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Effects of a Tranquilizer on Body Temperature. (29105)

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Since the mechanisms of body temperature regulation of homoiotherms are characteristically altered or ablated by the effects of general anesthetics(1), studies of thermal control are better performed on unanesthetized animals. The recent development of a variety of tranquilizers [pharmacological agents which reduce activity and agitation and make subjects more docile(2)] makes available a group of materials offering the hope of obtaining quiescent animal preparations retaining thermoregulatory ability. Earlier studies have investigated some of these materials as they produce changes in behavior(3,4,5), physiology(6,7,8), or to a more limited extent temperature regulation (9,10,11,12) in various species. The present program was designed to determine the effects of propiopromazine hydrochloride (Tranvet, Abbott Laboratories) on thermoregulatory ability in dogs exposed to 3 environmental temperatures.

Methods. Forty-eight 2-hour experiments were conducted using 4 young, adult mongrel dogs (11.5 to 16 kg) each exposed twice to 3 environmental temperatures: 4.4°C (40°F), 23.9°C (75°F), and 37.8°C (100°F), at 50% relative humidity, without the use of a tranquilizer and twice to each temperature tranquilized with 2.2 mg/kg propiopromazine (intravenously). No animal was given tranquilizer within 48 hours of a previous injection. All animals were placed in the environmental chamber with body tem-

peratures elevated by moderate exercise to force regulation and to provide more comparable initial rectal temperatures within the group. The animals were unrestrained, but were restricted to a small area by a collar and a short rope. Rectal temperature was continuously monitored by a thermistor probe inserted 10 cm into the lower colon and recorded on a Grass Polygraph Recorder (model 5C) through an appropriate bridge.

In addition to the above experiments, one animal was exposed to each of the environmental temperatures without prior exercise to indicate the influence of this single variable on internal body temperature.

Results. During a 2-hour exposure to an ambient temperature of 23.9°C, untranquilized animals fell from the average initial temperature of 39.23°C to 38.31°C (−0.92°C) and tranquilized animals decreased rectal temperature from (39.15°C to 38.15°C) (−1.00°C) in the same period (Fig. 1A).

At 37.8°C rectal temperatures of the tranquilized animals rose from 39.35°C to 39.61°C (+0.26°C), while the untranquilized group dropped rectal temperature from 39.44°C to 38.88°C (−0.56°C) (Fig. 1B).

At 4.4°C the tranquilized dogs dropped internal temperature from 39.32°C to 38.25°C (−1.07°C) in 2 hours with a low temperature of 38.02°C (−1.30°C) reached at 80 minutes. The control animals, with an initial temperature of 39.04°C demonstrated regulation at a level of 38.60°C (−0.44°C) after

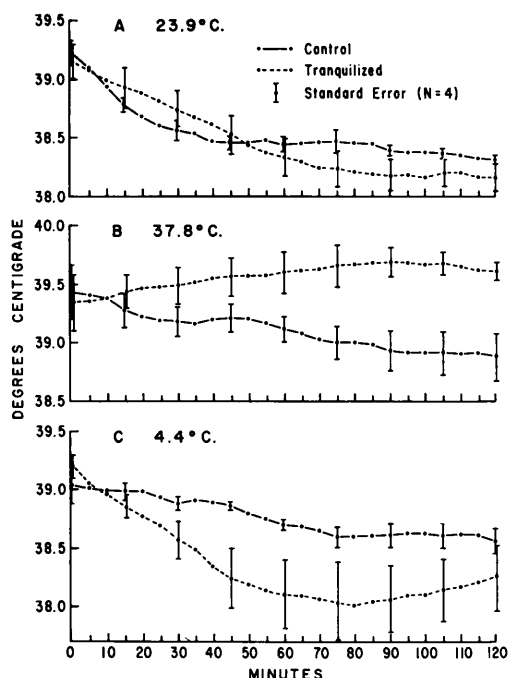


FIG. 1. Rectal temperatures of control and tranquilized animals during exposure to three environmental temperatures.

75 minutes and remained near that level throughout the remainder of the exposure (Fig. 1C).

Testing without prior exercise indicated that rectal temperatures similar to those recorded after exercise were reached within 25 minutes at 23.9°C, within 45 minutes at 37.8°C and within one hour at 4.4°C. Thus, even though the initial rectal temperatures without exercise were, on the average, 0.74°C lower than with exercise, the final body temperatures were the same at all environmental temperatures.

Discussion. Although small differences are reported between tranquilized and control dogs during exposure to an ambient temperature of 23.9°C (Fig. 1A), propiopromazine appeared to reduce thermoregulatory ability during thermal stress (4.4°C and 37.8°C) (Fig. 1B, 1C). During cold exposure, the drop in internal body temperature could be due to peripheral vasodilatation and consequent incurred heat loss mediated through sympatholytic actions of this phenothiazine

derivative(1,2). A further contributory factor could be the loss of muscle tone and ability to shiver, thus reducing heat production. During heat exposure, the rise in internal body temperature could be due to the reduction of contractility of skeletal muscles, decreasing panting. Panting appeared to be less pronounced in the tranquilized animals.

It would appear that when panting, shivering or vasomotor activity are not of critical importance, *i.e.*, during exposure to 23.9°C, the tranquilized dog is able to maintain body temperature as well as the non-tranquilized animal. No significant difference exists at any time interval at even the 0.10 level (Table I). However, when thermal defense mechanisms become important, *i.e.*, during exposure to 4.4°C and 37.8°C, the tranquilized dog is not able to maintain body temperature as well as the control animal. For the heat exposure, a 0.10 level of significance appears at 40 minutes and is at the $\leq .001$ level for the last 50 minutes of exposure. During the cold exposure the level of significance is $\leq .01$ at 40 minutes and increases gradually, with the difference during the last 20 minutes again being above the 0.10 level (Table I).

These results for propiopromazine are similar to those reported for another phenothiazine derivative, chlorpromazine(2), except that propiopromazine did not show the marked hypothermia produced at non-stressful environmental temperatures. However, both agents apparently interfere with heat loss and heat conservation due to a possible direct effect on the diencephalon(1,2). A similar response has been shown for chlor-

TABLE I. Analysis of Variance.

Level of significance for difference between control and tranquilized animals.

Time in min.	23.9°C	37.8°C	4.4°C
0	.68	.79	.40
20	.24	.26	.11
40	.41	.09	.01*
60	.52	.02*	.04*
80	.12	.001*	.08
100	.12	.001*	.08
120	.18	.001*	.35

* = $\leq .05$ level of significance.

promazine during cold exposure of hamsters (11).

The use of propiopromazine and chlorpromazine would, therefore, seem contraindicated in tests involving thermal stress. However, this study indicates that propiopromazine shows less interference with temperature regulation than chlorpromazine at a non-stressful environmental temperature.

These tranquilizers could be of benefit as an adjunct to the induction of hypo- or hyperthermia in animals without the artifacts introduced by emotional excitation or general anesthesia.

Summary. Four young adult mongrel dogs were exposed twice untranquilized to each of 3 environmental temperatures: 4.4°C, 23.9°C and 37.8°C and exposed twice tranquilized with 2.2 mg/kg propiopromazine hydrochloride. Rectal temperatures were monitored and recorded continuously during 2-hour exposures. Little difference was noted in rectal temperature response for tranquilized and untranquilized animals at the 23.9°C exposure. Tranquilized animals showed a greater decline in internal temperature at an environmental temperature of 4.4°C than control and when tranquilized showed a rise in rectal temperature during heat exposure (37.8°C)

while control animals showed a decline. These results indicate an impairment in both heat loss and heat conservation mechanisms in the tranquilized animals during thermal stress, but little, if any alteration of temperature control at a non-stressful ambient temperature.

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Anti-Fibrinolytic Effect of ϵ -Aminocaproic Acid as Measured by *in vivo* Clot Lysis.* (29106)

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ϵ -Aminocaproic acid (EACA) was first described as *in vitro* fibrinolytic inhibitor in a British patent issued to a Japanese firm in

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1957(1). The anti-fibrinolytic action has been confirmed by other investigators(2,3). *In vitro* studies by Alkjaersig *et al*(4) and by Troll and Sherry(5) have shown that plasminogen activation includes a proteolytic step in which bonds between lysine and other amino acids are split, and that lysine and ornithine both act as inhibitors of this activation. In view of the close structural resemblance of EACA to these compounds, Sherry and his associates(2) suggested that the main inhibitory action of EACA is on