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**LOCAL FLUID SHIFTS
AND EDEMA IN HUMANS
DURING SIMULATED MICROGRAVITY**

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A. Mechanisms of Headward Edema Formation during Head-Down Tilt

Co-Investigators: S.E. Parazynski, M. Aratow, B. Tucker, J. Styf, and A. Crenshaw

Recent Results:

To understand the mechanism, magnitude and time course of facial puffiness that occurs in microgravity, seven male subjects were tilted 6° head-down for 8 hours, and all four Starling transcapillary pressures were directly measured before, during, and after tilt (1-4). Head-down tilt (HDT) caused facial edema and a significant elevation of microvascular pressures measured in the lower lip: capillary pressure increased from 27.7 ± 1.5 mm Hg pre-HDT to 33.9 ± 1.7 mm Hg by the end of tilt (Fig. 1). Subcutaneous and intramuscular interstitial fluid pressures in the neck also increased as a result of HDT, while interstitial fluid colloid osmotic pressures in these tissues remained unchanged. Plasma colloid osmotic pressure dropped significantly by 4 hours of HDT (21.5 ± 1.5 mm Hg pre-HDT to 18.2 ± 1.9 mm Hg at 4 hours HDT), suggesting a transition from fluid filtration to absorption in capillary beds between the heart and feet during HDT (Fig. 2). After 4 hours of seated recovery from HDT, microvascular pressures (capillary and venule pressures) remained significantly elevated from baseline values, despite a significant HDT diuresis and the orthostatic challenge of an upright, seated posture. These results suggest that facial edema resulting from HDT is primarily caused by elevated capillary pressure in the head and decreased plasma colloid osmotic pressure. Post-tilt maintenance of elevated cephalic capillary pressure may suggest a compensatory vasodilation to maintain microvascular perfusion.

Significance and Future Plans:

This study represents the first direct measurement of all four Starling pressures in humans and the first time that micropuncture was applied to the human microcirculation above heart level (5). These results have elucidated the mechanism of facial puffiness during microgravity. Our results also indicate the need for measurement of intracranial pressure (ICP) during head-down tilt and actual microgravity. These results have important implications to long-duration missions because some cosmonauts had facial edema for up to one year and intracranial edema may limit performance. Future plans will: 1) investigate the post-tilt recovery period for longer times, 2) hopefully investigate ICP in rhesus monkeys during a future Cosmos mission, and 3) develop a noninvasive ICP technique for application to studies of crew during actual microgravity.

B. Postural Responses of Head and Foot Microcirculations and their Sensitivity to Bed Rest

Co-Investigators: M. Aratow, J.-U. Meyer, and S.B. Arnaud

Recent Results:

To explore further the mechanism of facial puffiness, headache, and nasal congestion associated with microgravity, the postural responses of the cutaneous microcirculation in the forehead and dorsum of the foot of 8 healthy men were studied by changing body position on a tilt table and measuring blood flows with a laser-Doppler flowmeter (6-8). Increasing arterial pressure in the feet by moving from a 6° head-down tilt to a 60° head-up posture significantly decreased foot cutaneous flow by $46.5 \pm 12.0\%$ (Fig. 3). Raising arterial pressure in the head by tilting from the 60° head-up to 6° head-down posture significantly increased forehead cutaneous flow by $25.5 \pm 7.2\%$. To investigate the possibility that these opposite responses could be modified by simulated microgravity, tilt tests were repeated after 7 days of 6° head-down tilt bed-rest. On the 1st and 2nd days after bed-rest, flows in the foot were decreased by $69.4 \pm 8.8\%$ and $45.8 \pm 18.7\%$, respectively, and increased in the head by $39.3 \pm 8.6\%$ and $15.5 \pm 5.9\%$, respectively. These responses were not significantly different from those recorded before bed-rest.

Significance and Future Plans:

Cutaneous microcirculatory flow in the feet is well regulated to prevent edema when shifting to an upright position, whereas there is little regulation in the head microcirculation with head-down tilt. The lack of regulation in the forehead cutaneous microcirculation increases capillary flow, and consequently increases fluid filtration. This phenomenon helps explain the facial edema associated with the simulated or actual microgravity environment. Future plans include longer-term bed-rest experiments and studies of intracranial blood flow by transcranial Doppler and correlation of blood flow alterations with performance indices in human subjects. The development of arterial and microvascular adaptations to gravitational blood pressure gradients is well documented in tall species such as humans and giraffes. It is expected that some or all of this vascular adaptation will be lost during long-duration flight.

C. Transcapillary Fluid Transport Associated with LBNP with and without Saline Ingestion

Co-Investigators: S. Fortney, M. Aratow, D.E. Watenpaugh,
and A. Crenshaw

Recent Results:

Lower body negative pressure (LBNP) may enhance fluid replacement during spaceflight by sequestering fluids in the lower body to help maintain plasma volume and post-flight orthostasis. We hypothesized that saline ingestion during LBNP would further increase transcapillary fluid filtration into leg interstitium and further improve postflight orthostatic tolerance. Six subjects underwent 4 h of 30 mm Hg LBNP and 50 min of recovery on two separate days with and without drinking one liter of isotonic saline during LBNP (9-11). Interstitial fluid pressures (IFP), venous pressure (VP), and change in circumference (LC) were continuously measured in the leg. Whole-body transcapillary fluid transport rate (TFT, net filtration if $TFT < 0$) was determined by subtracting urine production and insensible fluid loss from changes in plasma volume. Leg IFPs decreased in parallel with LBNP (3.0 ± 2.6 mm Hg to -26.5 ± 2.9 mm Hg, $p < 0.05$), yet VP remained constant (Fig. 4). Although IFPs returned to baseline after LBNP alone, LC remained $4.1 \pm 1.3\%$ above baseline at 50 min of recovery ($p < 0.05$) (Fig. 5). Saline ingestion increased post-LBNP IFP and LC relative to LBNP alone. TFT was 145 ± 10 ml/h (723 ± 43 ml) during LBNP with saline ingestion, compared to -7 ± 12 ml/h (-40 ± 64 ml) during LBNP alone.

Significance and Future Plans:

Increased vascular transmural pressure during LBNP led to venous pooling and filtration into lower body interstitium, yet reabsorption from upper-body interstitium compensated for this filtration during LBNP alone. Saline ingestion with LBNP supplemented lower-body interstitial volume. Post-LBNP reabsorption of fluid from lower-body interstitium was similar with and without saline ingestion, which indicates about half of the fluid load remained in the interstitial space at 50 min of recovery. Future plans may include studies of other types of fluid ingestion and LBNP as well as evaluation of the effect on post bed-rest orthostatic intolerance. These results provide objective data on possible use of LBNP and saline ingestion to improve orthostatic tolerance following short-duration as well as long-duration flight.

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Figure Legends:

- Figure 1: Capillary blood pressure increased significantly in the lip within the first half hour of HDT and remained elevated throughout HDT and in the recovery period. Lower bar indicates period of HDT.
- Figure 2: Plasma colloid osmotic pressure decreased significantly after 4 hours HDT. Lower bar indicates period of HDT.
- Figure 3: Responses of the forehead and dorsal foot cutaneous microcirculations to an arterial pressure increase before and after a one week period of bedrest. Forehead microcirculatory flow increases significantly whereas that in the foot decreases significantly with increased local blood pressure. The clear bars represent the percentage change in forehead cutaneous flow caused by a tilt to the head-down position, and the response of the foot cutaneous flow caused by a tilt to the head-up position is represented by the shaded bars. The magnitudes of these changes due to 7 days of bed rest were not significantly different from each other.
- Figure 4: Tissue fluid and foot venous pressures during LBNP with and without saline ingestion. The lower rectangle labelled "LBNP" in each graph represents the time period during which LBNP was applied to each subject. The subdivisions at the beginning and end of the rectangle represent the ramp up and ramp down of the chamber pressure. The rectangle in each graph labelled "saline" represents the time period over which the subject was required to drink 1 liter of isotonic saline.
- Figure 5: Calf circumference change, calculated plasma volume, and serum colloid oncotic pressure during LBNP with and without saline ingestion. The lower rectangle labelled "LBNP" in each graph represents the time period during which LBNP was applied to each subject. The subdivisions at the beginning and end of the rectangle represent the ramp up and ramp down of the chamber pressure. The rectangle in each graph labelled "saline" represents the time period over which the subject was required to drink 1 liter of isotonic saline.

FIGURE 1

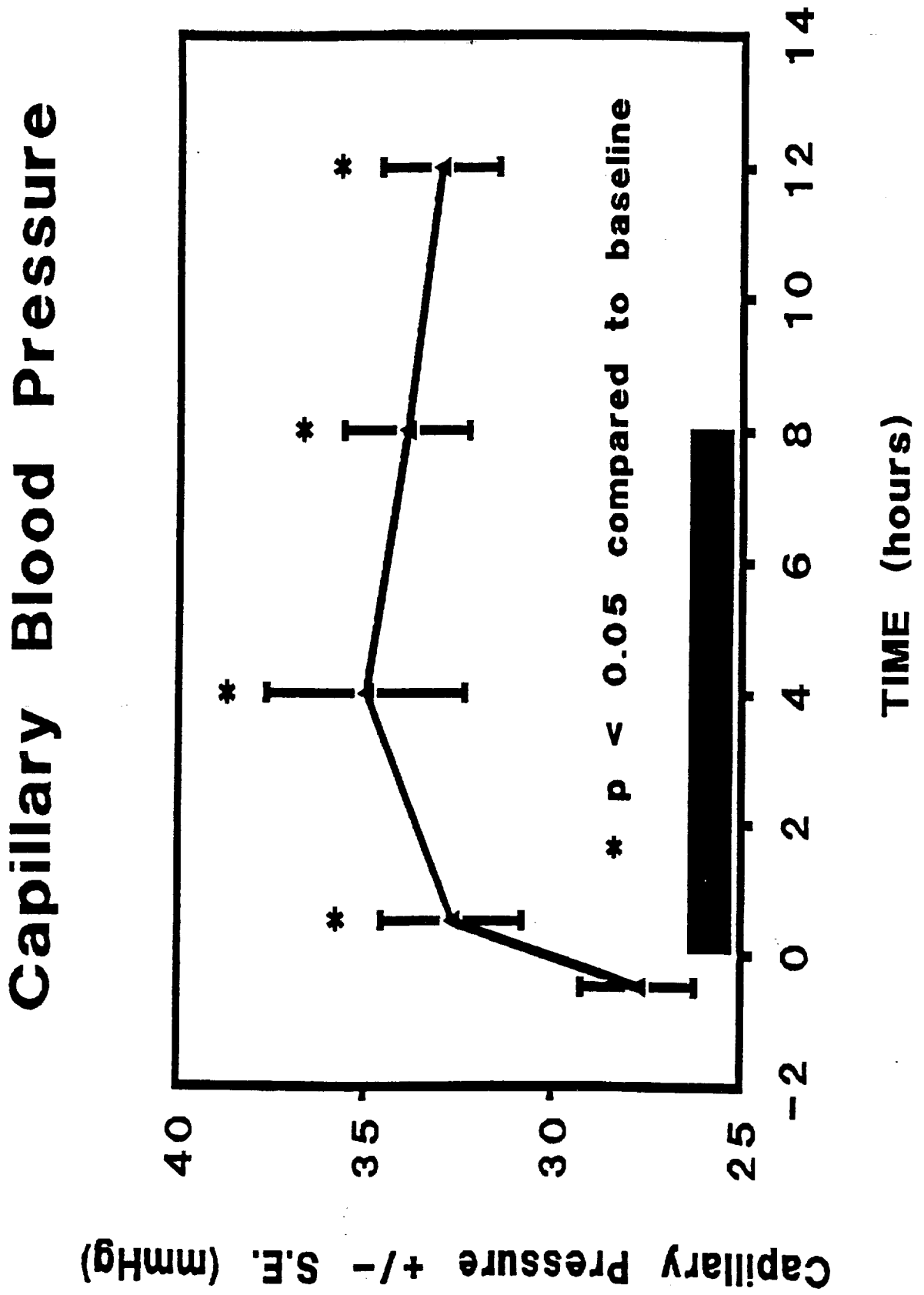


FIGURE 2

Plasma Colloid Osmotic Pressure

Colloid Osmotic Pressure +/- S.F. (mmHg)

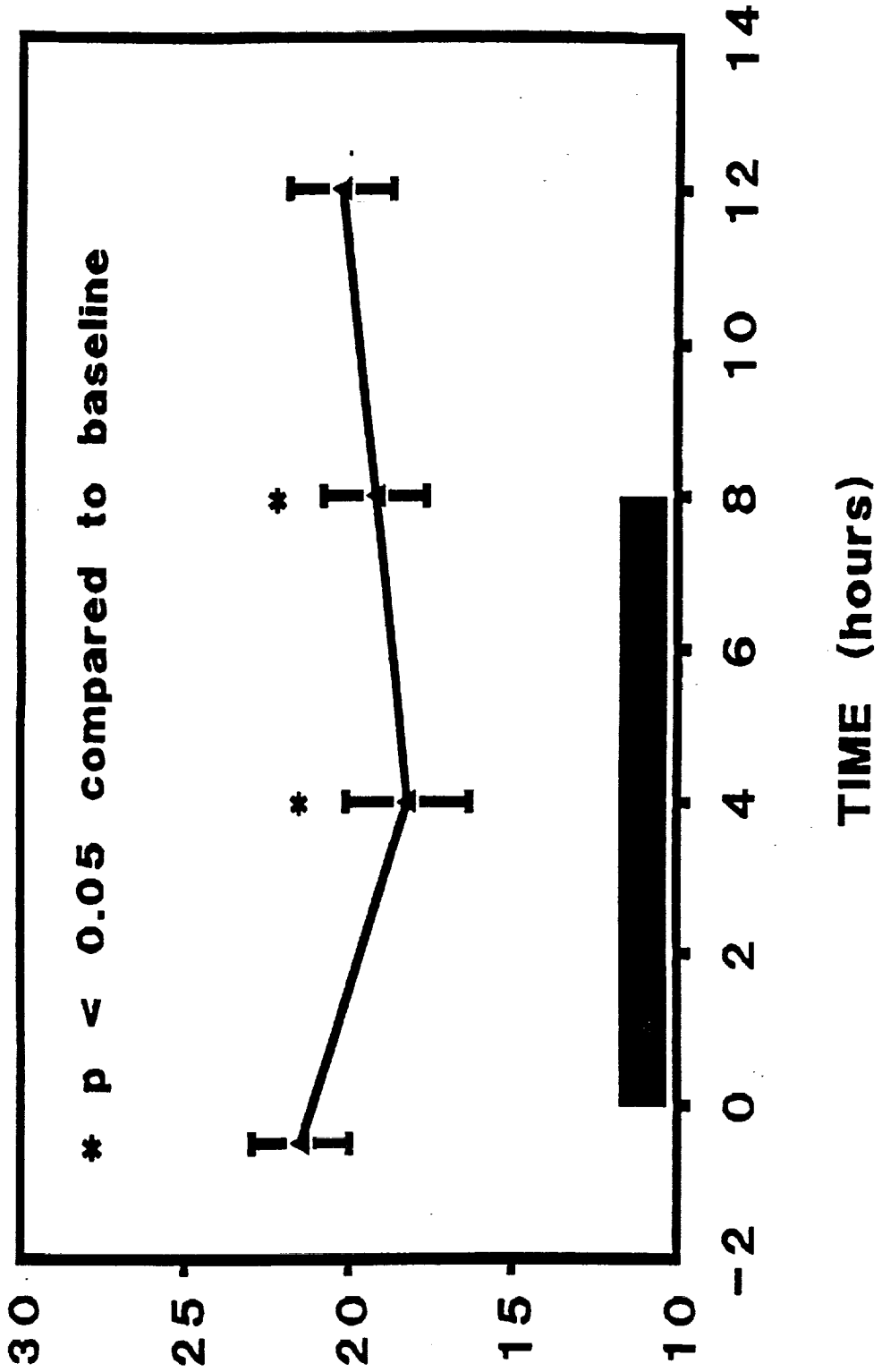
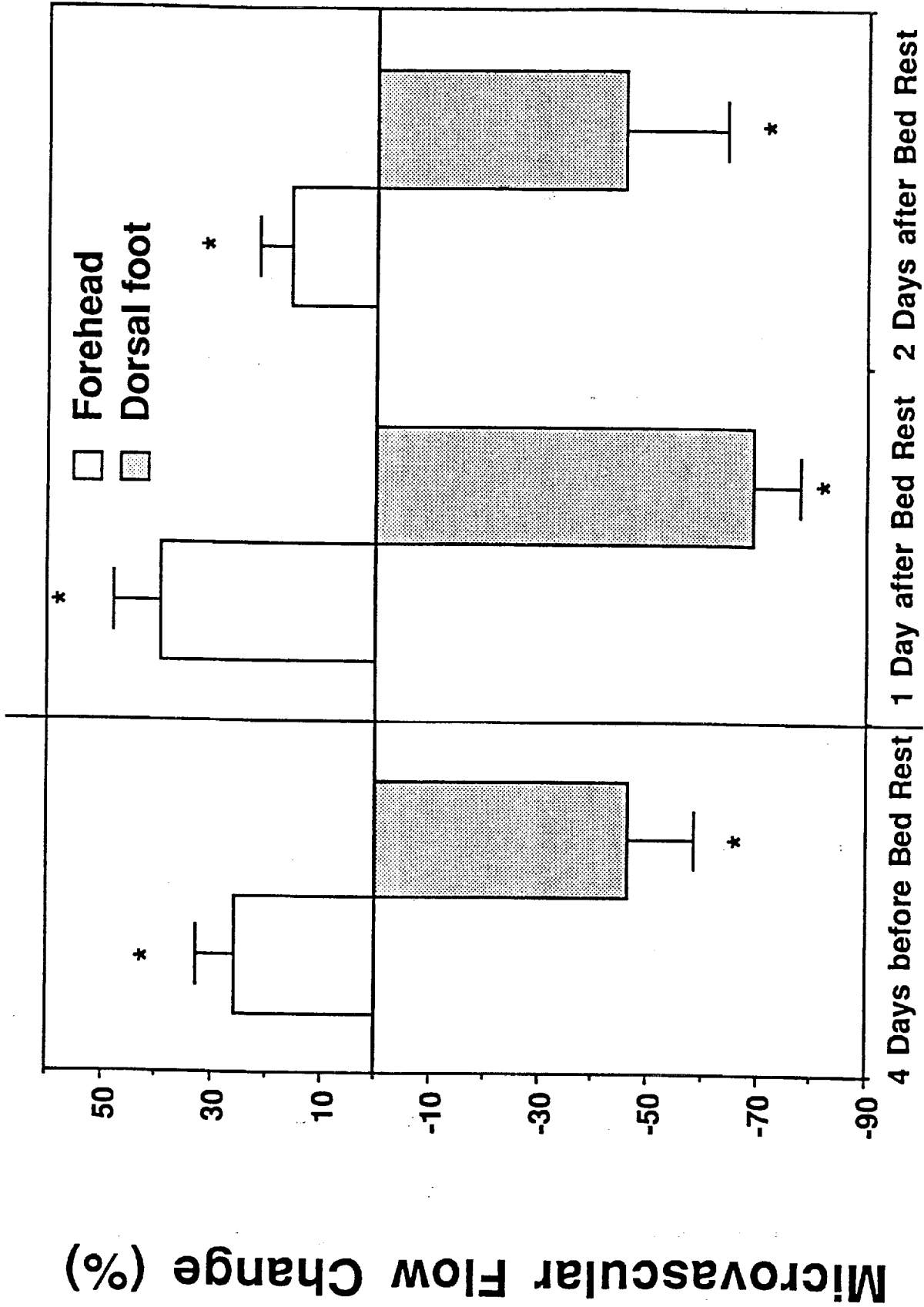


FIGURE 3



*p < 0.05 compared to pre-tilt microvascular flow

FIGURE 4

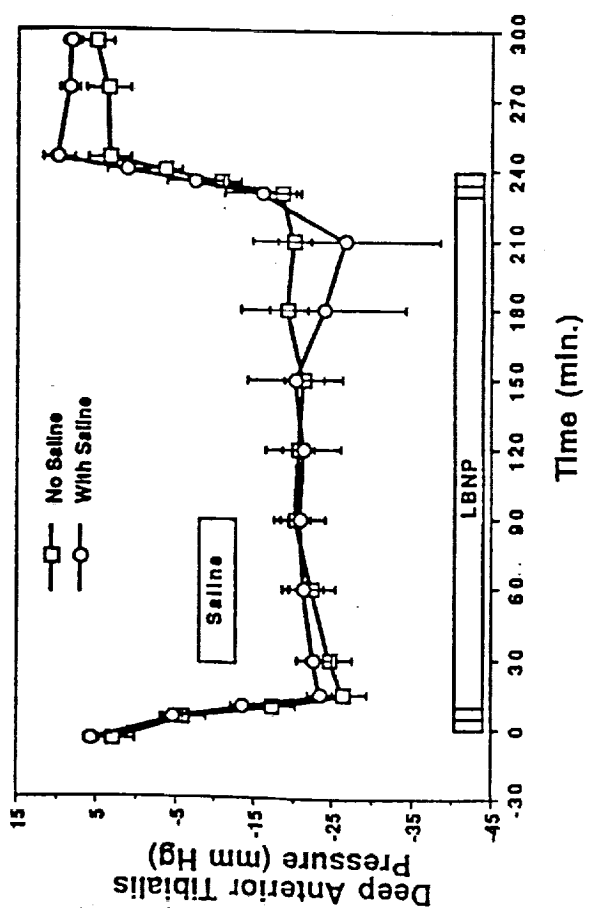
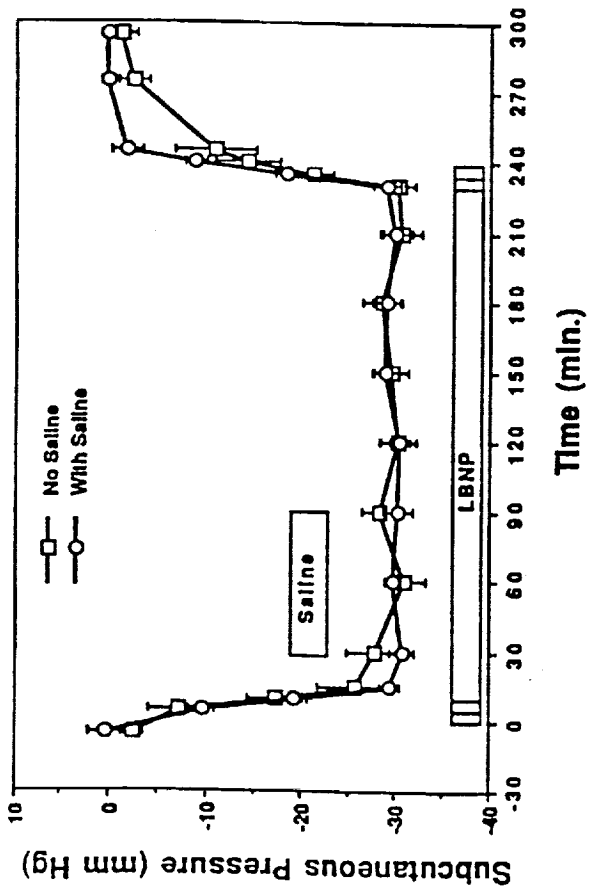
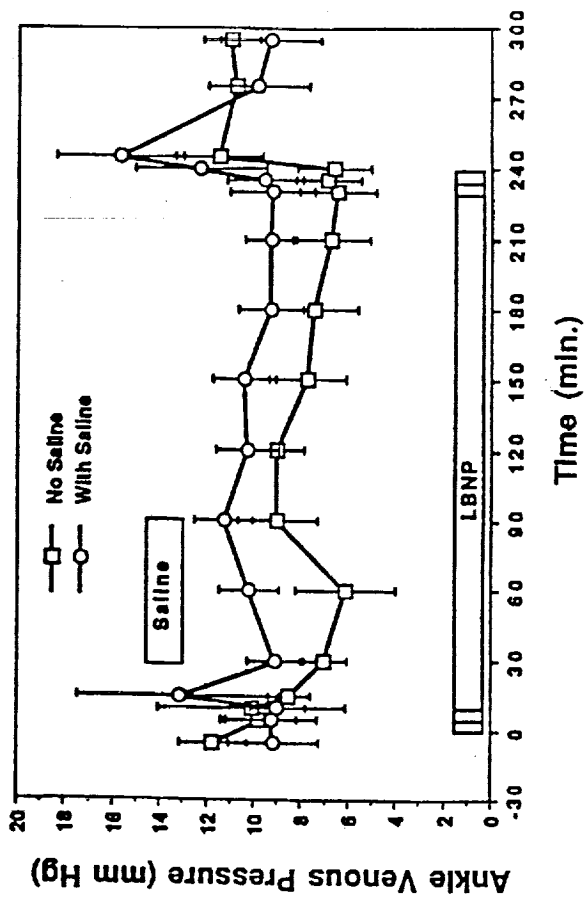
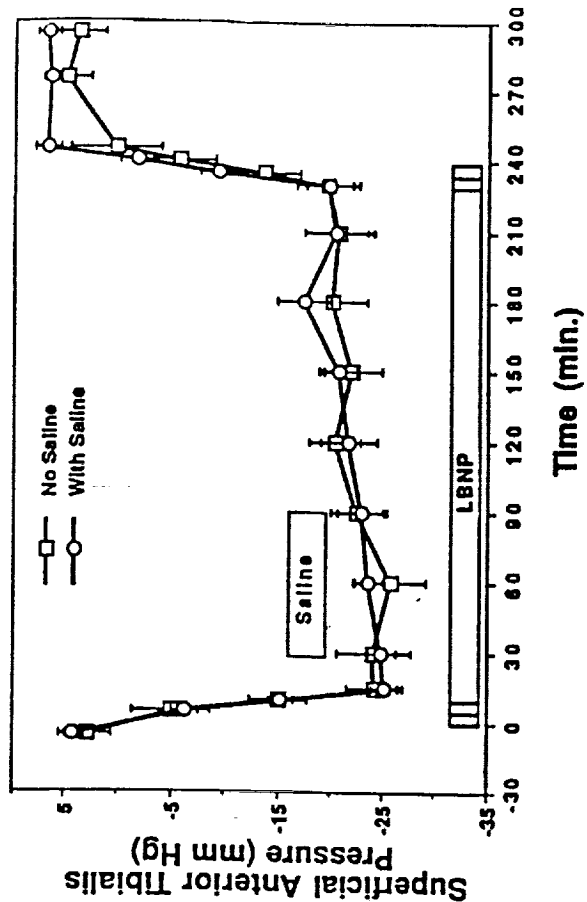
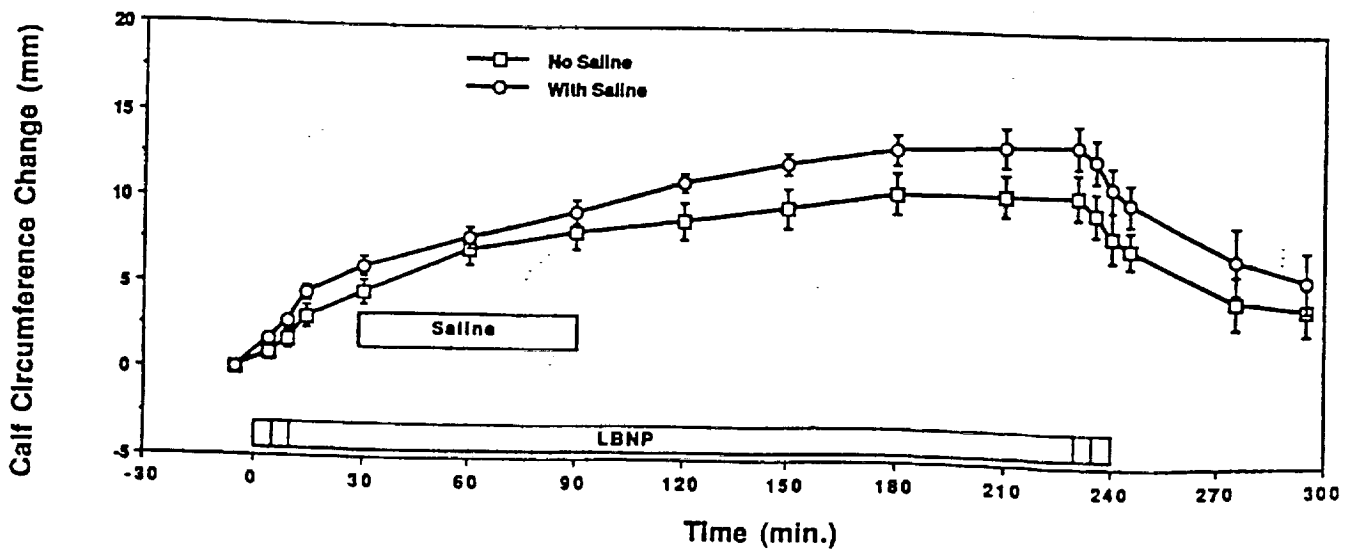
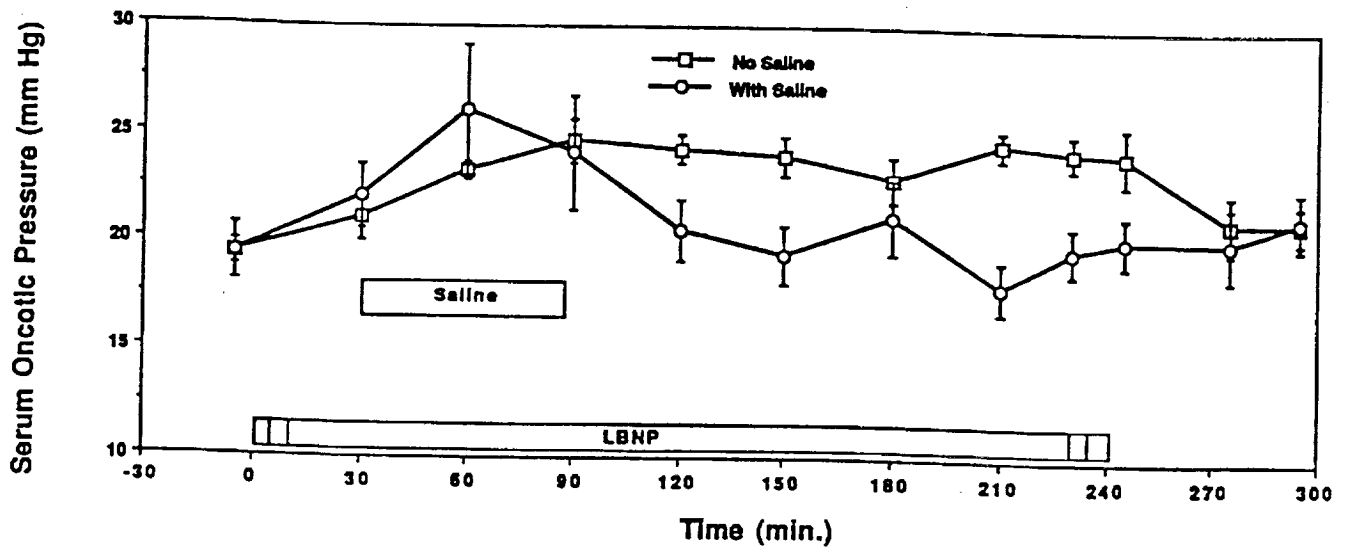
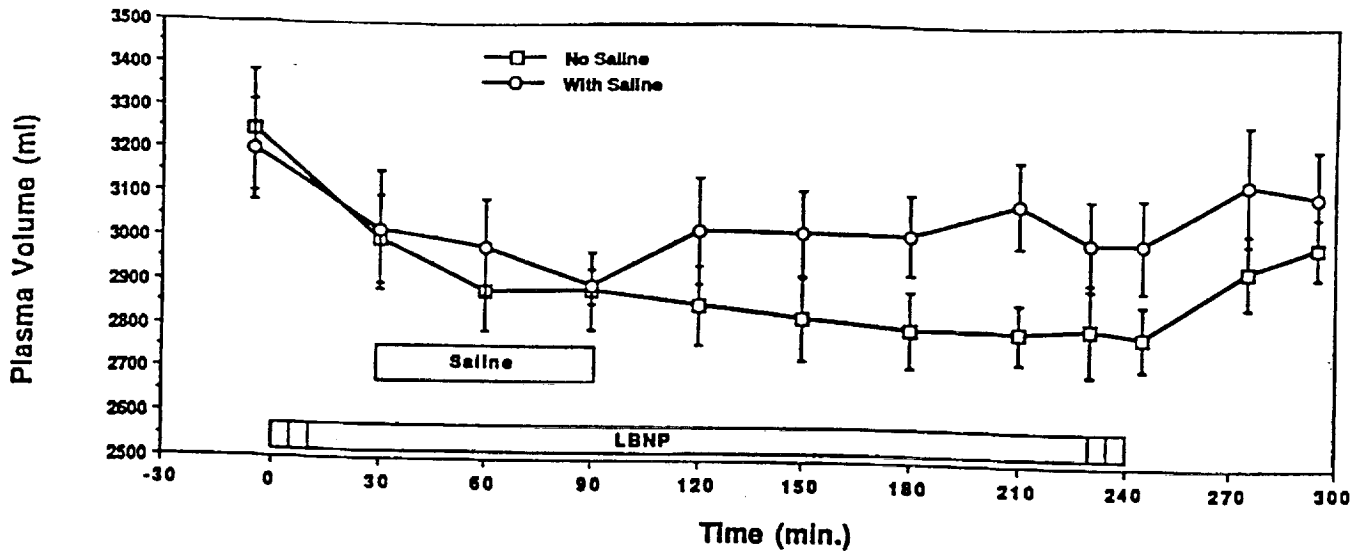


FIGURE 5





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