

Proceedings
of the
Society
for
Experimental Biology and Medicine

VOL. 55

FEBRUARY, 1944

No. 2

SECTION MEETINGS

CLEVELAND, OHIO

Lakeside Hospital

January 19, 1944

MINNESOTA

University of Minnesota

January 19, 1944

PACIFIC COAST

Western Regional Laboratory, Albany, Calif.

January 22, 1944

14469 P

Growth and Reproduction During Chronic Exposure to Carbon Monoxide.*

VIRGINIA SUHRIE AND A. T. MILLER, JR. (Introduced by John H. Ferguson).

From the Department of Physiology, School of Medicine, University of North Carolina, Chapel Hill.

In the course of studies on the role of heredity in determining individual differences in resistance to anoxia, observations have been made on growth and reproduction of rats during chronic anoxia produced by exposure to carbon monoxide. These experiments differ importantly from similar ones reported by other workers^{1,2,3,4} in that the concentration of carbon monoxide (0.04%) was below the level at which acute toxic symptoms or general impairment of health occur.

Monge⁵ discusses at length the deleterious influence on fertility resulting from residence at high altitudes. Miscarriages, abortions, sudden death of the new-born and complete sterility have been reported, both for the human and for domestic animals. In many cases (perhaps all) normal fertility is restored on return to lower altitudes. A fact of great interest is that the native inhabitants

of high altitudes (both man and domestic animals) have normal fertility, presumably the result of a slow process of acclimatization requiring generations for completion.

The authors know of no reports of impairment of fertility resulting from stagnant or histotoxic anoxia.

Methods. Newly weaned rats (Vanderbilt

* Aided by grants to one of us (A. T. M.) from the Sigma Xi Alumni Research Fund and from the Committee on Therapeutic Research, Council on Pharmacy and Chemistry, American Medical Association.

¹ Buresch, H., *Arch. f. Hyg.*, 1933, **109**, 211.

² Campbell, J. A., *Quart. J. Exp. Physiol.*, 1934, **24**, 271.

³ Williams, I. R., and Smith, E., *Am. J. Physiol.*, 1935, **110**, 611.

⁴ Killick, E. M., *J. Physiol.*, 1937, **91**, 279.

⁵ Monge, C., *Physiol. Rev.*, 1943, **23**, 166.

strain) were used. Litter mates were divided into 2 equal groups for experimental and control animals. A total of 24 males and 24 females was used for each group. The experimental animals were exposed to carbon monoxide, by a method previously described,⁶ 8 hours daily, except Saturday and Sunday.

Results. Sixteen of the control females have borne litters; 4 of them have borne 2 litters each. Of the 20 litters, 16 were weaned, averaging 5.0 to a litter (all litters were reduced to 6 at birth). This is somewhat below normal fertility, but the rats were taken from a newly established colony, unselected for breeding. During this same period there were 15 pregnancies in the experimental group. Four of these terminated in abortion and 11 litters were delivered at term. It was impossible to determine accurately the number of young in each litter, because the mother usually ate some of the young soon after birth. The average litter size (including stillborns) was 3.9. The average weight of the young was 3 to 5 g, while the average weight for the young of control animals was 5 to 7 g. In every case the mother refused to nurse her young, and death of all the young usually occurred in 1 to 3 days; the longest survival period was 8 days.

The growth curves for experimental and control animals were identical within limits of normal variation. At 114 days the average weights were: male controls 310 g, male

experimentals 300 g, female controls 176 g, female experimentals 179 g. These results differ from those of Campbell,² in which much higher concentrations of carbon monoxide were used. He observed that during the first 100 days, when acclimatization was developing, the mortality rate was high and growth lagged behind that of the controls. Killick⁴ observed a loss of weight in adult mice during acclimatization to gradually increasing concentrations of carbon monoxide.

Discussion. Our results emphasize the importance of Campbell's² insistence that acclimatization to carbon monoxide (or to any form of anoxia) cannot be considered complete unless fertility (pregnancy leading to the birth of normal young) is unimpaired. We would like to suggest, tentatively, that normal lactation leading to the weaning of healthy young be included, since, in at least one of our cases, a litter of normal size and average weight failed to nurse after 5 days and died in 8 days. Further studies are needed to determine the cause of the invariable failure of mothers exposed to carbon monoxide to nurse their young.

Conclusions. Rats exposed daily to carbon monoxide (0.04%) grow normally and have about the same incidence of pregnancy as do control litter mates. However, there is a tendency toward abortion, the average size of the litter and the average weight of the young at birth are subnormal, and the mothers invariably fail to nurse their young. The cause of this lactation deficiency is under investigation.

⁶ Miller, A. T., Jr., *J. Lab. and Clin. Med.*, 1943, **28**, 1854.

14470

Acetylation in Patients with Myasthenia Gravis. The Elimination of Para-amino Benzoic Acid.

CLARA TORDA AND HAROLD G. WOLFF.

From the New York Hospital, and Department of Medicine (Neurology) and Psychiatry, Cornell University Medical College, New York.

The weakness of certain skeletal muscles and the easy fatiguability observed in patients with myasthenia gravis is probably due to an insufficient production of acetylcholine (Torda

and Wolff¹). This decreased synthesis of

¹ Torda, C., and Wolff, H. G., *Science*, 1943, **98**, 224.