Title: MICROVASCULAR PERMEABILITY IN THE LIVER DURING ENDOTOXIN SHOCK.

GH Sigurdsson, HA Youssef, JT Christenson, A Owunwanne.
Depts of Anaesthesia, Surgery and Nuclear Medicine,
Faculty of Medicine, Kuwait University, Kuwait.

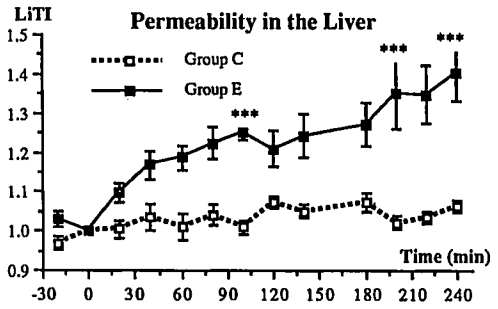
Acute lung injury (ARDS) caused by endotoxemia and sepsis is characterized by increased pulmonary vascular permeability to plasma proteins resulting in lung edema, hypoxia, decreased lung compliance and pulmonary hypertension. Until recently rather little attention has been paid to the role of the liver and the gut in endotoxin shock and sepsis, but lately increasing evidence has appeared suggesting involvement of these organs at an early stage.

The aim of this experimental series was to study microvascular permeability in the lungs as well as in abdominal organs during endotoxin shock using a double isotope method. We followed the dynamic behavior of In-111 labeled transferrin and Tc-99 labeled erythrocytes in multiple organs, including the liver, during endotoxin shock in sheep (group E; n = 7). A control group (group C; n = 7) was treated identically to group E, but received no endotoxin.

An experimental protocol was designed to mimic a clinical condition in an intensive care setting as far as possible. The animals were mechanically ventilated with 50% oxygen to avoid hypoxemia and IV fluids were given to reduce adverse effects of hypovolemia. A moderate dose of E coli endotoxin (10 µg/kg bwt) was given by IV infusion to induce shock. The animals were anaesthetized w ketamine and pancuronium and placed in supine position under a gamma camera linked to a STAR computer. An organ transferrin index (TI) which describes the net accumulation of plasma equivalents in the lung, was calculated. Arterial, central venous and Swan-Ganz catheters were incerted and connected to recorders for monitoring of the circulation.

The endotoxin infusion caused immediate increase in TI, both in the lungs(LuTI) as well as in the liver (LiTI) compared with the controls ($p<0.01$). These changes were accompanied by a sharp increase in PAP, decreased PaO2 and worsened lung compliance. No significant changes were noted in the kidneys or the over the gut.

It was concluded that there was a marked increase in the liver transferrin index during endotoxin shock in sheep. This may indicate that microvascular injury occurs just as early in the liver as in the lungs during endotoxin shock.



Title: EFFECTS OF HYPOTHERMIA AND POTASSIUM VARIATIONS ON MAXIMUM DIASTOLIC POTENTIAL

Authors: A Laszlo MD, J Sprung MD, PhD., S Polic, MD, PhD, JP Kampine MD PhD, and ZJ Bosnjak PhD
Affiliation: Department of Anesthesiology, The Medical College of Wisconsin, Milwaukee, WI 53226

Hypothermia induces redistributional hypokalemia which is in direct relationship to the depth of hypothermia and it is fully reversible with rewarming. Supplementation with exogenous K^+ may present the load that hypothermic organism, mostly in the process of rewarming, cannot handle resulting in "overshoot" hyperkalemia with arrhythmias.[1] Hypothermic effects on K^+ homeostasis may be important factor in determining transmembrane potential (TMP). One of the cellular mechanisms for dysrhythmias is loss of membrane potential (LMP) in "fast response" fibers that leads to depressed fast response conduction and may induce re-entry, abnormal forms of automaticity and/or heart blocks.[2] We evaluated how hypothermia and changes in extracellular K^+, $[K^+]_e$, effect maximum diastolic potential (MDP) of isolated canine Purkinje fibers, as a potential pathogenetic mechanisms for cardiac arrhythmias. Purkinje fibers from dog heart were cut and pinned in a 2 ml bath of oxygenated Krebs solution (37°C). The TMPs were recorded using a fine tip glass microelectrodes. Two stages of hypothermia, 32°C and 28°C, were achieved by adjusting temperature of the bath solution. K^+ variation was achieved by exchanging the normokalemic bath solution with one containing low (2.3 mM) or high (6.7 mM) K^+ content. Cells were stimulated with bipolar surface electrode.

Our results (Fig.1) show that hypothermia has stabilizing effect on MDP regardless of the value of $[K^+]_e$. Hypokalemia in conjunction with hypothermia shifts the membrane potential curve to the more negative level and gives significant additional protection against LMP. Hyperkalemia depolarizes Purkinje cell and hypothermia opposes this effect. Low body temperature induces the loss of $[K^+]_i$[3] what corresponds to reduction of MDP in hypothermic spontaneously beating cell.[4] Our study did not confirm this hypothermic effect on MDP. To exclude a possibility that the mode of cell activation (spontaneous vs. stimulated) is underlying cause for found discrepancies we repeated the study on spontaneously beating cell, and the results were similar. Presently we have no explanation for hyperpolarizing effect of hypothermia. In vivo hypothermic $[K^+]_i$ depletion is simultaneously accompanied by decrease in K_s^+. If the proportion of this hypothermic K^+ shifts is preserved, $[K^+]_i/[K^+]_e$ ratio and MDP are maintained in normal range. Besides this, in vivo, stabilizing effect of hypothermia on MDP mediated via $[K^+]_i/[K^+]_e$ ratio, our experiments,in vitro, proved that hypothermia in addition stabilizes MDP by some other, still unknown mechanism. In spite of constant $[K^+]_e$ (high, normal or low), hypothermia consistently hyperpolarized the cell membrane. Hypothermia and especially hypothermic hypokalemia are thus a physiologic, protective mechanism against increased cardiac irritability. The correction of hypothermic hypokalemia, only because the serum K^+ is low, will induce LMP, and therefore appears to be unnecessary since it may create potential for arrhythmias. In hypothermic setting, when $[K^+]_i$ is depleted, this may happen at lower K^+_s, as compared to normothermia.

References: 1. Inten Care Med 9:257,1983. 2. Anesthesiology 72:347, 1990. 3. Jpn J Thorac Surg 23:191-203,1975. 4. Helv Physiol Acta 12:32,1954.

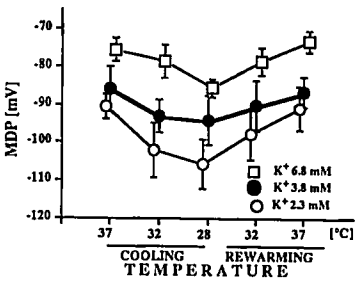


Fig. 1 Regardless of the level of K_s^+ and its effect on TMP, hypothermia showed tendency to hyperpolarize Purkinje cell membrane. Maximal effect was achieved at hypothermia of 28°C and K_s^+ 2.3 mM, when MDP increased to -106±6.5 mV.