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CARTAS AL EDITOR

Influence of Ambient Temperature on Erythropoietin Production in Carbon Monoxide-Intoxicated Mice

Previous work has shown that carbon monoxide (CO) intoxication causes in the mouse a promt and large increase in erythropoietin (EPO) production (4). In those studies it was observed that day by day variations in the ambient temperature resulted in large differences in plasma EPO concentration in mice exposed to the same degree of CO-intoxication. This paper reports the results of further studies on the influence of ambient temperature on EPO production in CO-intoxicated mice.

One third of ml per gram of body weight of CO were injected under the skin in the dorsal area to form a gas pocket and groups of 25 mice each were kept at 32, 24, 18, 16 and 14° C respectively for a four-hour period and then bled to obtain plasma. Plasma EPO content was assayed in transfused-policythemic mice (2).

The highest EPO concentration was found in the plasma of mice maintained at 32° C. As the ambient temperature was lowered below 24° C, EPO production decreased abruptly and no EPO content was detectable in the plasma of mice kept at 16° C or below (table I).

This striking, change can not be fully explained by these studies. It should be mentioned however that O_2 consumption, as measured by the method of GRAD (1), for small rodents, was larger in the groups maintained at or above 24° C relative to O_2 consumption in mice kept at lower temperatures.

Since a better utilization of O_2 could have improved the tissue pO_2, this result appear conflictive with the current concept that postulates tissue hypoxia as the fundamental stimulous for EPO formation. The possibility of a more severe degree of tissue hypoxia in the groups exposed to low temperatures was confirmed by the measurement of this parameter using the gas pocket technique (3). Mice bearing an air gas pocket over the last 24 hours were

Table I. *Erythropoietic activity oxygen consumption, tissue pO_2 and heart rate of mice kept at various temperatures.*

Temperature (°C)	Erythropoietic activity per cent ^{59}Fe uptake	O_2 consumption	Tissue pO_2	Heart rate
32	35.5±2.4 *	3.9±0.9	18.0±1.8	94
24	30.0±1.9	3.7±1.1	16.0±1.8	88
22	24.0±1.8	3.8±1.0	16.0±1.4	88
18	2.9±0.6	3.0±0.9	14.0±1.0	70
16	1.0±0.2	2.7±0.6	12.0±1.1	64
14	0.7±0.08	2.4±0.6	11.4±0.9	59

* Mean ± standard error of the mean.

then injected intraperitoneally with 3 ml of CO. Three hours later the examination of O_2 tension in the gas mixture in the pocket showed the lower tissue pO_2 in the mice exposed to the lower range of temperature.

A tentative explanation for this dramatic and paradoxical effect of ambient temperature in CO-intoxicated mice may be based in a possible action of low temperatures on circulatory efficiency. Electrocardiographic tracing obtained in lead II, showed a significant decrease in heart rate and in the net amplitude of the ORS and T deflections. These changes that were more conspicuous within the 1 to 3 hour-interval that follows CO injection, might reflect a fall on the blood flow efficiency and a greater deterioration of O_2 transport. An extremely low tissue pO_2 would created an unfavorable condition for the utilization of O_2 in the metabolic process from which EPO formation depends. In this way, notwithstanding the fact that the hypoxemic condition would still be a potent stimulous for EPO production, the biochemical processes involved in the biogenesis of the hormone would be so seriously affected as to lead to its total abolition.

Although more evidence is needed to validate this hypothesis. This finding reflects the importance of controlling the ambient temperature in experiments designed either to evaluate EPO formation or to estimate the erythropoietic response elicited by endogenous EPO.

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E. E. GUIDI, MARÍA C. BUYS, ADRIANA MADANES, CARMEN MIRANDA, J. L. SCARO and M. A. CARRERA.

Instituto de Biología de la Altura
Facultad de Medicina
Universidad Nacional de Tucumán
S. S. de Jujuy (Argentina)

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