211 ENDOTOXIN LIBERATION DURING THERAPY FOR GRAM-NEGATIVE BACTERIAL SEPSIS. Jerry Shenep, Fred Barrett, Gregory Stidham, David Westenkirchner and Patricia Flynn. St. Jude Children's Research Hospital, UTCHS, and LeBonheur Children's Medical Center, Memphis, TN.

To determine if plasma levels of free endotoxin increase during the initial hours of antibiotic therapy for gram-negative bacterial sepsis, serial blood samples were obtained from 24 patients presenting with suspected sepsis. For each sample the level of bacteremia was determined by quantitative culture, and the levels of free (filterable) and bacterial cell-bound plasma endotoxin were measured by Limulus lysate assay. Fourteen patients had no detectable bacteremia or endotoxemia. Five patients with constant or declining levels of free endotoxemia had transient gram-negative bacteremia (2), no detectable bacteremia (2), or overwhelming gram-positive bacterial sepsis (1). The remaining five patients had gram-negative bacterial sepsis ranging from 30 to 10^7 cfu/ml blood. Plasma free endotoxin increased in all of these patients during the initial hours of antibiotic therapy, while levels of bacteremia and cell-bound endotoxin were decreasing. Plasma free endotoxin subsequently cleared in four of these patients, but continued to rise in the other patient, associated with progressive purpura fulminans and irreversible shock. These results are consistent with the hypothesis that antibiotic-induced endotoxin release may be responsible for the deterioration observed in some patients with gram-negative bacterial sepsis during antibiotic therapy.

● 212 PERSISTENT PULMONARY VASOCONSTRICTION AFTER POSITIVE END-EXPIRATORY PRESSURE. Deborah.L. Smith-Wright, Michael F. Sweeney, Thomas P. Green, and Bradley P. Fuhrman, Ped. Crit. Care, U. of Minnesota, Minneapolis 55455.

To study recovery of the pulmonary vasculature after cessation of positive end-expiratory pressure(PEEP) in the intact, infant lamb, electromagnetic flow probes were placed about R and L pulmonary arteries(PA) and the L atrium(LA) was catheterized through a L thoracotomy. 1 wk later, under chloralose, probe terminals and LA catheters were exteriorized. A custom-made endobronchial tube was inserted, and R and L lungs were subjected to independent, volume regulated ventilation. In each study, PEEP (11mmHg) was applied for 4 minutes to the L lung only. Aortic(Ao), PA and LA pressures, left lung peak airway pressure(Lpmax), and R and L lung blood flows(QR,QL) were recorded during and for 4 minutes after abrupt cessation of PEEP.

	PEEP	10 sec	30 sec	1 min	2 min	4 min
QL ml/min	160±30*	280±30*	330±30*	350±30*	380±30*	410±30
QL % recovery:		50±3*	68±4*	79±2*	91±2*	100
PA mmHg	30±2*	28±1	27±1	27±1	27±1	27±1
LA mmHg	13±.5*	11±.6	11±.6	12±.5	11±.5	12±.5
Lpmax mmHg	35±1*	15±1	15±1	16±1	16±1	16±1

*p<.01 paired t vs value after 4 min recovery

Data was complete in 18 trials among 6 preparations. Cessation of unilateral PEEP did not measurably alter Ao pressure or cardiac output(CO). PA and LA pressures and Lpmax recovered completely within 10 seconds of cessation of PEEP. QL, however, recovered more slowly and remained depressed for at least 2 minutes (p<.01). PEEP has an effect on pulmonary vascular tone that persists after airway pressure returns to baseline.

213 CENTRAL HEMODYNAMIC EFFECTS OF DOPAMINE AND VOLUME EXPANSION IN ACUTE ABDOMINAL DISTENSION (AAD). Deborah Smith-Wright, Stanley Einzig, Donna Howland, Bradley Fuhrman. Univ. of Minn, Dept. of Pediatrics, Mpls., MN

In children AAD often follows major trauma, surgery, or infection. We have shown that AAD reduced cardiac output 36% in the dog. This decrease in CO was attributed to either a decrease in contractility or actual fall in ventricular preload. To elucidate the mechanism of this change we studied the central hemodynamic effects of dopamine (D) and volume expansion (V) in dogs with AAD. 7 dogs were anesthetized, paralyzed, ventilated, and their abdomens distended by N_2 to mmHg. Animals were instrumented to measure right atrial, pulmonary artery wedge, left ventricle, aortic (Aop), and abdominal pressures and heart rate (HR). Each experiment had five 30 minute steps--two control distension (C) periods, three intervention periods (D at 10 µg/kg/min; V (D_5LR) at 40 ml/kg/30'; or V+D). CO was measured and Systemic vascular resistance and stroke volume (SVR,SV) calculated. (Results X±SEM, *p<0.05 vs C; †p<0.01 vs C).

	C	D	V	V+D
Aop(mmHg)	114±15	110±10	132±13	119±14
CO(L/min)	1.5±0.2	1.6±0.1	2.6±0.4*	2.2±0.3
SV(ml)	8.2±0.9	9.1±1.0	17.8±2.7†	13.8±2.5
SVR(units)	74.9±8.7	71.3±9.5	58.3±11	57.4±7.8*
HR(b.p.m.)	190±9	182±14	148±9*	171±12

V increased CO, SV, and decreased HR and SVR. D had little effect. These results suggest that the central hemodynamic effects of AAD are primarily due to reduced ventricular preload rather than diminished left ventricular contractility.

● 214 EFFECT OF DOPAMINE AND VOLUME EXPANSION ON VISCERAL BLOOD FLOW IN ACUTE ABDOMINAL DISTENSION (AAD). Deborah Smith-Wright, Stanley Einzig, Robyn Schutjer, Elizabeth Lorenz, and Bradley Fuhrman. Dept. of Pediatrics, U of Minnesota, Minneapolis, MN 55455.

We have shown that AAD reduces visceral blood flow(BF),cardiac index(CI), and urine output(UO) in the dog. To see if BF and UO could be restored by dopamine (D) and/or volume expansion (V), 7 chloralose anesthetized dogs had their abdomens distended with N_2 gas to 20 mmHg. Each experiment had five 30 minute steps--two distention control(C) periods and three intervention periods (D at 10µg/kg/min; V(D_5LR) at 40 ml/kg/30'; or V+D). Left ventricular, pulmonary artery, aortic(Aop), inferior vena cava(IVC), and abdominal pressures were measured. Animals were sacrificed and renal cortical(ren), small bowel(sbo), and liver(lvr) samples obtained. BF was measured by radioactive microspheres. Results (X±SEM, *p<0.05 vs C; †p<0.01 vs C)

	C	D	V	V+D
(Aop-IVC)(mmHg)	95±16	91±11	113±15	97±15
CI (ml/gm/min)	0.08±0.01	0.08±0.01	0.14±0.02	0.12±0.02
sbo	0.16±0.02	0.23±0.02*	0.35±0.08*	0.63±0.21
ren	3.03±0.53	4.17±0.65	4.10±0.66	4.18±0.38
lvr	0.34±0.13	0.32±0.15	0.73±0.28	0.58±0.29
urine(ml/30')	18±17	26±12	92±18*	182±42†

In the presence of AAD, both V and D enhance abdominal visceral BF apparently in excess of their effects on driving pressure (Aop-IVC). UO and CI were significantly increased by V but unaltered by D. Thus, in the setting of AAD, V appears superior to D in restoring UO and systemic perfusion.

215 HYPERURICEMIA IS ASSOCIATED WITH INCREASED MORTALITY IN CHILDREN ADMITTED TO A PEDIATRIC INTENSIVE CARE UNIT. F. Bruder Stapleton, Yaun H. Chen and Gregory L. Stidham. Dept. Peds., Univ. Tenn Ctr. Health Sci., and LeBonheur Children's Medical Center, Memphis, Tennessee.

Severe tissue hypoxia results in depletion of intracellular phosphates which results in the metabolism of adenosine to uric acid. Hyperuricemia (HU) has been associated with hypoxic cellular injury as well as increased mortality in adult patients admitted to a coronary intensive care unit (ICU). We examined admission serum uric acid (SUA) and urinary UA concentrations as prognostic indices in 94 children admitted to a pediatric ICU. Admission SUA, fractional excretion of UA (FEUA), pH are shown in HU and normouricemic pts as mean±SD. †P<0.001, ‡P<0.01.

	n	Age mos	SUA mg/dl	FEUA %	pH	Death
High SUA	26	31±55	13.1±4.9†	21.6±16	7.18±0.36‡	13(50%)†
Normal SUA	68	51±58	4.8±1.5	22.3±17	7.36±0.10	7(10%)

Pts with HU had a higher mortality, lower pH, higher serum creatinine (1.5 vs 0.9 mg/dl, P<0.05) and a higher fractional sodium excretion (2.8 vs 1.2%, P<0.05) than did pts with normouricemia (NU). HU pts who died were older than NU fatalities (2.6 yrs vs 17.5 wks). There was no statistical difference in mortality between acidotic and non-acidotic HU pts. Temperature, pO_2, blood pressure, hemoglobin concentration and FEUA were similar between HU and NU pts. We conclude that increased admission SUA is associated with a higher mortality in pediatric ICU pts and that HU should alert physicians to the possibility of profound cellular injury.

216 ALTERED URINARY NITROGEN EXCRETION IN SEPSIS AND LIVER FAILURE IN CRITICALLY-ILL CHILDREN, D.Steinhorn MD, Peds ICU, W.Radmer, S.Weisdorf, MD, Peds GI,Univ. of Minn, Minneapolis, MN (Spons. by Thomas Green, MD)

Urinary nitrogen determination provides important information regarding dietary protein intake and relative state of catabolism and anabolism. Stress, e.g. surgery, sepsis, organ system failure, causes increased tissue breakdowm resulting in increased body nitrogen loss. Urea, formed in the liver, is the primary means in humans for nitrogen removal through urinary excretion (UUN). UUN has been shown to be 80-85% of Total Urinary Nitrogen (TUN) in adults but somewhat less in children. We examined UUN vs. TUN excretion in 16 Peds ICU patients over 25 patient days (PD).

	Mean UUN*	Mean TUN*	% TUN
Grp. #1 (Liver Fail.n=6)	3.2 (1.0)	7.4 (2.3)	41 (2.0)
Grp. #2 (Sepsis n=5)	2.6 (0.4)	7.3 (.86)	35 (4.3)
Grp. #3 (Post-surg.n=14)	2.8 (0.4)	6.0 (.63)	48 (2.9)
Grps. 1+2+3 (n=25)	2.9 (.37)	6.6 (.65)	44 (2.2)

*=gm/M2/day (--)=Std.Err.of Mean

The values for TUN and UUN agree with values in the literature. We found that patients with liver failure and bacterial or fungal sepsis have UUN production similar to post-surgical patients but higher TUN production. We conclude that stress associated with these two conditions causes an increase in non-urea nitrogen excretion.