THE EFFECTS OF A TRANQUILIZER ON BODY TEMPERATURE

63-23

FEDERAL AVIATION AGENCY
CIVIL AEROMEDICAL RESEARCH INSTITUTE
AERONAUTICAL CENTER
OKLAHOMA CITY, OKLAHOMA

OCTOBER 1963

Civil Aeromedical Research Institute, Federal Aviation Agency Oklahoma City, Oklahoma. CARI Report 63-23. **THE EFFECTS OF A TRANQUILIZER ON BODY TEMPERATURE** by E. Arnold Higgins, P. F. Iampietro, Thomas Adams, and D. D. Holmes.

1. Drugs
2. Temperature Regulation
3. Body Temperatures

Four young adult mongrel dogs were exposed twice untranquilized to each of three 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 two 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.

Civil Aeromedical Research Institute, Federal Aviation Agency Oklahoma City, Oklahoma. CARI Report 63-23. **THE EFFECTS OF A TRANQUILIZER ON BODY TEMPERATURE** by E. Arnold Higgins, P. F. Iampietro, Thomas Adams, and D. D. Holmes.

1. Drugs
2. Temperature Regulation
3. Body Temperatures

Four young adult mongrel dogs were exposed twice untranquilized to each of three 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 two 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.

Civil Aeromedical Research Institute, Federal Aviation Agency Oklahoma City, Oklahoma. CARI Report 63-23. **THE EFFECTS OF A TRANQUILIZER ON BODY TEMPERATURE** by E. Arnold Higgins, P. F. Iampietro, Thomas Adams, and D. D. Holmes.

1. Drugs
2. Temperature Regulation
3. Body Temperatures

Four young adult mongrel dogs were exposed twice untranquilized to each of three 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 two 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.

Civil Aeromedical Research Institute, Federal Aviation Agency Oklahoma City, Oklahoma. CARI Report 63-23. **THE EFFECTS OF A TRANQUILIZER ON BODY TEMPERATURE** by E. Arnold Higgins, P. F. Iampietro, Thomas Adams, and D. D. Holmes.

1. Drugs
2. Temperature Regulation
3. Body Temperatures

Four young adult mongrel dogs were exposed twice untranquilized to each of three 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 two 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.

THE EFFECTS OF A TRANQUILIZER ON BODY TEMPERATURE

E. ARNOLD HIGGINS, P. F. IAMPIETRO, THOMAS ADAMS AND D. D. HOLMES

Environmental Physiology Branch

63-23

FEDERAL AVIATION AGENCY
CIVIL AEROMEDICAL RESEARCH INSTITUTE
AERONAUTICAL CENTER
OKLAHOMA CITY, OKLAHOMA

OCTOBER 1963

THE EFFECTS OF A TRANQUILIZER ON BODY TEMPERATURE

E. ARNOLD HIGGINS, P. F. IAMPIETRO, THOMAS ADAMS and D. D. HOLMES

ABSTRACT

Four young adult mongrel dogs were exposed twice untranquilized to each of three 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 two hour exposures. Little difference was noted in rectal temperature response for tranquilized and untranquilized animals at 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 temperaure control at a non-stressful ambient temperature.

Since the mechanisms of body temperature regulation of homiotherms 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 three environmental temperatures.

Methods

Forty-eight two hour experiments were conducted using four young, adult mongrel dogs (11.5 to 16 kg) each exposed twice to three 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 previous injection. All animals were placed in the environmental chamber with body temperatures 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 two 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 two 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 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 (Figs. 2A, 2B, 2C). 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) (Figs. 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. As indicated in Table I, no significant difference exists at any time interval at even the 0.10 level. 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 35 minutes and is at the $\leq$ .001 level for the last 50 minutes of exposure. During cold exposure the level of significance is $\leq$ 0.10 at 25 minutes, $\leq$ 0.01 at 35 to 45 minutes and increases until at 105 minutes the difference is again 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 nonstressful 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 chlorpromazine 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.

TABLE I

ANALYSIS OF VARIANCE
LEVEL OF SIGNIFICANCE FOR DIFFERENCE
BETWEEN CONTROL AND TRANQUILIZED ANIMALS

Time in minutes	23.9°C	37.8°C	4.4°C
0	0.68	0.79	0.40
5	0.90	0.83	0.80
10	0.70	0.97	0.84
15	0.44	0.48	0.15
20	0.24	0.26	0.11
25	0.24	0.16	0.09*
30	0.32	0.15	0.06*
35	0.41	0.08*	0.01α
40	0.41	0.09*	0.01α
45	0.68	0.09*	0.01α
50	0.95	0.07*	0.02**
55	0.56	0.09*	0.07*
60	0.52	0.02**	0.04**
65	0.35	0.04**	0.07*
70	0.24	0.01α	0.07*
75	0.18	0.001ε	0.12
80	0.12	0.001ε	0.08*
85	0.12	0.001ε	0.10*
90	0.15	0.001ε	0.08*
95	0.15	0.001ε	0.08*
100	0.12	0.001ε	0.08*
105	0.16	0.001ε	0.11
110	0.18	0.001ε	0.12
115	0.18	0.001ε	0.18
120	0.18	0.001ε	0.35
Average	0.31	0.03**	0.10*

* = ≤ .10 level of significance; ** = ≤ .05 level of significance;
α = ≤ .01 level of significance; ε = ≤ .001 level of significance.

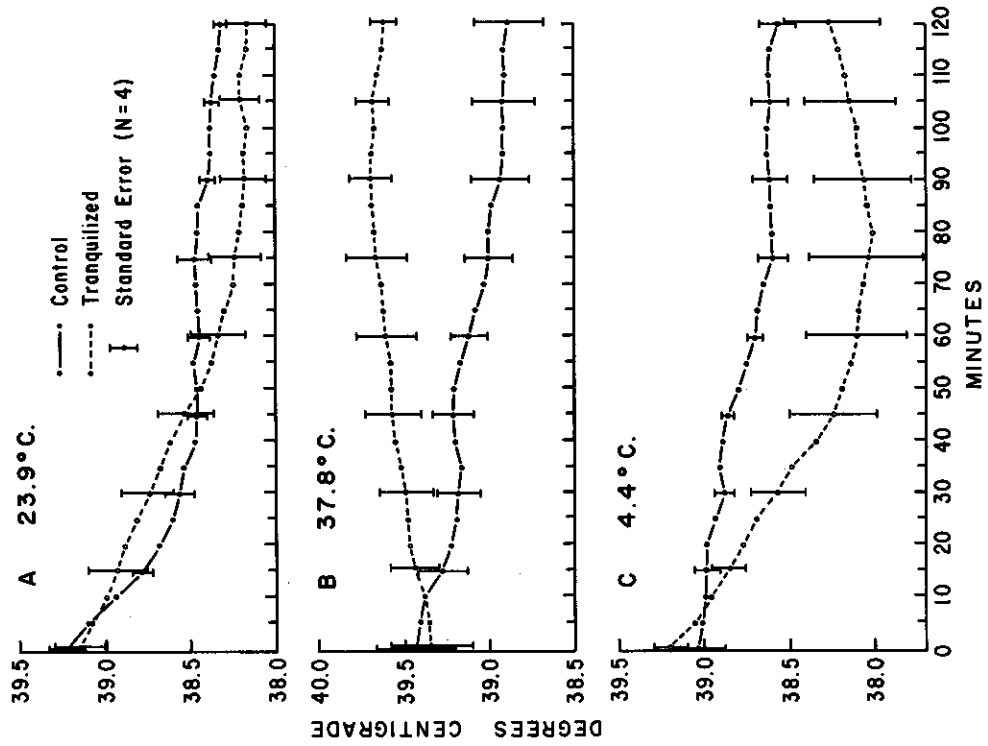

FIGURE 1. Rectal temperatures of control and tranquilized animals during exposure to three environmental temperatures.

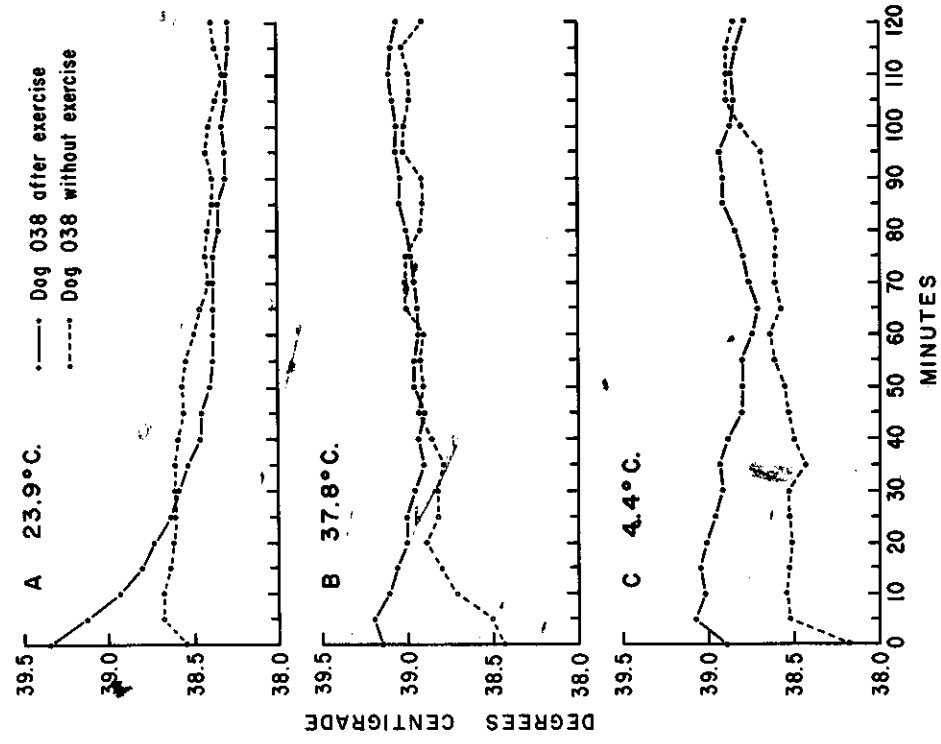

FIGURE 2. Rectal temperatures of one dog with and without prior exercise during exposure to three environmental temperatures.

REFERENCES

1. Grollman, Arthur, *Pharmacology and Therapeutics*, Lea and Febiger, Philadelphia, 1962, pp. 75 & 247.
2. Drill, V. A., *Pharmacology in Medicine*, McGraw-Hill Book Co., Inc., New York, 1958, pt. 7, Ch. 24.
3. Rickels, K., Snow, L., Baumm, C., Mock, J., *Amer. J. Psychiat.*, 1963, v119, 1093.
4. Symposium, *Ann. N. Y. Acad. Sci.*, 1957, v66, 417.
5. Tuteur, W., *Amer. J. Psychiat.*, 1963, v119, 776.
6. Lear, E., Chiron, A. E., Pallin, I. M., *New York J. Med.*, 1963, v63, 409.
7. Supek, A., Uroic, B., Gjiris, V., Marjan, N., *J. Pharm. Pharmacol.*, 1962, v14, 284.
8. Wortis J., Jackim, E., *Amer. J. Psychiat.*, 1962, v119, 363.
9. Hoffman, R. A., *Amer. J. Physiol.*, 1958, v195, 751.
10. Hoffman, R. A., *ibid*, 1958, v195, 755.
11. Hoffman, R. A., Zarrow, M. X., *ibid*, 1958, v193, 547.
12. Laverty, R., *J. Neurochem.*, 1963, v10, 151.

☆ U. S. GOVERNMENT PRINTING OFFICE : 1964 O - 719-718

Civil Aeromedical Research Institute, Federal Aviation Agency Oklahoma City, Oklahoma. CARI Report 63-23. **THE EFFECTS OF A TRANQUILIZER ON BODY TEMPERATURE** by E. Arnold Higgins, P. F. Iampietro, Thomas Adams, and D. D. Holmes.

1. Drugs
2. Temperature Regulation
3. Body Temperatures

Four young adult mongrel dogs were exposed twice untranquilized to each of three 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 two 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.

Civil Aeromedical Research Institute, Federal Aviation Agency Oklahoma City, Oklahoma. CARI Report 63-23. **THE EFFECTS OF A TRANQUILIZER ON BODY TEMPERATURE** by E. Arnold Higgins, P. F. Iampietro, Thomas Adams, and D. D. Holmes.

1. Drugs
2. Temperature Regulation
3. Body Temperatures

Four young adult mongrel dogs were exposed twice untranquilized to each of three 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 two 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.

Civil Aeromedical Research Institute, Federal Aviation Agency Oklahoma City, Oklahoma. CARI Report 63-23. **THE EFFECTS OF A TRANQUILIZER ON BODY TEMPERATURE** by E. Arnold Higgins, P. F. Iampietro, Thomas Adams, and D. D. Holmes.

1. Drugs
2. Temperature Regulation
3. Body Temperatures

Four young adult mongrel dogs were exposed twice untranquilized to each of three 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 two 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.

Civil Aeromedical Research Institute, Federal Aviation Agency Oklahoma City, Oklahoma. CARI Report 63-23. **THE EFFECTS OF A TRANQUILIZER ON BODY TEMPERATURE** by E. Arnold Higgins, P. F. Iampietro, Thomas Adams, and D. D. Holmes.

1. Drugs
2. Temperature Regulation
3. Body Temperatures

Four young adult mongrel dogs were exposed twice untranquilized to each of three 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 two 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.