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☐ Original Article ☐

Hematologic Changes in Acute Carbon Monoxide Intoxication

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This study was performed to investigate the hematologic changes and its pathogenesis in acute carbon monoxide (CO) intoxication. Serial complete blood counts (CBC) were obtained in 17 patients with acute CO intoxication five times in two weeks. Peripheral blood smear, bone marrow aspiration and biopsy were obtained in 7 patients within the first week. We analyzed the results of serial CBC's. Levels of hemoglobin and hematocrit rose only initially, probably due to dehydration and hemoconcentration rather than hypoxia. Leukocytosis, mainly neutrophilic, observed during the first few days seemed to be a physiological phenomena due to a stressful situation, such as hypoxia. Levels of platelet increased steadily after a initial decrease. We found no specific findings in bone marrow.

Key Words: Acute carbon monoxide intoxication, RBC, WBC, platelet

Carbon monoxide (CO) intoxication dates back to the roots of industrialization, and its significance increases mainly with present environmental pollution caused by motorization and partly with smoking habits. Since coal is still used as domestic fuel for cooking and under-the-floor heating in our country, acute CO intoxication is seen more frequently.

The pathophysiology of acute CO intoxication was first revealed by Claude Bernard (1857), who said that the cause was tissue hypoxia rather than CO's toxicity (Winter and Miller 1976). In 1927, Haldane described the symptoms caused by carboxyhemoglobin (COHb) saturation. Carbon monoxide affects brain and heart most severely, but other systemic manifestations were noted not infrequently (Choi 1991). The laboratory findings of acute CO intoxication are also diverse. Red blood cell (RBC) counts, hemoglobin (Hb), and hematocrit (Hct) were raised (Ramsey 1969a). White blood cell (WBC) counts were also increased(Whang and Choi 1990). The urinalysis showed positive for glucose, protein, and myoglobin. There were increases of serum creatine kinase (CK), lactic dehydrogenase (LDH), glutamic pyruvic transaminase (SGPT), glutamic oxaloacetic transaminase (SGOT), and glucose (Whang and Choi 1990). But these delineations are far from distinguishing with that of chronic CO intoxcation. They are known to cause reactive erythropoiesis (Jaeger and McGrath 1975; Penney and Bishop 1978; James *et al.* 1979), leukocytosis secondary to inflammation (Vanuxem *et al.* 1984; Bridges *et al.* 1986), and platelet dysfunction (Mansouri and Perry 1982; Madsen and Dyerberg 1984; Renaud *et al.* 1984).

So we performed this study to investigate the hematologic changes of acute CO intoxication which could be different from that of chronic CO intoxication, and, if possible, elucidate the mechanisms of the changes by doing serial tests of complete blood counts (CBC), peripheral blood smear, and bone marrow aspiration and biopsy.

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MATERIALS AND METHODS

Nine male and eight female patients with acute CO intoxication, from 15~74 years of age (mean 38.9 years), who were admitted to Wonju Christian Hospital, Wonju College of Medicine, Yonsei University, from May 1, 1991 to March 31, 1992 were evaluated. Patients who were admitted after 24 hours of discovery, with past history of hematologic diseases, who were pregnant, immediate postpartum or postoperational state were excluded. Also excluded were patients with purpura, hematuria, infection, or disseminated intravascular coagulation in the course of hospitalization.

Patients were evaluated by careful history taking, physical and neurological examination, and divided into several groups according to the mental state (Table 1, Snyder *et al.* 1980). Results of COHb and serial CBC were followed. CBC's were done on the day of onset, 3, 5, 7, and 14 days later. In four male and three female patients, we performed bone marrow aspiration and biopsy within 7 days after intoxication.

Complete blood counts were done using the Coulter S plus IV autoanalyzer, and the differential counts of WBC was done manually by counting two hundred WBC's. We used the Wright-Giemsa stain for the peripheral blood smear, and Wright-Giemsa stain and Prussian blue stain for the bone marrow aspiration. Hematoxylin-Eosin stain was used for the bone marrow biopsy. We evaluated the following parameters serially 5 times, during the 2 week duration of the study; Hb, Hct, RBC, WBC with differential count, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), mean platelet volume (MPV), platelet distribution width (PDW). For statistical analyses, independent Student t-test was used for comparison between male and female patients, and nonparametric Friedman test was used for daily comparison of each item and for mental states and hematologic changes. We also studied the relationship between the results of CBC's and bone marrow exam.

RESULTS

1) The mental state of the 17 patients were listed in Table 1. There were no significant statistical difference between male and female patients, and between mental states and hematologic changes.

2) Hematocrit, WBC, platelet, and MPV in both male and female patients, and Hb, RBC, MCHC, and differential counts of WBC in male patients, and PDW in female patients showed daily changes with statistical significance (Table 2). In both male and female patients, Hb (Fig. 1) and Hct (Fig. 2) increased on the day of onset, decreased on the fifth day, and showed variable changes afterwards. Red blood cell counts showed similar changes only in male patients (Fig. 3). But these changes of Hb, Hct, and RBC counts were all in normal limit. White blood cell counts revealed an abrupt rise on the day of onset, then slowly decreased to normal ranges in both male and female patients. The increase in WBC was mainly due to neutrophilia (Fig. 4). Platelet counts also showed an initial decrease and later increased in both male and female patients, but the changes were also within normal limit (Fig. 5). In male patients, MCHC showed a little increase first, then slowly decreased (Fig. 6). Mean platelet volume reached peak on third day, and gradually

Table 1. Mental state of 17 patients with acute CO intoxication at emergency room

Score	Response to pain	No. of patients
0	alert	1
1	drowsy, confused, respond to verval command	3
2	localize and resist to pain	3
3	withdrawal response to pain	2
4	decorticate rigidity to pain	6
5	decerebrate rigidity to pain	2
6	no response to pain	0

Table 2. Hematologic changes and its statistical significance in patients with acuth CO intoxication

	Sex	OD	3rd D	5th D	7th D	14 th D	Significance*
Hb(g/dl)	M	14.96±1.19	13.82±1.93	12.66±1.38	13.30±1.97	13.21±1.32	.0103
	F	14.12±1.09	12.57±1.12	12.26±1.74	12.37±1.85	11.77±2.53	.0518
Hct(%)	M	42.76±4.03	40.48±6.25	37.25±4.90	38.98±5.36	38.96±3.93	.0192
	F	41.43±3.37	37.27±3.66	36.50±5.32	36.73±5.20	35.67±7.45	.0314
RBC($10^4/\mu l$)	M	460.1±57.3	431.3±79.1	396.8±66.9	416.5±79.9	407.6±59.9	.0138
	F	458.2±38.6	414.5±51.8	407.0±58.3	399.1±59.5	423.5±83.1	.0518
WBC($10^2/\mu l$)	M	189.7±62.8	145.8±42.6	89.4±18.4	81.7±19.8	80.3±18.5	.0024
	F	200.3±75.5	156.2±72.9	92.1±31.7	100.7±30.9	84.5±26.2	.0314
Plt($10^3/\mu l$)	M	320.2±76.6	245.7±62.5	232.0±48.8	288.7±42.7	392.8±118.4	.0003
	F	323.5±109.4	232.8±72.9	226.8±65.7	228.8±77.9	464.7±112.5	.0113
MCV(fl)	M	93.41±5.72	94.48±5.72	94.44±6.02	94.66±6.99	96.15±5.32	.1209
	F	90.62±6.60	90.37±6.72	90.26±6.62	90.75±7.38	84.57±8.65	.3546
MCH(pg)	M	32.74±2.32	32.34±2.17	32.24±2.63	32.21±2.06	32.61±1.72	.1074
	F	30.92±2.28	30.55±2.79	30.48±2.45	30.58±2.56	27.92±3.27	.1680
MCHC(g/dl)	M	35.04±1.04	34.22±0.97	34.14±1.06	34.06±1.19	33.93±0.85	.0289
	F	34.16±0.93	33.78±1.04	33.60±0.57	33.75±0.77	33.02±0.42	.1712
RDW(%)	M	12.97±0.58	12.95±0.51	12.72±0.49	12.57±0.36	12.56±0.43	.3121
	F	13.30±1.40	13.28±1.43	12.83±1.55	12.90±1.68	13.40±1.74	.2977
MPV(fl)	M	7.46±0.84	8.11±0.83	7.97±0.75	7.70±0.64	7.30±0.78	.0319
	F	8.01±0.78	8.31±0.63	8.12±0.77	8.22±0.52	7.55±0.77	.0159
PDW(%)	M	16.81±0.55	16.73±0.38	16.94±0.45	16.96±0.96	16.85±0.77	.8500
	F	16.62±0.19	16.96±0.39	17.23±0.58	17.28±0.41	16.50±0.35	.0302
Seg	M	78.2±16.4	79.3±11.6	68.2±11.0	60.8±9.5	58.0±12.0	.0186
	F	81.5±8.8	81.7±13.4	73.3±11.0	72.0±8.6	59.0±21.2	.2532
Band(%)	M	4.3±5.9	2.0±2.2	0.6±1.6	0.2±0.4	0.0±0.0	.0221
	F	2.7±3.4	1.0±1.6	0.6±1.4	0.6±0.8	0.5±0.5	.8355
Lymph(%)	M	11.6±12.4	12.8±7.2	22.1±10.1	28.2±9.3	29.8±7.0	.0966
	F	12.0±8.0	14.0±11.4	21.0±9.3	20.6±8.2	32.2±17.5	.3139
Mono(%)	M	4.2±2.5	3.6±2.1	6.2±3.1	6.0±2.8	6.3±2.0	.1241
	F	2.6±2.3	3.2±2.6	3.3±1.6	4.8±2.3	5.7±1.8	.2442

( ) are unit and values are mean±standard deviation. Significance*: daily changes were compared by Friedman test. Abbreviations: OD: onset day, D; day, Hb; hemoglobin, Hct; hematocrit, RBC; red blood cell, WBC; white blood cell, Plt; platelet, MCV; mean corpuscular volume, MCH; mean corpuscular hemoglobin, MCHC; mean corpuscular hemoglobin concentration. RDW; red cell distribution width, MPV; mean platelet volume, PDW; platelet distribution width, Seg; segmented neutrophil, Band; bandform, Lymph; lymphocyte, mono; monocyte

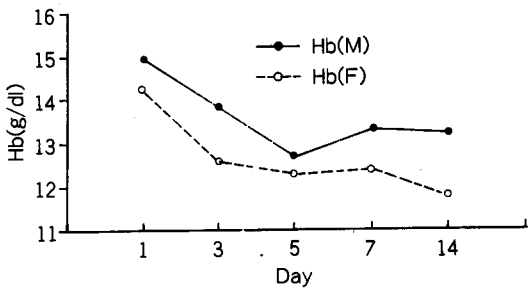

Fig. 1. *Serial changes of hemoglobin in patients with acute CO intoxication. The values were mean (N=17, M=9, F=8). (Hb: hemoglobin)*

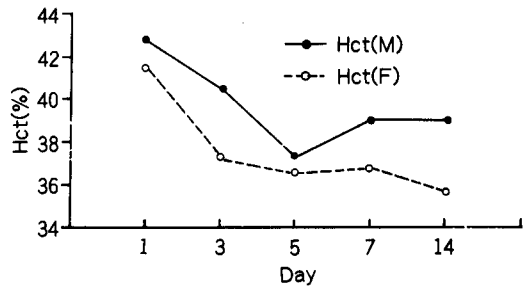

Fig. 2. *Serial changes of hematocrit in patients with acute CO intoxication. The values were mean (N=17, M=9, F=8). (Hct: hematocrit)*

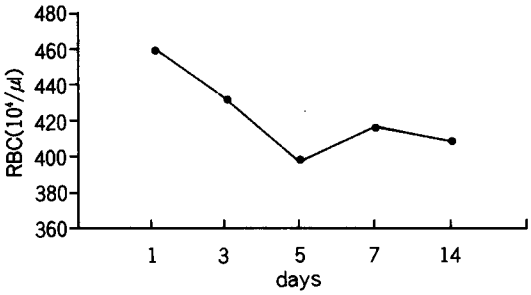

Fig. 3. *Serial changes of red blood cell in male patients with acute CO intoxication. The values were mean (N=9). (RBC: red blood cell)*

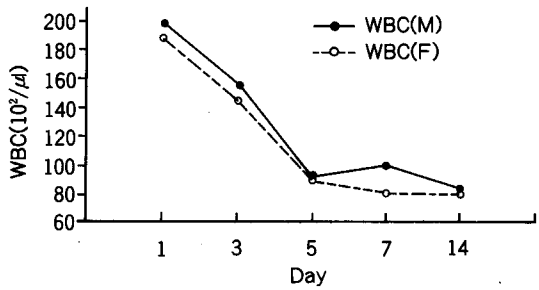

Fig. 4. *Serial changes of white blood cell in patients with acute CO intoxication. The values were mean (N=17, M=9, F=8). (WBC: white blood cell)*

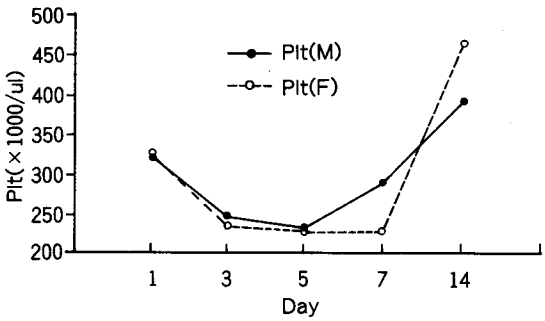

Fig. 5. *Serial changes of platelet in patients with acute CO intoxication. The values were mean (N=17, M=9, F=8). (Plt: platelet)*

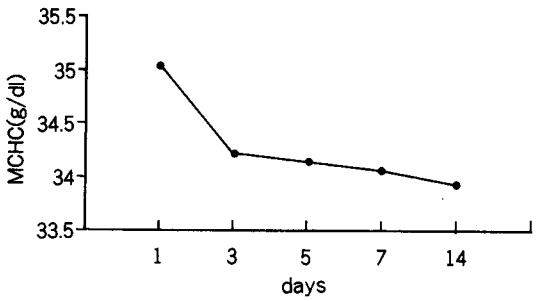

Fig. 6. *Serial changes of mean corpuscular hemoglobin concentration in male patients with acute CO intoxication. The values were mean (N=9). (MCHC: mean corpuscular hemoglobin concentration)*

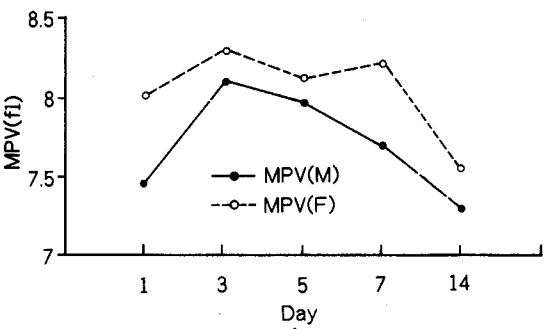

Fig. 7. *Serial changes of mean platelet volume in patients with acute CO intoxication. The values were mean (N=17, M=9, F=8). (MPV: mean platelet volume)*

fell (Fig. 7).

3) In peripheral blood smear, RBC looked normal in six cases and showed slight anisocytosis in one male. There were neutrophilia and giant form platelets in all cases with toxic changes of WBC (Fig. 8). In spite of abnormal peripheral blood smear, following CBC showed normal platelet indices. Normal cellularity was seen in six out of seven bone marrow exam, and only in one case, hypocellularity was revealed. In three cases, mild shift to left maturation of myeloid cell was seen. In all cases, there were no increase of stem cells including megakaryocyte that meant overproduction of blood cells in bone marrow.

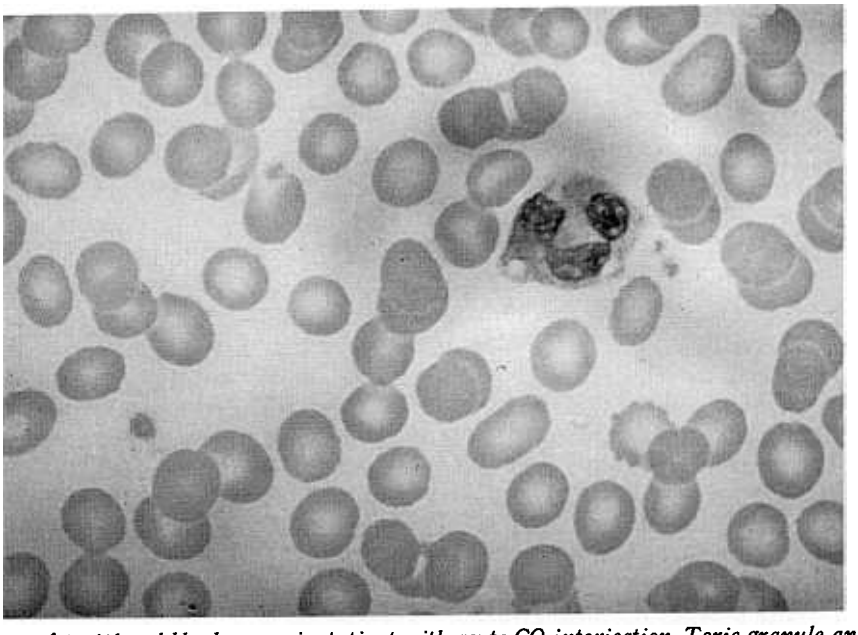

Fig. 8. Findings of peripheral blood smear in patient with acute CO intoxication. Toxic granule and vacuole were seen (Wright-Giemsa stain, × 1,000)

DISCUSSION

Many experimental exposures on animals and man have been performed using automotive exhaust, cigarette smoke, and pure CO, and some evaluations have been made concerning their effect on Hb and erythrocytic proportions in blood. The results of several such studies, when compared, appear somewhat discrepant. Rossiter (1942) commented on a study involving six students exposed to 400 ppm of CO for 68 days with resulting increase in Hb and RBC counts. On the other hands, Eckardt *et al.* (1972) insisted that very low level of CO, such as 20 to 60 ppm, did not alter Hb or Hct even when given chronically. Prigge and Hochrainer (1977) found that the exposure to 250 to 500 ppm of CO caused a sharp depression in fetal Hb and Hct, coincident with a marked reduction of the weight of fetus. But in general, later increases in Hb, Hct and RBC counts were reported (Jaeger and McGrath 1975; Penney and Thomas 1975; James *et al.* 1979; Penney *et al.* 1988). The earlier reports suggested that erythropoiesis was the main cause of increase in Hb, Hct and RBC counts in chronic CO exposure (Auerbach *et al.* 1969). Penney and Bishop (1978) reported Hb, Hct, and RBC counts showed initial increase after 4~7 days, reaching plateau after 25~30 days, and returned to control value after quitting exposure to CO. Polycythemia and hypervolemia caused by CO exposure resulted in cardiomegaly, especially right heart (James *et al.* 1979; Penney 1990).

But studies on hematologic changes in acute CO intoxication were meager. Ramsey (1969a) found that when his students were exposed weekly for varied times to varied concentration of CO, their Hb and Hct showed immediate postexposure increase and maintained for 2 months after exposure had ceased. Ramsey (1969b) also reported similar results in his animal study. Syvertsen and Harris (1972) commented that Hb and Hct increased after 48 hours in dogs exposing to 195 ppm of CO to

72 hours. But the pathogenesis of this rapid increase in Hb and Hct were controversial. Neither hemoconcentration due to shift of fluid (Asmussen and Nielsen 1945) nor erythropoiesis (Parving 1972) proved to be right until now. Smith and Landaw (1978) reported both hemoconcentration and erythropoiesis occurred in cigarette smokers. We found that Hb, Hct, and RBC increased on the onset day, but decreased immediately thereafter and showed only mild increase after the 5th day after the intoxication. The changes were all in normal ranges. Therefore we thought the initial increase was due to hemoconcentration rather than erythropoiesis, and following decrease might be related to intravenous fluid supply during the hospital stay.

Another characteristic hematologic change in CO intoxication is the toxic changes of WBC, such as initial leukocytosis and neutrophilia. Vanuxem *et al.* (1984) commented the relationship between CO concentration and leukocytosis in cigarette smokers, and Bridges *et al.* (1986) reported that CO rather than nicotine was related to leukocytosis. But Taylor *et al.* (1986) reported only nicotine concentration was related to WBC counts in both smoker and nonsmoker. All these studies were derived from chronic or repetitive low-level exposure of CO, resulting in chronic leukocytosis. In our study of acute CO intoxication, the initial leukocytosis and neutrophilia were thought to be similar with that of strenuous physical exercise, hypoxia, excessive stress, and in case of epinephrine injection (Davey and Nelson 1991). The neutrophilia resulted from increase in circulating neutrophils, whose nature were to stick to endothelium, was changed by cyclic AMP released by beta receptors of endothelium stimulated by epinephrine (Boxer *et al* 1980). The effects of acute CO intoxication upon platelets are not well known. Stonesifer *et al.* (1980) did a case report on thrombotic thrombocytopenic purpura in CO poisoning. He found decrease in platelet count, but not the mechanism. Mansouri and Perry (1982) showed that both cigarette smoke and CO pretreatment inhibited significant platelet release reaction. And they thought the dysfunction of platelet was due to CO. But other investigators (Madsen and Dyerberg 1984; Renaud *et al.* 1984) emphasized nicotine but not CO as the cause of platelet dysfunction in their experiment using bleeding time or clotting time. Although the changes of platelets we observed were within ranges of normal limit, the changes seemed to be similar with that of cyanotic congenital heart disease (Goldschmidt *et al.* 1974) or chronic obstructive pulmonary disease (Johnson *et al.* 1978) which were related to hypoxia. We observed continuing increase in platelet counts after initial decrease and normal megakaryocytes on bone marrow examination. It seems that the destruction of platelets was the cause of transient decrease in platelet counts, and not a decrease in production in the marrow.

The effects of acute CO intoxication upon bone marrow are also not well known. This study revealed only one case of shift to left maturation of myeloid cell and no other abnormal findings. Therefore we believe that the acute CO intoxication has no specific effects on the bone marrow, although our numbers of cases are small.

REFERENCES

Asmussen E, Nielsen M: Studies on the initial increase in O2-capacity of the blood at low O2-pressure. *Acta Physiol Scand 9: 75-87, 1945*

Auerbach O, Hammond EC, Kirman D, Garfinkel L: Emphysema produced in dogs by cigarette smoking. *JAMA 199: 89-94, 1969*

Boxer LA, Allen JM, Baehner RL, Amick V: Diminished polymorphonuclear leukocyte adherence. *J Clin Invest 66: 268-274, 1980*

Bridges RB, Wyatt RJ, Rehm SR: Effects of smoking on inflammatory mediators and their relationship to pulmonary dysfunction. *Eur J Respir Dis 69 (suppl 146): 145-152, 1986*

Choi IS: Clinical manifestations amd sequelae of carbon monoxide intoxication. *J Korean Med Assoc 34: 955-959, 1991*

Davey FR, Nelson DA: *Leukocytic disorders.* In Henry JB ed. *Clinical diagnosis and management by laboratory methods.* 18th ed. Philadelphia, WB Saunders, *1991, pp 677-689*

Eckardt RE, MacFarland HN, Alarie YC, Busey

WM: The biologic effect from long-term exposure of primates to carbon monoxide. *Arch Environ Health 25: 381-387, 1972*

Goldschmidt B, Sarkadi B, Gardos G, Matlary A: Platelet production and survival in cyanotic congenital heart disease. *Scan J Haematol 13: 110-115, 1974*

Haldane JBS: Carbon monoxide as a tissue poison. *Biochem J 21: 1068-1075, 1927*

Jaeger JJ, McGrath JJ: Hematological and biochemical effects of chronic CO exposure on the Japanese quail. *Respir Physiol 24: 365-372, 1975*

James WE, Tucker CE, Grover RF: Cardiac function in goats exposed to carbon monoxide. *J Appl Physiol 47 (2): 429-434, 1979*

Johnson TS, Ellis JH, Steele PP: Improvement of platelet survival time with oxygen in patients with chronic obstructive airway disease. *Am Rev Respir Dis 117: 255-257, 1978*

Madsen H, Dyerberg J: Cigarette smoking and its effects on the platelet-vessel wall interaction. *Scand J Clin Lab Invest 44: 203-206, 1984*

Mansouri A, Perry CA: Alteration of platelet aggregation by cigarette smoke and carbon monoxide. *Thromb Haemost (Stuttgart) 48: 286-288, 1982*

Parving HH: The effects of hypoxia and carbon monoxide exposure on plasma volume and capillary permeability to albumin. *Scand J Clin Lab Invest 30: 49-56, 1972*

Penney DG: Acute carbon monoxide poisoning: animal models: A review. *Toxicology 62: 123-160, 1990*

Penney DG, Bishop PA: Hematologic changes in the rat during and after exposure to carbon monoxide. *J Environ Pathol Toxicol 2: 407-415, 1978*

Penney DG, Davidson SB, Gargulinski RB, Caldwell-Ayre TM: Heart and lung hypertrophy, changes in blood volume, hematocrit and plasma renin activity in rats chronically exposed to increasing carbon monoxide concentrations. *J Appl Toxicol 8 (3): 171-178, 1988*

Penney DG, Thomas M: Hematological alterations and response to acute hypobaric stress. *J Appl Physiol 39: 1034-1037, 1975*

Prigge E, Hochrainer D: Effects of carbon monoxide inhalation on erythropoiesis and cardiac hypertrophy in fetal rats. *Toxicol Appl Pharmacol 42: 225-228, 1977*

Ramsey JM: The time course of hematological response to experimental exposures of carbon monoxide. *Arch Environ Health 18: 323-329, 1969a*

Ramsey JM: The immediate hematological response in the rat to experimental exposures of carbon monoxide. *J Physiol 202: 297-304, 1969b*

Renaud S, Blache D, Dumont E, Thevenon C, Wissendanger T: Platelet function after cigarette smoking in relation to nicotine and carbon monoxide. *Clin Pharmacol Ther 36: 389-395, 1984*

Rossiter FS: Carbon monoxide. *Industr Med 11: 586-589, 1942*

Smith JR, Landaw SA: Smokers' polycythemia. *N Eng J Med 298: 6-10, 1978*

Snyder BD, Loewenson RB, Gumnit R, Hauser AW, Leppick IE, Lassepas MR: Neurologic prognosis after cardiopulmonary arrest II. Level of consciousness. *Neurology 30: 52-58, 1980*

Stonesifer LD, Bone RC, Hiller FC: Thrombotic thrombocytopenic purpura in carbon monoxide poisoning: report of a case. *Arch Intern Med 140: 104-105, 1980*

Syvertsen GR, Harris JA: Erythropoietin production in dogs exposed to high altitude and carbon monoxide. *Am J Physiol 225: 293-299, 1972*

Taylor RG, Woodman G, Clarke SW: Plasma nicotine concentration and white blood cell count in smokers. *Thorax 41: 407-408, 1986*

Vanuxem D, Sampol J, Weiller PJ, M'Barki J, Grimaud C: Influence du tabagisme chronique sur les leukocytes. *Respiration 46: 258-264, 1984*

Whang SH, Choi IS: Studies on the clinical and laboratory findings of acute carbon monoxide intoxication. *J Korean Med Assoc 33: 997-1005, 1990*

Winter PM, Miller JN: Carbon monoxide poisoning. *JAMA 236: 1502-1504, 1976*