Title : HYPERTHERMIC ALTERATION OF SYMPATHETIC ACTIVITY

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Introduction: The cardiovascular responses to an elevation of core temperature, regardless of the etiology, are an increase in cardiac index (CI) and heart rate (HR) in association with increased cutaneous perfusion and reduced splanchnic perfusion. Since the sympathetic nervous system (SNS) plays a major role in the regulation of cardiovascular response, it might then be expected that changes in core temperature would differentially alter regional SNS activity.

Methods: Sixteen patients with advanced cancer undergoing whole body hyperthermia were studied after giving informed consent to this institutionally-approved protocol. Prior to anesthetizing the patients and inducing hyperthermia, radial arterial and thermodilution Swan-Ganz catheters were inserted percutaneously. Anesthesia was established with a continuous infusion of thiopental (7 mg/kg/hr) and fentanyl (3 ug/kg/hr). Core temperature was elevated to 41.5 C by means of a high-flow, low-volume, heated water perfusion suit over a period of approximately 2 hours. Blood samples for radioenzymatic assay of catecholamines were obtained simultaneously from the radial artery, pulmonary artery and cutaneous forearm vein after the induction of anesthesia at 37, 39.5 & 41.5 C. Systemic and pulmonary arterial pressures, pulse and cardiac output were determined concurrently.

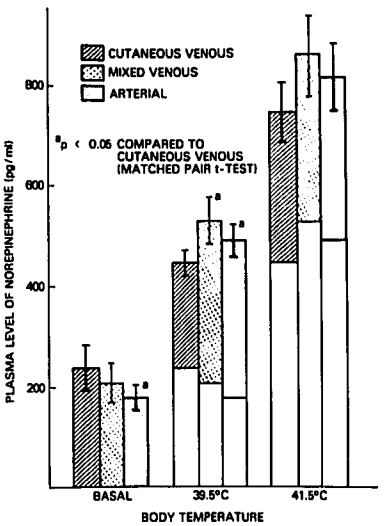
Results: Changes in hemodynamics and plasma norepinephrine (NE) levels are summarized in the accompanying table and figure. Baseline values at 37 C were recorded after the induction of anesthesia. At a core temperature of 39.5 C, CI and HR had increased by approximately 50% and there was a 10 torr reduction in the mean arterial pressure (MAP). Cutaneous, mixed venous and arterial NE levels were all increased, with the greatest increase evident in the mixed venous sample. No significant increases were seen in the epinephrine (EPI) levels from any of the vascular beds. At the final temperature of 41.5 C, further increases in CI and HR were seen and MAP decreased further. Additional increases in NE were seen at all sites with again the greatest increase from baseline values evident in the mixed venous samples. A small, but statistically significant rise in EPI was seen at this time. Stepwise, multiple regression analysis showed a close correlation of plasma NE with either HR or CI. No other correlation between hemodynamic data and catecholamines could be demonstrated at a confidence level of $p \leq 0.05$.

Discussion: The hemodynamic changes in anesthetized cancer patients at 41.5 C were not as profound as those described in healthy, unanesthetized volunteers[1] at 39.5 C. The induction of hyperthermia produced parallel increases in HR and CI, which correlated directly with increases in plasma NE. The elevated plasma NE is an index of increased SNS activity.[2] At basal body temperature and under anesthesia, cutaneous plasma NE levels exceeded arterial; mixed venous NE levels were intermediate. As the temperature rose, proportionately greater increases were seen in the arterial and mixed venous levels of NE than in the cutaneous plasma. This differential increase in mixed venous and arterial NE levels in excess of cutaneous NE, provides direct evidence that during hyperthermia, cutaneous SNS activity is decreased while in other areas, i.e. splanchnic and cardiac, SNS activity is increased. The absolute increase in cutaneous NE with the induction of hyperthermia is merely a reflection of increased circulating background NE and does not represent increased cutaneous liberation of NE; in fact, there is a net loss of NE through the cutaneous circulation as evidenced by the fact that arterial NE levels were greater than cutaneous levels. These findings are consistent with changes in SNS activity directly measured in experimentally-heated animals and support the view that alterations in regional SNS activity modulate the hemodynamic changes observed with the elevation of core temperature in man.

Hemodynamic Responses:

	37 C	39.5 C	41.5 C
CI	4.0+.2	6.0+.2	6.9+.2 (L/min/m^2)
HR	88+4.5	124+3.3	141+3.7 (bpm)
PCWP	7.4+.7	5.0+.7	4.1+.6 (torr)
MAP	85+2.2	74+2.3	71+2.7 (torr)

Norepinephrine levels:



References:
1. Rowell LB, Brengelmann GL, Murray JA: Cardiovascular responses to sustained high skin temperature in resting man. J Appl Physiol 27:673-680, 1969
2. Lake CR, Ziegler MG and Kopin IJ: Use of plasma norepinephrine for evaluation of sympathetic neuronal function in man. Life Sci 18:1315-1326, 1976.