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Blood Sugar, Insulin, and Dextrose Tolerance in Albino Rat Treated with Carbon Monoxide.

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Claude Bernard opened the modern history of CO asphyxia with his publication on toxic substances in 1857. He is credited with recognizing that CO displaces the O_2 in oxyhemoglobin, producing COHb. In the same year he published data concerning hyperglycemia and glycosuria induced by CO asphyxia in man: Makami[1] reported similar findings in rabbits, cats and dogs.

Experimental—Albino rats were used throughout the experiments herein reported. The data concern:

1. The relation of the per cent saturation of the Hb with CO to the blood sugar level, subsequent to single exposures to the gas.

2. Insulin tolerance and dextrose tolerance after exposure to CO daily for several weeks.

The sugar analyses were made by the direct microtitration method of Miller and Van Slyke[2] using samples of tail blood. The degree of saturation of the Hb with CO was determined by the method of Sayers and Yant[3] using vena cava blood.

1. Table I shows the blood sugar-COHb relationship.

Pretreatment blood sugar levels in 68 control male rats averaged 100.1±0.05. The blood sugar rises as the COHb increases until at

TABLE I.
Blood Sugar in Relation to COHb.
(Animals exposed once to CO, then sacrificed.)

No. of rats	%COHb	Blood sugar. Mean in mg/100 cc	Range
68	0	100.1 ± 0.05	93.0-109.0
10	10	114.9 ± 1.80	109.7-116.3
12	20	115.8 ± 1.00	111.6-120.2
12	30	117.4 ± 0.50	114.3-121.2
12	40	125.6 ± 1.40	118.2-135.1
12	50	132.0 ± 1.60	123.4-143.9
10	60	154.8 ± 4.10	137.8-162.3
19	85	166.6 ± 2.10	139.0-183.4

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1 Mikami, Shozo, *Tohoku J. Exp. Med.*, 1926, **8**, 113.

2 Miller, Benjamin F., and Van Slyke, Donald D., *J. Biol. Chem.*, 1936, **114**, 583.

3 Sayers, R. R., and Yant, W. P., U. S. Bureau of Mines, Technical Paper 373.

TABLE II.
Insulin Tolerance in Controls and CO Treated.
Blood sugar readings in mg%.

	No. of determinations	Pre-injection levels	Post-injection levels				
			½ hr	1½ hr	2½ hr	3½ hr	Mean
Control	50	104	74	61	60	93	72±6.6
Actual reading		98	71	60	50	79	65
CO treated							
Initial difference							
6 mg% added	50	104	77	66	56	85	71

the lethal saturation, 85% COHb, the mean hyperglycemia is 166.6±2.10.

II. Glucose and Insulin Tolerance. Four-months-old female rats were exposed over periods of 5 to 12 weeks for one hour daily to 0.32% CO-air mixture. This treatment induces a COHb of 60% to 70% which falls to between 5% and 10% within 24 hours. Rats thus treated constantly carry CO in their blood. Polycythemia is induced and the hemoglobin values range from 16 to 20 g per 100 cc of blood.

Insulin Tolerance—Pre-injection blood samples were withdrawn, then 2 units of insulin per kilo of body weight were injected subcutaneously; blood sugar determinations were made at ½ hour intervals for 3½ hours. Since the pre-injection blood sugar values were 6 mg % lower in the CO treated than in the controls, for a true comparison, 6 was added to all readings for CO treated animals. Both readings are shown in Table II.

The number of blood samples per rat was limited because some animals went into insulin coma. The control hypoglycemic average was 72±6.6 mg%. In the CO treated rats it was 65 mg% preceding and 71 mg% after addition of 6 to the initial readings. This variation is within the standard range of deviation mathematically.

Dextrose Tolerance—Initial blood samples were withdrawn, then dextrose in 20% solution was injected intraperitoneally in doses of 2 g per kilo of body weight. Here the difference in pre-injection blood

TABLE III
Dextrose Tolerance in Controls and CO Treated.
Blood sugar readings in mg%.

	No. of determinations	Pre-injection levels	½ hr	1 hr	1½ hr	2½ hr	3½ hr	Total Mean
Controls	50	107	138	151	140	110	105	129±6.9
Actual reading		99	140	158	145	110	105	132
CO treated								
Initial difference								
8 mg% added	50	107	148	166	153	118	113	140

sugar levels was 8 mg%, hence we have added 8 to the readings for CO treated animals.

The control hyperglycemic average was 129±6.9 mg%. In the CO treated it was 132 mg%, but after addition of the initial difference it becomes 140 mg%. This difference is well beyond the range of normal variation.

Conclusions. 1. Acute carbon monoxide asphyxia raises the blood sugar in direct proportion to the percentage of COHb induced. 2. Repeated exposure to carbon monoxide seems not to change the insulin tolerance significantly but to reduce the dextrose tolerance below the limits of normal variation. It reduces the fasting blood sugar 6-8 mg below that of untreated litter mates.

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Spatial Configuration and Preparation of Canavanine.

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Canavanine is one of the few amino acids whose spatial configuration has not yet been established. Since this compound, found to exist in a free form in the Jack Bean, is a product of nature it would be of interest to establish its spatial configuration by the method of Lutz and Jirgensons.[1] This method is based on the observation of these workers that the naturally occurring amino acids show a change in specific rotation toward the positive with increasing amount of HCl.

Optical rotation measurements were carried out on 0.1 M canavanine solutions with varying molecular equivalents of HCl and NaOH. In Fig. 1 is shown the curve thus obtained. From this one readily sees that there is a decided shift toward the positive with increasing amount of HCl. Dextrorotatory canavanine therefore should be designated as l(+) canavanine.

Experimental. Preparation of Canavanine. Jack Bean meal is extracted several times with 50% alcohol (by weight). The extracts are concentrated to remove the alcohol and then made up to a volume approximately one-tenth the volume of the extracts with 5% sulfuric acid. To this acid solution is now added sufficient flavianic acid to precipitate the canavanine. The solution is warmed gently to redissolve

[1] Lutz, O., and Jirgensons, B., *Ber. chem. Ges.*, 1930, **63**, 448; 1931, **64**, 1221.