J Epidemiol Community Health; Vol 40, ISS 1, 1986, P80-5

AB - Blood nicotine, cotinine, and carboxyhemoglobin (COHb) concentrations were measured in 392 smokers (255 women and 137 men) of middle tar (17-22 mg), low to middle (11-16 mg), and low tar (less than 11 mg) cigarettes. As tar intake cannot yet be measured directly, an index was devised to estimate it, based on the use of measured levels of an intake marker (blood nicotine) and the ratio of the tar to marker yields of the cigarettes. This approach was validated by its ability to enhance the prediction of levels of one marker by use of another. In a practical test, using COHb and the CO/nicotine yield ratio of the cigarettes, the mean blood nicotine concentration of the low tar smokers was predicted to be 31.9 ng/ml compared with the measured mean of 31.8 ng/ml. Despite substantial compensatory increases in inhalation, the low tar smokers took in about 25% less tar, about 15% less nicotine, and about 10% less carbon monoxide than smokers of middle and low to middle tar cigarettes. These results indicate that low tar cigarettes of the type available in Britain since the late 1970s are likely to prove less harmful than other brands. Monitoring of smoke intakes could supplement epidemiological approaches and provide earlier evidence of whether changing cigarette designs leads to any significant dosage reduction that could affect the risk of disease.

AU - Woodman G

AU - Newman SP

AU - Pavia D

AU - Clarke SW

TI - Inhaled smoke volume, puffing indices and carbon monoxide uptake in asymptomatic cigarette smokers

SI - TOXBIB/87/003373

SO - Clin Sci; Vol 71, ISS 4, 1986, P421-7

AB - Nine asymptomatic smokers each smoked one cigarette of their usual brand on four separate occasions. The inhaled smoke volume was measured by tracing the smoke with the inert gas Kr-81m. Puffing indices were recorded by using an electronic smoking analyser and a flowhead/cigarette holder. The expired air carbon monoxide concentration was measured immediately before and within 5 min of finishing smoking. The inhaled smoke percentage (total inhaled smoke volume/total puff volume) averaged 46% to 85% in different subjects. Neither the mean inhaled smoke volume per puff nor the total inhaled smoke volume per cigarette was significantly correlated with any of the puffing indices. Smokers took significantly smaller and shorter puffs, paused longer between puffs and inhaled less smoke as the cigarette was smoked (P less than 0.01), although the proportion of the puff that was subsequently inhaled did not change significantly. No significant intra-subject difference existed in any index from one visit to another.

AU - Stitzer ML

AU - Bigelow GE

TI - Contingent reinforcement for reduced breath carbon monoxide levels: target-specific effects on cigarette smoking

SI - TOXBIB/86/126341

SO - Addict Behav; Vol 10, ISS 4, 1985, P345-9

AB - This study determined the effects on smoking behavior of providing contingent reinforcement for nonsmoking versus reduced smoking afternoon breath carbon monoxide (CO) target levels. For the study, 28 chronic smoker volunteers were hired and randomly assigned to one of three experimental conditions during a 10-day intervention: (a) 8 ppm target CO, \$5 per day incentive (n = 11); (b) 16 ppm target CO, \$4 per day incentive (n = 8); or (c) 8 ppm target CO, no incentive (n = 9). Both payment groups showed significantly lower CO levels and greater amounts of daytime smoking reduction than the no-pay group. A specific effect of CO target was also seen; 45% of subjects in the 8 ppm group compared with 0% of subjects in the 16 ppm target and no-pay groups produced average afternoon CO levels of 8.5 ppm or lower during the intervention. Average levels of CO and smoking reduction did not differ for the two paid groups, however, because some subjects in the 8 ppm group failed to reduce CO sufficiently to contact the reinforcer. Contingent reinforcement, based on expired air CO levels, can exercise powerful and precise (target-specific) control over smoking behavior, but there may be individual differences in ability to meet reinforcement contingencies if difficult targets are introduced abruptly.

Plastic and Wood Sources

AU - Huttlinger PA

AU - Hilado CJ

TI - Carbon monoxide toxicant from plastics and wood

SI - TOXBIB/81/247535

SO - Proc West Pharmacol Soc; Vol 24, 1981, P251-4

3.0 Papers Relating to Human Studies

3.1 Human Studies

AU - Annau Z

AU - Fechter LD

TI - The effects of prenatal exposure to carbon monoxide

SI - DART/T/94000864

SO - Prenatal Exposure to Toxicants: Developmental Consequences (The Johns Hopkins Series in Environmental Toxicology) 1994;:249-67

TI - What are the potential delayed health effects of high-level carbon monoxide exposure?

SI - TOXBIB/94/351394

SO - J Occup Med; Vol 36, ISS 6, 1994, P595-7 (REF: 34)

AU - Balasubramanian S

AU - Lambright DG

AU - Simmons JH

AU - Gill SJ

AU - Boxer SG

TI - Determination of the carbon monoxide binding constants of myoglobin mutants: comparison of kinetic and equilibrium methods

SI - TOXBIB/94/304847

SO - Biochemistry; Vol 33, ISS 27, 1994, P8355-60

AB - The carbon monoxide (CO) binding constants of human myoglobin (Mb) and several single-site mutants have been determined using two different methods. In the kinetic method, which is commonly used for this ligand, the overall association (k_{on}) and dissociation (k_{off}) rates of CO were measured by flash photolysis and NO replacement, respectively, and the ratio $k_{\text{on}}/k_{\text{off}}$ was calculated. In the equilibrium method, the binding constant K_{eq} was measured directly using a thin-layer technique. These two measurements yield similar results for human wild-type Mb but differ significantly for some of the mutants. Possible reasons for these discrepancies are analyzed. A model assuming the presence of interconverting conformers with different association and dissociation rates is considered in light of infrared measurements on the CO stretching frequency in the MbCO forms of the same proteins (Balasubramanian et al. [1993a] Proc. Natl. Acad. Sci, U.S.A. 90, 4718). It is suggested that in the case of some mutants which exhibit multiple conformations, this model may lead to nonequilibrium kinetics, which could produce the observed discrepancies between the kinetic and equilibrium determinations of the binding constant. These results suggest that both equilibrium and kinetic data should be obtained, even for a monomeric protein such as Mb, before the relative stabilities of mutants can be meaningfully compared.

AU - Grau C

AU - Nordsmark M

AU - Khalil AA

AU - Horsman MR

AU - Overgaard J

TI - Effect of carbon monoxide breathing on hypoxia and radiation response in the SCCVII tumor in vivo

SI - TOXBIB/94/274456

SO - Int J Radiat Oncol Biol Phys; Vol 29, ISS 3, 1994, P449-54

AB - PURPOSE: To study the influence of a clinically relevant concentration of carbon monoxide (CO) on tumor oxygenation and response to irradiation. METHODS AND MATERIALS: The murine tumor model was the SCCVII squamous cell carcinoma transplanted to the feet of C3H/Km mice. RESULTS: Breathing CO at 200 ppm for 60 minutes resulted in a carboxyhemoglobin level of 15%. This action resulted in a reduction in p50 (the oxygen partial pressure at which hemoglobin is 50% saturated) to 78% of the control value, and a decrease in tumor blood perfusion to 73% of the control value. The combined effect of a decrease in effective hemoglobin and blood perfusion resulted in a reduction in tumor oxygen supply to 62% of the control value. In agreement with this, intra-tumoral pO₂ measurements showed a significant increase in tumor hypoxia, such that the percentage of measurements with low pO₂ (< or = 5 mmHg) increased from 33% to 62%. The fraction of clonogenic hypoxic cells, measured radiobiologically by paired cell survival curves, similarly increased from 0.2% to 3.8%. Radiation sensitivity, evaluated from in vivo-in vitro excision assay, was significantly decreased by CO breathing with both single dose and fractionated irradiation. The observed enhancement ratios for radiation given in 1, 4, 8, and 12 fractions were 0.71, 0.77, 0.83, and 0.71, respectively. CONCLUSION: The present SCCVII tumor data confirm the general experimental observation that CO breathing significantly increases tumor hypoxia and reduces the effectiveness of ionizing irradiation.

AU - Perry GF

TI - What are the potential delayed health effects of high-level carbon monoxide exposure? [column - Occupational Medicine Forum]

SO - JOM; Vol 36, No 6, June, 1994

AU - Thorpe M

TI - Chronic carbon monoxide poisoning [letter]

SI - TOXBIB/94/251696

SO - Can J Psychiatry; Vol 39, ISS 1, 1994, P59-61

AU - Grau C

AU - Khalil AA

AU - Nordmark M

AU - Horsman MR

AU - Overgaard J

TI - The relationship between carbon monoxide breathing, tumour oxygenation, and local tumour control in the C3H mammary carcinoma in vivo

SI - TOXBIB/94/114353

SO - Br J Cancer; Vol 69, ISS 1, 1994, P50-7

AB - The effect of acute carbon monoxide (CO) breathing on blood oxygenation and tumour hypoxia was related to the radiation response of the C3H/Tif mammary carcinoma. Blood gas analysis showed that CO breathing caused a time- and dose-dependent formation of carboxyhemoglobin (HbCO), a significant left shift of the oxygen dissociation curve and a reduction in tumour blood perfusion. These factors all contributed to a marked drop in tumour oxygen supply. In agreement with this, tumour hypoxia was found to be significantly increased. Microelectrode PO₂ measurements showed a clear

relationship between CO concentration and the proportion of low PO₂ measurements (< or = 5 mmHg). The fraction of clonogenic hypoxic cells increased from 8% in air-breathing animals to 13%, 18%, and 54% with 75,220 and 660 ppm CO respectively. The tumour hypoxia resulted in significant radiation modification. The local tumour control after single-dose and fractionated irradiation gave TCD50 enhancement ratios (relative to air-breathing controls) of 0.90, 0.85 and 0.89 for single dose and 5 or 10 fractions given in 5 days (P < 0.005 for all values). For 15 fractions in 5 days with 6- 6- and 12 h intervals, the TCD50 was similar in CO- and air-breathing mice, presumably as a consequence of insufficient reoxygenation during the short inter-fraction intervals. It is concluded that elevated HbCO levels leads to increased tumour hypoxia and that induced hypoxia has a significant impact on the local tumour control also after fractionated irradiation.

AU - Jha R

AU - Kher V

AU - Kale SA

AU - Jain SK

AU - Arora P

TI - Carbon monoxide poisoning: an unusual cause of acute renal failure

Department of Nephrology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India.

Language: Eng

SO - Ren Fail 1994 Nov;16(6):775-9

Unique Identifier: 95207487

AB - Carbon monoxide poisoning in a family of three persons resulted in renal failure with neurological damage in a 40-year-old husband and a fatal neurological injury in 35-year-old wife, whereas the newborn child survived without any ill effects. Rhabdomyolysis and myoglobinuria secondary to anoxia was the probable cause of acute renal failure. The recognition of nontraumatic rhabdomyolysis-related acute renal failure is important in preventing fatality if neurological salvage is done at the right time.

AU - Kolarzyk E

TI - The effect of acute carbon monoxide poisoning on the respiratory system efficiency. Values of spirometric parameters in different degrees of poisoning.

Department of Occupational Medicine, Jagiellonian University School of Medicine, Cracow, Poland.

Language: Eng

SO - Int J Occup Med Environ Health 1994;7(3):225-35

Unique Identifier: 95144449

AB - The examination of 91 patients, performed as soon as possible after CO poisoning, revealed the values of ventilatory parameters obtained from the flow-volume loop recorded by a computer-aided spirometer were significantly lower than those after treatment. Ventilatory efficiency closely related with the degree of poisoning, was assessed according to age, COHb concentration, blood lactate level, and neurological symptoms. Ventilatory parameters in 48 persons with medium and acute poisoning were significantly lower than in the group of slightly poisoned patients. The strong relationship between the major spirometric parameters, blood lactate level, and duration of exposure to carbon monoxide was noted. However, the correlation between ventilatory parameters and the degree of poisoning, taken as a total of all mentioned parameters, was strongest.

AU - Denays R
AU - Makhoul E
AU - Dachy B
AU - Tondeur M; Noel P
AU - Ham HR
AU - Mols P

TI - Electroencephalographic mapping and 99mTc HMPAO single-photon emission computed tomography in carbon monoxide poisoning

Department of Neurology, St Pierre Hospital, Free University of Brussels, Belgium.

Language: Eng

SO - Ann Emerg Med 1994 Nov;24(5):947-52

Unique Identifier: 95069255

AB - STUDY OBJECTIVE: To investigate whether topographic analysis of EEG mapping and technetium-99m (99mTc) hexamethylpropylenamine oxide (HMPAO) brain single-photon emission computed tomography (SPECT) can detect cerebral anomalies in the acute phase of carbon monoxide poisoning. DESIGN: Twelve patients aged 18 to 55 years with severe carbon monoxide poisoning and no history of neurologic disorder were evaluated. Either nasal (5 patients) or hyperbaric (7 patients) oxygen therapy was administered. Criteria for hyperbaric oxygen therapy were blood CO of more than 20%, loss of consciousness, pregnancy, or signs of cardiac injury. After oxygen treatment, all patients had a blood CO value of 0% and no patient had persistent acute signs of toxicity. Patients then were investigated by conventional EEG, EEG mapping, and 99mTc HMPAO brain SPECT. These procedures were performed on the day of admission. PARTICIPANTS: After nasal (5 patients) or hyperbaric (7 patients) oxygen therapy was administered, 12 adults with severe carbon monoxide poisoning were evaluated. All studies were performed on the day of admission. MEASUREMENTS: Conventional EEG, EEG mapping, and 99mTc HMPAO brain SPECT. RESULTS: While classic EEG was normal in 9 of 12 patients and showed diffuse anomalies in 3, EEG mapping and 99mTc HMPAO brain SPECT demonstrated unilateral or bilateral regional anomalies in 8 of 12 patients. Anomalies were localized in temporo-parieto-occipital areas, the watershed areas of the major cerebral arteries, or in temporal cortex. CONCLUSION: These preliminary results suggest that EEG mapping and 99mTc HMPAO brain SPECT can be complementary tools to diagnose early regional cerebral anomalies in carbon monoxide-poisoned patients.

AU - Lee SS
AU - Choi IS
AU - Song KS

Hematologic changes in acute carbon monoxide intoxication

Department of Neurology, Yonsei University Wonju College of Medicine, Korea.

Language: Eng

SO - Yonsei Med J 1994 Sep;35(3):245-51

Unique Identifier: 95066202

AB - This study was performed to investigate the hematologic changes and its pathogenesis in acute carbon monoxide (CO) intoxication. Serial complete blood counts (CBC) were obtained in 17 patients with acute CO intoxication five times in two weeks. Peripheral blood smear, bone marrow aspiration and biopsy were obtained in 7 patients within the first week. The results of serial CBCs were analyzed. Levels of hemoglobin and hematocrit rose only initially, probably due to dehydration and

hemoconcentration rather than hypoxia. Leukocytosis, mainly neutrophilic, observed during the first few days seemed to be a physiological phenomena due to a stressful situation, such as hypoxia. Levels of platelet increased steadily after a initial decrease. No specific findings in bone marrow were found.

AU - Jones JS

AU - Lagasse J

AU - Zimmerman G

TI - Computed tomographic findings after acute carbon monoxide poisoning

Emergency Medicine Residency Program, Butterworth Hospital, Grand Rapids, MI.

Language: Eng

SO - Am J Emerg Med 1994 Jul;12(4):448-51

Unique Identifier: 94304452

AB - Selective necrosis and degeneration of the globus pallidus are characteristic autopsy findings in patients with severe carbon monoxide (CO) poisoning. The objective of this study was to show that computed tomography (CT) may demonstrate these morphological changes in the brain during life, and provide a clue to prognosis. The authors reviewed the medical records of 19 consecutive patients with acute CO poisoning who underwent CT examination during hospitalization. Abnormal CT findings were found in 10 of the 19 patients (53%). The most common abnormal findings were low-density areas in the basal ganglia. These lesions were found in 7 of the 10 cases, and varied from small (limited to the globus pallidus) to large (extending to the internal capsule). Of the 10 patients with abnormal CT scans, 9 survived to hospital discharge, but all had some degree of functional neurological impairment. Of the patients with normal CT scans 89% (8 of 9) were discharged neurologically intact. Awareness of the potential for basal ganglia lesions in CO poisoning should lead to more accurate CT interpretation and may have significant prognostic implications.

AU - Wolff E

TI - Carbon monoxide poisoning with severe myonecrosis and acute renal failure. St Francis Hospital, Roslyn, NY.

Language: Eng

SO - Am J Emerg Med 1994 May;12(3):347-9

Unique Identifier: 94235080

AB - A case of carbon monoxide (CO) poisoning with severe myonecrosis and acute renal failure (ARF) is presented with extremely high values of CPK, but with preservation of myocardial tissue. A discussion of the broad effects of CO intoxication is undertaken with a review of the pertinent literature. Diagnostic and therapeutic mainstays are presented with some pitfalls and alternatives to their implementation. Computed tomography of affected muscles is presented as an alternative to muscle biopsy, and a unique modality of noninvasive diagnosis of myonecrosis.

AU - Marks GS

AU - Nakatsu K

AU - Brien JF

TI - Does endogenous zinc protoporphyrin modulate carbon monoxide formation from heme?

Implications for long-term potentiation, memory, and cognitive function

SI - TOXBIB/94/192086

SO - Can J Physiol Pharmacol; Vol 71, ISS 10-11, 1993, P753-4 (REF: 12)

AB - Carbon monoxide, which is formed endogenously from heme catabolism catalyzed by heme oxygenase and shares some of the chemical and biological properties of nitric oxide, may play a similar

role as a widespread signal transduction mechanism for the regulation of cell function and communication. Zinc protoporphyrin, an inhibitor of heme oxygenase, prevents induction of long-term potentiation. Zinc protoporphyrin is an endogenous substance that may have a physiological role by modulating heme oxygenase activity and, therefore, formation of carbon monoxide from heme. This reaction, in turn, would modulate long-term potentiation, memory, and cognitive function.

AU - Rumel D

AU - Riedel LF

AU - Latorre M do r

AU - Duncan BB

TI - Myocardial infarct and cerebral vascular disorders associated with high temperature and carbon monoxide in a metropolitan area of southeastern Brazil

SI - TOXBIB/94/143698

SO - Rev Saude Publica; Vol 27, ISS 1, 1993, P15-22

AB - Many studies have been published about the relationship between life style and genetic risk factors and stroke and heart attack, but few of them have been about the relationship between atmospheric pollution, specifically with carbon monoxide, and temperature and stroke and heart attack. With a view to filling this gap, the relationship between values of carbon monoxide concentration in the air, maximum and average by day, and maximum temperature by day and the number of new cases of CVA and IM admitted as emergencies at the biggest hospital complex of S. Paulo city was analysed. It was concluded, by the use of multivariable regression analysis, that 2.1% and 4.9% of heart attack admissions were due to carbon monoxide air pollution and high temperature, respectively. High temperatures caused 2.8% of stroke admissions. Stroke and carbon monoxide were not associated in this population.

AU - Song CP

TI - Health effects on workers exposed to low concentration carbon monoxide at high altitude

SI - TOXBIB/93/358687

SO - Chung Hua Yu Fang I Hsueh Tsa Chih; Vol 27, ISS 2, 1993, P81-4

AB - Workers exposed to carbon monoxide (CO) at a concentration of 26.8 mg/m³ at an altitude of 2300 meters above sea level were compared with a control group of local inhabitants. Significant differences appeared in symptoms of headache, vertige fatigue and weakness memory impairment, insomnia, palpitation and neurobehavioral functions. CO concentration in respiratory air and HbCO in blood was higher, but partial pressure of oxygen (PO₂) and saturation of oxygen (SaO₂) in blood was lower in the exposed group than the control group. Self-comparison of CO in respiratory air and HbCO in blood was higher, after work than before work. Neurasthenia rate was significantly higher but PO₂ and SaO₂ significantly lower at the high altitude than in the plain. The results indicated that, under same CO concentrations, the hazards to workers at high altitude were greater than to those working in the plain. The author recommends that at high altitude the CO permissible level should be appropriately lowered.

AU - Prabhu SS

AU - Sharma RR

AU - Gurusinghe NT

AU - Parekh HC

TI - Acute transient hydrocephalus in carbon monoxide poisoning: a case report [letter]

SI - TOXBIB/93/280609

SO - J Neurol Neurosurg Psychiatry; Vol 56, ISS 5, 1993, P567-8

AU - Smith CJ

AU - Steichen TJ

TI - The atherogenic potential of carbon monoxide [published erratum appears in Atherosclerosis 1993 Jun;101(1):127]

SI - TOXBIB/93/277600

SO - Atherosclerosis; Vol 99, ISS 2, 1993, P137-49 (REF: 41)

AB - This paper reviews the available evidence concerning the atherogenic potential of carbon monoxide. The evidence comes from two different types of studies—epidemiology studies on populations of humans chronically exposed to carbon monoxide, and animal studies conducted under conditions of controlled exposure to carbon monoxide. Data from both epidemiology and animal studies suggest that carbon monoxide is not atherogenic. Therefore, the increased levels of atherosclerosis associated with smoking, as reported in epidemiology studies of human smokers, probably cannot be attributed to CO exposure.

AU - Dahms TE

AU - Younis LT

AU - Wiens RD

AU - Zarnegar S

AU - Byers SL

AU - Chaitman BR

TI - Effects of carbon monoxide exposure in patients with documented cardiac arrhythmias

SI - TOXBIB/93/147383

SO - J Am Coll Cardiol; Vol 21, ISS 2, 1993, P442-50.

AB - **OBJECTIVE:** This study was designed to determine whether carbon monoxide has proarrhythmic effects at rest and during upright exercise in patients with myocardial ischemia and moderate baseline ectopic activity. **BACKGROUND:** Exposure of patients with documented myocardial ischemia to low levels of carboxyhemoglobin (COHb) alters the myocardial response to exercise. Anecdotal reports from patients with myocardial ischemia have noted the development of arrhythmias related to carbon monoxide exposure. Increased frequency of arrhythmias related to carbon monoxide exposure in patients performing supine bicycle exercise has been recently reported. **METHODS:** The study included 28 nonsmoking men and 5 nonsmoking women with documented coronary artery disease and a minimum of 30 ventricular ectopic beats/h over a 20-hour period were studied. Subjects were exposed in a randomized double-blind fashion to either room air or sufficient carbon monoxide to elevate their COHb concentration to 3% or 5% in 1 hour, followed by a maintenance exposure to carbon monoxide. The subjects then left the laboratory and resumed their normal daily activity to determine changes in ventricular ectopic beats after carbon monoxide exposure. **RESULTS:** No significant change was present in the frequency of single ventricular ectopic beats at rest from 115 +/- 28 (in room air) to 121 +/- 31 at 3% COHb to 94 +/- 23 at 5% COHb. Exercise itself increased the frequency of ventricular ectopic beats, but no additional effect was found of carbon monoxide exposure on the exercise-induced increase in isolated ectopic beats or complex ectopic waveforms. Analysis of the data, based on grouping of the subjects by the severity of disease (ventricular ectopic beat frequency, ejection fraction, presence of exercise-induced ischemia), indicated

no proarrhythmic effect of carbon monoxide. **CONCLUSIONS:** In patients with frequent ventricular ectopic activity ($>$ or $=$ 30 ectopic beats/h), exposure to carbon monoxide producing either 3% or 5% COHb does not increase arrhythmia frequency of single or multiple beats during rest or exercise.

AU - Choi IS
AU - Kim SK
AU - Choi YC
AU - Lee SS
AU - Lee MS

TI - Evaluation of outcome after acute carbon monoxide poisoning by brain CT

Department of Neurology, Yongdong Severance Hospital, Yonsei University College of Medicine, Seoul, Korea.

Language: Eng

SO - J Korean Med Sci 1993 Feb;8(1):78-83

Unique Identifier: 93344017

AB - Of 129 patients with carbon monoxide (CO) poisoning, 62 (48.0%) had characteristic computed tomographic (CT) findings. The most common finding, seen in 42 patients, was low-density in the cerebral white matter, and the second characteristic feature, seen in 33 patients, was low-density in both globus pallidi. Abnormal CT findings tended to increase in accordance with the duration of unconsciousness during acute CO poisoning, but such findings occurred even when the mental state was clear during acute illness. The prognosis of acute CO poisoning depended on low-density lesions of the cerebral white matter, rather than on those of the globus pallidus. A significant correlation seemed to exist between the cerebral white matter changes in the initial CT scan and the development of delayed neurologic sequelae after acute CO poisoning, particularly in middle age or older patients, but no correlation between the CT findings and the clinical outcome of delayed neurologic sequelae.

AU - Gotoh M
AU - Kuyama H
AU - Asari S
AU - Ohmoto T
AU - Akioka T
AU - Lai MY

TI - Sequential changes in MR images of the brain in acute carbon monoxide poisoning

Department of Neurological Surgery, Okayama University Medical School, Japan.

Language: Eng

SO - Comput Med Imaging Graph 1993 Jan-Feb;17(1):55-9

Unique Identifier: 93193097

AB - Two cases of acute carbon monoxide poisoning are presented in this paper. Sequential magnetic resonance (MR) images of the brain showed abnormal lesions in the bilateral globus pallidus or in the subcortical white matter. The MR images disclosed the severity of the white matter lesions correlated with the prognosis in acute carbon monoxide poisoning. However, the images did not always correspond to the neurological condition in the acute and subacute stages.

AU - Dueva LA

AU - Tolmachev DA

AU - Volkova AP

TI - Cellular immunity indices in combined chronic exposure to stress and low concentrations of carbon monoxide (II). Experimental research.

SI - TOXBIB/93/202502

SO - Gig Tr Prof Zabol, ISS 8, 1992, P25-7

AB - Studies of the chronic combined effects of carbon monoxide low concentrations and psychoemotional stress revealed changes in the peripheral lymphocyte subpopulation in all groups of examinees, connected with the defense activation of the humoral immunity and functional decrease of T lymphocytes. Analysis of correlations of cell subpopulations revealed disorders of their relationships, augmenting with the intensity of exposure. Combined action of carbon monoxide in the maximal of studies concentrations with stress resulted in the most severe changes of nonspecific immunity, which proves decompensated decrease of immunity.

AU - Chaitman BR

AU - Dahms TE

AU - Byers S

AU - Carroll LW

AU - Younis LT

AU - Wiens RD

TI - Carbon monoxide exposure of subjects with documented cardiac arrhythmias

SI - TOXBIB/93/039855

SO - Res Rep Health Eff Inst, ISS 52, 1992, P1-26; discussion 27-37

AB - The impact of low-level carbon monoxide exposure on ventricular arrhythmia frequency in patients with ischemic heart disease has not been thoroughly studied. The issue is of concern because of the potential proarrhythmic effect of carbon monoxide in patients with ischemic heart disease. The study included 30 subjects with well-documented coronary artery disease who had an average of at least 30 ventricular ectopic beats per hour over a 20-hour monitoring interval. By using appropriate inclusion and exclusion criteria, subjects were selected and enrolled in a randomized double-blind study to determine the effects of carbon monoxide exposure on ventricular arrhythmia frequency at rest, during exercise, and during ambulatory activities. The carbon monoxide exposure was designed to result in 3% or 5% carboxyhemoglobin levels, as measured by gas chromatography. The carbon monoxide exposure protocol produced target levels in 60 minutes, and the levels were maintained for an additional 90 minutes to provide adequate time to assess the impact of carbon monoxide on the frequency of ventricular ectopic beats. The data on total and repetitive ventricular arrhythmias were analyzed for seven specific time intervals: 1) two hours before carbon monoxide exposure; 2) during the two-hour carbon monoxide or air exposure; 3) during a 2-hour rest period; 4) during an exercise period; 5) during an exercise recovery period; 6) six hours after carbon monoxide or air exposure; and 7) approximately 10 hours after exposure, or the remaining recording interval on the Holter monitor. No increase in ventricular arrhythmia frequency after carbon monoxide exposure was noted, regardless of the level of carboxyhemoglobin or the type of activity. During steady-state conditions at rest, the number of ventricular ectopic beats per hour was 115 +/- 153 (SD) for room air exposure (0.7% carboxyhemoglobin), 121 +/- 171 for the lower carbon monoxide exposure (3.2% carboxyhemoglobin), and 94 +/- 129 for the higher carbon monoxide exposure (5.1% carboxyhemoglobin). The frequency of complex ventricular ectopy was not altered at the levels of carbon monoxide studied. Secondary analysis of the impact of carbon monoxide on ventricular ectopic beat frequency stratified

by baseline ejection fraction, baseline ventricular ectopic beat frequency, and exercise-induced ST-segment changes did not indicate an effect of carbon monoxide on ventricular arrhythmias. In conclusion, low levels of carbon monoxide exposure resulting in blood levels of 3.2% and 5.1% carboxyhemoglobin, as measured by gas chromatography, do not have a proarrhythmic effect on patients with coronary artery disease and frequent ventricular ectopy. (ABSTRACT TRUNCATED AT 400 WORDS)

AU - Manno M

AU - Rugge M

AU - Cocheo V

TI - Double fatal inhalation of dichloromethane

Institute of Occupational Medicine, University of Padua Medical School, Italy.

Language: Eng

SO - Hum Exp Toxicol 1992 Nov;11(6):540-5

Unique Identifier: 93098971

AB - Two cases of lethal poisoning following acute inhalation of extremely high concentrations of dichloromethane (DCM) are reported. The concentrations of the solvent found in the blood of the two subjects collected at autopsy and analysed by gas chromatography/mass spectrometry (572 and 601 mg l⁻¹) were compatible with those measured in the air a few hours after the discovery of the bodies (up to 168,000 ppm). Extensive brain and lung oedema and congestion, microhaemorrhagic changes of the stomach and congestion in other organs were observed on macroscopic and microscopic examination of both subjects. In addition, and in both cases, high but not lethal carboxyhemoglobin (COHb) levels (30%) were found in the blood collected at autopsy. Narcosis and respiratory depression due to the effect of DCM on the central nervous system (CNS) appear to have played a critical role in the death of the two men. However, biotransformation of the solvent to toxic metabolites, including carbon monoxide (via oxidative dehalogenation by the cytochrome P450-dependent mixed function oxidase system) or formaldehyde, formic acid, inorganic chloride, and carbon dioxide (via the glutathione-S-transferase pathway) may have also contributed significantly to fatal toxicity.

AU - McCabe MJ

AU - Weston CF

AU - Fraser AG

Acute myocardial infarction related to smoke inhalation and myocardial bridging

Department of Cardiology, University Hospital of Wales, Health Park, Cardiff, UK.

Language: Eng

SO - Postgrad Med J 1992 Sep;68(803):758-61

Unique Identifier: 93126192

AB - A previously healthy 26-year-old woman who was exposed to smoke during a house fire developed acute anterior myocardial infarction complicated by ventricular fibrillation. Subsequent left ventriculography confirmed anterior infarction, but coronary arteriography was normal apart from myocardial bridging over a segment of the left anterior descending artery. The development of acute myocardial infarction in this patient suggests that, in the presence of bridging, carbon monoxide inhalation may cause regional infarction.

AU - Shimosegawa E

AU - Hatazawa J

AU - Nagata K

AU - Okudera T
AU - Inugami A
AU - Ogawa T
AU - Fujita H
AU - Itoh H
AU - Kanno I
AU - Uemura K

TI - Cerebral blood flow and glucose metabolism measurements in a patient surviving one year after carbon monoxide intoxication

Department of Radiology and Nuclear Medicine, Research Institute of Brain and Blood Vessels, Akita, Japan.

Language: Eng

SO - J Nucl Med 1992 Sep;33(9):1696-8

Unique Identifier: 92389045

AB - A 29-yr-old woman was studied for 1 year after acute carbon monoxide intoxication, following an attempted suicide by inhalation of automobile exhaust fumes. The patient demonstrated impaired responsiveness to stimuli without any specific neurological deficits for 1 year after carbon monoxide intoxication. Repeated brain magnetic resonance imaging consistently displayed only bilateral globus pallidus lesions, but no lesions in either deep white matter or cerebral cortex. Position emission tomography measurements of regional cerebral blood flow, and glucose utilization rate were made in this patient at 6 months and 1 year following carbon monoxide intoxication. Impairment of both blood flow and glucose metabolism were found not only in the basal ganglia, but also in morphologically normal frontal cortex. The decrease in glucose utilization in the frontal cortex was greater than that in the basal ganglia. During the period of 6 months to 1 year, blood flow and glucose metabolism in the basal ganglia recovered to the normal range. In the frontal cortex, however, blood flow and glucose metabolism remained approximately 20% lower than normal mean values. This prolonged dysfunction in the frontal cortex may therefore be responsible for the impaired responsiveness of the subject.

AU - Florkowski CM
AU - Rossi ML
AU - Carey MP
AU - Poulton K
AU - Dickson GR
AU - Ferner RE

TI - Rhabdomyolysis and acute renal failure following carbon monoxide poisoning: two case reports with muscle histopathology and enzyme activities.

West Midlands Poisons Unit, Dudley Road Hospital, Birmingham, United Kingdom.

Language: Eng

SO - J Toxicol Clin Toxicol 1992;30(3):443-54

Unique Identifier: 92381775

AB - Two patients with carbon monoxide poisoning are presented, both of whom suffered rhabdomyolysis complicated by acute renal failure. One patient, an attempted suicide, developed a compartment syndrome of the right thigh that required fasciotomy and recovered after a period of hemofiltration and hemodialysis. Muscle biopsy appearances were consistent with partial muscle infarction. The other patient, rescued from a smoke-filled room, exhibited raised creatine kinase but no evidence of muscle swelling. He developed anuric renal failure and adult respiratory distress syndrome and died despite maximum intensive care. Muscle biopsy showed early evidence of muscle

necrosis. In both cases, a marked reduction of enzyme activities existed in the muscle biopsy consistent with metabolic derangement. Although a clinical compartment syndrome was present in the first case, no muscle swelling was seen at the time of biopsy or subsequently in the second case. A direct toxic effect of carbon monoxide may thus have been an important mechanism contributing to the muscle necrosis in the second case, although local ischemia may have been an exacerbating factor in the first case.

AU - Tikuisis P

AU - Kane DM

AU - McLellan TM

AU - Buick F

AU - Fairburn SM

TI - Rate of formation of carboxyhemoglobin in exercising humans exposed to carbon monoxide

SI - TOXBIB/92/276167

SO - J Appl Physiol; Vol 72, ISS 4, 1992, P1311-9

AB - The purpose of this study was to test the CFK equation for its prediction of the rate of formation of carboxyhemoglobin (HbCO) in exercising humans by use of measured values of the respiratory variables and to characterize the rate of appearance of HbCO with frequent blood sampling.

Nonsmoking male subjects (10) were exposed to carbon monoxide (CO) on two separate occasions distinguished by the level of activity. Steady-state exercise was conducted on a cycle ergometer at either a low (approximately 45 W) or moderate (approximately 90 W) power output. Each experiment began with an exposure of 3000 ppm CO for 3 min during a rest period followed by three intermittent exposures ranging from 3000 ppm CO for 1 min at low exercise to 667 ppm CO for 3 min at moderate exercise. Increases in HbCO were normalized against predicted values to account for individual differences in the variables that govern CO uptake. No difference in the normalized uptake of CO was found between the low- and moderate-exercise trials. However, the CFK equation underpredicted the increase in HbCO for the exposures at rest and the first exposure at exercise, whereas it overpredicted for the latter two exposures at exercise. The net increase in HbCO after all exposures (approximately 10% HbCO) deviated by less than 1% HbCO between the measured and predicted values. The rate of appearance of HbCO fits a sigmoidal shape with considerable overshoot at the end of exposure. This pattern can be explained by delays in the delivery of CO to the blood sampling point (dorsal hand vein) and by a relatively small blood circulation time compared with other regions of the body. A simple circulation model is used to demonstrate the overshoot phenomenon.

AU - Adir Y

AU - Kol S

AU - Melamed Y

TI - Carbon monoxide and coronary artery disease

SI - TOXBIB/92/225416

SO - Harefuah; Vol 122, ISS 4, 1992, P249-51 (REF: 22)

AU - Chang KH

AU - Han MH

AU - Kim HS

AU - Wie BA

AU - Han MC

TI - Delayed encephalopathy after acute carbon monoxide intoxication: MR imaging features and distribution of cerebral white matter lesions.

Department of Diagnostic Radiology, Seoul National University Hospital, Korea.

Language: Eng

SO - Radiology 1992 Jul;184(1):117-22

Unique Identifier: 92302501

AB - Magnetic resonance (MR) images obtained in 15 patients with delayed encephalopathy after acute carbon monoxide (CO) intoxication were reviewed. Images had been obtained 4-9 weeks after exposure to CO, during the relapse of neuropsychiatric symptoms after initial recovery. Bilateral symmetric confluent high signal intensity in the periventricular white matter and centrum semiovale was seen on long-repetition-time images (n = 15). The high intensity extended into the corpus callosum (n = 11), subcortical U fibers (n = 12), and external (n = 9) and internal (n = 7) capsules. Bilateral diffuse low-intensity signal in the thalamus and putamen on T2-weighted images, suggesting iron deposition, was demonstrated in 10 patients. Bilateral ischemia or necrosis of the globus pallidus was seen in nine patients. In three of four patients with follow-up MR imaging studies, a decrease in extent and signal intensity of white matter lesions accompanied lessening of clinical symptoms. These results suggest that the main pathologic feature of delayed encephalopathy associated with CO intoxication is a reversible demyelinating process of the cerebral white matter.

AU - Penney DG

AU - Howley JW

TI - Is there a connection between carbon monoxide exposure and hypertension?

SI - TOXBIB/92/331546

SO - Environ Health Perspect; Vol 95, 1991, P191-8 (REF: 91)

AB - Exposure to carbon monoxide in our society is a frequent occurrence, from auto exhaust, industrial effluents, and cigarette smoke, and takes place over a wide range of concentrations. It has been suggested that chronic CO inhalation may alter blood pressure, even possibly provoking hypertension by acting alone or in combination with other environmental stressors. Some studies examining the response to CO exposure have reported decreases in blood pressure, whereas others have found increases or no change. Blood pressure in long-term cigarette smokers is generally decreased relative to nonsmokers, albeit a slight decrease. The strength of this finding is somewhat clouded by the effect of the lower body weight in smokers. The increases in blood pressure observed acutely with smoking are mainly due to nicotine. Chronically, the hypertensive action of nicotine is largely offset by the hypotensive action of CO. Several studies support the notion that environmental CO exposure or smoking accelerates or exacerbates hypertension in some people. It has been asserted that chronic CO exposure increases the development of atherosclerotic disease; however, convincing evidence from animal experiments is lacking. Nevertheless, CO may elevate plasma cholesterol and does appear to enhance atherosclerosis when serum cholesterol is greatly elevated by diet. Using the borderline hypertensive rat, an animal model reputed to have increased sensitivity to environmental stimuli, no evidence was found to suggest a provocatory role for CO in the development of hypertension; instead, CO exposure produced hypotension. On the whole, the human and animal literature, as well as these studies, fail to support the hypothesis that long-term CO exposure is capable of provoking an increase in blood pressure, even in borderline hypertensive or sensitive individuals.

AU - Sedov AV

AU - Akin'shin AV

AU - Lukicheva TA

TI - Prognostication of physical work capacity under the effect of carbon monoxide and raised air temperature and decreased oxygen contents

SI - TOXBIB/91/331353

SO - Gig Tr Prof Zabol, ISS 5, 1991, P25-7

AB - Experimental studies performed on volunteers resulted in formulating an equation which characterized degrees of physical working capacity decrease depending on the carbon monoxide concentration levels and duration of its influence at high temperature levels (+50 degrees C) of the air and lowered barometric pressure (560 mm). A nomogram was charted to forecast degrees of physical working capacity decrease in man at the carbon monoxide concentration levels from 500 to 2000 mg/m³ at time intervals ranging from 0 to 30 min.

AU - Marks GS

AU - Brien JF

AU - Nakatsu K

AU - McLaughlin BE

TI - Does carbon monoxide have a physiological function?

SI - TOXBIB/91/320387

SO - Trends Pharmacol Sci; Vol 12, ISS 5, 1991, P185-8 (REF: 30)

AB - Recently, endothelium-derived relaxing factor (EDRF) has been identified as nitric oxide. The source of the nitric oxide is L-arginine, and the L-arginine-nitric oxide pathway has been proposed to function as a widespread transduction mechanism for the regulation of cell function and communication. Gerald Marks and colleagues suggest that carbon monoxide, which is formed endogenously from heme catabolism and which shares some of the chemical and biological properties of nitric oxide, may play a similar role. This combination would be achieved by carbon monoxide binding to the iron atom of the heme moiety of soluble guanylyl cyclase and to the iron-sulfur centers of macrophage enzymes.

AU - Allred EN

AU - Bleecker ER

AU - Chaitman BR

AU - Dahms TE

AU - Gottlieb SO

AU - Hackney JD

AU - Pagano M

AU - Selvester RH

AU - Walden SM

AU - Warren J

TI - Effects of carbon monoxide on myocardial ischemia

SI - TOXBIB/91/249757

SO - Environ Health Perspect; Vol 91, 1991, P89-132

AB - The purpose of this study was to determine whether low doses of carbon monoxide (CO) exacerbate myocardial ischemia during a progressive exercise test. The effect of CO exposure was evaluated using the objective measure of time to development of electrocardiographic changes indicative of ischemia and the subjective measure of time to onset of angina. A total of 63 male subjects (41-75 years) with well-documented coronary artery disease, who had exertional angina pectoris and ischemic ST-segment changes in their electrocardiograms, were studied. Results from three randomized, double-blind test visits (room air, low, and high CO) were compared. The effect of

CO exposure was determined from the percent difference in the end points obtained on exercise tests performed before and after a 1-hour exposure to room air or CO. The exposures resulted in postexercise carboxyhemoglobin (COHb) levels of 0.6% +/- 0.3%, 2.0% +/- 0.1%, and 3.9% +/- 0.1%. The results obtained on the 2%-COHb day and 3.9%-COHb day were compared to those on the room air day. Compared to the control day 5.1% ($p = 0.01$) and 12.1% (p less than or equal to 0.0001) decreases were found in the time to development of ischemic ST-segment changes after exposures producing 2.0 and 3.9% COHb, respectively. In addition, 4.2% ($p = 0.027$) and 7.1% ($p = 0.002$) decreases were found in time to the onset of angina after exposures producing 2.0 and 3.9% COHb, respectively, also compared to the control day. A significant dose-response relationship was found for the individual differences in the time to ST end point and angina for the pre- versus postexposure exercise tests at the three carboxyhemoglobin levels. These findings demonstrate that low doses of CO produce significant effects on cardiac function during exercise in subjects with coronary artery disease.

AU - Levesque B
 AU - Lavoie R
 AU - Dewailly E
 AU - Prud'homme D
 AU - Allaire S

TI - An experiment to evaluate carbon monoxide absorption by hockey players in ice skating rinks
 SI - TOXBIB/91/205742

SO - Vet Hum Toxicol; Vol 33, ISS 1, 1991, P5-8

AB - Carbon monoxide (CO) released from the exhaust of ice resurfacing machinery is frequently found in indoor ice skating rinks. A study was conducted with 14 male adult non-smokers unexposed occupationally, who played hockey games in 4 different atmospheric CO concentrations. To document absorption, their alveolar carbon monoxide (alvCO) was measured. Exposure was the average CO level in the rink during the game. Environmental concentrations were between 0.0 (undetected) and 76.2 parts per million (ppm). The exposure-absorption relationship was linear (regression parameters: $r^2 = 0.93$, slope = 0.411, intercept = -1.45). Thus, for each 10 ppm of CO in the indoor air, the players absorbed enough CO to raise their alvCO by 4.1 ppm (approximately 0.76% carboxyhemoglobin). Taking into account the duration of the games, the regression coefficients were almost similar to those of an earlier study made with 122 adult male hockey players playing in recreational leagues of the Quebec city area. These results show the exposure-absorption relationship for an acute 60-minute exposure, in a design which eliminated certain of the uncontrolled variables of the first study. It also emphasizes the importance of prevention for CO pollution in indoor skating rinks.

AU - Sedov AV
 AU - Kustov VV
 AU - Surovtsev NA
 AU - Lukicheva TA
 AU - Akin'shin AV
 AU - Nazarov LIu

TI - Quantitative evaluation of combined effects of carbon monoxide, toluene and hot microclimate on humans

SI - TOXBIB/91/177346

SO - Gig Tr Prof Zabol, ISS 8, 1990, P11-4

AB - As a result of the proposed study, it was established that a complex action of carbon oxide and

toluene++ in 300 mg/m³ concentration in a combination with heating microclimate (leading to a maximum heat labour condition) results in an increased total biological effect. The coefficient to the complex action of carbon oxide and heating microclimate is equal to 2.5 and toluene++ and heating microclimate to 1.9. These coefficients should be taken into account in establishing hygienic norms for the chemical compounds.

AU - Norman CA

AU - Halton DM

TI - Is carbon monoxide a workplace teratogen? A review and evaluation of the literature

SI - TOXBIB/91/052900

SO - Ann Occup Hyg; Vol 34, ISS 4, 1990, P335-47 (REF: 44)

AB - Case reports of carbon monoxide exposures involving 60 pregnant women are reviewed. The circumstances, under which carbon monoxide exposures adversely affected pregnancy and the types of effects seen, are summarized. Severe acute exposures to carbon monoxide caused foetal death or toxic effects, including anatomical malformations and functional alterations. Foetal outcome was related to two major indices of carbon monoxide exposure: maternal blood carboxyhemoglobin levels and maternal toxicity.

AU - Haab P

TI - The effect of carbon monoxide on respiration

SI - TOXBIB/91/071353

SO - Experientia; Vol 46, ISS 11-12, 1990, P1202-6 (REF: 32)

AB - In this review, the effects of carbon monoxide on tissular oxygenation, at doses which are compatible with life, are considered. In a first section, the relative CO-O₂ affinity (M*) of various O₂ carrying proteins is compared; M* is about 220 for hemoglobin, 20-25 for myoglobin and close to unity for cytochrome oxidases. Thus, most of the acute CO toxicity should not be considered as due to malfunction of the intracellular respiratory chain. In addition, the differences in M* are caused more by the changes in O₂ affinity than by those in CO affinity. The second section deals with the changes in the O₂ equilibrium curve (OEC) induced by the presence of HbCO in blood, i.e., the hyperbolization of this curve due to the progressive loss of allostery due to the preferential binding of CO to Hb. The functional importance of this phenomenon lies in the fact that the lower part of the OEC is shifted to the left, whereas the upper part is shifted to the right to an extent which depends upon the amount of HbCO. Thus, the effects of the so-called CO anemia are considered to be due to the reduction of functional Hb and to the reduced partial pressure in the hypoxic range of the OEC. The third section presents recent data concerning the effect of HbCO on the VO₂ max of the isolated gastrocnemius preparation. The results were obtained in hypoxia under conditions where perfusion and arterial O₂ content, i.e., O₂ delivery, were the same with and without 30% HbCO. The salient finding is a 26% reduction of VO₂ max under conditions of CO anemia as compared to hypoxia alone. Interestingly, the PO₂ of the venous effluent of the muscle is found to be the same in both cases, which leads to the interpretation that it is not the reduction of the mean capillary PO₂, but rather a decrease of the blood-to-mitochondria O₂ conductance that causes the fall in VO₂ max.

AU - King CE

TI - Muscle oxygenation and performance during low level carbon monoxide exposure

SI - TOXBIB/91/263821

SO - Adv Exp Med Biol; Vol 277, 1990, P533-40

AU - Sedov AV
AU - Kustov VV
AU - Surovtsev NA
AU - Lukicheva TA
AU - Akin'shin AV
AU - Nazarov LIu
AU - Stroganov VP
TI - Substantiation of the permissible level of exposure of the body to carbon monoxide, heat and hypoxic hypoxia in aviation accidents
SI - TOXBIB/91/200688
SO - Gig Tr Prof Zabol, ISS 11, 1990, P20-3

AU - Perutz MF
TI - Mechanisms regulating the reactions of human hemoglobin with oxygen and carbon monoxide
SI - TOXBIB/90/233747
SO - Annu Rev Physiol; Vol 52, 1990, P1-25 (REF: 49)

AU - Kleinman MT
AU - Davidson DM
AU - Vandagriff RB
AU - Caiozzo VJ
AU - Whittenberger JL
TI - Effects of short-term exposure to carbon monoxide in subjects with coronary artery disease
SI - TOXBIB/90/120690
SO - Arch Environ Health; Vol 44, ISS 6, 1989, P361-9
AB - A sample of 24 male subjects with stable angina pectoris performed graded exercise tests after being exposed to either carbon monoxide (CO) or clean air in a randomized crossover double-blind experiment in which each subject acted as his own control. Subjects' blood carboxyhemoglobin levels were increased from a baseline level of approximately 1.5% to 3% of saturation, post-CO exposure. Cardiographic and respiratory gas exchange data were obtained during the tests in which the subjects exercised to the point of onset of anginal pain. The goal of the study was to determine if low-level CO exposure compromised the ability of these individuals to perform work. Data were evaluated statistically using a 2-factor analysis of variance with repeated measures; the factors were exposure ATMOSPHERE (clean air vs. CO) and ORDER of exposure (clean air first, CO second vs. CO first, clean air second). One-tailed tests were used, and differences were considered significant at the p less than 0.05 level. The time to onset of angina was reduced 6% ($p = 0.046$) after CO exposure relative to clean air. Oxygen uptake (VO_2) at angina was reduced by approximately 3% ($p = 0.04$). A subgroup of individuals who exhibited depression in the ST segment of their electrocardiograph tracings showed a 12% reduction in time to onset of angina and a 20% reduction in the time to onset of 0.1 mV ST segment depression; both of these findings were also statistically significant.

AU - Allred EN
AU - Bleecker ER
AU - Chaitman BR
AU - Dahms TE
AU - Gottlieb SO
AU - Hackney JD

AU - Hayes D
AU - Pagano M
AU - Selvester RH
AU - Walden SM
AU - et al

TI - Acute effects of carbon monoxide exposure on individuals with coronary artery disease
SI - TOXBIB/90/104702

SO - Res Rep Health Eff Inst, ISS 25, 1989, P1-79

AB - The purpose of this study was to determine, using more objective evidence than reported in previous studies, whether or not exposures to carbon monoxide that produce approximately 2% or 4% blood carboxyhemoglobin levels cause an exacerbation of myocardial ischemia during a progressive exercise test. The objective measurements were based on the development of electrocardiographic evidence of ischemia. In addition, time to onset of angina pectoris was studied. Male subjects, ages 35 to 75, with stable exertional angina pectoris and positive exercise treadmill tests with reproducible ischemic ST-segment changes in their electrocardiograms, were studied. In addition, each subject fulfilled at least one of the following criteria of coronary artery disease: angiographic evidence of at least a 70% occlusion of one or more major coronary artery; prior documented myocardial infarction; or a positive exercise thallium test. Each subject was evaluated on four separate occasions, a qualifying visit and three blinded test visits, which involved exposure (in random order) to air without added carbon monoxide and to air that contained carbon monoxide concentrations calculated to produce approximately 2.2% or 4.4% carboxyhemoglobin, measured by gas chromatography, at the end of the exposure period. These immediate postexposure target levels were set 10% higher than the desired postexercise carboxyhemoglobin levels of 2.0% and 4.0%, because exercise while breathing room air results in loss of carbon monoxide. The actual 1-minute postexercise levels reached were 2.0% +/- 0.1% (mean +/- standard error of the mean) and 3.9% +/- 0.1%. On each test day, the subject performed a symptom-limited exercise test on a treadmill, was exposed for approximately 1 hour to air or to one of two levels of carbon monoxide in air, and then performed a second exercise test. Time to the onset of ischemic ST-segment changes and time to the onset of angina were determined for each exercise test. The percent difference for these endpoints on the pre- and postexposure exercise tests was determined, and the results on the 2%-COHb-target day and the results on the 4%-COHb-target day were compared to those on the control day. Data from the 63 subjects who completed the three test visits and met all protocol criteria were analyzed. Compared to the control day, 5.1% (p = 0.01) and 12.1% (p less than or equal to 0.0001) (trimmed mean) decreases were found in the time to development of ischemic ST-segment changes after the 2%- and 4%-COHb-target exposures, respectively, compared to the control day. (ABSTRACT TRUNCATED AT 400 WORDS)

AU - Pankow D
AU - Hoffmann P

TI - Dichloromethane metabolism to carbon monoxide can be induced by isoniazid, acetone and fasting
SI - TOXBIB/89/373646
SO - Arch Toxicol Suppl; Vol 13, 1989, P302-3

AU - Di Cera E
AU - Doyle ML
AU - Morgan MS
AU - De Cristofaro R
AU - Landolfi R

AU - Bizzi B

AU - Castagnola M

AU - Gill SJ

TI - Carbon monoxide and oxygen binding to human hemoglobin F0

SI - TOXBIB/89/274197

SO - Biochemistry; Vol 28, ISS 6, 1989, P2631-8

AB - Differential binding curve measurements of carbon monoxide and oxygen binding to human hemoglobin F0 under near-physiological conditions (0.1 M NaCl and 15 mM 2,3-diphosphoglyceric acid, pH 7.35, and 37 degrees C) have allowed a detailed description of the binding and linkage between these two gaseous ligands. Comparison with human hemoglobin A0 under identical solution conditions shows that fetal hemoglobin F0 binds oxygen and carbon monoxide with higher affinity than human hemoglobin A0, but with the same cooperativity. Construction of the partition coefficient surface for carbon monoxide and oxygen binding reveals a failure of Haldane's laws for both hemoglobins. Linkage graphs are used to explore the phenomenological properties of the system. The graphs provide a quantitative description of the mechanism of carbon monoxide toxicity on oxygen transport by hemoglobin in vivo and demonstrate striking similarities between the functional properties of fetal and adult hemoglobins.

AU - Hinderliter AL

AU - Adams KF Jr

AU - Price CJ

AU - Herbst MC

AU - Koch G

AU - Sheps DS

TI - Effects of low-level carbon monoxide exposure on resting and exercise-induced ventricular arrhythmias in patients with coronary artery disease and no baseline ectopy

SI - TOXBIB/89/192495

SO - Arch Environ Health; Vol 44, ISS 2; 1989, P89-93

AB - The effects of acute elevation of carboxyhemoglobin (COHb) concentrations on resting and exercise-induced ventricular arrhythmias were evaluated in 10 patients who had ischemic heart disease and in whom no ectopy during baseline monitoring was noted. After an initial training session, patients were exposed to air, 100 ppm carbon monoxide (CO), or 200 ppm CO on successive days in a randomized, double-blind, cross-over fashion. After exposure to 100 and 200 ppm CO, venous COHb levels averaged 4% and 6%, respectively. Symptom-limited supine exercise was performed after exposure. A total of 8 of the 10 patients had evidence of exercise-induced ischemia (either angina, 1.0 mm ST depression, or abnormal ejection fraction response) during 1 or more exposure days. Ambulatory electrocardiograms were obtained on each day and analyzed for arrhythmia frequency and severity. On air and CO exposure days, each patient had only 0-1 ventricular premature beat/hour in the 2 hours prior to exposure, during the exposure period, during the subsequent exercise test, and in the 5 hours following exercise. In conclusion, low-level CO exposure is not arrhythmogenic in patients with coronary artery disease and no ventricular ectopy at baseline.

AU - Horvath SM

AU - Agnew JW

AU - Wagner JA

AU - Bedi JF

TI - Maximal aerobic capacity at several ambient concentrations of carbon monoxide at several altitudes

SI - TOXBIB/90/057015

SO - Res Rep Health Eff Inst, ISS 21, 1988, P1-21

AB - In order to assess the combined effects of altitude and acute carbon monoxide exposure, 11 male and 12 female subjects, nonsmokers in good health, were given incremental (two minutes at each workload) maximal aerobic capacity tests at four levels of ambient carbon monoxide (0, 50, 100, and 150 parts per million) at four altitudes (55, 1,524, 2,134, and 3048 m). Five male and four female subjects completed all 16 experiments. The remaining subjects completed either 8 or 12 experiments; at least 8 male and 8 female subjects were tested at each combination of carbon monoxide and altitude. Test conditions were double-blind. Subjects initially were screened with a medical history questionnaire, a 12-lead electrocardiogram, pulmonary function tests, anthropometric and body fat measurements, blood volume determinations, and a maximal aerobic capacity test. Each subject, after attaining the required altitude and ambient carbon monoxide level, performed the maximal aerobic capacity test (maximum VO_2) meeting required conditions to assure that a maximal level was attained. Blood samples were drawn prior to the aerobic capacity test; at workloads of 50 watts, 100 watts, 150 watts, and maximum; at the fifth minute of recovery; and prior to repressurization to sea level. Blood was analyzed for hemoglobin, hematocrit, plasma proteins, lactates, and carboxyhemoglobin. Carbon-monoxide-carboxyhemoglobin uptake rates were derived from the submaximal workloads. Maximum VO_2 was similar at 55 m and 1524 m, and decreased from the 55-m value by 4% at 2134 m and by 8% at 3048 m. Despite increases in carboxyhemoglobin, no additional significant decreases in maximal aerobic capacity were observed. With increasing carbon monoxide, a decrease in maximum VO_2 independent of altitude was observed. Carboxyhemoglobin concentrations at maximum VO_2 were highest at 55 m and lowest at 3048 m. Carboxyhemoglobin concentrations were lower in female subjects than in male subjects. Immediately prior to and at maximal workloads, carbon monoxide shifted into extravascular spaces and returned to the vascular space within five minutes after exercise stopped. The tests demonstrated that altitude hypoxia and carbon monoxide hypoxia act independently on the parameters of the maximal aerobic capacity test. Also demonstrated was a decrease in the carbon monoxide concentration to carboxyhemoglobin as altitude increased, which can be attributed to the decrease in driving pressure of carbon monoxide at altitude.

AU - Di Cera E

TI - Interaction of carbon monoxide with human hemoglobin: violation of Haldane's law under physiological conditions

SI - TOXBIB/89/143052

SO - Medicina (Firenze); Vol 8, ISS 2, 1988, P168-70

AU - Alderman BW

AU - Baron AE

AU - Savitz DA

TI - Maternal exposure to neighborhood carbon monoxide and risk of low infant birth weight

SI - TOXBIB/87/290433

SO - Public Health Rep; Vol 102, ISS 4, 1987, P410-4

AB - This case-control study investigated the potential association between ambient levels of carbon monoxide in a pregnant woman's neighborhood of residence and her chance of delivering a low birth weight infant. Low birth weight infants and normal birth weight infants were contrasted with respect to ambient levels of CO during the 3 months prior to delivery in the neighborhoods where their

mothers lived at birth. After adjustment for the confounding effects of maternal race and education, no association was present between higher CO exposure and higher odds of low birth weight. These data do not support a strong association between maternal exposure to neighborhood CO during pregnancy and odds of delivering a low birth weight infant. Further investigation of the effects of CO exposure on birth weight, with direct measurement of total CO exposure, is needed.

AU - Iastrebov VE

AU - Kustov VV

AU - Razinkin SM

TI - Short-term action of high carbon monoxide concentrations on the psychophysiological functions of a human operator

SI - TOXBIB/88/092199

SO - Kosm Biol Aviakosm Med; Vol 21, ISS 5, 1987, P47-50

AB - Experiments on volunteers, aged 26-40, demonstrated that a 10-minute exposure to carbon monoxide at a concentration of $900 \pm 20 \text{ mg/m}^3$ caused a significant decline of the quality of their operator's function. The task they performed was a 2-dimensional compensatory tracking task combined with mental arithmetic. Some of the test subjects showed symptoms of mild CO intoxication which preceded disorders in their work and were accompanied by an increase of HbCO to $10 \pm 0.57\%$. Such an exposure to CO should be regarded as hazardous, because it may increase the probability of erroneous actions, particularly of the flying personnel.

AU - Benignus VA

AU - Muller KE

AU - Barton CN

AU - Prah JD

TI - Effect of low level carbon monoxide on compensatory tracking and event monitoring

SI - TOXBIB/87/314823

SO - Neurotoxicol Teratol; Vol 9, ISS 3, 1987, P227-34

AB - Experiments by Putz et al. (19XX) concerning the effect of carbon monoxide (CO) exposure on compensatory tracking and monitoring in healthy young men were replicated. Task and procedural variables were reproduced as closely as practical. Subjects were exposed to either room air or 100 ppm CO. Mean carboxyhemoglobin (COHb) levels in the high CO exposure groups were 5.1% for Putz et al. (19XX) (70 ppm exposure), and 8.24% for the present study (100 ppm exposure). In both studies, elevated COHb produced a statistically significant increase over time in log mean absolute deviation scores (tracking error) with respect to control groups. The magnitude of the effect was smaller in the present study, perhaps because of subtle methodological or training differences between studies. The relationship between task difficulty and magnitude of CO-induced dysfunction remains unresolved. In contrast to Putz et al. (19XX), no statistically significant effect of COHb in monitoring behavior was found. The failure to replicate this feature of what may reflect the large differences in baseline performance, and higher variance in the present study.

AU - Hussein A

AU - Rottschäfer T

AU - von der Hardt H

TI - Transfer factor (diffusion capacity) of the lung for carbon monoxide: reference values for the inhalation method in children aged 7-18 years

SI - TOXBIB/87/260554

SO - Prax Klin Pneumol; Vol 41, ISS 5, 1987, P170-6

AU - Kustov VV

AU - Iastrebov VE

AU - Razinkin SM

TI - Data providing a basis for the maximum allowable concentration of carbon monoxide during short-term exposure

SI - TOXBIB/87/248188

SO - Gig Tr Prof Zabol, ISS 4, 1987, P34-6

AU - Fechter LD

AU - Mactutus CF

AU - Storm JE

TI - Carbon monoxide and brain development

SI - TOXBIB/87/065834

SO - Neurotoxicology; Vol 7, ISS 2, 1986, P463-73 (REF: 13)

AU - Dolan MC

TI - Carbon monoxide poisoning

Language: Eng

SO - Can Med Assoc J 1985 Sep 1;133(5):392-9

Unique Identifier: 85281876

AB - Carbon monoxide poisoning is a significant cause of illness and death. Its protean symptoms probably lead to a gross underestimation of its true incidence. Low levels of carbon monoxide aggravate chronic cardiopulmonary problems, and high levels are associated with cardiac arrhythmias and cerebral edema. Patients who survive acute poisoning are at risk of delayed neurologic sequelae. The measurement of carboxyhemoglobin levels does not reveal the tissue levels of carbon monoxide, but is useful in determining therapy. Treatment includes the monitoring and management of cardiac arrhythmias and oxygenation. Hyperbaric oxygenation is beneficial, but currently no definite criteria exist for its use.

AU - Ferguson LS

AU - Burke MJ

AU - Choromokos EA

TI - Carbon Monoxide Retinopathy

SO - Arch Ophthalmol; Vol 103, 1985, P66-67

AB - Recently, three family members with acute carbon monoxide intoxication resulting from a single accidental exposure were examined. The family group included a stepfather with a normal fundus, a mother with scattered superficial retinal hemorrhages, and her child with multiple large subinternal limiting membrane hemorrhages, peripapillary hemorrhages, severe venous tortuosity, and disc edema. All three had comparable carboxyhemoglobin levels and no evidence of hypertension, diabetes, or anemia. The different fundus presentations illustrated the variable clinical manifestations of carbon monoxide retinopathy. Early detection could prevent a lethal outcome.

AU - Goldmann RW

AU - Kindwall EP

TI - Adrenocortical function after acute carbon monoxide exposure in humans

SI - TOXBIB/85/224412

SO - Arch Environ Health; Vol 40, ISS 2, 1985, P88-90

AB - The effect of acute carbon monoxide (CO) exposure on plasma adrenocorticotrophic hormone (ACTH), renin activity (PRA), aldosterone, and cortisol levels was studied in patients approximately 80-90 min after removal from the scene of exposure. Nine patients had carboxyhemoglobin (COHb) levels below 15%. Seven patients had COHb levels that exceeded 15% (Group II). Plasma ACTH, cortisol, and aldosterone levels were significantly higher in Group II (elevated COHb). Plasma cortisol and aldosterone levels were appropriate for the levels of ACTH and PRA achieved. The conclusion was: (a) acute carbon monoxide poisoning leads to elevated plasma corticosteroid levels, and (b) the adrenal gland appears to function normally acutely after exposure to carbon monoxide.

AU - Zorn H

TI - Medical and biologic effects of carbon monoxide

SI - TOXBIB/86/261671

SO - Schriftenr Ver Wasser Boden Lufthyg; Vol 69, 1986, P177-9

AU - Britten JS

AU - Myers RA

TI - Effects of hyperbaric treatment on carbon monoxide elimination in humans

SI - TOXBIB/86/098283

SO - Undersea Biomed Res; Vol 12, ISS 4, 1985, P431-8

AB - A theoretical model of carbon monoxide elimination from the acutely poisoned individual is presented. The model is derived from a one-compartment system with the rate-limiting step that of alveolar ventilation, assuming equilibration of carbon monoxide and oxygen between alveolar gas and pulmonary capillary blood and incorporates the effect of the carboxyhemoglobin-oxyhemoglobin equilibrium in the pulmonary capillary. The model is applied to groups of patients treated for carbon monoxide intoxication both by conventional means and by hyperbaric medicine and to some animal studies found in the literature with satisfactory fit of data to the model. Finally, a number of factors responsible for the variability of CO elimination are discussed in terms of the model.

AU - Kuller LH

AU - Radford EP

TI - Epidemiological bases for the current ambient carbon monoxide standards

SI - TOXBIB/84/084494

SO - Environ Health Perspect; Vol 52, 1983, P131-9

AB - Carbon monoxide is widely distributed in the environment, and acute or chronic toxic effects may be of considerable public health significance. A review of the basis for current ambient standards is given. Mortality and morbidity studies have been negative or equivocal in relating carbon monoxide levels to health effects, but studies in human subjects with compromised coronary or peripheral circulation support an effect of acute exposure to CO at blood levels equivalent to about 20 ppm over several hours. It is possible that some of the cardiovascular effects of smoking may be related to the high levels of CO in cigarette smoke, but it has been difficult to isolate the contribution of CO independent of the effects of other smoke constituents.

AU - Gliner JA
AU - Horvath SM
AU - Mihevic PM
TI - Carbon monoxide and human performance in a single and dual task methodology
SI - TOXBIB/84/023567
SO - Aviat Space Environ Med; Vol 54, ISS 8, 1983, P714-7
AB - Does carbon monoxide (CO) exposure limit man's ability to time share two concurrent tasks? In our study 15 subjects underwent two different 2.5-hour exposures to either filtered air or to 100 ppm CO. They performed two tasks singly and in combination. The central task was a compensatory tracking task with three levels of difficulty, whereas the peripheral task was a signal detection task with three probabilities of signal occurrence. When HbCO levels reached 5% (during the last half hour of the exposure), performance on the peripheral signal detection task was altered. This decline in performance was demonstrated by a 6% decline in signals detected correctly (p less than 0.05). This decline in signals detected was found when the signal detection task was performed alone. These results suggested that exposure to CO decreased arousal and interacted with fatigue to produce decreases in performance.

AU - Mihevic PM
AU - Gliner JA
AU - Horvath SM
TI - Carbon monoxide exposure and information processing during perceptual-motor performance
SI - TOXBIB/83/236970
SO - Int Arch Occup Environ Health; Vol 51, ISS 4, 1983, P355-63
AB - This study examined the influence of exposure to ambient carbon monoxide resulting in final carboxyhemoglobin (COHb) levels of approximately 5.0% on the ability to process information during motor performance. Subjects ($n = 16$) performed a primary reciprocal tapping task and a secondary digit manipulation task singly or concurrently during a 2.5 hour exposure to room air (0 ppm CO) or 100 ppm CO. Five levels of tapping difficulty and two levels of digit manipulation were employed. Tapping performance was unaffected when COHb levels were as high as 5%. However, at this level of COHb it was noted that CO exposure interacted with task difficulty of both tasks to influence reaction time on the digit manipulation task. It was concluded that motor performance was not influenced by exposure to CO leading to COHb concentrations of 5%. Task difficulty was a significant factor mediating behavioral effects of CO exposure.

AU - Stupfel M
AU - Perramon A
AU - Demaria Pesce VH
AU - Merat P
AU - Gôurlet V
AU - Thierry H
TI - Genetic factors and acute carbon monoxide intoxication
SI - TOXBIB/82/249828
SO - Sci Total Environ; Vol 23, 1982, P189-96

AU - Kustov VV
AU - Litau VG
AU - Razinkin SM

TI - Combined action of carbon monoxide and total vibration on the body
SI - TOXBIB/82/262873
SO - Gig Tr Prof Zabol, ISS 6, 1982, P15-8

AU - Honigman B
AU - Cromer R
AU - Kurt TL
TI - Carbon monoxide levels in athletes during exercise in an urban environment
Language: Eng
SO - J Air Pollut Control Assoc 1982 Jan;32(1):77-9
Unique Identifier: 82098933

AU - Turino GM
TI - Effect of carbon monoxide on the cardiorespiratory system. Carbon monoxide toxicity: physiology and biochemistry
SI - TOXBIB/81/065142
SO - Circulation; Vol 63, ISS 1, 1981, P253A-259A (REF: 60)

AU - Whorton MD
TI - Carbon monoxide intoxication: a review of 14 patients.
Language: Eng
SO - JACEP 1976 Jul;5(7):505-9
Unique Identifier: 76241321
AB - In 14 cases of carbon monoxide poisoning, medical records were available for retrospective review in which blood samples for carboxyhemoglobin (COHgb) were obtained. Twelve victims (86%) were overcome while at work. Correlation of the clinical picture and COHgb saturation was not always possible although hypertension was not uncommon initially. On follow-up only three patients were mildly hypertensive. Skin or mucous membrane color changes were difficult to detect. Three cases are presented to illustrate factors in the diagnosis and possible sequelae.

AU - Stewart RD
AU - Baretta ED
AU - Platte LR
AU - Stewart EB
AU - Kalbfleisch JH
AU - Van Yserloo B
AU - Rimm AA
TI - Carboxyhemoglobin levels in American blood donors
Language: Eng
SO - JAMA 1974 Aug 26;229(9):1187-95
Unique Identifier: 74280869

AU - Stewart RD
AU - Newton PE
AU - Hosko MJ
AU - Peterson JE
TI - Effect of carbon monoxide on time perception

Language: Eng
SO - Arch Environ Health 1973 Sep;27(3):155-60
Unique Identifier: 73230028

AU - Stewart RD
AU - Peterson JE
AU - Fisher TN
AU - Hosko MJ
AU - Baretta ED
AU - Dodd HC
AU - Herrmann AA
TI - Experimental human exposure to high concentrations of carbon monoxide
Language: Eng
SO - Arch Environ Health 1973 Jan;26(1):1-7
Unique Identifier: 73070773

AU - Peterson JE
TI - Postexposure relationship of carbon monoxide in blood and expired air
Language: Eng
SO - Arch Environ Health 1970 Aug;21(2):172-3
Unique Identifier: 70237997

AU - Peterson JE
AU - Stewart RD
Absorption and elimination of carbon monoxide by inactive young men
Language: Eng
SO - Arch Environ Health 1970 Aug;21(2):165-71
Unique Identifier: 70237996

AU - Chance B
AU - Erecinska M
AU - Wagner M
TI - Mitochondrial responses to carbon monoxide toxicity
Language: Eng
SO - Ann N Y Acad Sci 1970 Oct 5;174(1):193-204
Unique Identifier: 72082770

3.2 Animal Studies

AU - Causey Z
AU - Moore-Cheatum L
AU - Singh J
TI - Alterations in fetal brain protein in protein-deprived and carbon monoxide exposed mice
SI - DART/T/94000799
SO - Teratology 1994 May;49(5):412

AB - Carbon monoxide (CO) is a deadly air pollutant gas. Everyone in modern society is at risk to CO exposure. Protein deficiency is fairly common in the diets of poor pregnant women. Experiments were conducted to estimate the fetal brain protein concentrations in CO-exposed and protein-deprived mice. Pregnant CD-1 mice were placed on diets of 27, 16, or 8% protein throughout gestation. The dams were exposed to 0 or 250 ppm of CO for six hours per day during the first two weeks of pregnancy. The dams were sacrificed on gestation day 18. Fetal brains were removed, weighed and prepared for protein estimation. Protein estimation was carried out by the New ICN Protein Determination Reagent. Fetal brain protein concentrations were related to the dietary protein levels and inversely related to the CO exposure levels. Further work is in progress.

AU - Hill M

AU - Moore-Cheatum L

AU - Singh J

TI - Carbon monoxide pollution alters maternal and placental hematology in protein deprived mice

SI - DART/T/94000779

SO - Teratology 1994 May;49(5):407

AB - Carbon monoxide (CO) pollution is of serious public health concern. When CO exposure combines with protein deficiency, its harmful effects are increased. Studies were conducted to determine the alterations in white blood cells (WBC), red blood cells (RBC), hematocrit (HCT), and hemoglobin (HGB) of maternal (M) and placental (P) blood in protein-deprived mice. Mated dams were placed on diets of 16, 8 or 4% protein throughout gestation. The dams were exposed to 0, 125, or 250 ppm of CO, for six hours per day for the first two weeks of pregnancy. Dams were sacrificed on gestation day 18 and M and P blood samples were collected for hematological estimation. The amounts of WBC and RBC in the M and P blood were related to CO exposure levels; the concentration of HGB in the M blood was also related to CO exposure levels. The amounts of WBC, RBC, and HGB in the P blood were related to dietary protein levels.

AU - Singh J

AU - Moore-Cheatum L

TI - Carbon monoxide pollution increases spontaneous abortion rate in protein-deficient mice

SI - DART/T/94000778

SO - Teratology 1994 May;49(5):407

AB - Carbon monoxide (CO) is one of the most commonly encountered air pollutants. Exposure to CO produces fetal mortality and malformations. Protein deficiency is wide spread in the diets of poor pregnant women. Experiments were carried out to estimate the rate of spontaneous abortions due to CO exposure in protein-deficient mice. Mated dams of CD-1 strain were maintained on diets of 27, 16, 8 or 4% protein throughout gestation. The dams were exposed to 0 (control), 65, 125 or 250 ppm of CO for six hours per day during the first week of pregnancy. The dams were killed on gestation day 18 and examined for spontaneous abortions. The rate of spontaneous abortions was related to the CO exposure levels and inversely related to the dietary protein levels. The rate was particularly high in the protein-deficient animals. The data may explain the reasons for decreasing rate of pregnancy in the American population.

AU - Benignus VA

AU - Annau Z

TI - Carboxyhemoglobin formation due to carbon monoxide exposure in rats

SI - TOXBIB/94/360430

SO - Toxicol Appl Pharmacol; Vol 128, ISS 1, 1994, P151-7

AB - The Coburn-Forster-Kane equation (CFKE) is a well-tested model for prediction of carboxyhemoglobin (COHb) formation due to carbon monoxide (CO) exposure in humans. A few relatively poorly tested attempts have been made to implement a CFKE for rats. Such an implementation is of interest because many experiments on the effects of CO in rats were done without measuring COHb. To extrapolate from rats to humans requires a rat version of the CFKE. Rats were exposed to 150, 250, 500, and 1000 ppm CO for up to 240 min. Blood gases and COHb were measured. A CFKE was implemented for rats by using parameters found in the literature and estimating them from the data. It was deduced from the blood-gas data that rats hyperventilate slightly as COHb increases. The blood-gas data were used to estimate ventilation and alveolar capillary oxygen partial pressure. The hyperventilation required an iterative solution to the CFKE. The iterative CFKE predictions were found to differ statistically from observations, but in explainable ways or in small amounts

AU - Maurice T

AU - Hiramatsu M

AU - Kameyama T

AU - Hasegawa T

AU - Nabeshima T

TI - Behavioral evidence for a modulating role of sigma ligands in memory processes. Reversion of carbon monoxide-induced amnesia

SI - TOXBIB/94/349130

SO - Brain Res; Vol 647, ISS 1, 1994, P57-64

AB - This study examined the effect of low doses of sigma ligands on amnesia induced in mice by successive carbon monoxide (CO) exposure. Mice were exposed three consecutive times to CO (10 ml/min, 30-50 s) at 38 degrees C. Spatial working memory impairment was investigated 5 days later by monitoring spontaneous alternation behavior in a Y-maze. Delayed amnesia was examined 7 days after CO exposure by using a step-down passive avoidance test. The preadministration of the sigma ligand 1,3-di-(2-tolyl) guanidine (DTG), at doses of 1 to 1000 µg/kg, s.c., 30 min before CO exposure did not affect the resulting amnesia in either test. However, when administered 30 min before the test, i.e., 5 or 7 days after CO exposure, this agent completely reversed the CO-induced decrease in alternation performance, at doses of 10 to 100 µg/kg. The same effect was observed with (+)-N-allylnormetazocine ([+]-SKF 10,047), at doses of 100 to 300 µg/kg, but not with (-)-SKF 10,047. DTG, at the same dose range that reversed the decrease in alternation, also totally reversed the CO-induced decrease in step-down latency in the passive avoidance test. The curve for these effects was bell-shaped; the effects were not observed at the dose of 1 µg/kg. Moreover, alpha-(4-fluorophenyl-2-pyrimidinyl)-1-piperazine butanol (BMY 14802), a putative sigma antagonist (1-10 µg/kg i.p.), did not affect CO-induced amnesia, but when simultaneously administered with DTG, it completely prevented its effect in both tests. (ABSTRACT TRUNCATED AT 250 WORDS)

AU - Maurice T

AU - Hiramatsu M

AU - Kameyama T

AU - Hasegawa T

AU - Nabeshima T

TI - Cholecystokinin-related peptides, after systemic or central administration, prevent carbon monoxide-induced amnesia in mice

SI - TOXBIB/94/238459

SO - J Pharmacol Exp Ther; Vol 269, ISS 2, 1994, P665-73

AB - The neuroprotective actions of cholecystokinin (CCK) peptides were investigated in a mouse hypoxia model, in which the animals were successively exposed to CO gas. Working memory impairment 5 days after CO exposure was examined by using a Y-maze test; delayed amnesia was examined 7 days after CO exposure, by using a step-down type passive avoidance test. Ceruletide (1-100 µg/kg, given s.c. 30 min before CO exposure) significantly prevented the CO-induced impairment of performance in both tests, the improvement being correlated with the severity of hypoxia. This severity was increased by maintaining the body temperature at 38 degrees C. Ceruletide was less effective when injected immediately after a single CO exposure. The order of potency of the CCK-peptides administered systemically was: ceruletide > CCK-8S > CCK-8NS >> CCK-4. Ceruletide (0.03-0.3 mg/mouse) and CCK-8S (0.03-1 mg/mouse) prevented CO-induced amnesia after i.c.v. administration. Under all experimental conditions, dizocilpine (MK-801, [+]-5-methyl-10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5,10-imine maleate, 500 µg/kg s.c. or 10 micrograms/mouse i.c.v.) prevented completely the CO-induced amnesia. The protective effects of systemic ceruletide were blocked, partially but significantly, by the preadministration of L-364,718 (3S-[-]-N-[2,3-dihydro-1-methyl-2-oxo-S-phenyl-1H-1,4-benzodiazepine-3-yl]-1H-indole-2-carboxamide, 1-10 µg/kg i.p.), a selective CCK-A receptor antagonist. L-365,260 ([3R-[+]-2,3-dihydro-1-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepine-3-yl]-N' - [3-methyl-phenyl] urea), a CCK-B antagonist, also decreased ceruletide-induced protection. (ABSTRACT TRUNCATED AT 250 WORDS)

AU - Penney DG

AU - Giraldo AA

AU - Van Egmond EM

TI - Coronary vessel alterations following chronic carbon monoxide exposure in the adult rat

SI - TOXBIB/94/209551

SO - J Appl Toxicol; Vol 14, ISS 1, 1994, P47-54

AB - Adult male rats were exposed to 500 ppm CO continuously for 30 days, while litter-mate controls remained in room air (AIR). Heart weight-to-body weight ratio and hematocrit were increased significantly. Right ventricle (RV) free wall thickness was increased significantly, as was right to left heart diameter and average heart diameter. Cross-sectional areas of the left ventricle (LV) free wall, interventricular septum (S) and RV midway between the apex and base were increased significantly. Morphometric analysis of the CO-exposed and AIR hearts revealed no significant differences in the number of small (27-114 microns) or larger (> 114 microns) blood vessels in any region; however, a trend was noticed toward an increased number of the smaller vessels, both arterioles and venules, in the CO-exposed rats. The larger arteries in the S and RV were significantly larger in the CO-exposed rats. A significant overall effect of CO was found on larger artery diameter across all heart regions, consistent with the appearance of heart radiographs taken. No differences in the diameter of the small vessels were noticed in any region of the heart between the CO-exposed and AIR rats. The vessel cross-sectional area of the larger vessels tended to be increased in all regions of the heart. The cross-sectional area of the large arteries in the LV was increased significantly. Arterial wall thickness was decreased significantly in RV and there was a significant overall effect of CO in decreasing wall thickness and the ratio of wall thickness-to-vessel luminal diameter in these vessels. No vascular

pathology was observed. The results of this study suggest changes in coronary vessel architecture during chronic CO-induced cardiac hypertrophy and are consistent with earlier hemodynamic and morphometric studies of CO-exposed hearts.

AU - Tucker A

AU - Penney DG

TI - Pulmonary vascular responsiveness in rats following neonatal exposure to high altitude or carbon monoxide

SI - TOXBIB/94/109359

SO - Exp Lung Res; Vol 19, ISS 6, 1993, P699-713

AB - Exposure of adult and neonatal rats to high altitude increases pulmonary vascular responsiveness during the exposure. A study was undertaken to determine if a short exposure of neonatal rats to either high-altitude or carbon monoxide (CO) hypoxia would cause persistent alterations in pulmonary vascular responsiveness postexposure. One-day-old male Sprague-Dawley rats were obtained as 16 litters of 10-12 pups each. At 2 days of age, 4 litters were exposed to CO (500 ppm) for 32 days, and 4 litters were exposed to ambient air (AIR) in Detroit (200 m). Another 4 litters were exposed to 3500 m altitude (ALT) in a chamber for 32 days, and 3 litters were exposed to ambient conditions in Fort Collins (CON, 1524 m). After the exposures, all rats were maintained at 1524 m. At 2, 40, 76, and 112 days postexposure, lungs were isolated and perfused with Earle's salt solution (+Ficoll, 4 g%). Pulmonary vascular responsiveness was assessed by dose responses to angiotensin II (AII, 0.025-0.40 μ g) and acute hypoxia (3% O₂ for 3 min). AII responses were higher in ALT vs CON rats at all ages, but no differences were noted between CO and AIR rats. Acute hypoxic responses were higher in ALT versus CON rats at 2 and 40 days postexposure, but no differences were noted between CO and AIR rats. Baseline pulmonary vascular resistance and pulmonary arterial pressure (in isolated lungs) were higher in ALT rats at all four ages compared to the other three groups. Both the ALT and CO rats displayed hypertrophy of the right ventricle (RV) and the left ventricle (LV) at the termination of treatment and elevated hematocrit. LV hypertrophy and polycythemia regressed with time, but RV hypertrophy remained significant in the ALT rats through 112 days postexposure. The results indicate that neonatal exposure to ALT, but not CO, causes a persistent increase in pulmonary vascular responsiveness and RV hypertrophy for at least 112 days after termination of the exposure.

AU - Carratu MR

AU - Renna G

AU - Giustino A

AU - De Salvia MA

AU - Cuomo V

TI - Changes in peripheral nervous system activity produced in rats by prenatal exposure to carbon monoxide

SI - DART/M/93378553

SO - Arch Toxicol 1993;67(5):297-301

AB - The present experiments were designed to investigate whether alterations of peripheral nervous system activity may be produced in male Wistar rats by prenatal exposure (from day 0 to day 20 of pregnancy) to relatively low levels of CO (75 and 150 ppm). The voltage clamp analysis of ionic currents recorded from sciatic nerve fibres showed that prenatal exposure to CO produced modifications of sodium current properties. In particular, in 40-day-old rats exposed to CO (75 and 150 ppm) during gestation, the inactivation kinetics of transient sodium current were significantly slowed. Analysis of the potential dependence of steady-state Na inactivation, h_{∞} (V), showed

that the percentage of the maximum number of activable Na channels at the normal resting potential (-80 mV) was increased to approximately 85% in CO-exposed rats. Moreover, the voltage-current relationship showed a negative shift of sodium equilibrium potential in CO treated animals. In 270-day-old CO-exposed rats, parameters of sodium inactivation were not significantly modified; the reversal potential was still lower with respect to controls. The results indicate that prenatal exposure to mild CO concentrations produces reversible changes in sodium inactivation kinetics and irreversible change in sodium equilibrium potential. These alterations could reflect CO influence on the rate of ion channel development.

AU - Di Giovanni V

AU - Cagiano R

AU - De Salvia MA

AU - Giustino A

AU - Lacomba C

AU - Renna G

AU - Cuomo V

TI - Neurobehavioral changes produced in rats by prenatal exposure to carbon monoxide

SI - DART/M/93364723

SO - Brain Res 1993 Jul 9;616(1-2):126-31

AB - Wistar female rats were exposed to relatively mild concentrations of carbon monoxide (75 and 150 ppm) from day 0 to day 20 of pregnancy. The results show that prenatal exposure to CO (150 ppm) produced a significant reduction in the minimum frequency of ultrasonic calls emitted by rat pups removed from their nest. Moreover, a significant decrease in the responsiveness (rate of calling) to a challenge dose of diazepam (0.25 μ g/kg) was found in male pups exposed to CO (150 ppm) during gestation. Prenatal CO (75 and 150 ppm) did not significantly affect locomotor activity or D-amphetamine-induced hyperactivity in either 14- and 21-day-old animals. Furthermore, adult male rats exposed to this chemical (150 ppm) during gestation exhibited significant alterations in the acquisition of an active avoidance task. CO-induced learning disruption does not seem to be linked to changes in the emotionality of animals. These findings suggest that gestational exposure to CO induces in rat offspring both short- and long-term behavioral changes characterized by altered ontogeny of emotional responsiveness to environmental challenges and by learning impairment.

AU - Singh J

AU - Moore-Cheatum L

TI - Carbon monoxide pollution reduces pregnancy rate in protein deficient mice

SI - DART/T/93001087

SO - Teratology 1993 May;47(5):404-5

AB - Carbon monoxide (CO) is produced by incomplete combustion of carbon in fuels. Everyone in modern society is at risk of CO exposure. Protein deficiency is wide spread in the diets of poor pregnant women. Experiments were conducted to estimate the rate of pregnancy in protein deficient and CO exposed mice. Mated dams of CD-1 mice were maintained on diets of 16 (control), 8 or 4% protein throughout gestation. The dams were exposed to 0 (control) or 65 ppm of CO for 6 hours per day during the first trimester of pregnancy. The pregnancy status of dams was examined on gestation day 18. The rates of pregnancy in the 8 and 4% dietary protein dams were significantly lower than that of the 16% dietary protein dams. The rate of pregnancy in the 65 ppm CO exposed dams was also significantly lower than that of the control exposed dams. The rate of pregnancy in the 8% dietary protein dams exposed to 65 ppm CO was also significantly lower than that of the control exposed

dams. The data indicate that gestational inhalation of CO pollution at low levels reduces the rate of pregnancy in protein deficient mice. Special groups at risk may include drug abusers, cigarette or marijuana smokers, and humans exposed to indoor or outdoor CO pollution who experience protein deficiency during gestation.

AU - Katzman GM

AU - Penney DG

TI - Electrocardiographic responses to carbon monoxide and cyanide in the conscious rat

SI - TOXBIB/94/024955

SO - Toxicol Lett; Vol 69, ISS 2, 1993, P139-53

AB - Carbon monoxide (CO) and cyanide (CN), commonly found in exhaust fumes and smoke, act as hypoxic agents in eliciting morbid and lethal effects. This study explored the effects of these two toxicants on the ECG in a controlled and well-characterized animal model. Levine-prepared awake female rats were treated with 1500 and 2400 ppm CO for 90 min, CN at 4 $\mu\text{g/kg}$, or 1500 ppm CO plus 4 $\mu\text{g/kg}$ CN. As in past studies, CO initially induced hyperglycemia and many-fold increases in blood lactate concentration, and rebound increases in blood glucose during recovery. CN produced hyperglycemia, however, no glucose rebound, nor a significant increase in lactate was noted. CN plus 1500 ppm CO produced glucose changes similar to that of CO alone. CO exposure also induced hypothermia and hypotension, while CN produced little change in these parameters. CO increased heart rate, while CN tended to decrease heart rate. PR interval was increased significantly 4.5-17.0 ms by exposure to CO, with or without combination with CN, while CN alone produced minimal change in the PR interval. QT interval was increased up to 20 ms by exposure to CO, with or without combination with CN. CN alone produced no change in the QT interval. T wave duration was increased up to 22.5 ms by exposure to 1500 ppm CO, with or without combination with CN. CN alone produced minimal changes in T wave duration. No changes occurred in duration of the (Q)RS complex or of the R wave. QT interval lengthening was positively correlated with the decrease in systolic blood pressure (0-30 min, $r = 0.657$, $P < 0.05$; 0-60 min, $r = 0.704$, $P < 0.05$). Hypothermia was correlated with increase in lactate concentration ($r = 0.73$, $P < 0.05$) and with decrease in blood pressure ($r = 0.69$, $P < 0.05$). No correlation between body temperature and QT interval was observed. The results indicate that CO at the concentrations used in the Levine-prepared rat has major effects on the ECG in slowing AV conduction and ventricular repolarization. In contrast, CN at 4 mg/dl has little or no effect on either conduction or repolarization in this animal model. These findings are discussed in light of past animal and human studies.

AU - Penn A

TI - Determination of the atherogenic potential of inhaled carbon monoxide

SI - TOXBIB/94/000529

SO - Res Rep Health Eff Inst, ISS 57, 1993, P1-20; discussion 21-30

AB - The effects of chronic exposure to moderate levels of carbon monoxide upon the augmentation of arteriosclerotic plaque development were investigated in a series of in vivo studies in the cockerel (young rooster). This animal model has been well-characterized, especially regarding the role of environmental agents in exacerbating early stages of plaque development. Cockerels injected with subtumorigenic doses of carcinogens exhibit markedly accelerated development of aortic arteriosclerotic plaques. Inhalation of mainstream smoke from two packs of cigarettes (100 minutes/day for 16 weeks) causes small but statistically significant increases in plaque size. As is the case with many animal models of plaque development, raised fat-proliferative plaques also appear in these animals following cholesterol feeding. Carbon monoxide is a ubiquitous pollutant in urban environments,

where it is derived largely from mobile sources and cigarette smoke. Exposure to chronically elevated carbon monoxide levels has been implicated in a number of health-related problems. Whether such exposure plays a role in the development of arteriosclerosis has not been determined conclusively. In the present study, three questions were posed: 1) Will inhaled carbon monoxide at levels of 50 to 200 parts per million (ppm) (two hours/day for 16 weeks) be sufficient to augment arteriosclerotic plaque development in cockerels, in the absence of other plaque-promoting agents? 2) Will the inhalation of 100 ppm carbon monoxide (two hours/day for 16 weeks), concomitant with the feeding of low levels (0.1%) of cholesterol, yield larger plaques than those obtained with either of these agents administered alone? 3) Will inhalation of 100 ppm carbon monoxide (two hours/day for 11 or 22 weeks), by cockerels in whom plaques have already appeared, further augment plaque development? Cockerels were exposed to carefully regulated levels of carbon monoxide in stainless-steel and Plexiglas dynamic exposure chambers. The volume percentage of plaques in the wall of the abdominal aorta of each exposed and control animal was determined by a point-counting method. Chronic inhalation of carbon monoxide at levels as high as 200 ppm did not affect augmentation of arteriosclerotic plaque development. (In separate studies involving inhalation of 200 ppm carbon monoxide, carboxyhemoglobin levels 10 minutes after exposures ended were 11% to 12%.) When administered at the same time that plaque development was being promoted by cholesterol feeding, carbon monoxide had no further effect upon plaque development. (ABSTRACT TRUNCATED AT 400 WORDS)

AU - Penney DG

AU - Formolo JM

TI - Carbon monoxide-induced cardiac hypertrophy is not reduced by alpha- or beta-blockade in the rat

SI - TOXBIB/93/318271

SO - Toxicology; Vol 80, ISS 2-3, 1993, P173-87

AB - The stimulus for carbon monoxide-induced cardiac hypertrophy was investigated. Two experiments were carried out in which adult male Sprague-Dawley rats were exposed continuously to 700 ppm CO for 30 days (CO) or inhaled room air (Air). In each experiment, two-thirds of the rats received either the beta-1-adrenergic blocker, atenolol, or the alpha-1 adrenergic blocking agent, prazosin, in the food daily, at low and high doses. Systolic blood pressure (SBP) was significantly lowered (20-25 mmHg) by CO alone. Atenolol alone lowered SBP, but only at the high dose. Low dose and particularly high dose atenolol, lowered SBP even more in the CO rats. Prazosin lowered SBP, particularly at the high dose and further lowered SBP in the CO rats. Heart rate was significantly lowered by atenolol and prazosin alone at both doses in the Air rats. Heart rate remained the same or was slightly elevated by CO exposure. Heart rate in the presence of CO was significantly depressed by prazosin, but not by atenolol. Carbon monoxide alone resulted in 30-43% and 18-25% weight increases in right ventricle free-wall (RV) and left ventricle + septum (LV+S), respectively, relative to untreated controls. Neither low nor high dose prazosin significantly decreased RV and LV+S weights in the CO rats. Low dose atenolol failed to alter RV and LV+S weights in the CO rats; however, high dose atenolol, significantly ($P < 0.01$) increased RV weight in the CO rats. Right ventricle weight was positively correlated with SBP lowering by CO and/or atenolol, or prazosin. Carbon monoxide exposure increased lung/body weight ratio; atenolol, but not prazosin, attenuated this effect. Hematocrit increased from 50% in the Air to 77% in the CO rats; it was unaltered by prazosin or atenolol treatment. Thus, CO-induced cardiac hypertrophy develops in spite of lowered SBP (i.e. lowered LV afterload), and the blockade of either alpha or beta-1 receptors. It is suggested that increased ventricular preload caused by atenolol and prazosin is directly responsible for the cardiac hypertrophy, regardless of the ameliorating effects of decreased inotropicity and heart rate produced by the adrenergic blocking agents. The results suggest the potentially powerful role of enhanced preload

in driving myocardial hypertrophy.

AU - Leichter J

TI - Fetal growth retardation due to exposure of pregnant rats to carbon monoxide

SI - DART/T/94000288

SO - Biochemical Archives 1993;9:267-72

AB - To determine whether retarded fetal growth caused by maternal cigarette smoke exposure is due mainly to the carbon monoxide content in smoke, pregnant rats were exposed to carbon monoxide daily for a 2-hour period throughout gestation. The concentration of carbon monoxide was between 1100 and 1200 ppm. Appropriate pair-fed and ad libitum control animals were included to separate the effect of carbon monoxide on fetal growth from maternal underfeeding. Body weights of fetuses exposed to carbon monoxide were significantly lower than those of the pair-fed and ad libitum controls. However, the difference in fetal body weight between the pair-fed and ad libitum controls was not significant. Litter size was not significantly different among the three groups. The carbon monoxide exposed dams had significantly higher hematocrit values than the other two groups. The results of this study indicate that carbon monoxide is probably the primary constituent of cigarette smoke responsible for fetal growth retardation.

AU - Giustino A

AU - Cagiano R

AU - Carratu MR

AU - De Salvia MA

AU - Panaro MA

AU - Jirillo E

AU - Cuomo V

TI - Immunological changes produced in rats by prenatal exposure to carbon monoxide

SI - DART/M/94159521

SO - Pharmacol Toxicol 1993 Nov;73(5):274-8

AB - Wistar female rats were exposed to relatively mild concentrations of carbon monoxide (CO) (75 and 150 ppm) from day 0 to day 20 of pregnancy. The results show that splenic macrophage phagocytosis of *Candida albicans* was significantly decreased in 15- and 21-day old male rats exposed to CO (150 ppm) during pregnancy. Moreover, splenic macrophage killing was significantly reduced in 15-day old male pups prenatally exposed to 75 and 150 ppm of CO. Prenatal CO (150 ppm) significantly decreased splenic macrophage O₂-release in both 15- and 21-day old pups. CO-induced alterations in the immune system were not observed in 60-day old rats. These findings indicate that gestational exposure to relatively mild concentrations of CO induces in rat offspring reversible immunological changes characterized by an altered splenic macrophage function.

AU - Wittenberg BA

AU - Wittenberg JB

TI - Effects of carbon monoxide on isolated heart muscle cells

SI - TOXBIB/94/206473

SO - Res Rep Health Eff Inst, ISS 62, 1993, P1-12; discussion 13-21

AB - By sequestering intracellular myoglobin of cardiac muscle cells in the nonfunctioning carboxymyoglobin form, carbon monoxide blocks myoglobin-facilitated diffusion of oxygen, as well as

myoglobin-mediated oxidative phosphorylation. Here, the hypothesis is that carbon monoxide blockade of myoglobin function may be responsible at the cellular level for a component of the cardiotoxicity of carbon monoxide observed during exercise. Suspensions of isolated rat cardiac myocytes were held in near steady states of oxygen pressure near the intracellular partial pressure of oxygen of the working heart (2 to 5 torr) and near the end-venous partial pressure of oxygen (20 torr). These suspensions were exposed to CO at low pressure (0.07 to 70 torr; 90 to 90,000 parts per million). The fraction of intracellular carboxymyoglobin, determined spectrophotometrically, was in good agreement with the fraction predicted from the ratio of carbon monoxide partial pressure to oxygen partial pressure. The effects observed were related to the fraction of intracellular myoglobin bound to CO. At physiological oxygen pressures no greater than 5 torr, after sequestration of approximately 50% of the myoglobin, steady-state oxygen uptake decreased significantly and was significantly less than the respiration of cell groups for which the fraction of carboxymyoglobin was 0% to 40%. When respiration is diminished, the rate of aerobic adenosine triphosphate synthesis (oxidative phosphorylation) also decreases. As in the whole heart, cytoplasmic adenosine triphosphate concentration in isolated heart cells is controlled at a constant level by the creatine phosphokinase equilibrium. When adenosine triphosphate utilization is unchanged, a sensitive monitor of the decreased adenosine triphosphate synthesis is the ratio of phosphocreatine to adenosine triphosphate. When carboxymyoglobin was at least 40% of the total intracellular myoglobin, the ratio of phosphocreatine to adenosine triphosphate in carbon monoxide-treated heart cells was significantly lower than that in control cells from the same preparation. Thus, the study concluded that sequestering intracellular myoglobin as carboxymyoglobin significantly decreased the rate of oxidative phosphorylation of isolated cardiac myocytes. It is estimated that intracellular myoglobin-dependent oxidative phosphorylation will be inhibited when approximately 20% to 40% of the arterial hemoglobin in the whole animal is carboxyhemoglobin.

AU - Packianathan S

AU - Cain CD

AU - Stagg RB

AU - Longo LD

TI - Ornithine decarboxylase activity in fetal and newborn rat brain: responses to hypoxic and carbon monoxide hypoxia

SI - DART/M/94139035

SO - Brain Res Dev Brain Res 1993 Nov 19;76(1):131-40

AB - In response to acute maternal hypoxia, ornithine decarboxylase (ODC) activity increased significantly in fetal rat brain, peaking at 4 hours. This increase was associated with increased ODC mRNA and elevated polyamine concentrations. To correlate this response with development, ODC activity was measured in the rat from gestational day E 17 to postnatal day P 10. The extent hypoxia induces increased ODC activity in adult rat brains and whether the response to chronic hypoxia differed from that to acute hypoxia were also examined. To test the hypothesis that this increased activity is due to hypoxic hypoxia per se, pregnant dams were exposed to inspired carbon monoxide concentrations ranging from 150 to 1000 ppm and ODC activity was assayed in the fetal brain 4 hours later. In the fetus, ODC activity was elevated on E 17 in the cerebrum and cerebellum. It declined gradually to about one-tenth E 17 levels by E 21 and remained low thereafter, except for a postnatal elevation in the cerebellum on P 3. In response to 10.5% O₂, in the 3-day-old rat, ODC activity peaked between 2 and 3 hours of hypoxia, increasing 3-fold in the hippocampus and 2-fold in cerebellum. Similar increases were seen in the hypoxic adult rat brain. In inspired oxygen dose-response studies, exposure of P 3 rat pups to 13.25% O₂ for 2.5 h produced a 1.5-fold increase in ODC activity; 10.5% O₂ produced a

2-3-fold increase, while in response to 9% O₂, ODC activity remained at baseline levels. With maternal CO-hypoxia, ODC activity increased in the fetal brain at 4 hours, as seen with hypoxic-hypoxia. For example, in hippocampus, ODC activity doubled at 500 ppm and tripled at 600 ppm. The conclusion: 1) apparently, the ability to respond thus is not lost as the animal ages and may represent an important cellular response to acute hypoxia; 2) the increase in hypoxic-induced ODC activity is relative to the already elevated activity seen from E 17 to E 20; a vast reserve for the induction of fetal ODC activity probably exists and may indicate the importance of this enzyme during this time frame for differentiation and growth promotion; and 3) the CO-hypoxia studies suggest that some aspects of the cellular responses to CO- and hypoxic-hypoxia are similar.

AU - Singh J

AU - Aggison L Jr

AU - Moore-Cheatum L

TI - Teratogenicity and developmental toxicity of carbon monoxide in protein-deficient mice

SI - DART/M/94024698

SO - Teratology 1993 Aug;48(2):149-59

AB - Experiments were carried out to determine the teratogenicity and developmental toxicity of carbon monoxide (CO) in mice fed protein-deficient diets. Pregnant CD-1 mice were fed 27 (control), 16, 8, or 4% protein diets throughout gestation and each group was exposed to 0 (control), 65, 125, 250, or 500 ppm of CO from gestation days 8-18. The CO exposure was continuous except for daily watering, feeding, or cage changing. The animals were killed on gestation day 18. Pregnancy status of the dams was examined. Fetuses were examined for gross and skeletal malformations. The percentages of dead or resorbed fetuses and of grossly malformed fetuses per litter were related to the CO exposure levels and inversely related to the dietary protein levels. All levels of CO and 8 or 4% protein diets significantly decreased the fetal weight of normal fetuses. The most commonly seen gross malformations were brachygnathia accompanied by protruding tongue, microstomia, microcephaly, open mouth, or open eyes. Most of the grossly malformed fetuses also had dry, bleached and wrinkled skin. An increased incidence of skull (interparietal or supraoccipital), and jaw (mandible or premaxilla) malformation; wavy ribs and scoliosis of spine; and limb unossifications were observed in the litters of dams fed protein-deficient diet and all levels of CO exposure. Malformed litters in each protein diet were related to CO exposure levels. The data suggest that CO is teratogenic under protein-deficient conditions. Protein deficiency had additive effect on CO teratogenicity and synergistic effect on fetal mortality. Special groups at risk may include cigarette or marijuana smokers and malnourished or undernourished populations.

AU - Penney DG

AU - Giraldo AA

AU - Van Egmond EM

TI - Chronic carbon monoxide exposure in young rats alters coronary vessel growth

SI - TOXBIB/93/274705

SO - J Toxicol Environ Health; Vol 39, ISS 2, 1993, P207-22

AB - The goal of this study was to determine whether chronic monoxide exposure in the developing heart produces long-lasting coronary vasculature alterations. One-day-old male rat pups were exposed to 500 ppm CO continuously for 30 days, while littermate controls remained in room air (AIR). At 61 and 110 days of age, hearts were removed, perfusion fixed, x-rayed, and processed for analysis of coronary vessel architecture. Body weight (BW) and heart weight (HW) increased with age; the ratio of HW/BW decreased. No differences were observed in HW and ventricular dimensions at either age

due to prior CO exposure. Morphometric analysis of the fixed hearts from CO-exposed and AIR rats revealed no significant individual group differences in the number of small (27-114 microns) or larger (> 114 microns) vessels in any heart region. The septum (S) in CO rats was an exception: More small veins were found at 61 days of age and more large veins at 110 days of age. A significant increase was seen in the number of small arteries at both ages in the CO rats across all heart regions, and in the smaller veins at 61 days of age. The large vessels in the S at 61 days of age had a significantly greater diameter in CO compared to AIR rats. This fact was also true for the large arteries in the S and right ventricle (RV) of the 110-day-old rats. Taking all heart regions together, the large arteries in CO rats were larger than in AIR rats. Previous CO exposure significantly increased large artery and total cross-sectional area in the S and RV at 61 days of age, and in RV at 110 days of age. Total cross-sectional area of veins in the S was also increased. Taking all heart regions together, CO significantly increased small artery cross-sectional area at 61 days of age, and small, large, and total artery cross-sectional area at 110 days of age. With one exception (small veins, 110 days of age), no effect was noted of CO on vein cross-sectional area. These changes resulted in the percentage of total cross-sectional area contributed by the larger vessels to increase. Pathological examination showed nothing abnormal. The results suggest profound and persistent changes in coronary vessel architecture following chronic neonatal CO exposure.

AU - Ludbrook GL

AU - Helps SC

AU - Gorman DF

AU - Reilly PL

AU - North JB

AU - Grant C

TI - The relative effects of hypoxic hypoxia and carbon monoxide on brain function in rabbits

SI - TOXBIB/93/088293

SO - Toxicology; Vol 75, ISS 1, 1992, P71-80

AB - New Zealand white rabbits were exposed to control conditions (n = 11), or to either a progressive hypoxic hypoxia produced by dilution of oxygen (O₂) with nitrogen (n = 10) or a 1% carbon monoxide (CO) admixture for 15 min (n = 11). Both exposures caused a significant increase in cerebral blood flow (CBF) of up to 300%, so that O₂ delivery to the brain was unchanged. In the hypoxia group, a cortical somatosensory evoked response (CSER) was unaffected until the arterial O₂ tension was below 20 mmHg. At this time, the rabbits became hypotensive, O₂ delivery to the brain decreased dramatically and the CSER could not be elicited. In contrast, despite the maintenance of O₂ delivery to the brain during and after the CO exposure, the CSER voltages were halved during the exposure and only recovered to about 80% of baseline subsequently. The conclusion is that primary toxicity of CO to the brain in rabbits is not due to a reduction in O₂ delivery.

AU - Penn A

AU - Currie J

AU - Snyder C

TI - Inhalation of carbon monoxide does not accelerate arteriosclerosis in cockerels

SI - TOXBIB/93/076878

SO - Eur J Pharmacol; Vol 228, ISS 2-3, 1992, P155-64

AB - The effects of chronic exposure to moderate levels of carbon monoxide (CO) upon the augmentation of arteriosclerotic plaque development were investigated in a series of in vivo studies. Cockerels were exposed to carefully regulated CO levels in dynamic exposure chambers. The plaque

volume percentage in the aortic walls of experimental and control animals was determined by point-counting. Chronic CO inhalation, at levels up to 200 ppm, did not stimulate arteriosclerotic plaque development (at 200 ppm CO, carboxyhemoglobin (COHb) levels 10 min after exposures ended were 11-12%). When administered concomitantly with cholesterol feeding, CO did not augment plaque development. When administered after either carcinogen-associated or diet-promoted plaque size increases had occurred, CO elicited no further plaque size increases. Thus, in this animal model, daily exposures to moderately high CO levels were without discernable effect upon arteriosclerotic plaque development, although high COHb levels were attained.

AU - Doolette DJ

AU - Kerr DI

TI - Comparison of carbon monoxide and nitrogen induced effects on synaptic transmission in the rat hippocampal slice

SI - TOXBIB/93/025806

SO - Neurosci Lett; Vol 138, ISS 1, 1992, P9-13

AB - A comparison has been made of the effects of carbon monoxide (CO) or nitrogen (N₂) exposure on synaptic transmission in the hippocampal slice. CA1 field potentials, evoked by Schaffer collateral stimulation, were unaffected by superfusion of slices with artificial cerebral spinal fluid (ACSF) equilibrated with either 15% CO or 15% N₂ for 120 min. However, superfusion with hypoxic ACSF equilibrated with either 85% CO or 85% N₂ caused a rapid depression of synaptic transmission. Reperfusion with control ACSF following 30 min hypoxia led to recovery of evoked responses and a slight hyperexcitability. In the hippocampal slice, synaptic transmission, as assessed by input/output curves, was not different during or following hypoxia induced by exposure to CO or N₂. In the short term, CO is not toxic.

AU - Hiramatsu M

AU - Koide T

AU - Ishihara S

AU - Shiotani T

AU - Kameyama T

AU - Nabeshima T

TI - Involvement of the cholinergic system in the effects of nefiracetam (DM-9384) on carbon monoxide (CO)-induced acute and delayed amnesia

SI - TOXBIB/93/011541

SO - Eur J Pharmacol; Vol 216, ISS 2, 1992, P279-85

AB - The effects of N-(2,6-dimethylphenyl)-2-(2-oxo-1-pyrrolidinyl)-acetamide (DM-9384, nefiracetam), a cyclic derivative of GABA, were investigated in the carbon monoxide (CO)-induced amnesia model in mice using the passive avoidance task. Memory deficiency occurred when mice were exposed to CO before memory was completely consolidated after training (acute amnesia), at 7 days before training and 7 days after training (delayed amnesia). DM-9384 prolonged the step-down latency in mice with CO-induced amnesia. Scopolamine blocked the anti-amnesic effect of DM-9384 on delayed amnesia that had been induced by pre- or post-training exposure to CO. Bicuculline had a tendency to antagonize the anti-amnesic effect of DM-9384, but this tendency was not significant. Under these conditions, no significant change in the activity of choline acetyltransferase and glutamic acid decarboxylase was observed in the frontal cortex, striatum, and hippocampus. These results suggest that DM-9384 potentiates cholinergic neuronal function and that it may modify acquisition or consolidation of memory.

AU - Singh J

AU - Smith CB

AU - Moore-Cheatum L

TI - Additivity of protein deficiency and carbon monoxide on placental carboxyhemoglobin in mice

SI - DART/M/92411312

SO - Am J Obstet Gynecol 1992 Sep;167(3):843-6

AB - OBJECTIVES: The purpose of the study was to estimate maternal and placental carboxyhemoglobin in protein-deficient and carbon monoxide-exposed mice. STUDY DESIGN: Pregnant CD-1 mice were placed on diets containing 27% (control), 16%, 8%, or 4% protein on gestation day 1. The dams were exposed to carbon monoxide concentrations of 0 (control), 65, 125, 250, or 500 ppm from gestation days 8 to 18. The dams were killed on gestation day 18, and blood samples were collected from the maternal hearts and placentas for carboxyhemoglobin determination. RESULTS: Maternal carboxyhemoglobin levels were related to the carbon monoxide exposure levels and were not affected by protein deficiency. Placental carboxyhemoglobin levels were higher than maternal carboxyhemoglobin levels, were related to carbon monoxide exposure levels, and were inversely related to dietary protein levels. CONCLUSION: The data suggest that maternal protein deficiency enhances the placental carboxyhemoglobin levels resulting from carbon monoxide exposure and exacerbates hypoxic conditions for the developing fetus. Special groups at risk may include drug abusers and cigarette or marijuana smokers.

AU - Brown SD

AU - Piantadosi CA

TI - Recovery of energy metabolism in rat brain after carbon monoxide hypoxia

SI - TOXBIB/92/147886

SO - J Clin Invest; Vol 89, ISS 2, 1992, P666-72

AB - Carbon monoxide (CO) may inhibit mitochondrial electron transport in the brain and increase the toxic effects of the gas. This hypothesis was investigated in anesthetized rats during CO exposure and recovery at either normobaric or hyperbaric O₂ concentrations. During exposure and recovery, the oxidation level of cerebrocortical cytochrome c oxidase was measured by differential spectroscopy and biochemical metabolites known to reflect aerobic energy provision in the brain. CO exposure (HbCO = 71 +/- 1%) significantly decreased blood pressure and cytochrome oxidation level. Cerebral ATP was maintained while lactate/pyruvate, glucose, and succinate rose, and phosphocreatine (PCr) fell, relative to control (P less than 0.05). Intracellular pH (pHi) calculated from the PCr equilibrium also declined during the exposures. During recovery, HbCO fell more rapidly at hyperbaric than at normobaric O₂ levels, but returned to 10% or less in both groups by 45 min. Cytochrome oxidation state improved to 80% of control after 90 min at normobaric O₂, but recovered completely after hyperbaric O₂ (P less than 0.05). In normobaric O₂, PCr and pHi continued to fall for 45 min after CO exposure and did not recover completely by 90 min. PCr and pHi in animals after hyperbaric O₂ improved within 45 min, but also remained below control at 90 min. These data indicate that intracellular uptake of CO can impair cerebral energy metabolism, despite the elimination of HbCO from the blood.

AU - Bambach GA

AU - Penney DG

AU - Negendank WG

TI - In situ assessment of the rat heart during chronic carbon monoxide exposure using nuclear magnetic resonance imaging

SI - TOXBIB/91/217351

SO - J Appl Toxicol; Vol 11, ISS 1, 1991, P43-9

AB - Ventricular hypertrophy induced in male Sprague-Dawley rats by inhalation of 500 ppm carbon monoxide (40% carboxyhemoglobin level) for 0-62 days was assessed by contiguous 2-mm thick axial cardiac cross-sections, using 32 accumulated averages of ungated fast-scan gradient-recalled nuclear magnetic resonance (NMR) images. Following final imaging, the rats were sacrificed and the hematocrit and heart mass were determined. The mean outside diameter of the left ventricle plus interventricular septum (LV + S) showed a strong correlation ($r = 0.73$, P less than 0.01) with the duration of CO exposure, while the correlation coefficients for the LV + S lumen diameter and wall thickness were marginally significant. The mean pleural space diameter also increased significantly ($r = 0.64$, P less than 0.05) with the duration of CO exposure. The ratio of the LV + S wall thickness and the lumen radius was 0.53 in the rats exposed to CO for 0-8 days; this value did not change with longer CO exposure. The LV + S outside and lumen diameter showed significant correlations to the hematocrit ($r = 0.72$, p less than 0.05 and $r = 0.66$, P less than 0.05, respectively), and the LV + S outside diameter correlated with the increase in the LV + S mass ($r = 0.72$, P less than 0.05). The results achieved with NMR imaging are consistent with past morphometric studies of CO-induced ventricular hypertrophy, where heart dimensions were determined in relaxed frozen tissue, and corroborate the eccentric nature of CO-induced ventricular hypertrophy.

AU - Pankow D

AU - Matschiner F

AU - Weigmann HJ

TI - Influence of aromatic hydrocarbons on the metabolism of dichloromethane to carbon monoxide in rats

SI - TOXBIB/91/335479

SO - Toxicology; Vol 68, ISS 1, 1991, P89-100

AB - The influence of prior or simultaneous oral administration of benzene, toluene, o-, m-, or p-xylene on the carboxyhemoglobin (COHb) level after a single dose of dichloromethane (DCM) was investigated in male rats. Six hours after administration of DCM, 6.2 mmol/kg, the mean maximum COHb level was $9.3 \pm 1.9\%$. This level was significantly enhanced by prior administration of benzene (16.9 mmol/kg) at 12-24 h, of toluene (18.8 mmol/kg) at 20-28 hours, of o-xylene (16.6 mmol/kg) and m-xylene (16.3 mmol/kg) at 20-32 h, and of p-xylene (16.2 mmol/kg) at 24-32 h. The corresponding maximum COHb levels were 20.7 ± 1.3 , 18.6 ± 1.1 , 18.9 ± 1.1 , 22.7 ± 1.2 , and $13.2 \pm 1.0\%$, respectively. After simultaneous administration of both DCM and the aromatic solvent, the COHb formation was inhibited: values of 1.3 ± 0.3 , 1.7 ± 0.4 , 3.6 ± 0.2 , 1.9 ± 0.2 , and $2.0 \pm 0.2\%$ COHb, respectively, were found. The inhibition was also evident when DCM was administered 12 hours after toluene or m-xylene and 12, 16 or 20 hours after p-xylene. The inhibition was dose-related as seen after combined gavage of o-, m-, or p-xylene and DCM. The o- and m-, but not the p-methylhippuric acid (MHA) excretion in the urine was significantly reduced after simultaneous administration of equimolar doses of DCM and the corresponding xylenes. In conclusion, it seems the stimulation or inhibition of the COHb formation after DCM caused by pretreatment with or by simultaneous administration of the aromatic solvents is due to the induction of cytochrome P-450 IIE1 or to competition between DCM and the aromatic solvent on this isozyme of cytochrome P-450.

AU - Moore SJ

AU - Ho IK

AU - Hume AS

TI - Severe hypoxia produced by concomitant intoxication with sublethal doses of carbon monoxide and cyanide

SI - TOXBIB/91/306117

SO - Toxicol Appl Pharmacol; Vol 109, ISS 3, 1991, P412-20

AB - It has long been known that a number of tissue hypoxicants are generated in the fire scenario. However, until recently few investigators have undertaken to correlate smoke inhalation deaths with the simultaneous exposure to histotoxic hypoxicants. Carbon monoxide and hydrogen cyanide are two histotoxic hypoxicants that are generated in nearly every fire. Prior studies have demonstrated that death can result from concomitant exposure to otherwise sublethal concentrations of carbon monoxide and cyanide. Because most smoke inhalation victims exhibit acid/base anomalies, it was important to investigate whether the death associated with simultaneous exposure to these two hypoxicants, at concentrations widely held to be nonlethal, could be explained by acid/base imbalances. Male ICR mice were exposed to 0.35% carbon monoxide immediately after having been injected with potassium cyanide solution, or were challenged with either agent alone. Animals challenged with cyanide or carbon monoxide alone demonstrated significant hypoxia. However, animals challenged with both agents demonstrated much greater hypoxia than could be explained by an additive effect alone. Controls demonstrated no alteration in acid/base homeostasis. Blood pH perturbations were found to be due to severe lactic acidosis coupled with inadequate respiratory compensation. Thus, it appears that the synergistic lethal effect of simultaneous administration of carbon monoxide and cyanide are related to a precipitous decrease in blood pH, the tissue hypoxia, and its resulting complications.

AU - Rowan JD

AU - Fountain SB

TI - Carbon monoxide exposure reduces the rewarding quality of brain-stimulation reward in rats

SI - TOXBIB/91/260574

SO - Neurotoxicol Teratol; Vol 13, ISS 2, 1991, P175-9

AB - The effect of carbon monoxide (CO) exposure on hypothalamic brain-stimulation reward (BSR) was examined. Rats were trained in a procedure that daily determined their stimulus duration threshold (SDT), that is, the shortest electrical stimulus to the posterior lateral hypothalamus that would support discrete-trial leverpress responding for BSR. After a stable SDT baseline was established using a single response lever, rats were exposed to 0, 5, 10, 20, and 40 ml/kg pure CO by IP injection. The SDT was significantly elevated by the 40 ml/kg exposure (corresponding to approximately 65% carboxyhemoglobin in the blood) compared to control exposures of an equal volume. No change was observed in response rate at any dose in this 1-lever task. No tolerance was observed when 40 ml/kg CO exposure was repeated on alternating days for 14 exposures, but a small reduction in response rate was observed in this procedure. When rats of a second group were required to alternate responses on two levers some distance apart, SDT was elevated by the highest exposure (40 ml/kg) as before. Additionally, response rate was also significantly suppressed by the highest exposure in this 2-lever task. The results support the view that CO has a direct effect on brain reward systems assessed by the SDT task. Response rate changes due to CO exposure may be due to direct effects on brain reward systems and to other effects, such as hypoxia-induced fatigue.

AU - Nabeshima T

AU - Katoh A

AU - Ishimaru H

AU - Yoneda Y

AU - Ogita K

AU - Murase K

AU - Ohtsuka H

AU - Inari K

AU - Fukuta T

AU - Kameyama T

TI - Carbon monoxide-induced delayed amnesia, delayed neuronal death and change in acetylcholine concentration in mice

SI - TOXBIB/91/108724

SO - J Pharmacol Exp Ther; Vol 256, ISS.1, 1991, P378-84

AB - This study investigated the interrelationship of delayed amnesia, delayed neuronal death and changes in acetylcholine concentration induced by carbon monoxide (CO) exposure in mice. In the test for retention of the passive avoidance task, amnesia was observed 5 and 7 days after CO exposure when the mice were exposed to CO 1 day after training; in the case where the mice were exposed to CO 5 and 7 days before training, amnesia was also observed in a retention test given 1 day after training. The number of pyramidal cells in the hippocampal CA1 subfield was lower than that of the control 3, 5, and 7 days after CO exposure. But the neurodegeneration in the parietal cortex, area 1, was not observed until 7 days after CO exposure. The findings indicated the amnesia and the neuronal death were produced after a delay when the mice were exposed to CO. In addition, the delayed amnesia was closely related to the delayed neuronal death in the hippocampal CA1 subfield.

Moreover, [3H]glutamate and [3H]glycine binding sites did not change after CO exposure but, 7 days after CO exposure, the concentration of acetylcholine and the binding of [3H]quinuclidinyl benzilate in the frontal cortex and the striatum were found to have significantly changed, but those in the hippocampus did not show significant change. Therefore, delayed amnesia induced by CO exposure may result from delayed neuronal death in the hippocampal CA1 subfield and dysfunction in the acetylcholinergic neurons, in the frontal cortex, the striatum, or the hippocampus.

AU - Singh J

AU - Moore-Cheatum L

TI - Carbon monoxide may be teratogenic under protein deficient conditions

SI - DART/T/91000705

SO - Teratology 1991 May;43(5):456

AB - Carbon monoxide (CO) is one of the most widely encountered occupational and environmental contaminants. Protein deficiency in the diets of poor pregnant women is wide-spread. Experiments were carried out to determine the teratogenicity of CO under protein deficient conditions. Pregnant CD-1 mice were placed on protein diets of 27 (control), 16, 8, or 4% on gestation day one. These animals were exposed to 0 (control), 65, 125, 250, or 500 ppm of CO from gestation day 8 to 18. The animals were sacrificed on gestation day 18 for teratological examination of the fetuses. The percentages of dead or resorbed fetuses and grossly malformed fetuses per litter were directly proportional to the CO levels and inversely proportional to the dietary protein levels. All levels of CO, and 8 and 4% protein diets significantly reduced the fetal weight of normal fetuses. CO exposure at 250 or 500 ppm significantly increased the head length and decreased the head width in normal fetuses. Protein diets at 4% or 8% significantly decreased the head width in normal fetuses. The most commonly seen

malformations were micrognathia, microstomia, open mouth and eyes, protruding tongue and microcephaly. The data indicate that CO is teratogenic under protein deficient conditions.

AU - Penney DG

AU - Skikun RM

TI - Hypertension is not exacerbated by chronic carbon monoxide exposure, with or without added salt, in the borderline hypertensive rat

SI - TOXBIB/92/215124

SO - Arch Toxicol Suppl; Vol 14, 1991, P118-23

AU - Farber JP

AU - Schwartz PJ

AU - Vanoli E

AU - Stramba-Badiale M

AU - De Ferrari GM

TI - Carbon monoxide and lethal arrhythmias

SI - TOXBIB/91/229768

SO - Res Rep Health Eff Inst, ISS 36, 1990, P1-17; discussion 19-27

AB - The effect of acute exposure to carbon monoxide on ventricular arrhythmias was studied in a previously described chronically maintained animal model of sudden cardiac death. In 60% of dogs with a healed anterior myocardial infarction, the combination of mild exercise and acute myocardial ischemia induces ventricular fibrillation. The events in this model are highly reproducible, thus allowing study by internal control analysis. Dogs that develop ventricular fibrillation during the test of exercise and acute myocardial ischemia are considered at high risk for sudden death and are defined as susceptible; dogs that survive the test without a fatal arrhythmia are considered at low risk for sudden death and are defined as resistant. In the current study, the effects of carboxyhemoglobin levels ranging from 5 to 15% were tested in resistant and susceptible dogs. A trend toward higher heart rates was observed at all levels of carboxyhemoglobin, although significant differences were observed only with 15% carboxyhemoglobin. This trend was observed at rest and during exercise in both resistant and susceptible dogs. In resistant animals, in which acute myocardial ischemia is typically associated with bradycardia even under the control condition, this reflex response occurred earlier and was augmented after exposure to carbon monoxide. This effect may depend on the increased hypoxic challenge caused by carbon monoxide, and thus on an augmentation of the neural reflex activation or a sensitization of the sinus node to acetylcholine induced by hypoxia. In both resistant and susceptible dogs, carbon monoxide exposure induced a worsening of ventricular arrhythmias in a minority of cases. This worsening was not reproducible in subsequent trials. These data indicate that acute exposure to carbon monoxide is seldom arrhythmogenic in dogs that have survived myocardial infarction. Nevertheless, the observation that carbon monoxide exposure increases heart rate at rest and during moderate exercise may have clinical implications relevant to patients with coronary artery disease. (ABSTRACT TRUNCATED AT 400 WORDS)

AU - Mattsson JL

AU - Albee RR

AU - Eisenbrandt DL

TI - Neurotoxicologic evaluation of rats after 13 weeks of inhalation exposure to dichloromethane or carbon monoxide

SI - TOXBIB/90/332820

SO - Pharmacol Biochem Behav; Vol 36, ISS 3, 1990, P671-81

AB - Male and female Fischer 344 rats were exposed to dichloromethane (methylene chloride, DCM) or carbon monoxide (CO) for 6 hr/day, 5 days/week, for 13 weeks. Because oxidative metabolism of DCM to CO and CO₂ is a saturable process, DCM exposure concentrations were selected clearly below saturation (50 ppm), just below saturation (200 ppm), and well above saturation (2000 ppm). At saturation of metabolism, metabolic CO causes about 10% carboxyhemoglobinemia (COHb). Therefore, as a control for CO effects, a separate group of rats was exposed to 135 ppm CO to induce approximately 10% COHb. Postexposure functional tests included an observational battery, hindlimb grip strength, and a battery of evoked potentials (flash, auditory brainstem, somatosensory, caudal nerve). After functional tests were completed, rats from all groups were perfused with fixative and a comprehensive set of nervous tissues from the high DCM exposure group and from controls were examined by light microscopy. Although some miscellaneous functional and morphologic variations were recorded, none were related to treatment. Thus, subchronic exposures as high as 2000 ppm DCM or 135 ppm CO had no deleterious effects on any of the measures of this study.

AU - Tomita M

AU - Okuyama T

AU - Shimosato K

AU - Kondo Y

AU - Ijiri I

TI - Effect of ethanol on fatal carbon monoxide poisoning in awake mice (correction of rats)

SI - TOXBIB/90/176787

SO - Toxicol Lett; Vol 50, ISS 2-3, 1990, P151-7

AB - The effect of ethanol on fatal carbon monoxide (CO) poisoning was investigated in mice injected intraperitoneally with ethanol. Ethanol (1.5 and 3.0 g/kg) was injected 15 min prior to exposure to gas containing 6.6% CO. The survival period was significantly lengthened with ethanol in proportion to the doses injected, although the carboxyhemoglobin (CO-Hb) saturation level in postmortem blood was almost the same in all groups. On the other hand, the CO-Hb level in the blood of mice injected with ethanol was significantly lower than that of control mice during the early exposure period when all mice were still alive. Our results showed that the acute ethanol injection did not influence the CO-Hb saturation level in blood at death, but did affect the duration of survival, probably because of ethanol's ability to decrease blood flow and CO intake.

AU - Shimazu T

AU - Ikeuchi H

AU - Hubbard GB

AU - Langlais PC

AU - Mason AD Jr

AU - Pruitt BA Jr

TI - Smoke inhalation injury and the effect of carbon monoxide in the sheep model

SI - TOXBIB/90/156454

SO - J Trauma; Vol 30, ISS 2, 1990, P170-5

AB - The role of carbon monoxide (CO) in causing the physiologic and anatomic changes characteristic of smoke inhalation injury was evaluated in 34 sheep. The smoke-exposed group received a dose of smoke known to produce mild inhalation injury. The CO group received a pure gas mixture that contained concentrations of oxygen, carbon dioxide, and CO similar to those in the smoke. Cardio-pulmonary function was measured immediately after exposure, and 24 and 72 hours after exposure.

The CO group showed a transient increase in cardiac output, but the smoke group showed no such response. The CO group maintained normal PaO₂ levels during the 72-hour study period; the smoke group gradually developed hypoxemia. The lungs of the CO exposed animals had no discernible histologic changes; lungs of the smoke group showed progressive inflammatory changes. These results indicate that CO per se is not the primary etiologic agent of smoke inhalation injury.

AU - Verrier RL

AU - Mills AK

AU - Skornik WA

TI - Acute effects of carbon monoxide on cardiac electrical stability

SI - TOXBIB/91/151595

SO - Res Rep Health Eff Inst, ISS 35, 1990, P1-14

AB - The objective of this project was to determine the effects of acute carbon monoxide exposure on cardiac electrical stability. To obtain a comprehensive assessment, diverse biological models were employed. These involved cardiac electrical testing in the normal and ischemic heart in anesthetized and conscious dogs. The experimental plan was designed to examine the direct effects of carbon monoxide exposure on the myocardium and to evaluate possible indirect influences through alterations in platelet aggregability or changes in central nervous system activity in the conscious animal. Results indicate that exposure to relatively high levels of carbon monoxide, leading to carboxyhemoglobin concentrations of up to 20%, is without significant effect on ventricular electrical stability. This conclusion appears to be the case in the acutely ischemic heart, as well as in the normal heart. It is important to note the total exposure period was in the range of 90 to 124 minutes. The possibility that longer periods of exposure or exacerbation from nicotine in cigarette smoke could have a deleterious effect cannot be excluded. Whether or not alterations in platelet aggregability, due to carbon monoxide exposure, could be a predisposing factor for cardiac arrhythmias was also examined. A model involving partial coronary artery stenosis was used to simulate the conditions under which platelet plugs could lead to myocardial ischemia and life-threatening arrhythmias. No changes were found either in the cycle frequency of coronary blood flow oscillations or in platelet aggregability during carbon monoxide exposure. Thus, carbon monoxide exposure does not appear to alter platelet aggregability or its effect on coronary blood flow during stenosis. In the final series of experiments, the effects of carbon monoxide exposure in the conscious state were examined. The rationale was to take into consideration possible adverse consequences mediated by the central nervous system. No adverse effects on cardiac excitable properties were found in response to either a 2-hour or 24-hour-exposure paradigm. This response appears to argue against major deleterious influences of carbon monoxide exposure as a result of direct myocardial actions or indirect actions mediated through effects on central nervous system activity.

AU - Thom SR

TI - Antagonism of carbon monoxide-mediated brain lipid peroxidation by hyperbaric oxygen

SI - TOXBIB/91/020152

SO - Toxicol Appl Pharmacol; Vol 105, ISS 2, 1990, P340-4

AB - The effects of oxygen at 1, 2, and 3, atmospheres absolute (ATA) were assessed on brain lipid peroxidation caused by carbon monoxide (CO) poisoning in a rat model. Oxygen at 3 ATA, but not 1 ATA, was found to prevent brain lipid peroxidation when administered to rats for 45 min, beginning 45 min subsequent to CO poisoning. Oxygen at 2 ATA had an intermediate effect. The action of hyperbaric oxygen could not be attributed to a more rapid diminution of carboxyhemoglobin, and appears to occur at the level of the brain tissue.

AU - Tachi N
AU - Aoyama M
TI - Postnatal growth in rats prenatally exposed to cigarette smoke or carbon monoxide
SI - DART/M/91091548
SO - Bull Environ Contam Toxicol 1990 Nov;45(5):641-8

AU - Norman CA
AU - Halton DM
TI - Is carbon monoxide a workplace teratogen? A review and evaluation of the literature
SI - DART/M/91052900
SO - Ann Occup Hyg 1990 Aug;34(4):335-47
AB - The review included 60 case reports of carbon monoxide exposures involving pregnant women. The circumstances under which carbon monoxide exposures adversely affected pregnancy and the types of effects seen are summarized. Severe acute exposures to carbon monoxide caused foetal death or toxic effects, including anatomical malformations and functional alterations. Foetal outcome was related to two major indices of carbon monoxide exposure: maternal blood carboxyhemoglobin levels and maternal toxicity.

AU - Moessinger AC
AU - Shen CT
AU - Kiu GT
AU - Daniel SS
AU - James LS
TI - Maternal exposure to carbon monoxide inhibits fetal lung cell multiplication
SI - DART/T/91001290
SO - Pediatr Res 1990 Apr;27(4 Pt 2):48A
AB - Maternal smoking during pregnancy adversely affects fetal lung development (Ann NY Acad Sci 1989, 562:101). Because carbon monoxide (CO) is a major component of cigarette smoke, pregnant guinea pigs (GP) were exposed to CO between days 45 & 65 of gestation (term = 67). Using a computer-controlled environmental chamber, O₂, CO₂, CO, T, and H₂O were kept within narrow margins. In the study, three groups of GP were exposed: Group 1 (n = 7) 130-150 ppm CO; Group 2 (n = 5) Hypoxia (Hy) 11.5-12.5% O₂; Group 3 (n = 5). Normoxia controls 20-21% O₂. Other variables and caloric intake were kept constant. The fetuses were delivered abdominally on day 65. Fetal body and organ weights were determined to the nearest .01 mg. From each group, 10 fetuses were used for dry wt. and DNA contents, i.e. 2 fetuses per litter (1 female and 1 male) with body weights closest to the mean of the litter. Weights in grams for groups 1,2,3: (Table: see text). Fetal HbCO was 16.2 +/- 5% in group 1 and negligible in groups 2 and 3. Hematologic responses to CO and Hy were different with a predominantly fetal effect (CO) or maternal effect (Hy). The weight differences were confirmed by dry wts and DNA contents, p less than 0.05. Percent dry wts. of lungs were significantly more in groups 1 and 2, p less than 0.01. CO exposure during the last third of pregnancy selectively interferes with fetal lung growth in the GP. This situation occurs via a hypoxic effect with decreased pulmonary blood flow and altered fetal lung fluid dynamics.

AU - Clubb FJ Jr
AU - Penney DG
AU - Bishop SP
TI - Cardiomegaly in neonatal rats exposed to 500 ppm carbon monoxide

SI - TOXBIB/90/040739

SO - J Mol Cell Cardiol; Vol 21, ISS 9, 1989, P945-55

AB - Increased hemodynamic workload was induced in growing neonatal rats to study alterations in myocyte structure and number and to determine if carbon monoxide (CO) produced a volume-induced model of cardiomegaly. Newborn rats were exposed to 500 ppm CO for up to 32 days of age, at which time the remaining CO exposed rats and ambient air controls continued development in room air to 200 days of age. In the CO group, ventricular weight to body weight ratio was 26% greater than controls at 6 days of age, more than double at 15 days, and remained 47% greater at 28 days. Although absolute myocyte volumes were not different between the two groups at any time period, the CO group did have greater myocyte volume relative to body weight during the CO exposure period. Binucleated myocytes of both ventricles were longer than controls during the exposure period, but did not have increased width. By 200 days of age, myocytes from left ventricle plus septum of CO exposed rats were significantly shorter and CO exposed rats had more total myocytes than controls (36×10^6 versus 32×10^6 for controls, P less than 0.05). In this study, cardiomegaly induced by 500 ppm CO from birth to 32 days of age was primarily due to myocyte hypertrophy with myocytes having increased length to width ratios (i.e., alterations consistent with a volume-induced model). Following removal from CO exposure, cardiomegaly and myocyte hypertrophy was regressive. With increasing time after removal from CO, myocytes tended to become shorter and smaller compared to age matched controls. This trend was present at 105 days and statistically significant by 200 days of age, resulting in an increased number of myocytes in the myocardium long after removal of rats from CO exposure. It was concluded that neonatal exposure to CO causes cardiomegaly by increase in cell length and cell volume, consistent with a volume overload model of cardiac hypertrophy.

AU - McGrath JJ

TI - Cardiovascular effects of chronic carbon monoxide and high-altitude exposure

SI - TOXBIB/90/104704

SO - Res Rep Health Eff Inst, ISS 27, 1989, P1-23

AB - At higher altitudes, ambient carbon monoxide levels are increasing with the number of residents and tourists and their use of motor vehicles and heating devices (such as fireplaces, furnaces, and stoves). Although chronic exposure to carbon monoxide or high altitude causes pronounced cardiovascular changes in humans as well as in animals, little information is found on the effects elicited by these stressors combined. Data from acute studies and theoretical considerations suggest that carbon monoxide inhaled at altitude may be more detrimental than carbon monoxide inhaled at sea level. It is not known, however, if the cardiovascular system adapts or deteriorates with continuous, concurrent exposure to carbon monoxide and high altitude. Male laboratory rats were exposed for six weeks in steel barometric chambers to altitudes ranging from 3300 ft (ambient) to 18,000 ft and to concentrations ranging from 0 to 500 parts per million (ppm)². Carbon monoxide had no effect on body weight at any altitude. A tendency was found for hematocrit to increase even at the lowest concentration of carbon monoxide (9 ppm), but the increase did not become significant until 100 ppm. At 10,000 ft, total heart weight tended to increase in rats inhaling 100 ppm carbon monoxide. Although its effects on the heart at altitude are complex, carbon monoxide, in concentrations of 500 ppm or less, had little effect on the right ventricle; it did not exacerbate any effects due to altitude. The left ventricle weight tended to increase with exposure to 35 ppm carbon monoxide at altitude, but the increase was not significant until 100 ppm carbon monoxide. Heart rate, blood pressure, cardiac output, and peripheral resistance were unaffected by exposure to 35 ppm carbon monoxide or 10,000-ft altitude singly or in combination. It was concluded that six weeks of exposure to 35 ppm carbon monoxide does not produce measurable effects in the healthy laboratory rat, nor does it exacerbate the

effects produced by exposure to 10,000-ft altitude. Basal carboxyhemoglobin (COHb) level (due to endogenous carbon monoxide production) was increased from 0.7% to 1.0% at 10,000 ft, and to 1.7% at 15,000 ft. These figures suggest that the high-altitude resident has a greater initial body burden of COHb and will attain the COHb level associated with the National Ambient Air Quality Standard for carbon monoxide more quickly than the sea-level resident.

AU - Knisely JS

AU - Rees DC

AU - Balster RL

TI - Effects of carbon monoxide in combination with behaviorally active drugs on fixed-ratio performance in the mouse

SI - TOXBIB/90/081618

SO - Neurotoxicol Teratol; Vol 11, ISS 5, 1989; P447-52

AB - The effects of carbon monoxide (3.75, 7.5, 15, and 30 ml/kg, IP) alone and in combination with ethanol (1.1 g/kg), nicotine (1.1 μ g/kg), caffeine (36.1 μ g/kg), chlorpromazine (2.2 μ g/kg), diazepam (10 μ g/kg), pentobarbital (23.1 μ g/kg), d-amphetamine (1.4 μ g/kg), or morphine (13.3 μ g/kg) were evaluated in mice. Animals were trained to lever press under a fixed-ratio 32 schedule of water reinforcement. Response rates following CO-drug combinations were compared with the expected additive effects determined by the sum of the effects of each agent administered alone. CO (15 and 30 ml/kg) in combination with ethanol produced supra-additive effects. CO-chlorpromazine and CO-d-amphetamine combinations often produced greater than additive response-rate suppression, although differences from additivity did not reach statistical significance. The effects on response rates following CO in combination with nicotine, caffeine, diazepam, pentobarbital, or morphine were additive. These results suggest that concurrent use of therapeutic or abused drugs and CO exposure may place an individual at higher risk for behavioral toxicity.

AU - Nanji AA

AU - Jui LT

AU - French SW

TI - Effect of chronic carbon monoxide exposure on experimental alcoholic liver injury in rats

SI - TOXBIB/90/013885

SO - Life Sci; Vol 45, ISS 10, 1989, P885-90

AB - Two groups of experimental animals with pair-fed controls were studied to evaluate the effect of chronic carbon monoxide (CO) exposure on progression of experimental alcoholic liver injury. Eight pairs of male Wistar rats were continuously infused liquid diet and ethanol or isocaloric dextrose for four months. Four pairs were also exposed to CO. Liver damage was followed monthly by serum ALT and morphologic assessment of liver biopsy. Serum levels of ALT were significantly higher in the CO-ethanol group compared to other groups. Electron microscopy revealed a greater degree of cell necrosis in the CO-exposed group, which explained the significantly higher ALT activity in these animals. Both experimental groups (CO-ethanol and air-ethanol) had significantly greater liver damage than controls. Carboxyhemoglobin levels were not different in the ethanol-fed and control group. Results show that chronic CO exposure enhances liver cell necrosis in ethanol-fed rats, thereby lending support to the hypothesis that ethanol and hypoxia enhance cellular disruption in the liver which could be important in the pathogenesis of alcoholic liver disease in rats.

AU - Vanoli E

AU - De Ferrari GM

AU - Stramba-Badiale M

AU - Farber JP

AU - Schwartz PJ

TI - Carbon monoxide and lethal arrhythmias in conscious dogs with a healed myocardial infarction

SI - TOXBIB/89/132307

SO - Am Heart J; Vol 117, ISS 2, 1989, P348-57

AB - Environmental studies suggested that exposure to carbon monoxide (CO) increases cardiovascular mortality among patients with coronary artery disease. The study investigated whether, in dogs with a healed anterior myocardial infarction at low and high risk for ventricular fibrillation, acute exposure to CO has adverse effects during acute myocardial ischemia combined with exercise. One month after myocardial infarction, 17 dogs had ventricular fibrillation and 16 survived during the combined exercise and ischemia test. These tests were then repeated in all dogs with different concentrations of carboxyhemoglobin (COHb) (from 5% to 15%). With 15% COHb, heart rate (HR) at rest and during exercise was higher (p less than 0.05) than in the control tests. Surprisingly, the reflex HR response to acute ischemia was also altered; namely, the HR reduction characteristic of the low-risk animals was anticipated and accentuated (-31 ± 25 versus 2 ± 30 beats/min, p less than 0.05). Conversely, the HR increase characteristic of the high-risk group was reduced by CO (44 ± 52 versus 72 ± 43 beats/min, p less than 0.05). With 15% COHb, malignant arrhythmias occurred in two of the low-risk dogs and in none of the high-risk dogs. In the latter, CO was tested with a combination of exercise work load and myocardial ischemia duration not associated with ventricular fibrillation (VF) in the control condition. This study demonstrated that brief exposure to CO: 1) profoundly alters the reflex HR response to exercise and to acute myocardial ischemia, and 2) does not enhance the occurrence of malignant arrhythmias in conscious dogs with a healed myocardial infarction.

SI - TOXBIB/89/068769

SO - J Tongji Med Univ; Vol 8, ISS 1, 1988, P60-5

AU - Lin H

AU - McGrath JJ

TI - Vasodilating effects of carbon monoxide

SI - TOXBIB/89/210400

SO - Drug Chem Toxicol; Vol 11, ISS 4, 1988, P371-85

AB - The vasodilator effects of carbon monoxide (CO) were studied in an isolated perfused rat thoracic aorta preparation. Thoracic aortas from male Sprague-Dawley laboratory rats were dissected free of surrounding tissue, cannulated proximally, and tethered to in situ length. The vessels were perfused with oxygenated Krebs-Henseleit (KH) solution at 37 degrees C in a constant flow system with a circumferentially-applied, pulsatile (300/min), basal systolic pressure of 100 mm Hg. Aortas were precontracted with high-potassium (K+) or norepinephrine (NE). Changes in perfusion pressure were indicative of changes in vascular resistance induced by the test gas mixtures. Oxygen (O₂) content of the perfusate was kept constant, while CO and nitrogen (N₂) were altered. CO (2.5, 5, and 10%) dilated both K+-contracted and NE-contracted aortas in a dose-dependent manner. A significant vasodilation in response to 5% CO (24.5% of maximal), but not to 5% N₂, was obtained in the K+-contracted aortas. After the endothelium was removed chemically, the aortas continued to dilate in response to CO. These results suggest that CO has a direct vasorelaxant effect on vascular smooth muscle that is nonspecific and is not endothelium-dependent.

AU - Mikiskova H

AU - Frantik E

TI - Animal model of cardiotoxicity: carbon monoxide induced ECG hypoxia masked in light narcosis

SI - TOXBIB/88/147341

SO - Act Nerv Super (Praha); Vol 29, ISS 4, 1987, P274-8

AB - Inhalation exposure of restrained conscious rats to carbon monoxide (1000 ppm, 120 min.) led to a peak carboxyhemoglobin concentration of 40-45%. At these concentrations, spontaneous motor activity was not affected significantly, but the physical capacity at endurance run was depressed by 70%. From the 30th min. of exposure, a typical 2-phasic change in heart rate with initial tachycardia and obvious but unstable hypoxic changes in ECG were observed. Quieting of animals (light anesthesia with phenobarbitone; 100 µg/kg ip) removed almost completely all pathological changes. The level and fluctuations of functional requirements to the circulation seem thus substantial for the development of the cardiotoxic effects.

AU - Annau Z

TI - Complex maze performance during carbon monoxide exposure in rats

SI - TOXBIB/88/013702

SO - Neurotoxicol Teratol; Vol 9, ISS 2, 1987, P151-5

AB - Most human victims of residential fires die of smoke inhalation. The cause of death of the victims is attributed to high levels of carboxyhemoglobin, but it is not clear why the victims are unable to escape even from locations remote from flaming combustion. In an attempt to provide a model of escape from toxic gases using animals, a complex maze was built for rats with eight choice points. The animals were 24-hour water deprived and trained to remain in the start box for 15 min. Following this period, a rat was released in the maze and had to learn to avoid blind alleys and reach the goal box for water reinforcement within 15 min. Total time to traverse and total distance in the maze were recorded. Each animal was given one trial per day. After stable running times were established, different groups of six rats were exposed to 2000, 3000, 3500, and 4000 ppm of carbon monoxide (CO) when placed in the maze. Each animal was exposed to CO only once. On the day after CO exposure the rats were implanted with an arterial cannula and on the next day each animal was exposed to the same CO concentration it had previously experienced for 30 min. Blood samples were taken every 5 min. The effect of increasing CO concentrations was to increase maze running times, as well as to decrease the number of animals reaching the goal. At 3500 ppm no animal reached the goal. At 2000 ppm, the animals that failed to reach the goal moved a greater distance than animals that reached the goal. (ABSTRACT TRUNCATED AT 250 WORDS)

AU - McFaul SJ

AU - McGrath JJ

TI - Studies on the mechanism of carbon monoxide-induced vasodilation in the isolated perfused rat heart

SI - TOXBIB/87/179048

SO - Toxicol Appl Pharmacol; Vol 87, ISS 3, 1987, P464-73

AB - The effects of dissolved CO on isolated potassium-arrested (K+) perfused rat hearts were investigated. Hearts from male Sprague-Dawley rats were perfused via the aorta with oxygenated Krebs-Henseleit solution containing 20 mM K+. Coronary flow (Qt) averaged 48.8 +/- 1.6 (SE), 48.1 +/- 1.7, and 55.6 +/- 1.7 ml/min/g dry wt when the perfusate was equilibrated with 95% O₂-5% CO₂, 5% N₂-90% O₂-5% CO₂, and 5% CO-90% O₂-5% CO₂, respectively. The change in Qt was statistically significant when CO was present in the perfusion medium, but was not significant when N₂

was present. Furthermore, the effect was reversible because coronary flow returned to control levels when CO was removed. Myocardial oxygen consumption (MVO_2) did not change significantly when hearts were perfused with either N_2 or CO. The magnitude of CO-induced vasodilation was not affected significantly by the addition of either 5 μM propranolol, 2 μM phentolamine, 1 unit of adenosine deaminase, or 0.1 mM indomethacin to the perfusate. In addition, CO reversed the vasoconstrictive effects of the α -agonist methoxamine. These results indicate that CO exerts a vasodilatory effect on coronary vasculature that is not the result of decreased O_2 content in the perfusate and is not mediated by adrenergic influences, adenosine, or prostaglandins.

AU - Fukui Y

AU - Akane A

AU - Takahashi S

AU - Matsubara K

AU - Maseda C

TI - Derivative spectrophotometric studies on cytotoxic effects of carbon monoxide

SI - TOXBIB/87/163750

SO - Forensic Sci Int; Vol 33, ISS 2, 1987, P75-82

AB - Characteristics of cytochrome oxidase prepared from hearts of Sprague-Dawley male rats were studied with the use of the fourth derivative spectrophotometry in respect to the cytotoxic effects of carbon monoxide (CO). CO-exposed rats tended to show lower specific activities of cytochrome oxidase than control and recovered rats. Moreover, a significant difference was found in the fourth derivative spectral features of the enzyme: CO-exposed groups indicated peaks at 412 nm in the spectra while controls at 408 nm. This spectral difference seemed to reflect specific effect of CO on cytochrome oxidase, though such a trace remained for not more than a day after death.

AU - Levin BC

AU - Paabo M

AU - Gurman JL

AU - Harris SE

AU - Braun E

TI - Toxicological interactions between carbon monoxide and carbon dioxide

SI - TOXBIB/88/071482

SO - Toxicology; Vol 47, ISS 1-2, 1987, P135-64

AB - Fischer 344 male rats were subjected to 30-min individual or combined exposures of carbon monoxide (CO) and carbon dioxide (CO_2). All deaths from CO occurred during the exposures, and the LC_{50} values were 4600 and 5000 ppm, depending on experimental conditions. Animals exposed to CO_2 concentrations ranging from 1.3 to 14.7% for 30 min were neither incapacitated nor fatally injured. The addition of nonlethal concentrations of CO_2 (1.7 to 17.3%) to sublethal concentrations of CO (2500 to 4000 ppm) caused deaths of the exposed rats both during and following (up to 24 h) the 30-min exposures. The most toxic combination of these two gases (2500 ppm CO plus 5% CO_2) increased the rate of carboxyhemoglobin (COHb) formation 1.5 times that found in rats exposed to 2500 ppm of CO alone. The COHb equilibrium levels were the same. Exposure to both CO and CO_2 produced a greater degree of acidosis and a longer recovery time than that observed with either gas alone. The results fit a mathematical model indicating a synergistic interaction. Combustion of 11 materials at their LC_{50} values indicated that CO was probably the primary toxicant in one case and that the combined CO plus CO_2 was the cause of the deaths in three other cases. Additional fire gases need to be studied to explain deaths from the other materials.

AU - Fechter LD

TI - Neurotoxicity of prenatal carbon monoxide exposure

SI - DART/M/90057007

SO - Res Rep Health Eff Inst 1987 Sep(12):3-22

AB - Despite the very wide recognition that carbon monoxide (CO) is a significant neurotoxicant, the level at which subtle effects occur, and the existence of sensitive periods in development for such toxicity, has been undetermined. In terms of risk to the fetus, a potentially susceptible sub-population, concerns include, first, the level of exposure at which neurotoxicity occurs may be different from the adult, and second, the site of toxic action and subsequent neurotoxic effects of CO may be different in the immature and mature brain. The investigator studied the susceptibility of the developing brain to moderate levels of CO maintained chronically through the period of neuronal proliferation, and into the period of synapse formation. Carbon monoxide may be thought of as a prototypical hypoxic agent, and a significant public health hazard in its own right. Carbon monoxide is a ubiquitous toxic agent that accounts for large numbers of deaths and significant morbidity in human populations. Subtle neurotoxic effects of this agent may be even more common, but they may go largely undetected, or fail to be associated with CO exposure. Prenatal CO exposure at moderate levels can produce significant neurotoxic effects in rats. The data obtained from the cerebellum and neostriatum, in particular, suggest that chronic, moderate perinatal CO exposure may disrupt neuronal proliferation and certain markers for neurochemical transmission, as well.

AU - Vyskocil A

AU - Tusl M

AU - Zaydlar K

TI - The effect of carbon monoxide on hormone levels and organ weights in rats

SI - TOXBIB/87/110352

SO - J Appl Toxicol; Vol 6, ISS 6, 1986, P443-6

AB - Male Wistar rats were exposed continuously for 1 or 2 months to 25 or 100 ppm CO. The concentrations of noradrenaline in the hypothalamus, corticosterone and thyroxine in serum and of adrenal catecholamines were estimated. After exposure to 25 ppm CO, no significant changes were observed in the serum corticosterone and thyroxine, hypothalamic noradrenaline, adrenal catecholamines levels, or in the weights of lung, spleen, adrenal glands, liver, and the whole body. Exposure to 100 ppm CO induced a decrease in hypothalamic noradrenaline and serum thyroxine and an increase in adrenal catecholamines and serum corticosterone. Whole-body and organ weights were unchanged except for a slight decrease in liver weight. The results suggest a non-specific stress response in the rat to 100 ppm CO, and a concentration of 25 ppm CO without any stress effect.

AU - Young LJ

AU - Caughey WS

TI - Mitochondrial oxygenation of carbon monoxide

SI - TOXBIB/87/100080

SO - Biochem J; Vol 239, ISS 1, 1986, P225-7

AB - A variety of mitochondria have been observed to oxidize ^{13}CO to $^{13}\text{CO}_2$ in the presence of dioxygen, and on the basis of earlier studies (Young & Caughey [1986] Biochemistry 25, 152-161; Young (1981) Ph.D. Dissertation, Colorado State University), this activity is attributed to cytochrome c oxidase. Implications of these findings in respect to some aspects of the pathological biochemistry of CO poisoning are discussed.

AU - Kwak HM

AU - Yang YH

AU - Lee MS

TI - Cytogenetic effects on mouse fetus of acute and chronic transplacental in vivo exposure to carbon monoxide: induction of micronuclei and sister chromatid exchanges.

SI - TOXBIB/87/095909

SO - Yonsei Med J; Vol 27, ISS 3, 1986, P205-12

AU - Norris JC

AU - Moore SJ

AU - Hume AS

TI - Synergistic lethality induced by the combination of carbon monoxide and cyanide

SI - TOXBIB/86/262460

SO - Toxicology; Vol 40, ISS 2, 1986, P121-9

AB - Carbon monoxide (CO) and hydrogen cyanide are recognized pyrolytic products of plastic materials in fires. Lethal blood concentrations of CO and cyanide are found in fire victims and considered to be the cause of death. However, fire victims are reported with sublethal concentrations of both CO and cyanide and no other attributed reason for their deaths. Thus, the purpose of this study was to investigate lethality induced by low concentrations of CO and cyanide. Male ICR mice were used in these studies. Doses of potassium cyanide (4-9 $\mu\text{g/kg}$, ip) were administered to animals pretreated for 3 min with either air or CO (0.63-0.66%). From these data, the LD50 value of potassium cyanide (KCN) was determined in these animals pretreated with either air or CO. A significantly lower LD50 value for KCN was found in CO-pretreated animals, as compared to air-pretreated animals. In another series of experiments, animals were pretreated with either saline or KCN (1.00-6.35 $\mu\text{g/kg}$, ip) and then placed in the chamber containing a CO atmosphere (0.325-0.375%). Of saline-pretreated animals 10-20% were dead at the end of the monitoring period. Sublethal doses of KCN (3.5-6.35 $\mu\text{g/kg}$, ip) produced a synergistic lethality, as compared to the saline-pretreated animals. Blood was analyzed for CO and cyanide content to determine if any changes could explain this augmented lethality. No difference was found in CO or cyanide blood concentrations between these treatment groups. From these data, a synergistic lethality induced by the combination of CO and cyanide was demonstrated that could not be explained by altered CO or cyanide blood concentrations.

AU - Chen KC

AU - McGrath JJ

TI - Response of the isolated heart to carbon monoxide and nitrogen anoxia

SI - TOXBIB/86/097847

SO - Toxicol Appl Pharmacol; Vol 81, ISS 3 Pt 1, 1985, P363-70

AB - The effects of carbon monoxide (CO) or nitrogen (N_2) anoxia were assessed and compared in stimulated (360 beats/min) and unstimulated isolated rat hearts. The hearts were perfused through the aorta with Krebs-Henseleit solution aerated with 95% O_2 -5% CO_2 (O_2). Heart rate, pulse pressure, perfusate flow, and perfusate lactate concentrations were recorded. After 30 min of O_2 perfusion, the hearts were challenged with 95% CO -5% CO_2 (CO) or 95% N_2 -5% CO_2 (N_2) for 10 min. The preparations were then reoxygenated and allowed to recover for 10 min. In the unstimulated hearts, CO depressed heart rate, pulse pressure, and perfusate flow earlier than did N_2 . Lactate concentrations increased to a greater extent with N_2 than with CO. With reoxygenation heart rate, pulse pressure, and lactate concentrations returned to control values earlier in the CO hearts. The differences observed in

pulse pressure and lactate concentrations with CO and N₂ anoxia disappeared with stimulation. No significant differences were noted in water or glycogen contents after CO or N₂ in either the unstimulated or stimulated preparations. These results suggest that CO may have a direct effect on the myocardium in addition to its well-known anoxic effect.

AU - Mactutus CF

AU - Fechter LD

TI - Moderate prenatal carbon monoxide exposure produces persistent, and apparently permanent, memory deficits in rats

SI - TOXBIB/85/168826

SO - Teratology; Vol 31, ISS 1, 1985, P1-12

AB - The effects of moderate (150 +/- 2 ppm) prenatal carbon monoxide (CO) exposure (maternal HbCO concentrations of 15.6 +/- 1.1%) on learning and memory were assessed in young and aged adult rats using a 2-way active avoidance paradigm. In experiment 1, the prenatal CO-exposed rats at 120 days of age acquired a conditioned avoidance response equally as well as control animals in a 100-trial session. However, following a 24-hour interval the CO-exposed rats failed to demonstrate significant retention of the task, as indicated by the absence of significant improvement in performance. Over the previous day, control subjects did show significant retention. In experiment 2, in which 120-day-old animals received 50 training trials per day until a criterion of 10 consecutive avoidance responses was met, the prenatal CO-exposed subjects again acquired the task, as well as the control animals. When tested for retention 28 days later, a significant memory impairment was again observed in terms of trials required to reattain the avoidance criterion, as well as in total percent avoidance responding. In neither experiment did an analysis of initial or average latency to escape the footshock stimulus reveal any significant alterations. These latter results suggest the observed performance impairment reflected a memory deficit and not a disruption of sensory, motor, or motivational factors. In experiment 3, prenatal CO-exposed rats approximately 1 year of age (300-360 days of age) showed impairment relative to air-exposed controls in both the original learning and retention of the 2-way avoidance response. Again, however, no evidence appeared for alterations in performance factors per se. Collectively, these data indicate that while young adult rats prenatally exposed to 150 ppm CO demonstrate an associative deficit restricted to memory impairment, aged adults similarly exposed during the prenatal period display a more pronounced deficit, similar to that recently reported for animals tested as juveniles. The importance of parametric manipulations in uncovering long-term toxicity is also discussed.

AU - Pankow D

AU - Ponsold W

TI - Effect of carbon monoxide exposure on heart cytochrome c oxidase activity of rats

SI - TOXBIB/85/121844

SO - Biomed Biochim Acta; Vol 43, ISS 10, 1984, P1185-9

AB - The activity of cytochrome c oxidase in heart muscle of rats was within the control range 1 and 24 hours after commencement of CO exposure (56% COHb) and was significantly decreased 3 hours thereafter. A decrease of the enzyme activity was also detectable 3 hours following repeated CO exposure demonstrating that cytochrome c oxidase does not seem to play a role in the adaptive response of organism to chronic CO exposure.

AU - Penney DG

AU - Barthel BG

AU - Skoney JA

TI - Cardiac compliance and dimensions in carbon monoxide-induced cardiomegaly

SI - TOXBIB/84/233905

SO - Cardiovasc Res; Vol 18, ISS 5, 1984, P270-6

AB - Adult male rats inhaled 500 ppm CO continuously for 38 to 47 days to produce significant cardiomegaly. In a first experiment in which heart wall stiffness was examined, haematocrit rose 45.1% and the ratio of the sum of right ventricle (RV) and left ventricle (LV) to body weight (mg x g⁻¹) increased from 2.69 to 3.34. Compliance (ml x mmHg⁻¹) of CO LVs and RVs studied from 0 to 25 mmHg intraluminal pressure, was generally greater than that of LVs and RVs from controls at the same pressure. These differences were greater for RVs. No difference was present between control RVs and LVs at the same distending pressure. The differences between treated and control groups disappeared when compliance was normalised per g heart weight. In a second experiment in which heart dimensions were examined, haematocrit ratio increased 48.6% and 2V (RV + LV) to body weight ratio (mg x g⁻¹) increased from 2.77 to 3.45. Atrial weight was also greater. LV apex to base length increased 6.4% and LV outside diameter increased 7.3. No significant differences in LV, RV or interventricular septum (S) thickness resulted from CO exposure, as measured at three sites in each, in four cross-sections of the heart between the apex and base. In general, LV wall was slightly thicker than S, while RV was about 35% that of LV. The findings suggest that chronic carboxyhaemoglobinaemia produces largely eccentric cardiomegaly, and no intrinsic change in wall stiffness.

AU - McGrath JJ

TI - The effects of carbon monoxide on the heart: an in vitro study

SI - TOXBIB/85/113402

SO - Pharmacol Biochem Behav; Vol 21 Suppl 1, 1984, P99-102

AB - Experiments were conducted to assess the effects of increasing concentrations of carbon monoxide (CO) on the isolated spontaneously beating rat heart. Hearts removed from male Sprague Dawley rats were perfused via the aorta with Krebs-Henseleit solution. Coronary flow was timed and collected in a calibrated vessel. Heart rate and pulse pressure were measured by a catheter inserted in the left ventricle and attached to a pressure transducer. After 30 min, the hearts were challenged for 10 min with perfusate containing increasing concentrations of CO and decreasing concentrations of O₂. Coronary flow increased in response to CO concentrations below 50%. After 8 min, coronary flow increased by 40% in response to 10% CO challenge. Heart rate and pulse pressure were generally depressed by CO. Heart rate was depressed at the end of 8 min by 5, 10, 38, and 64%, respectively, by solutions equilibrated against 10, 25, 50, and 95% CO. Pulse pressure decreased with concentrations of 50% CO and higher. These results indicate that coronary flow appears to be the most sensitive indicator of CO toxicity in the isolated heart.

AU - Shiotsuka RN

AU - Drew RT

AU - Wehner RW

TI - Carbon monoxide enhances development of hypertension in Dahl rats

SI - TOXBIB/85/041243

SO - Toxicol Appl Pharmacol; Vol 76, ISS 2, 1984, P225-33

AB - The influence of carbon monoxide (CO) on the development of systemic hypertension was studied in Dahl rats selectively bred for susceptibility (DS) and resistance (DR) to NaCl-induced hypertension. This study was designed to examine the interactions among rat line (DS or DR), NaCl content of diet,

and exposure to CO. The rats were exposed to 500 ppm CO or conditioned air, 21 hours/day, for 62 to 63 consecutive days. Carbon monoxide exposures affected blood pressure only in DS rats fed a high NaCl diet, where it enhanced the development of NaCl-induced hypertension. Whole-body weights were not affected by CO, but organ weight changes in the form of cardiomegaly ranging from 22% (DR, low NaCl) to 36% (DS, high NaCl), and splenomegaly ranging from 29% (DR, low NaCl) to 98% (DS, high NaCl) were observed. The mean equilibrium carboxyhemoglobin concentration was 42% in the CO-exposed rats. The hematologic responses to the CO exposures were elevated total hemoglobin and hematocrit.

AU - Singh J

AU - Scott LH

TI - Threshold for carbon monoxide induced fetotoxicity

SI - TOXBIB/85/041030

SO - Teratology; Vol 30, ISS 2, 1984, P253-7

AB - Carbon monoxide (CO) is said to be the most widely encountered occupational and environmental contaminant. Threshold for CO-induced fetotoxicity was studied using mice as the experimental animal. Pregnant animals of CD-1 strain were exposed to 0, 65, 125, 250, or 500 ppm CO from gestation day 7 to 18. The animals were sacrificed on gestation day 18, and their uterine horns were examined for live or resorbed fetuses. The data suggest that maternal CO exposure to as low as 125 ppm affects fetal growth and higher levels affect viability. The data also suggest the developing organism is sensitive to chronic CO exposure, and this sensitivity is dose dependent. The fetal mouse is influenced at levels of exposure below those found transiently for human cigarette smokers and ambient CO concentrations associated with various occupations.

AU - Chen KC

AU - Lee EW

AU - McGrath JJ

TI - Effect of intermittent carbon monoxide inhalation on erythropoiesis and organ weights in rats

SI - TOXBIB/84/265774

SO - J Appl Toxicol; Vol 4, ISS 3, 1984, P145-9

AB - Sprague-Dawley rats were exposed to 450 ppm carbon monoxide (CO) for 6 hours per day, 5 days per week for 33 days. The effect of CO on reticulocyte count, hematocrit, hemoglobin concentration, body weight and selected organ weights was measured. Exposure to CO caused a 3-fold increase in the youngest reticulocyte population, concomitant with an increase in the total reticulocyte count. Despite continued CO exposure, reticulocyte number and distribution returned to normal by day 9, suggesting that reticulocyte response of the organism to CO had changed. Both hematocrit and hemoglobin concentrations began to increase 16 days after CO exposure and remained at the increased level for the duration of the exposure period. No changes in kidney, liver and adrenal weights were observed throughout the course of study. However, spleen weight was increased after 5 days of CO exposure. Left and right ventricular organ weight ratios increased equally at the same time during the study. These results indicate the increase in the young reticulocyte population and the subsequent increase in total reticulocyte count are the earliest erythropoietic responses to intermittent CO exposure and that CO-induced polycythemia is associated with cardiac hypertrophy in rats.

AU - Mactutus CF

AU - Fechter LD

TI - Prenatal exposure to carbon monoxide: learning and memory deficits

SI - TOXBIB/84/097544

SO - Science; Vol 223, ISS 4634, 1984, P409-11

AB - Exposing pregnant rats to carbon monoxide (150 parts per million) produced only minor reductions in the birth weights of the pups and gave no evidence of overt teratogenesis. However, behavioral evaluation of learning and memory processes in a 2-way avoidance task suggested a functional deficit in the central nervous system of the exposed offspring. Multiple dependent measures and specific control groups confirmed this deficit was independent of nonassociative or motivational alterations.

AU - Vyskocil A

AU - Tusl M

AU - Zaydlar K

TI - The effect of chronic exposure to 100 ppm carbon monoxide on brain biamines, serum corticosterone, and organ weights in rats

SI - TOXBIB/84/240863

SO - J Appl Toxicol; Vol 3, ISS 6, 1983, P307-9

AB - The effect of chronic exposure to 100 ppm (0.01 %) CO on pituitary-adrenal activity was evaluated by measuring serum corticosterone and brain bioamine levels in the rat. Exposure to CO for 1 month induced a decrease in the brain serotonin levels. Serum corticosterone, brain dopamine, and noradrenaline, as well as the weight of the adrenal glands, lungs, spleen, and liver were unchanged. After two months of exposure, serum corticosterone and brain serotonin levels were elevated and the liver weight was significantly lower. These changes suggest that at this chronic low concentration CO acts as a stressor, and the organism initiates a general defensive reaction. The effect of CO on the pituitary-adrenal axis could be mediated by a central neuronal pathway.

AU - Pankow D

AU - Haerting J

AU - Ponsold W

AU - Adam J

TI - Seasonal variations of carbon monoxide-induced polycythemia in rats

SI - TOXBIB/83/282730

SO - Biomed Biochim Acta; Vol 42, ISS 2-3, 1983, P255-63

AB - Fluctuations of the extent of polycythemia in rats, due to repeated exposure to carbon monoxide, prompted a study to determine whether the differences were caused by seasonal variations. Data from 18 independent experiments, involving the hemoglobin values of 206 CO-exposed and 208 control rats over a period of nearly 3 years, were available. Because the experiments were not designed for chronobiological studies, several methods of quasilinear and nonlinear regression analysis were applied to fit periodic models to the data. The best fit was obtained by a single cosine function with a period of nearly 12 months and with maximum values in winter and minimum values in summer. Experiments to elucidate mechanism(s) of seasonal variations showed that following a single CO exposure to the nocturnally active rodents, the rate of CO release from the body was higher in the dark span, that reduced food supply produced a potentiation of the CO-induced hemoglobin increase, and that adaptive CO response was not affected by testosterone or thyroidectomy, but inhibited by L-thyroxine. Thus, it seems that influences of light, CO elimination rate, food intake, metabolic rate, and related hormones play a role for seasonal variations.

AU - Stupfel M

AU - Demaria Pesce VH

AU - Perramon A

AU - Merat P

AU - Gourlet V

AU - Thierry H

TI - Inter and intraspecies genetic differences in survival to an acute carbon monoxide challenge in mice, rats, guinea pigs, quails, and chickens

SI - TOXBIB/83/181361

SO - Comp Biochem Physiol [A]; Vol 74, ISS 4, 1983, P933-7

AB - 1. Groups of small laboratory vertebrates, of both sexes, have been submitted to an acute carbon monoxide challenge, close to a LD50. 2. An interspecific classification, from low to high CO sensitivity, gives: guinea pigs-mice-chickens-rats-quails. 3. Interstrain statistical differences were observed in all species, with the exception of guinea pigs. Furthermore, among two selected genotypes of Japanese quails, one was resistant to acute nitrogen hypoxia and to carbon monoxide intoxication and the other sensitive to both these types of hypoxia. 4. Interspecific comparisons show similarities of genetic differences to acute CO intoxication and acute nitrogen normobaric hypoxia.

AU - Mullin LS

AU - Krivanek ND

TI - Comparison of unconditioned reflex and conditioned avoidance tests in rats exposed by inhalation to carbon monoxide, 1,1,1-trichloroethane, toluene, or ethanol

SI - TOXBIB/83/037715

SO - Neurotoxicology; Vol 3, ISS 1, 1982, P126-37

AB - The sensitivity of unconditioned reflex and conditioned avoidance tests in evaluating behavioral toxicity was compared. Male rats were exposed by inhalation up to four hours to 0, 200, 400, 800, or 1600 ppm carbon monoxide (CO); 0, 1500, 3000, 6000, or 12,000 ppm 1,1,1-trichloroethane; 0, 800, 1600, 3200, or 6400 ppm toluene; or 0, 4000, 8000, 16,000, or 32,000 ppm ethanol. Animals were tested for behavioral changes at 0.5, 1, 2, and 4 hours during exposure and 18 hours after exposure ended. In unconditioned reflex testing, the presence or absence of specific unconditioned reflexes (such as corneal, placing, grasping, and righting reflexes) and simple behavior patterns, including locomotor activity and coordination, were observed. The conditioned reflex task consisted of shock avoidance by lever press following simultaneous light and sound stimuli. Rats began to fail unconditioned reflex tests at 800 ppm CO, 3000 ppm trichloroethane, 800 ppm toluene, and 8000 ppm ethanol. Decrements in conditioned avoidance were observed at 800 ppm CO, 6000 ppm trichloroethane, 3200 ppm toluene, and 8000 ppm ethanol. Neither test was consistently more sensitive than the other in detecting behavioral changes. For both methods, the concentrations at which changes were detected in rats were 2 to 10 times higher than those reported for human effects.

AU - Umeda M

AU - Ishikawa K

AU - Kinouchi N

TI - On susceptibility for carbon monoxide exposure. The effect of carbon monoxide exposure on hepatic drug metabolizing enzymes of mice

SI - TOXBIB/83/216903

SO - Sangyo Igaku; Vol 24, ISS 6, 1982, P663-71

AB - Male mice were exposed to three levels of carbon monoxide, i.e. 500, 1000, and 3000 ppm for 60, 10, and 7 minutes per day, respectively. Durations of the exposure were 1 and 5 days and 3, 6,

and 9 weeks. As the effect of carbon monoxide exposure, induction of the drug metabolizing enzyme was observed, which was ascertained by the decrease of sleeping time by pentobarbital and by the increase of activities of liver microsomal p-nitroanisole demethylase and of aniline hydroxylase. These results should be due to an adaptive response to carbon monoxide exposure, but the mechanisms of the enzyme induction were not fully explained in this study. In 5 days of exposure to carbon monoxide, a dose-response relationship was observed between the degree of carbon monoxide exposure and the extent of enzyme induction. But in the prolonged exposure to higher concentrations of carbon monoxide (1000 and 3000 ppm), the increase of drug metabolism became less pronounced and by 9 weeks of exposure to 1000 ppm carbon monoxide, little induction of the drug metabolizing enzyme was observed. These results suggest that induction of the drug metabolizing enzyme by carbon monoxide exposure has a certain limit.

AU - Thomas WC

AU - O'Flaherty EJ

TI - The cardiotoxicity of carbon monoxide as a component of polymer pyrolysis smokes

SI - TOXBIB/82/250984

SO - Toxicol Appl Pharmacol; Vol 63, ISS 3, 1982, P363-72

AU - Funata N

AU - Okeda R

AU - Takano T

AU - Miyazaki Y

AU - Higashino F

AU - Yokoyama K

AU - Manabe M

TI - Electron microscopic observations of experimental carbon monoxide encephalopathy in the acute phase

SI - TOXBIB/82/226700

SO - Acta Pathol Jpn; Vol 32, ISS 2, 1982, P219-29

AB - The cerebral and cerebellar lesions of the cats that were exposed to 0.3% carbon monoxide gas under artificial respiration were examined at different intervals by an electron microscope. During the first few days, the most outstanding features were segmental empty axonal swelling, dilatation of the extracellular space, swelling and necrosis of astrocytes and oligodendroglia, and lamellar separation of the myelin sheath predominantly in the deep cerebral white matter. These changes subsided within one week. Instead, collapsed myelin increased in number and phagocytosis of disintegrated myelin was occasionally observed. Astrocytes and oligodendroglia became prominent in size and number. Changes suggestive of selective damage of myelin or oligodendroglia were not encountered. CO, followed by Wallerian degeneration, and the pathogenesis of CO-encephalopathy were discussed.

AU - Davies DM

AU - Jolly EJ

AU - Pethybridge RJ

AU - Colquhoun WP

TI - The Effects of Continuous Exposure to Carbon Monoxide on Auditory Vigilance in Man

SO - Int Arch Occup Environ Health Vol 48, 1981, P25-34

AB - Six different groups of non-smoking young male subjects were studied separately for 18 consecutive days, each in a closed controlled-environment human exposure chamber. Each group was

subjected to a 5-day control period in fresh air followed successively by an 8 day period of continuous exposure to 50 ppm, 15 ppm, or 0 ppm (control) by volume of carbon monoxide (CO) in air, and a 5-day recovery period in fresh air. The subjects performed a 1-hour auditory vigilance task every day at the same time of day in a fixed qualitative, quantitative, and temporal relationship with food intake, consumption of stimulating beverages, physical activity, and sleep. It was concluded that such CO exposure, involving the continuous carriage of carboxyhemoglobin loads up to 7%, was without significant effect on auditory vigilance.

AU - Shamarin AA

AU - Iurasova OI

AU - Goev GB

TI - Evaluation of the state of the hemato-encephalic barrier in studying the neurotoxic action of carbon monoxide

SI - TOXBIB/82/073825

SO - Gig Sanit, ISS 10, 1981, P33-5

AU - Negrienko KV

AU - Shubik VM

TI - Immunological reactivity of experimental animals exposed to carbon monoxide

SI - TOXBIB/82/005245

SO - Gig Sanit, ISS 6, 1981, P76-7

AU - Marshall M

AU - Hess H

TI - Acute effects of low carbon monoxide concentrations on blood rheology, platelet function, and the arterial wall in the minipig (author's transl)

SI - TOXBIB/81/200511

SO - Res Exp Med (Berl); Vol 178, ISS 3, 1981, P201-10

AB - While investigating the initial effects of low carbon monoxide concentrations on haemorheology and the arterial wall, minipigs were exposed to CO-air mixtures with 160, 185, and 420 ppm CO. The daily exposure time was 4 hours. Exposure to 160 and 185 ppm CO led to a significant increase of platelet aggregation. Four hundred twenty ppm CO caused an increase in haematocrit, blood and plasma viscosity, and in platelet aggregation. When examined by light microscopy, no changes were found in the arterial wall, whereas scanning electron-microscopic examinations revealed adhesions of shape-changed platelets on the arterial endothelium in some cases after a single 4-hour exposure to 160 or 185 ppm CO. After 4 x 4-hour exposures to 420 ppm CO, mixed microthrombi were present on the arterial endothelium. According to preliminary transmission electron-microscopic studies, these adhesions of platelets, and also adhesions of mononuclear elements, can always be related to foci of degeneration in the endothelial cells. These examinations showed that low concentrations of carbon monoxide can cause both haemorheological and morphological changes in the arterial wall. The further development of these changes under chronic CO exposure and a possible significance of the environmental hygiene beyond cigarette smoking must be clarified by long-term experiments.

3.3 Tobacco Related Papers

AU - Mennear JH

TI - Carbon monoxide and cardiovascular disease: an analysis of the weight of evidence

SI - TOXBIB/93/181568

SO - Regul Toxicol Pharmacol; Vol 17, ISS 1, 1993, P77-84 (REF: 20)

AB - The role, if any, of environmental tobacco smoke (ETS) in the causation or exacerbation of cardiovascular disease remains to be proven and defined. Earlier workers suggested that ETS-associated carbon monoxide, nicotine, or polyaromatic hydrocarbons may be causative factors. The purpose of this review was to assess the weight of evidence supporting a role for ambient carbon monoxide in the etiology of human ischemic cardiovascular disease. The findings show that scant clinical or experimental evidence to support a role for carbon monoxide in the causation of ischemic heart disease. Further, the results of field studies of relative air quality in nonsmoking and smoking homes, offices, and public places show that ETS contributes only minor and toxicologically insignificant increments in ambient carbon monoxide concentrations. These increments are variable and easily masked by other common carbon monoxide sources, such as internal combustion engines and the burning of cooking and heating fuels. It is concluded that if ETS plays a role in the etiology of cardiovascular disease, it is most likely not mediated through carbon monoxide.

AU - Lando HA

AU - McGovern PG

AU - Kelder SH

AU - Jeffery RW

AU - Forster JL

TI - Use of carbon monoxide breath validation in assessing exposure to cigarette smoke in a worksite population

SI - TOXBIB/92/007653

SO - Health Psychol; Vol 10, ISS 4, 1991, P296-301

AB - Assessed the usefulness of carbon monoxide (CO) breath validation of self-reported smoking status in a large worksite population (N = 4,647). CO assessment was performed as part of a baseline survey procedure. CO levels differed substantially in relation to self-reported smoking status and amount smoked. Correcting for ambient exposure (estimated by mean CO levels among never smokers) produced more satisfactory results than uncorrected CO levels. Striking company differences were observed in mean CO exposures among self-reported never smokers. An unexpected finding was that 17.1% of current smokers reported smoking less than daily. Although the CO measure was excellent in detecting moderate and heavy smokers, it was inadequate in detecting occasional and light smokers. If detection of occasional or lighter smoking is critical to the purposes of the study, the more expensive (but more accurate) cotinine measure is preferred.

AU - Doolittle DJ

AU - Rahn CA

AU - Lee CK

TI - The effect of exposure to nicotine, carbon monoxide, cigarette smoke or cigarette smoke condensate on the mutagenicity of rat urine

SI - TOXBIB/91/226461

SO - Mutat Res; Vol 260, ISS 1, 1991, P9-18

AB - Cigarette smokers have been reported to void urine which is more mutagenic than that voided by non-smokers, but the specific urinary mutagen(s) have not been identified. Because mechanistic studies are best performed in animal models, the objective of this study was to determine if a model to study the role of cigarette smoke and its components in urinary mutagenicity could be developed in rats. XAD-2 resin was used to concentrate the urine and the microsuspension modification of the Ames test used to quantify mutagenicity. Nicotine administered by intraperitoneal injection at 0.8 $\mu\text{g/kg}$ (the maximum tolerated dose) or inhalation of carbon monoxide for 14 days at the maximum tolerated dose (1800 ppm, resulting in 68% carboxyhemoglobin) did not increase urinary mutagenicity. Cigarette smoke condensate (CSC) prepared by electrostatic precipitation of mainstream smoke increased urinary mutagenicity at doses of 100 and 200 $\mu\text{g/kg}$ when administered acutely by either i.p. injection or gavage, verifying the assay system was capable of detecting cigarette smoke-related mutagens in the urine. However, cigarette smoke administered by the appropriate route of exposure, nose-only inhalation, for 1, 7, 14, or 90 days (1 hour per day) did not increase urinary mutagenicity. The smoke concentration administered was at or near the maximum tolerated dose as evidenced by carboxyhemoglobin concentrations of approximately 50%, and of 10% or more weight loss in exposed animals. Thus, although cigarette smoke condensate is mutagenic in vitro and mutagenic urine was observed when rats were given high doses of CSC by inappropriate routes of administration, acute or subchronic inhalation exposure to the maximum tolerated dose of whole cigarette smoke did not increase urinary mutagenicity in rats. These results indicate that the rat may be an inappropriate model to study urinary mutagenicity following the inhalation of tobacco smoke.

AU - Krzyzanowski M

AU - Sherrill DL

AU - Paoletti P

AU - Lebowitz MD

TI - Relationship of respiratory symptoms and pulmonary function to tar, nicotine, and carbon monoxide yield of cigarettes

SI - TOXBIB/91/119296

SO - Am Rev Respir Dis; Vol 143, ISS 2, 1991, P306-11

AB - The data from consecutive surveys of the Tucson Epidemiologic Study (1981-1988) were used to evaluate the relationship in cigarette smokers of respiratory symptoms and pulmonary function to tar, nicotine, and carbon monoxide (CO) yields of the cigarette. In at least one survey, a total of 690 subjects over age 15 reported smoking regularly. After adjustment for intensity and duration of smoking and for depth of inhalation, the risk of chronic phlegm, cough, and dyspnea were not related to the tar and nicotine yields. In 414 subjects with pulmonary function tested in at least one of the three surveys, the spirometric indices used were significantly related to the daily dose of tar, nicotine, and CO (product of the cigarette yield and daily number of cigarettes smoked). The effects were more pronounced for past than for current doses. However, the differentiation of pulmonary function due to various yields of cigarettes was small in comparison to the difference in pulmonary function between smokers and nonsmokers.

AU - Allen DR

AU - Browse NL

AU - Rutt DL

AU - Butler L

AU - Fletcher C

TI - The effect of cigarette smoke, nicotine, and carbon monoxide on the permeability of the arterial wall

SI - TOXBIB/88/091181

SO - J Vasc Surg; Vol 7, ISS 1, 1988, P139-52

AB - The association between cigarette smoking and the development of atherosclerosis is well established, but the mechanism that makes cigarettes such a potent risk factor is not understood. Normally, plasma macromolecules constantly permeate the arterial wall. Fibrinogen and lipids are two of the large molecules involved in atherosclerosis. Therefore, the study investigated the effect of cigarette smoke, nicotine, and carbon monoxide on the permeability of the canine arterial wall to ¹²⁵I-labeled fibrinogen. The results show that inhaled cigarette smoke significantly and rapidly increases the permeability of the arterial wall to fibrinogen and that this effect can be produced with carbon monoxide alone, but not with intravenous nicotine.

AU - Effeney DJ

TI - Prostacyclin production by the heart: effect of nicotine and carbon monoxide

SI - TOXBIB/87/141425

SO - J Vasc Surg; Vol 5, ISS 2, 1987, P237-47

AB - Smoking has been linked to the development and progression of atherosclerosis, but the mechanism by which smoking exerts its deleterious effects remains unknown. This study was designed to examine in a systematic way the effects of nicotine and carbon monoxide on platelets, arterial walls, and the heart. Results of experiments designed to assess the effect of nicotine and carbon monoxide on the production of prostacyclin (PGI₂) by the rabbit heart are reported. Animals exposed to carbon monoxide showed carboxyhemoglobin raised to at least 12% by breathing an atmosphere enriched with carbon monoxide. Nicotine was infused at 50 µg/kg/hour for 1 week. Nicotine was measured by gas/liquid chromatography. PGI₂ was measured by radioimmunoassay of 6-keto-PGF₁ α, and its biologic activity was assessed by inhibition of platelet aggregation. Nicotine is concentrated in the heart and blood vessel wall and causes a statistically significant reduction in PGI₂ production. Carbon monoxide raised PGI₂ production significantly in all chambers, and the combination of nicotine and carbon monoxide further raised PGI₂ production. The difference between the effects of nitrogen and carbon monoxide alone and nitrogen and a combination of nitrogen and carbon monoxide was significant in all chambers. It is hypothesized that nicotine exerts a direct metabolic effect in lowering PGI₂ production. Carbon monoxide may make the endothelial cell relatively hypoxic, a powerful stimulus of PGI₂ production, or, less likely, exert a direct toxic effect on the endothelial cell.

AU - Mannisto J

AU - Puustinen T

AU - Uotila P

TI - Carbon monoxide is not responsible for the cigarette smoke-induced changes in the pulmonary metabolism of arachidonic acid and prostaglandin E₂

SI - TOXBIB/85/247667

SO - Acta Pharmacol Toxicol (Copenh); Vol 56, ISS 3, 1985, P265-8

AB - Cigarette smoke is known to interfere with the pulmonary metabolism of arachidonic acid and prostaglandin E₂ (PGE₂). The possible role of carbon monoxide in these cigarette smoke-induced alterations was investigated in this study. ¹⁴C-Arachidonic acid (50 nmol) was infused into the pulmonary circulation of isolated perfused hamster lungs, and the radioactive metabolites in the perfusion effluent, as well as the distribution of incorporated radioactive arachidonic acid within the lung lipids, were analysed. Carbon monoxide, added into the ventilatory air, had no effect on the oxidative metabolism of arachidonic acid or on the distribution of radioactive arachidonic acid within

the lung. In addition, carbon monoxide had no effect on the metabolism of PGE2 following infusion of 100 nmol of 14C-PGE2 into the rat pulmonary circulation. The present study suggests that carbon monoxide is not responsible for the cigarette smoke-induced changes in the pulmonary metabolism of arachidonic acid and PGE2.

AU - Borland C

AU - Chamberlain A

AU - Higenbottam T

AU - Shipley M

AU - Rose G

TI - Carbon monoxide yield of cigarettes and its relation to cardiorespiratory disease

SI - TOXBIB/84/054201

SO - Br Med J (Clin Res Ed); Vol 287, ISS 6405, 1983, P1583-6

AB - Estimates of the carbon monoxide yield of their cigarettes have been obtained for 4910 smokers (68% of all smokers) in the Whitehall study of men aged 40 to 64. In the 10 years after examination, 635 men died. When men smoking cigarettes with high carbon monoxide yield were compared with those smoking cigarettes with a low yield, and after adjusting for age, employment grade, amount smoked, and tar yield, the risk of death was 32% lower for coronary heart disease, 49% higher for lung cancer, and 10% lower for total mortality; these differences were not statistically significant. Among men who said that they inhaled, the risk of fatal coronary heart disease was 51% lower in the high carbon monoxide group (p less than 0.01), while the risk of lung cancer was 75% higher. These results provide no evidence that a smoker can reduce his risk of death by smoking a brand with a low carbon monoxide yield; he might even increase it. The complex interactions between characteristics of the smoker, smoking behaviour, constituents of tobacco smoke, and health are again demonstrated.

AU - Klausen K

AU - Andersen C

AU - Nandrup S

TI - Acute effects of cigarette smoking and inhalation of carbon monoxide during maximal exercise

SI - TOXBIB/84/028612

SO - Eur J Appl Physiol; Vol 51, ISS 3, 1983, P371-9

AB - The acute effect of inhaling the smoke of three cigarettes was compared to the effect of inhalation of an amount of carbon monoxide (CO), giving the same CO-saturation of the arterial blood as smoking during rest and during maximal exercise on a Krogh cycle ergometer. The 16 male subjects were tested in the morning: 1) after about 8 hours without smoking (control); 2) after inhalation of the smoke of three cigarettes (smoke); and 3) after CO-inhalation (CO). It was found that the average maximal rate of O₂-uptake (VO₂max) decreased during both smoke and CO by about 7%. Endurance time at VO₂ max decreased 20% during smoke but only 10% during CO. A significant decrease in maximal heart rate (HR), and an increase in HR at rest, was demonstrated only during smoke. The peak lactate concentration (HLA) following maximal exercise was significantly decreased after smoke. The results suggest the decrease in VO₂ max during smoke is due to the CO-saturation of the blood, and hence to a decrease in the oxygen capacity of the blood, while the decrease in endurance time during smoke is combined effect of the CO-saturation and an increased cost of breathing caused by the smoke particles. It is further suggested that nicotine, or possibly some other components of the smoke, have an enhancing effect on the heart at rest, while an inhibition is seen during maximal exercise. (ABSTRACT TRUNCATED AT 250 WORDS)

AU - Penn A
AU - Butler J
AU - Snyder C
AU - Albert RE

TI - Cigarette smoke and carbon monoxide do not have equivalent effects upon development of arteriosclerotic lesions

SI - TOXBIB/84/279449

SO - Artery; Vol 12, ISS 2, 1983, P117-31

AB - Experiments were performed to test whether exposure to mainstream cigarette smoke, without any diet modification, was sufficient to exacerbate arteriosclerotic lesion development in cockerels. Additionally, the experiments were designed to test whether any such effect could be attributed solely to carbon monoxide (CO) in the smoke. Three groups of cockerels (7/group) were exposed 5 days/week in standard inhalation chambers. Each day, one group (smoke) was exposed to smoke produced from the combustion of two packs of cigarettes. A second group (CO) was exposed to CO at levels equivalent to those produced during the combustion of two packs of cigarettes. A third group was sham-exposed. Following sacrifice, the abdominal aorta of each animal was cut into 5 mm segments and the extent of arteriosclerotic lesion development was measured. In smoke animals, compared to those in either of the other two groups, more aortic segments were found with measurable lesions present and the cross-sectional areas of these segments were greater. On a comparative basis, the smoke lesions were three times larger than in either of the other two groups, despite the fact that blood carboxyhemoglobin levels were the same in CO and smoke animals. The location of the lesions and their histological appearance were very similar to those previously described for spontaneous and carcinogen-associated lesions in the cockerel. These results demonstrate that as little as four months of daily exposure to cigarette smoke, in the absence of a cholesterol supplemented diet, can help accelerate arteriosclerotic lesion development. Further, this accelerated development cannot be attributed solely to CO in the smoke.

AU - Jarvis MJ
AU - Russell MA
AU - Feyerabend C

TI - Absorption of nicotine and carbon monoxide from passive smoking under natural conditions of exposure

SI - TOXBIB/84/073857

SO - Thorax; Vol 38, ISS 11, 1983, P829-33

AB - Seven non-smokers were exposed to tobacco smoke under natural conditions for two hours in a public house. Measures of nicotine and cotinine in plasma, saliva, and urine and expired air carbon monoxide all showed reliable increases. The concentrations of carbon monoxide and nicotine after exposure averaged 15.7% and 7.5%; respectively, of the values found in heavy smokers. Although the increase in expired air carbon monoxide of 5.9 ppm was similar to increases in smokers after a single cigarette, the amount of nicotine absorbed was between a tenth and a third of the amount taken in from one cigarette. Since this represented a relatively extreme acute natural exposure, any health risks of passive smoking probably depend less on quantitative factors than on qualitative differences between sidestream and mainstream smoke.

AU - Kaufman DW
AU - Helmrich SP
AU - Rosenberg L

AU - Miettinen OS

AU - Shapiro S

TI - Nicotine and carbon monoxide content of cigarette smoke and the risk of myocardial infarction in young men

SI - TOXBIB/83/115140

SO - N Engl J Med; Vol 308, ISS 8, 1983, P409-13

AB - To evaluate whether the nicotine and carbon monoxide content of cigarette smoke is related to the risk of nonfatal first myocardial infarction in young men, 502 cases were compared with 835 hospital controls, all between the ages of 30 and 54 years. As expected, the estimated risk of myocardial infarction increased with the number of cigarettes smoked; overall, the relative-risk estimate for current smokers was 2.8 (95% confidence interval, 2.0 to 4.0). The risk did not appear to vary according to the amount of nicotine or carbon monoxide in the cigarette, and the mean amounts of both substances per cigarette were similar for the cases and controls. The results suggest that men who smoke the newer cigarettes with reduced amounts of nicotine and carbon monoxide do not have a lower risk of myocardial infarction than those who smoke cigarettes containing larger amounts of these substances.

4.0 Papers Relating to Measurement

AU - Touger M

AU - Gallagher EJ

AU - Tyrell J

TI - Relationship between venous and arterial carboxyhemoglobin levels in patients with suspected carbon monoxide poisoning

Department of Medicine, Bronx Municipal Hospital, Albert Einstein College of Medicine.

Language: Eng

SO - Ann Emerg Med 1995 Apr;25(4):481-3

Unique Identifier: 95225523

AB - STUDY OBJECTIVE: To test the hypothesis that venous carboxyhemoglobin (V-COHb) levels accurately predict arterial (A-COHb) levels. DESIGN: Prospective comparison of A-COHb and V-COHb levels in patients with suspected carbon monoxide (CO) poisoning. SETTING: Municipal hospital emergency department with contiguous multiplace hyperbaric chamber staffed 24 hours a day. PARTICIPANTS: Unselected convenience sample of 61 adults with suspected CO toxicity. INTERVENTION: Simultaneous sampling of arterial and venous blood. RESULTS: Correlation between V-COHb and A-COHb showed an r value of 0.99 (95% CI, 0.99 to 0.99), and an r^2 value of 0.98. Agreement between V-COHb and A-COHb levels was examined by use of a plot of arteriovenous differences against the mean of the two measurements. The mean arteriovenous difference was 0.15% COHb (95% CI, 0.13% to 0.45%), with 95% of the differences ranging from 2.4% COHb to -2.1% COHb. CONCLUSION: Venous COHb levels predict arterial levels with a high degree of accuracy. Patients with suspected CO poisoning can be screened with the use of venous blood, without the need for arterial puncture.

AU - Lee PS

AU - Schreck RM

AU - Hare BA

AU - McGrath JJ

TI - Biomedical applications of tunable diode laser spectrometry: correlation between breath carbon monoxide and low level blood carboxyhemoglobin saturation

SI - TOXBIB/94/338033

SO - Ann Biomed Eng; Vol 22, ISS 1, 1994, P120-5

AB - Tunable diode laser spectrometry was used to measure breath carbon monoxide (CO) concentrations in nonsmoking subjects. Corresponding blood carboxyhemoglobin (COHb) saturations between physiological levels and levels after 1 and 8 hours exposure to 9 ppm CO, the maximum permissible concentration in the air under federal regulations, were also determined. A good linear correlation between breath CO and blood COHb saturation for low levels representing ambient conditions was established, with a correlation coefficient better than 0.999 for the means and 0.945 for the individual data points. Similar studies on the other compounds of concern are also possible using tunable diode laser spectrometry, requiring only a breath sample and with no sample preparation. This technique will facilitate fast, noninvasive environmental health effect and biomedical studies.

AU - Van Dam J

AU - Daenens P

TI - Microanalysis of carbon monoxide in blood by head-space capillary gas chromatography

SI - TOXBIB/94/253779

SO - J Forensic Sci; Vol 39, ISS 2, 1994, P473-8

AB - A gas chromatographic procedure for the determination of carboxyhaemoglobin in blood was improved by using a capillary system in combination with a micro thermal conductivity detector. This system is very sensitive with high resolutions. The analytical time is reduced to approximately two minutes. Using sulphuric acid as the liberating agent of carbon monoxide, a gradual and reproducible release of carbon monoxide was seen. This process shortens the time in emergency cases for sample preparation.

AU - Cardeal ZL

AU - Pradeau D

AU - Hamon M

AU - Abdoulaye I

AU - Pailler FM

AU - Lejeune B

TI - New calibration method for gas chromatographic assay of carbon monoxide in blood

SI - TOXBIB/93/382064

SO - J Anal Toxicol; Vol 17, ISS 4, 1993, P193-5

AB - The calibration method described is based on the in situ formation of carbon monoxide in a closed system by the reaction of hot concentrated sulfuric acid with formic acid. Carbon monoxide is released from hemoglobin by treatment with 85% phosphoric acid, diluted 1:2 (v/v). Carbon monoxide is analyzed by means of headspace gas chromatography on a Porapak Q 80-100 column, following catalytic reduction to methane, using a flame-ionization detector. The method was validated by comparing the results obtained for blood samples from patients suffering from carbon monoxide poisoning and previously analyzed by means of spectrophotometry.

AU - Lechnitz K

TI - Determination of the time-weighted average concentration of carbon monoxide in air using a long-term detector tube

SI - TOXBIB/93/293280

SO - IARC Sci Publ, ISS 109, 1993, P346-52

AU - Mage DT

TI - Determination of carbon monoxide in indoor air with a direct-reading instrument

SI - TOXBIB/93/293279

SO - IARC Sci Publ, ISS 109, 1993, P342-5

AU - Lee K

AU - Yanagisawa Y

AU - Spengler JD

AU - Billick IH

TI - Measurement of personal carbon monoxide exposures by mailed passive sampler

SI - TOXBIB/93/119600

SO - J Air Waste Manage Assoc; Vol 42, ISS 9, 1992, P1212-3

AU - Balkon J

TI - Results of a multilaboratory check sample analysis program for carbon monoxide and cyanide

SI - TOXBIB/92/072272

SO - J Anal Toxicol; Vol 15, ISS 5, 1991, P232-6

AB - A blind check sample analysis program, designed to evaluate global performance in the determination of fire-related analytes (carbon monoxide and cyanide), was implemented and processed using 10 field forensic toxicology laboratories. Each participant received, on a quarterly basis, a set of four calibrators and a set of four unknown check samples. Each participant was asked to determine the presence and quantity of carbon monoxide (carboxyhemoglobin in percent saturation of hemoglobin units) and cyanide (in mg/L units), using the calibrators for reference. The results were to be reported anonymously. Prior to and during the analysis period, all batches of calibrators and check samples were validated for analyte stability using gas chromatography, CO-oximetry, and ion chromatography. The performance of the laboratories in the analysis of carboxyhemoglobin was evaluated over a concentration range of 3 to 40% saturation yielding a correlation with validation concentrations of 0.986. In some cases, false negatives and false positives were reported. The performance of laboratories in the analysis of cyanide was evaluated over a concentration range of 0.1 to 2.5 mg/L. Laboratory results yielded a correlation of 0.443 with validated concentrations. False negatives and false positives were also reported. Based upon the correlation estimates, it was concluded that forensic toxicology laboratories are likely to generate reliable carboxyhemoglobin data.

AU - Iffland R

AU - Balling P

AU - Eiling G

TI - Optimizing carbon monoxide detection in biological material

SI - TOXBIB/90/056392

SO - Beitr Gerichtl Med; Vol 47, 1989, P87-94

AB - The determination of the CO-content is difficult in heated or putrified samples of blood and tissues. The preparation of these materials and a sensitive gas-chromatographic detection of small amounts of carbon-monoxide with head-space technique are described. The iron-content of a sample is a measure for the complete saturation with carbon-monoxide. This content is measured with AAS in the same vessel used before to determine CO. The presented method is also suited for ecological studies.

AU - Bogusz M

AU - Aderjan R

AU - Bosche J

TI - The determination of carbon monoxide in blood by means of electrochemical pocket gas meter

SI - TOXBIB/89/038468

SO - J Anal Toxicol; Vol 12, ISS 4, 1988, P225-8

AB - The Comopac electrochemical device for CO determination in the workplace was adapted for CO and COHb determination in blood. The method enables the determination of COHb from 1 to 95% in 0.5 mL of blood in 20 min. Comparison of results obtained with the Comopac, spectrophotometry, and gas chromatography showed comparable accuracy and precision. The specificity of the electrochemical method was better than spectrophotometry and comparable with gas chromatography.

AU - Mage DT
TI - Determination of carbon monoxide in indoor air with a direct-reading detector
SI - TOXBIB/88/113969
SO - IARC Sci Publ, ISS 81, 1987, P191-201

AU - Adams JD
AU - O'Mara-Adams KJ
TI - Determination of carbon monoxide in sidestream tobacco smoke
SI - TOXBIB/88/113968
SO - IARC Sci Publ, ISS 81, 1987, P185-90

AU - Mironova NP
AU - Il'in VP
AU - Semikina LG
TI - Comparative evaluation of the methods of tracing carbon monoxide in the air of the work area
SI - TOXBIB/87/305677
SO - Gig Tr Prof Zabol, ISS 6, 1987, P54-6

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AU - Ott WR
AU - Rodes CE
AU - Drago RJ
AU - Williams C
AU - Burmann FJ
TI - Automated data-logging personal exposure monitors for carbon monoxide
SI - TOXBIB/87/009435
SO - J Air Pollut Control Assoc; Vol 36, ISS 8, 1986, P883-7

AU - Costantino AG
AU - Park J
AU - Caplan YH
TI - Carbon monoxide analysis: a comparison of two co-oximeters and headspace gas chromatography.
Language: Eng
SO - J Anal Toxicol 1986 Sep-Oct;10(5):190-3
Unique Identifier: 87037974
AB - Three methods (IL-182 Co-Oximeter, IL-282 Co-Oximeter, and headspace gas chromatography) for the analysis of carbon monoxide in postmortem blood were studied and compared using a prepared reference standard, Quanta control materials, and 62 postmortem blood specimens. The methods compared favorably with one another. The linear regression equations for the 62 postmortem blood samples (range = 1.0 to 86% saturation) were: IL-282 vs. IL-182, $y = 1.11x - 3.10$, $r = 0.981$; IL-182 vs. GC, $y = 0.88x + 2.97$, $r = 0.973$; IL-282 vs. GC, $y = 1.00x - 1.24$, $r = 0.986$.

AU - Hanika G
TI - Gas chromatography measurement of carbon monoxide in exhaled air in the ppm area
SI - TOXBIB/86/098984
SO - Z Gesamte Hyg; Vol 31, ISS 10, 1985, P574-6

AU - Aviado DM
TI - Carbon monoxide as an index of environmental tobacco smoke exposure
SI - TOXBIB/84/208534
SO - Eur J Respir Dis Suppl; Vol 133, 1984, P47-60 (REF: 93)

AU - Kedik LM
AU - Novikova IS
TI - Use of the gas chromatography technic to determine carbon monoxide in air
SI - TOXBIB/84/237625
SO - Gig Sanit, ISS 4, 1984, P45-6

AU - Gonzalez LA
AU - Sefton MV
TI - Stain length passive dosimeter for monitoring of carbon monoxide
SI - TOXBIB/83/305513
SO - Am Ind Hyg Assoc J; Vol 44, ISS 7, 1983, P514-20
AB - A new passive dosimeter for the personal monitoring of carbon monoxide exposure in the workplace has been developed. This new type of sampling device does not require follow-up analysis of the collected sample to determine the exposure. Rather, the time-weighted average concentration is determined directly from the length of a colored stain which is produced instantaneously during the exposure period in a specially prepared indicator tube. The colored stain length is a function of contaminant concentration and exposure time. The effects of carbon monoxide concentration in the range of 0.5 T TLV to 2.0 x TLV on the response of the dosimeter were evaluated in a dynamic exposure chamber. In this range of concentration, plots of stain length against exposure collapsed onto a single curve. At the TLV exposure, the stain length was 2.1 cm and the 95% confidence interval about this point was +/- 17%. Relative humidity in the range of 26 to 92% and face velocity in the range of 0.01 to 1.0 m/s (2 to 200 fpm) did not significantly affect the dosimeter response. These data were fitted to the appropriate model equation with a correlation coefficient of 0.968. By eliminating the need for follow-up analysis, this stain length dosimeter significantly reduces the cost of monitoring. The instantaneous readout eliminates the delay between exposure and quantification, enabling more careful control of the workplace environment.

AU - Palus J
AU - Majka J
AU - Sokal J
TI - Determination of low concentrations of carbon monoxide in the air by gas chromatography
SI - TOXBIB/83/218353
SO - Med Pr; Vol 33, ISS 5-6, 1982, P283-8
AB - Determination of carbon monoxide by gas chromatography was described. Having been separated from other air components, carbon monoxide is reduced to methane in the presence of nickel catalyst and determined on the flame-ionization detector. A rectilinear dependence was found between the peak surface or height and CO concentration within 0.5-1000 ppm. The low detectability limit was 0.2 ppm.

Pacific Northwest National Laboratory

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