Title **MULTIPLE ORGAN FAILURE AND PLATELET TRAPPING IN THE INTESTINE IN CRITICALLY ILL PATIENTS.**

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Recent clinical and experimental data suggests that the gastro-intestinal tract may be an important source of endotoxin and bacteria, causing sepsis and multiple organ failure (MOF) in critically ill patients (1). It is known that platelets aggregate and sequestrate wherever there is microvascular injury, such as occurs in the lungs during ARDS and in the liver and the lungs during experimental endotoxemia. However, no data is available on platelet sequestration in the liver and in the gut in sick patients. The aim of this study was to follow the behavior of platelets in multiple organs of critically ill patients, who had been resuscitated after major trauma or sepsis. Fifteen patients were studied. The patients in group A (n=10) had been resuscitated after septic shock of extra-abdominal origin (n=2) or a severe trauma (ISS>30, n=8). They had a mean APACHE II score of 20±6 on admission. Group C (n=5) had severe head injuries, but no other significant injuries (ISS:16-29 and APACHE II=12±4). In addition, they had all been circulatory stable and not had any signs of sepsis prior to the study. The study was approved by the Ethical Committee for Human Research of K.U.

Autologous platelets were labeled in vitro with In-III oxine, 135-295 µCi. Cadmium-telluride minidetectors connected to preamplifiers and a microcomputer (custom built mobile unit) were used to measure the counts over the organs studied, lungs, liver, kidneys, spleen, gut, brain, muscle and heart. Measurements were done daily (for 7 days or until death) over each organ (a mean value of 3 measurements., each done during 100 sec). The data were presented as a ratio: organ activity over heart activity.

Seven of the patients in group A developed MOF and 4 of them died, 5 to 38 days after the initial insult. None of the control patients (group C) developed MOF and all survived. All the patients in group A, who developed MOF (n=7), had significant increase in platelet trapping in the liver and the lungs. The other three, who did not develop MOF, as well as two of the controls had slight increase in the liver and a significant rise in the lungs. Furthermore, all the patients who died had a marked increase in platelet activity (trapping) in the gut (more than 7 times the activity in blood), while none of the survivors had ($p<0.01$). Furthermore, this increase was recorded 1-3 days prior to the first clinical signs of sepsis and up to a week before the development of MOF.

The results of this preliminary study support the hypothesis that the gut may be a source of endotoxin and bacteria causing sepsis and multiple organ failure in critically ill patients. In patients resuscitated after severe trauma or shock, increased sequestration of platelets in the gut, as measured by radioisotope labeled autologous platelets, may predict the development of sepsis and multiple organ failure.

(1) Border JR, Hypothesis: Sepsis, multiple systems organ failure and the macrophage. Arch Surg, 123, 285-286.

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TITLE: EFFECT OF INDIVIDUAL BRANCHED CHAIN AMINO ACIDS ON CONTRACTILITY AND FATIGUE OF DIAPHRAGM

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We have found that branched chain amino acids(BCAA) improve recovery from fatigue induced by direct stimulation of isolated rat hemidiaphragm. This study investigate the contribution of the individual amino acids.

Five groups of hemidiaphragms were equilibrated with Krebs Ringer Buffer solution(KRB) alone(as paired controls, n=24), KRB plus leucine(n=6), valine(n=6), isoleucine(n=6), or all three(BCAA, n=6). Hemidiaphragms were stimulated directly under complete neuromuscular block. Fatigue was induced by 10 min. stimulation with 30 trains/min of 5 Hz at a 50 % duty cycle. Isometric tensions elicited by single and tetanic(10 to 100 Hz) stimulation were measured at baseline, after 2 hours of equilibration(T2), and at 0, 10, 30, and 60 minutes(T6) after induction of fatigue.

The per cent of baseline at T6 elicited by stimulation at 100 Hz (mean±SE) was 58±5, 78±2 ($p<0.01$), 76±2 ($p<0.01$), 70±5 (ns), and 64±5 (ns) for KRB, BCAA, leucine, valine and isoleucine, respectively. As illustrated in figure, tension difference(% of baseline in treatment - % of baseline in paired control), at T2 and T6, there were significant differences in leucine and BCAA compared with control, but not in valine or isoleucine.

The data suggest that a major part of the effect of BCAA on reduction of fatigue in isolated rat hemidiaphragm is mediated by leucine.