

# Carbon Monoxide Accumulation in Closed Circle Anesthesia Systems

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Small amounts of carbon monoxide are endogenously produced by the breakdown of hemoglobin. Accumulation of carbon monoxide was measured in a series of patients anesthetized with a closed circle system; clinically significant values were occasionally reached. Factors affecting carbon monoxide levels were blood transfusion before and during operation and prolonged use of the closed system.

SINCE the late nineteenth century, it has been known that carbon monoxide was present in the blood, but its source has been recognized only in recent years. In 1951 Sjöstrand<sup>1</sup> compared the carbon monoxide content of ambient air with that of expired air. He found the concentration in ambient air to be  $0.00007 \pm 0.000003$  per cent and that in expired air to be  $0.000023 \pm 0.00001$  per cent. He concluded, therefore, that carbon monoxide is produced endogenously. Coburn *et al.*<sup>2</sup> measured carbon monoxide production in man by collecting expired air over periods of two to five hours in a closed system into which oxygen was admitted through a one-way valve and carbon dioxide extracted with a soda lime absorber. In normal subjects, the rate of carbon monoxide production was  $0.42 \pm 0.07$  S.D. ml./hour.

An anesthesia machine, employing a closed technique, is equivalent to the system in which

Coburn *et al.* measured carbon monoxide production. It was the purpose of this study to determine whether the use of the closed system, in anesthetized patients, allows the build up of carbon monoxide to levels that exert significant effects.

## Materials and Methods

A group of 22 adult surgical patients at the Latter-day Saints Hospital in Salt Lake City, Utah, was randomly chosen and their anesthetics administered using a completely closed circle anesthetic technique (exceptions noted in tables). Gas samples of 350 ml. volume were taken from a side-arm in the expiration tubing. These were analyzed using a Monoxor (Bacharach Industrial Instrument Company, Pittsburgh), an instrument used in industry to detect and quantitate potentially hazardous sources of carbon monoxide. The instrument measures carbon monoxide by means of a chemical reaction which discolors an indicator tube of silica gel to a length proportional to the carbon monoxide concentration. The accuracy is in the range of 0.0005 per cent in samples of 350 ml. Readings must be corrected for temperature and altitude.<sup>4</sup> The readings made in this study were corrected for an altitude of 4,500 feet and body temperature.

Gas samples were taken immediately after closure of the system and again before the system was opened. In some cases, samples were taken at hourly intervals throughout the anesthetic period. Note was made of known smoking history, recent transfusions or anemia.

Samples of the anesthetic gases or vapors used in this series (cyclopropane, halothane cylinder oxygen) were taken before administration, and carbon monoxide content was not detected by the Monoxor.

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TABLE 1. Overall Data in 22 Patients

	Total	CO Increased	CO Un- changed or Decreased
Number of patients	22	15	7
Percentage of patients	100	68.2	31.8
Average change in CO concentration	54.5 ppm.	80 ppm.	0
Range of change in CO concentration	0-210 ppm.	20-210 ppm.	0
Smoking history	2	1	1
Duration of CO sampling (hours)	1.8	2.15	1.08
Range of duration of CO sampling (hours)	0.16-3.5	0.16-3.5	0.33-1.75
Transfusion history	12	10	2
Percentage with trans- fusion history	54.5	66.7	28.5

Results

In the 22 cases, 15 showed increasing carbon monoxide concentrations, as shown in table 1. Those cases in which CO increased were of longer average duration than those in which the CO was unchanged and were more frequently associated with a history of recent blood transfusion.

Table 2 lists the corrected CO sampling data, surgical procedure, anesthetic technique, hematocrit, smoking and transfusion history of each of the 22 cases. Carbon monoxide values were unchanged in cases 5, 7, 8, 11, 17, and 19. In only one case did the concentration of carbon monoxide decrease (number 9). The cause for the decrease was not evident. In all other cases, the carbon monoxide increased.

The highest value of carbon monoxide concentration was found in a patient known to be a heavy cigarette smoker (case 15) and most likely represents carbon monoxide of exogenous rather than endogenous origin.\*

\* The low incidence of smokers in the group studied may be explained by the fact that the religious tenets of the Latter-day Saint Church forbid smoking.

One case in which a semiclosed technique was used was included in the series because of a significant increase in the carbon monoxide concentration (number 6). This was one in which a large transfusion was given during a cardiac bypass procedure.

In case number 10 frequent sampling traced the effect of opening and closing the system on the carbon monoxide concentration. Only the data from the first 1½ hours (or until the system was first opened) are included in table 1.

Discussion

Carbon monoxide in alveolar air may be of endogenous or exogenous origin. ~~Exogenous sources include cigarette smoke, automobile exhaust, and by-products of a wide variety of industrial processes.~~ Endogenous carbon monoxide is a by-product of hemoglobin catabolism according to the reaction shown in figure 1.<sup>3</sup>

The porphyrin ring is opened by expulsion of the carbon atom in the alpha position; this occurs after replacement of the methene group by C-OH which is then dehydrogenated to CO. The production of carbon monoxide has been found to be proportional to hemoglobin catabolism, thereby implicating hemoglobin as the only source of endogenous CO.<sup>5</sup> ~~An average of 4 g. of hemoglobin is broken down each day with the production of 6.8 mg. of CO.~~ These quantity are proportional to the relative molecular weights of hemoglobin and CO.

The affinity of hemoglobin for carbon monoxide is approximately 300 times that of oxygen, and the resulting product, carboxyhemoglobin, is much more stable than oxyhemoglobin. The concentration of COHgb in blood can be predicted by determination of the partial pressure of carbon monoxide in alveolar air.<sup>5</sup>

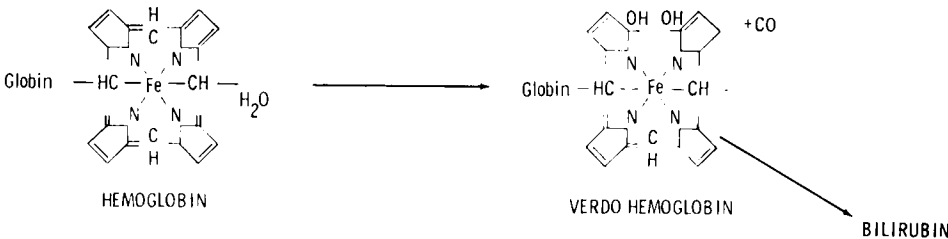


FIG. 1. Structural formulas indicating catabolism of hemoglobin.

TABLE 2. Anesthesia, Operation, and Carbon Monoxide Levels in the Group of Patients Studied

Case	Surgical Procedure Indication	Anesthetic Technique	HMT/HGB	Smoking History	Transfusion History	Carbon Monoxide Sampling Data (Values Corrected) for Temperature and Pressure
1	Gastric resection, bleeding duodenal ulcer	Pento-succinyl ind., d-Tc IV Cyclo-O <sub>2</sub> IT O <sub>2</sub> 60%	41%	None	2 U. WB 12 days preop.	Sample 1 0.013 2 0.027 1½ hr. 3 0.034 3½ hr.
2	Abdominal perineal resection, ulcerative colitis	Pento-succinyl ind., d-Tc, Pentobarbital IV O <sub>2</sub> IT 70%	43%	None	3 U. PC 4 days preop. 2 U. PC 3 days preop. 1 U. WB 7 days preop.	Sample 1 0.010 2 0.019 3 hr.
3	Radical mastectomy, carcinoma	Pento-succinyl ind., Meperidine IV Halo-O <sub>2</sub> IT		None	3 U. WB in O.R.	Sample 1 0.003 2 0.022 3½ hr.
4	Hiatus hernia repair	Pento-succinyl ind., d-Tc IV cyclo-O <sub>2</sub> IT O <sub>2</sub> 65%	41%	None		Sample 1 0.005 2 0.011 2 hr.
5	Vaginal hysterectomy	Pento-succinyl ind., d-Tc IV O <sub>2</sub> IT	43%	None		Sample 1 0.005 2 0.005 1 hr.
6	Correction of aortic stenosis	Pento-succinyl ind., d-Tc IV N <sub>2</sub> O-Halo-O <sub>2</sub> IT (semiclosed) cardiac bypass	40%	None	WB in cardiac bypass Machine	Sample 1 trace 2 trace 2½ hr. 3 0.009 4 hr. (2 hr. off bypass)
7	Abdominal hysterectomy	Pento-succinyl ind., cyclo-O <sub>2</sub> IT d-Tc IV		None		Sample 1 0.005 2 0.005 1 hr.
8	Thyroidectomy	Pento-succinyl ind., cyclo-O <sub>2</sub> IT	46%	None		Sample 1 0.004 2 0.004 1 hr.
9	Gastric resection	Pento-succinyl in I., d-Tc IV, cyclo-O <sub>2</sub> IT	42%	Occasional smoker	2 U. WB 4 days preop.	Sample 1 0.013 2 0.016 1 hr. 3 0.011 1½ hr.
10	Tetralogy of fallot repair	Pento-succinyl ind., Pentobarbital d-Tc IV O <sub>2</sub> IT, cardiac bypass (system open while on bypass)	56%, 18.7g. %	None	3 U. WB  6 U. WB in bypass machine	System closed Sample 1 0.004 2 0.004 ½ hr. 3 0.016 1½ hr.  On bypass (system open) Sample 1 0.016 4 min. on bypass 2 0.003 ½ hr. 3 0.009 2 hr. Off bypass (system closed) Sample 1 0.011 ½ hr. off bypass 2 0.014 1½ hr.
11	Cholecystectomy	Pento-succinyl ind., cyclo-O <sub>2</sub> IT d-Tc IV	45%	None		Sample 1 0.008 2 0.008 1 hr.
12	Laparotomy	Pento-succinyl ind., cyclo-O <sub>2</sub> IT d-Tc IV		None		Sample 1 0.005 2 0.009 1 hr.
13	Salpingectomy, ruptured tubal pregnancy	Pento-succinyl ind., cyclo-O <sub>2</sub> (mask) d-Tc IV	27%, 9.3g. %	None	4 U. WB in O.R.	Sample 1 0.003 2 0.016 1 hr.
14	Radical mastectomy, carcinoma	Pento-succinyl ind., cyclo-O <sub>2</sub> IT		None	1 U. WB in O.R.	Sample 1 0.027 2 0.030 ½ hr.
15	Cervical fusion	Pento-succinyl ind., Pentobarbital, morphine 804 IV, O <sub>2</sub> IT	47.5%	Heavy smoker		Sample 1 0.067 2 0.071 1 hr. 3 0.081 3 ½ hr.
16	Salpingectomy, ruptured ectopic pregnancy	Pento-succinyl ind., cyclo-O <sub>2</sub> IT	36%, 12g. %	None	1 U. WB in O.R.	Sample 1 0.008 2 0.009 10 min. 3 0.012 ½ hr.
17	Salpingectomy, ruptured ectopic pregnancy	Pento-succinyl ind., cyclo-O <sub>2</sub> IT		None	2 U. WB in O.R.	Sample 1 0.012 2 0.012 ½ hr.

Abbreviations: Pento, Sodium thiopental; Succinyl, Succinylcholine; IT, Intratracheal; IV, Intravenous; Cyclo, Cyclopropane; Halo, halothane; d-Tc, d-tubocurarine; O<sub>2</sub> %, measured by O<sub>2</sub> analyzer; WB, whole blood; PC, packed cells.

TABLE 2.—(Continued)

Case	Surgical Procedure Indication	Anesthetic Technique	HMT, HGB	Smoking History	Transfusion History	Carbon Monoxide Sampling Data (Values Corrected) for Temperature and Pressure
18	Thyroidectomy	Pento-succinyl ind., cyclo-O <sub>2</sub> IT, O <sub>2</sub> 60%		None		Sample 1 0.001 2 0.005 2 hr.
19	Abdominal hysterectomy	Pento-succinyl ind., cyclo-O <sub>2</sub> IT, d-Tc IV	40%	None		Sample 1 0.005 2 0.005 1 1/2 hr.
20	Colon resection	Pento-succinyl ind., cyclo-O <sub>2</sub> IT, d-Tc IV		None		Sample 1 0.004 2 0.007 3 hr.
21	Gastric resection	Pento-succinyl ind., cyclo-O <sub>2</sub> IT, d-Tc IV		None	2 U. WB 10 days preop. 2 U. WB 9 days preop. 2 U. WB 8 days preop. 1 U. WB 5 days preop.	Sample 1 0.001 2 0.004 2 1/2 hr.
22	Abdominal hysterectomy	Pento-succinyl ind., cyclo-O <sub>2</sub> IT, d-Tc IV	46%	None		Sample 1 0.004 2 0.011 2 hr.

Toxicity of carbon monoxide depends upon the concentration of the gas in the alveolar air, the duration of exposure, and the physical condition of the person exposed. "Safe" concentrations have been variously designated: Hamilton and Hardy<sup>8</sup> consider this to be an exposure of 100 ppm. (0.01 per cent) for 8 hours or 400 ppm. for less than an hour; however, this represents characteristic industrial exposure in presumably healthy, active industrial workers. Henderson's and Haggard's<sup>9</sup>

index of toxic effects has been widely used for prediction of toxicity:

$$\text{CO concentration (ppm.)} \times \text{Time (hours)} \\ = \text{Index of toxic effect}$$

300—no perceptible effect  
600—just perceptible effect  
900—nausea and headache  
1,500—dangerous to life

Our cases fall into the category between just perceptible or no perceptible effect.

The effect of carbon monoxide at nonlethal concentrations seems to be entirely that of the binding to hemoglobin and interference with oxygen transport. In this regard, carbon monoxide is effective in minute concentrations. A concentration of 0.01 per cent (100 ppm.) in the alveolar air will bind 16 per cent of the body's hemoglobin as COHgb.<sup>10</sup> Because viscosity of blood and Po<sub>2</sub> remain constant, compensatory circulatory mechanisms of vasodilation and increased cardiac output are delayed. Since high levels of COHgb modify the oxygen dissociation curve (see fig. 2), there results an anemia, the effect of which is more severe than can be explained simply by binding of hemoglobin.

The "anemia" produced by the levels of carbon monoxide encountered in this series might be easily tolerated by normal healthy subjects with adequate hemoglobin levels. In the severely ill patient, however, increased

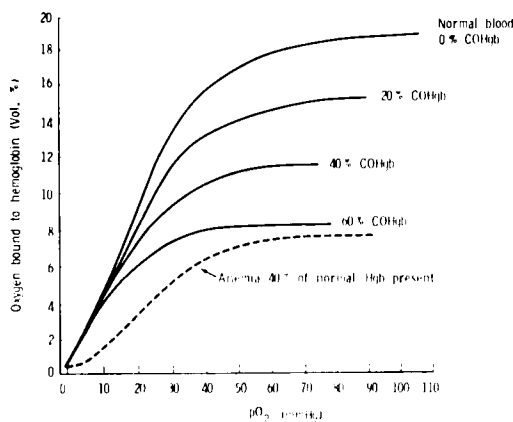


FIG. 2. The oxygen dissociation curve as modified by high levels of carbon monoxide-hemoglobin. Reproduced, by permission, from Roughton, F. J. W., and Darling, R. C.: The effect of carbon monoxide on the oxyhemoglobin dissociation curve, *Amer. J. Physiol.* 141: 17-31, 1944.

COHgb levels and diminished oxygen transport easily might become a matter of critical importance.

Complete closure of the anesthetic system allows build up of carbon monoxide while semiclosed and open techniques allow carbon monoxide to escape. It is, therefore, recommended when closed techniques are employed that the system be opened and flushed at regular intervals to prevent carbon monoxide accumulation. It is estimated that hourly intervals would be adequate for ordinary patients, but the frequency should be increased in patients with histories of hemolytic anemia, recent transfusion, or in patients whose histories of heavy smoking or occupational exposure indicate the possibility of rebreathing exogenous carbon monoxide.

### Conclusion

Closed system anesthetic techniques allow the accumulation of endogenous and exogenous carbon monoxide which causes binding of hemoglobin and impaired oxygen transport, when present in even minute concentrations. Accumulation can be prevented by intermittently opening and flushing the anesthetic system.

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**LOCAL ANESTHETICS** Peripheral vasodilating action of local anesthetics was investigated by means of a magnetic flowmeter inserted in a dog's femoral vein, while local anesthetics were injected into the femoral artery of the same leg. Dogs were anesthetized with either pentobarbital or halothane, no significant differences being noted in the results as between the anesthetic methods. The local influence of lidocaine, Citanest (propylamino-2-methylpropionanilide), mepivacaine, dibucaine, tetracaine and cocaine was tested with reference to saline, 5 per cent glucose and/or vasopressors as controls. All these local anesthetics caused a similar increase of venous return except cocaine, which caused a decrease of flow following an initial rise. (Kuba, T., and others: *Studies on Local Anesthetics. I. Vasodilating Effects (Japanese)*, *Jap. J. Anaesth.* **13**: 646, 1964.)