

Sodium Pentobarbital on Temperature and Heart Rate of Rats Subjected to Cold.* (29822)

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A study was reported(1) of the effects of a standard dose of sodium pentobarbital on the body temperatures and heart rates of rats before and after subjection to 5°C for 46 hours. Normal, thyroidectomized and hypermetabolic rats were used. It was found that after subjection to cold the body temperatures and heart rates had more ability to recover after the barbiturate administration than in rats without previous exposure to cold. The thyroidectomized rats did not recover before or after subjection to cold. The hypermetabolic rats for the most part had the property of recovering in the cold after the barbiturate. All of these tests were made with the rats in a cold air bath at 5°C.

This work has been extended by carrying out similar experiments with the duration of exposure to 5°C varying from 16 hours to 45 days. Also repetition of the administration of the barbiturate and subjection to cold was carried out in the rats previously subjected to cold and then allowed to remain at room temperature for varying periods. These results have been reported in abstract(2).

Methods. White male albino rats were obtained from Carworth Farms. The standard test for each experiment was to inject the rat intraperitoneally with 4.8 mg of sodium pentobarbital (Nembutal Sodium, Abbott) in 1 ml/100 g body weight and then to place the rat in a divided wire cage attached to leads to a portable electrocardiograph (Sanborn) in order to obtain heart rates. A resistance thermometer (Tele-thermometer, Yellow Springs Instrument Co.) was inserted 6 cm to 8 cm into the rectum. The rat in this cage was placed in a refrigerator with the air temperature maintained at 5°C by a constant temperature device. Body temperature and heart rate were recorded at once

after placing the rat in the refrigerator, then every 15 minutes for a period of hours. This procedure is called "the standard experiment." The rats were then subjected to cold by placing them at 5°C for periods varying from 16 hours to 49 days. They were removed for injection of the sodium pentobarbital, placed in the wire cage, and immediately returned to the refrigerator. It had been demonstrated that repetition of the injection of barbiturate and subjection to cold did not alter the response of body temperature and heart rate from that of the previous experiment. Therefore, the results are not due to modification of the response to the barbiturate on the second injection but due to the exposure to cold between the experiments. All of the rats weighed approximately 300 g. It is very important to use rats of a standard weight both from the standpoint of their reaction to cold and to their response to the barbiturate.

Results. Body temperatures and heart rates of normal rats under sodium pentobarbital and 5°C respond in one of 3 ways (Fig. 1): The usual response is a rapid fall of body temperature and heart rate. These rats were removed from the cold when their body temperatures fell to 27°C for, from previous experiments, they did not recover if the body temperature fell much below this value. In a few rats, there is a plateau reached on which body temperatures and heart rates are maintained followed by a late rise or additional fall. The third response is a recovery of body temperatures and heart rates during the exposure to cold. The results are reported in terms of these 3 responses. In tests on 58 normal rats (Fig. 2, A), in 87.9% body temperatures and heart rates fell rapidly and the experiments were discontinued. In 5.2% there was a plateau while in 6.9% there was a recovery. When 16 rats were placed in an air bath at 5°C for 16-24 hours before experiment (Fig. 2, B), the results changed,

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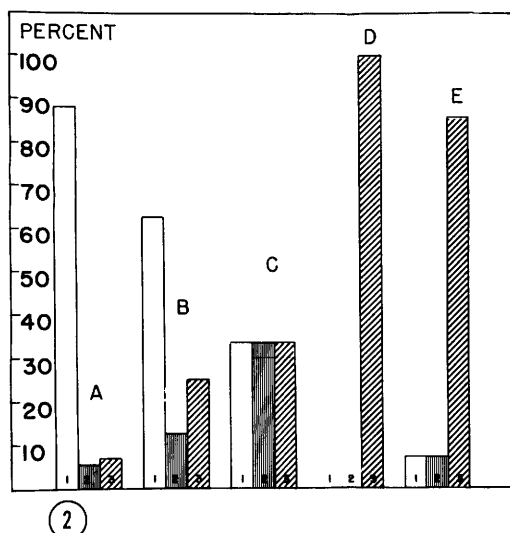
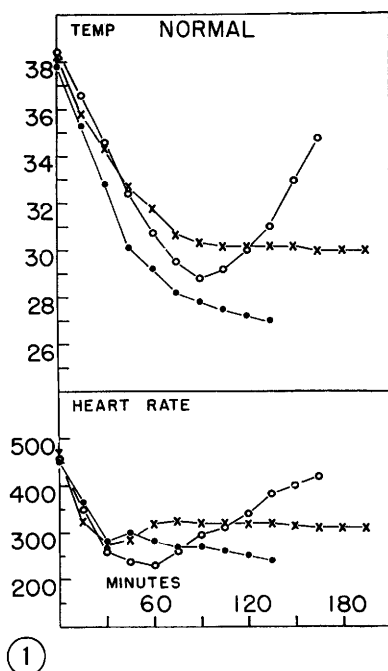


FIG. 1. Responses of rats to 5°C after sodium pentobarbital. Abscissae, min; ordinates, upper curves, body temperature; lower curves, heart rate per min. I.P. injection of 4.8 mg of sodium pentobarbital per 100 g body weight. The 3 types of responses are illustrated (●) fall in body temperature, plateau (×) and recovery (○). Fall in heart rate (●) was not so marked as in body temperature, while plateau (×) and recovery (○) followed changes in body temperature.

FIG. 2. Responses of rats to 5°C after sodium pentobarbital and previous exposure to cold. Ordinates, % of total group. Open blocks, rats having marked fall in body temperature and heart rate;

blocks with vertical lines, rats having a plateau; blocks with cross lines, rats having recovery. A. Normal rats without previous exposure to cold. B. Normal rats with 16 to 24 hours previous exposure to cold. C. Normal rats with 46 hours previous exposure to cold. D. Normal rats with 37 to 49 days previous exposure to cold. E. Normal rats with 37 to 49 days exposure to cold and then removed to room temperature for periods of 30 to 83 days before the standard experiment.

with more rats recovering and fewer having the rapid fall. When 18 rats were kept for 46 hours (Fig. 2, C) (results described previously(1)), there were still more recoveries. When 16 rats were kept at 5°C for periods varying from 37 to 49 days (Fig. 2, D), all of the rats recovered in the standard test. However, it was noticed in the rats that recovered, that generally there was a rise in heart rate preceding the rise in body temperature. When the 14 rats from the latter group were allowed to remain at room temperature (27°C) for periods of 30 to 83 days (Fig. 2, E), most of these animals retained their ability to recover. In only one of 14 rats was body temperature lowered to 27°C and one had a plateau. Heart rates followed very closely the changes in body temperature and are not reported in Fig. 2.

Conclusions. It was found that under a standard test of subjecting a rat to sodium pentobarbital and 5°C, previous exposure to cold modified the body temperatures and heart rates. After 16 hours previous exposure the rats had more ability to recover than did rats without previous exposure. After 37 to 45 days previous exposure, all of the rats had the ability to recover their body temperatures and heart rates. When these rats were allowed to remain at room temperature for periods of 30 to 83 days, most of the rats retained their ability to recover. These results are of interest from the standpoint of modification of a drug response to cold exposure which may be due to the cold exposure affecting the metabolic rate of the pentobarbital. However, no definite conclusions can be made as to the mechanisms involved in these results.

1. Gemmill, C. L., Browning, K. M., *Am. J. Physiol.*, 1962, v203, 758.

2. ———, *Va. J. Sci.*, 1964, v15, 340.