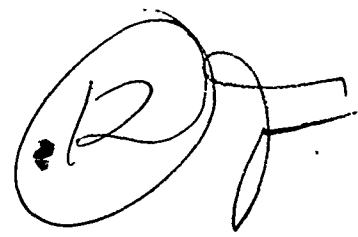


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**A STUDY OF EFFECTS OF HYPERTHERMIA ON LARGE,
SHORT-HAIRED MALE DOGS: A SIMULATED AIR
TRANSPORT ENVIRONMENTAL STRESS**

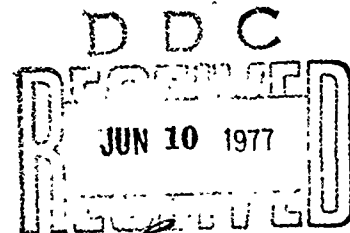
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16. Abstract When dogs are shipped by air transport, they can encounter environmental temperatures as high as 130.0° F during the summer months. Normally, little concern is given to the effects of hyperthermia on animals; however, heat-induced hyperthermia can be a major problem in dogs. To assess some aspects of the heat stress problem, 20 dogs were exposed to an ambient temperature of 130.0° F for 30 minutes--10 dogs at 15% percent relative humidity and 10 at 35% percent relative humidity. Transient and permanent changes were seen; however, no dogs died from exposure. All dogs exhibited increases in heart rate, rectal temperature, blood pH, hemoglobin, packed cell volume, and red blood cell count while body weight and blood carbon dioxide decreased. There were also differences between the two groups for blood pH, blood carbon dioxide, rectal temperature, and weight loss. The major histological tissue changes attributed to hyperthermia were fragmentation of the myocardium, acute cortical necrosis in the kidneys, and marked degenerative changes in the cerebellum and cerebral cortex that were considered severe and permanent.		
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A STUDY OF EFFECTS OF HYPERTHERMIA ON LARGE, SHORT-HAIRED MALE DOGS: A SIMULATED AIR TRANSPORT ENVIRONMENTAL STRESS

I. Introduction.

In the early 1970's, the general public let it be known that they were concerned about the safe, efficient, and humane treatment of animals during shipments by air freight. In 1973 the Special Studies Subcommittee of the Committee on Government Operations, House of Representatives, conducted hearings on problems in air shipment of domestic animals.¹⁷ Testimony before this committee made quite evident that of the environmental stresses animals can be exposed to during shipment, heat is the most serious. It has been reported that in an air carrier on the ground in the summer, temperatures may reach 130.0° F or higher in the cargo compartment.^{17 18}

When animals are exposed to ambient temperatures that exceed their normal body temperatures, they may experience hyperthermia.¹³ The degree of hyperthermia in an animal depends on such factors as humidity, ventilation, and the animal's muscular exertion, hair coat, and physical condition. During an episode of hyperthermia, an animal may show little clinical evidence of harm; however, transient and permanent changes can occur. Because of public concern more attention has been given to the dog and its well-being than to other domestic small animals.

The dog, unlike man, produces little sweat but promotes heat loss through panting. By panting, the dog is able to evaporate moisture from its tongue and upper respiratory tract. However, as the relative humidity (RH) increases or when ventilation is inadequate, this process becomes less effective in dissipating heat. Prolonged exposure to these factors can tax a dog's ability to maintain a normal body temperature, and heat hyperpyrexia or heatstroke can result.²

In the past decade, little progress has been made in studying the biochemical and histopathological effects of hyperthermia on animals. It is a question, so far unanswered, of what degree and duration of hyperthermia will damage the central nervous system.¹³ In 1927, Hall and Wakefield⁴ studied hyperthermia in female dogs in an environment in which the dry-bulb temperature ranged between 131.0° and 141.0° F and the wet-bulb temperature ranged between 95.0° and 115.0° F. After 20-75 minutes of exposure, the dogs' rectal temperatures ranged between 106.0° and 113.4° F. They noted increases in blood urea nitrogen (BUN), sugar, chlorides, lactic acid, creatinine, and calcium (Ca) and decreases in plasma carbon dioxide (CO₂) combining power, inorganic phosphate, and serum pH. Histopathology showed cellular degeneration in the lung, kidney, liver, heart, and brain.

Jacobsen and Hosoi⁸ used radiotherapy on dogs. Eleven dogs received single exposures ranging from 37 minutes to 12 hours with resultant maximum rectal temperatures of 108.0° to 111.0° F. Of the 11 dogs exposed, 6 died within 40 minutes after heating. Histopathology showed changes in the heart, lung, spleen, gastrointestinal tract, kidney, and brain. Knudson and Schaible¹² studied canine physiological and biochemical changes resulting from exposure to an ultrahigh frequency field. Exposure times ranging from 30 minutes to 5 hours 15 minutes resulted in rectal temperatures ranging from 104.0° to 109.9° F. Weight loss ranged from 1.9 percent to 11.1 percent in dogs that were given no water during treatment. Most dogs were exposed more than once. The biochemical changes in the blood were similar to those reported by Hall and Wakefield. Hartman and Major⁵ reported pathological changes in female dogs, resulting from 5 to 7 hours of exposure at 150.0° to 157.0° F and humidities of 30 percent to 40 percent. The

maximum rectal temperatures varied from 106.2° to 110.4° F. Kanter,^{9 10 11} in his studies, reported exposing unanesthetized female dogs to 120.0° F and a humidity lower than 20 percent for 4 hours. His results showed hypoglycemia, a fall in plasma phosphate and potassium (K) levels, an increase in plasma sodium and chloride, and an increase in arterial pH. Higgins⁶ exposed dogs weighing 19.8 to 37.4 lb to temperature of 100.0°, 110.0°, and 120.0° F and 30-percent humidity until rectal temperatures reached 107.6° F. At each temperature his results showed increases in blood pH, packed cell volume (PCV), oxygen (O₂), Ca, and chlorides and decreases in blood CO₂. Blood sodium (Na) decreased at 100.0° and 120.0° F but increased at 110.0° F whereas K showed a decline at 100.0° F, increased slightly and leveled off at 110.0° F, and increased at 120.0° F. Nemoto and Frankel¹⁶ exposed anesthetized dogs to temperatures of between 110.0° and 115.0° F and rectal temperatures reached 104.0°, 107.6°, and 109.4° F. Results indicated that blood pH and O₂ increased and CO₂ decreased at 104.0° and 107.6° F while pH at 109.4° F decreased to control levels.

After reviewing the literature on hyperthermia in dogs, we felt there was a need for further study on biochemical and histological changes in hyperthermia dogs. Our approach was to use a high environmental temperature, one that could possibly develop during transport. Since humidity also plays an important role in hyperthermia, we used two humidities (one high, one low) that would be reasonable to expect at such a temperature. The length of exposure was one that could reasonably be expected to occur when an animal is at a terminal awaiting transport or between flights.

II. Materials and Methods.

For this study we chose to use large male dogs between 2 and 7 years of age, short haired, of the hound/pointer/bird-dog type and body conformation. This size of dog allowed us to withdraw volumes of blood without ill effects. All dogs were maintained on a dry-food diet plus a vitamin-mineral supplement. During the conditioning period the dogs were immunized against canine distemper, canine infectious hepatitis, leptospirosis, and rabies. Internal and external parasites were eliminated.

Since we were also studying two humidity levels (15 percent and 35 percent), there were two groups of 10 dogs. At the time of exposure, the 15-percent group weighed from 44.1 to 54.5 lb while the 35-percent group weighed from 47.1 to 69.2 lb. To prevent drug influence, no dog received any medication for at least 14 days prior to exposure, and all were in very good condition at the time of exposure. All were studied individually and unanesthetized. Food was withheld for 24 hours prior to exposure but water was available.

The dogs were exposed to heat and humidity in the Civil Aeromedical Institute environmental chamber. Before each exposure, the proper temperature and humidity were established in the chamber and maintained throughout the exposure. One group experienced a temperature of 130.0° F at 15-percent RH for 30 minutes. The second group was exposed to 130.0° F at 35-percent RH for 30 minutes. The dogs were lightly restrained in a sling-type device secured to a movable laboratory cart. Heart rate and rectal temperatures were monitored and recorded at 5-min intervals. Venous blood samples (10 ml each) were obtained from a cephalic vein, using a sterile vacuum tube and needle, just prior to exposure and at 15 and 30 min of exposure. The pH, O₂, and total content of CO₂ were determined with an IL Ultra-Micro pH and Blood Gas Analyzer. White blood cell counts (WBC), PCV, and differentials were determined manually. Blood glucose, BUN, Ca, total protein, globulins, albumin, cholesterol, serum glutamic oxalacetic transaminase (SGOT), total lipids, alkaline phosphatase, hemoglobin (Hb), and red cell counts (RBC) were determined with a Biodynamics Unimeter 300. Blood determinations were made as soon as possible after withdrawal.

A different dog was used for each exposure. Each experiment consisted of a 30-min control period and a 30-min heat/humidity exposure. Each dog was weighed at the beginning of the control period. After the control period (ambient 72.0° to 76.0° F), each dog was moved into the chamber. The chamber was lighted and well ventilated, and noise was kept to a minimum. Following exposure, the dog was removed from the chamber, the third blood sample was taken, monitoring leads were removed, and the dog was reweighed and returned to its living quarters.

Four dogs (two from each humidity group) were sacrificed at 4, 28, 52, 100, and 196 h after exposure. Immediately after sacrifice they were necropsied and brain, heart, kidney, and lung tissues were preserved and later prepared for microscopic examination.

III. Results.

During the control period, all dogs remained calm. About midway of the exposure period, most dogs became restless and panted heavily. Oral mucous membranes became hyperemic, the sclera became injected, and salivation became excessive. Following removal from the chamber, the dogs appeared exhausted, seemed thirsty, and wanted to lie on the cool cement floor. However, within an hour they appeared to have recovered fully.

As indicated in Table 1, both the 15-percent-RH and 35-percent-RH groups showed significant increases in blood pH, Hb, PCV, and RBC and a decrease in Pv_{CO_2} . The changes for both blood Pv_{CO_2} and pH were significantly greater in the 35-percent-RH group than in the 15-percent-RH group.

Table 2 presents the temperature and heart rate data. There were significant increases in rectal temperature in both the 15-percent-RH and 35-percent-RH groups. In the 15-percent-RH group, the rectal temperature of only 1 of the 10 dogs was higher than 105.0° F following exposure. Five of the ten dogs in the 35-percent-RH group had rectal temperatures higher than 105.0° F and one dog's temperature reached 107.4° F by the end of the 30-min exposure. The temperature increase was significantly greater in the 35-percent-RH group than in the 15-percent-RH group. The heart rate increased significantly in both the 15-percent-RH and 35-percent-RH groups.

During exposure the mean weight loss for the 15-percent-RH group was 0.3 lb, or 0.6 percent of the initial body weight. The 35-percent-RH group lost 0.6 lb, or 1.1 percent of the initial weight. The weight loss of dogs in the 35-percent-RH group was significantly greater ($p \leq 0.01$) than that of dogs in the 15-percent-RH group.

In order of significance, the following organs showed histopathological changes: cerebellum, cerebral cortex, heart, kidney, and lung.

The most consistent and remarkable changes were in the cerebellum, where Purkinje cells showed marked degenerative changes ranging from cell deformity, hyperchromatic cytoplasm, and loss of nuclear definition to cytolysis. Many specimens showed separation of the glial layer of Bergmann, oligodendroglial hydropic changes in the deep cerebellar white matter, and fragmentation of the neuropil in the molecular layer. Microhemorrhages were often seen in the white matter, particularly in the dogs exposed to 35-percent RH. Some specimens showed slight conglutination of the internal granular layer and congestion in the deep cerebellar white matter.

The neurons of the cerebral cortex generally showed deformity, hyperchromatic cytoplasm, and loss of nuclear definition. In some instances the neurons retained a degree of cellular integrity but exhibited satellitosis, glial activity, and early signs of degeneration. In those specimens showing more advanced degenerative changes, the glial activity appeared to be minimal. All specimens except one from each group showed evidence of edema as indicated by a clear zone around the neurons, separation of neuropil, hydropic changes of the oligodendroglia, and distention of the perivascular spaces. Half the specimens from the 35-percent-RH group showed microhemorrhages in the cortex and white matter.

Following exposure, 9 of the 10 dogs in each group showed degenerative changes in the heart muscle. Histological examination revealed fragmentation of the myocardium in many specimens. The myofibrillar striations were poorly defined and/or absent to some degree in all specimens except for one from each group. Some degree of pyknosis of the nuclei was evident in more than half the specimens. Microhemorrhages were often seen in the tissues, but there was no inflammatory reaction. Fraying and separation of muscle fibers were frequently seen.

More than half the dogs showed kidney changes following exposure, and those varied in degree of involvement. In many specimens the glomeruli were hypercellular. Occasionally, there were congested glomeruli. Bowman's capsules were dilated to some degree in about half the specimens, and occasionally there was blood in Bowman's spaces. In 5 of 10 dogs in the 15-percent-RH group and 6 of 10 in the 35-percent-RH group, the epithelium of the convoluted tubules showed degenerative changes that

TABLE 1. Blood Constituents in Dogs as Affected by Exposure to 130.0° F and a Relative Humidity of 15 Percent or 35 Percent*

Items	Duration of Exposure (Min) at 15% RH		Duration of Exposure (Min) at 35% RH		
	0	15	0	15	
Hematologic					
pH	7.38 (0.03)	7.45 (0.05)	7.50 (0.07)**	7.56 (0.07)	7.64 (0.07)**
P _v CO ₂ (mm Hg)	35.73 (2.91)	28.58 (2.96)	24.69 (3.32)**	41.38 (5.94)	17.08 (4.89)
P _v O ₂ (mm Hg)	45.34 (6.88)	53.64 (7.94)	50.96 (8.92)	44.01 (6.11)	48.53 (16.59)
Hb (gm/100 ml)	13.05 (1.54)	13.63 (1.52)	14.18 (1.53)**	12.80 (0.63)	14.93 (1.69)
PCV (percent)	43.40 (3.44)	45.50 (4.38)	46.30 (4.97)**	47.60 (3.06)	52.80 (5.83)**
RBC (10 ⁶ /cmm)	4.82 (0.49)	5.10 (0.45)	5.30 (0.65)**	5.15 (0.47)	5.68 (0.65)**
WBC (10 ³ /cmm)	8.33 (1716)	8.09 (1507)	7.83 (1630)	8.41 (1503)	8.83 (1547)
Serum Chemistries					
Glucose (mg/100 ml)	68.20 (6.97)	74.20 (12.03)	76.00 (16.22)	66.90 (17.32)	71.70 (14.73)
Calcium (mg/100 ml)	10.40 (0.98)	10.26 (1.09)	10.29 (1.06)	8.76 (0.56)	9.11 (0.65)
Bilirubin, Total (mg/100 ml)	0.46 (0.20)	0.51 (0.27)	0.59 (0.29)	0.76 (0.33)	0.98 (0.48)
Cholesterol, Total (mg/100 ml)	166.50 (26.88)	165.00 (34.48)	175.00 (31.97)	157.30 (29.71)	163.90 (27.47)
Lipids (mg/100 ml)	380.70 (19.71)	384.00 (21.96)	389.70 (22.03)	390.10 (43.94)	388.10 (51.36)
BUN (mg/100 ml)	10.95 (3.05)	11.70 (2.76)	13.26 (4.04)	12.44 (4.56)	11.74 (4.45)
Inorganic Phosphorus (mg/100 ml)	1.64 (0.88)	1.35 (1.13)	1.75 (1.11)	2.60 (0.64)	2.19 (0.54)
Protein, Total (gm/100 ml)	6.84 (0.67)	6.95 (0.56)	7.05 (0.52)	6.09 (0.76)	6.30 (0.92)
Albumin (gm/100 ml)	1.59 (0.74)	1.50 (0.53)	1.61 (0.34) [†]	2.88 (0.55)	3.00 (0.73)
Globulin (gm/100 ml)	5.26 (0.67)	5.35 (0.54)	5.32 (0.57)	3.21 (0.33)	3.27 (0.28)
SGOT (Karmen Units)	25.30 (4.08)	26.10 (6.85)	25.50 (4.88)	28.75 (9.22)	34.10 (11.31)
Alkaline Phosphatase (I.U.)	15.22 (6.48)	13.44 (6.51)	13.90 (7.13)	10.10 (5.78)	9.40 (6.64)

* 10 dogs each at 15-percent and 35-percent RH

** P < 0.01 statistical test by analysis of variance

Table entries are means; standard deviations are given in parentheses.

The 15-min entries at 35-percent RH are the means of nine dogs.

Alkaline phosphatase at 15-percent RH at 0 and 15 min are means of nine and eight dogs respectively.

TABLE 2. Heart Rates and Rectal Temperatures in Dogs as Affected by Exposure to 130.0° F and a Relative Humidity of 15 Percent or 35 Percent*

Items	Duration of Exposure (Min) at 15% RH						Duration of Exposure (Min) at 35% RH						
	0	5	10	15	20	30	0	5	10	15	20	25	30
Heart Rate (beats/min)	85 (27)	95 (32)	97 (26)	102 (33)	107 (28)	113 (33)	111 (24)	134 (19)	135 (22)	135 (21)	143 (28)	147 (23)	149** (22)
Rectal Temperature (° F)	101.5 (0.28)	101.6 (0.26)	101.8 (0.21)	102.2 (0.17)	102.7 (0.15)	103.2 (0.25)	101.7 (0.35)	102.0 (0.44)	102.4 (0.51)	103.0 (0.50)	103.7 (0.53)	104.5 (0.58)	105.3** (0.67)

* 10 dogs each at 15-percent and 35-percent RH
 ** P < 0.01

Table entries are means; standard deviations are given in parentheses.

were suggestive of early cortical necrosis. In the tissues showing tubular necrosis, the changes were present as early as 28 h and as late as 100 h postexposure. In one dog necropsied at 28 h, the changes were so profound that, in our experience, if the dog had been allowed to live it would probably have experienced renal failure.

The lung from all the exposed dogs showed some degree of pathology. Those necropsied at 28, 52, and 100 h revealed more lung changes than those sacrificed at 100 and 196 h. The predominant histopathological findings were thickening and congestion of the alveoli septi, hemorrhage and/or edema in the alveolar spaces, and engorgement of the blood vessels. Occasionally, a specimen had hemorrhage or debris in a few of the bronchi.

IV. Discussion.

The results of this study showed significant ($p \leq 0.01$) changes in heart rate, rectal temperature, Pv_{CO_2} , blood pH, Hb, RBC, PCV*, and weight that can be related to the exposure environment. The effects of humidity produced significant differences between the 15-percent-RH and 35-percent-RH groups for Pv_{CO_2} , blood pH, rectal temperature, and weight loss. Peak heart rate increase occurred in 5 of the 10 dogs of the 15-percent-RH group before the end of the 30-min exposure whereas 7 of the 10 in the 35-percent-RH group peaked before the end of exposure. Although no significant change was found in BUN, 2 of 10 dogs showed a decrease in BUN at the 15-percent-RH exposure whereas 7 of 10 at the 35-percent-RH exposure showed a decrease. Some of the remaining parameters showed changes that were not significant.

Hemolysis was also noted in samples from a few of the dogs exposed to the 35-percent humidity, but the quantity was not measurable. Iampietro *et al.*⁷ showed that hemolysis occurred in dogs exposed to temperatures ranging from 70.0° to 120.0° F at 50-percent RH for up to 60 min. He states that hemolysis might have been the result of extremely low blood CO_2 and/or high pH brought about by hyperventilation and/or high body temperature.

Throughout the available literature, we found few reports that histology had been performed on surviving victims of hyperthermia. Hartman and Major⁵ reported histological changes in anesthetized dogs exposed to temperatures of from 150.0° to 175.0° at 30- to 40-percent RH. Histological changes in animal tissues have been reported by Jacobsen and Hosoi⁸ and by Mortimer¹⁵ in studies of experimental hyperthermia induced by ultrahigh frequency oscillators or high frequency current. Hall and Wakefield⁴ showed that degenerative changes occurred in the brain, heart, kidney, and lung of dogs that died from experimental heatstroke. Malamud *et al.*¹⁴ studied 125 fatal cases of heatstroke in military personnel who had undergone strenuous muscular exercise at high temperatures. According to their description, the histopathological changes of the brain and viscera in these cases closely parallel the changes found in our dogs. Freeman and Dumoff,³ in their report on cerebellar syndrome following heatstroke in man, state that periods of exposure must be brief because at high temperatures the pathological alterations in the body cells rapidly become irreversible.

In our study, the histopathological changes in the brain, heart, kidney, and lung examined provided the most interesting and valuable information. It is our opinion that most of the changes in the cerebellum and cerebral cortex are considered severe and permanent and that the neuronal changes developed during the period of hyperthermia. We believe the fragmentation of the myocardium, loss of myofibrillar striations, and pyknotic nuclei are attributable to hyperthermia. In those dogs whose kidneys showed acute cortical necrosis, this was, we believe, related to hyperthermia in that none of the dogs experienced any clinical signs of shock. In general, the changes observed in the lungs were minimal to moderate with those necropsied at 100 and 196 hours showing signs of recovery. We were unable to detect any qualitative or quantitative relationship in tissue changes between the two humidity groups. Although all dogs survived acute hyperthermia with no signs of illness, there were histological changes in the tissues examined.

V. Conclusions.

In view of the results obtained from this limited study, we should remember that 130.0° F is on the high side of the ambient temperature scale to which dogs could be exposed during air transport. With a dog's average rectal temperature being 101.5° F, the question remains: At what ambient temperature will a dog sustain permanent damage from hyperthermia? We should not assume that all dogs will respond to a given temperature in the same manner. Aside from health problems that can influence a dog's ability to withstand various temperatures, there

are at least three anatomical characteristics that should be considered. First, there is a wide range of size in breeds weighing from 3 to 175 pounds and, therefore, considerable variation in the area of body surface exposed. Second, the hair coats of various breeds differ in density, length, and texture. Third, the brachycephalic breeds of dogs have short, narrow nasal passages, pendulous soft palates, and heavily muscled throats—characteristics that increase the effort of accelerated breathing during panting. These factors should be studied further before the FAA can recommend thermal limits for the air transportation of dogs.

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