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Gross Muscular Activity and Temperature Regulation in the Restrained Rat.* (22509)

ROSCOE G. BARTLETT, JR.,† VERNON C. BOHR, GLENN L. FOSTER, MILTON A. MILLER, AND ROGER H. HELMENDACH.
Department of Physiology, College of Medical Evangelists, Loma Linda, Calif.

Several explanations have been offered for the production of restraint hypothermia(1-4). One which has received particular attention is the suggestion that lightly restrained animals become hypothermic because of restricted muscular activity(3,4). While studying restraint hypothermia it appeared that those animals which struggled more experienced a greater drop in body temperature. This paper reports an experiment in which an attempt was made to correlate quantitatively the degree of struggling with the body temperature drop of restrained rats maintained in the cold.

Methods and materials. Thirty-six healthy adult male Sprague-Dawley rats (225-275 g) were enclosed in individual loosely fitting restraining cages and placed in a cold room (0° C ± 1°) on pivoted platforms of a "ballistograph" so fashioned that movements of the animals were transmitted to rocker arms which vertically deflected writing levers. The frequency response was such that non-visible shivering would not have been recorded. No resonant effect which would give overshoot was observed. Gross shivering was not observed but would have been recorded as well as other gross movements. Records were obtained on a long paper kymograph with a paper speed of about 8 cm/hr. In order to quantitate the degree of struggling, the kymograph records were placed on a shadow box and the area within the struggling curves (*i.e.*, the curves drawn along the upper and lower borders of the kymograph records of the amount of struggling) was traced on 100% rag coordinate paper. These curves were then cut out and weighed on an analytical balance to the nearest mg. The weight of a known area of paper was found, and the weight of the cut-out curves converted to sq. cm.

Body temperatures of animals were obtained with indwelling thermometers inserted in the rectum to read high colonic temperature at a depth of 6-8 cm. These indwelling thermometers should be considered a portion of the stressing technic.

Results. A typical record from the tests (Fig. 1) shows that there was a marked relationship between the degree of struggling and thermolability. That those animals which

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† Present address: Laboratory of Physical Biology, N.I.H., Bethesda, Md.

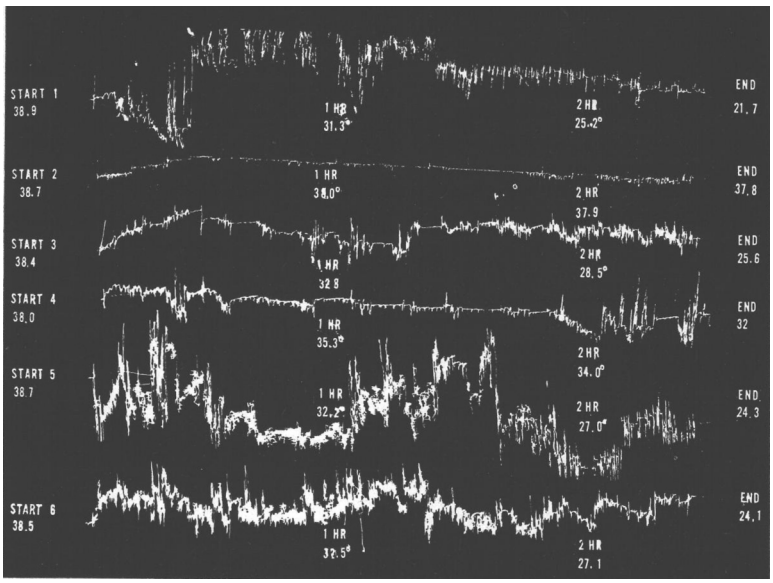

FIG. 1. Reproduction of a kymograph tracing from a typical test. Because the 6 records were obtained simultaneously, these 6 tracings were originally staggered. To improve the visual presentation, the tracings were separated and placed one above the other. The body temperature readings at the beginning, 1 hr, 2 hr, and at the termination of the tests are indicated on the records.

struggled more also became the more hypothermic is convincingly demonstrated in these records. The correlation coefficient between body temperature drop and degree of struggling was 0.56 $\pm$ 0.13, a significant level. When the fall in body temperature was plotted against the units of activity (both over a 2-hour period) for all animals a curve through the points rose to a plateau indicating that body temperature fall tended not to continue after the animals exceeded a certain activity level.

Discussion. The finding that marked and prolonged struggling seemed to limit the extent of body temperature drop is of interest. It appears that such struggling ultimately enables an animal to stabilize its temperature at a lower level. It is reasonable that if an animal's body temperature continues to fall it will ultimately restrict movement. It was observed that the lowering of body temperature did limit the amount of struggling in that an animal which struggled vigorously early in the test, thus experiencing a large drop in body temperature, struggled less later in the experiment.

It is not possible from the available data to determine a cause and effect relationship between struggling and the body temperature fall. It is likely that both struggling and thermolability are the effects of another cause. It has been demonstrated that those rats which are the more emotional become the more hypothermic when exposed to the stress of restraint in the cold(5). The relationship of struggling to emotionality is obvious, that of thermolability is not yet clear. It is known, however, that animals restrained in the cold consume more oxygen (and, therefore, presumably produce more heat) than do non-restrained, cold-exposed control animals(6). It may be, then, a matter of alteration of circulation within the skin which results in a greater net heat loss in spite of the increased heat production. Another possible relationship is that those animals which were rendered thermolabile by the stress of restraint experienced a drop in temperature which then initiated the struggling. If this were the sequence of events the struggling may actually have retarded the rate of body temperature fall. By inspection the records do not bear this out. It seems even less likely that the reverse relationship is true; *i.e.* struggling initi-

ated the body temperature fall.

The exact age of the animals was not known but their size (225-275 g) indicates that they were well over 60 days of age with well developed temperature regulating mechanisms(7).

The quantitative data presented here support our hypothesis that struggling and thermolability (hypothermia) are positively correlated in the restrained rat. We have no ready explanation for this apparent paradox. However, these data do negate the contention of some that body temperature drop in the restrained rat is a result of muscular inactivity.

Summary. Body temperature drop is positively correlated with gross body movement of rats restrained in the cold. It is concluded that restraint hypothermia cannot be explained on the basis of restricted muscular activity.

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Independence of Phosphatide Induced Hypercholesteremia and Hepatic Function.* (22510)

SANFORD O. BYERS AND MEYER FRIEDMAN.
(With technical assistance of Clarence Omoto and Warren Hayashi.)
Harold Brunn Institute, Mount Zion Hospital, San Francisco, Calif.

Previous studies(1-5) have suggested that the pathogenesis of various hypercholesteremias rested primarily on the retention and accumulation ("trapping") of cholesterol in plasma and plasma alone. Since phospholipid and/or neutral fat rises accompany all hypercholesteremic states, studies were done first with both these lipids together(6) and then with each lipid separately(7). The results showed that a prior plasma accumulation of either neutral fat or phospholipid was quickly succeeded by hypercholesteremia.

In the present study, the role of the liver in the hypercholesteremia induced by prior elevation of plasma phospholipid was investigated. This type of hypercholesteremia could be produced in the complete absence of functioning liver tissue.

I. *Cholesterol content of liver before and after induction of phosphatide induced hypercholesteremia.* To determine whether cholesterol accumulating in plasma following sustained hyperphospholipidemia(7) was accompanied by hepatic depletion of cholesterol, the following experiments were done.

Methods. Fifty male rats of Long Evans strain (Wt: appx. 315 g) between 14-18 weeks of age and which had been starved for 18 hours were used. Fifteen of these were injected intravenously with 3.0 ml of a 2% soybean phospholipide† solution containing 5% dextrose, and then injected continuously at an approximate rate of 1.0 ml per hour for 24 hours with the same concentration of phosphatide solution. Plasma samples obtained before and 24 hours after the beginning of

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† This phospholipide mixture was furnished by Glidden Co., labeled "Soya Lecithin, 'oil-free' RG Brand." Prior to injection, the soy phosphatides were freed from $Ca_3(PO_4)_2$. Phosphatides were further purified before injection into 10 of the 15 rats by successive reprecipitation from diethyl ether and from glacial acetic acid. The reprecipitated product showed no apparent sterol content by our analytical methods.