Gezondheidsraad

Commentaar op conceptadvies Koolmonoxide

Comments on draft report Carbon monoxide

Inhoud

Dit document bevat de letterlijke weergave van de commentaren (deels Engelstalig) van:

- NIOSH, *National Institute for Occupational Safety and Health* (commentaar van 5 reviewers)
- Caesar Consult namens Koninklijke Metaalunie en Vereniging FME
- Mr. Donnay
- Prof. Lindhout
- Mr. Van Slooten

This document contains the comments (some in Dutch) by:

- NIOSH, National Institute for Occupational Safety and Health (comments by 5 reviewers)
- Caesar Consult on behalf of *Koninklijke Metaalunie* and *Vereniging FME*
- Mr. Donnay
- Prof. Lindhout
- Mr. Van Slooten

Comments on DECOS draft document on Carbon monoxide

By: Barbara M. Alexander, General Engineer
NIOSH/Division of Field Studies and Engineering
Cincinnati, Ohio, USA

PAGE NUMBER, LINE NUMBER	COMMENT
General Comments	The Committee's recommendations are well-supported. Feasibility of compliance with the new occupational exposure limit is likely not under consideration here. However, the new limit is largely based on the study of Lee et al.[36] That study is a meta-analysis of 26 studies, 6 of which include ambient concentrations of CO that are higher than the new occupational exposure limit. Compliance with a limit that is lower than levels that can be reached in ambient air is likely to be quite difficult. Multiple issues of grammar and spelling were observed, such as poor agreement between subject and verb (for example, plural subject and singular verb), and misspellings such as "Swedisch."
Specific Comments	
Page 11, Table 1	Under "Synonyms," the words, "carbon monoxide," appear twice. It is possible that the second occurrence is meant to be "carbon monooxide" (three o's instead of two).
Page 13, line 15	Replace the word, "and," with "an."
Page 17, Table 2	On the 7th line of Table 2, the word, "stuff," does not seem to make sense. Should there be a different word in its place?
Page 19, line 7	Spell out "American Conference of Governmental Industrial Hygienists" on first use, replace "ACHIH" with "ACGIH" and replace "Indice" with "Index."
Page 20, line 4	The words, "of or across," do not make sense in this context.
Page 21, line 6	The word, "minimally," is used twice in this sentence. Please delete one.
Page 21, line 21	Delete "upon."
Page 23, Table 4	In the third row of the table, "To protect for excitotoxicity and ischaemic insults in neurons," does not sound like an adverse outcome, and should probably be deleted.
Page 33, line 28	Delete "in."
Page 34, line 16	Replace "one chronic" with "one is a chronic."

Page 38, line 15	Please spell out the phrase for which "GRADE" is an acronym, "Grading of Recommendations Assessment, Development and Evaluation."
Page 39, Table 11	Under Causality determination, for respiratory morbidity, long-term, replace "of" with "to infer."
Page 41, line 27	Replace "en" with "and."
Page 42, lines 20–21	Replace "were intervened for a primary percutaneous coronary artery" with "had a primary percutaneous coronary artery intervention."
Page 50 (page number missing), line 14	Replace "during to carbon monoxide pregnancy to carbon monoxide" with "to carbon monoxide during pregnancy."
Page 52, line 16	It may be worth noting in this section that NIOSH has established a Ceiling concentration of 200 ppm and an Immediately Dangerous to Life or Health (IDLH) concentration of 1200 ppm.

Comments on DECOS draft document on Carbon monoxide

By: Cherie F. Estill, Deputy Associate Director of Science
NIOSH/Division of Field Studies and Engineering
Cincinnati, Ohio, USA

PAGE NUMBER, LINE NUMBER	COMMENT
Page 48, lines 11–18	This section says that the report by Sari et al. [2008] is the only occupational study in the reports mentioned by the expert groups. However, the report by Stern et al. [1988] of bridge and tunnel workers is an occupational study. The Stern paper is mentioned in section 8.1.3 of the World Health Organization (WHO) indoor air quality report.

Comments on DECOS draft document on Carbon monoxide

By: Evan A. Frank, Toxicologist
NIOSH/Division of Science Integration
Cincinnati, Ohio, USA

PAGE NUMBER, LINE NUMBER	COMMENT
General Comments	None.
Specific Comments	
Page 18, Table 3	I recommend including the date these Occupational Exposure Limits (OELs) were published so the reader may take this into consideration.
Page 18, Table 3	Also recommend adding a footnote in this table noting that NIOSH recommends an Immediately Dangerous to Life or Health (IDLH) value of 1200 ppm for Carbon monoxide. CDC - Immediately Dangerous to Life or Health Concentrations (IDLH): Carbon monoxide - NIOSH Publications and Products https://www.cdc.gov/niosh/idlh/630080.html

Comments on DECOS draft document on Carbon monoxide
By: Douglas Johns, Ph.D, Division Director
NIOSH/Spokane Mining Research Division
Spokane, Washington, USA

PAGE NUMBER, LINE NUMBER	COMMENT
General Comments	The document is well-written, relatively comprehensive, with generally well-reasoned conclusions and recommendations. The document correctly acknowledges that the majority of evidence of adverse health effects resulting from carbon monoxide (CO) exposure comes from studies evaluating short term exposures. Given that, I was somewhat surprised to see the meta-analysis presented in Lee et al. [2020] of short-term exposures (~24h) used as a basis for recommending a TWA to protect workers from low-level exposures over a working lifetime. Note, I am not familiar with the referenced World Health Organization (WHO) outdoor air report, but am well-versed with the Environmental Protection Agency (EPA)'s science assessment for Carbon Monoxide. EPA has concluded there is limited evidence that long-term low-level exposures to CO result in adverse health effects.
Specific Comments	
Page 10, line 2 & Page 24, line 2	I recommend including the EPA Integrated Science Assessment (ISA) as a significant source of scientific data explicitly, rather than solely referencing the document through the work of WHO.
Page 32, line 24	Delete "and the Environmental Protection Agency (EPA)" from this sentence. ATSDR did publish a toxicological profile for Carbon Monoxide in 2012, which is referenced correctly in the draft advisory report. However, while staff from EPA may have reviewed that document, it is in no way an EPA document.
Page 53, line 3	I would recommend including among the groups at extra risk those with cardiovascular disease and obstructive lung disease. These conditions are prevalent (diagnosed or undiagnosed) even among working populations.

Comments on DECOS draft document on Carbon monoxide

By: Janet A. Thompson, PhD, Biologist
NIOSH/Health Effect Laboratory Branch
Morgantown, West Virginia, USA

PAGE NUMBER, LINE NUMBER	COMMENT
General Comments	The Committee's HBR-OEL recommendation of 7.5 mg per m^3 air (6.4 ppm) for carbon monoxide is appropriate and supported by the evidence cited in the literature regarding adverse effects of carbon monoxide exposure.
Specific Comments	
Page 11, Table 1, Synonyms	Remove repeated "carbon monoxide."
Page 11, Table 1	Define "n.a." as found in table.
Page 13, lines 8–9	Change "has also" to "also has"; "As background…COHb levels." is an incomplete sentence. Recommend combining with the previous sentence to read "…limitations as background COHb levels between individuals…."
Page 13, line 15	Change "and underestimation" to "an underestimation."
Page 13, line 24	Move citation "[15]" outside the period for consistency.
Page 16, line 31	Remove repeated ",".
Page 31, line 24	Font change at "which are…".
Page 41, line 27	Change "1-day en" to "1-day and…".
Page 41, line 30	Add subscript, change "NO2" to "NO_2."
Pages 43 and 45	Missing page number.
Page 50, line 30	Two periods appear after "…populations.."; one should be removed. Also, there is no page number on the bottom of page 50.
Page 51, line 7	"Lee et al (2020)" is missing a period; change to "Lee et al. (2020)."
Page 67, top row of table	"s of uterine.." should the "s" be part of malformation(s) on the previous page ?

Comments on DECOS draft document on Carbon monoxide

By: Daniel Jay Hardt, MS, CIH, Research Industrial Hygienist
NIOSH/Western States Division
Spokane, Washington, USA

PAGE NUMBER, LINE NUMBER	COMMENT
General Comments	The DECOS Committee recommends reducing the 8-hour time-weighted average occupational exposure limit (OEL) for carbon monoxide (CO) in the Netherlands from 23 mg/m^3 to 7.5 mg/m^3. The rationale for this reduction is that studies show that non-hypoxic cardiovascular effects occur at lower CO concentrations than hypoxic effects that originally formed the basis for the current Dutch OEL, and all other OELs for CO. If adopted, this new OEL would be the lowest (most protective) OEL for CO among all OECD countries.
Specific Comments	
Page 19, line 7	Change "ACHIH" to "American Conference of Governmental Industrial Hygienists (ACGIH)."
Pages 43–44, Table 12	This document would be improved by additional discussion about the fact that the literature cited within Table 12 involves epidemiological studies of hospital admissions based upon environmental (not occupational) exposures to several pollutants—CO, as well as particulate matter and several other toxic gases produced by combustion. While these studies may be relevant to the dose-response relationship between CO exposure and cardiovascular events, more discussion about the potential confounders within these exposure data is warranted.
Page 48, lines 12–24	The DECOS Committee clearly states here that occupational study data are not currently available to determine accurate toxicological thresholds for CO-mediated, non-hypoxic mechanistic effects.
Page 51, lines 18–23	The DECOS Committee chooses here to derive their new 8-hr TWA OEL based on the observed cardiovascular effects upon the general population during extended environmental exposures (24 hrs. per day). This methodology should be protective to workers since constant exposure to CO usually poses more health risk than intermittent exposure.

caesar consult
RISICOBEOORDELING VAN CHEMISCHE STOFFEN
CHEMICAL SUBSTANCES RISK ASSESSMENT

Koninklijke Metaalunie en Vereniging FME
p/a Zilverstraat 69
2718 RP Zoetermeer

Date 7 April 2024
from: dr. J.G.M. van Rooij (PhD)
Your reference: Your email message dated 18 March 2024
Contact person: Mr. K. Halm (FME)
Our reference: project number 2024.005 (proposal dated 2024-02-16)
Concerns: Review draft report of Health Council (DECOS): Carbon monoxide (December 2023)

Dear Mr. K. Halm,

Thank you for sending us the draft report of the Dutch Expert Committee on Occupational Safety (DECOS) of the Health Council, entitled: Carbon monoxide – Health based recommended occupational exposure level (Dec 2023).

You are asking me to review this draft report on Carbon monoxide, based on my knowledge of toxicology and occupational hygiene.

Please find the results of my review in the attachment. If you have any questions or comments, please contact me by phone or email.

Yours sincerely,

dr. J.G.M. van Rooij (PhD)
toxicologist / occupational hygienist

Review of draft report of the Health Council of the Netherlands:

Carbon monoxide - Health based recommended occupational exposure level.
Dutch Expert Committee on Occupational Safety (DECOS), The Hague, public draft, version date 20 December 2023

Place, Date:	Nijmegen The Netherlands, April 7, 2024.
By:	dr. J.G.M. van Rooij (PhD), toxicologist / occupational hygienist at Caesar Consult
On behalf of:	Koninklijke Metaalunie en Vereniging FME

1. Introduction

In December 2023, the *Dutch Expert Committee on Occupational Safety* (DECOS) of the Health Council published a draft advice for a health based recommended occupational exposure level for carbon monoxide (Public draft, version date December 20, 2023)[1].

DECOS recommends a health-based occupational exposure limit for carbon monoxide of 7.5 mg per m^3 air (6.4 ppm), which represents a mean concentration during an 8-hour working day.

As the Committee has not identified literature suitable for derivation of a recommended OEL for short term exposure, the Committee cannot recommend a STEL or ceiling value.

The recommended health-based occupational exposure limit for carbon monoxide of 7.5 mg per m^3 air is considerably stricter than the current Dutch legal limit value for carbon monoxide of 23 mg/m^3 (20 ppm, 8-hour TWA), and also lower than the EU indicative occupational exposure limit value of 23 mg/m^3 (20 ppm, 8 -hour TWA).

This advice may have major consequences for the metal sector. Koninklijke Metaalunie and Vereniging FME have asked dr. J.G.M. van Rooij, toxicologist/occupational hygienist at Caesar Consult in The Netherlands, to carry out a review of the draft Health Council report.

2. Aim

Critical assessment of the findings and conclusions of the DECOS committee of the Health Council of the Netherlands in their draft report entitled: *Carbon monoxide - Health-based recommended occupational exposure level. Dutch Expert Committee on Occupational Safety (DECOS). The Hague, the Netherlands, public draft, version date 20 December 2023*

3. Approach

In this review special attention is given to the Committees' working methods, the inventory and processing of the current and available toxicological and epidemiological data, the selection of the critical effect(s) and the key-study/studies, the quality of the selected key-study/studies, and the interpretation of the selected research data.
In this review the instructions of the Health Council for submitting comments were followed.[2]

[1] Health Council of the Netherlands: Carbon monoxide - Health-based recommended occupational exposure level. Dutch Expert Committee on Occupational Safety (DECOS). The Hague, the Netherlands, public draft, version date 20 December 2023.
[2] Health Council of the Netherlands: Instructions for submitting comments on the draft advisory report Carbon monoxide (The Hague NL, December 21, 2023)

4. Expertise

The review was conducted by dr. J.G.M. van Rooij (PhD). He is a EUROTOX registered toxicologist and senior occupational hygienist at Caesar Consult, The Netherlands.

5. Results of the review

Studying the Health Council report shows that DECOS make a number of assumptions, choices and conclusions that have a major influence on the evaluation and the recommended limit value for carbon monoxide, but which are insufficiently substantiated with scientific data.

The results of the review in broad terms is presented in § 5.1. Detailed comments and suggestions are presented in § 5.2.

5.1 Main findings (review in broad terms)

The Health Council has published a guidance for recommending health-based occupational exposure limits: *Guidance for recommending classifications and health-based occupational exposure limits*. Health Council of the Netherlands, The Hague**,** 2021.

According to this guidance's the evaluation of the available toxicological and epidemiological studies is an essential part of the process/working procedure of deriving of a health-based occupational exposure limit.

But for the evaluation of carbon monoxide, the DECOS has decided to deviate from this guidance:

> "*Given the complex toxicity profile of carbon monoxide (i.e. several potential health effects that might occur at a similar (low) exposure levels) and the large amount of available data, the Committee has decided to use assessment reports previously published by other scientific organizations as a starting point, and only address underlying literature when needed*."

DECOS prefers to use an air quality guideline derived by the WHO in order to protect the general population, as a starting point for deriving a workplace limit value for carbon monoxide, while extensive evaluations of carbon monoxide were recently carried out by respected institutes that are specialized in evaluation of hazards of chemicals in an occupational setting, such as Nordic expert group (NEG, 2012) and Swedish Criteria Group for occupational Standards (2017).

This is an interesting but not a very desirable development and, moreover, confusing.

Confusing because very recently, DECOS published a very extensive evaluation draft report on respirable crystalline silica, remarkably enough in close cooperation with the Nordic Expert Group. Respirable crystalline silica has also a complex toxicity profile (several health effects that might occur at a similar low exposure level) and a very large amount of available data, even more than for carbon monoxide.

Was respirable crystalline silica more interesting for DECOS than carbon monoxide? Is it because of the strong preference of DECOS for epidemiological studies and for the risk-based approach? Or was the availability of a recent epidemiological study on respirable crystalline silica published by a Dutch research institute (IRAS) the reason to fully focus on respirable crystalline silica?

Is this the start of a new DECOS working method? Will DECOS also use the other air quality guidelines drawn up by the WHO for the derivation of health based occupational exposure limit values? This doesn't seem like a good development to me.

DECOS is kindly requested to adhere to its own guidelines with its working methods. This will have a positive effect on the authority of DECOS and will increase the acceptance of its recommended limit values, both nationally and internationally.

5.2 Detailed comments and suggestions

Samenvatting

Page 5 – 6:
DECOS is kindly requested to adjust the *Samenvatting* based on the changes and corrections made in the main body of the report (see below).

Executive Summary

Page 7 – 8:
DECOS is kindly requested to adjust the *Executive summary* based on the changes and corrections made in the main body of the report (see below).

1. Scope

Page 9, line 8-8
DECOS states: "*A letter of the request {remark JvR: of the Minister of SZW) can be found on the website of the Health Council*."

The formal request of the Minister of SZW for an advise on Carbon monoxide is not available via the web-site.

DECOS is kindly requested to include the letter from the Minister of SZW with the formal request for advice on carbon monoxide in the appendix of the report.

Page 9, line 25-26
DECOS states: "*For the evaluation of carbon monoxide, the Committee has decided to deviate from this guidance. Given the complex toxicity profile of carbon monoxide (i.e. several potential health effects that might occur at a similar (low) exposure levels) and the large amount of available data, the Committee has decided to use assessment reports previously published by other scientific organizations as a starting point, and only address underlying literature when needed*."

Is this the start of a new DECOS working method? Will DECOS also use the other air quality guidelines drawn up by the WHO for the derivation/update of other health based occupational exposure limit values? This doesn't seem like a good development to me.

DECOS is kindly requested to clarify whether the use of WHO air quality guidelines will become part of the DECOS working method for the derivation/update of other health based occupational exposure limit values.

2. Identity of the substance, existing guidelines and exposure monitoring

No further comments or suggestions.

3. Sources

Page 14, line 27-30
DECOS writes: "*It is estimated that approximately 33% of the carbon monoxide in the troposphere originates from environmental sources.* [5,12] *A typical concentration in the troposphere is around 0.1 mg/m*^{3} *(100 ppb), especially clean air can have concentrations as low as 0.06 mg/m*^{3} *(50 ppb).*"

'Troposphere' is not a common term among HSE experts.

DECOS is kindly requested to explain what is meant by troposphere.

4. Exposure levels

No comments or suggestions.

5. Current EU occupational exposure limits and classification and labelling

No comments or suggestions.

6. Kinetics

Page 21, line 8 – 14
DECOS writes: "*The elimination half-life (t1/2) of COHb depends on the concentration of oxygen inhaled. When the t1/2 was calculated in a single human subject immediately after smoking a cigarette, it was almost 5 hours at sea level and atmospheric pressure but decreased to 75 minutes at 40% normobaric (1 atmosphere pressure) oxygen and to 21 minutes at 100% oxygen. Another study showed a COHb half-life of 74 minutes in 93 carbon monoxide -poisoned patients (carbon monoxide from various sources) at 100% oxygen".*

The provided information on elimination half-life (t1/2) of COHb in relation to the oxygen concentration is very confusing and not very relevant for evaluating occupational exposures.

DECOS is kindly requested to provide the elimination half-live (t1/2) of COHb under standard conditions among adults: about 4 – 5 hours.

7. Mechanism of toxicity

Page 21, line20 until page 23, 1 - 2
The organization of this chapter, in relation to the chapter title, is not logical and leads to confusion.

First, I suggest to rename '§ 7.1 Hypoxia' to '§ 7.1 Hypoxic mechanisms (of toxicity)' and '§7.2 Non-hypoxia' to '§ 7.2 Non-hypoxic mechanisms (of toxicity)'.

Second, I propose to replace the following text :

7.3 Molecular events

No specific adverse outcome pathways have been described up to date. Although the involvement of carbon monoxide to the various listed processes is known and has been reviewed in existing literature,[25-30] the precise mechanisms are not always clear. Table 4 shows a list of carbon monoxide-mediated effects that may play a role in hypoxic and non-hypoxic effects observed after carbon monoxide exposure.

…. with:

~~7.3 Molecular events~~

~~No specific adverse outcome pathways have been described up to date.~~ Table 4 shows a list of carbon monoxide-mediated effects that may play a role in hypoxic and non-hypoxic effects observed after carbon monoxide exposure. Although the involvement of carbon monoxide to the various listed processes is known and has been reviewed in existing literature,[25-30] the precise mechanisms are not always clear.

DECOS is kindly requested to consider the proposed text adjustments in this chapter 7. Mechanisms of toxicity.

8. Effects

Page 24, line 1
The chapter title **'8. Effects'** does not cover the content of this chapter.

I recommend replacing the title of this chapter with **8. Health effects: Evaluations by other expert groups and recent literature**

DECOS is kindly requested to consider the proposed adjustment of the title of chapter 8..

Page 40, line 15 – 16
Paragraph 8.1 provides a lot of information on all kind of effects and evaluations of other expert groups.

To give the reader more insight into what other expert groups consider a critical effect(s), key-studies and which (occupational/environmental) limit value they recommend, I propose to summarizing this in a table in the new paragraph '8.1.8 Summary of evaluations by other expert groups'.
I recommend the following structure of this new table number 11a: Expert group (year) - Critical health effect(s) – Key publication(s) (first author, year) - Recommended limit value(s) (average time) - Remark. In this Remark column one can add some additional clarification if needed.

DECOS is kindly requested to consider an extra paragraph '§ 8.1.8 Summary of evaluations by other expert groups' and to add a table that summarizes the identified critical effects and recommended limit values.

Page 40, line 16 until page 49, line 10 (§ 8.2 Evaluation of recent literature, § 8.3 DECOS' evaluation of previous reports and recent literature)

The following information in *§ 8.2 Evaluation of recent literature* and *§ 8.3 DECOS' evaluation of previous reports and recent literature*, is missing:

Based on the study of recently published literature DECOS should answer the following questions: (i) Are their new insights regarding the critical health effects of carbon monoxide?, and (ii) Have there been any studies recently published that can/should be regarded as new key studies?

In order to answer these questions, DECOS will first have to gain insight into the critical health effects and the underlying key studies previously selected by the expert groups (this should be clearly described and summarized in *§ 8.1 Previous reports from other expert group*) .

It can then be assessed whether, based on new studies, there is sufficient reason to choose a different critical effect and/or a different key-study. Any new study that shows this, must then be assessed as to whether it is of sufficient quality to be classified as a key study.

DECOS is kindly requested to report whether recently published literature provide new insights regarding the critical health effects of carbon monoxide, and whether there are any studies recently published that can/should be regarded as new key studies (revision of § 8.2 and § 8.3).

Page 47, line 17-22
DECOS writes: '*The Committee has assessed both the scope and methodology of the above mentioned reports. The Committee notes that the reports show little or no overlap in assessed information and for most reports the main information provided did not involve primary data sources which were not systematically retrieved. The Committee considers these reports therefore informative from an overall point of view, but not suitable as a single primary source for the Committee's evaluation from a methodological point of view*.'

This disqualification of the work of other expert groups seems very inappropriate to me. And it is not supported by valid arguments. The accusation is all the more painful since DECOS itself has chosen not to conduct any literature research (with the exception of the period between 2012 and April 2023). It is also noted that one of the expert groups that is disqualified by DECOS is the Nordic Expert Group, a group DECOS collaborates closely with (see the recent joint report on respirable crystalline silica, December 2023).

My urgent advice to DECOS is to first get your homework in order before you disqualify the evaluations of other expert groups. This includes a systematic review of the available literature by DECOS itself.

If that is too much work, DECOS may indeed consider to review previous evaluations of the expert groups, but with special focus on the selected critical effects and the underlying key-studies.

DECOS must then answer the following questions: (i) Are their new insights regarding the critical health effects of carbon monoxide?, and (ii) Have there been any studies recently published that can/should be regarded as new key studies? To answer these questions, a study of recently published literature is an obvious approach.

DECOS is advised to remove the unsubstantiated disqualification of the work of other expert groups from the report.

DECOS is kindly requested to perform a systematic review of the evaluations of the expert groups with special focus on the selected critical effects and the underlying key-studies (revision § 8.1). Additional literature research should clarify whether there are new insights into critical effects and whether there are studies that can/should be regarded as new key studies (revision of § 8.2).

Page 47, line 31 – page 49, line 11

'Usability of COHb for HBROEL derivation'
DECOS takes the position that studies that use COHb-levels as measure of exposure are not useful in deriving a health-based limit value. This is a remarkable view that will not be shared by the majority of scientific community involved in hazard and/or risk assessment of carbon monoxide.

'Use of occupational studies'
DECOS further states: '*For carbon monoxide, limited information is available on adverse effects and occupational exposure. Only one occupational study (excluding case reports) is included in the reports of the mentioned expert groups, namely the study by Sari et al (2008)."*

The suggestion that there are hardly any occupational studies on carbon monoxide is remarkable and actually quite embarrassing. Four of them are described by DECOS itself !? (see page 31 of the DECOS report). But there are of course many other publications on this subject. DECOS could have discovered this itself if it had made the effort to search also the literature before 2012.

What DECOS does not mention in *§ 8.3 DECOS' evaluation of previous reports and recent literature*, is that there are numerous studies with volunteers who have been exposed to carbon monoxide under controlled conditions and who have been subjected to extensive medical testing. Most expert groups make eager use of these volunteer studies.

'Conclusions'
DECOS concludes: ' …*the study by Lee et al. (2020) provides the most robust starting point for quantitative hazard assessment. In this study the relation between ambient carbon monoxide exposure and clinical cardiovascular outcome - a study also used by the WHO for its outdoor guideline - was assessed*.'

DECOS has chosen to put aside findings from other expert groups and to put aside studies using COHb as exposure measure, occupational exposure studies and even volunteer studies!?

DECOS does not seem to realize that the uncertainties associated with epidemiological studies of the effects of an air pollutant such as carbon monoxide in the general population, are much greater.

This concerns uncertainties that arise from, among other things, the relatively low level and low variation in exposure, the exposure characterization of the general population and possible contribution of other (confounding) air pollutants such as nitrogen dioxide.

The fact that WHO used this study to derive the air quality guideline for carbon monoxide in outdoor air, does not necessarily mean that this study is of good quality or that this study shows a convincing association between carbon monoxide and myocardial infarction. WHO chose this study for lack of anything better (apparently WHO does not use occupational exposure studies).

The weakness of the association between carbon monoxide and myocardial infarction is evident from the so-called *forest plot* that has been taken from the publication of Lee et al. (2020) and included in the appendix 1 of this report.

The researchers themselves recognize that this type of research has major limitations. Lee et al. (2020) write about this:

> "*We acknowledge several limitations in this review. First, the vast majority of studies originated from high-income countries with only five out of thirty studies conducted in low- or middle-income countries. This may limit the generalisability of our findings. Second, the pooling of evidence from only observational studies is prone to bias. However, this is an issue that is common to environmental epidemiological studies in this field where it is not possible to conduct a randomised controlled trial.*

Finally, very few studies have performed multi-pollutant analyses. Ambient carbon monoxide concentrations may be highly correlated with other air pollutants such as nitrogen dioxide which may significantly confound the observed risk estimates."

And furthermore, Lee et al. (2020) conclude:

"In summary, the overall quality of the evidence on the association between short-term exposure to carbon monoxide and myocardial infarction was assessed to be of moderate certainty.'

DECOS is urgently requested to put aside the epidemiological study of Lee et al. (2020) and to look for a more robust and reliable key study that can serve as a starting point for the quantitative hazard of carbon monoxide among workers. A systematic review of the previous evaluations of the expert groups with special focus on the selected critical effects and the underlying key-study, supplemented with a search in recent literature for possible new key studies, can contribute to this.

9. Hazard assessment

Page 51, line 15 – 21

DECOS states:

"*For the extrapolation to the working population, the Committee applies the following default factors (See also the Committee's Guidance for recommending classifications and health-based occupational exposure limits)[2]:*

Exposure duration (hours)	*24/8 (24 hours for general population/8 hours for workers)*
	7/5 (7 days for general population/5 days for worker)
Respiratory rate (m3)	*6.7/10 (standard conditions for general population/light exercise for workers)*
Sensitivity of the population	*10/5 (general population/workers)*
Effect	*1/3 (assessment factor NOAEL/LOAEL)*

Taking into account these factors, the Committee derives a HBR-OEL based on cardiovascular effects of:

*4 mg/m^3 x (24/8 * 7/5 * 6.7/10 * 10/5 * 1/3) = 7.5 mg/m^3 (6.4 ppm)*

The DECOS calculation is incorrect. In the derivation of the HBR-OEL, DECOS failed to apply adjustment factors for:

- the difference in exposure weeks per year: 52/48 (52 weeks for general population 48 weeks for workers)
- the difference in years of exposure: 80/40 (80 years for general population, 40 years for workers)
- the difference in protection: 1.6/1 (99-th % for general population, 95-th % for workers)

Note: The WHO AQG level is assumed to protect the general population on 99 percent of the year, which means that exceedance is accepted on 1% of the days in the year, or 3.65 days per year (see footnote to table 3.26 in appendix 2). Workplace limit values are assumed to protect workers on 95 percent of the year, which means that exceedance is accepted on 5% of the days in the work year (5% of 240 days = 12 days per year). Assuming a GSD of 2.0, the 99-th percentile is 1.6 times higher than the 95-th percentile.

Taking into account these factors, the recalculated HBR-OEL based on cardiovascular effects is:

*4 mg/m^3 x (24/8 * 7/5 * 6.7/10 * 10/5 * 1/3 * 52/48 * 80/40 * 1.6/1) = 26.0 mg/m^3 (22.3 ppm)*

DECOS is kindly requested to adjust and correct the calculation of the HBR-OEL.

Appendix 1. Forest plot of the association between carbon monoxide and admission for Myocardial Infarction or mortality from Myocardial infarction across all included studies

Source: *K.K. Lee et al. (2020) Short term exposure to carbon monoxide and myocardial infarction: A systematic review and meta-analysis. Environment international, 143 2020*

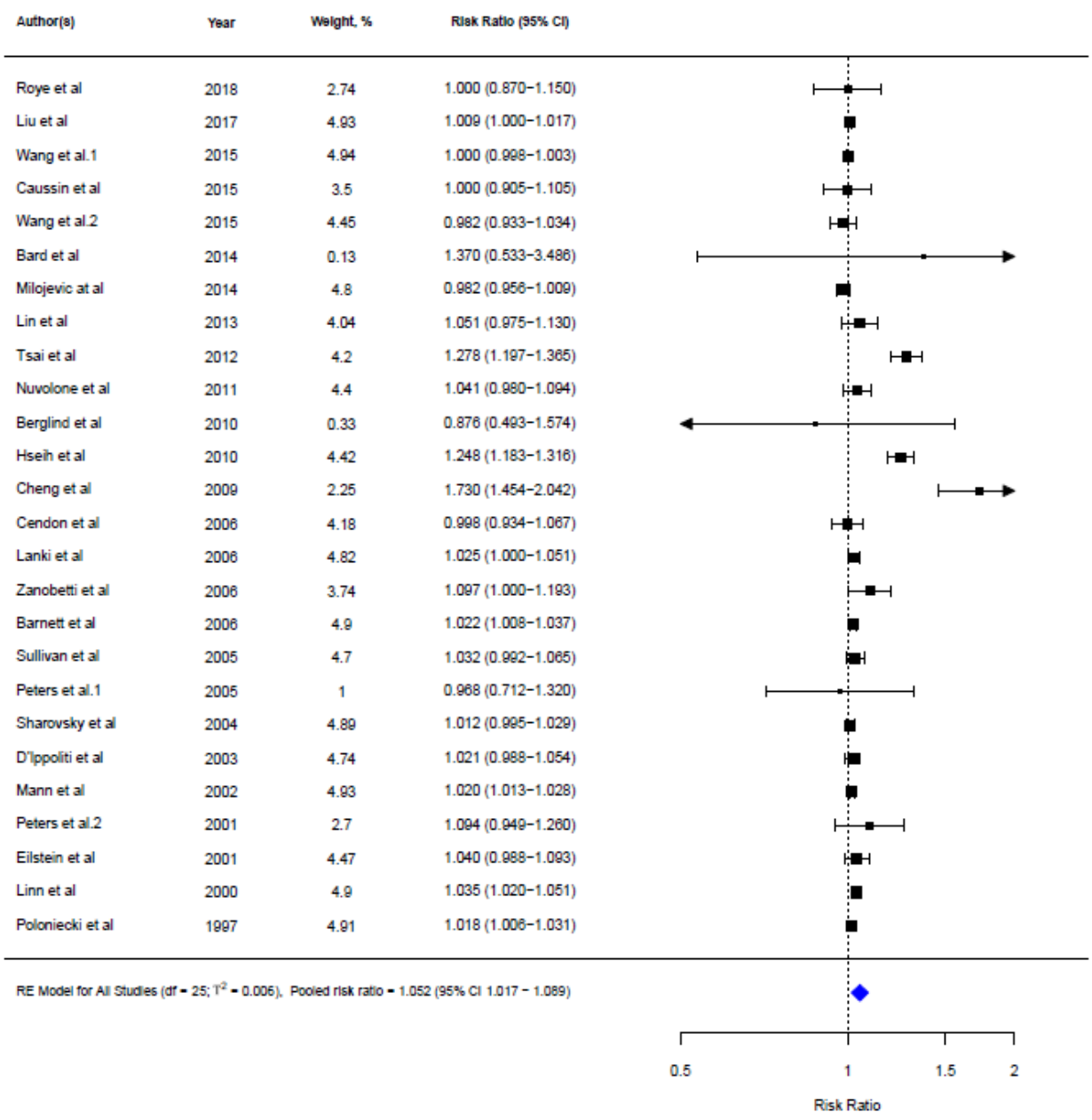

Fig. 2. Forest plot of the association between carbon monoxide and admission for MI or mortality from MI across all included studies.

Appendix 2. Recommended Air Quality Guidelines WHO 2021

Bron : WHO global air quality guidelines. Particulate matter (PM2.5 and PM10), ozone, nitrogen dioxide, sulfur dioxide and carbon monoxide. Geneva: World Health Organization; 2021

Table 3.26. Recommended 2021 AQG levels and 2005 air quality guidelines

Pollutant	Averaging time	2005 air quality guideline	2021 AQG level
$PM_{2.5}$, μg/m³	Annual	10	5
	24-hour[a]	25	15
PM_{10}, μg/m³	Annual	20	15
	24-hour[a]	50	45
O_3, μg/m³	Peak season[b]	–	60
	8-hour[a]	100	100
NO_2, μg/m³	Annual	40	10
	24-hour[a]	–	25
SO_2, μg/m³	24-hour[a]	20	40
CO, mg/m³	24-hour[a]	–	4

[a] 99th percentile (i.e. 3–4 exceedance days per year).
[b] Average of daily maximum 8-hour mean O_3 concentration in the six consecutive months with the highest six-month running-average O_3 concentration.

Public Comments
submitted 8 April 2024
to: Dutch Expert Committee on Occupational Safety (DECOS)
c/o Dr. S.R. Vink, Scientific Secretary
draftOSH@gr.nl

from: Albert Donnay, MS, MHS
title: Consulting Toxicologist and Environmental Health Engineer
business: Donnay Detoxicology LLC
location: Hyattsville, Maryland, United States

Thank you for giving the public the opportunity to submit comments on the draft report about Carbon Monoxide (CO) by the Dutch Expert Committee on Occupational Safety (the report) related to any of the following:

Issue 1: "the publications and scientific data used (is the report comprehensive and exhaustive?)"
Issue 2: "the interpretation of the scientific data"
Issue 3: "errors and inconsistencies"

My comments are informed by my professional training and experience as a consulting toxicologist and environmental health engineer in the United States who has specialized in CO poisoning since 1999. These comments are my own and not those of any client.

As the authors do in their report, I abbreviate new references by author/year in my comments but also provide the full references at the end of each comment, including the abstract and doi where these are available from PubMed.gov.

Thank you for your consideration. I look forward to seeing the final report.

Part 1: Comments regarding "the publications and scientific data used"
(is the report comprehensive and exhaustive?)

Comment 1.1 Given the definitions below from dictionary.com of
comprehensive, meaning "*of large scope; covering or involving much; inclusive"*;
and exhaustive, meaning *"exhausting a subject, topic, etc.; comprehensive; thorough";*
this report is neither, as evidenced by the facts presented in comments 1.2 to 1.7 below:

Comment 1.2 On page 10, line 14: The authors write they only reviewed original CO studies published from 2012 up to April 2023, and relied on reviews of CO literature conducted for other national governments or the WHO to identify and summarize any important earlier studies. The 62 references they include in the literature list starting on page 54 line 1 and running through page 58 line 26 include only 3 peer-reviewed studies of occupational CO poisoning (Stern 1988 (#32 in literature list), Ely 1995 (#33), and Sari 2008 (#34)), which is less than 5% of the total.

Among the rest, 29% (18) are animal studies on the effects of prenatal or perinatal exposure to CO, which has little relevance to setting occupational exposure limits; 24% (15) are self-published reports of government and scientific organizations; 15% (9) review articles that focus on various issues about CO exposures and testing generally (none specifically about occupational exposures); 13% (8) are population level epidemiology studies about correlations between outdoor ambient CO exposures (mostly below 2 mg/m3) and changes in the rates of hospitalization and/or death for various causes among the general populations;

and 5 (8%) are clinical studies of acute CO poisoning cases, (none of them occupational).

Such a thin review is neither “exhaustive” nor “comprehensive.”

I recommend the authors expand the literature list in the report to include all the studies listed below published from January 2012 through April 2023 that are related to occupational CO exposures (comments continue on page 58)

They were identified by searching www.PubMed.gov for:
("carbon monoxide" and ("occupational" or "worker" or "employee" or "workplace" or "job")).
Full references for each are provided below with titles in bold. They include the abstract and doi where available.

Note these studies address a more diverse range of occupational CO exposures than the report, and all are more relevant than animal studies of prenatal exposures. They include measurements of CO in bars and restaurants, parking garages, tunnels, mines, ice skating rinks, surgical operating rooms, vehicles, ships, and coffee roasting facilities, as well as in some outdoor settings, such as when operating chainsaws, directing traffic, and fighting wildfires. This collection also can be viewed, sorted, and saved on PubMed via this link:

https://pubmed.ncbi.nlm.nih.gov/?term=23813888,25684497,23307861,30450122,26611218,23325913,27918460,30427286,32300027,22594934,24142221,29028252,33703981,23298425,30130361,33350528,28471692,23868822,26788681,27624690,34482929,25995848,26803678,30364347,25216817,34397541,22697403,36147587,22693522,29718778,37302076,22788370,28582531,23183022,35297489,23095154,23738842,37384051,33616228,33668116,34285366,34759449,24116669,31737615,29751534,25125950,24736103,24625483,33298031,34626220,30024867,33249041,30270967,26811352&format=abstract

To skip ahead to next comment, search for comment 1.3

54 More References on Occupational Exposures to Carbon Monoxide from Jan 2012 to April 2023

Items 1-54 of 54

1. **Exposure of wildland firefighters to carbon monoxide, fine particles, and levoglucosan**

Ann Occup Hyg. 2013 Oct;57(8):979-91. doi: 10.1093/annhyg/met024. Epub 2013 Jun 27.

Authors

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Affiliation

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- PMID: 23813888
- DOI: 10.1093/annhyg/met024

Abstract

Wildland firefighters are occupationally exposed to elevated levels of woodsmoke. Eighteen wildland firefighters were monitored for their personal exposure to particulate matter with median aerodynamic diameter of 2.5 microns (PM2.5),

levoglucosan (LG), and carbon monoxide (CO) at 30 prescribed burns at the Savannah River Site, South Carolina. Linear mixed effect models were used to investigate the effect on exposure of various factors and to examine whether the firefighters were able to qualitatively estimate their own exposures. Exposure to PM2.5 and CO was higher when firefighters performed 'holding' tasks compared with 'lighting' duties, whereas exposures to CO and LG were higher when burns were in compartments with predominantly pine vegetation ($P < 0.05$). Exposures to PM2.5 (64-2068 μg m(-3)) and CO (0.02-8.2 p.p.m.) fell within the ranges observed in previous studies. Some recommended shorter term exposure limits for CO were exceeded in a few instances. The very low LG:PM2.5 ratios in some samples suggest that the exposures of wildland firefighters to pollutants at prescribed burns may be substantially impacted by non-woodsmoke sources. The association of the qualitative exposure estimation of the firefighters with actual PM2.5 and CO measurements ($P < 0.01$) indicates that qualitative estimation may be used to assess exposure in epidemiology studies.

Keywords: carbon monoxide; levoglucosan; occupational exposure; particulate matter; prescribed burn; wildland firefighter.

- Cited by 11 articles

Full text links

2. **Opportunistic insights into occupational health hazards associated with waterpipe tobacco smoking premises in the United Kingdom**

Asian Pac J Cancer Prev. 2015;16(2):621-6. doi: 10.7314/apjcp.2015.16.2.621.

Authors

Ali Al-Bakri [1], Mohammed Jawad, Pascale Salameh, Mustafa al'Absi, Saba Kassim

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- PMID: 25684497
- DOI: 10.7314/apjcp.2015.16.2.621

Free article

Abstract

Background: Smokefree laws aim to protect employees and the public from the dangers of secondhand smoke. Waterpipe premises have significantly increased in number in the last decade, with anecdotal reports of poor compliance with the smokefree law. The literature is bereft of information pertaining to waterpipe premise employees. This study aimed to opportunistically gather knowledge about the occupational health hazards associated with working in waterpipe premises in London, England.

Materials and methods: Employees from seven convenience-sampled, smokefree-compliant waterpipe premises in London were observed for occupational activities. Opportunistic carbon monoxide (CO) measurements were made among those with whom a rapport had developed. Observations were thematically coded and analysed.

Results: Occupational hazards mainly included environmental smoke exposure. Waterpipe-serving employees were required to draw several puffs soon after igniting the coals, thereby providing quality assurance of the product. Median CO levels were 27.5 ppm (range 21-55 ppm) among these employees. Self-reported employee health was poor, with some suggestion that working patterns and smoke exposure was a contributory factor.

Conclusions: The smokefree law in England does not appear to protect waterpipe premise employees from high levels of CO. Continued concerns surrounding chronic smoke exposure may contribute to poor self-reported physical and mental wellbeing.

- Cited by 3 articles

Full text links

Fatal carbon monoxide intoxication after acetylene gas welding of pipes

3.

Ann Occup Hyg. 2013 Jun;57(5):662-6. doi: 10.1093/annhyg/mes104. Epub 2013 Jan 9.

Authors

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- PMID: 23307861
- DOI: 10.1093/annhyg/mes104

Abstract

Acetylene gas welding of district heating pipes can result in exposure to high concentrations of carbon monoxide. A fatal case due to intoxication is described. Measurements of carbon monoxide revealed high levels when gas welding a pipe with closed ends. This fatality and these measurements highlight a new hazard, which must be promptly prevented.

Keywords: carbon monoxide; district heating; gas welding; welding.

- Cited by 2 articles

Full text links

Prevalence of hidden carbon monoxide poisoning in auto service workers; a prospective cohort study

4.

J Occup Med Toxicol. 2018 Nov 6:13:35. doi: 10.1186/s12995-018-0214-9. eCollection 2018.

Authors

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- [2] 2Gaziosmanpasa University Emergency Medicine, Tokat, Turkey.
- [3] 3Erciyes University Emergency Medicine, Kayseri, Turkey.

- PMID: 30450122
- PMCID: PMC6219102
- DOI: 10.1186/s12995-018-0214-9

Abstract

Background: Carbon monoxide (CO) is formed as a result of the incomplete burning of hydrocarbon-containing fuels such as natural gas, coal, liquid petroleum gas, and wood. CO is a colorless, odorless, and poisonous gas that produces various acute and chronic effects in CO-exposed people. In this study, we aimed to measure CO levels in auto care repairmen with chronic CO-related illnesses using a serial, non-invasive method.A prospective cohort study.

Methods: A total of 99 people from six different auto-repair services were included in the study. Carboxyhemoglobin (COHb) levels were measured at four different times with 2-hour intervals starting at 08:00 AM. Data concerning employees' ages, working hours, smoking statuses, and types of home heating fuel were collected. A control group of 100 cases was created based on this data. The measurements were done on the control group in the morning with a Masimo Rad-57 CO-oximeter.

Results: The highest mean (± SD) COHb value was 7.04% ± 3.32% after the third measurement. The mean value for the control group was 1.61% ± 1.43%. A statistically significant difference between the groups was found for each value.

Discussion: We determined that the risk of being affected by CO is high in buildings in which the auto services were located. The effects of chronic or prolonged exposure to low amounts of CO were found to be ambiguous. However, in some studies, it was found that low-grade CO exposure could lead to coronary artery disease and some neurological complications. Therefore, it is necessary to be careful about the health of employees who have been exposed to CO.

Conclusions: We concluded that there is a need for more detailed studies concerning chronic CO poisoning. Also, in workplaces in which there is high exposure to CO, proper workplace safety measures should be taken to reduce this gas's harmful effects to employees.

Conflict of interest statement

Kayseri Erciyes University Ethics Committee approval date: 04.12.2012 and the Decision Number: 2012/701. In addition, the contents of the work to all service officers were explained and permission was given to do this work during working hours.Not applicableThe authors declare that they have no competing interests.Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

- Cited by 1 article
- 16 references
- 2 figures

Full text links

5. **Carbon Monoxide Exposure in Norwegian Rescue Helicopters**

Air Med J. 2015 Nov-Dec;34(6):328-32. doi: 10.1016/j.amj.2015.06.010.

Author

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Affiliation

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- PMID: 26611218
- DOI: 10.1016/j.amj.2015.06.010

Abstract

Objective: Exposure to exhaust fumes from combustion engines can lead to carbon monoxide (CO) poisoning. Sea King Rescue helicopter crews are frequently subjected to engine exhaust. This study investigates the extent of CO exposure and potential for intoxication for flight crews during standard operational training procedures.

Methods: Over a 2-week period, rescue helicopter flight crews were monitored for exposure to exhaust fumes and clinical symptoms of CO intoxication by means of a written survey and measurements of carboxyhemoglobin saturation (SpCO) with a handheld pulse CO oximeter (RAD-57; Masimo, Irvine, CA). Normal ranges for SpCO were defined as ≤ 4%.

Results: Sixty-nine completed surveys and 138 SpCO measurements of 37 crewmembers were included in the study. Sixty-four percent (n = 44) experienced subjective exposure to engine exhaust during training. Clinical symptoms were reported in 8.6% (n = 6) and included exhaustion (n = 4), headache (n = 1), and nausea (n = 1). Twenty-nine percent (n = 20) showed postflight SpCO levels outside the normal range (≥ 4%). The maximum postflight SpCO level among all measurements was 7%.

Conclusion: Exposure to engine fumes is common, even more so during open cargo door operations. However, clinical symptoms are infrequent and mild. Toxic SpCO levels were not reached in this study, but approximately one third of postflight SpCO levels were outside the normal range.

Full text links

6. **Urinary cotinine and breath carbon monoxide levels among bar and restaurant employees in ankara**

Nicotine Tob Res. 2013 Aug;15(8):1446-52. doi: 10.1093/ntr/nts345. Epub 2013 Jan 16.

Authors

Ozge Karadag Caman [1], Berrin I Erguder, Hilal Ozcebe, Nazmi Bilir

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- PMID: 23325913
- DOI: 10.1093/ntr/nts345

Abstract

Introduction: Hospitality sector employees constitute one of the key groups with respect to their secondhand tobacco smoke exposure at work. This study aimed to detect urinary cotinine and breath carbon monoxide (CO) levels among bar and restaurant employees in Ankara, as well as the employees' opinions on the new antitobacco law, changes in smoking behavior, and subjective health status before and after the law entered into force.

Methods: This before-after study was conducted in 19 premises, with the participation of 65 employees before implementation and 81 employees 3 months after implementation of the new antitobacco law in the hospitality sector. Data in both phases were collected through face-to-face surveys, breath CO measurements, and urinary cotinine analysis. Descriptive statistics were used to summarize data, whereas chi-square test, paired and unpaired t tests, and analysis of variance were used to compare groups.

Results: Most of the restaurant and bar employees were male and below 35 years old. Before-after comparison showed that health complaints of the hospitality sector employees such as watering and itching in the eyes, difficulty in breathing, and cough ($p < .001$), as well as breath CO ($p < .001$) and urinary cotinine levels ($p < .001$) decreased significantly 3 months after implementation of the law. Among the smoking employees, mean number of cigarettes smoked was also found to decrease ($p = .012$). Majority of the employees (83.8%) were found to support the smoking ban in enclosed public places.

Conclusions: Results of this study provide solid evidence on the positive health effects of smoke-free laws and employees' support for smoke-free workplaces.

- Cited by 2 articles

Full text links

Indoor Air Quality in the Metro System in North Taiwan

7.

Int J Environ Res Public Health. 2016 Dec 2;13(12):1200. doi: 10.3390/ijerph13121200.

Authors

Ying-Yi Chen [1], Fung-Chang Sung [2 3], Mei-Lien Chen [4], I-Fang Mao [5 6], Chung-Yen Lu [7 8]

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- PMID: 27918460
- PMCID: PMC5201341
- DOI: 10.3390/ijerph13121200

Abstract

Indoor air pollution is an increasing health concern, especially in enclosed environments such as underground subway stations because of increased global usage by urban populations. This study measured the indoor air quality of underground platforms at 10 metro stations of the Taipei Rapid Transit system (TRTS) in Taiwan, including humidity, temperature, carbon monoxide (CO), carbon dioxide (CO_2), formaldehyde (HCHO), total volatile organic compounds (TVOCs), ozone (O_3), airborne particulate matter (PM_{10} and $PM_{2.5}$), bacteria and fungi. Results showed that the CO_2, CO and HCHO levels met the stipulated standards as regulated by Taiwan's Indoor Air Quality Management Act (TIAQMA). However, elevated PM_{10} and $PM_{2.5}$ levels were measured at most stations. TVOCs and bacterial concentrations at some stations measured in summer were higher than the regulated standards stipulated by Taiwan's Environmental Protection Administration. Further studies should be conducted to reduce particulate matters, TVOCs and bacteria in the air of subway stations.

Keywords: indoor air; metro; particulate matter; subway; transit.

Conflict of interest statement

The authors declare no conflict of interest.

- Cited by 9 articles
- 28 references
- 1 figure

Full text links

8. **Characterization of CO and NO_2 exposures of ice skating rink maintenance workers**

J Occup Environ Hyg. 2019 Feb;16(2):101-108. doi: 10.1080/15459624.2018.1540875. Epub 2019 Feb 27.

Authors

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- PMID: 30427286
- DOI: 10.1080/15459624.2018.1540875

Abstract

Air quality is a common concern among indoor ice rink facilities due to the use of gasoline/propane ice resurfacing equipment. Although previous studies have investigated spectator, guest, and skater exposures, a review of the literature revealed little published research regarding ice maintenance employees' exposures. Ice maintenance includes edging and resurfacing. The resurfacer is commonly referred to as a Zamboni®. Edging is almost always followed by resurfacing, but resurfacing frequently happens independently of edging. The purpose of this study was to characterize ice rink maintenance employees' exposures to CO and NO_2. Employees from four ice rinks in Salt Lake County, Utah were sampled using direct reading instruments during routine ice maintenance activities. Maintenance was divided into four activities: 1) Edging only, 2) Resurfacing after edging (not including edging), 3) Edging and resurfacing (Activities 1 and 2 combined), and 4) Resurfacing only (independent of edging). Activities 1, 2 and 3 were sampled twenty-four (n = 24) times. Activity 4 was sampled eight times. Sampling results were graphed and summarized using descriptive statistics. The highest measured CO concentration was 202 ppm, which occurred during edging. Average CO concentrations for all activities ranged from 0 ppm to 60.4 ppm. Minimal CO exposure was observed when resurfacing occurred without edging, which implies that elevated CO exposure measured while using the resurfacer may be residual CO from prior edging activities. NO_2 concentrations were negligible for all rinks and all activities. Results confirmed that gasoline edgers significantly contribute to indoor CO levels, with peak levels exceeding some recommended exposure levels. Indoor ice rink facilities should monitor employees' CO exposures and implement procedures to limit exposures. This may be achieved by limiting the number of laps taken with the edger or replacing gasoline powered edgers with electric edgers.

Keywords: Indoor air quality; combustion equipment; edger; ice resurfacing; occupational exposure.

9. **Hookah venue employees' knowledge and perceptions of hookah tobacco smoking**

Tob Control. 2021 May;30(3):299-304. doi: 10.1136/tobaccocontrol-2019-055461. Epub 2020 Apr 16.

Authors

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- PMID: 32300027
- DOI: 10.1136/tobaccocontrol-2019-055461

Abstract

Background: Recent years showed sharp proliferation of hookah bars worldwide with scarcity of workplace safety regulations. Hookah server employees are at high risk for elevated harm. This study reported hookah smoke exposure, assessed acute problems and evaluated factors related to knowledge of hookah-smoking harm and toxicity among high-risk hookah servers.

Methods: A mixed methods design was employed. A self-reported questionnaire was distributed online, and semistructured in-depth interviews were used. Hookah server employees were recruited using snowball sampling, with 52 participants included in quantitative analyses and 10 participating in semistructured interviews.

Results: Hookah server employees took a median 389 hookah puffs per workday compared with 169-170 per session for customers. Servers were limited in knowledge of potential hookah harms and smoke toxicant exposure. Almost all believed that hookah water bowls filtered out toxicants. Smoking with family members (p=0.012) was associated with lower knowledge scores for hookah harms and exposure. Hookah server employees reported carbon monoxide-poisoning symptoms of dizziness, headaches and fainting during work but believed their bodies would adapt. Home remedies were taken to alleviate symptoms. Work environment and salary attracted hookah server employees to their position and none considered quitting for reasons of harm.

Conclusion: Findings demonstrate need for workplace policies and regulations to protect hookah server employees and provide targets for educational interventions for high-risk hookah server employees.

Keywords: global health; non-cigarette tobacco products; smoking caused disease; smoking topography.

Conflict of interest statement

Competing interests: None declared.

Full text links

10. **Evaluation of an exposure assessment used in epidemiological studies of diesel exhaust and lung cancer in underground mines**

Crit Rev Toxicol. 2012 Aug;42(7):599-612. doi: 10.3109/10408444.2012.689755. Epub 2012 May 18.

Authors

Kenny Crump [1], Cynthia Van Landingham

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- PMID: 22594934
- PMCID: PMC3423303
- DOI: 10.3109/10408444.2012.689755

Free PMC article

Abstract

NIOSH/NCI (National Institute of Occupational Safety and Health and National Cancer Institute) developed exposure estimates for respirable elemental carbon (REC) as a surrogate for exposure to diesel exhaust (DE) for different jobs in eight underground mines by year beginning in the 1940s-1960s when diesel equipment was first introduced into these mines. These estimates played a key role in subsequent epidemiological analyses of the potential relationship between exposure to DE and lung cancer conducted in these mines. We report here on a reanalysis of some of the data from this exposure assessment. Because samples of REC were limited primarily to 1998-2001, NIOSH/NCI used carbon monoxide (CO) as a surrogate for REC. In addition, because CO samples were limited, particularly in the earlier years, they used the ratio of diesel horsepower (HP) to the mine air exhaust rate as a surrogate for CO. There are considerable uncertainties connected with each of these surrogate-based steps. The estimates of HP appear to involve considerable uncertainty, although we had no data upon which to evaluate the magnitude of this uncertainty. A sizable percentage (45%) of the CO samples used in the HP to CO model was below the detection limit which required NIOSH/NCI to assign CO values to these samples. In their preferred REC estimates, NIOSH/NCI assumed a linear relation between C0 and REC, although they provided no credible support for that assumption. Their assumption of a stable relationship between HP and CO also is questionable, and our reanalysis found a statistically significant relationship in only one-half of the mines. We re-estimated yearly REC exposures mainly using NIOSH/NCI methods but with some important differences: (i) rather than simply assuming a linear relationship, we used data from the mines to estimate the CO-REC relationship; (ii) we used a different method for assigning values to nondetect CO measurements; and (iii) we took account of statistical uncertainty to estimate bounds for REC exposures. This exercise yielded significantly different exposure estimates than estimated by NIOSH/NCI. However, this analysis did not incorporate the full range of uncertainty in REC exposures because of additional uncertainties in the assumptions underlying the modeling and in the underlying data (e.g. HP and mine exhaust rates). Estimating historical exposures in a cohort is generally a very difficult undertaking. However, this should not prevent one from recognizing the uncertainty in the resulting estimates in any use made of them.

- Cited by 8 articles
- 21 references
- 4 figures

Full text links

Relation between workplace accidents and the levels of carboxyhemoglobin in motorcycle taxi drivers

11.

Rev Lat Am Enfermagem. 2013 Sep-Oct;21(5):1119-26. doi: 10.1590/S0104-11692013000500015.

[Article in English, Portuguese, Spanish]

Authors

Luiz Almeida da Silva [1], Maria Lúcia do Carmo Cruz Robazzi, Fábio de Souza Terra

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- PMID: 24142221
- DOI: 10.1590/S0104-11692013000500015

Free article

Abstract

Objective: To investigate the relation between workplace accidents and the levels of carboxyhemoglobin found in motorcycle taxi drivers.

Method: Correlational, quantitative study involving 111 workers and data obtained in July 2012 through a questionnaire to characterize the participants and blood collection to measure carboxyhemoglobin levels.

Result: 28.8% had suffered workplace accidents; 27.6% had fractured the lower limbs and significant symptoms of carbon monoxide exposure were verified in smokers. The carboxyhemoglobin levels were higher among smokers and victims of workplace accidents.

Conclusion: Motorcycle taxi drivers had increased levels of carboxyhemoglobin, possibly due to the exposure to carbon monoxide; these levels are also increased among smokers and victims of workplace accidents. The study provides advances in the knowledge about occupational health and environmental science, and also shows that carboxyhemoglobin can be an indicator of exposure to environmental pollutants for those working outdoors, which can be related to workplace accidents.

- Cited by 2 articles

Full text links

12. **Surveillance and Analysis of Occupational Carbon Monoxide Poisoning in the Paris Region**

Ann Work Expo Health. 2017 Oct 1;61(8):986-993. doi: 10.1093/annweh/wxx063.

Authors

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Affiliations

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- [4] INSERM U 705; CNRS, UMR 7157, Paris-Descartes University, Paris, France.

- PMID: 29028252

- DOI: 10.1093/annweh/wxx063

Abstract

Objectives: Acute carbon monoxide poisoning is common and often severe. Domestic causes have been extensively documented, while occupational exposures have been reported less frequently. We analyse occupational carbon monoxide poisonings from the available data of the carbon monoxide poisoning surveillance network for Paris and its region, and identify predictive factors of severity for occupational poisoning in order to identify priority prevention actions.

Methods: We retrospectively reviewed all events of acute accidental carbon monoxide exposures which occurred in the Paris region, at the work place, and notified to the surveillance network from 1 January 2005 to 31 December 2011.

Results: Over the 7-year study period, 362 exposed workers were identified, representing 8.15% of all cases of carbon monoxide exposures. The largest number of events occurred in the building sector and most commonly affected occupations were craft and related trades workers. The most common sources of exposure were internal combustion engine equipment that was involved in almost half of cases. Minor severity was observed in 86% of cases, and 13% were moderate or more. We identify that the use of internal combustion engine equipment was significantly associated with increased severity.

Conclusions: Occupational carbon monoxide poisoning is reported less frequently than domestic poisoning and has different and more numerous causes. It can be potentially severe, especially when it is caused by internal combustion engine equipment. Information about risks, compliance with instructions and cleaning rules, and establishment of collective and individual protective equipment would significantly reduce the frequency and severity of carbon monoxide poisoning.

Keywords: carbon monoxide; occupational health; poisoning.

- Cited by 1 article

Descriptive epidemiology of clinically significant occupational poisonings, United States, 2008-2018

13.

Clin Toxicol (Phila). 2021 Dec;59(12):1259-1263. doi: 10.1080/15563650.2021.1892717. Epub 2021 Mar 11.

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- PMID: 33703981
- DOI: 10.1080/15563650.2021.1892717

Abstract

Introduction: References listing common occupational poisons often include agents that were observed decades prior to the introduction of worker protective laws and regulations. Current causes of work-related acute poisonings have not been characterized. This study's primary objective was to describe the most common poisons and routes of exposure

responsible for clinically significant occupational poisonings. A secondary objective was to determine the crude rate of clinically significant occupational poisonings and occupational poisoning-related deaths over the study period.

Methods: This was a retrospective cohort study using electronic data from the American Association of Poison Control Centers' (AAPCC) National Poison Data System (NPDS), and open source data from the United States Bureau of Labor Statistics (BLS). The NPDS was queried for all cases with exposure reason coded as "Unintentional-Occupational" for the period 1 January 2008 to 31 December 2018. A case of clinically significant occupational poisoning (CSOP) was defined as a case with moderate or severe clinical effects reported, to include fatal cases. A descriptive analysis was conducted using unadjusted odds ratios to assess the strength of association between main variables of interest and CSOP.

Results: 329,437 exposure cases were available for analysis. Of these, 54,254 were considered CSOP and included 196 deaths. The top five poisons responsible for occupational fatalities were hydrogen sulfide, ammonia, carbon monoxide, simple asphyxiants, and chlorines. Fatalities were 3.7 times (OR: 3.7; 95% CI: 2.2-6.4) more likely to be men and 5.7 times (OR: 5.7; 95% CI: 4.0-8.1) more likely to have had an inhalational exposure, compared to those workers with CSOP without fatality. The crude rate of occupational fatal poisoning reported to US poison centers was 11.3 deaths per 100,000,000 worker-years during the study period. The crude rate of clinically significant occupational poisoning was 3.1 per 100,000 worker-years. These rates remained generally stable over the study period.

Conclusion: Occupational poisonings continue to be a significant cause of morbidity and mortality in the workplace despite significant improvements in workplace chemical safety over the last four decades. Workplace education and proper preventive measures devoted to inhalational toxicants and respiratory protection are opportunities for improvement.

Keywords: Occupational; Occupational Safety and Health Administration; Poison Center; occupational disease; poisoning; toxicity.

- Cited by 2 articles

Full text links

14. **Personal carbon monoxide exposures among firefighters at prescribed forest burns in the Southeastern United States**

Arch Environ Occup Health. 2013;68(1):55-9. doi: 10.1080/19338244.2011.633126.

Authors

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Affiliation

- [1] National Institute for Occupational Safety and Health, Cincinnati, OH, USA.

- PMID: 23298425
- DOI: 10.1080/19338244.2011.633126

Abstract

Exposure to combustion products from wildland fires causes respiratory irritation and decreased lung function among firefighters. The authors evaluated carbon monoxide (CO) exposures of a group of wildland firefighters who conducted prescribed burns in the southeastern United States of America. A total of 149 person-days of samples were collected using data logging CO monitors. A questionnaire was administered to collect data on job tasks and self-reported smoke exposure. Overall, the highest exposures were seen amongst firefighters assigned to holding and mop-up tasks (geometric mean [GM]: 2.6 ppm), whereas the lowest were associated with lighting and jobs such as burn boss (GM: 1.6 and 0.3 ppm, respectively). The self-reported smoke exposure showed a significant linear trend with increasing CO exposure. The numbers of acres burned or burn duration, however, were not good predictors of exposure.

- Cited by 2 articles

Full text links

15. **Exposure to a firefighting overhaul environment without respiratory protection increases immune dysregulation and lung disease risk**

PLoS One. 2018 Aug 21;13(8):e0201830. doi: 10.1371/journal.pone.0201830. eCollection 2018.

Authors

Stephen J Gainey [1], Gavin P Horn [2], Albert E Towers [3], Maci L Oelschlager [4], Vincent L Tir [4], Jenny Drnevich [5], Kenneth W Fent [6], Stephen Kerber [7], Denise L Smith [2 8], Gregory G Freund [1 3 4]

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- PMID: 30130361
- PMCID: PMC6103500
- DOI: 10.1371/journal.pone.0201830

Abstract

Firefighting activities appear to increase the risk of acute and chronic lung disease, including malignancy. While self-contained breathing apparatuses (SCBA) mitigate exposures to inhalable asphyxiates and carcinogens, firefighters frequently remove SCBA during overhaul when the firegrounds appear clear of visible smoke. Using a mouse model of overhaul without airway protection, the impact of fireground environment exposure on lung gene expression was assessed to identify transcripts potentially critical to firefighter-related chronic pulmonary illnesses. Lung tissue was collected 2 hrs post-overhaul and evaluated via whole genome transcriptomics by RNA-seq. Although gas metering

showed that the fireground overhaul levels of carbon monoxide (CO), carbon dioxide (CO2), hydrogen cyanine (HCN), hydrogen sulfide (H2S) and oxygen (O2) were within NIOSH ceiling recommendations, 3852 lung genes were differentially expressed when mice exposed to overhaul were compared to mice on the fireground but outside the overhaul environment. Importantly, overhaul exposure was associated with an up/down-regulation of 86 genes with a fold change of 1.5 or greater ($p<0.5$) including the immunomodulatory-linked genes S100a8 and Tnfsf9 (downregulation) and the cancer-linked genes, Capn11 and Rorc (upregulation). Taken together these findings indicate that, without respiratory protection, exposure to the fireground overhaul environment is associated with transcriptional changes impacting proteins potentially related to inflammation-associated lung disease and cancer.

Conflict of interest statement

The authors have declared that no competing interests exist.

- Cited by 9 articles
- 54 references
- 3 figures

Full text links

16. **Determinants of ultrafine particles, black carbon, nitrogen dioxide, and carbon monoxide concentrations inside vehicles in the Paris area: PUF-TAXI study**

Indoor Air. 2021 May;31(3):848-859. doi: 10.1111/ina.12779. Epub 2020 Dec 22.

Authors

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- [4] Department of Occupational and Environmental Diseases, Hotel-Dieu Hospital, APHP, Centre - Paris University, AP-HP, Paris, France.

- PMID: 33350528
- DOI: 10.1111/ina.12779

Abstract

This study presents real-time concentrations of traffic-related air pollutants during 499 trips conducted by 50 Parisian taxi drivers from PUF-TAXI project. Ultrafine particles (UFP), black carbon (BC), and nitrogen dioxide (NO_2)/carbon monoxide (CO) were measured inside vehicles by Diffusion Size Classifier Miniature®, microAeth®, and Gas-Pro®, respectively, for nine hours. Vehicle/trip data characteristics were collected by questionnaires and on ambient conditions by monitoring stations. The associations between pollutant levels and their potential determinants were analyzed using generalized estimating equation model. Determinants of in-vehicle pollutants levels were identified: (1) ambient factors (meteorology and ambient pollution)-affecting BC, NO_2, and CO; (2) vehicle characteristics-affecting all pollutants; and (3) trip-related

driving habits-affecting UFP, BC, and CO. We highlight that commuters can, therefore, avoid high in-vehicle air pollutant concentrations mainly by (1) closing windows and activating air-conditioning under air recirculation mode in congested traffic; (2) smooth driving; and (3) maintaining cabin air filters.

Keywords: black carbon; determinants; occupational exposure; taxi drivers; traffic-related air pollutants; ultrafine particles.

- Cited by 1 article
- 68 references

Full text links

Carbon Monoxide Exposure in Workplaces, Including Coffee Processing Facilities

17.

Am J Respir Crit Care Med. 2017 Oct 15;196(8):1080-1081. doi: 10.1164/rccm.201703-0513LE.

Authors

Brie Hawley [1], Jean M Cox-Ganser [1], Kristin J Cummings [1]

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- PMID: 28471692
- PMCID: PMC5649989
- DOI: 10.1164/rccm.201703-0513LE

No abstract available

Comment in

- Reply: Carbon Monoxide Exposure in Workplaces, Including Coffee Processing Facilities.

  Rose JJ, Wang L, Xu Q, McTiernan CF, Shiva S, Tejero J, Gladwin MT.

  Am J Respir Crit Care Med. 2017 Oct 15;196(8):1081-1082. doi: 10.1164/rccm.201704-0773LE.

  PMID: 28471722Free PMC article.No abstract available.

Comment on

- Carbon Monoxide Poisoning: Pathogenesis, Management, and Future Directions of Therapy.

Rose JJ, Wang L, Xu Q, McTiernan CF, Shiva S, Tejero J, Gladwin MT.

Am J Respir Crit Care Med. 2017 Mar 1;195(5):596-606. doi: 10.1164/rccm.201606-1275CI.

PMID: 27753502Free PMC article.Review.

- Cited by 7 articles
- 7 references

Full text links

Occupational carbon monoxide fatalities in the US from unintentional non-fire related exposures, 1992-2008

18.

Am J Ind Med. 2013 Nov;56(11):1280-9. doi: 10.1002/ajim.22226. Epub 2013 Jul 19.

Authors

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- PMID: 23868822
- PMCID: PMC4552320
- DOI: 10.1002/ajim.22226

Abstract

Objective: To analyze characteristics of, and trends in, work-related carbon monoxide (CO) fatalities in the US.

Methods: Records of unintentional, non-fire related fatalities from CO exposure were extracted from the Bureau of Labor Statistics' Census of Fatal Occupational Injuries and the Occupational Safety and Health Administration's Integrated Management Information System for years 1992-2008 and analyzed separately.

Results: The average number of annual CO fatalities was 22 (standard deviation=8). Fatality rates were highest among workers aged≥65, males, Hispanics, winter months, the Midwest, and the Fishing, Hunting, and Trapping industry subsector. Self-employed workers accounted for 28% of all fatalities. Motor vehicles were the most frequent source of fatal CO exposure, followed by heating systems and generators.

Conclusions: CO has been the most frequent cause of occupational fatality due to acute inhalation, and has shown no significant decreasing trend since 1992. The high number of fatalities from motor vehicles warrants further investigation.

Keywords: CFOI; carbon monoxide; fatalities; occupational; surveillance.

Conflict of interest statement

Disclosure Statement: The authors report no conflicts of interests.

- Cited by 8 articles
- 39 references
- 2 figures

Full text links

Carbon Monoxide Poisonings from Forklift Use During Produce Packing Operations

19.

J Agromedicine. 2016;21(2):132-5. doi: 10.1080/1059924X.2016.1142915.

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- PMID: 26788681
- DOI: 10.1080/1059924X.2016.1142915

Abstract

In August 2013, the North Carolina Division of Public Health investigated a carbon monoxide (CO) exposure on a farm. Two employees were overcome by CO and lost consciousness while using a propane-powered forklift to load produce into a refrigerated trailer backed up to a warehouse. One employee died, and the second employee was admitted to the hospital for hyperbaric oxygen treatment. Eighteen people, ranging in age from 18 to 69 years, were potentially exposed to CO, including the two employees, a family member who discovered the employees, two bystanders who stopped to offer assistance, and 13 first responders. Thirteen people who assisted in the emergency response experienced symptoms such as headache and dizziness, and all 16 who assisted were evaluated in a local hospital emergency department and released after receiving 100% oxygen. Blood tests showed five people (the two employees, family member, and two bystanders) had elevated blood carboxyhemoglobin levels, but all first responders had levels within normal range. Firefighters measured a peak CO concentration of 2214 parts per million in the warehouse. The North Carolina Division of Occupational Safety and Health investigated and determined that the forklift, operated inside the trailer with no ventilation, was the source of the CO. Public health investigation activities included interviewing responders, obtaining ambient CO concentration measurements from the fire department, advising the local health director, reviewing medical records, and developing a line listing of exposed persons. To prevent CO poisoning, employers should consider replacing gas-powered equipment with electric equipment, which does not produce CO.

Keywords: CO poisoning; Carbon monoxide poisoning; forklift.

- Cited by 1 article

20. **Exploring chainsaw operator occupational exposure to carbon monoxide in forestry**

J Occup Environ Hyg. 2017 Jan;14(1):D1-D12. doi: 10.1080/15459624.2016.1229483.

Authors

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- PMID: 27624690
- DOI: 10.1080/15459624.2016.1229483

Abstract

Exposure to carbon monoxide (CO) emitted by chainsaws can negatively impact health in forestry workers. This exploratory study measures CO concentration within the breathing zone of chainsaw operators during motor-manual operations, and discusses the potential influences on CO exposure levels. A CO monitoring instrument was paired with a concurrent video recording of task activities to enable correlation of exact working operations to critical exposure levels. Multiple streams of meteorological data were also collected from sensors worn by the eight professional tree fellers/log makers. Time-weighted averages were applied to investigate levels of CO exposure during a nominal 1-hr monitoring period. The differing task demands and environment were found to influence worker exposure to CO, supporting previous research. Pending further investigation, a number of possible actions are recommended to reduce observed high exposure levels and/or emission concentration.

Keywords: 2-stroke engine exhaust; concentration; forest harvesting; logging; petrol-driven.

- Cited by 2 articles

21. **Comprehensive analysis and investigation of accident/occupational disease responsibility rates: A case study for accidental CO poisoning**

Sci Justice. 2021 Sep;61(5):493-504. doi: 10.1016/j.scijus.2021.05.001. Epub 2021 May 18.

Authors

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- PMID: 34482929
- DOI: 10.1016/j.scijus.2021.05.001

Abstract

One of the major problems of courts and insurance companies is the lack of a proper technique to determine the rate of responsibility of the parties involved in the accident. The aim of this study was to determine the Accident/Occupational Diseases Responsibility Rates (AOD RR) for complex events. Accordingly, a case study of a complex accident of carbon monoxide (CO) poisoning was selected and Occupational Accident Tree Analysis (OATA) and Occupational Accident Component Analysis (OACA) techniques, which were solely used to investigate occupational accidents, were used with the new names Accident/Occupational Disease Tree Analysis (AOD TA) and Accident/Occupational Disease Component Analysis (AOD CA) to evaluate their applicability to investigate non-occupational accidents and occupational diseases. For this purpose, causes of CO penetration to victims' room was assessed using gas tracking methods. Finally, Fuzzy Accident/Occupational Disease Tree/Component Analysis (FAOD TA and FAOD CA) techniques were developed and used for determining AOD RR in fuzzy environment. The results showed that the AOD RR obtained by AOD TA and AOD CA based on the average of experts' personal opinions and consensus between experts, and AOD TA and AOD CA in a fuzzy environment were close to each other, with the power terminal and the power cable crossing route being the main routes of transmission and penetration of CO to the victims' room. Also, the owner, contractor, tenant, and serviceman were responsible for the CO poisoning of victims. It can be concluded that any hole, crack, or fission in the building can result in CO penetration to the individuals' living rooms, and gas tracking in early winter, especially in older buildings, plays a very significant role in preventing residents' poisoning. Further, due to the uncertainty of AOD TA and AOD CA techniques, it is recommended to use FAOD TA and FAOD CA techniques for increasing the accuracy of the results. This will enhance the court and insurance companies' trust in the opinions of accident investigation experts, decrease delays in the proceedings, and prevent any violation of the individual rights.

Keywords: Accident; Carbon monoxide poisoning; Chimney; Gas detector; Occupational disease; Responsibility rates.

Full text links

22. **Carbon monoxide poisoning-induced cardiomyopathy from charcoal at a barbecue restaurant: a case report**

Ann Occup Environ Med. 2015 Apr 28:27:13. doi: 10.1186/s40557-015-0063-2. eCollection 2015.

Authors

Hyun-Jun Kim [1], Yun Kyung Chung [1], Kyeong Min Kwak [1], Se-Jin Ahn [1], Yong-Hyun Kim [1], Young-Su Ju [1], Young-Jun Kwon [1], Eun-A Kim [2]

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- PMID: 25995848
- PMCID: PMC4438634
- DOI: 10.1186/s40557-015-0063-2

Abstract

Objective: Acute carbon monoxide poisoning has important clinical value because it can cause severe adverse cardiovascular effects and sudden death. Acute carbon monoxide poisoning due to charcoal is well reported worldwide, and increased use of charcoal in the restaurant industry raises concern for an increase in occupational health problems. We present a case of carbon monoxide poisoning induced cardiomyopathy in a 47-year-old restaurant worker.

Materials and methods: A male patient was brought to the emergency department to syncope and complained of left chest pain. Cardiac angiography and electrocardiography were performed to rule out acute ischemic heart disease, and cardiac markers were checked. After relief of the symptoms and stabilization of the cardiac markers, the patient was discharged without any complications.

Results: Electrocardiography was normal, but cardiac angiography showed up to a 40% midsegmental stenosis of the right coronary artery with thrombotic plaque. The level of cardiac markers was elevated at least 5 to 10 times higher than the normal value, and the carboxyhemoglobin concentration was 35% measured at one hour after syncope. Following the diagnosis of acute carbon monoxide poisoning induced cardiomyopathy, the patient's medical history and work exposure history were examined. He was found to have been exposed to burning charcoal constantly during his work hours.

Conclusions: Severe exposure to carbon monoxide was evident in the patient because of high carboxyhemoglobin concentration and highly elevated cardiac enzymes. We concluded that this exposure led to subsequent cardiac injury. He was diagnosed with acute carbon monoxide poisoning-induced cardiomyopathy due to an unsafe working environment. According to the results, the risk of exposure to noxious chemicals such as carbon monoxide by workers in the food service industry is potentially high, and workers in this sector should be educated and monitored by the occupational health service to prevent adverse effects.

Keywords: Carbon monoxide poisoning; Cardiomyopathy; Charcoal; Restaurant worker.

- Cited by 2 articles
- 24 references
- 1 figure

Full text links

23. **A cross-sectional study with an improved methodology to assess occupational air pollution exposure and respiratory health in motorcycle taxi driving**

Sci Total Environ. 2016 Apr 15:550:1-5. doi: 10.1016/j.scitotenv.2016.01.068. Epub 2016 Jan 22.

Authors

Herve Lawin [1], Gildas Agodokpessi [2], Paul Ayelo [3], Jacqueline Kagima [4], Rodrigue Sonoukon [3], Bertrand H Mbatchou Ngahane [5], Olayemi Awopeju [6], William M Vollmer [7], Benoit Nemery [8], Peter Burney [9], Benjamin Fayomi [3]

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- PMID: 26803678
- DOI: 10.1016/j.scitotenv.2016.01.068

Abstract

Introduction: Motorcycle taxi driving is common in many African cities. This study tested whether this occupation is associated with more respiratory disorders in a context of widespread urban air pollution with an improved methodology.

Methods: In a cross sectional study we compared 85 male motorcycle taxi drivers in the capital city of the Republic of Benin (Cotonou) with an age and neighborhood matched control group. All participants carried a portable carbon monoxide data logger for 8 hours per day to assess exposure to air pollution. Respiratory symptoms were obtained using a standardized questionnaire and pulmonary function was assessed by spirometry.

Results: The two groups did not differ significantly (p>0.10) in their age, height, educational level, and exposures to smoke from biomass fuels and tobacco products. The taxi drivers were exposed to higher mean (SD) levels of carbon monoxide (7.6±4.9ppmvs. 5.4±3.8ppm p=0.001). They reported more phlegm and tended to have slightly lower levels of lung function, although these differences were not statistically significant.

Conclusion: In this cross sectional study of young motorcycle taxi drivers with substantial exposure to urban traffic and a matched control group, we found no evidence for respiratory impairment. A follow-up of such study population with other pollution exposure surrogate and other clinical endpoint may provide a more robust conclusion regarding the exposure response in this professional group.

- Cited by 6 articles

Full text links

24. **Comparison of motorcycle taxi driver's respiratory health using an air quality standard for carbon monoxide in ambient air: a pilot survey in Benin**

Pan Afr Med J. 2018 Jun 12:30:113. doi: 10.11604/pamj.2018.30.113.14975. eCollection 2018.

Authors

Herve Lawin [1 2], Lucie Ayi Fanou [3], Arsene Amadohoue Kpangon [4], Antoine Vikkey Hinson [1], John Balmes [5], Jacqueline Wanjiku [6], Boni Maxime Ale [7], Benjamin Fayomi [1 2]

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- PMID: 30364347
- PMCID: PMC6195239
- DOI: 10.11604/pamj.2018.30.113.14975

Abstract

Introduction: Ambient air quality standards are not designed to protect people occupationally exposed to outdoor air pollution on a routine basis. This study aimed to assess the effect of exceeding the US ambient air quality standard for carbon monoxide (CO) on motorcycle taxi drivers respiratory health.

Methods: A cross-sectional study of 85 current motorcycle taxi drivers with at least 5 years of job tenure in Cotonou (Benin) was conducted. Personal CO was measured with a portable CO data logger for 8 hours per day during working hours. A questionnaire on respiratory symptoms was administered to participants and spirometry was performed. Participants were divided into two groups, those with exposure to CO >9 ppm and ≤9 ppm, according to the US Environmental Protection Agency (EPA) National Ambient Air Quality Standard which is an 8-hour average of 9ppm. 8 and 10 ppm were also used an exposure limit. Analysis was done using these two groups.

Results: Socio-demographic characteristics were well balanced between the two study groups. The drivers with a CO exposure of more than 9ppm had non-significantly more respiratory symptoms (OR=1.67; 95%CI:0.26,10.74), lower FVC and FEV1 compared to the less exposed group but they have a significant lower PEF (-10%, p=0.02). When we used an exposure limit of 8 or 10 ppm the results were not statistically different.

Conclusion: Drivers with a CO exposure >9 ppm tend to have more respiratory problems. More research is needed to reinforce this result in order to improve air quality standards to protect workers occupationally exposed to outdoor air pollution.

Keywords: Occupational exposure; air quality standards; carbon monoxide; lung function; respiratory symptoms.

Conflict of interest statement

The authors declare no competing interests.

- Cited by 2 articles
- 23 references

Full text links

25. **The concentration of carbon monoxide in the breathing areas of workers during logging operations at the motor-manual level**

Int J Occup Med Environ Health. 2014 Oct;27(5):821-9. doi: 10.2478/s13382-014-0300-x. Epub 2014 Sep 12.

Author

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- PMID: 25216817
- DOI: 10.2478/s13382-014-0300-x

Free article

Abstract

Objectives: This article compares 2 variants of logging technologies at the motor-manual level: variant A - cutting and delimbing by means of a petrol chainsaw, skidding with the use of a cable winch mounted on a tractor (67-74 kW); variant B - cutting by means of a petrol chainsaw, skidding, debranching and cutting to length by means of a processor aggregated with a farm tractor (61 kW).

Material and methods: Direct dosimetry and non-parametric (moving block bootstrap) methods were used in order to specify the characteristics of the collected sets.

Results: Bootstrap average values show that the average CO concentration at a skidding tractor operator's station during early thinning was 2.54 mg×m(-3). At processor operator's station it amounted to 10.35 mg×m(-3). Such results allow to conclude that a higher CO concentration at the above-mentioned 2 work stations was observed during early thinning. In the case of a petrol chainsaw operator, it was observed that the permissible exposure limit (23 mg×m(-3)) was exceeded and the short-term permissible exposure limit (117 mg×m(-3)) was not. The average concentration value for a chainsaw operator working individually during late thinning interventions was substantially lower (15.01 mg×m(-3)), which results from the lack of technological pressure that can be observed while cooperating with a processor operator.

Conclusions: The risk increases along with conditions that generate the concentration of exhaust produced by 2-stroke petrol chainsaw engines.

- Cited by 1 article

Full text links

Gaseous and Particulate Content of Laser Tattoo Removal Plume

26.

Dermatol Surg. 2021 Aug 1;47(8):1071-1078. doi: 10.1097/DSS.0000000000003089.

Authors

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- PMID: 34397541
- PMCID: PMC9241128
- DOI: 10.1097/DSS.0000000000003089

Abstract

Background: There is increasing awareness of the potential hazards of surgical plumes. The plume associated with laser tattoo removal remains uncharacterized.

Objective: To determine the gaseous, particulate, and microbiological content of the laser tattoo removal plume.

Materials and methods: Air sampling was performed during laser tattoo removal from pig skin and from patients. Measurement of metals, volatile organic compounds (VOCs), carbon monoxide (CO), hydrogen sulfide (HS), and ultrafine particulates (UPs) as well as bacterial 16S ribosomal DNA sequencing were performed.

Results: Metals were identified in the plume from both pig and human skin. Volatile organic compounds were found at similar levels within and outside the treatment room. Several bacterial phyla were detected in the treatment room, but not outside. High levels of UPs were measured throughout the treatment room during tattoo removal from pig skin. Ultrafine particulates were detected at low levels in the room periphery during tattoo removal from human skin, but at higher levels in the immediate treatment zone. HS and CO were not detected.

Conclusion: Metals, VOCs, HS, and CO were found at levels below applicable occupational exposure limits. The presence of bacteria is of uncertain significance, but may be hazardous. High levels of UPs require further investigation.

- 33 references
- 3 figures

Full text links

A human factors analysis of an EMS crew's exposure to carbon monoxide

27. Prehosp Disaster Med. 2012 Jun;27(3):297-8. doi: 10.1017/S1049023X12000684. Epub 2012 Jun 15.

Authors

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- PMID: 22697403
- DOI: 10.1017/S1049023X12000684

Abstract

The safety of personnel and resources is considered to be a cornerstone of prehospital Emergency Medical Services (EMS) operations and practice. However, barriers exist that limit the comprehensive reporting of EMS safety data. To overcome these barriers, many high risk industries utilize a technique called Human Factors Analysis (HFA) as a means of error reduction. The goal of this approach is to analyze processes for the purposes of making an environment safer for patients and providers. This report describes an application of this approach to safety incident analysis following a situation during which a paramedic ambulance crew was exposed to high levels of carbon monoxide.

- Cited by 1 article

Full text links

Carbon monoxide poisoning-induced encephalopathy in a carbon dioxide arc welder: a case report

28. Ann Occup Environ Med. 2022 Aug 3:34:e19. doi: 10.35371/aoem.2022.34.e19. eCollection 2022.

Authors

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- PMID: 36147587
- PMCID: PMC9483627
- DOI: 10.35371/aoem.2022.34.e19

Abstract

Background: It is widely known that carbon dioxide (CO_2) arc welding generates carbon monoxide (CO). However, to the best of our knowledge, no case reports have been published regarding CO poisoning in CO_2 arc welders. Therefore, we aimed to report a case of CO poisoning-induced encephalopathy in a CO_2 arc welder in the Republic of Korea to inform about the dangers of CO exposure among CO_2arc welders.

Case presentation: A 40-year-old man working as a CO_2 arc welder for 15 years visited a local hospital with a tremor, involuntary urination, and speaking gibberish, on April 9, 2019. He stated that he had intermittent headache and forgetting symptoms for the last 5 years, and had been lost on the way to work several times. On April 9, 2019, he was diagnosed with CO poisoning-induced encephalopathy through brain magnetic resonance imaging. He received hyperbaric oxygen therapy, and some of his symptoms improved. According to the exposure assessment of his work environment, he was continuously exposed to high concentrations of CO for 15 years while operating CO_2 arc welding machines.

Conclusions: After evaluating the patient's work environment and evaluating his medical history, we concluded that his encephalopathy was caused by CO exposure during CO_2 arc welding. Thus CO_2 arc welders must be aware of the risk of CO poisoning and strive to avoid CO exposure.

Keywords: Carbon monoxide poisoning; Encephalopathy; Metal workers.

Conflict of interest statement

Competing interests: The authors declare that they have no competing interest.

- 35 references
- 3 figures

Full text links

Should any workplace be exempt from smoke-free law: the Irish experience

29. J Environ Public Health. 2012:2012:545483. doi: 10.1155/2012/545483. Epub 2012 May 24.

Authors

M McCaffrey [1], P Goodman, A Gavigan, C Kenny, C Hogg, L Byrne, J McLaughlin, K Young, L Clancy

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- PMID: 22693522
- PMCID: PMC3368201
- DOI: 10.1155/2012/545483

Abstract

Background: In 2004, the Irish Government introduced national legislation banning smoking in workplaces; with exemptions for "a place of residence". This paper summarises three Irish studies of exempted premises; prisons, psychiatric hospitals and nursing homes.

Methods: PM(2.5) and nicotine were measured in nursing homes and psychiatric hospitals, in addition to ultrafine particles in the hospitals. In the prisons, officers (n = 30) completed exhaled breath Carbon Monoxide (CO) measurements. Questionnaires determined officers' opinion on introducing smoking prohibitions in prisons. Nursing home smoking policies were examined and questionnaires completed by staff regarding workplace secondhand smoke (SHS) exposure.

Findings: Ultrafine particle concentrations in psychiatric hospitals averaged 130,000 cm(3), approximately 45% higher than Dublin pub (35.5 µg/m(3)) pre ban. PM(2.5) levels in psychiatric hospitals (39.5 µg/m(3)) were similar to Dublin pubs (35.5 µg/m(3)) pre ban. In nursing homes permitting smoking, similar PM(2.5) levels (33 µg/m(3)) were measured, with nicotine levels (0.57 µg/m(3)) four times higher than "non-smoking" nursing homes (0.13 µg/m(3)). In prisons, 44% of non-smoking officers exhibited exhaled breath CO criteria for light to heavy smokers.

Conclusions: With SHS exposure levels in some exempted workplaces similar to Dublin pubs levels pre ban, policies ensuring full protection must be developed and implemented as a right for workers, inmates and patients.

- Cited by 6 articles
- 13 references
- 7 figures

Full text links

Exposure assessment of non-electric ice resurfacer operators in indoor ice rinks: a pilot study

30. Int J Occup Environ Health. 2017 Jul;23(3):228-233. doi: 10.1080/10773525.2018.1468130. Epub 2018 May 2.

Authors

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- PMID: 29718778
- PMCID: PMC6060872
- DOI: 10.1080/10773525.2018.1468130

Abstract

Exposure of ice resurfacer operators to indoor air contaminants was measured in six indoor ice arenas. A standardized questionnaire on technical and operational features was employed and indoor airborne concentrations of carbon monoxide (CO), carbon dioxide (CO_2), nitric oxide (NO), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and total volatile organic compounds (VOCs) were measured. Air samples were collected using a range of direct reading instruments attached to the driver's seat of the resurfacer. The range of mean exposure concentrations via positional sampling (i.e. as close as able to the operator's breathing zone) were 5.7-7.4 ppm, 694-2171 ppm, <0.5 to 0.5 ppm, and < 0.1 to 0.2 ppm, for CO, CO_2, NO, and NO_2, respectively. Exposure levels for SO_2 and VOC were below detection. Overall, each of the measured indoor air contaminants was found to be below its respective occupational exposure limits (OEL), suggesting that the risk of hazardous exposure is low. The use of natural gas as a fuel source is believed to contribute to low contaminant concentrations.

Keywords: Occupational exposure; combustion byproducts; ice rinks; indoor air quality; non-electric ice resurfacer.

- 24 references
- 1 figure

Full text links

Long-term effects of carbon monoxide poisoning at Miike coal mine: A 33-year follow-up study

31. Undersea Hyperb Med. 2023 Second Quarter;50(2):111-143. doi: 10.22462/01.01.2023.40.

Authors

Koichi Mimura [1], Masazumi Harada [2], Shiro Sumiyoshi [3], Gyo Toya [4], Motoaki Takagi [5], Eisuke Fujita [1], Akira Takata [6], Seijun Tatetsu [7]

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- PMID: 37302076
- DOI: 10.22462/01.01.2023.40

Abstract

On November 9, 1963, a coal dust explosion occurred at the Miike Mikawa Coal Mine (Omuta, Kyushu Region of Japan). This resulted in a massive release of carbon monoxide (CO) gas that resulted in 458 fatalities and 839 victims of CO poisoning. After the accident, the Department of Neuropsychiatry, Kumamoto University School of Medicine (including the authors) immediately began to conduct periodic medical examinations of the victims. Such a long-term follow up of so many CO-poisoned patients is globally unprecedented. When the Miike Mine was closed in March of 1997, 33 years after the disaster, we conducted the final follow-up study.

Keywords: MRI; Miike coal mine; carbon monoxide poisoning; coal dust explosion; long-term prognosis follow-up study.

Conflict of interest statement

The authors of this paper declare no conflicts of interest exist with this submission.

Wildland smoke exposure values and exhaled breath indicators in firefighters

32.

J Toxicol Environ Health A. 2012;75(13-15):831-43. doi: 10.1080/15287394.2012.690686.

Authors

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- PMID: 22788370
- DOI: 10.1080/15287394.2012.690686

Abstract

Smoke from forest fires contains significant amounts of gaseous and particulate pollutants. Firefighters exposed to wildland fire smoke can suffer from several acute and chronic adverse health effects. Consequently, exposure data are of vital importance for the establishment of cause/effect relationships between exposure to smoke and firefighter health effects. The aims of this study were to (1) characterize the relationship between wildland smoke exposure and medical parameters and (2) identify health effects pertinent to wildland forest fire smoke exposure. In this study, firefighter exposure levels of carbon monoxide (CO), nitrogen dioxide (NO_2), and volatile organic compounds (VOC) were measured in wildfires during three fire seasons in Portugal. Personal monitoring devices were used to measure exposure. Firefighters were also tested for exhaled nitric oxide (eNO) and CO before and after their firefighting activities. Data indicated that exposure levels during firefighting activities were beyond limits recommended by the Occupational Exposure Standard (OES) values. Medical tests conducted on the firefighters also indicated a considerable effect on measured medical parameters, with a significant increase in CO and decrease in NO in exhaled air of majority of the firefighters.

- Cited by 14 articles

Biomarkers of Secondhand Smoke Exposure in Waterpipe Tobacco Venue Employees in Istanbul, Moscow, and Cairo

33.

Nicotine Tob Res. 2018 Mar 6;20(4):482-491. doi: 10.1093/ntr/ntx125.

Authors

Katherine A Moon [1 2], Ana M Rule [1], Hoda S Magid [1], Jacqueline M Ferguson [1], Jolie Susan [1], Zhuolu Sun [1], Christine Torrey [1], Salahaddin Abubaker [1], Vladimir Levshin [3], Asli Çarkoglu [4], Ghada Nasr Radwan [5], Maha El-Rabbat [4 5], Joanna E Cohen [6], Paul Strickland [1], Patrick N Breysse [1], Ana Navas-Acien [1 2 7]

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- PMID: 28582531
- PMCID: PMC6350617
- DOI: 10.1093/ntr/ntx125

Abstract

Background: Most smoke-free legislation to reduce secondhand smoke (SHS) exposure exempts waterpipe (hookah) smoking venues. Few studies have examined SHS exposure in waterpipe venues and their employees.

Methods: We surveyed 276 employees of 46 waterpipe tobacco venues in Istanbul, Moscow, and Cairo. We interviewed venue managers and employees and collected biological samples from employees to measure exhaled carbon monoxide (CO), hair nicotine, saliva cotinine, urine cotinine, urine 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL), and urine 1-hydroxypyrene glucuronide (1-OHPG). We estimated adjusted geometric mean ratios (GMR) of each SHS biomarker by employee characteristics and indoor air SHS measures.

Results: There were 73 nonsmoking employees and 203 current smokers of cigarettes or waterpipe. In nonsmokers, the median (interquartile) range concentrations of SHS biomarkers were 1.1 (0.2, 40.9) µg/g creatinine urine cotinine, 5.5 (2, 15) ng/mL saliva cotinine, 0.95 (0.36, 5.02) ng/mg hair nicotine, 1.48 (0.98, 3.97) pg/mg creatinine urine NNAL, 0.54 (0.25, 0.97) pmol/mg creatinine urine 1-OHPG, and 1.67 (1.33, 2.33) ppm exhaled CO. An 8-hour increase in work hours was associated with higher urine cotinine (GMR: 1.68, 95% CI: 1.20, 2.37) and hair nicotine (GMR: 1.22, 95% CI: 1.05, 1.43). Lighting waterpipes was associated with higher saliva cotinine (GMR: 2.83, 95% CI: 1.05, 7.62).

Conclusions: Nonsmoking employees of waterpipe tobacco venues were exposed to high levels of SHS, including measurable levels of carcinogenic biomarkers (tobacco-specific nitrosamines and PAHs).

Implications: Smoke-free regulation should be extended to waterpipe venues to protect nonsmoking employees and patrons from the adverse health effects of SHS.

- Cited by 11 articles
- 50 references

Full text links

Generation rate of carbon monoxide from CO2 arc welding

34.

J Occup Health. 2013;55(1):39-42. doi: 10.1539/joh.12-0180-br. Epub 2012 Nov 27.

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- PMID: 23183022
- DOI: 10.1539/joh.12-0180-br

Free article

Abstract

Objectives: CO poisoning has been a serious industrial hazard in Japanese workplaces. Although incomplete combustion is the major cause of CO generation, there is a risk of CO poisoning during some welding operations. The aim of the present study was to evaluate the generation rate of CO from CO2 arc welding under controlled laboratory conditions and estimate the ventilation requirements for the prevention of CO poisoning.

Methods: Bead on plate welding was carried out with an automatic welding robot on a rolled steel base metal under several conditions. The concentration of emitted CO from the welding was measured by a real-time CO monitor in a well-ventilated laboratory that was free from ambient CO contamination. The generation rate of CO was obtained from the three measurements-the flow rate of the welding exhaust gas, CO concentration in the exhaust gas and the arcing time. Then the ventilation requirement to prevent CO poisoning was calculated.

Results: The generation rate of CO was found to be 386-883 ml/min with a solid wire and 331-1,293 ml/min with a flux cored wire respectively. It was found that the CO concentration in a room would be maintained theoretically below the OSHA PEL (50 ppm) providing the ventilation rate in the room was 6.6-25.9 m3/min. The actual ventilation requirement was then estimated to be 6.6-259 m3/min considering incomplete mixing.

Conclusions: In order to prevent CO poisoning, some countermeasures against gaseous emission as well as welding fumes should be taken eagerly.

- Cited by 3 articles

Full text links

35. **Video Exposure Monitoring and Position Tracking for Evaluating Particulate and Gas Exposures in a Fully Enclosed Small Arms Firing Range**

Ann Work Expo Health. 2022 Jul 2;66(6):768-780. doi: 10.1093/annweh/wxac007.

Authors

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- PMID: 35297489
- DOI: 10.1093/annweh/wxac007

Abstract

The exposure environment in small arms firing ranges is dynamic since ventilation conditions vary in space and time and instructors continuously move around throughout the range. Understanding the impact of engineering controls and instructor behavior on the levels of particulates and gases in the breathing zone is required for providing recommendations to mitigate exposure. In this study, video exposure monitoring (VEM) and position tracking technologies were used in conjunction with real-time measurements of ultrafine particle (UFP) and carbon monoxide (CO) exposures in the breathing zone of instructors in an enclosed small arms firing range. VEM was completed using Enhanced Video Analysis of Dust Exposure 2.1 developed by the National Institute for Occupational Safety and Health. With this program, video recordings of Combat Arms instructor activity were synced with exposure data collected in real-time during small arms training. Position tracking was completed using a system by Pozyx, which uses ultra-wideband (UWB) technology. Position tracking data was aligned with real-time sensor data via time-synchronization. VEM identified that the largest peaks in UFP and CO concentrations generally occurred when instructors were close to the firing line assisting shooters during live fire and when instructors were located near the center of the range near the back wall where the air supplies transition between the Left-Hand-Side (LHS) and Right-Hand-Side (RHS). The UWB position tracking results agreed with the VEM results, confirming that peak exposures occurred when firing range instructors were near the center of the range close to the back wall where the LHS and RHS air supplies transition. Without these exposure visualization technologies, this observation could not have been made. Thus, exposure visualization is a valuable tool to identify gaps in exposure assessment, although future technologies should focus on automation to expedite analysis.

Keywords: aerosols; direct-reading instruments; exposure assessment; exposure assessment methodology; exposure data evaluation; particle monitoring—ultrafines.

- Cited by 1 article

36. **Indoor air quality in Portuguese archives: a snapshot on exposure levels**

J Toxicol Environ Health A. 2012;75(22-23):1359-70. doi: 10.1080/15287394.2012.721168.

Authors

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- PMID: 23095154
- DOI: 10.1080/15287394.2012.721168

Abstract

Indoor air quality recently entered legislation in Portugal. Several parameters must be evaluated and kept within limits in order to obtain a certification for air quality and energy consumption. Certification parameters were analyzed in two Portuguese archives in order to assess indoor air quality both for people attending or working on these premises and for maintenance of a written heritage that must be retained for future generations. Carbon monoxide (CO) and carbon dioxide (CO_2), formaldehyde, and fungal counts were kept within stipulated limits. Relative humidity (RH), volatile organic compounds (VOC), particulate matter (PM_{10}), and ozone (O_3) showed values above legislated levels and justified the implementation of corrective measures. In terms of conservation, studies on the limit values are still needed, but according to the available international guidelines, some of the analyzed parameters such as PM_{10}, O_3, and RH were also above desirable values. Corrective measures were proposed to these institutions. Although this study was only of a short duration, it proved valuable in assessing potential eventual problems and constitutes the first Portuguese indoor air quality assessment taking into consideration both aspects of an archive such as human health and heritage safekeeping.

- Cited by 2 articles

37. **Evaluation of oxidative stress and DNA damage in traffic policemen exposed to vehicle exhaust**

Biomarkers. 2013 Aug;18(5):406-11. doi: 10.3109/1354750X.2013.801517. Epub 2013 Jun 5.

Authors

Badabagni Siva Prasad [1], Peddireddy Vidyullatha, Rekhadevi Perumalla Venkata, Vani Gudimella Tirumala, Sreedevi Varre, Usha Rani Penagaluru, Paramjit Grover, Hema Prasad Mundluru, Pardhanandana Reddy Penagaluru

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- PMID: 23738842
- DOI: 10.3109/1354750X.2013.801517

Abstract

Objective: We aimed to study the genotoxic effects in traffic police who are occupationally exposed due to higher free radical generation.

Methods: Ambient and breathing zone air samples were analyzed blood samples were collected for analysis of antioxidant enzymes Superoxide Dismutase (SOD), Glutathione Peroxidase (GPx) and free radicals - nitric oxide (NO) and malondialdehyde (MDA) levels using a spectrophotometer. DNA damage was measured with the comet assay.

Results: Higher levels of benzene (BZ), toluene (TOL), carbon monoxide (CO), benzo([a])pyrene (BaP) and sulfur dioxide (SO2) was observed in traffic police. Elevated levels of NO, MDA and comet tail length and lower SOD and GPx levels observed in traffic police.

Conclusion: The studied biomarkers, related to oxidative stress and DNA damage positively correlated in traffic police exposed to environmental air pollutants.

- Cited by 3 articles

Full text links

38. **Assessment of Carbon Monoxide in Exhaled Breath using the Smokerlyzer Handheld Machine: A Cross-Sectional Study**

Tob Use Insights. 2023 Jun 23:16:1179173X231184129. doi: 10.1177/1179173X231184129. eCollection 2023.

Authors

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- PMID: 37384051
- PMCID: PMC10293515
- DOI: 10.1177/1179173X231184129

Abstract

Introduction: Nicotine dependence is known to be a chronic remitting and relapsing addictive disorder. Among cancer patients who smoke, nicotine addiction has been found to be more when compared with smoking healthy individuals. Smokerlyzer machine can be used to test smoking substance use and de-addiction services can be provided at Preventive Oncology units. The objectives of the study include: (i) To assess eCO using a Smokerlyzer hand-held machine and correlate it with the smoking status, (ii) To assess the cut-off value for smoking use, and discusses the benefits of this method.

Methods: In this cross-sectional study, healthy individuals at the workplace were tested for exhaled CO (eCO), which is used as a biological marker for monitoring the tobacco smoking. We discuss the feasibility of testing and its implications for cancer patients. The Bedfont EC50 Smokerlyzer machine was used to measure the concentration of CO in the end-tidal expired air.

Results: Among 643 study subjects, we found a statistically significant difference (P < .001) of median (IQR) eCO (measured in ppm) among smokers and non-smokers 2(1,5) vs 1(1,2). A significant and moderate positive correlation (Spearman rank correlation coefficient: .463) was observed between eCO and subjects who used cigarettes (measured in pack years). The ROC curve shows a cut off value for eCO as 2.5 with sensitivity 43.6% and 1 - specificity 2.76% (Specificity: 97.24%), which was rounded to 3. The area under the curve is 74.9%, which indicates a moderate discrimination performance of the test. The diagnostic accuracy of the test is 82.89%, which shows the proportion of correct test results.

Conclusion: Estimating eCO in health care settings will enable monitoring the smoking substance use which has important impact on clinical outcomes. In cancer hospitals, when the goal is complete abstinence a stringent CO cutoff in the range of 3-4 ppm should be used.

Keywords: Breath tests; carbon monoxide; carboxyhaemoglobin; neoplasm; smoking; smoking cessation.

Conflict of interest statement

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

- 25 references
- 3 figures

Full text links

A rare case of Holmes tremor in a worker with occupational carbon monoxide poisoning

39. Am J Ind Med. 2021 May;64(5):435-449. doi: 10.1002/ajim.23235. Epub 2021 Feb 22.

Authors

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- PMID: 33616228
- DOI: 10.1002/ajim.23235

Abstract

Parkinsonism and encephalopathy are frequently seen in patients who survive carbon monoxide (CO) poisoning. Neurological findings associated with CO poisoning can emerge immediately after cessation of exposure or following a brief period of pseudo-recovery. When present, the tremor associated with CO poisoning is typical of the postural/intention type. Here, we report on a rare case of toxic encephalopathy with a dominant-hand Holmes-type tremor, characterized by resting, as well as postural and kinetic/intentional components, in a previously healthy 53-year-old man exposed to CO while actively engaged in the process of performing a physically demanding skilled labor task. The unique neuropathological and functional changes that give rise to Holmes-type tremor and how this relates to the selective vulnerability of the inhibitory indirect pathway of the basal ganglia to glutamatergic excitotoxicity mediated by tissue hypoxia are discussed.

Keywords: Holmes tremor; Parkinsonism; carbon monoxide; occupational.

- Cited by 1 article
- 78 references

Full text links

Classification of Critical Levels of CO Exposure of Firefigthers through Monitored Heart Rate

40.

Sensors (Basel). 2021 Feb 24;21(5):1561. doi: 10.3390/s21051561.

Authors

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- [2] Centre for Environmental and Marine Studies (CESAM) & Department of Environment and Planning (DAO), University of Aveiro, 3810-193 Aveiro, Portugal.

- PMID: 33668116
- PMCID: PMC7956572
- DOI: 10.3390/s21051561

Abstract

Smoke inhalation poses a serious health threat to firefighters (FFs), with potential effects including respiratory and cardiac disorders. In this work, environmental and physiological data were collected from FFs, during experimental fires performed in 2015 and 2019. Extending a previous work, which allowed us to conclude that changes in heart rate (HR) were associated with alterations in the inhalation of carbon monoxide (CO), we performed a HR analysis according to different levels of CO exposure during firefighting based on data collected from three FFs. Based on HR collected and on CO occupational exposure standards (OES), we propose a classifier to identify CO exposure levels through the HR measured values. An ensemble of 100 bagged classification trees was used and the classification of CO levels obtained an overall accuracy of 91.9%. The classification can be performed in real-time and can be embedded in a decision fire-fighting support system. This classification of FF' exposure to critical CO levels, through minimally-invasive monitored HR, opens

the possibility to identify hazardous situations, preventing and avoiding possible severe problems in FF' health due to inhaled pollutants. The obtained results also show the importance of future studies on the relevance and influence of the exposure and inhalation of pollutants on the FF' health, especially in what refers to hazardous levels of toxic air pollutants.

Keywords: CO exposure; exposure classification; firefighters health; heart rate; physiological data.

Conflict of interest statement

The authors declare no conflict of interest.

- Cited by 2 articles
- 29 references
- 7 figures

Full text links

Carbon monoxide exposures in wildland firefighters in the United States and targets for exposure reduction

41.

J Expo Sci Environ Epidemiol. 2021 Sep;31(5):923-929. doi: 10.1038/s41370-021-00371-z. Epub 2021 Jul 20.

Authors

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- PMID: 34285366
- PMCID: PMC8448930
- DOI: 10.1038/s41370-021-00371-z

Abstract

Background: Every year thousands of wildland firefighters (WFFs) work to suppress wildfires to protect public safety, health, and property. Although much effort has been put toward mitigating air pollutant exposures for the public and WFFs, the current burden in this worker population is unclear as are the most effective exposure reduction strategies.

Objective: Quantify fireline carbon monoxide (CO) exposures in WFFs and identify predictors of exposures.

Methods: We collected 1-min breathing zone CO measurements on 246 WFFs assigned to fires between 2015 and 2017. We used generalized estimating equations to evaluate predictors of CO exposure.

Results: Approximately 5% of WFFs had fireline CO exposure means exceeding the National Wildfire Coordinating Group's occupational exposure limit of 16 ppm. Relative to operational breaks, direct suppression-related job tasks were associated with 56% (95% CI: 47%, 65%) higher geometric mean CO concentrations, adjusted for incident type, crew type, and fire location. WFF perception of smoke exposure was a strong predictor of measured CO exposure.

Significance: Specific job tasks related to direct suppression and WFF perceptions of smoke exposure are potential opportunities for targeted interventions aimed at minimizing exposure to smoke.

Keywords: Carbon monoxide; Occupational; Prevention; Wildland firefighter.

Conflict of interest statement

Conflicts of Interest

The authors declare no conflicts of interest.

- Cited by 3 articles
- 34 references
- 3 figures

Full text links

42. **A Comparison of Occupational CO Levels, HbCO, and Lung Functions Between Grill and Non-grill Street Vendors**

Med Arch. 2021 Aug;75(4):286-290. doi: 10.5455/medarh.2021.75.286-290.

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- PMID: 34759449
- PMCID: PMC8563034
- DOI: 10.5455/medarh.2021.75.286-290

Abstract

Background: There is a surge increase in grills-fast food outlet in the urban areas that plays an essential role in producing air pollution. Chronic accumulation of carbon monoxide might affect the airway and destroy alveolus as well as correlated with the disturbance of lung function.

Objective: The purpose of this study is to compare the occupational CO levels, HbCO, and lung functions between grill and non-grill street vendors.

Methods: This was an observational analytic study with a case-control design. The subjects were grill street vendors and non-grill street vendors in Medan city who fulfilled several inclusion criteria. The questionnaire was used to determine some characteristics, while smokerlyzer, and ELISA for expiration CO level and blood CO level, spirometer was used to determining lung function. Logistic regression was performed with p-value < 0.05 considered to be significant using SPSS ver 24.0.

Results: A total of 50 subjects enrolled into this study with the majority of subjects in the case group were in red (40%) zone in CO exhaled test with the results in pulmonary function test, predominantly restrictive (56%) and mixed-type (40%) with the mean value of HbCO was 486.16 (ng/mL). Meanwhile, the majority of subjects were green zone with mixed type of lung function disturbance in the control group with 540.15 (ng/mL) as HBCO mean value. Grilled street vendors have a higher level of exhaled CO level (p- value: 0.03) without significant difference in HbCO and lung functions (p-value > 0.05). Age, smoking status, HbCO, and lung function did not significantly affect the CO level (p-value: 0.05).

Conclusion: There was a significant difference in exhaled CO level between grill-and non-grill street vendors without significant difference in HbCO and lung functions.

Keywords: HbCO; Lung Functions; Occupational CO Levels.

Conflict of interest statement

There are no conflicts of interest.

- Cited by 1 article
- 36 references

Full text links

43. **Temporal variation of size-fractionated particulate matter and carbon monoxide in selected microenvironments of the Milan urban area**

J Occup Environ Hyg. 2013;10(11):652-62. doi: 10.1080/15459624.2013.831985.

Authors

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- PMID: 24116669
- DOI: 10.1080/15459624.2013.831985

Abstract

This article focuses on air pollution in specific urban microenvironments and conditions characterized by high relative concentration levels and by possible risk to human health. For this reason, monitoring of particle number concentration (PNC) with a wide, size-resolved particle-size range, and CO (an indicator of combustion sources, e.g., traffic), was performed in a variety of microenvironments. Concentrations of ultrafine particles (UFPs), size-fractionated particulate matter (PM), and carbon monoxide (CO) were measured in the central area of Milan over three-week-long periods, one each during summer, autumn, and winter, with three monitoring sessions per day. Experimental data were collected continuously during each monitoring period along an established urban pathway. To assess the relevance of time and spatial factors affecting atmospheric concentrations of UFPs, PM, and CO data were collected while walking or moving by different private and public means of transport. Measurements were divided on the basis of different microenvironments (MEs), seasons, days of the week, and periods of the day. Data analysis shows statistically significant differences across MEs and monitoring periods. The highest measured median concentrations and data variability were observed for busy streets, walking or moving by motorized vehicle (CO, UFP) and in metro trains (PM); the lowest concentrations were observed in park areas and in indoor environments. The highest concentrations were measured during working day morning monitoring sessions. Regarding seasonal variation, UFP, PM, and CO showed different patterns: the highest median concentrations were observed in summer for CO, and in autumn and winter for the UFP and PM. Appreciable differences among all MEs and monitoring periods were observed: concentration patterns and variations appear related to typical sources of urban pollutants (traffic), proximity to sources, and time of day. [Supplementary materials are available for this article. Go to the publisher's online edition of Journal of Occupational and Environmental Hygiene for the following free supplemental resource: a file containing Table VI: Tau b (Kendall) index for non-parametric correlation tau test.].

- Cited by 4 articles

44. **The Biotic and Abiotic Carbon Monoxide Formation During Aerobic Co-digestion of Dairy Cattle Manure With Green Waste and Sawdust**

Front Bioeng Biotechnol. 2019 Oct 29:7:283. doi: 10.3389/fbioe.2019.00283. eCollection 2019.

Authors

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- PMID: 31737615
- PMCID: PMC6828980
- DOI: 10.3389/fbioe.2019.00283

Abstract

Carbon monoxide (CO), an air pollutant and a toxic gas to humans, can be generated during aerobic digestion of organic waste. CO is produced due to thermochemical processes, and also produced or consumed by cohorts of methanogenic, acetogenic, or sulfate-reducing bacteria. The exact mechanisms of biotic and abiotic formation of CO in aerobic digestion (particularly the effects of process temperature) are still not known. This study aimed to determine the temporal variation

in CO concentrations during the aerobic digestion as a function of process temperature and activity of microorganisms. All experiments were conducted in controlled temperature reactors using homogeneous materials. The lab-scale tests with sterilized and non-sterilized mix of green waste, dairy cattle manure, sawdust (1:1:1 mass ratio) were carried out for 1 week at 10, 25, 30, 37, 40, 50, 60, 70°C to elucidate the biotic vs. abiotic effect. Gas concentrations of CO, O_2, and CO_2 inside the reactor were measured every 12 h. The CO concentrations observed for up to 30°C did not exceed 100 ppm v/v. For 50 and 60°C, significantly ($p < 0.05$) higher CO concentrations, reaching almost 600 ppm v/v, were observed. The regression analyses showed in both cases (sterile and non-sterile) a statistically significant effect ($p < 0.05$) of temperature on CO concentration, confirming that the increase in temperature causes an increase in CO concentration. The remaining factors (time, O_2, and CO_2 content) were not statistically significant ($p > 0.05$). A new polynomial model describing the effect of temperature, O_2, and CO_2 concentration on CO production during aerobic digestion of organic waste was formulated. It has been found that the proposed model for sterile variant had a better fit ($R^2 = 0.86$) compared with non-sterile ($R^2 = 0.71$). The model predicts CO emissions and could be considered for composting process optimization. The developed model could be further developed and useful for ambient air quality and occupational exposure to CO.

Keywords: CO emissions; aerobic digestion; biomass composting; biowaste; manure; mesophilic conditions; thermophilic conditions.

- Cited by 7 articles
- 46 references
- 6 figures

Full text links

Low-Cost, Distributed Environmental Monitors for Factory Worker Health

45. Sensors (Basel). 2018 May 3;18(5):1411. doi: 10.3390/s18051411.

Authors

Geb W Thomas [1], Sinan Sousan [2], Marcus Tatum [3], Xiaoxing Liu [4 5], Christopher Zuidema [6], Mitchell Fitzpatrick [7], Kirsten A Koehler [8], Thomas M Peters [9]

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- PMID: 29751534
- PMCID: PMC5982698
- DOI: 10.3390/s18051411

Abstract

An integrated network of environmental monitors was developed to continuously measure several airborne hazards in a manufacturing facility. The monitors integrated low-cost sensors to measure particulate matter, carbon monoxide, ozone and nitrogen dioxide, noise, temperature and humidity. The monitors were developed and tested in situ for three months in several overlapping deployments, before a full cohort of 40 was deployed in a heavy vehicle manufacturing facility for a year of data collection. The monitors collect data from each sensor and report them to a central database every 5 min. The work includes an experimental validation of the particle, gas and noise monitors. The R^2 for the particle sensor ranges between 0.98 and 0.99 for particle mass densities up to 300 μg/m³. The R^2 for the carbon monoxide sensor is 0.99 for concentrations up to 15 ppm. The R^2 for the oxidizing gas sensor is 0.98 over the sensitive range from 20 to 180 ppb. The noise monitor is precise within 1% between 65 and 95 dBA. This work demonstrates the capability of distributed monitoring as a means to examine exposure variability in both space and time, building an important preliminary step towards a new approach for workplace hazard monitoring.

Keywords: aerosol exposure; carbon monoxide gas sensors; noise sensors; occupational health and safety; occupational medicine; oxidizing gas sensors; particle sensors; personal exposure; sensor arrays; wireless sensor network.

Conflict of interest statement

The authors declare no conflict of interest.

- Cited by 13 articles
- 54 references
- 12 figures

Full text links

Effect of exhaust emissions on carbon monoxide levels in employees working at indoor car wash facilities

46. Hippokratia. 2014 Jan;18(1):37-9.

Authors

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- PMID: 25125950
- PMCID: PMC4103039

Abstract

Background: Exhaust emissions from motor vehicles threaten the environment and human health. Carbon monoxide (CO) poisoning, especially the use of exhaust gas CO in suicidal attempts is well known in the literature. Recently, indoor car wash facilities established in large shopping malls with closed parking, lots is a new risk area that exposes car wash employees to prolonged periods of high level CO emissions from cars. The aim of this study was to investigate how carboxyhemoglobin (COHb) blood levels of employees get affected in confined areas with relatively poor air circulation.

Methods: Twenty male volunteers working in indoor parking car wash facilities were included in the study. Participants were informed about the aim of this study and their consent was obtained. Their pulse COHb levels were measured twice, at the beginning and at the end of the working day using Rad-57 pulse CO-oximeter device, allowing non-invasive measurement of COHb blood levels to compare the changes in their COHb levels before and after work.

Results: The mean age of the male volunteers was 29.8 ± 11.9 (range 18-55). While the mean COHb levels measured at the start of the working day was 2.1 ± 2.0 (range 0-9), it was increased to 5.2 ± 3.3 (range 1-15) at the end of work shift (Wilcoxon test, p <0.001). There was a statistically significant difference in COHb levels between the beginning and the end of the work shift in smoker subjects, while the difference was not significant in the non-smoking group (Wilcoxon test, p=0.001, p=0.102, respectively).

Conclusion: The COHb blood levels of indoor car wash facility employees is directly impacted and gets elevated by motor vechile exhaust emissions. For the health of the employees at indoor parking car wash facilities, stricter precautions are needed and the government should not give permit to such operations.

Keywords: Gas poisoning; automobile exhaust; carbon monoxide (CO); carboxyhemoglobin (COHb); occupational exposure.

- Cited by 1 article
- 13 references

Full text links

Waterpipe cafes in Baltimore, Maryland: Carbon monoxide, particulate matter, and nicotine exposure

47.

J Expo Sci Environ Epidemiol. 2015 Jul-Aug;25(4):405-10. doi: 10.1038/jes.2014.19. Epub 2014 Apr 16.

Authors

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- PMID: 24736103
- PMCID: PMC4333110
- DOI: 10.1038/jes.2014.19

Abstract

Waterpipe smoking has been growing in popularity in the United States and worldwide. Most tobacco control regulations remain limited to cigarettes. Few studies have investigated waterpipe tobacco smoke exposures in a real world setting. We measured carbon monoxide (CO), particulate matter (PM)2.5, and airborne nicotine concentrations in seven waterpipe cafes in the greater Baltimore area. Area air samples were collected between two and five hours, with an average sampling duration of three hours. Waterpipe smoking behaviors were observed at each venue. Indoor air samplers for CO, PM2.5, and airborne nicotine were placed in the main seating area 1-2 m above the floor. Indoor airborne concentrations of PM2.5 and CO were markedly elevated in waterpipe cafes and exceeded concentrations that were observed in cigarette smoking bars. Air nicotine concentrations, although not as high as in venues that allow cigarette smoking, were markedly higher than in smoke-free bars and restaurants. Concentrations of PM approached occupational exposure limits and CO exceeded occupational exposure guidelines suggesting that worker protection measures need to be considered. This study adds to the literature indicating that both employees and patrons of waterpipe venues are at increased risk from complex exposures to secondhand waterpipe smoke.

48. **[Otoneurologic and cardiovascular abnormalities associated to carbon monoxide poisoning in occupational exposed workers]**

Rev Med Inst Mex Seguro Soc. 2014 Jan-Feb;52(1):44-9.

[Article in Spanish]

Authors

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- PMID: 24625483

Abstract

in English, Spanish

Background: Even though Federal Labor Law includes carbon monoxide poisoning in the list of occupational diseases, the registration of this intoxication rarely occurs in a work environment. The objective was to determine the association of this poisoning with cardiovascular and otoneurologic disorders, in order to establish adequately this diagnosis as a work-related illness.

Methods: Cross-sectional survey performed in a group of broiler production workers, compared with a control group (n = 54). The sample consisted of people aged between 18 and 74 years, males and females, smokers and non-smokers. We excluded those participants with clinical history of cardiac attack. We determined carboxyhemoglobin (COHb) rates in exhaled air, and performed an audiometric test, and a 12-lead electrocardiogram.

Results: We studied 54 workers (57 % males and 43 % females). We obtained a statistically significant difference ($p < 0.05$) to develop hearing loss between the two groups, an odds ratio > 1 also in regards to hearing loss, and cardiovascular manifestations (anterior fascicle hemiblock).

Conclusions: Otoneurologic and cardiovascular abnormalities in occupationally exposed workers to carbon monoxide are not casual, and suggest a cause-effect relationship.

INTRODUCCIÓN: aun cuando la Ley Federal del Trabajo incluye la intoxicación por monóxido de carbono, su registro es escaso en el ámbito laboral. El objetivo de esta investigación fue determinar la relación de trastornos otoneurológicos y cardiovasculares con la intoxicación por monóxido de carbono en el ambiente de trabajo, para la adecuada fundamentación de su diagnóstico como enfermedad de trabajo. MÉTODOS: estudio transversal y analítico de un grupo de asaderos que utilizaban leña y carbón para cocinar pollo, comparados con un grupo control (n = 54). La investigación se realizó de abril a noviembre de 2012, con trabajadores de uno u otro sexo, entre los 18 y 74 años de edad; no se excluyó a quienes fumaban, pero no se incluyó a quienes manifestaron antecedente de cardiopatía isquémica Se obtuvieron niveles de carboxihemoglobina en aire espirado, audiometría tonal y electrocardiograma de 12 derivaciones.

Resultados: se estudiaron 54 trabajadores, 57 % del sexo masculino y 43 %, del femenino. Se obtuvo una diferencia estadísticamente significativa ($p < 0.05$) respecto a la hipoacusia y, en ambos grupos, una razón de momios > 1 para la presencia de esta y hemibloqueo del fascículo anterior.

Conclusiones: las alteraciones otoneurológicas y cardiovasculares en la intoxicación ocupacional con monóxido de carbono no se deben al azar y muestran una relación de causa-efecto, trabajo-daño.

Keywords: Carbon moxide; Carboxyhemoglobin; Occupational diseases.

Smoking practices in relation to exhaled carbon monoxide in an occupational cohort

49.

BMC Public Health. 2020 Dec 9;20(1):1894. doi: 10.1186/s12889-020-09997-4.

Authors

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- PMID: 33298031
- PMCID: PMC7725030
- DOI: 10.1186/s12889-020-09997-4

Abstract

Background: Exposure to carbon monoxide (CO) remains a leading occupational hazard in firefighters, but cigarette and waterpipe smoking likely contributes to the other sources of CO in such workers. The aim of this study was to estimate the contribution of self-reported active cigarette smoking, waterpipe use, and potential job-related sources of CO to the level of exhaled CO in firefighters.

Methods: We surveyed the personnel of 18 fire stations (N = 842), median age 28 years, who participated at an annual screening not timed to coincide with recent firefighting. We surveyed smoking and waterpipe history, exposure to secondhand smoke (SHS), use of coal for health and biomass for cooking and time since last exposure to firefighting in the workplace. We measured exhaled CO with an instantaneous reading device (piCO Smokerlyzer). We used multivariable regression models to test the association of time since last smoked cigarette (≤12 h) and waterpipe (≤12 h) and time since last fire (≤6 h) with exhaled CO.

Results: In analysis limited to men (93.5% of all surveyed), 42% were daily cigarette; 1% were waterpipe smokers; 94% were exposed to SHS, 29% used coal for heating and 4% used biomass for cooking. The median CO was 4 (interquartile range 3;8) ppm. Age (beta 0.74 per 10 years, $p < 0.001$), use of biomass fuel for cooking (beta 1.38, $p = 0.05$), cigarette smoked in the last 12 h (beta 8.22, $p < 0.001$), waterpipe smoked in the last 12 h (beta 23.10, $p < 0.001$) were statistically associated with CO, but not time since last fire (≤6 h) (beta 4.12, $p = 0.12$). There was a significant interaction between older age and firefighting for exhaled CO ($p = 0.03$).

Conclusions: Cigarette and recent waterpipe smoking are associated with increased exhaled CO in firefighters. Firefighting itself was a less potent contributor to exhaled CO when measured at an annual screening, but an age interaction was manifested.

Keywords: Carbon monoxide; Firefighting; Smoking; Waterpipe; Work-related.

Conflict of interest statement

The authors declare that they have no competing interests.

- Cited by 1 article
- 19 references
- 1 figure

Full text links

Fractional exhaled NO in a metalworking occupational cohort

50.

Int Arch Occup Environ Health. 2022 Apr;95(3):701-708. doi: 10.1007/s00420-021-01801-z. Epub 2021 Oct 9.

Authors

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- PMID: 34626220
- DOI: 10.1007/s00420-021-01801-z

Abstract

Purpose: Secondary metalworking carries exposure to relatively heavy levels of respirable particulate. We investigated the extent to which metalworking is associated with increased exhaled nitric oxide (FeNO), an established inflammatory biomarker.

Methods: We studied 80 metalworking factory employees in Kazakhstan. Informed by industrial hygiene data, we categorized them into three groups: (1) machine operators (41%); (2) welders or assemblers (33%); and (3) all others, including administrative and ancillary staff (26%). Participants completed questionnaires covering occupational history, smoking, home particulate sources, respiratory symptoms, and comorbidities. We measured exhaled carbon monoxide (CO), exhaled fractional nitric oxide (FeNO), and spirometric function. We used mixed-effects modeling to test the associations of occupational group with FeNO, adjusted for covariates.

Results: The median age was 51.5 (interquartile range 20.5) years; 7% were women. Occupational group ($p < 0.01$), daily current cigarette smoking intensity ($p < 0.05$), and age ($p < 0.05$), each was statistically associated with FeNO. Welders, or assemblers (Group 2), who had intermediate particulate exposure, manifested significantly higher exhaled FeNO compared to machinists (Group 1, with the highest particulate exposure) and all others (Groups 3, the lowest particulate): adjusted Group 2 mean 44.8 ppb (95% confidence interval (CI) 33.8-55.9) vs. Group 1 24.6 ppb (95% 20.5-28.7) and Group 3, 24.3 ppb (95% CI 17.7-30.9). Secondhand smoking and height were not associated with FeNO.

Conclusion: In a metalworking industrial cohort, welders/assemblers manifested significantly higher levels of FeNO. This may reflect respiratory tract inflammation associated with airborne exposures specific to this group.

Keywords: Assembling; Exhaled nitric oxide; Inflammation; Mixed-effects model; Occupational; Welding.

- Cited by 4 articles
- 38 references

Full text links

Notes from the Field: Occupational Carbon Monoxide Exposure in an Industrial Kitchen Facility - Wisconsin, 2017

51. MMWR Morb Mortal Wkly Rep. 2018 Jul 20;67(28):786. doi: 10.15585/mmwr.mm6728a5.

Authors

Erica Wilson, Carrie Tomasallo, Jonathan Meiman

- PMID: 30024867
- PMCID: PMC6053995
- DOI: 10.15585/mmwr.mm6728a5

No abstract available

Conflict of interest statement

No conflicts of interest were reported.

- Cited by 1 article
- 5 references

Full text links

Characterization of occupational smoke exposure among wildland firefighters in the midwestern United States

52. Environ Res. 2021 Feb:193:110541. doi: 10.1016/j.envres.2020.110541. Epub 2020 Nov 27.

Authors

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- PMID: 33249041
- DOI: 10.1016/j.envres.2020.110541

Abstract

Wildland firefighters are repeatedly exposed to elevated levels of wildland fire smoke (WFS) while protecting lives and properties from wildland fires. Studies reporting personal exposure concentrations of air pollutants in WFS during fire suppression or prescribed burn activities have been geographically limited to the western and southeastern United States. The objective of this study is to characterize exposure concentrations of air pollutants in WFS emissions among wildland firefighters who conducted prescribed burns in the Midwest. Between 2016 and 2019, a total of 35 firefighters (31 males and 4 females, age of 35.63 ± 9.31 years) were recruited to participate in this study. Personal particulate matter 2.5 ($PM_{2.5}$) and carbon monoxide (CO) exposure concentrations were measured during prescribed burns. The level of black carbon (BC) in WFS particulates was determined using the light transmission technique, while trace metal composition was analyzed using inductively coupled plasma mass spectrometry (ICP-MS). The results showed geometric means for $PM_{2.5}$, CO, and BC concentrations were 1.43 ± 0.13 mg/m^3, 7.02 ± 0.69 ppm, and 58.79 ± 5.46 μg/m^3, respectively. Although no occupational exposure limits (OELs) were exceeded by 8-h time-weighted average (TWA) exposure concentration observed in the firefighters, a total of 28 personal CO exposure concentrations were above the National Institute for Occupational Safety and Health (NIOSH) Recommended Exposure Limit (REL) Ceiling (200 ppm) for CO. $PM_{2.5}$ and CO concentrations were about 2-7 times higher in the Midwest than the other regions. Firefighters who performed holding had higher CO exposure concentrations compared to firefighters who performed lighting ($p < 0.01$), while lighters were exposed to higher level of BC in the smoke particulates ($p < 0.01$), possibly due to the domination of exposure by different combustion sources and stages. The levels of trace metals in WFS particulates were well below the corresponding OELs and no task-related difference was observed except for manganese. Our results suggest that wildland firefighters in the midwestern region have higher WFS exposures while working at prescribed burns compared to those western and southeastern United States.

Keywords: Black carbon; Carbon monoxide; Particulate matter; Trace metals; Wildland fire smoke.

- Cited by 4 articles

Full text links

Numerical and experimental investigation of carbon monoxide spread in underground mine fires

53.

J Fire Sci. 2018;36(5):406-418. doi: 10.1177/0734904118793891. Epub 2018 Aug 14.

Authors

Lihong Zhou, Liming Yuan, Davood Bahrami, Richard A Thomas, James H Rowland

- PMID: 30270967
- PMCID: PMC6159219
- DOI: 10.1177/0734904118793891

Abstract

The primary danger with underground mine fires is carbon monoxide poisoning. A good knowledge of smoke and carbon monoxide movement in an underground mine during a fire is of importance for the design of ventilation systems, emergency response, and miners' escape and rescue. Mine fire simulation software packages have been widely used to predict carbon monoxide concentration and its spread in a mine for effective mine fire emergency planning. However, they are not highly recommended to be used to forecast the actual carbon monoxide concentration due to lack of validation

studies. In this article, MFIRE, a mine fire simulation software based on ventilation networks, was evaluated for its carbon monoxide spread prediction capabilities using experimental results from large-scale diesel fuel and conveyor belt fire tests conducted in the Safety Research Coal Mine at The National Institute for Occupational Safety and Health. The comparison between the simulation and test results of carbon monoxide concentration shows good agreement and indicates that MFIRE is able to predict the carbon monoxide spread in underground mine fires with confidence.

Keywords: Mine fire; carbon monoxide spread; mine fire simulation.

Conflict of interest statement

Declaration of conflicting interests The author(s) declared the potential conflicts of interest with respect to the research, authorship, and/ or publication of this article: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention.

- Cited by 2 articles
- 15 references
- 10 figures

Full text links

54. **Secondhand hookah smoke: an occupational hazard for hookah bar employees**

Tob Control. 2017 Jan;26(1):40-45. doi: 10.1136/tobaccocontrol-2015-052505. Epub 2016 Jan 25.

Authors

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- PMID: 26811352
- DOI: 10.1136/tobaccocontrol-2015-052505

Abstract

Background: Despite the increasing popularity of hookah bars, there is a lack of research assessing the health effects of hookah smoke among employees. This study investigated indoor air quality in hookah bars and the health effects of secondhand hookah smoke on hookah bar workers.

Methods: Air samples were collected during the work shift of 10 workers in hookah bars in New York City (NYC). Air measurements of fine particulate matter ($PM_{2.5}$), fine black carbon ($BC_{2.5}$), carbon monoxide (CO), and nicotine were collected during each work shift. Blood pressure and heart rate, markers of active smoking and secondhand smoke exposure (exhaled CO and saliva cotinine levels), and selected inflammatory cytokines in blood (ineterleukin (IL)-1b, IL-6, IL-8, interferon γ (IFN-γ), tumour necrosis factor (TNF-α)) were assessed in workers immediately prior to and immediately after their work shift.

Results: The $PM_{2.5}$ (gravimetric) and $BC_{2.5}$ concentrations in indoor air varied greatly among the work shifts with mean levels of 363.8 $\mu g/m^3$ and 2.2 $\mu g/m^3$, respectively. The mean CO level was 12.9 ppm with a peak value of 22.5 ppm CO observed in one hookah bar. While heart rate was elevated by 6 bpm after occupational exposure, this change was not statistically significant. Levels of inflammatory cytokines in blood were all increased at postshift compared to preshift testing with IFN-Y increasing from 0.85 (0.13) to 1.6 (0.25) (mean (standard error of the mean; SEM)) pg/mL ($p<0.01$). Exhaled CO levels were significantly elevated after the work shift with 2 of 10 workers having values >90 ppm exhaled CO.

Conclusions: These results demonstrate that hookah bars have elevated concentrations of indoor air pollutants that appear to cause adverse health effects in employees. These data indicate the need for further research and a marked need for better air quality monitoring and policies in such establishments to improve the indoor air quality for workers and patrons.

Keywords: Secondhand smoke; Smoking Caused Disease; Toxicology.

- Cited by 18 articles

Comment 1.3 On page 74 starting at line 16: in the description of the search criteria used to find studies about "carbon monoxide" and "occupational exposure", the authors say they searched for articles published "from 2012 until March 2023." But on page 10 at line 14 they wrote "up to April 2023." This is **inconsistent.** They also say they excluded all 191 studies they found by this search for various reasons, which should have led them to relax some of their exclusions or change their search terms, in order to have some recent studies to consider. Searching for studies on CO and "occupational", for example, instead of "occupational exposure" finds 616 studies over the same time frame, more than three times as many. This shows **the authors' search strategy was not exhaustive or comprehensive**.

I recommend the authors relax some of their exclusion criteria and reevaluate the results so their review may be informed by at least some studies of occupational CO exposures published after 2012.

Comment 1.4 In Appendix A starting on page 61, the authors present short descriptions and results from what they consider the most relevant results from 18 prenatal and perinatal animal studies of CO. But Appendix A does not give references for any of these studies, so there is no way to easily identify them in the literature list starting on page 54. There is no reason to include results of animal studies in this review of human occupational exposures, so I recommend not including them in the literature list. If they are removed, I recommend that Appendix A be replaced with a similar appendix giving details of much more relevant studies of CO exposure in humans. Whatever types of studies are included in Appendix A, the source of each should be identified and linked by either a number or the last name of the first author and year of publication (name, year) so the reader can look up the full references in the literature list.

Comment 1.5 Unlike with the animal studies discussed in comment 1.4 above, the report does not contain any appendix with the results of human CO studies. Instead, several tables are given in the report that contain short unreferenced descriptions of what the authors consider the most important human CO studies and results that other

governments and scientific organizations have cited in their self-published reports about CO health effects and exposure limits. I recommend that all studies from which any results are presented in any section or table of the final report be linked to a full reference in the literature list that starts on page 54.

I am not making any accusations here, but according to the Committee on Publication Ethics (COPE), republishing the results of other previously peer-reviewed and published studies without including a reference to the original work or any other acknowledgment of the actual authors is considered a form of plagiarism that warrants correction (as shown in this flowchart: https://publicationethics.org/resources/flowcharts/plagiarism-published-article).

Comment 1.6 Among the unreferenced human CO studies mentioned in comment 1.5 is one that is described slightly differently in each of the tables in which it is described, as shown below:

Page and Line	Table number: Title	Description of study involving people with coronary disease	Description of Exposure	Actual Exposure as reported by Allred et al (see below for full references)
page 35 line 1	9: "health risk evaluation studies of non-acute exposures (at least 1h), adapted from the NEG. These values exemplify the most critical endpoints as supported by the indicated literature for human and animal data."	"Cardiovascular function assessments during exercise challenge"	"136 and 295 mg/m3 (117 and 253 ppm) (2.4- 4.7%) COHb range: 2.9-5.9%"	Study reported ppm, not mg/m3, and exposed men with angina to individually determined CO levels that ranged from 42 to 202 ppm CO on the "low CO" day and 143 to 357 on the "high CO day" (yes, these ranges overlapped). This is shown correctly in Table 10 but Table 9 only gives the means of the individual exposure levels (117 on the low CO day and 253 on the high CO day). These exposures produced overlapping ranges of venous COHb as well, for which the mean levels post exposure and pre-exercise were 2.2 % on the low CO day and 4.4% on the high CO day. These peaks levels then decreased after exposure stopped and the men started exercising in fresh air. COHb was measured again when the men developed angina, at which point the low and high means were reported as 2.0% and 3.9%.
page 37 line 1	10: "health risk evaluation studies as indicated in section 'Dose-effect/dose-response relationships' (p44-46) by the 2 Swedish Criteria Group, and summarised by the Committee"	"Myocardial ischemia (decreased time to onset angina symptoms and ischemic ST segment changes)"	"49-235 mg/m3 (42-202 ppm); 2% COHb and 167-416 mg/m3 (143-357 ppm); 3.9% COHb"	Same as study 9

This is inconsistent. I recommend that this and any other study summarized in more than one table should be described in exactly the same way, as well as referenced the same way, so this is not hidden from readers.

This particular example is a famous study known as Allred et al that was commissioned by the US EPA from the Health Effects Institute (HEI) in 1983 to provide a scientific basis for the CO National Ambient Air Quality Standards

(NAAQS) adopted in 1971. It is the longest, largest, most expensive and most cited study of controlled CO exposures in US history. Its results were published 3 times—twice in 1989 (by HEI and the NEJM) and once in 1991 (by Environmental Health Perspectives, a journal of US CDC NIEHS)—and the US EPA still cites all 3 papers as the primary basis for both the 1-hour 35 ppm and 8-hour 9 ppm CO NAAQS limits established in 1971. The full references are given below with their abstracts (and doi were available)..

1. First and most comprehensive publication of Allred et al. Note the levels of CO exposure are not reported

Allred EN, Bleecker ER, Chaitman BR, Dahms TE, Gottlieb SO, Hackney JD, Hayes D, Pagano M, Selvester RH, Walden SM, Warren J. Acute effects of carbon monoxide exposure on individuals with coronary artery disease. Res Rep Health Eff Inst. 1989 Nov;(25):1-79.

Abstract: The purpose of this study was to determine, using more objective evidence than that 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 one-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 one 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 then 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. There were 5.1% (p = 0.01) and 12.1% (p less than or equal to 0.0001) (trimmed mean) decreases 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)

2. Second and shortest publication of Allred et al, which refers to the first as "in press."
Note the levels of CO exposure are not reported

Allred EN, Bleecker ER, Chaitman BR, Dahms TE, Gottlieb SO, Hackney JD, Pagano M, Selvester RH, Walden SM, Warren J. Short-term effects of carbon monoxide exposure on the exercise performance of subjects with coronary artery disease. N Engl J Med. 1989 Nov 23;321(21):1426-32.
doi: 10.1056/NEJM198911233212102.

Abstract: 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. Sixty-three 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-hr 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. There were 5.1% (p = 0.01) and 12.1% (p less than or equal to 0.0001) decreases in the time to development of ischemic ST-segment changes after exposures producing 2.0 and 3.9% COHb, respectively, compared to the control day. In addition, there were 4.2% (p = 0.027) and 7.1% (p = 0.002) decreases in time to the onset of angina after exposures producing 2.0 and 3.9% COHb, respectively, 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.

3. Third publication of Allred et al was requested by US EPA and is the longest ever published by EHP.
Note the levels of CO exposure are misreported as “one of two concentrations of carbon monoxide (117 +/- 4.4 ppm or 253 +/- 6.1 ppm)”. Those are only the mean levels of exposure to which the subjects were exposed, which ranged from 42 to 202 ppm in the low CO experiments and from 143 to 357 ppm in the high CO experiments. The time of exposure also varied, from 50 to 70 minutes, so no two subjects were exposed to the same level for the same time.

Effects of carbon monoxide on myocardial ischemia.
Allred EN, Bleecker ER, Chaitman BR, Dahms TE, Gottlieb SO, Hackney JD, Pagano M, Selvester RH, Walden SM, Warren J. Environ Health Perspect. 1991 Feb;91:89-132.
doi: 10.1289/ehp.919189.

Abstract: Patients with atherosclerotic cardiovascular disease may be adversely affected by the presence of carboxyhemoglobin, even at low concentrations. We investigated the effects of carbon monoxide exposure on myocardial ischemia during exercise in 63 men with documented coronary artery disease. On each test day, subjects performed two symptom-limited incremental exercise tests on a treadmill; the tests were separated by a recovery period and 50 to 70 minutes of exposure to either room air or air containing one of two concentrations of carbon monoxide (117 +/- 4.4 ppm or 253 +/- 6.1 ppm). The order of exposure was assigned randomly. On each occasion, neither the subjects nor the study personnel knew whether the subjects had been exposed to room air or to one of the concentrations of carbon monoxide. Exposure to room air resulted in a mean carboxyhemoglobin level of 0.6 percent, exposure to the lower level of carbon monoxide resulted in a carboxyhemoglobin level of 2.0 percent, and exposure to the higher level of carbon monoxide resulted in a level of 3.9 percent. An effect of carbon monoxide on myocardial ischemia was demonstrated objectively by electrocardiographic changes during exercise. We observed a decrease of 5.1 percent (90 percent confidence interval, 1.5 to 8.7 percent; P = 0.02) and a decrease of 12.1 percent (90 percent confidence interval, 9.0 to 15.3 percent; P less than or equal to 0.0001) in the length of time to a threshold ischemic ST-segment change (ST end point) after carbon monoxide exposures that produced carboxyhemoglobin levels of 2.0 percent and 3.9 percent, respectively. The length of time to the onset of angina decreased by 4.2 percent (90 percent confidence interval, 0.7 to 7.9 percent; P = 0.054) at the 2.0 percent carboxyhemoglobin level and by 7.1 percent (90 percent confidence interval, 3.1 to 10.9 percent; P = 0.004) at the 3.9 percent carboxyhemoglobin level. Significant dose-response relations were found in both the change in the length of time to the ST end point (P less than or equal to 0.0001) and the change in the length of time to the onset of angina (P = 0.02). We conclude that low levels of carboxyhemoglobin exacerbate myocardial ischemia during graded exercise in subjects with coronary artery disease.

Since Allred et al only studied 50- to 70-minute exposures that ranged from 42 to 357 ppm, their results should not be cited as evidence that any lower level of exposure is safe over 8 hours.

Critically, as detailed in a poster I presented to the Society of Toxicology Annual Meeting in 2015 that is available online here:

https://www.dropbox.com/scl/fi/9gxsyscl3kl6naxfjeuvy/Donnay-2023-VIAQ-on-CO-in-vehicles.pptx?rlkey=2hedwc63pgqg5u21jp1a9ddr0&dl=0
the Allred study results come from 3 clinical sites that were unable to replicate each other's primary results or even agree on their direction. Scatterplots of their combined results, published in the first of the authors' three papers, show no trends from the lowest to highest levels of CO exposure when measured in ppm*minutes.

However, even if the results of Allred et al were internally consistent, they cannot be extrapolated with any clinical or statistical confidence to much lower and/or longer CO exposures. So even though the US and other countries still cite Allred et al as the basis for both 1-hour and 8-hour CO exposure limits, I urge the authors not to repeat this error.

Part 2: Comments regarding "the interpretation of the scientific data"

Comment 2.1 Starting on page 51 and line 1, the authors derive an occupational limit for CO of 7.5 mg/m3 average over 8 hours by applying various correction factors to the WHO's 24-hour average CO guideline of 4 mg/m3.

Critically, the report does not cite any studies of any kind that tested 8-hour CO exposures up to an average of 7.5 mg/3 to see what effects they produce in working adults. So the authors cannot credibly say this level will be safe workers of all ages and genders. The WHO 2021 review made the same mistake, recommending a CO limit of 4mg/m3 as protective even though all the epidemiology studies its contractor reviewed found significantly increased risks of cardiovascular disease and death at lower levels of 24-hour exposure.

I recommend that the authors acknowledge this shortcoming and propose a lower occupational limit for 8 hours based on a broader review of the epidemiology literature (see comment 2.3 below).

These show the public is only protected from the significantly higher risks of morbidity and mortality associated with small increases in CO exposure when their average inhaled level remains below 1 ppm. By the authors conversion formula, this suggests workers who are only exposed 8 hours per day for 5 days per week instead of 24/7 may tolerate occupational exposures up to 2 ppm average.

Comment 2.2 On page 52 at line 5, the authors say there is not enough evidence to set a 15-minute short-term exposure limit (STEL, and at line 16, they say the same about a Ceiling limit for immediate evacuation. I oppose the decisions to not recommend STEL or ceiling limits as they are not based on an exhaustive and comprehensive review of the available literature on occupational CO poisonings, as discussed in Comment 1.2. These limits are needed to protect workers who might otherwise be legally exposed to much higher levels over shorter times, such as over 120 mg/m3 for 30 minutes. The current limits are better than nothing and should be retained if the authors cannot find any evidence to warrant lowering them. Given that employers and workers have become accustomed to working with their limits, they should not be discarded without some replacement. I recommend that the authors recommend a one-hour average CO limit that is no more than quadruple their 8-hour limit, and a STEL limit that is no more than double their 1-hour limit.

Comment 2.3 On page 43 in Table 12 starting on line 1 and in the literature list starting on page 54, I welcome the inclusion of 6 air pollution epidemiology studies that all found statistically significantly increased rates of hospitalization or death for mostly cardiac-related disorders correlated with small increases in ambient CO of just 1 or less above low background levels, below 3ppm. But I disagree with the authors' decision to limit their review to these studies. There are more than 720 other air pollution epidemiology studies published between 2012 and March 2023 that indicate workers would be at much greater risk for adverse outcomes if they were exposed to CO up to 7.5 mg/m3 average over 8 hours compared to if their average CO exposure was kept below 1 ppm. Rather than listing all 720 studies here with their abstracts, I am providing links to a 4-part PubMed collection where they can be viewed, sorted, merged, and saved: part 1, part 2, part 3, and part 4.

I recommend that the authors acknowledge that all the epidemiology studies of CO ambient exposures published from 2012 through March 2023 that found statistically significant risks of adverse outcomes associated with increases in CO exposure found these risks in environments where CO never exceeded 5 ppm and the 8-hour and 24-hour means remained below 2 ppm.

Comment 2.4 On page 12 starting at line 15: The authors incorrectly describe pulse oximeters that can measure CO, which they should describe as "pulse CO oximeters that use a fingertip clip or skin patch to give an estimate of arterial COHb." I recommend the authors also mention these pulse CO oximeters display a trademark measure that Masimo, the US-based developer, calls SpCo™ -- which is closer to arterial COHb than venous (just as SpO2 measured with traditional pulse oximeters is closer to arterial O2Hb). Whether or not SpCO overestimates arterial COHb is not clear since most published studies compared it only to venous COHb, under the mistaken belief that they would not be significantly different.

Comment 2.5 On page 52 starting at line 1: in the discussion of Groups at Extra Risk, I recommend the authors also list occupations that require working in confined microenvironments with limited ventilation in which lower acceptable levels of chemical exposure levels and/or shorter exposure times are recommended or required to protect against higher risks of poisoning and death, such as in mines, tunnels, storage tanks and silos, vehicles, enclosed garages, submarines, tanks, aircraft, and below deck on ships.

Comment 2.6 On page 18 at line 12: Authors correctly note that "Carbon monoxide is not classified for carcinogenic properties." But this concise wording is not the whole truth and conceals more than it discloses. I assume the authors verified this claim by looking up carbon monoxide in at least one database of carcinogens that have been classified by organizations such as the IARC and not finding it. But the fact that CO has not yet been evaluated by any cancer organizations does not mean CO has no carcinogenic properties. It also does not excuse the authors from considering the peer-reviewed literature on this vital topic, at least that published from 2012 until April 2023, to be consistent with the method they used to review all the other potential adverse health effects of occupational CO exposures.

Searching PubMed within these dates for literature on ("carbon monoxide" and ("cancer" or "cancerous" or "metastatic")) finds 1173 studies, which when limited to reviews, finds 16 that focus either solely on adverse effects (CO promotes the growth of many cancers) or also discuss beneficial effects (CO can slow the growth and metastasis of many cancers depending on the timing and level of exposure). Full references for the reviews are provided below, including abstracts and doi were available from PubMed.

I recommend the authors acknowledge this growing literature on the role of CO exposure in promoting some cancers and include some of these reviews in the literature list starting on page 54.

This collection also can be viewed, sorted, and saved on PubMed via this link:
https://pubmed.ncbi.nlm.nih.gov/?term=32108290,30583467,22145952,34945812,28257621,26392237,26416069,33868304,33440611,34841438,25956277,24413553,32455831,29599978,24927633,25642189&format=abstract

If you want to skip ahead to the next comment, search for 3.1

PubMed references on adverse role played by carbon monoxide in cancer

Items 1-16 of 16 (Display the 16 citations in PubMed)

1. **Heme Oxygenase-1 and Carbon Monoxide Regulate Growth and Progression in Glioblastoma Cells**

Mol Neurobiol. 2020 May;57(5):2436-2446. doi: 10.1007/s12035-020-01869-7. Epub 2020 Feb 27.

Authors

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- PMID: 32108290
- DOI: 10.1007/s12035-020-01869-7

Abstract

In human glioma tumours, heme oxygenase-1 (HO-1) is overexpressed when compared with normal brain tissues and during oligodendroglioma progression. However, the molecular mechanisms mediated by HO-1 to promote glioblastoma remain unknown. We therefore aimed at investigating the effect of HO-1 expression and its selective enzymatic inhibition in two different cell lines (i.e. A172 and U87-MG). HO-1 was induced by hemin treatment (10 μM), and VP13/47 (100 μM) was used as a specific non-competitive inhibitor of HO-1 activity. Cell proliferation was measured by cell index measurement (xCelligence technology) and clonogenic assay, whereas cell migration was assessed by wound healing assay. Carbon monoxide-releasing molecules (CORMs) (i.e. CORM-3 and CORM-A1) were also used in a separate set of experiments to confirm the effect of HO-1 by-product in glioblastoma progression further. Our results were further validated using GSE4412 microarray dataset analysis and comparing biopsies overexpressing HO-1 with the rest of the cases. Our results showed that hemin was able to induce both HO-1 gene and protein expression in a cell-dependent manner being A172 more responsive to pharmacological upregulation of HO-1. Hemin, but not CORMs treatment, resulted in a significant increase of cell proliferation following 24 h of treatment as measured by increased cell index and colony formation capacity and such effect was abolished by VP13/47. Interestingly, both hemin and CORMs showed a significant effect on the wound healing assay also exhibiting cell specificity. Finally, our dataset analysis showed a positive correlation of HO-1 gene expression with ITGBI and ITGBII which are membrane receptors involved in cell adhesion, embryogenesis, tissue repair, immune response and metastatic diffusion of tumour cells. In conclusion, our data suggest that HO-1 and its by-product CO exhibit a cell-specific effect on various aspects of disease progression and are associated with a complex series of molecular mechanisms driving cell proliferation, survival and metastasis.

Keywords: Biliverdin; Cancer; Carbon monoxide; Glioblastoma; Heme oxygenase; Nrf2; PUM2.

- Cited by 15 articles
- 56 references

Full text links

2. **A Dual Role of Heme Oxygenase-1 in Cancer Cells**

Int J Mol Sci. 2018 Dec 21;20(1):39. doi: 10.3390/ijms20010039.

Authors

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- PMCID: PMC6337503
- DOI: 10.3390/ijms20010039

Abstract

Heme oxygenase (HO)-1 is known to metabolize heme into biliverdin/bilirubin, carbon monoxide, and ferrous iron, and it has been suggested to demonstrate cytoprotective effects against various stress-related conditions. HO-1 is commonly regarded as a survival molecule, exerting an important role in cancer progression and its inhibition is considered beneficial in a number of cancers. However, increasing studies have shown a dark side of HO-1, in which HO-1 acts as a critical mediator in ferroptosis induction and plays a causative factor for the progression of several diseases. Ferroptosis is a newly identified iron- and lipid peroxidation-dependent cell death. The critical role of HO-1 in heme metabolism makes it an important candidate to mediate protective or detrimental effects via ferroptosis induction. This review summarizes the current understanding on the regulatory mechanisms of HO-1 in ferroptosis. The amount of cellular iron and reactive oxygen species (ROS) is the determinative momentum for the role of HO-1, in which excessive cellular iron and ROS tend to enforce HO-1 from a protective role to a perpetrator. Despite the dark side that is related to cell death, there is a prospective application of HO-1 to mediate ferroptosis for cancer therapy as a chemotherapeutic strategy against tumors.

Keywords: chemotherapy; ferroptosis; glutathione; heme oxygenase-1; iron; reactive oxygen species.

Conflict of interest statement

The authors declare no conflict of interest.

- Cited by 186 articles
- 117 references
- 3 figures

Full text links

3. **Carbon monoxide, generated by heme oxygenase-1, mediates the enhanced permeability and retention effect in solid tumors**

Cancer Sci. 2012 Mar;103(3):535-41. doi: 10.1111/j.1349-7006.2011.02178.x. Epub 2012 Jan 16.

Authors

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- PMID: 22145952
- PMCID: PMC7713620
- DOI: 10.1111/j.1349-7006.2011.02178.x

Abstract

The enhanced permeability and retention (EPR) effect is a unique pathophysiological phenomenon of solid tumors that sees biocompatible macromolecules (>40 kDa) accumulate selectively in the tumor. Various factors have been implicated in this effect. Herein, we report that heme oxygenase-1 (HO-1; also known as heat shock protein 32) significantly increases vascular permeability and thus macromolecular drug accumulation in tumors. Intradermal injection of recombinant HO-1 in mice, followed by i.v. administration of a macromolecular Evans blue-albumin complex, resulted in dose-dependent extravasation of Evans blue-albumin at the HO-1 injection site. Almost no extravasation was detected when inactivated HO-1 or a carbon monoxide (CO) scavenger was injected instead. Because HO-1 generates CO, these data imply that CO plays a key role in vascular leakage. This is supported by results obtained after intratumoral administration of a CO-releasing agent (tricarbonyldichlororuthenium(II) dimer) in the same experimental setting, specifically dose-dependent increases in vascular permeability plus augmented tumor blood flow. In addition, induction of HO-1 in tumors by the water-soluble macromolecular HO-1 inducer pegylated hemin significantly increased tumor blood flow and Evans blue-albumin accumulation in tumors. These findings suggest that HO-1 and/or CO are important mediators of the EPR effect. Thus, anticancer chemotherapy using macromolecular drugs may be improved by combination with an HO-1 inducer, such as pegylated hemin, via an enhanced EPR effect.

- Cited by 29 articles
- 49 references
- 6 figures

Full text links

4. **Expression Dynamics of Heme Oxygenase-1 in Tumor Cells and the Host Contributes to the Progression of Tumors**

J Pers Med. 2021 Dec 9;11(12):1340. doi: 10.3390/jpm11121340.

Authors

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- PMID: 34945812
- PMCID: PMC8704574
- DOI: 10.3390/jpm11121340

Abstract

Heme oxygenase (HO-1) plays an important role in cellular protection against various stresses. The induction of HO-1 is an effective strategy for reactive oxygen species-related diseases, inflammatory diseases, as well as suppressing carcinogenesis. On the other hand, the high expression of HO-1 is now well known in many tumors. In this study, we investigated the dynamics of HO-1 expression in the host and the tumor. In the mouse sarcoma S180 solid tumor model and the rat hepatoma AH136B ascitic tumor model, HO-1 expression in the tumor, as indicated by the end product of HO-1 activation, i.e., carbon monoxide, gradually increased along with tumor growth. Over-expression of HO-1 expression in mouse colon cancer C26 tumor cells significantly promoted tumor growth as well as lung metastasis, whereas opposite results were found when the HO-1 expression was reduced in the cells. On the other hand, upregulating HO-1 levels in the host by using an HO-1 inducer protected the progression of the xenograft tumor in mice, whereas lowering HO-1 expression in the host with an HO-1 inhibitor showed accelerated tumor growth and lung metastasis after subcutaneous tumor xenograft inoculation. These findings strongly suggest that the balance of HO-1 levels in the host and the tumor cells is essential for the occurrence, progression, and prognosis of cancer. Maintenance of appropriately high HO-1 levels in the host is favorable for cancer prevention, whereas suppression of HO-1 in the tumor cells may thus become a therapeutic strategy for cancer.

Keywords: carbon monoxide; carcinogenesis; heme oxygenase-1; tumor progression.

Conflict of interest statement

The authors declare no conflict of interest.

- Cited by 1 article
- 48 references
- 6 figures

Full text links

5. **The Heme Oxygenase System in Hematological Malignancies**

Antioxid Redox Signal. 2017 Aug 20;27(6):363-377. doi: 10.1089/ars.2016.6735. Epub 2017 May 19.

Authors

Giovanni Li Volti [1 2], Daniele Tibullo [3], Luca Vanella [4], Cesarina Giallongo [3], Francesco Di Raimondo [3], Stefano Forte [1 5], Michelino Di Rosa [1], Salvatore Santo Signorelli [6], Ignazio Barbagallo [4]

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- [5] 5 Istituto Oncologico del Mediterraneo Ricerca srl Viagrande, Catania, Italy.
- [6] 6 Department of Clinical and Experimental Medicine, University of Catania, Catania, Italy.
- PMID: 28257621
- DOI: 10.1089/ars.2016.6735

Abstract

Significance: Several lines of evidence suggest that hematological malignancies exhibit an altered redox balance homeostasis that can lead to the activation of various survival pathways that, in turn, lead to the progression of disease and chemoresistance. Among these pathways, the heme oxygenase-1 (HO-1) pathway is likely to play a major role. HO catalyzes the enzymatic degradation of heme with the simultaneous release of carbon monoxide (CO), ferrous iron (Fe^{2+}), and biliverdin. This review focuses on the role of HO-1 in various hematological malignancies and the possibility of exploiting such targets to improve the outcome of well-established chemotherapeutic regimens. Recent Advances and Critical Issues: Interestingly, the inhibition of the expression of HO-1 (e.g., with siRNA) or HO activity (with competitive inhibitors) contributes to the increased efficacy of chemotherapy and improves the outcome in animal models. Furthermore, some hematological malignancies (e.g., chronic myeloid leukemia and multiple myeloma) have served to explore the non-canonical functions of HO-1, such as the association between nuclear compartmentalization and genetic instability and/or chemoresistance.
Future directions: The HO system may serve as an important tool in the field of hematological malignancies because it can be exploited to counteract chemoresistance and to monitor the outcome of bone marrow transplants and may be an additional target for combined therapies. Antioxid. Redox Signal. 27, 363-377.
Keywords: cancer; hematology; heme oxygenase; leukemia; multiple myeloma.

- Cited by 26 articles

Full text links

6. **HO-1/CO system in tumor growth, angiogenesis and metabolism - Targeting HO-1 as an anti-tumor therapy**
Vascul Pharmacol. 2015 Nov:74:11-22. doi: 10.1016/j.vph.2015.09.004. Epub 2015 Sep 25.
Authors
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- [2] Department of Medical Biotechnology, Faculty of Biochemistry, Biophysics and Biotechnology, Jagiellonian University, Gronostajowa 7, 30-387 Krakow, Poland.
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- PMID: 26392237
- DOI: 10.1016/j.vph.2015.09.004

Abstract
Heme oxygenase-1 (HO-1, hmox-1) catalyzes the rate-limiting step in the heme degradation processes. Out of three by-products of HO-1 activity, biliverdin, iron ions and carbon monoxide (CO), the latter was mostly shown to mediate many beneficial HO-1 effects, including protection against oxidative injury, regulation of apoptosis, modulation of inflammation as well as contribution to angiogenesis. Mounting evidence suggests that HO-1/CO system may be of special benefit in protection in many pathological conditions, like atherosclerosis or myocardial infarction. By contrast, the augmented expression of HO-1 in tumor tissues may have detrimental effect as HO-1 accelerates the formation of tumor neo vasculature and provides the selective advantage for tumor cells to overcome the increased oxidative stress during tumorigenesis and during treatment. The inhibition of HO-1 has been proposed as an anti-cancer therapy, however, because of non-specific effects of known HO-1 inhibitors, the discovery of ideal drug lowering HO-1 expression/activity is still an open question. Importantly, in several types of cancer HO-1/CO system exerts opposite activities, making the possible treatment more complicated. All together indicates the complex role for HO-1/CO in various in vitro and in vivo conditions.
Keywords: Angiogenesis; Carbon monoxide; HO-1 inhibitors; MicroRNAs; Tumorigenesis.

- Cited by 82 articles

Full text links

7. **Association of heme oxygenase-1 polymorphisms with cancer risk: A systematic review and meta-analysis**
J BUON. 2015 Jul-Aug;20(4):1142-53.
Authors

Haiqing Luo [1], Yiming Shao, Na Yao, Xiaoyi Chen, Liren Hu, Taiping He

Affiliation

- [1] Oncology Center, the Affiliated Hospital of Guangdong Medical University, Zhanjiang, 524001, China.
- PMID: 26416069

Abstract

Purpose: Observational studies have recently focused on the association between heme oxygenase-1 (HMOX1) gene promoter polymorphisms and cancer risk. However, conflicting results have been obtained. To derive a precise estimate of the association, a systematic review and meta-analysis were conducted.

Methods: This study followed the guidelines for Preferred Reporting Items for Systematic Reviews and Meta-Analyses. PubMed, Medline, Embase and Web of Knowledge were systematically searched for relevant studies. Summary odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for the allelic and genotypic comparisons according to the homozygous, heterozygous, dominant, and recessive genetic models. Between-study heterogeneity was quantified through I2 statistics, and publication bias was appraised by using funnel plots. Sensitivity analyses were conducted to evaluate the robustness of the meta-analysis findings.

Results: Meta-analysis of 9 studies involving 2491 cases and 3380 controls did not reveal any significant association of the HMOX-1 (GT)n and 413A>T polymorphisms with cancer risk. Stratified analysis by ethnicity showed a statistically significant association between (GT)n repeat length variant and susceptibility to cancer for the heterozygous genetic model among Asian populations (OR=1.42, 95% CI: 1.04-1.95, Pheterogeneity=0.218), which is a robust finding according to sensitivity analysis. Funnel plot inspection did not reveal any publication bias.

Conclusion: In conclusion, this study comprehensively examined the available literature on the association of HMOX-1 (GT)n and 413A>T polymorphisms with cancer risk. Meta-analysis results suggest (GT)n repeat length polymorphism as a potential susceptibility variant for cancer in Asians. Additional large-scale and well-designed studies are needed to confirm these results.

- Cited by 6 articles

8. **The Diverse Roles of Heme Oxygenase-1 in Tumor Progression**

Front Immunol. 2021 Mar 31:12:658315. doi: 10.3389/fimmu.2021.658315. eCollection 2021.

Authors

Kim Ngan Luu Hoang [1], Joanne E Anstee [1], James N Arnold [1]

Affiliation

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- PMID: 33868304
- PMCID: PMC8044534
- DOI: 10.3389/fimmu.2021.658315

Abstract

Heme oxygenase-1 (HO-1) is an inducible intracellular enzyme that is expressed in response to a variety of stimuli to degrade heme, which generates the biologically active catabolites carbon monoxide (CO), biliverdin and ferrous iron (Fe^{2+}). HO-1 is expressed across a range of cancers and has been demonstrated to promote tumor progression through a variety of mechanisms. HO-1 can be expressed in a variety of cells within the tumor microenvironment (TME), including both the malignant tumor cells as well as stromal cell populations such as macrophages, dendritic cells and regulatory T-cells. Intrinsically to the cell, HO-1 activity provides antioxidant, anti-apoptotic and cytoprotective effects via its catabolites as well as clearing toxic intracellular heme. However, the catabolites of heme degradation can also diffuse outside of the cell to extrinsically modulate the wider TME, influencing cellular functionality and biological processes which promote tumor progression, such as facilitating angiogenesis and metastasis, as well as promoting anti-inflammation and immune suppression. Pharmacological inhibition of HO-1 has been demonstrated to be a promising therapeutic approach to promote anti-tumor immune responses and inhibit metastasis. However, these biological functions might be context, TME and cell type-dependent as there is also conflicting reports for HO-1 activity facilitating anti-tumoral processes. This review will consider our current understanding of the role of HO-1 in cancer progression and as a therapeutic target in cancer.

Keywords: angiogenesis; cancer; cytoprotection; heme oxygenase-1 (HO-1); metastasis; tumor associated macrophages (TAMs); tumor immunology.

Conflict of interest statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

- Cited by 47 articles

- 171 references
- 4 figures

Full text links

9. **Nuclear Localization of Heme Oxygenase-1 in Pathophysiological Conditions: Does It Explain the Dual Role in Cancer?**

Antioxidants (Basel). 2021 Jan 11;10(1):87. doi: 10.3390/antiox10010087.

Authors

Marilina Mascaró [1], Eliana N Alonso [1], Exequiel G Alonso [1], Ezequiel Lacunza [2], Alejandro C Curino [1], María Marta Facchinetti [1]

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- [2] Centro de Investigaciones Inmunológicas Básicas y Aplicadas (CINIBA), Facultad de Ciencias Médicas, Universidad Nacional de La Plata, La Plata CP1900, Argentina.

- PMID: 33440611
- PMCID: PMC7826503
- DOI: 10.3390/antiox10010087

Abstract

Heme Oxygenase-1 (HO-1) is a type II detoxifying enzyme that catalyzes the rate-limiting step in heme degradation leading to the formation of equimolar quantities of carbon monoxide (CO), free iron and biliverdin. HO-1 was originally shown to localize at the smooth endoplasmic reticulum membrane (sER), although increasing evidence demonstrates that the protein translocates to other subcellular compartments including the nucleus. The nuclear translocation occurs after proteolytic cleavage by proteases including signal peptide peptidase and some cysteine proteases. In addition, nuclear translocation has been demonstrated to be involved in several cellular processes leading to cancer progression, including induction of resistance to therapy and enhanced metastatic activity. In this review, we focus on nuclear HO-1 implication in pathophysiological conditions with special emphasis on malignant processes. We provide a brief background on the current understanding of the mechanisms underlying how HO-1 leaves the sER membrane and migrates to the nucleus, the circumstances under which it does so and, maybe the most important and unknown aspect, what the function of HO-1 in the nucleus is.

Keywords: cancer; heme oxygenase-1; nuclear localization; nuclear protein; nucleus; oxidative stress.

Conflict of interest statement

The authors declare no conflict of interest.

- Cited by 17 articles
- 92 references
- 3 figures

Full text links

10. **Association between HO-1 gene promoter polymorphisms and diseases (Review)**

Mol Med Rep. 2022 Jan;25(1):29. doi: 10.3892/mmr.2021.12545. Epub 2021 Nov 29.

Authors

Lin-Lin Ma[#1], Lei Sun[#1], Yu-Xi Wang [1], Bai-He Sun [1], Yan-Fei Li [1], Yue-Ling Jin [2]

Affiliations

- [1] School of Medical Technology, Shanghai University of Medicine & Health Sciences, Shanghai 201318, P.R. China.
- [2] Management Department of Scientific Research, Shanghai Science and Technology Museum, Shanghai 200127, P.R. China.

[#] Contributed equally.

- PMID: 34841438
- PMCID: PMC8669660
- DOI: 10.3892/mmr.2021.12545

Abstract

Heme oxygenase-1 (HO-1) is an inducible cytoprotective enzyme that degrades heme into free iron, carbon monoxide and biliverdin, which is then rapidly converted into bilirubin. These degradation products serve an important role in the regulation of inflammation, oxidative stress and apoptosis. While the expression level of HO-1 is typically low in most cells, it may be highly expressed when induced by a variety of stimulating factors, a process that contributes to the regulation of cell homeostasis. In the 5'-non-coding region of the HO-1 gene, there are two polymorphic sites, namely the (GT)n dinucleotide and T(-413)A single nucleotide polymorphism sites, which regulate the transcriptional activity of HO-1. These polymorphisms have been shown to be closely associated with the occurrence and progression of numerous diseases, including cardiovascular, pulmonary, liver and kidney, various types of cancer and viral diseases. The present article reviews the progress that has been made in research on the association between the two types of polymorphisms and these diseases, which is expected to provide novel strategies for the diagnosis, treatment and prognosis of various diseases.

Keywords: (GT)n dinucleotide polymorphism; HO-1; T(-413)A single nucleotide polymorphism; diseases; promoter polymorphism.

Conflict of interest statement

The authors declare that they have no competing interests.

- Cited by 11 articles
- 109 references
- 1 figure

Full text links

11. **Association between GT-repeat polymorphism at heme oxygenase-1 gene promoter and gastric cancer and metastasis**

Tumour Biol. 2015 Jun;36(6):4757-62. doi: 10.1007/s13277-015-3125-8. Epub 2015 May 10.

Authors

M Motovali-Bashi [1], M Hamidy

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- PMID: 25956277
- DOI: 10.1007/s13277-015-3125-8

Abstract

HO-1 gene encodes heme oxygenase-1 enzyme that catalyzes the oxidation of heme to carbon monoxide (CO). It has also been suggested that cells could be protected by the enzyme against stress. A (GT) n dinucleotide repeat at HO-1 promoter is a polymorphic region and modulates gene transcription and associated with some of diseases. In this study, length of polymorphism GT tandem repeat has been determined and classified into two alleles short (≤28) and long (≥29). In present study, association between GT-repeat polymorphism at heme oxygenase-1 gene promoter and increased risk of gastric cancer and metastasis was investigated. Blood samples from 100 control individuals and 60 gastric cancer cases had taken. Genotypic frequencies of (GT) n repeat for samples were determined using PCR technique and polyacrylamide PAGE electrophoresis. At final, higher frequency alleles were sequenced. Our results show that S-allele is significantly higher in cases in comparison with control groups (p = 0/000, odds ratio (OR) = 4/154). It has been shown that individuals with S/S and S/L genotypes are at high risk of having gastric cancer (p = 0/000, OR = 3/789). Statistic data show association between SS genotype and risk of gastric cancer metastasis (p = 0.017, OR = 3.889). But, there is no significant association between clinicopathological characteristics of the patients and risk of gastric cancer metastasis (p > 0.05). Significant association was found between short allele (SS + SL genotypes) and risk of gastric cancer, and also strong association was found between SS genotype and risk of gastric cancer metastasis.

- Cited by 3 articles
- 35 references

Full text links

12. **Brain tumors enhance plasmatic coagulation: the role of hemeoxygenase-1**

Anesth Analg. 2014 May;118(5):919-24. doi: 10.1213/ANE.0000000000000048.

Authors

Vance G Nielsen [1], G Michael Lemole Jr, Ryan W Matika, Martin E Weinand, Sana Hussaini, Ali A Baaj, Evangelina B Steinbrenner

Affiliation

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- PMID: 24413553
- DOI: 10.1213/ANE.0000000000000048

Abstract

Background: Patients with brain tumors suffer significant thrombotic morbidity and mortality. In addition to increased thrombin generation via tumor release of tissue factor-bearing microparticles and hyperfibrinogenemia, brain tumors and surrounding normal brain likely generate endogenous carbon monoxide (CO) via the hemeoxygenase-1 (HO-1) system. CO has been shown to enhance plasmatic coagulation via formation of carboxyhemefibrinogen (COHF). Thus, our goals in this study were to determine whether patients with brain tumors had increased HO-1 upregulation/CO production, plasmatic hypercoagulability, and formation of COHF.

Methods: Patients with brain tumors (N = 20) undergoing craniotomy had blood collected for determination of carboxyhemoglobin as a marker of HO-1 activity, plasmatic hypercoagulability (defined as clot strength > 95% confidence interval value of normal subject plasma), and COHF formation (determined with a thrombelastograph-based assay). Plasma obtained from commercially available normal subjects (N = 30) was used for comparison with brain tumor patient samples.

Results: Brain tumor patients had carboxyhemoglobin concentrations of 1.5% ± 0.5% (mean ± SD), indicative of HO-1 upregulation. Compared with normal subject plasma, brain tumor patient plasma had significantly ($P < 0.0001$) greater clot formation velocity (5.2 ± 1.5 vs 9.5 ± 2.3 dynes/cm/s, respectively) and significantly ($P = 0.00016$) stronger final clot strength (166 ± 28 vs 230 ± 78 dynes/cm, respectively). Ten of the brain tumor patients had plasma clot strength that exceeded the 95% confidence interval value observed in normal subjects, and 12 of the brain tumor patients had COHF formation. Five of the brain tumor patients in the hypercoagulable subgroup had COHF formation. Last, 5 of the hypercoagulable patients had primary brain tumors, whereas the other 5 patients had metastatic tumors or an inflammatory mass lesion.

Conclusions: A subset of patients with brain tumors has increased endogenous CO production, plasmatic hypercoagulability, and COHF formation. Future investigation of the role played by HO-1 derived CO in the pathogenesis of brain tumor-associated thrombophilia is warranted.

- Cited by 2 articles

Full text links

13. **Heme Oxygenase-1 in Central Nervous System Malignancies**

J Clin Med. 2020 May 21;9(5):1562. doi: 10.3390/jcm9051562.

Authors

Giuseppe Sferrazzo [1], Michelino Di Rosa [2], Eugenio Barone [3], Giovanni Li Volti [2 4], Nicolò Musso [1], Daniele Tibullo [2], Ignazio Barbagallo [1]

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- [4] EuroMediterranean Institute of Science and Technology, Via Michele Miraglia 20, 90139 Palermo, Italy.
- PMID: 32455831
- PMCID: PMC7290325
- DOI: 10.3390/jcm9051562

Abstract

Central nervous system tumors are the most common pediatric solid tumors and account for 20%-25% of all childhood malignancies. Several lines of evidence suggest that brain tumors show altered redox homeostasis that triggers the activation of various survival pathways, leading to disease progression and chemoresistance. Among these pathways, heme oxygenase-1 (HO-1) plays an important role. HO-1 catalyzes the enzymatic degradation of heme with the simultaneous release of carbon monoxide (CO), ferrous iron (Fe^{2+}), and biliverdin. The biological effects of HO-1 in tumor

cells have been shown to be cell-specific since, in some tumors, its upregulation promotes cell cycle arrest and cellular death, whereas, in other neoplasms, it is associated with tumor survival and progression. This review focuses on the role of HO-1 in central nervous system malignancies and the possibility of exploiting such a target to improve the outcome of well-established therapeutic regimens. Finally, several studies show that HO-1 overexpression is involved in the development and resistance of brain tumors to chemotherapy and radiotherapy, suggesting the use of HO-1 as an innovative therapeutic target to overcome drug resistance. The following keywords were used to search the literature related to this topic: nuclear factor erythroid 2 p45-related factor 2, heme oxygenase, neuroblastoma, medulloblastoma, meningioma, astrocytoma, oligodendroglioma, glioblastoma multiforme, and gliomas.

Keywords: NRF2; ROS; brain cancer; nuclear factor erythroid 2 p45-related factor 2; oxidative stress.

Conflict of interest statement

The authors declare no conflict of interest.

- Cited by 19 articles
- 138 references
- 3 figures

Full text links

14. **Association between heme oxygenase-1 gene promoter polymorphisms and cancer susceptibility: A meta-analysis**

Biomed Rep. 2018 Mar;8(3):241-248. doi: 10.3892/br.2018.1048. Epub 2018 Jan 25.

Authors

Rui Wang [1], Jun Shen [2], Rui Yang [3], Wan-Guo Wang [3], Ye Yuan [3], Zhong-Hua Guo [3]

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- [2] Department of Cardiology, Renmin Hospital, Hubei University of Medicine Shiyan, Hubei 442000, P.R. China.
- [3] Department of Orthopedics, People's Hospital of Dongxihu District, Wuhan, Hubei 430040, P.R. China.

- PMID: 29599978
- PMCID: PMC5867395
- DOI: 10.3892/br.2018.1048

Abstract

Numerous studies have focused on the association between heme oxygenase-1 (HO-1) gene promoter polymorphisms and susceptibility to cancer; however, results remain ambiguous. The present systematic Human Genome Epidemiology review and meta-analysis aimed to clarify this association. A systematic search was used to assess the association of HO-1 gene polymorphisms with cancer susceptibility in the PubMed, Web of Science, Cochrane Library, Wanfang Data and China National Knowledge Infrastructure databases, with all reviewed studies published before April 10, 2017. Review Manager 5.3 and Stata 12.0 software were used to perform the meta-analysis. A total of 14 studies were included in the analysis. Overall, no significant associations of the HO-1 (GT)n and T(-413)A polymorphisms with cancer susceptibility were identified. However, subgroup analyses by ethnicity and cancer type indicated that the LL and L-allele (LL+LS) genotypes of HO-1 (GT)n were associated with increased susceptibility to cancer compared with the SS+SL and SS genotypes in the following subgroups: East Asian [LL+LS vs. SS: odds ratio (OR)=1.51, 95% confidence interval (CI)=1.11-2.05, P=0.0003; LL vs. SS+SL: OR=1.44, 95% CI=1.04-2.01, P=0.03; LL vs. SS: OR=1.64, 95% CI=1.07-2.52, P=0.02]; squamous cell carcinoma (LL+LS vs. SS: OR=1.78, 95% CI=1.35-2.34, P<0.05; LL vs. SS+SL: OR=1.71, 95% CI=1.34-2.18, P<0.05; LL vs. SS: OR=2.26, 95% CI =1.62-3.14, P<0.05); and digestive tract cancer + East Asian (LL+LS vs. SS: OR=1.56, 95% CI=1.22-1.98, P<0.05; LL vs. SS: OR=1.80, 95% CI=1.06-3.05, P<0.05). These findings indicated that there was no association of the HO-1 (GT)n and T(-413)A polymorphisms with cancer susceptibility, while the L-allele genotypes (LL and LS) of HO-1 (GT)n may be susceptibility factors for cancer in East Asian, digestive tract cancer in East Asian and squamous cell carcinoma populations. Due to limitations of the reviewed studies, additional large-scale and refined studies are now required to confirm the present findings.

Keywords: cancer; genetics; heme oxygenase-1; meta-analysis; polymorphism.

- Cited by 2 articles
- 43 references
- 1 figure

Full text links

15. **Upregulation of heme oxygenase-1 in colorectal cancer patients with increased circulation carbon monoxide levels, potentially affects chemotherapeutic sensitivity**
BMC Cancer. 2014 Jun 14:14:436. doi: 10.1186/1471-2407-14-436.
Authors
Hongzhuan Yin, Jun Fang, Long Liao, Hiroshi Maeda, Qi Su [1]
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- PMID: 24927633
- PMCID: PMC4075569
- DOI: 10.1186/1471-2407-14-436

Abstract
Background: Heme oxygenase-1 (HO-1) and its major product carbon monoxide (CO) are known to be involved in the development and progression of many tumors. The present study was to elucidate the expression and function of HO-1 in colorectal cancer (CRC), specially focusing on the circulation CO levels in CRC patients and the possible roles of HO-1 in chemoresistance of colon cancer cells.
Methods: One hundred and eighteen patients received resection for colorectal cancer and polyps at China Medical University Sheng Jing Hospital, were collected in this study. HO-1 expression in CRC tissues was analyzed by immnuohistochemical staining; circulation CO levels as carboxyhemoglobin (COHb) in CRC patients were analyzed by an ABL800 FLEX blood gas analyzer. HO-1 expression in murine colon cells C26 and human colon cancer cells HT29 and DLD1 under HO-1 inducer hemin and anticancer drug pirarubicin (THP) treatment was examined by RT-PCR, and the cell viability after each treatment was investigated by MTT assay. Data were analyzed by student's t-test or one-way ANOVA followed by Bonferroni t-test or Fisher's exact test.
Results: HO-1 expression in tumor tissues of CRC (61.0%) was significantly higher than in normal colorectal tissues and polyps tissues (29.7%, $P < 0.01$); well-differentiated CRC seemed to express more HO-1 (81.5%) than moderately/poorly-differentiated cancers (59.5%, $P < 0.05$). However, the nuclear HO-1 expression is apparently higher in moderately/poorly differentiated CRC than well-differentiated CRC probably suggesting a new mechanism of function involved in HO-1 in cancer. In parallel with HO-1 expression, circulation CO levels in CRC patients also significantly accelerated. Moreover, HO-1 expression/induction also related to the chemosensitivity of colon cells; HO inhibitor zinc protoporphyrin significantly increased cytotoxicities of THP (i.e., 2.6 - 5.3 folds compared to cells without zinc protoporphyrin treatment).
Conclusions: These findings strongly suggested HO-1/COHb is a useful diagnostic and prognostic indicator for CRC, and inhibition of HO-1 may be a option to enhance the chemotherapeutic effects of conventional anticancer drugs toward CRC.
- Cited by 46 articles
- 52 references
- 6 figures

Full text links

16. **Heme oxygenase-1 in pregnancy and cancer: similarities in cellular invasion, cytoprotection, angiogenesis, and immunomodulation**
Front Pharmacol. 2015 Jan 14:5:295. doi: 10.3389/fphar.2014.00295. eCollection 2014.
Authors
Hui Zhao [1], Maide Ozen [1], Ronald J Wong [1], David K Stevenson [1]
Affiliation
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- PMID: 25642189
- PMCID: PMC4294126
- DOI: 10.3389/fphar.2014.00295

Abstract
Pregnancy can be defined as a "permissible" process, where a semi-allogeneic fetus and placenta are allowed to grow and survive within the mother. Similarly, in tumor growth, antigen-specific malignant cells proliferate and evade into normal tissues of the host. The microenvironments of the placenta and tumors are amazingly comparable, sharing similar mechanisms exploited by fetal or cancer cells with regard to surviving in a hypoxic microenvironment, invading tissues via degradation and vasculogenesis, and escaping host attack through immune privilege. Heme oxygease-1 (HO-1) is a

stress-response protein that has antioxidative, anti-apoptotic, pro-angiogenic, and anti-inflammatory properties. Although a large volume of research has been published in recent years investigating the possible role(s) of HO-1 in pregnancy and in cancer development, the molecular mechanisms that regulate these "yin-yang" processes have still not been fully elucidated. Here, we summarize and compare pregnancy and cancer development, focusing primarily on the function of HO-1 in cellular invasion, cytoprotection, angiogenesis, and immunomodulation. Due to the similarities of both processes, a thorough understanding of the molecular mechanisms of each process may reveal and guide the development of new approaches to prevent not only pregnancy disorders; but also, to study cancer.

Keywords: Placenta; alternatively activated macrophage (M2); angiogenesis; immunosuppression; tolerogenic dendritic cells (tDC); trophoblast invasion.

- Cited by 30 articles
- 90 references
- 2 figures

Part 3: Comments regarding errors and inconsistencies

Comment 3.1 On page 9 starting at line 26: Authors acknowledge they deviated from the standard DECOS guidance for recommending health-based occupational exposure limits: "Given the complex toxicity profile of carbon monoxide (i.e. several potential health effects **that might occur at a similar (low) exposure levels**) and the large amount of available data, the Committee has decided to use assessment reports previously published by other scientific organisations as a starting point, and only address underlying literature when needed. These reports were assessed for the quality of systematic approaches and considered for evidence that could support an 8h time-weighted average (TWA) exposure limit, a 15-min STEL, or a ceiling value." (emphasis added)

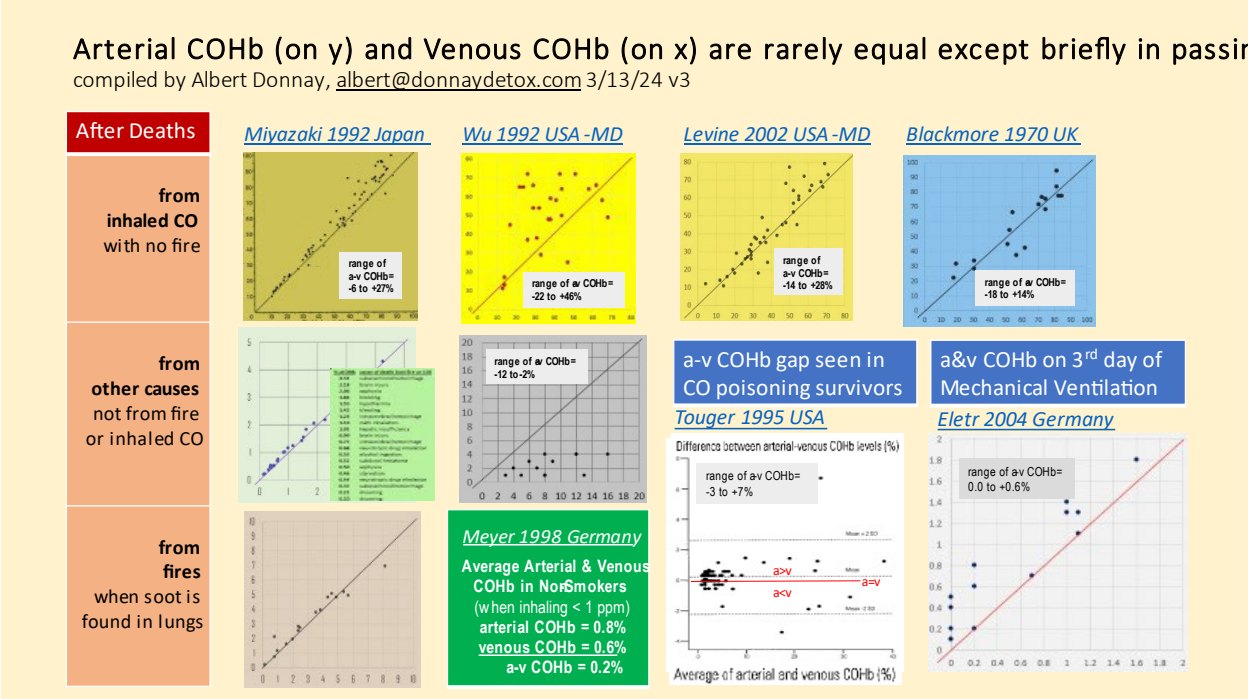
I recommend the bold phrase be changed to **"that may occur at low exposure levels"**

This report would be more informative if the authors placed less emphasis on reviewing the duplicative findings of the CO reports published by other national governments and instead reviewed more of the original studies on occupational CO exposures published from 2012 to 2023, such as the 54 that I recommend above in Comment 1.2.

Comment 3.2 In the literature list starting on page 54, the authors include 5 papers published from 2000 to 2017 (#24, 25, 27, 28, and 30), that discuss the clinical management of acute non-occupational CO poisonings caused by high exposures, which should have been excluded according to the search criteria on page 74. **This is inconsistent.**

I recommend the authors either delete these references and all discussion of them in the text, or change their report's exclusion criteria on page 74 to allow reports of acute non-occupational CO poisoning.

Comment 3.3 The authors do not mention any studies of CO exposure that reported both arterial and venous COHb levels. As shown in the scatterplots below, arterial and venous CO are rarely the same and not consistently correlated. Arterial COHb is usually but not always greater than venous and differences up to 46% have been reported. Full references for these studies are given below the figure along with abstract and doi where available.



These studies cast doubt on how to interpret results of the majority of CO exposure studies, including all the ones cited in the report, that only reported arterial or venous CO without identifying which was greater. For this reason, I recommend that the authors add these references in the literature list starting on page 54.

To skip ahead to next comment, search for 3.5

The determination of carbon monoxide in blood and tissue

1. Analyst. 1970 May;95(130):439-58. doi: 10.1039/an9709500439.

Author

D J Blackmore

- PMID: 5419714
- DOI: 10.1039/an9709500439

No abstract available

- Cited by 12 articles

Full text links

2. **Arteriovenous carboxyhemoglobin difference is not correlated to TNF-alpha, IL-6, PCT, CRP and leukocytes in critically ill patients**

Clin Chim Acta. 2004 Nov;349(1-2):75-80. doi: 10.1016/j.cccn.2004.06.005.

Authors

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- PMID: 15469858
- DOI: 10.1016/j.cccn.2004.06.005

Abstract

Background: It is still unclear as to whether the paradoxical arteriovenous carboxyhemoglobin (COHb) difference found in critical illness may represent a novel marker of the acute inflammatory response. We determined whether the arterial and central venous COHb concentration or their difference may be correlated to classical pro-inflammatory markers.

Methods: Arterial and matched central venous blood gases were obtained from non-smoking intensive care patients undergoing gastrointestinal surgery, and were correlated with plasma concentrations of tumor necrosis factor-alpha (TNF-alpha), interleukin-6 (IL-6), procalcitonin (PCT), C-reactive protein (CRP) and leukocytes.

Results: No correlation was found between arteriovenous COHb difference and the investigated pro-inflammatory mediators. While arterial and central venous COHb concentrations were positively correlated to plasma concentrations of TNF-alpha (P< or =0.01), IL-6 (P<0.05) and PCT (P< or =0.01), they were neither interrelated with PCT nor with leukocytes.

Conclusions: Arteriovenous COHb difference does not appear to be a marker of the acute inflammatory response. Future studies are needed to investigate whether arterial and central venous COHb concentrations by themselves may serve as indicators of systemic inflammation.

Full text links

3. **A comparison of carboxyhemoglobin saturation values in postmortem heart blood and peripheral blood specimens**

J Forensic Sci. 2002 Nov;47(6):1388-90.

Authors

Barry Levine [1], Karla A Moore, Jack M Titus, David Fowler

Affiliation

- [1] Office of the Chief Medical Examiner, State of Maryland, Baltimore, MD 21201, USA.

- PMID: 12455669

Abstract

The following is a study conducted to determine whether there was any significant difference in carboxyhemoglobin (COHb) saturation levels between the heart blood and blood collected from a peripheral site. The average heart blood to peripheral blood COHb saturation level ratio in the 42 cases studied was 1.09. Sixty-two percent (26 of 42) of the cases had a heart blood to peripheral blood ratio between 0.9 and 1.1; 74% (31 of 42) had a ratio between 0.8 and 1.2. Eighty-three percent (35 of 42) had a ratio between 0.7 and 1.3. There were four cases where the heart blood to peripheral blood ratio was either below 0.6 or greater than 1.4. The differences between the two sites were not statistically significant.

Arterio-venous carboxyhemoglobin difference suggests carbon monoxide production by human lungs

4. Biochem Biophys Res Commun. 1998 Mar 6;244(1):230-2. doi: 10.1006/bbrc.1998.8244.

Authors

J Meyer [1], T Prien, H Van Aken, H G Bone, R Waurick, G Theilmeier, M Booke

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- PMID: 9514911
- DOI: 10.1006/bbrc.1998.8244

Abstract

Carbon monoxide is hypothesized to be produced by the enzyme heme oxygenase predominantly in liver and spleen, bound to hemoglobin, and excreted by the lungs. Thus, venous carboxyhemoglobin is expected to be higher or equal to arterial carboxyhemoglobin. Unspecific inflammatory stimuli have been shown to induce heme oxygenase in lung tissue possibly leading to pulmonary carbon monoxide production. Arterial and central venous carboxyhemoglobin levels were measured in critically ill patients on the third day of ICU stay (n = 59) as well as in otherwise healthy humans prior to orthopedic surgery (n = 29). Arterial and central venous carboxyhemoglobin were higher in ICU patients than in healthy humans, respectively. In both groups, arterial carboxyhemoglobin was significantly higher than central venous carboxyhemoglobin. The arteriovenous carboxyhemoglobin differences were similar in both groups. The data suggest (a) increased CO-generation in critical illness and (b) pulmonary CO-production in healthy and critically ill humans.

- Cited by 5 articles

Full text links

Interpretation of COHb concentrations in the left and right heart blood of cadavers

5. Int J Legal Med. 1992;105(2):65-8. doi: 10.1007/BF02340825.

Authors

T Miyazaki [1], T Kojima, M Yashiki, F Chikasue, Y Iwasaki

Affiliation

- [1] Department of Legal Medicine, Hiroshima University School of Medicine, Japan.

- PMID: 1520638
- DOI: 10.1007/BF02340825

Abstract

Carbon monoxide hemoglobin (COHb) concentrations in left and right heart blood samples from cadavers both exposed and not exposed to fire or CO gas were analyzed by the gas chromatographic method. The COHb concentration ratio between samples of left and right heart blood (L/R ratio) does not appear to be useful for establishing whether death has occurred before or after exposure to fire with the exception of cases where no soot can be detected in the airways by the naked eye and the COHb concentration in the blood sample is within the level considered normal for tobacco smokers.

- 11 references

6. **Relationship between venous and arterial carboxyhemoglobin levels in patients with suspected carbon monoxide poisoning**

Ann Emerg Med. 1995 Apr;25(4):481-3. doi: 10.1016/s0196-0644(95)70262-8.

Authors

M Touger [1], E J Gallagher, J Tyrell

Affiliation

- [1] Department of Medicine, Bronx Municipal Hospital, Albert Einstein College of Medicine.

- PMID: 7710152
- DOI: 10.1016/s0196-0644(95)70262-8

Abstract

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 .99 (95%CI, .99 to .99), and an r2 value of .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 .15% COHb (95%CI, .13% to .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.

- Cited by 14 articles

Full text links

Analysis of spleen specimens for carbon monoxide

7.

J Anal Toxicol. 1992 Jan-Feb;16(1):42-4. doi: 10.1093/jat/16.1.42.

Authors

S C Wu [1], B Levine, J C Goodin, Y H Caplan, M L Smith

Affiliation

- [1] Office of the Chief Medical Examiner, State of Maryland.

- PMID: 1640697
- DOI: 10.1093/jat/16.1.42

Abstract

Crucial to the investigation of aircraft fatalities is the analysis of biological specimens for carbon monoxide (CO). In many cases, blood specimens are unavailable or unsuitable for analysis, and the testing of an alternate specimen for CO becomes necessary. Spleen specimens provide a rich source of red blood cells and hence can be a primary substitute for blood. To verify this, 40 paired blood and spleen specimens were analyzed for CO by using a gas chromatographic method. Ten specimens with a spleen CO saturation level (sat.) of less than 10% were associated with corresponding blood specimens with CO sat. less than 10%. Fifteen of the 18 spleen specimens with CO sat. greater than 29% were associated with blood specimens with greater than 48% sat. Results were inconclusive when the spleen CO sat. was between 10 and 29%. We concluded that spleen CO sat. can reflect blood CO sat. in certain situations, particularly when spleen CO sat. is high.

Comment 3.4 In the literature list starting on page 54, the authors include 5 studies (#24, 25, 27, 28, 30) that describe the management of acute poisoning cases caused by high CO exposures, which the methodology section of the report says were excluded. **This is not consistent.**

I recommend the authors either delete these references and all discussion of them in the text, or change the methodology section to acknowledge that reports of acute CO poisoning were considered.

Comment 3.5 On page 3 at line 28: Table of Contents is missing a line for the (cited) Literature section, which starts in text on page 54 at line 1 and runs the end of page 58. This section should be identified as number 10 in both the table of contents on page 3 and in the text on page 54.

Comment 3.6 On page 19 at line 7: **ACHIH** should be **ACGIH,** and Biological Exposure **Indice** should be **Index** (or Indices if plural).

Comment 3.7 On page 5 in Table 3 starting at line 1: The last line line in this table for US OSHA does not show any STEL for CO. **This is an error.** OSHA has long had a regulation requiring the evacuation of workers when CO is over 100ppm. See: https://www.osha.gov/laws-regs/regulations/standardnumber/1917/1917.24#:~:text=The%20carbon%20monoxide%20content%20of,carbon%20monoxide%20concentration%20exceeds%20a

Unfortunately, this only applies to workers in marine terminals, but I still recommend including it because there are many marine terminals in the Netherlands.

Comment 3.8 on page 31 starting at line 5, the same range of expected COHb (1-5%) is given for exposure to 10 ppm (which can at most raise COHb to 2%, given approximately 5ppm per 1% COHb) and exposure to 20 ppm (which can raise COHb to 4%). **This is an error.** I recommend authors correct this by deleting all discussion of this study since it is from a 1958 study that is no longer available and cannot be checked.

Comment 3.9 on page 34 starting at line 10, a report is cited as NRC 2010. But NRC does not appear in the literature list that starts on page 54. **This is an error.** I recommend the authors correct this by adding the full reference below to the literature list

US National Research Council Committee on Acute Exposure Guideline Levels. Acute Exposure Guideline Levels for Selected Airborne Chemicals: Volume 8. Washington (DC): National Academies Press; 2010.

The full text is available from https://www.ncbi.nlm.nih.gov/books/NBK220007/ Note this is a book that does not have an abstract or doi.

Comment 3.10 on page 36 starting at line 7, the authors refer to "existing criteria documents (NEG, WHO, EU, NIOSH, DECOS)." But there are no references for any documents by the EU, NIOSH or DECOS in the literature list that starts on page 54. **This is an error.**

I recommend the authors correct this by adding full references in the literature list. I am unable to provide them here because I do not know what "criteria documents" the authors are writing about.

Comment 3.11 On page 29 starting at line 15: in section 8.1.3, titled "WHO report indoor air quality", the authors review a WHO report published in 2010, for which the reference given in the literature list on page 54 is "**WHO. World Health Organization**. WHO guidelines for indoor air quality: selected pollutants. 2010; ISBN 978 92 890 0213 4." (emphasis added)

This is incorrect. This is actually a report of the **WHO Regional Office for Europe** (as shown on the cover and repeated on the title page at https://iris.who.int/bitstream/handle/10665/260127/9789289002134-eng.pdf?sequence=1). I recommend the authors correct this in the literature list.

More importantly, the 2010 report is outdated by a 2021 report from WHO entitled Global Air Quality Guidelines: particulate matter (PM2.5 and PM10), ozone, nitrogen dioxide, sulfur dioxide and carbon monoxide, which is already in the literature list (#9) and online here https://iris.who.int/bitstream/handle/10665/345329/9789240034228-eng.pdf

The 2021 report is discussed later in section 8.1.7, starting on page 28 at line 2, which (confusingly!) has the exact same title as section 8.1.3 ("WHO report indoor air quality"). **This is inconsistent** since the reports reviewed in 8.1.3 and 8.1.7 do not have the same title, publisher, or scope: the 2010 is focused exclusively on indoor exposures while the 2021 applies explicitly to both indoor and outdoor non-occupational exposures. I recommend the authors merge section 8.1.3 and 8.1.7 into a new section entitled "WHO air quality guidelines." The most recent global guidelines from 2021 should be discussed first in this section (what is now 8.1.7), followed by the now superseded guidelines for Europe from 2021 (what is now 8.1.3), which the authors should note allowed 75% more CO over a 24-hour average (7 mg/m3 instead of the current 4).

In this way, the report can still include the authors' reviews of the 4 occupational studies (starting on page 31 at line 2) that were included in the 2010 guidelines but not the 2021.

The authors also should note that, although the global WHO guidelines from 2021 cite the same 1-hour and 8-hour average CO exposure limits as WHO Regional Office for Europe published in 2010, the 1-hour limit of 35 mg/m3 is 17% higher than 30 mg/m3 the WHO recommended in 2000, in the second edition of its Guidelines for Air Quality (see Table 2 on page 32 at https://iris.who.int/bitstream/handle/10665/107335/9789289013581-eng.pdf). The WHO has never published any explanation of this change, so it is not publicly known whether this was done inadvertently or because of new studies showing people can tolerate a higher level of CO exposure for one hour than previously thought.

If the authors make these changes, they will also need to change the following phrase that appears on page 34 starting at line 18, in reference to the Sari study of indoor barbecue workers. I recommend changing
from:
"which is summarised in section on the WHO indoor air report (2010) (see Section 8.1.3 'WHO report outdoor air quality')."
to:
"which is summarised in a report by the WHO Regional Office for Europe on guidelines for indoor air quality (2010)."

# # #

Mennen, R.H. (Gina)

Van: Dick Lindhout <dl@KNMG.ORG>
Verzonden: woensdag 10 januari 2024 15:11
Aan: Vink, S.R. (Stefan)
Onderwerp: OCR carbon monoxide
Bijlagen: Zhang_et_al-Am_J_Transl_Res-2023-15(11)-6558_6564-carbon_monoxide-delayed_encephalopathy-assessment.pdf; Suzuki_et_al-PLoS_ONE -2021-16(3)-e0249395-carbon_monoxide-delayed-encephalopathy-risk_factors.pdf; Rissanen_et_al-Neurotoxicology-2010-31-2010-403_407-carbon_monoxide-nigrostriatal_dopaminergic_dysfunction-PET.pdf; Dorman-Handbook_Clinical_Neurology-2015-131-chapter_13-extrapyramidal_system_neurotoxicity-animal_models.pdf; Huang_et_al-Neural_Regen_Res-2020-15(12)-2286_2295-carbon_monoxide-delayed_encephalopathy-mechanisms.pdf; Kudo_et_al-Kudo et al. BMC_Emergency_Medicine-2014-14-3-carbon_monoxide-delayed_encephalopathy-predictors.pdf; Hu_et_al-Am_J_Emerg_Med-2011-29-261_264-carbon_monoxide-delayed_encephalopathy-prognostic_factors.pdf

Geachte secretaris, beste Stefan,

Deze GR-draft met belangstelling diagonaal gelezen en wel om de volgende reden:

In de beginperiode van mijn werlk als klinisch geneticus aan de EUR te Rotterdam (1985-2000) werd naar mij verwezen een man met de (waarschijnlijkheidsdiagnose chorea van Huntington.
De familie-anamnese was negatief en de voorgeschiedenis vermeldde een acute koolmonoxide intoxicatie met aanvankellijk volledig herstel.

De ziektegeschiedenis werd doorgenomen met prof. Busch, neuroloog, Dijkzicht Ziekenhuis/EUR, die concludeerde dat patiënt hoogstwaarschijnlijk leed aan een Huntington-like lange-termijn effect van de CO intoxicatie.

Destijds relatief weinig relevante literatuur gevonden, maar nu naar aanleiding van het GR-draft nog eens een poging gewaagd met de zoektermen carbon monoxide, delayed encephalopathy, chorea, extrapyramidal, neurodegeneration in diverse combinaties. Een kleine selectie uit de verkregen hits bijgevoegd.

Alhoewel in de draft het volgende wordt gesteld (Pag 29, Regel 31-32): "High exposure levels that can be lethal and **delayed effects were not examined**
", vergt het vetgedrukte gedeelte mijn inziens een toelichting **waarom** late effecten zijn uitgesloten, **waarom** deze effecten niet relevant voor de vraagstelling zouden zijn, terwijl die ook bij accidentele blo
.
otstellingen klinisch uiterst relevant zijn.

De cie zou kunnen overwegen om er juist wél aandacht aan te geven, dan wel steekhoudende argumenten te vermelden waarom zij daarvan afziet.

Veel succes met de verdere afronding.

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Commentaar op het concept advies Koolmonoxide
Gezondheidsraad; 20 december 2023.

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Inleiding

Gedurende mijn jarenlange werk als consulent industriële veiligheid en hygiëne in meer dan 20 landen, had ik veel ervaringen met de negatieve aspecten van koolmonoxide (CO), ook op vliegvelden en in vliegtuigen. Daarom heb ik daar een praktische en theoretische studie aan gewijd. Mijn commentaar op het concept advies is dus niet gebaseerd op eigen wetenschappelijk medisch onderzoek, maar op talloze praktijkwaarnemingen, het volgen van de medisch-wetenschappelijke literatuur en deelname aan bijeenkomsten en congressen. Ook publiceerde ik artikelen in vakbladen, in kwaliteitskranten en in huis-aan-huisbladen.

In 2016 publiceerde de Onderzoeksraad voor de Veiligheid (OvV) het advies ***"Koolmonoxide. Onderschat en onbegrepen gevaar".*** Het is een goed advies over acute vergiftiging door het inademen van hoge concentraties CO. De OvV waarschuwde dat artsen onvoldoende weten van CO intoxicatie en ook de symptomen vaak niet herkennen. Daarom heb ik in 'Medisch Contact' (28/02/2017) aandacht gevraagd voor de gevaren van een chronische CO intoxicatie, waarvan de symptomen nog veel bedrieglijker zijn dan die van een acute vergiftiging. Zie https://www.medischcontact.nl/actueel/laatste-nieuws/artikel/chronische-koolmonoxidevergiftiging-vaak-gemist

Begin 2017 heb ik Prof. Pim van Gool, voorzitter van de Gezondheidsraad (GR), benaderd en hem aangeraden om de gevolgen van lage concentraties CO te onderzoeken. Dat resulteerde in juli 2019 in het advies ***"Gezondheidsrisico's door lage concentraties koolmonoxide***". Aan dat advies werkte ik niet mee, maar ik had wel enkele keren contact met de medewerker drs. H.F.G. van Dijk.
Ook dit advies bevestigde dat medische opleidingen meer aandacht moeten hebben voor de gevaren van CO.
Na dit advies publiceerde 'Medisch Contact' op 20/02/2020 mijn (omslag)artikel **"Chronische koolmonoxidevergiftiging is onderschat gevaar"**. Zie https://www.medischcontact.nl/actueel/laatste-nieuws/artikel/chronische-co-vergiftiging-is-onderschat-gevaar Het leverde positieve reacties op, o.a. van het Nationaal Vergiftigingen Informatie Centrum, dat mijn mening onderschrijft dat bij onbegrepen gezondheidsklachten ook altijd gedacht moet worden aan koolmonoxide als

mogelijke oorzaak. Dat gebeurt nauwelijks en huisartsen beschikken bovendien niet over een ademtester om een CO intoxicatie snel aan te tonen.

De afgelopen jaren was ik als bedrijfsadviseur veel in het buitenland en dan neem ik altijd twee meetapparaten voor CO mee: een Bedfont 'Micro' en een Lascar CO Datalogger. De Bedfont is geschikt voor het meten van de CO concentratie van 0 tot 500 ppm in omgevingslucht en adem. De Datalogger meet de CO concentratie van 0 tot 300 ppm in de omgevingslucht en legt dat vast in het geheugen dat later kan worden uitgelezen met een computer. Met de Datalogger deed ik o.a. de volgende verontrustende metingen:

1. Vrijwel voortdurend 5-7 ppm CO in de cabinelucht tijdens een retourvlucht naar Indonesië. Ik schrijf dit toe aan het recirculeren en accumuleren van endogeen CO. Omdat de luchtdruk in vliegtuigcabines is verlaagd, is 5-7 ppm CO te hoog tijdens lange vluchten. Ik heb dit gemeld aan het RIVM/NAC.
2. 180 ppm CO in de cabine van een vliegtuig tijdens het 'boarden' aan de gate op Schiphol. Ik schreef dit toe aan de uitlaatgassen van andere vliegtuigen die langs taxieden en/of aan de APU van het toestel zelf.
   De conclusie is dat vliegvelden en vliegtuigcabines een hoog risico opleveren op chronische CO intoxicatie van werkers, bemanningsleden en passagiers.
3. Metingen tot 200 ppm CO op straatniveau tijdens een winterse autorit van Bilthoven naar Doorn over binnenwegen op de Utrechtse Heuvelrug, veroorzaakt door rookgassen van houtkachels en/of cv ketels langs de route.

Helaas is mij de afgelopen jaren gebleken dat het lastig is om met artsen in gesprek te komen over de gevaren van CO en het probleem van de vele 'ziekmakende' woningen. Dit merkte ik o.a. bij deelname aan bijeenkosten van Studium Generale in Utrecht, over problemen en preventie in de zorg.

De onwetendheid t.a.v. de gevaren van CO blijkt ook uit het besluit van Amsterdam en Den Bosch om de maximumsnelheid te verlagen naar 30 km/uur. Dat geeft tragere doorstroming en méér files en opstoppingen, waardoor de luchtvervuiling in de binnenstad toeneemt. Een driewegkatalysator werkt namelijk alleen goed bij een gelijkmatig draaiende motor. En zonder goed werkende katalysator kan de concentratie CO in de uitlaatgassen oplopen tot 25.000 ppm (onderzoek in Zweden). Ook zijn er verkeersdeelnemers zonder katalysator (scooters, brommers, motorfietsen, oldtimers).
De gezondheidssituatie zal dus verslechteren door deze maatregel, met name voor mensen die op straat werken, zoals politie, verkeersregelaars, vuilnisophalers, besteldiensten, bestuurders van bussen, trams en taxi's. De voorlichtingsbrochure van de gemeente Amsterdam over dit besluit gaat alleen over een (mijns inziens onderschatte) toename van NOx en fijnstof, terwijl het veel gevaarlijker CO wordt verzwegen. Dit is typerend voor de nonchalance en onwetendheid in Nederland.

In september 2023 had het Nederlands Militair Geneeskundig Tijdschrift (NMGT) mijn artikel "**Chronische koolmonoxide intoxicatie: een verhoogd risico binnen de krijgsmacht**". Daarin pleitte ik o.a. voor meer bewustzijn t.a.v. de vele gevaren van CO en het gebruik van ademtesters om een snelle diagnose te kunnen stellen.
Het NMGT van september 2023 is te downloaden op de medische website van de NAVO https://www.coemed.org/resources/medicalmessenger/NMGT

Commentaar op het 'draft advisory report carbon monoxide'

1. Met de voorgestelde norm van 6.4 ppm als maximale gemiddelde blootstelling aan CO gedurende 8 werkuren ben ik het eens.
2. Die voorgestelde norm is echter aanzienlijk lager dan het bereik van de CO detectoren die worden verkocht in bouwmarkten e.d. Zulke detectoren zijn dus niet geschikt om de veiligheid van een arbeidsplaats te bewaken. In 2019 adviseerde uw Raad al dat de Europese norm voor CO detectoren moet worden aangepast aan de nieuwe inzichten, maar dat is nog niet gebeurd. Er bestaan detectoren die de CO concentratie vanaf 5 ppm aangeven en dan zelfs alarm slaan (bv. van het Canadese merk 'CO Experts'), maar die zijn prijzig en lastig te vinden.
3. Op basis van mijn waarnemingen concludeer ik dat CO intoxicatie (veel) vaker voorkomt dan gedacht , maar dat het in de medische wereld (huis- en bedrijfsartsen en SEH afdelingen) nog schort aan deskundigheid en alertheid op dit specifieke gebied, en aan een goed en snel diagnosemiddel.
4. Ik adviseer de Raad om zo snel mogelijk een proef te nemen met ademtesters bij geïnstrueerde huisartsen en SEH afdelingen. Dit geldt ook voor consultatiebureaus voor zwangere vrouwen, omdat CO erg gevaarlijk is voor de foetus en geboorteafwijkingen veroorzaakt. (NB: in Engeland krijgen zwangere vrouwen een ademtest aangeboden bij iedere controle).
5. CO is biologisch actief en het speelt o.a. een belangrijke rolbij de regulering van lichaamsfuncties bij mens en dier. Die biologische werking van CO is 'hormetisch', dus te weinig is niet goed en teveel is erg slecht. Daartussen ligt het gebied waarin CO doet wat het eigenlijk moet doen.
   Naar mijn mening geldt die hormetische activiteit van CO ook voor virussen en andere micro-organismen. Tijdens de coronapandemie waren tussen landen en regio's namelijk grote verschillen in morbiditeit en mortaliteit, die veroorzaakt werden door de variaties in lucht- en milieukwaliteit. Dat kan wellicht verklaren waarom corona in Afrika kalmer verliep dan in Europa, want de gemiddelde CO concentratie in de lucht is in Afrika hoger dan in Europa.
   De effecten van CO op de functies en functionaliteit van micro-organismen verdienen in elk geval urgent wetenschappelijke aandacht.