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Title : HYPERTHERMIC CARDIAC ARREST AND IRREVERSIBLE SHOCK IN MONKEYS

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Introduction. Approx. 4,000 hyperthermia related deaths occur each year in the U.S.A., most of them due to "heat stroke", which may be triggered by hot environment, dehydration, exercise and infection . Protection of vital organs against hyperthermia is also important for cancer therapy. The pathophysiology of dying in lethal hyperthermia is poorly understood. Resuscitation from hyperthermic cardiac arrest is unexplored. In 1978 we initiated a laboratory research program in hyperthermia.

Pilot experiments. In dogs and rhesus monkeys under light anesthesia brain temp was raised to 42°C for ½-1 hour (by immersion heating), followed by normothermia. Partial recovery (lucid period) was followed by diffuse bleeding and irreversible shock in spite of standard life support measures.

Model. In 9 rhesus monkeys the natural course of dying was studied when brain temp was maintained at 42°C during spontaneous breathing with light halothane (n5), ketamine (n2) or thiopental anesthesia (n2). All 9 monkeys followed a similar pattern. Cardiac arrest occurred at about the same time irrespective of the anesthetic used. Monitored were EKG, MAP, heart rate, CVP, pulmonary artery wedge pressure, EEG (skull screws), intracranial pressure (ICP) (supracortical catheter), epidural temp (burr hole), rectal and nasopharyngeal temp, $PETCO_2$, arterial blood gases, hematocrit, clotting variables, and serum sodium, potassium, calcium, osmolality and glucose.

The monkeys were heated by immersion into warm water to raise and maintain epidural temp at 42±0.5°C until death (apnea, no arterial pulsations, EEG silence, electric asystole). Within 1 minute of death perfusion fixation with formalin was performed.

When epidural temp reached 40°C, tachycardia, tachypnea and hypocarbia occurred. This was followed by moderate hypotension, sometimes with PVC's and VT; and later by profound hypotension, terminal hypoventilation and agonal gasping, brief hypercarbia without hypoxemia, and pulselessness after approx. 90 min above 41°C. Rectal and nasopharyngeal temp's rose faster than brain temp. The heart arrested in asystole or electromechanical dissociation in 7; with VF in 2. The EEG remained active without convulsive patterns and flattened with hypotension. There was no signif rise in ICP. CVP and PAWP remained unchanged. There were metabolic acidemia and profound hypoglycemia with blood sugar values of 25 mg/dl (13-42). 5 dogs under light ketamine followed the same course, but cardiac arrest occurred later (at 190-350 min). In the arrest model, no GI bleeding occurred because of the rapidity of dying. There was no evidence of DIC nor were there elevated blood endotoxin levels. At autopsy, however, there were petechial hemorrhages in all organs, particularly the heart; however, the brain seemed grossly normal.

When in 3 monkeys the hyperglycemia was prevented by IV glucose 50%, cardiac arrest occurred 60 min later. In five additional monkeys, the empirical addition of a septic shock "cocktail" (ATP-glucose-insulin-magnesium chloride, steroid) did not extend tolerance further.

Cardiac resuscitation. Pigtail monkeys were used. They followed the same course to arrest (see model). Group A (n6) received standard CPR with fluid resuscitation. Group B (n6) received in addition hypertonic glucose, steroid and glucagon. After 1 min of cardiac arrest, CPR was started and accompanied by surface cooling and cold saline IV. Temp reached 39°C within 15 min. Spont circ. was restored in 8/12 with temp still high. Immed. post-CPR, all animals irrespective of therapy developed an irreversible shock state, resembling a mixture of oligemic, cardiogenic and distributive shock. It was resistant to IV colloids, salt and water; norepinephrine; calcium; and the special treatment of group B. Group A deteriorated to re-arrest at a mean of 131 min post-CPR and group B at 190 min. 5% glucose IV (group A) normalized blood sugar. EEG recovered slowly in group A, promptly in group B. At autopsy there was hemorrhagic fluid in all serosal cavities, GI bleeding, hemorrhagic myocardial contusion or infarction, and terminal pulmonary edema or hemorrhage. Again the brains appeared grossly normal.

Conclusions. A reproducible monkey model of lethal hyperthermia was developed. Severe hypoglycemia is a consistent and correctable factor. Hyperthermic cardiac arrest is reversible. Following correction of temp pre-or post-arrest a lucid period is followed by irreversible shock.

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