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From the report "Fresh Meat in Consumer Packaging" with modified gas containing CO_2 [illegible]

IV. Report by Tore Aune: "Fresh Meat in Consumer Packaging – A Toxicological Evaluation of the Use of up to 0.5% CO in a Gas Mixture."

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FRESH MEAT IN CONSUMER PACKAGING – A TOXICOLOGICAL EVALUATION OF THE USE OF UP TO 0.5% CO IN A GAS MIXTURE

By Tore Aune

Carbon monoxide (CO) is a colorless gas that is primarily generated by incomplete combustion of organic material. The background concentration of CO in the atmosphere is approximately 0.01-0.09mg/m^3 (0.009-0.08 ppm), while the concentration in larger cities may excede 50mg/m^3 as an 8 hour mean, depending on traffic.

General Health Effects

CO attaches to the iron of the hemoglobin in the red blood cells during generation of carboxyhemoglobin (COHb), and can thus affect the transport of oxygen in the blood and the supply of oxygen to the tissues. Compared to its affinity to oxygen, hemoglobin has approximately 240 times greater affinity to CO. CO also attaches to myoglobin, cytochromes, and some other enzymes, but these reactions are considered less important than the formation of carboxyhemoglobin (WHO 1979). The health impact on humans is mainly restricted to effects on the cardiovascular system, the nervous system, and certain types of proteins and cells in the bloodstream, as well as effects on embryos (SFT 1992).

The carboxyhemoglobin percentage (COHb %) is a function of the CO concentration in the inhaled air, the exposure time and the level of physical activity (Coburn et al., 1965) (see Table 1). A CO exposure resulting in a COHb concentration above 2% in the bloodstream of the most sensitive individuals (cardiovascular patients) has been shown to give symptoms of localized oxygen deficit and chest pains. Reduced work capacity occurs at a somewhat higher COHb%, and persons suffering from angina can tolerate less strain before an attack occurs. No health effects have been detected in healthy adults at COHb concentrations below 5%.

Table 1: Blood carboxyhemoglobin percentage as a function of CO concentration in air, exposure time and different degrees of physical activity (Coburn et al., 1965):

Exposure		COHb%		
CO Conc.	Time in Hours:	At rest	Moderate Activity	Strenuous Activity
10 mg/m^3	8	1.3	1.4	1.4
25 mg/m^3	1	1.0	1.5	2.0
40 mg/m^3	1	1.3	2.2	2.9

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CO attachment to the hemoglobin is reversible. The half-life at ventilation at rest is approximately 4.5 hours.

A small amount of CO is continually formed in the body as a result of the decomposition of substances such as hemoproteins. This results in a COHb% of approximately 0.5. The uptake of CO through inhalation comes in addition to that. The average COHb level in non-smokers is estimated at 1.2-1.5%, while the level is 3-4% in smokers.

Survey of Health Effects Associated with CO Exposure

The negative health effects of CO are due to the fact that CO competes with oxygen for points of attachments on the hemoglobin molecule. Moreover, the release of oxygen in the tissues is reduced (WGHO 1987). Myoglobin is closely related to hemoglobin. It stores oxygen and promotes the diffusion of oxygen to muscle cells. In cardiac and skeletal muscles, myoglobin binds CO with an affinity that is 30-50 times higher than the corresponding affinity for oxygen. No reported studies have shown that the binding of CO to myoglobin can cause any health effect at a COHb level of 4-5%.

Uptake and liberation of CO occur at a relatively slow pace (hours), which means that short-time exposure to elevated CO levels will not result in any noticeable increase in the COHb level. SFT report No. 92/16 (1992) includes an overview of the correlation between blood COHb levels and health effects (Table 2).

Table 2: Correlation between blood carboxyhemoglobin levels and health effects (SFT 1992):

COHb%	Observed Effects in Humans:
50 and above	Unconsciousness, lethal when untreated.
30 and above	Headache, dizziness, nausea, and vomiting.
10 and above	May be lethal to cardiovascular patients. Headache in healthy individuals.
5 and above	Reduction of peak oxygen consumption under strenuous activity in healthy individuals.
5 and above	Impaired vision, learning ability and fine motor response.
5 and above	Exposure during pregnancy may affect the embryo.
2.9 and above	Individuals suffering from angina can tolerate less strain before an attack occurs.
2.3 and above	Reduced capacity for physical work, especially stamina.
2 and above	Possible reduced ability to concentrate and pay attention.
2 and above	Symptoms of localized oxygen deficit and incipient chest pains in cardiac patients.

The literature in the field does not seem to indicate that health effects have been proven in healthy adults exposed to CO resulting in a blood COHb concentration of less than 5%.

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However, the data indicate that a COHb level of 2-3% may have negative effects on sick and sensitive individuals, such as people suffering from cardiovascular diseases.

Exposure to CO through the Air

With regard to CO as an air pollution factor, a team of Norwegian experts (SFT 1992) suggested air quality criteria at CO concentrations resulting in a maximum of 1.5% COHb during light physical activity (including the CO produced endogenically). The correlation between CO concentration, activity level, and exposure time in order not to exceed 1.5% blood COHb is shown in Table 3.

Table 3: Calculation of CO concentrations in the air resulting in a COHb level of 1.5%, including endogenic CO production (SFT 1992):

	CO Concentration, mg/m^3		
Exposure Time:	At Rest:	Moderate Physical Activity:	Strenuous Physical Activity:
15 min	170	80	52
30 min	86	42	29
1 hour	48	24	18
8 hours	11.5	9.2	9.2

Exposure to CO through Consumption of Fresh Meat Treated with a Gas Mixture

There is a paucity of information in scientific literature concerning exposure to CO through the consumption of fresh meat treated with a gas mixture containing CO. One of the most interesting references in this regard is a 1954 publication by A. L. Tappel et al., which is unfortunately not easily accessible. However, their work has been cited in other publications, e.g. in the study by Clark et al. (1976): Tappel et al. considered a US industrial sanitary norm for CO of 50 ppm (8 hours/day), and found that such exposure would result in a blood COHb level over a longer period of time that is approximately 14 times higher than the temporary increase caused by consumption of approximately 225 g meat, provided that the myoglobin and hemoglobin in the meat are saturated with CO, and that 100% of CO from this source is transferred to the blood of the consumer (an estimate representing a hypothetical worst-case scenario). According to the authors, such treatment of meat will thus cause only a very minor effect in comparison to what is considered the safety limit, even when assuming maximum uptake of CO. Watts et al. (1978) exposed beef to a gas containing 1% CO for 3 days, and found that this resulted in a CO saturation of approximately 30% of the myoglobin. CO was lost under such storage conditions, with a half-life of approximately 3 days. After cooking, the CO concentration in the meat decreased to

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below 0.09 ppm (equivalent to approximately 0.1 mg/kg). Maximum loss after cooking (on burner at 195°C) amounted to approximately 85%.

Comparison of CO Exposure through Air and Meat (CO Treated)

There is little data available for such a comparison, but a rough overview nevertheless provides some points of reference. An adult inhales 10-20m^3 air per 24 hours (depending on the activity level). This is the equivalent of 0.42-0.84m^3 per hour (or 3.36-6.72 m^3 per 8 hours).

To stay within a maximum blood COHb level of 1.5%, the CO concentration in the air must be 24 mg/m^3 for 1 hour at moderate physical activity, at 9.2 mg/m^3 for 8 hours (according to Table 3). In comparison, the CO exposure is 0.1 mg/kg after consumption of 250 g of heated CO-treated meat that has been treated for 72 hours in a gas containing 1% CO (Watts et al., 1978). Table 4 shows a calculation of CO intake from the air and a meal of CO-treated meat.

Table 4: Comparison of CO intake from air within a range without any health impact and theoretical intake of CO through consumption of a meal of CO-treated meat:

Path of Exposure:	CO Intake, 1 hour:	CO Intake, 8 hours
Lungs (15 m^3/24 hours)	24mg x 0.625 = 15.1mg	9.2mg x 5 = 46.0mg
Meat	0.025mg	0.025 mg

For CO balance between air and blood is only achieved after a considerable period of time (hours). The absorption of gases from the intestinal canal to the blood is probably considerably less efficient than from the lungs, where the tissue allows for maximum gas exchange between the alveoli and the bloodstream. This implies that intake of CO through meat probably won't cause any demonstrable increase in the blood CO level (in the form of COHb). And at any rate, the exposure from meat is much lower (approximately one thousand times lower) than through the airways, as shown in the calculations above.

According to the Norwegian Institute of Air Research (SFT 1992), the CO concentration in larger Norwegian cities is on average between 1 and 2 mg/m^3 during the winter. Maximum hourly values have been measured to approximately 60 mg/m^3, and maximum values for 8 hours to about 40 mg/m^3.

Evaluation of Other Gases Used in Foods in the EU

EU's Research Committee on Foods (SCF) has not considered CO. However, the expert team has considered other gases (EUR 1981), such as carbon dioxide (CO_2) and nitrogen oxide (NO). In this connection, the committee employed the following evaluation method, which should be applicable for CO, as well:

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CO_2: This compound is a natural product of metabolism, and people are constantly exposed to carbon dioxide from the atmosphere, food and drink. Compared to this exposure, the residual content from its use as an extraction agent is insignificant. Establishing an ADI for this compound is unnecessary. The committee considers this compound acceptable as an extraction agent. It is unnecessary to determine concentration values for the residue.

N_2O: The pharmacological and pharmacokinetic properties of this gas are well known from the extensive use of N_2O as an anaesthetic. Even though no data on residual content are available, such amounts are probably so minor that they are not hazardous to the consumer. The committee finds that it is unnecessary to establish an ADI, and considers the use of N_2O as an extraction agent acceptable.

Toxicological Evaluation of the Use of CO as a Packaging Gas for Meat

People are continually exposed to carbon monoxide, both by means of endogenic production and by inhaled air. Toxicologically, it is the amount of CO bound to the blood hemoglobin (the carboxyhemoglobin percentage) that determines any health effects. The very first effects in sensitive individuals occur at COHb concentrations from approximately 2-3%. To prevent possible health effects even in the most sensitive individuals, a team of Norwegian experts has suggested limits for CO in the air that do not result in COHb concentrations above 1.5%, including the endogenic production at 0.5%. The above-mentioned estimates indicate that even if all CO in the prepared meat is transferred to the consumer's blood, the CO concentration – even a temporary concentration – will remain well below accepted limits in air. From a health perspective, the use of CO in concentrations below 0.5-1 % for fresh meat thus represents no toxicological risk.

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