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# Heat Stroke in Dogs: A Retrospective Study of 54 Cases (1999–2004) and Analysis of Risk Factors for Death

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The medical records of 54 dogs presented to the Hebrew University Veterinary Teaching Hospital and diagnosed with heat stroke were retrospectively reviewed. Data abstracted included history, clinical and clinicopathological signs at admission, treatment, disease progression, and outcome. Exertional and environmental heat stroke were present in 63% (34 of 54) and 37% (20 of 54) of the dogs, respectively, and 78% (42 of 54) were examined between June and August. The mean temperature and heat discomfort index in the particular days of heat stroke were significantly increased ($P < .001$, $P < .001$, respectively) compared with their corresponding average daily values. In 27 dogs the body temperature was ≥41°C (105.8°F). Belgian Malinois (15%, odds ratio [OR] = 24, 95% confidence interval [$CI_{95\%}$] 8.2–64.5), Golden and Labrador Retrievers (21%, OR = 2.08, $CI_{95\%}$ 0.95–4.2), and brachycephalic breeds (25%, OR = 1.7, $CI_{95\%}$ 0.81–3.21) were overrepresented, whereas small breeds (<8 kg) were underrepresented (2%, OR = 0.08, $CI_{95\%}$ 0.002–0.48). Thrombocytopenia (45 of 54 dogs) and prolongation of the prothrombin (PT) and activated thromboplastin (aPTT) times (27 of 47 dogs) were recorded during hospitalization. Disseminated intravascular coagulation ($P = .013$) and acute renal failure ($P = .008$), diagnosed in 28 of 54 and 18 of 54 of the cases, respectively, were risk factors for death. The overall mortality rate was 50%. Hypoglycemia (<47 mg/dL, $P = .003$), prolonged PT (>18 seconds, $P = .05$), and aPTT (>30 sec, $P < .001$) at admission were associated with death. Serum creatinine >1.5 mg/dL ($P = .003$) after 24 hours, delayed admission (>90 minutes, $P = .032$), seizures ($P = .02$), and obesity ($P = .04$) were also risk factors for death. Heat stroke in dogs results in serious complications and high fatality rate despite appropriate treatment.

**Key words:** Canine; Discomfort index; Disseminated intravascular coagulation; Heat stress; Rhabdomyolysis.

Hyperthermia can be a pyrogenic or a nonpyrogenic increase in body temperature above the normal hypothalamic set point.[1] Nonpyrogenic hyperthermia occurs when heat dissipating mechanisms cannot adequately compensate for heat production or when these are impaired.[2] More than 70% of the total body heat loss in dogs is dissipated through radiation and convection from body surfaces.[2–4] As the environmental temperature increases, approaching body temperature, evaporation, primarily through panting, becomes more important in maintaining normothermia. The nasal turbinates provide a large surface area for water loss from the moist mucous membranes and have an important role in the evaporative cooling mechanism. Hypersalivation improves evaporation efficiency. High environmental temperatures and increased humidity (>35%) reduce evaporation efficiency, and when the humidity is >80%, evaporation will be negated.[2,5]

Heat stroke is a severe illness characterized by core temperatures >40°C (104°F) in human patients, and >41°C (105.8°F) in dogs, as well as central nervous system dysfunction.[1,2] It results from exposure to a hot and humid environment (classical heat stroke) or to strenuous physical exercise (exertional heat stroke). It is associated with a systemic inflammatory response syndrome leading to multiple organ dysfunction.[1]

Heat stroke is a commonly recognized syndrome in dogs and occurs particularly during the summer months, mainly in hot and humid environments.[6,7] Most data on this condition in veterinary medicine are on the basis of studies of humans.[2,6] However, dogs are considered unsuitable models for human heat-related disease, in part because of the intrinsic thermal resistance of the canine brain.[8] Thus, it is reasonable to assume that information derived from human patients may not be applied without reservations to dogs. The research of heat stroke in dogs is limited to one retrospective study of heat-induced illness in 42 patients, conducted between 1976 and 1993.[6] Research of heat stress effects on canine physiology, hemostasis, central nervous system function, immune response, and renal function has expanded since that study.[8–11] Improvements in clinicopathological testing have been introduced and have become routine in veterinary practice. This retrospective study describes the history, clinical, and clinicopathological signs on admission, disease progression, therapy, and outcome in 54 cases of canine heat stroke, as well as provides an assessment of the risk factors for death.

## Materials and Methods

### *Selection of Cases and Collection of Data*

The medical records of all dogs admitted to the Emergency and Critical Care Unit of the Hebrew University Veterinary Medicine Teaching Hospital (HUVTH) between 1999 and 2004 were retrospectively reviewed. Eight dogs were excluded because of incomplete medical records (4) and other concurrent illness (2 dogs with ehrlichiosis and 2 with neoplasia).The dogs selected for the present study had no other coexisting medical condition apart from heat-related illness on the basis of their history, and their clinical signs had developed only after exposure to a warm environment, strenuous activity, or both. These signs included central nervous system dysfunction, collapse and tachypnea, or both. The dogs

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were divided into 3 groups on the basis of their body temperature on admission and were defined as markedly hyperthermic (≥41°C, [105.8°F]), normothermic to moderately hyperthermic (37.6–40.9°C [99.7–105.7°F]), and hypothermic (<37.6°C [99.7°F]). Nonsurvivors included dogs that died naturally (19 dogs) or were euthanized (8 dogs) during hospitalization.

### *Definitions of Environmental Heat Stress and Collection of Meteorological Data*

All of the meteorological data (environmental temperature, humidity, and discomfort index [DI]) in the individual days when the heat stroke had occurred, average daily temperature, humidity, and DI with their respective standard deviation (SD) were collected from the Israeli National Meteorological Service (INMS).[a] The DI was calculated as [Wet Bulb Globe (°C) + Dry Bulb Globe (°C)]/2.[12] The wet bulb globe is the temperature measured with a thermometer bearing a wetted wick. The purpose of this measure is to determine the amount of cooling provided to a human subject through evaporation, which is a function of air speed and humidity. The dry bulb globe is the temperature measured with a standard air thermometer shielded from radiant heat. It measures the effect of the convection and conduction heating or cooling a human. This index combines air temperature, humidity, airflow, and radiant heat to measure the risk of heat stress disorders in humans,[a] The DI was subdivided to mild (22.1–24) moderate (24.1–28), and severe (>28) on the basis of the definitions used by the INMS[a] for the purpose of risk factor analysis.

### *Definition of Secondary Complications*

All dogs diagnosed with disseminated intravascular coagulation (DIC) had thrombocytopenia (<150,000/μL) and at least 2 of the following: prolongation (>25%) of the prothrombin time (PT) or activated partial thromboplastin time (aPTT) and clinical signs compatible with DIC (including petechiae, echymoses, hematochezia, hematemesis, or hematuria). Dogs were diagnosed with acute renal failure if creatinine concentration was >2 mg/dL after 24 hours of aggressive continuous IV fluid therapy. The dogs were divided into 2 groups on the basis of their mental status on admission for the purpose of risk factor analysis. Group 1 included dogs with neurological signs of disorientation up to stupor, and group 2 included dogs presented with semicoma or coma.

### *Laboratory Tests*

Blood samples for hematological, electrolyte, and dry biochemistry analyses and coagulation tests were collected in potassium-EDTA, heparin, and trisodium-citrate tubes, respectively, and analyzed within 30 minutes from collection. CBC was performed on admission and before treatment in 50 dogs, with an automated blood impedance analyzer calibrated for canine blood.[b,c] Packed cell volume was measured by centrifugation of heparinized capillaries (in 52 dogs), and total plasma protein was determined with a standard refractometer[d] calibrated weekly (50 dogs). Differential white cell counts (19 dogs) were performed manually by counting 100 leukocytes in Giemsa-stained blood smears. Nucleated red blood cells (NRBC) counts and a semiquantitive evaluation of platelet numbers were performed manually. Blood for wet serum biochemistry (19 dogs) was collected on admission in plain tubes, centrifuged within 30 minutes from collection, and sera were refrigerated (4°C) pending analysis that was performed within 24 hours from collection with an autoanalyzer.[e] Specific dry chemistry analyses (50 dogs, glucose and creatinine only) were performed with dry chemistry analyzers.[f] Electrolyte analysis (39 dogs) was performed with a specific-electrode electrolyte analyzer.[g] Coagulation tests (47 dogs) included PT and aPTT and were performed with analyzers calibrated for canine blood.[h]

### *Statistical Analysis*

Statistical analysis for independence of dichotomous variables was performed by using Fisher's exact test. A chi-square test was used for statistical significance assessment of the independence between nominal variables that consisted of more than 2 categories. The Mantel test was used for the linear trend assessment association in these variables. Mean, median, and SD were calculated for continuous variables. The overall assessment of the association of continuous variables with survival and occurrence of DIC was analyzed by the receiver operation characteristics (ROC) procedure, by calculation of the area under the curve (AUC) with its 95% confidence interval ($CI_{95\%}$) by the nonparametric method. The cutoff points that optimized the overall correct predictors of survival and nonsurvival on the ROC curve were selected for the division of continuous variables and their dichotomic transformation. The results of the PT and aPTT of the survivors and nonsurvivors were logarithmically transformed and compared by using the independent *t*-test. Temperature, humidity, and DI in the particular days of heat stroke events were compared to the average daily values of their respective months (1987–2002) by using the independent *t*-test. Total weighted comparison was performed for the entire daily values in the study.

Because the data concerning survival within the study group can be regarded as originating in a cohort study, risk ratios (RRs) were calculated. Risk factor analysis was performed for all nonsurvivor dogs versus survivors, as well as for nonsurvivors that died naturally (euthanized cases excluded) versus survivors. Assessment of breed as a risk factor for developing heat stroke was performed by comparison of breed frequencies in the study group to their frequencies in the general HUVTH population (years 1999–2004). Odds ratios (OR) were calculated for each breed or group of breeds. For the calculation of the OR of small breeds (<8 kg), mixed breed dogs were excluded from both the study and the HUVTH population. In this analysis, we relied on the pure breed dogs' standard weight. Exact $CI_{95\%}$s for the RRs and ORs were calculated. Statistical analysis was performed by using statistical software.[i–k] *P*-value ≤.05 was considered statistically significant for all analyses.

## Results

### *Environmental Factors*

Fifty-four dogs with heat stroke admitted to the HUVTH between 1999 and 2004 were included in this study. All were presented between March and October; however, most had occurred during the hot summer months of June (28%), July (31%), and August (19%). The DI was mild, moderate, and severe in 1, 33, and 13 dogs, respectively. It was <22.1 (ie, no heat stress) in 4 dogs, of which 3 had exertional heat stroke, and 1 had environmental heat stroke because of excessive hair drying with a fan. The average temperature and DI, but not the humidity in the particular days of the heat stroke, were significantly increased ($P < .001$, $P < .001$, and $P = .53$, respectively; Table 1) compared with their corresponding average daily (1987–2002) values. The DI, but not the temperature and humidity in the particular days of the heat stroke events, was positively and significantly associated with occurrence of DIC (AUC = 0.677, $P = .03$). There was no association

**Table 1.** Meteorological variables of the time of heat stroke events compared to average daily data (1987–2002).

| | | Temperature (°C) (Mean ± SD) | | | Relative humidity (%) (Mean ± SD) | | | Discomfort Index (°C) (Mean ± SD) | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Month | n | Days of Heat Stress Insult | Other Days | *P* | Days of Heat Stress Insult | Other Days | *P* | Days of Heat Stress Insult | Other Days | *P* |
| March | 3 | 23.2 ± 5.9 | 19.2 ± 3.6 | .056 | 35.5 ± 26.2 | 53 ± 15.0 | .045 | 18.1 ± 3.1 | 16.5 ± 2.7 | .31 |
| April | 0 | | 23.2 ± 4.7 | | | 47 ± 15.0 | | | 19.7 ± 3.2 | |
| May | 5 | 31.2 ± 4.6 | 25.8 ± 3.6 | .001 | 34.8 ± 10.7 | 49 ± 13.0 | .015 | 25.8 ± 3.5 | 22.2 ± 2.5 | .002 |
| June | 15 | 29.2 ± 2.9 | 28.4 ± 2.2 | .17 | 52.1 ± 11.7 | 52 ± 10.0 | .97 | 25.6 ± 1.7 | 24.9 ± 1.6 | .1 |
| July | 17 | 31.3 ± 1.3 | 30.3 ± 1.3 | .002 | 55.1 ± 6.8 | 55 ± 6.0 | .95 | 27.6 ± 0.8 | 26.9 ± 1.1 | .01 |
| August | 10 | 31.6 ± 0.7 | 30.7 ± 1.0 | .005 | 54.8 ± 4.6 | 55 ± 5.0 | .9 | 28.3 ± 0.7 | 27.3 ± 1.0 | .002 |
| September | 2 | 29.4 ± 0.9 | 29.8 ± 1.6 | .72 | 52.5 ± 0.7 | 52 ± 8.0 | .93 | 25.8 ± 1.0 | 26.2 ± 1.3 | .66 |
| All cases | 52 | 29.3 ± 2.9 | 26.8 ± 1.4 | <.001 | 47.5 ± 11.1 | 51.9 ± 4.1 | .53 | 26.5 ± 2.4 | 23.4 ± 0.8 | <.001 |

between the meteorological data and the heat stroke type (ie, exertional and environmental heat stroke).

Exertional heat stroke was observed in 63% (34 of 54) of the cases ($CI_{95\%}$ 49–75%). The mean exertion time was 58 minutes (29/34 dogs, median 30, range 6–300). The mean exposure duration to environmental heat stress in 8 of 20 dogs diagnosed with environmental heat stroke of which these data were available, was 191 minutes (SD 75, median 210, range 90–300). There was no difference in case fatality rate between dogs with environmental heat stroke compared with dogs with exertional heat stroke (10 of 20 and 17 of 34, respectively; Table 2). The results were similar when euthanized cases were excluded from the analysis.

The median time lag from the collapse due to the predisposing event to admission (available for 49 dogs) was 240 minutes (range 12–2880). The dogs were divided into 2 time lag groups (≤90 minutes, 15 dogs [31%]; >90 minutes, 34 dogs [69%]) by means of a ROC curve. The mortality rate was significantly ($P = .032$) higher in the dogs with time lag >90 minutes (62% versus 27%; Table 2). The results were similar when euthanized cases were excluded from the analysis. Late admission (time lag >90 minutes) was significantly associated with the occurrence of DIC ($P = .04$).

Twenty-six dogs (48%) were cooled by their owners before admission. There was no significant difference in the mortality (Table 2) and prevalence of DIC and acute renal failure in this group (17 and 10 dogs, respectively) compared with the other dogs (12 and 9 dogs, respectively); however, survival was 100% in 6 dogs that were cooled by their owners before admission and admitted within a time lag ≤90 minutes. The results were similar when euthanized cases were excluded from the analysis. Cooling was negatively and significantly ($P = .005$) associated with the rectal temperature on admission in dogs admitted to the HUVTH within a time lag ≤ 4 hours (39.46°C versus 41.17°C [103.03°F versus 106.11°F]), but not in dogs admitted to the HUVTH within a time lag >4 hours.

**Table 2.** Risk factors for death in 54 dogs with heat stroke.

| | RF Present | | RF Not Present | | | | |
|---|---|---|---|---|---|---|---|
| Variable | n | No. of Deaths (%) | n | No. of Deaths (%) | RR | Exact $CI_{95\%}$ | *P* |
| Timelag >90 minutes | 34 | 21 (62) | 15 | 4 (27) | 2.32 | 1.08–5.90 | .032 |
| Cooling by owners before admission | 26 | 10 (39) | 28 | 17 (61) | 0.63 | 0.35–1.12 | .173 |
| Obesity | 11 | 9 (82) | 36 | 15 (42) | 1.96 | 1.11–3.21 | .040 |
| Coma/semicoma on admission | 22 | 15 (68) | 20 | 8 (41) | 1.71 | 0.95–3.32 | .060 |
| Seizures during illness | 19 | 14 (74) | 35 | 13 (37) | 2.00 | 1.17–3.37 | .020 |
| Prothrombin time >18 seconds on admission | 8 | 7 (88) | 39 | 18 (46) | 1.90 | 1.05–2.94 | .050 |
| aPTT >30 seconds on admission | 14 | 13 (93) | 33 | 12 (36) | 2.55 | 1.57–4.28 | <.001 |
| Thrombocytopenia during illness[a] | 42 | 19 (45) | 8 | 3 (37) | 0.83 | 0.28–1.80 | 1.000 |
| Creatinine >1.5 mg/dL at 24 hours after admission | 20 | 15 (75) | 17 | 4 (24) | 3.19 | 1.41–8.39 | .003 |
| Glucose <47 mg/dL on admission | 12 | 10 (83) | 12 | 5 (42) | 2.00 | 1.01–5.27 | .03 |
| Presence of DIC | 28 | 19 (68) | 26 | 8 (31) | 2.21 | 1.22–4.31 | .013 |
| Presence of acute renal failure | 18 | 14 (78) | 36 | 13 (36) | 2.15 | 1.28–3.64 | .008 |
| Presence of DIC + acute renal failure | 12 | 11 (92) | 21 | 6 (29) | 3.21 | 1.63–7.01 | .001 |
| Presence of environmental heat stroke | 20 | 10 (50) | 34 | 17 (50) | 1.00 | 0.55–1.72 | 1.000 |
| Presence of exertional heat stroke | 34 | 17 (50) | 20 | 10 (50) | 1.00 | 0.58–1.82 | 1.000 |

RF, risk factor; RR, relative risk; $CI_{95\%}$, 95% confidence interval, aPTT, activated partial thromboplastin time, DIC, disseminated intravascular coagulation.

[a] Platelet count $<150 \times 10^3/mm^3$.

**Table 3.** Prevalence of different breeds and their odds ratio for heat stroke.

| Breed | n | % | Odds Ratio | $CI_{95\%}$ | % General Hospital Population |
|---|---|---|---|---|---|
| Mixed breed | 11 | 20 | 0.7 | 0.3–1.3 | 28.3 |
| Belgian Malinois | 8 | 15 | 24 | 8.2–65 | 0.7 |
| Golden and Labrador Retrievers | 11 | 20 | 2.1 | 0.95–4.2 | 10.9 |
| Boxer | 4 | 7 | 1.4 | 0.35–3.9 | 5.5 |
| Rottweiler | 3 | 6 | 2.1 | 0.4–6.8 | 2.7 |
| English Bulldog | 3 | 6 | 2.7 | 0.5–9 | 2.1 |
| Brachycephalic breeds[a] | 13 | 25 | 1.7 | 0.8–3.21 | 16.5 |
| Small pure breeds (<8 kg) | 1 | 2[b] | 0.1[b] | 0.002–0.5[b] | 22.9[b] |

$CI_{95\%}$, 95% confidence interval
[a] Brachycephalic dogs in this study include Boxer, English Bulldog, Sharpei, Pekinese, Dog de Bordeaux, and Staffordshire Bull Terrier.
[b] Excluding mixed breed dogs.

### *Signalment*

There was no difference between the prevalence of males and females in the study (32 of 54 [59%] versus 22 of 54 [40%], respectively). The median age was 3 years (range 1–12; Table 3). Eight dogs were police or military dogs, of which 7 were Belgian Malinois. Six of these working dogs had exertional heat stroke, and 2 had environmental heat stroke. The body weight (available in 47 dogs) was 30 kg (median, range 4–50 kg), and 11 dogs (20%) were obese. The case fatality was significantly ($P = .04$) higher in the obese dogs (82% versus 42%; Table 2).

### *Clinical Signs*

The body temperature on admission was recorded in 51 dogs, and was ≥41°C (105.8°F), 37.6–40.9°C (99.7–105.7°F), and <37.6°C (<99.7°F) in 21 (40%), 23 (46%), and 7 (14%) dogs, respectively. Interpretation of a ROC curve did not reveal a temperature cutoff beyond which the outcome was significantly different. In 6 referred dogs that were cooled before admission, the body temperature measured by the referring veterinarians was >41°C (>105.8°F), however, was normal on admission.

The heart rate on admission was 145 bpm (median, range 84–220). Tachycardia (>120 bpm) was recorded in 71% of the dogs. The mental status on admission was recorded in 42 of 54 (77%) dogs. The most common clinical signs in the history and physical examination were collapse (51 of 54), tachypnea (33 of 41), bleeding (eg, petechiae, hematemesis, hematochezia; 33 of 54), shock (23 of 54), disorientation/stupor (22 of 42), and semicoma/coma (20 of 42).

Dogs presenting semicoma/coma tended ($P = .06$) to have a higher mortality compared to dogs in the disorientation/stupor group (70% versus 41%, respectively). The results were similar when euthanized cases were excluded from the analysis. Nineteen dogs (35%) exhibited at least 1 episode of seizures during the disease course, with a significantly ($P = .02$) higher mortality compared with that of dogs that did not present seizures (74% versus 37%, respectively; Table 2). The results were similar when euthanized cases were excluded from the analysis.

Fourteen (25%) dogs presented cardiac arrhythmias during the initial 12 hours of hospitalization, including ventricular premature complexes (7 dogs), sustained ventricular tachycardia (3), idioventricular rhythm (3), and atrial fibrillation (1).

### *Hematological and Coagulation Tests*

The most common hematological findings were thrombocytopenia (on admission, 62%, 31 of 50 dogs; during hospitalization, 83%, 45 of 54 dogs), increased packed cell volume (51%), and hemoglobin concentration (77%; Table 4). Thrombocytopenia was not a risk factor for death (RR 0.88, $P = 1.0$; Table 2). NRBCs were detected in 13 of 19 dogs (68%), of which a blood smear was evaluated on admission (median 10, range 1–67), and the NRBC/polychromatic RBC ratio was >1 in all cases.

Coagulation tests were performed in 47 dogs on admission (Table 4), of which 22 survived and 25 died. Mean PT and aPTT (logarithmically transformed) in the nonsurvivors were significantly ($P = .004$ and $P < .001$, respectively) longer compared with that of the survivors (mean 14.8 ± 5.3 versus 10.2 ± 2.8 seconds, and mean 28.1 ± 16.6 versus 16.5 ± 12 seconds, respectively). By means of ROC analysis of the PT and aPTT ranges, cutoff points were set at 18 and 30 seconds, respectively. Dogs with prolonged PT (>18 seconds) and aPTT (>30 seconds) had a significantly ($P = .05$, and $P < .001$, respectively) higher mortality (Table 2). The results were similar when euthanized cases were excluded from the analysis.

### *Serum Biochemistry Results*

The most commonly observed serum biochemistry abnormalities on admission included increased serum activities of creatine kinase (CK, 100% of the dogs), alanine aminotransferase (ALT, 83%), aspartate aminotransferase (AST, 82%), and alkaline phosphatase (ALP, 79%). Additional abnormalities included hypoglycemia (63%) and increased serum creatinine concentration (52%; Table 5).

Serum creatinine concentration on admission and at 24 hours after admission, were available in 51 and 37 dogs, respectively. By means of a ROC curve, the dogs

**Table 4.** Hematological data of dogs with heat stroke.

| Variable | n | Median | Range | Reference Interval |
|---|---|---|---|---|
| White blood cells on admission ($10^3$/mm$^3$) | 49 | 8.9 | 1.31–41 | 6.00–17.00 |
| Platelets on admission ($10^5$/mm$^3$) | 50 | 104 | 0–614 | 150–500 |
| Packed cell volume on admission (%) | 53 | 56 | 41–72 | 37.0–55.0 |
| Hemoglobin on admission (g/dL) | 51 | 19.1 | 13.2–24.1 | 12.0–18.0 |
| Packed cell volume at 24 hours after admission (%) | 27 | 44.0 | 24.0–76.0 | 37.0–55.0 |
| Total protein on admission (g/dL) | 51 | 7.8 | 6.6–10 | 5.5–7.5 |
| Total protein at 24 hours after admission (g/dL) | 27 | 6.2 | 4.4–9.2 | 5.5–7.5 |
| Prothrombin time on admission (sec) | 47 | 11.0 | 6.0–60.0 | 6.0–8.4 |
| aPTT on admission (sec) | 47 | 19.0 | 8.0–61.0 | 11.0–17.4 |

aPTT, activated partial thromboplastin time.

were divided into 2 groups on the basis of their 24-hour serum creatinine concentration, with a cutoff point at 1.5 mg/dL. Dogs with creatinine >1.5 mg/dL had a significantly ($P = .003$) higher fatality rate (Table 2) and occurrence of DIC ($P = .02$). The dogs were divided into 2 groups on the basis of their serum glucose concentration on admission (24 dogs) by means of a ROC curve, with a cutoff point at 47 mg/dL. Dogs with glucose concentration ≤47 mg/dL had a significantly ($P = .03$) higher mortality (Table 2). The results were similar when euthanized dogs were excluded from the analysis. Seizures were observed in 67% of these dogs and in 25% of the dogs with glucose >47 mg/dL; however, this difference was not significant.

### *Treatment*

Treatment in all dogs included IV lactated Ringer's solution and whole body cooling when indicated. Fresh frozen plasma (FFP) was administered in 37 of 54 dogs (69%; mean ± SD 2 ± 1 units/dog, median 14.3 mL/kg, range 6.3–188.5) during hospitalization. Other common medications included mannitol[l] (26 dogs), $H_2$-receptor blockers (25), antibiotics (25), furosemide[m] (19), glucose (15), heparin[n] (11), dexamethasone-sodium-phosphate[o] (11), dopamine[p] (9), and diazepam[q] (9).

### *Complications and Outcome*

The overall mortality rate was 50% (27 of 54), of which 63% (17 dogs) died (of which 4 were euthanized) within 24 hours of admission. DIC and acute renal failure were significant ($P = .013$ and .008, respectively) risk factors for death (Table 2). The fatality rate in dogs with concurrent DIC and acute renal failure was significantly higher ($P = .001$) compared with that of dogs without either DIC or acute failure (92% versus 29%, respectively; Table 2). The results were similar when euthanized dogs were excluded from the analysis. There was no difference in the prevalence of DIC and acute renal failure between dogs with environmental and exertional heat stroke. Other recorded complications

**Table 5.** Serum biochemistry data of dogs with heat stroke.

| Variable | n | Median | Range | Reference Interval |
|---|---|---|---|---|
| Alanine aminotransferase (U/L) | 18 | 136 | 45–1810 | 10–70 |
| Albumin (g/dL) | 14 | 2.86 | 2.25–4.5 | 2.60–4.00 |
| Alkaline phosphatase (U/L) | 14 | 294 | 51–749 | 13–190 |
| Amylase (U/L) | 12 | 901 | 224–7950 | 340–1100 |
| Aspartate aminotransferase (U/L) | 11 | 253 | 9–5900 | 14–80 |
| Total calcium (mg/dL) | 12 | 8.9 | 5.8–12.0 | 8.5–11.3 |
| Ionized calcium (mmol/L) | 35 | 1.2 | 0.86–1.53 | 0.90–1.30 |
| Chloride (mmol/L) | 3 | 118.0 | 115.0–141.0 | 102.0–117.0 |
| Cholesterol (mg/dL) | 13 | 231 | 140–600 | 118–309 |
| Creatine kinase (U/L) | 14 | 7350 | 348–182,000 | 20–160 |
| Creatinine (at 24 hours; mg/dL) | 37 | 1.66 | 0.50–12.00 | 0.50–1.50 |
| Creatinine (on admission; mg/dL) | 51 | 1.32 | 0.50–8.00 | 0.50–1.50 |
| γ-glutamyltransferase (U/L) | 11 | 6.0 | 3.0–38.0 | 1.0–13.0 |
| Globulin (g/dL) | 12 | 3.45 | 2.05–4.9 | 1.9–3.5 |
| Glucose (mg/dL) | 24 | 48.5 | 10–200 | 65.0–103.0 |
| Potassium (mmol/L) | 39 | 3.9 | 2.2–5.7 | 3.8–5.6 |
| Lactate dehydrogenase (U/L) | 4 | 725 | 5.8–2390 | 34–360 |
| Sodium (mmol/L) | 39 | 152 | 47–163 | 140.0–155.0 |
| Phosphorus (mg/dL) | 12 | 4.2 | 1.4–27.1 | 2.63–5.8 |
| Total bilirubin (mg/dL) | 15 | 0.3 | 0.13–1.22 | 0.02–0.54 |
| Total protein (g/dL) | 12 | 6.15 | 4.3–8.8 | 5.5–7.5 |
| Triglycerides (mg/dL) | 4 | 85 | 65–141 | 15–100 |
| Urea (mg/dL) | 19 | 54 | 26–714 | 11–50 |

included acute respiratory distress syndrome (ARDS, 4 of 54), pancreatitis, and pneumonia (1 of 54 each).

Postmortem examination, performed in 6 dogs, revealed acute tubular necrosis and renal infarcts (5 of 6), diffuse hemorrhages in the serosal surfaces and skeletal muscles, multiple petechiae and diffuse gastrointestinal bleeding (5 of 6), icterus (2 of 6), cerebral hemorrhage, and pancreatitis (1 of 6 each).

## Discussion

There is no clear-cut definition of heat stroke in dogs, but there is general agreement that it should be considered when heat-related illness leads to an acute onset of severe systemic clinical signs in an otherwise healthy animal.[2,6] However, it has been reported that delay in rectal temperature measurement in both humans and dogs hinders a prompt diagnosis of heat stroke on admission, and that a presence of lower body temperatures does not negate a positive diagnosis of heat stroke.[6,13,14] The selection criteria for all cases in the present study included presence of systemic clinical signs of an acute onset, along with a history of exposure to a warm environment, strenuous activity, or both, in otherwise healthy dogs, with no other concurrent unrelated disease. In the present study, there was a high variability in the body temperature on admission, as has been reported previously in canine heat-induced illness.[6] Twenty-six dogs went through whole body cooling by their owners, before admission, and some were admitted later than 3 hours after the heat insult had occurred. Thus, hyperthermia on admission should not have been an exclusive selection criterion. In contrast, neurological manifestations (ie, muscle tremors, seizures, convulsions, disorientation, stupor, coma) were detected on admission only in 42 of 54 dogs, whereas in all the remaining 12 dogs, hyperthermia (>41°C [105.8°F]), tachypnea, and acute collapse were all present. Thus, presence of neurological abnormalities probably should also not be an exclusive selection criterion for canine heat stroke, or alternatively, if the human definition of heat stroke (ie, hyperthermia with presence of neurological dysfunction) is accepted, then such cases should be classified as a less severe form of heat-induced illness. However, as stated earlier, the canine brain has an intrinsic thermal resistance,[8] and it is reasonable to assume that this definition, derived from human medicine, may not be applied without reservations to dogs.

Although there was no statistically significant difference in case fatality rate between dogs that were cooled by their owners before admission and dogs that were not ($P = .173$, Table 2), there was a major difference in the proportion of nonsurvivors between these groups (38% versus 61%, respectively). Thus, although the results of the present study do not clearly prove that whole body cooling is essential for survival, they do suggest that it may be beneficial, as cooling was negatively and significantly ($P = .005$) associated with the rectal temperature on admission in dogs admitted to the HUVTH within a time lag ≤4 hours (39.5°C versus 41.2°C [103.0 versus 106.1°F]). The lack of statistical significance concerning the effect of whole body cooling by the owners before admission on survival probably resulted from a high variability in cooling efficacy (depending on the method, intensity, and duration), type of hair coat, and its interaction with other parameters (eg, obesity, time lag to admission). A small sample size might have led to a lack of statistical power to reach significance.

All cases in this study had occurred between March and October, but in contrast to a previous report[6] in which most cases were presented in the early summer, in the present study, 79% of the dogs were presented during the peak of the hot season and heat stress. This dissimilarity may be attributed to the fact that the winter in central Israel is relatively warm (mean 16°C [60.8°F], range 7.3–28.5°C [39.2–83.3°F]) and humid, so acclimation from winter to summer in Israel occurs gradually and does not play a role in the pathogenesis of heat stroke. As both the average temperature and DI in the particular days of heat stroke were significantly increased compared with their corresponding average daily values (Table 1), owners should be advised to avoid exposure of their dogs to such environmental conditions, and clinicians should be aware that the likelihood of heat stroke is higher. Moreover, this study has found that DI in the particular days of heat stroke events was positively and significantly associated with occurrence of DIC.

Although in humans environmental (classical) heat stroke is of major concern, in this study, exertional heat stroke was observed more commonly. However, the distinction between environmental and exertional heat stroke may not be clear-cut in dogs, and heat stroke should be a major concern when dogs are exposed to stressful physical activities in a particularly hot and humid environment. This is exemplified by the fact that there was no association between the meteorological data and HS type (ie, exertional and environmental). It should be noted that delays in diagnosis of human heat stroke occur most commonly in moderate environments when the suspicion of exertional heat stroke is low.[13]

The overrepresentation of Belgian Malinios (OR 24, 14.5%) in this study was due to their exposure to strenuous activity as working military or police dogs, and 7 of 8 had exertional heat stroke. The fact that these highly trained dogs developed heat stroke after a relatively short duration of physical activity exemplifies the potential hazardous consequences of the combination of strenuous physical activity and a high environmental heat stress. Dog trainers should probably be educated to restrict strenuous physical exercise, especially when heat stress conditions are severe. Obesity and an active playful character might have played a role in the overrepresentation of Golden and Labrador Retrievers (OR = 2.1) in this study. Brachycephalic dogs had a trend toward overrepresentation (OR = 1.7) and are probably predisposed to heat stroke because of their poor ineffective evaporation ability and their tendency to develop laryngeal edema during heat stress.[2,15,16] English Bulldogs are particularly predisposed to heat

stroke because of a combination of a brachycephalic conformation and obesity.

Obesity was found to be a significant ($P = .04$) risk factor for death in the present study. Obesity and high body weight were reported to be risk factors for developing heat-induced illness in both people and dogs.[2,19–22] Excess body fat increases thermal insulation and impairs normal heat dissipation in obese people and animals.[2] All dogs, with the exception of one in this study, were of large breed, suggesting that the body weight/body surface ratio is an important factor in the heat dissipation mechanism under heat stress. However, the possibility that large dogs are more active compared with small and toy breed dogs and thus are over-represented, cannot be excluded. Owners of large breed, obese, and brachycephalic dogs should probably restrict the activity and exposure of such dogs to heat stress conditions.

In a retrospective study of human heat stroke, there was no significant correlation between the body temperature on admission and the morbidity or mortality,[21] whereas in a previous study of canine heat-related illness, hypothermia on admission was a poor prognostic indicator.[6] In the present study, there was no association between the body temperature on admission and fatality rate.

The lesions of heat stroke are related to the primary thermal insult; however, secondary deterioration occurs because of dehydration, shock, and a poor perfusion. Thus, early diagnosis and intervention are crucial to the prevention of further cerebral and renal deterioration and exacerbation of coagulation abnormalities.[1,2,5] This statement is supported by the finding that delayed admission (>90 minutes) was found to be a significant ($P = .032$) risk factor for death in the present study. Normalization of the core body temperature and supportive care are important, as they inhibit fibrinolysis, but are not enough, as the activation of the coagulation cascade continues in a pattern that resembles that encountered in sepsis.[22,23] Thus, early admission to an intensive care facility where additional therapy and monitoring are available is advised, although the latter have not been shown to result in a better outcome in the present study.

Endothelial cell injury, diffuse microvascular thrombosis, and formation of DIC are prominent features of heat stroke.[1,17,22] Injured endothelium releases tissue thromboplastin and factor XII, which activate the coagulation and complement cascades, inducing a systemic inflammatory response syndrome and widespread coagulation.[17,22] Hepatic injury due to hypoperfusion and microembolism can exacerbate the hemostatic abnormalities.[2,6,10] Concurrently, fibrinolysis is also highly activated during heat stroke and is manifested by increased plasmin-antiplasmin complexes and D-dimer, and decreased plasminogen concentrations.[10,22,25] In contrast to a previous study in which no association between coagulation test results and outcome was detected,[6] in the present study, occurrence of DIC and prolonged PT and aPTT on admission were found to be significant risk factors for death ($P = .013$, $P = .004$, $P < .001$, respectively). As DIC may appear hours to days after the initial hyperthermic insult, dogs with heat stroke should be monitored for coagulation abnormalities and clinical signs of DIC during the first 48 hours after insult.[25,26]

The treatment of the hemostatic abnormalities in DIC is based on stabilization of the coagulation, with concurrent prevention of thrombosis. Indeed, FFP was part of the treatment in 68% of the dogs in the present study, and heparin was given in 11 dogs (20%). The latter should be initiated only when antithrombin III concentrations are adequate, because its presence is required for heparin to exhibit its beneficial effects.[24,27] Although not proven effective, preincubation of whole blood or plasma with heparin was suggested to activate donor antithrombin III.[28]

Thrombocytopenia was present in 45 (83%) of the dogs in this study; however, only 28 were diagnosed with DIC. Thrombocytopenia was most likely caused by secondary platelet consumption due to vasculitis, gastrointestinal bleeding, and hyperthermia-induced platelet aggregation.[17,29,30] Delayed onset thrombocytopenia was observed in 14 dogs and probably resulted from development of DIC and decreased bone marrow platelet release due to megakaryocyte susceptibility to high temperatures.[17] Presence of metarubricytosis (68%) in the present study was not related to erythroid hyperplasia, as the ratio of NRBC to polychromatic RBC was >1 and thus can be considered as pathological. Similar results (58%) have also been previously reported in canine heat-induced illness, and it has been suggested that direct thermal bone marrow injury might have resulted in the premature release of NRBC.[6] Endothelial cell injury and diffuse microvascular thrombosis that are commonly associated with DIC may also be implicated as contributing factors in lesions to the blood-bone marrow barrier.[1,17,22]

The most remarkable biochemical abnormalities observed in the present study were increased serum activities of muscle enzyme activities (CK, LDH, AST), hepatic enzyme activities (ALP, ALT), azotemia, and hypoglycemia. The increase in serum CK activity on admission was marked and ranged from 7.5- to 1100-fold in most (12 of 14) of the dogs (Table 5). Thus, it is reasonable to assume that rhabdomyolysis was present in all these dogs and probably resulted from direct thermal muscular damage, increased muscular activity, and seizures. There were not enough data to determine whether dogs with high serum CK activities were predisposed to acute renal failure; however, this possibility should be further investigated. Rhabdomyolysis of different causes, including heat stroke, has been associated with myoglobinuric acute renal failure in people.[31]

Azotemia is a common finding in heat stroke and results from prerenal and renal mechanisms, such as severe hemoconcentration and direct renal tissue damage,[32] leading to tubular necrosis, as observed at postmortem examination of 5 dogs in this study. This probably occurs as a result of a direct renal thermal injury, dehydration, hypoxia, endotoxemia, release of cytokines and vasoactive mediators, and microthrom-

bosis associated with DIC.[1,2,18,32] Aggressive fluid therapy over the first 24 hours of hospitalization probably eliminated the prerenal component. Therefore, measurement of serum creatinine after 24 hours should be a more sensitive marker of renal damage compared with serum creatinine on admission. In the present study, acute renal failure ($P = .008$) and serum creatinine >1.5 mg/dL ($P = .003$) after 24 hours were both risk factors for death. Supportive treatment should protect against further renal deterioration but cannot eliminate the primary renal insult that induces tubular necrosis. It is for this reason that acute renal failure did develop in one third of the dogs in the present study, despite the early and aggressive IV fluid therapy employed.

Hypoglycemia can result from increased utilization or decreased production of glucose. Increased glucose utilization results from increased ATP demand, associated with high body temperatures, seizures, and respiratory efforts.[6,10,32] Sepsis may also be involved in the pathogenesis of heat stroke–induced hypoglycemia. Patients with heat stroke have an increased risk of bacterial translocation or endotoxin leakage, and develop bacteremia, endotoxemia, and sepsis because of gastrointestinal mucosal damage and a decline in host defenses.[6,33] Hepatic failure can lead to decreased glucose production and consequently to hypoglycemia.[6] Severe hypoglycemia (<47 mg/mL) on admission was found to be significantly ($P = .03$) associated with death, as has been previously described in dogs and humans with heat-induced illness.[6,34] This result exemplifies the importance of restoring and maintaining normoglycemia in dogs with heat stroke as part of the routine treatment. Hypoglycemia may be a risk factor for the development of central nervous system abnormalities in canine heat stroke.

Severe hyperthermia results in cerebral hypoperfusion, neuronal necrosis, direct vascular damage, cerebral edema, hemorrhage, and multifocal vascular thrombosis with tissue infarction that may lead to central nervous system abnormalities and death.[2,8,35] However, in experimentally induced hyperthermia in dogs (42.5°C [108.5°F] for 90 minutes), there were no significant differences in the morphological and biochemical indicators of neuronal injury between the study and the control groups, indicating that the canine brain is intrinsically resistant to sublethal hyperthermia. Thus, it has been suggested that central nervous system lesions in the dogs occur because of the presence of other physiological derangements rather than the direct thermal effect on the neuronal tissue.[7] Whatever the mechanisms leading to central nervous system lesions in canine heat stroke are, presence of seizures and semicoma/coma were found to be risk factors ($P = .02$ and $P = .06$, respectively) for death in the present study. Similarly, in previous studies in human and canine heat stroke, there was a statistically significant association between the mental status (comatose versus noncomatose) and the outcome.[6,36] In a retrospective study of human heat stroke, 11% had seizures and convulsions and 39% were comatose,[21] whereas in a previous study in dogs 24% presented coma.[6] In the present study, 35% of the dogs presented seizures, and 47% had semicoma or coma.

The presence of ECG abnormalities detected in 14 of 54 dogs might have resulted from a direct thermal myocardial damage, as has been reported previously[2]; however, extracardiac causes, such as hypoperfusion, lactic acidosis, electrolyte imbalance, and microthrombosis could lead to myocardial ischemia and arrhythmias.[7,37] Thus, dogs with heat stroke will probably benefit from oxygen supplementation, and an improvement in cardiac function should be expected once rehydration and restoration of the metabolic imbalances have occurred. Antiarrhythmic therapy should probably be considered only if the patient has related clinical signs.

Other complications of heat stroke observed in this study included ARDS (4), pancreatitis (1), and pneumonia (1), and all have been previously reported in human heat stroke and are attributed to systemic inflammatory response syndrome and multiple organ dysfunction.[1,38] These complications also should be looked for and considered in canine heat stroke when compatible clinical signs are present.

## Footnotes

[a] Israeli National Meteorological Service, Beit Dagan 50250, Israel
[b] Minos, ST-Vet, Montpelier, France
[c] Abacus, Diatron, Vienna, Austria
[d] Atago Co Ltd, Tokyo, Japan
[e] Kone Progress Selective Chemistry Analyzer, Kone Corporation Instrument Group, Helsinki, Finland
[f] Reflotron, Boehringer Mannheim, Germany or Reflovet Plus, Roche, Basel, Switzerland
[g] Nova 8, Nova Biomedical, Waltham, MA
[h] KC 1A Micro, Amelung, Germany; ACL 200, Instrumentation Laboratory, Barcelona, Spain
[i] SPSS 12.0 for Microsoft Windows, SPSS Inc. Chicago, IL
[j] StatXact, Citel Software Corp, Cambridge, MA
[k] PEPI 4.0, Computer Programs for Epidemiologists, 4th ed, Sagebrush Press, Salt Lake City, UT
[l] Osmitrol, Baxter Healthcare Corporation, Deerfield, IL
[m] Fusid, Teva, Petach Tikva, Israel
[n] Heparin sodium, Kamada, Rehovat, Israel
[o] Dexacort, Teva, Petach Tikva, Israel
[p] Docard, Dexon Ltd, Or Akiva, Israel
[q] Assival, Teva, Petach Tikva, Israel

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