Osmotic Thirst Suppression during 2,4-Dinitrophenol (DNP) Hyperthermia in the Dog

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Summary. The effect of generalized body hyperthermia elicited by intravenous infusion of 2,4-dinitrophenol (DNP) on the reactivity of the thirst mechanism to osmotic stimuli was examined in conscious dogs.

DNP increased deep body temperature by $1.53 \pm 0.18^\circ C$ in 18 out of 20 experiments. Impairement of thirst sensation was observed at the same time. The animals did not drink enough water to compensate for its total and evaporative loss. In consequence water deficit developed, reaching maximum value of $2.7 \pm 0.6\%$ of body weight. The deficit was accompanied by an increase in plasma osmolarity, plasma protein concentration and hematocrit. A significant correlation between evaporative water loss and water deficit as well as between increase in deep body temperature and water deficit was found.

The cellular dehydration developed in the course of DNP hyperthermia was higher by $3.3 \pm 0.6\%$ of intracellular water ($P < 0.001$) than that which was necessary to elicit drinking under conditions of normothermia.

It is concluded that DNP hyperthermia changes the osmotic reactivity of the thirst mechanism so that the body fluids osmolarity is regulated at a higher level. This finding is discussed with regard to voluntary dehydration.

Key words: Hyperthermia — Osmotic Thirst — Voluntary Dehydration.

Impairement of thirst sensation resulting in voluntary dehydration is often observed in man [2,8,10,17] and animals [7,11] exposed to a high ambient temperature, especially when the exposure is accompanied by physical exercise.

As heating the preoptic region suppresses osmotic thirst in the dog [23,24] a hypothesis was advanced [24] that this is an increase in body temperature, particularly in the basal forebrain that accounts for a phenomenon of voluntary dehydration.

A locally applied heating of the brain tissue is an artificial situation, in which the temperature increase in the small area often results in lowering of the whole body temperature. Therefore it was attempted to examine the reactivity of the thirst mechanism to osmotic stimuli and thereby to assess its efficiency in maintaining water balance under
conditions of generalized body hyperthermia elicited by 2,4-dinitrophenol (DNP), simulating the increase in internal body temperature during physical exercises.

DNP uncouples oxidation and phosphorylation in the mitochondria [19]. This results in an increase in tissue metabolism and oxygen consumption. It was claimed that the hypermetabolism induced by DNP is essentially similar to that occurring during physical exercises [15]. The hyperthermia developing as a result of heat overproduction stimulates the heat dissipating mechanisms. It increases evaporative water loss and raises body fluids osmolality. The latter change is expected to stimulate thirst and enhance water intake in order to prevent severe dehydration. DNP hyperthermia experimental design enables also to induce an increase in body temperature without the effect of heat on skin thermoreceptors, which cannot be separated in the case of hyperthermia developing during an exposure to a high ambient temperature.

Material and Methods

Animals. Experiments were performed on 12 conscious, mongrel male dogs weighing 12.4–22.6 kg, trained to rest quietly on a Pavlovian stand. The animals were kept fasting for 18 hrs preceding the experiments, but they had free access to water before and during the experiments.

Two variants of experiments were carried out. In series I the ability of the dogs to replenish body water loss in the course of DNP hyperthermia was examined in 18 experiments on 10 animals. In series II the osmotic reactivity of the thirst mechanism under conditions of normothermia was measured in 9 out of 10 dogs used in series I. The order of experiments of series I and II varied at random.

Experimental Design. Experiments were done at the same time of the day at ambient temperature ranging from 20 to 25°C and relative air humidity of 40–50%. Series I. The experiment started at 9 a.m. The dog was standing on a stand for 30 min. During this time a semiconductor thermosensitive probe was placed to measure rectal temperature (T<sub>r</sub>) and the hypothalamic temperature sensor was connected to milivoltometer to measure hypothalamic temperature (T<sub>h</sub>). A 1.2 mm polyethylene catheter was introduced into the saphenous vein for taking blood samples. A bladder catheter was introduced through the urethra, the bladder was emptied by air flushing and the urine output during 20 min was measured. The blood sample to measure hematocit (Hct), plasma osmolarity (P<sub>osm</sub>) and plasma protein concentration (P<sub>p</sub>) was drawn at the end of this period. At 9.30 a.m. the dog was weighed and an intravenous infusion of 100 mg/100 ml 2,4-dinitrophenol in 0.9% NaCl at a rate of 10 mg/min was started. The infusion was stopped when the dose of DNP infused reached 10 mg/kg. The blood sample was taken at the end of the infusion. At 10.40 the bladder was catheterized again and volume of urine was measured. Diuresis was also measured during 20 min which followed and the urine sample was taken. At 10.50 the blood sample was taken. At 11.00 body weight was measured. The schedule from 10.40 to 11.00 was repeated every hour until body temperature went down to the preinfusion level. Rectal and hypothalamic temperatures were recorded every 5 min. The incidence and size of the individual draughts of water as well as the cumulative water intake were measured throughout the whole experiment.