0022-5282/92/3206-0704$03.00/0
THE JOURNAL OF TRAUMA
Copyright © 1992 by Williams & Wilkins
Vol. 32, No. 6
Printed in U.S.A.

Effects of Hypertonic Saline Dextran Resuscitation on Oxygen Delivery, Oxygen Consumption, and Lipid Peroxidation After Burn Injury

RIFAT TOKYAY, MD,[a] STEPHEN T. ZEIGLER, MD,[a] GEORGE C. KRAMER, PHD,[b,c] CHRISTIAN S. ROGERS, BS, JOHN P. HEGGERS, PHD,[a,d] DANIEL L. TRABER, PHD,[b,c] AND DAVID N. HERNDON, MD[a]

We compared the effects of lactated Ringer's (LR) and hypertonic saline dextran (HSD) on postburn cardiovascular function, O_2 consumption, lipid peroxidation, and bacterial translocation. Miniature pigs with 40% total body surface area (TBSA), third-degree burns received, 30 minutes postburn, either Parkland resuscitation (LR group, n = 8) or HSD, 10 mL/kg/30 minutes, followed by LR, 4 mL/kg/%burn over the next 23 hours (HSD group, n = 8). The HSD prevented the early decrease in cardiac index (CI); the early increase in the resistance of the systemic, mesenteric, celiac, and renal vascular beds; and the decrease in mesenteric O_2 consumption seen after burns when LR alone is used for resuscitation. The HSD also moderated the systemic and mesenteric lipid peroxidation. Bacterial translocation was less in the HSD group (3 of 8 animals) compared with the LR group (5 of 8 animals), but was not statistically different. Hypertonic saline dextran may be beneficial in improving the postburn microcirculation and attenuating postburn oxidant-induced lipid peroxidation in the systemic tissues and the gut.

Resuscitation from circulatory shock with hypertonic solutions has been reported to restore systemic hemodynamics more effectively and more rapidly than isotonic solutions.[1-6] In particular, hypertonic saline dextran has been used as a rapid expander of intravascular volume in hypovolemic shock[7-13] and in burn injury,[14,15] although in burn injury the improvement seems to be transient and total fluid requirements and edema formation remain unchanged.[15]

While normalizing standard indices of circulatory function such as cardiac output (CO), mean arterial pressure (MAP), and urine output can be adequate to reverse uncomplicated hypovolemic shock, recent evidence suggests that unrecognized O_2 debt is present in many forms of critical illness,[16,17] including burns.[18] It may be necessary to augment O_2 delivery to greater than normal levels to ensure adequate O_2 delivery. Such an approach has been shown to decrease subsequent organ failure and increase survival in critically ill patients.[19,20]

Standard burn resuscitation is inadequate in restoring O_2 delivery to the tissues with increased O_2 demands.[18] Since administration of hypertonic saline dextran improves postburn depressed cardiac function and increases cardiac output,[14] the first aim of our study was to determine if addition of hypertonic saline dextran to the standard burn resuscitation regimen would increase postburn O_2 transport to the tissues.

On the other hand, increasing O_2 delivery may result in increased production of oxygen-derived free radicals in ischemic tissues during reperfusion and may contribute to tissue damage.[21] Reperfusion of a burn wound has been shown to release oxidants into the systemic circulation, resulting in lipid peroxidation in the skin[22] as well as other organs such as the lungs,[23,24] liver, spleen[22] and circulating red blood cells.[25] This damage may be either direct or the result of complement activation.[24] Because of the possibility of increased oxidant production by improving cardiac output and O_2 transport to ischemic tissues, the second aim of our study was to determine if hypertonic saline dextran resuscitation accentuated postburn reperfusion injury. Since peroxidative decomposition of membrane lipids has been considered the basis of oxidant-induced cell injury[26] and since postburn circulating conjugated diene levels have been shown to

From the [a] Department of Surgery, [b] Department of Anesthesiology, [c] Department of Physiology and Biophysics, and [d] Department of Microbiology, University of Texas Medical Branch and the Shriners Burns Institute, Galveston, Texas.

Supported by the Shriners Burns Institute Galveston Unit Grant # 15852.

Presented at the Fifty-first Annual Session of the American Association for the Surgery of Trauma, September 11-14, 1991, Philadelphia, Pennsylvania.

Address for reprints: David N. Herndon, MD, Chief of Staff, SBI and Jesse H. Jones Professor of Surgery, UTMB, 610 Texas Ave., Galveston, TX 77550.

correspond with the degree of local wound and distal systemic tissue lipid peroxidation,[23,24,27] we measured plasma conjugated diene levels to determine the degree of systemic reperfusion injury.

Thermal trauma can cause gastrointestinal mucosal injury and impaired barrier function resulting in increased permeability[28,29] to luminal microbes and their products.[30–33] This process may play a role in the evolution of subsequent sepsis and multiple organ failure.[29,30,34,35] Although the mechanism of posttraumatic mucosal injury is not completely understood, current evidence suggests that oxygen-derived free radicals play an important role in this process.[36–39] Jones et al.[40] as well as our own group[41–44] have shown that after major burns, mesenteric blood flow is significantly reduced. This reduction continues during the early phase of resuscitation with lactated Ringer's, even if arterial pressure and cardiac output have been returned to normal levels.[45] Postburn mesenteric hypoperfusion or the reperfusion afterward as well as the circulating oxidants from the burn wound[23] may damage the intestinal mucosa and impair its barrier function. Therefore, the third aim of our study was to evaluate the effects of hypertonic saline dextran resuscitation on postburn mesenteric blood flow, mesenteric O_2 delivery and consumption, the degree of oxidant-induced injury in the gut, and the rate of bacterial translocation from the gut.

METHODS

Operative Preparation. Studies were done in 16 female, 6-month-old, Hanford-Pittmann-Moore miniature pigs weighing between 17 and 26 kg each. These animals were prepared surgically for the study five days before the experiment. After an overnight fast, anesthesia was induced with intramuscular (IM) ketamine (30 mg/kg) followed by 2%–2.5% halothane. After induction, the trachea of each miniature pig was intubated and the animal was placed on a ventilator. A left flank incision was made and retroperitoneally, the superior mesenteric, celiac, and left renal arteries were identified at their origins from the abdominal aorta. Transit time ultrasonic flow probes (4 or 6 mm, Transonic Systems, Inc., Ithaca, NY) were placed on each of these vessels. The flow probes were fixed to the psoas muscle to prevent rotation. Through the same incision, intraperitoneally, a 6.5F catheter was threaded into the superior mesenteric vein via a small branch. After the flank incision was closed, the pig was then placed in its run for five days with free access to food and water.

On the day of the experiment, with the animal under ketamine (20 mg/kg, IM) and local lidocaine anesthesia, a catheter was placed through a neck incision via the right common carotid artery into the abdominal aorta and a Swan-Ganz thermal dilution catheter (Model 93 A-131-5F, American Edwards Laboratories, Anasco, PR) was positioned in the pulmonary artery through the right jugular vein.

Experimental Design. The animals were kept in special slings for monitoring purposes. These slings allowed them to rest on their sides when data were not being collected. Throughout the study period the animals were not fed orally. Baseline data were collected after the animals had completely recovered from the anesthesia.

The pigs were randomized into two groups: (1) The LR group (n = 8) received a 40% total body surface area (TBSA), third-degree flame burn under anesthesia. The animals were resuscitated according to the Parkland formula and received lactated Ringer's solution, 4 mL/kg/(%TBSA burn), starting 30 minutes after the burn. Half of the total resuscitation fluid was given in the first eight hours postburn and the remainder in the next 16 hours. (2) The HSD group (n = 8) received the same burn injury but the animals were resuscitated initially with 7.5% NaCl in 6% dextran 70, 10 mL/kg as an IV infusion starting 30 minutes after the burn and continuing for 30 minutes. Lactated Ringer's solution was administered during the next 23 hours at a rate of 4 mL/kg/(%TBSA burn).

Systemic, renal, and splanchnic hemodynamics were measured and blood samples were drawn for determinations of aortic, mixed venous, and superior mesenteric venous hemoglobin, electrolytes, blood gases, and conjugated diene levels at baseline and 1, 2, 3, 4, 8, 16, and 24 hours after the burn. At the end of the 24 hours, animals were anesthetized with 5 mL/kg ketamine IV and killed with 5 mL intravenous saturated KCl. Using aseptic technique, peritoneal fluid and tissue samples from the mesenteric lymph nodes, spleen, liver, kidney, lung, jejunum, ileum, and cecum were taken through a midline laparotomy incision, for bacteriologic culture.

Burn Injury. We created the third-degree burn by techniques that have previously been used in our laboratory. While the animal is under deep anesthesia with 2% halothane, an area corresponding to 40% TBSA is outlined. The flame from a Meeker burner is then applied to the skin until it begins to contract. We then move the burner to a new unburned skin area until we have completely burned the entire outlined area. The burned skin is then observed and the burner is reapplied to areas that are pink, which may indicate a second-degree burn. We confirm the full-thickness lesion of the burned skin by histologic evaluation at autopsy.

All experimental protocols were approved by the Animal Care and Use Committee of the University of Texas Medical Branch (ACUC 90-09-103).

Systemic and Splanchnic Hemodynamics and Blood Gas Measurements. Aortic (MAP), central venous (CVP), and portal venous (PVP) pressures were measured using transducers (P231D, Statham Gould, Oxnard, CA) that were adapted with continuous flushing devices. The transducers were connected to an Electronic Medicine Honeywell Recorder (Model OM-9 patient monitor) with graphic and digital display for electronically calculated mean pressures. A horizontal plane through the shoulder was taken as the zero reference point for pressure measurements. Cardiac output was determined by the thermal dilution technique utilizing a Swan-Ganz catheter and a cardiac output computer (Model 9520, American Edwards Laboratories, Irvine, CA). Dextrose solution (5%) at 5°C was used as the indicator. Arterial, mixed venous, and mesenteric venous blood gas measurements were performed with a blood gas analyzer (System 1302, Instrumentation Laboratory, Inc., Cidra, PR). The results were corrected to the body temperature of the animal. Arterial (Sa_{O_2}), mixed venous (Sv_{O_2}), and mesenteric venous (Sm_{O_2}) O_2 saturations were determined with a Co-Oximeter (Model 282, Instrumentation Laboratory, Inc., Cidra, PR). Mesenteric (m), celiac (c), and renal (r) arterial blood flows (Q) were measured with transit time ultrasonic flow probes connected to a T101 ultrasonic meter (Transonic Systems, Inc., Ithaca, NY).[23,46] The accuracy of the flow was confirmed at autopsy when the vessels were perfused in situ.

Systemic (Rs), mesenteric (Rm), celiac (Rc), and renal (Rr) vascular resistances were calculated with the following formulas:

$$Rs = [(MAP - CVP)\cdot(80)]/CO$$
$$Rm = [(MAP - PVP)\cdot(80)]/Qm$$
$$Rc = [(MAP - PVP)\cdot(80)]/Qc$$
$$Rr = [(MAP - CVP)\cdot(80)]/Qr$$

Systemic O_2 delivery (Do_2), systemic O_2 consumption (Vo_2), mesenteric O_2 delivery (mDo_2), and mesenteric O_2 consumption (mVo_2) were calculated with the following formulas:

$$Do_2 = [(Sao_2 \cdot 1.34 \cdot Hba) + (Pao_2 \cdot 0.03)] \cdot (CO)$$

$$Vo_2 = ([(Sao_2 \cdot 1.34 \cdot Hba) + (Pao_2 \cdot 0.03)] - [(Svo_2 \cdot 1.34 \cdot Hbv) + (Pvo_2 \cdot 0.03)]) \cdot (CO)$$

$$mDo_2 = [(Sao_2 \cdot 1.34 \cdot Hba) + (Pao_2 \cdot 0.03)] \cdot Qm$$

$$mVo_2 = ([(Sao_2 \cdot 1.34 \cdot Hba) + (Pao_2 \cdot 0.03)] - [(Smo_2 \cdot 1.34 \cdot Hbm) + (Pmo_2 \cdot 0.03)]) \cdot Qm$$

where Hba, Hbv, and Hbm are the aortic, mixed venous, and mesenteric venous Hb, and Pao_2, Pvo_2, and Pmo_2 are the arterial, mixed venous, and mesenteric venous O_2 tensions.

Quantitative Bacteriologic Culture of Tissue Samples. Aseptically collected tissue samples were weighed and 0.5 g of each were homogenized in a tissue grinder with 4.5 mL nonbacteriostatic saline to create a 1:10 dilution of the original sample. One tenth (0.1) and 0.01 mL (of the 1:10 dilution) was inoculated to a MacConkey agar plate and a CNA plate for isolation of gram-negative and gram-positive organisms, respectively. Therefore, one colony would represent 1×10^2 and 1×10^3 CFUs per gram of tissue, respectively, for each inoculum size. Limits of detection were 100 organisms/gram of tissue. Inoculated plates were incubated at 37°C for 24 and 48 hours and read with a Darkfield Quebec Colony Counter (Model 3330, American Optical Co., Buffalo, NY) to determine bacterial counts. Positive cultures were interpreted as those greater than 100 colonies/gram of tissue.

Plasma Conjugated Diene Assay. Conjugated dienes were measured according to the method of Till et al.[47] Conjugated dienes were extracted from the plasma by using a 2:1 (vol/vol) mixture of chloroform and methanol. Seven milliliters of the chloroform-methanol mixture preheated to 45°C was added to 0.5 mL plasma. The mixture was then vigorously agitated for 2 minutes and centrifuged at 3,000 rpm for 5 minutes at 4°C. The lower layer was aspirated and pipetted into a test tube and dried under a direct flow of nitrogen gas. The residue that remained was reconstituted with 1.5 mL heptane and read spectrophotometrically at 233 nm (Spectronic 1001; Milton Roy Co., Houston, TX).

Statistical Analysis. Data are presented as the mean ± SEM and were analyzed as a two-factor factorial experiment with repeated measures. Comparative statistics on the effects of time were analyzed using Dunnett's t test after ANOVA by comparing the individual time periods to baseline values within each group. Between groups, data at each time point were compared by using the Student's unpaired t test. Bacteriologic tissue culture results were analyzed by Fisher's exact test. Statistical significance was accepted when $p < 0.05$.[48,49]

RESULTS

Data (mean ± SEM) are presented in Table 1 and Figures 1 through 5.

Central venous pressure (CVP), pulmonary wedge pressure (PWP), and portal pressure (PortP) were maintained at preburn values throughout the study period by both regimens of fluid resuscitation. Mean arterial pressure was increased above the baseline value in both groups between two and four hours postburn. The blood hemoglobin (Hb) level was decreased in the LR group through the fourth hour, while in the HSD group the Hb level was decreased at two hours (Table 1).

Changes in postburn CI were within 20% of the preburn values and were not significantly different from the baseline values in either of the resuscitation groups. However, the difference between the two groups was significant at one hour postburn (Fig. 1).

Systemic vascular resistance was significantly increased from the baseline values at one hour postburn in the LR group. The HSD group did not show this increase in systemic vascular resistance, and the difference between the two groups was statistically significant at this time point (Fig. 1).

As shown in Table 1 and Figure 2, mesenteric blood flow decreased significantly at two and three hours postburn and the resistance in the mesenteric vascular bed was significantly increased from the baseline values during the first three hours postburn. The HSD group, on the other hand, did not show any significant changes in either variable from the preburn level. The difference in mesenteric vascular resistance between the two groups was significant at one hour postburn.

Although celiac blood flow did not change until the last eight hours of the study period in the LR group, celiac vascular resistance started to increase with the onset of the injury, but changes from baseline reached significance at three hours postburn. Celiac vascular resistance was unchanged in the HSD group despite the increase in celiac blood flow at one hour postburn. The difference between the two groups was significant throughout the first three hours after injury (Table 1, Fig. 2).

The most dramatic difference between the two groups was noticed in changes in the renal vascular resistance from the baseline values. In the LR group, renal vascular resistance increased more than four fold from the baseline figure at one hour and more than three fold at two hours postburn, while it was virtually unchanged in the HSD group. The difference between the two groups was statistically significant during the first four hours postburn (Fig. 2). Renal blood flow was a mirror image of the renal vascular resistance. It decreased at one, two, and three hours postburn in the LR group and was unaltered in the HSD group (Table 1).

In both groups, systemic O_2 delivery remained within 80% of the preburn value (Fig. 3), with no statistically significant changes within or between the groups. Systemic O_2 consumption, however, although unchanged from the baseline value in either group, was significantly higher in the HSD group at two hours postburn when compared with the LR group (Fig. 3).

Mesenteric O_2 delivery in the LR group remained significantly below the baseline value throughout the study period. In the HSD group, mesenteric O_2 delivery stayed within 20% of the baseline value, and the difference between the two groups reached statistical significance at eight and 24 hours postburn (Fig. 4). Mesenteric O_2 consumption, on the other hand, was reduced below the baseline value in both groups at two hours after injury. In the HSD group, however, it returned to and

TABLE 1
Systemic and mesenteric hemodynamic response of burned swine to resuscitation with LR and HSD+LR

Group	Hours	MAP (mm Hg)	CVP (mm Hg)	PWP (mm Hg)	PortP (mm Hg)	Q (mL/min) (mesenteric)	Q (mL/min) (celiac)	Q (mL/min) (renal)	Blood Hb (g/dl)
LR	0	104 ± 4	7 ± 1	12 ± 2	13 ± 1	305 ± 41	365 ± 83	253 ± 15	10.6 ± 0.1
	1	111 ± 5	6 ± 2	9 ± 2†	12 ± 1	151 ± 21*	396 ± 78	99 ± 28*	
	2	124 ± 5*	13 ± 4	11 ± 2	13 ± 2	224 ± 41*	415 ± 86	110 ± 33*	10.6 ± 0.3
	3	123 ± 3*	12 ± 3	11 ± 2	12 ± 2	279 ± 52	369 ± 88	139 ± 31*	
	4	117 ± 2*	9 ± 2	11 ± 2	12 ± 1	267 ± 42	389 ± 61	157 ± 30	9.4 ± 0.2*
	8	113 ± 5	9 ± 2	11 ± 1	13 ± 2	291 ± 39	490 ± 80	236 ± 33	8.1 ± 0.4*
	16	109 ± 5	9 ± 2	12 ± 2	11 ± 2	292 ± 45	493 ± 58*	288 ± 34	7.7 ± 0.3*
	24	107 ± 5	10 ± 2	12 ± 2	11 ± 2	303 ± 33	505 ± 51*	290 ± 45	7.0 ± 0.6*
HSD	0	108 ± 3	10 ± 2	12 ± 1	15 ± 3	245 ± 30	258 ± 23	204 ± 40	11.2 ± 0.6
	1	122 ± 4	8 ± 2	13 ± 1	20 ± 6	202 ± 19	326 ± 31*	194 ± 41	
	2	134 ± 5*	8 ± 2	11 ± 2	19 ± 5	241 ± 32	292 ± 29	198 ± 38	9.3 ± 0.3*
	3	133 ± 6*	11 ± 3	14 ± 2	14 ± 4	224 ± 19	310 ± 35	205 ± 45	
	4	131 ± 6*	9 ± 3	13 ± 2	14 ± 1	228 ± 23	301 ± 33	222 ± 39	9.5 ± 0.3*
	8	121 ± 4	8 ± 3	9 ± 2	13 ± 1	248 ± 34	306 ± 33†	224 ± 34	10.1 ± 0.4
	16	116 ± 5	7 ± 2	10 ± 1	11 ± 1	263 ± 18	289 ± 30†	225 ± 31	9.2 ± 0.4*
	24	108 ± 4	7 ± 1	9 ± 1	13 ± 2	247 ± 17	287 ± 37†	235 ± 31	8.8 ± 0.4*

Abbreviations: MAP, mean aortic pressure, CVP, central venous pressure; PWP, pulmonary wedge pressure; PortP, portal pressure; Q, blood flow; Hb, hemoglobin; LR, lactated Ringer's; HSD; hypertonic saline dextran.
* $p < 0.05$ vs. baseline.
† $p < 0.05$ between groups.

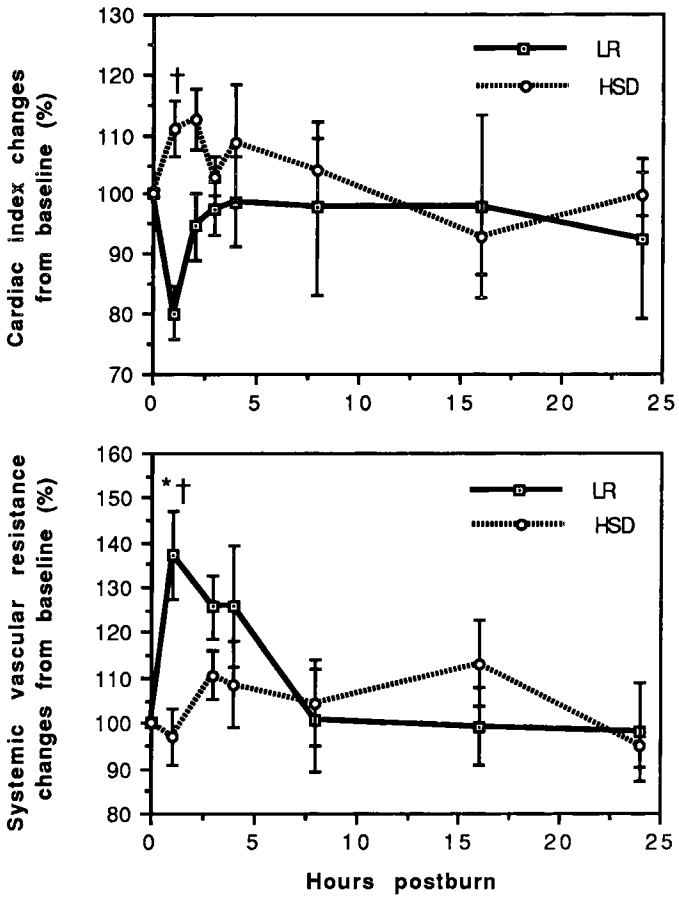

FIG. 1. Changes from preburn values in cardiac index and systemic vascular resistance. Cardiac index in the HSD group was significantly above that in the LR group at two hours postburn. At this time point, systemic vascular resistance was significantly elevated in the LR group. LR, lactated Ringer's; HSD, hypertonic saline dextran; * $p < 0.05$ vs. baseline; † $p < 0.05$ LR vs. HSD group.

stayed at preburn levels after two hours, while in the LR group mesenteric O_2 consumption remained significantly below the baseline value throughout the study period, making the difference between groups significant at eight hours postburn (Fig. 4).

Arterial plasma conjugated diene levels were increased in the LR group at four and eight hours postburn. Levels of conjugated dienes were also increased in the HSD group, but this increase was earlier (at two hours postburn), of shorter duration, and was of a lesser magnitude than that of the LR group. The difference between the two groups was significant at four and eight hours postburn (Fig. 5). Superior mesenteric venous plasma conjugated diene levels increased in the LR group (at two hours postburn) but not in HSD group. However, this increase was not as pronounced as that seen in the arterial plasma, and the difference in SMV plasma conjugated diene levels between the two groups was not statistically significant (Fig. 5).

The bacterial translocation rate from the gut to the systemic tissues and organs was 62.5% in the LR group and 37.5% in the HSD group. The difference between the two groups was not statistically significant.

At two hours postburn, serum sodium levels were significantly higher in the HSD group (152 ± 2 mEq/L) and significantly lower in the LR group (136 ± 1 mEq/L) when compared with the preburn values of 140 ± 1 and 143 ± 3 mEq/L, respectively. The difference between the two groups was significant during the first eight hours postburn.

DISCUSSION

The attractiveness of HSD in thermal resuscitation was borne from the extensive work done using HSD in

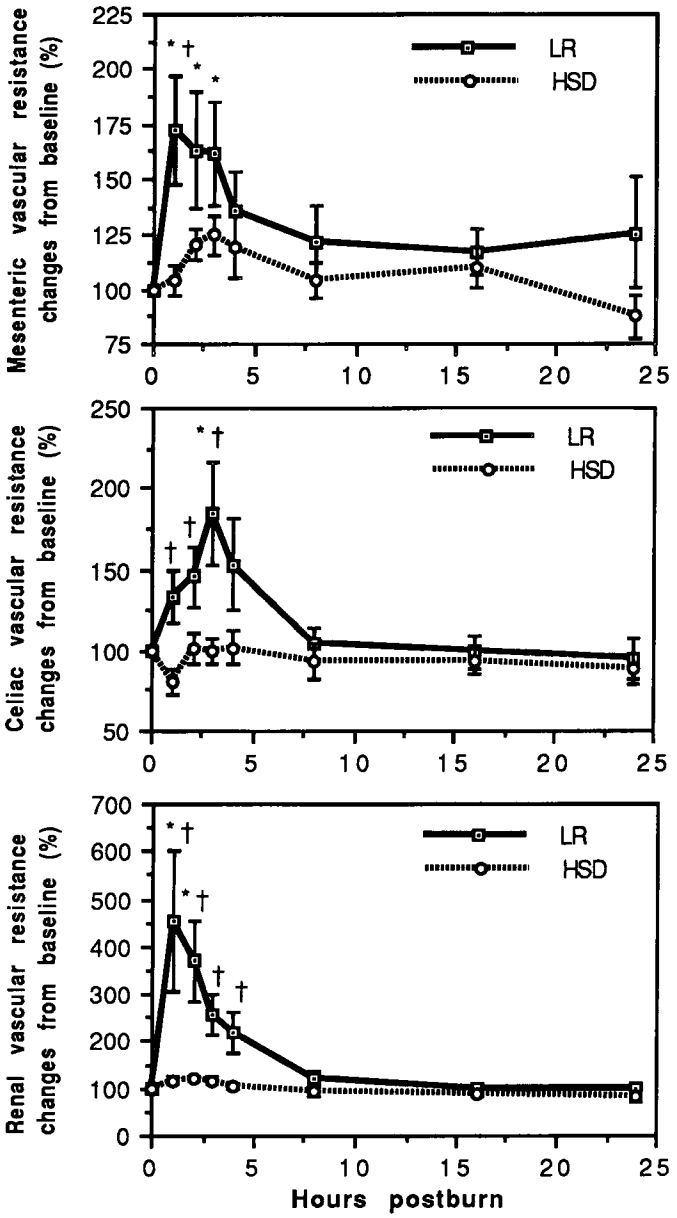

FIG. 2. Changes from preburn values in the resistance of the mesenteric, celiac, and renal vascular beds. Resistances in all three vascular beds were elevated during the early postburn period in the LR group but were unchanged in the HSD group. LR, lactated Ringer's; HSD, hypertonic saline dextran; * $p < 0.05$ vs. baseline; † $p < 0.05$ LR vs. HSD group.

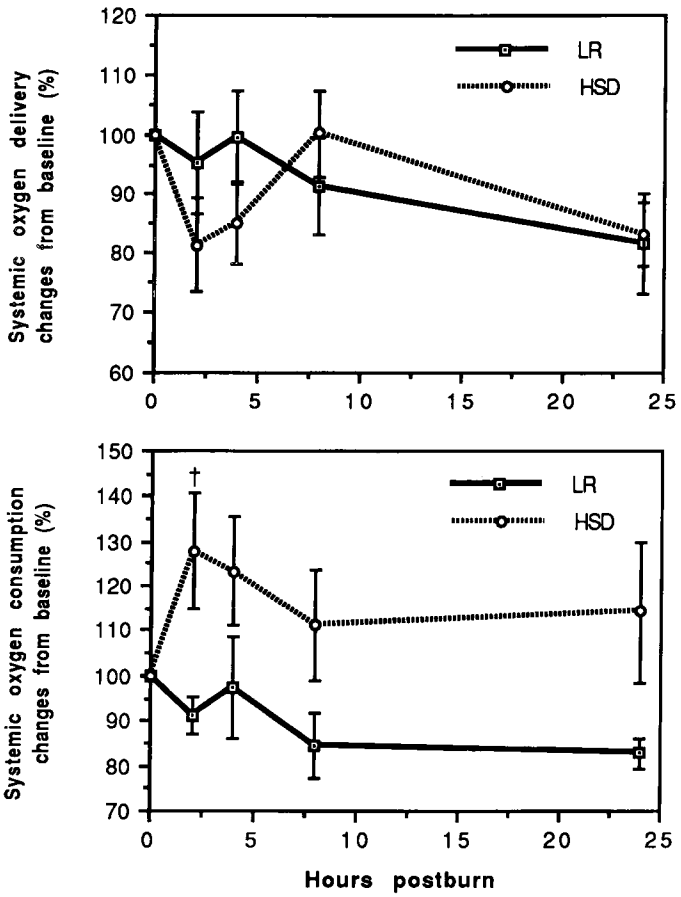

FIG. 3. Changes from preburn levels in systemic O_2 delivery and consumption. Although systemic O_2 delivery was unchanged in both groups, systemic oxygen consumption was significantly higher in the HSD group at two hours postburn. LR, lactated Ringer's; HSD, hypertonic saline dextran; * $p < 0.05$ vs. baseline; † $p < 0.05$ LR vs. HSD group.

the treatment of hemorrhagic shock. Small volume resuscitation with HSD permits its use during transport of a traumatized patient without delaying treatment at the scene. Hypertonic saline dextran therefore has the potential for use in thermally injured patients before the institution of crystalloid resuscitation. In this experiment we sought to evaluate the effects of standard burn resuscitation compared with standard burn resuscitation with the addition of HSD.

Recent work by Onarheim et al. using an anesthetized sheep model of thermal injury showed that a HSD (4 mL/kg) bolus over 2 minutes improved cardiovascular function compared with an equal volume of 0.9% saline following thermal injury.[15] These improvements were only transient. We chose an infusion of 10 mL/kg HSD similar to the dose that Maningas used in the hemorrhagic shock model[11] and infused this volume over 30 minutes to simulate patient transport time. We purposely did not choose to infuse equal volumes of fluid during the initial 30 minutes of resuscitation so that we could assess the effects HSD supplemented burn resuscitation versus a standard burn resuscitation formula. By experimental design the HSD group therefore received more fluid initially, 10 mL/kg HSD (200 mL during first 30 minutes), compared with the LR group (100 mL over first 30 minutes according to the Parkland formula). We do not believe this 100 mL volume difference explains the better outcome with HSD given the nearly 3,200 mL infused over the 24-hour period of resuscitation. This conclusion is supported by the work with HSD in hemorrhagic and burn shock. Kramer et al.,[15] Maningas,[11] and Onarheim et al.[15] showed that equal volumes of normal saline bolus infusions did not produce any significant improvement in cardiovascular function following shock. Rather, it is likely that physi-

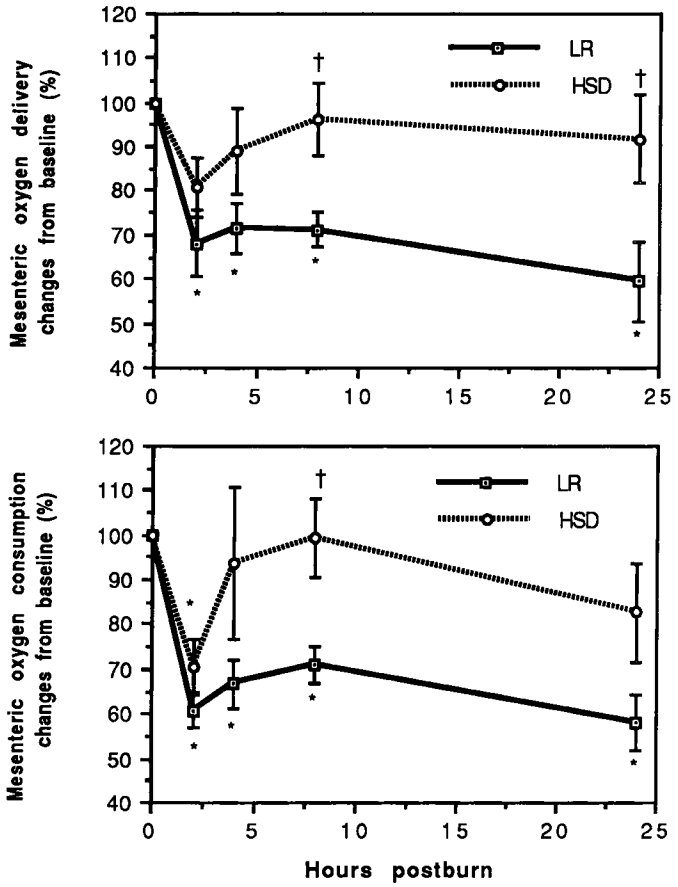

FIG. 4. Changes from preburn levels in mesenteric O_2 delivery and consumption. Mesenteric O_2 delivery and consumption were decreased in the LR group throughout the study period. In the HSD group, except for a decrease in mesenteric O_2 consumption at two hours postburn, these measurements stayed stable. LR, lactated Ringer's; HSD, hypertonic saline dextran; * $p < 0.05$ vs. baseline; † $p < 0.05$ LR vs. HSD group.

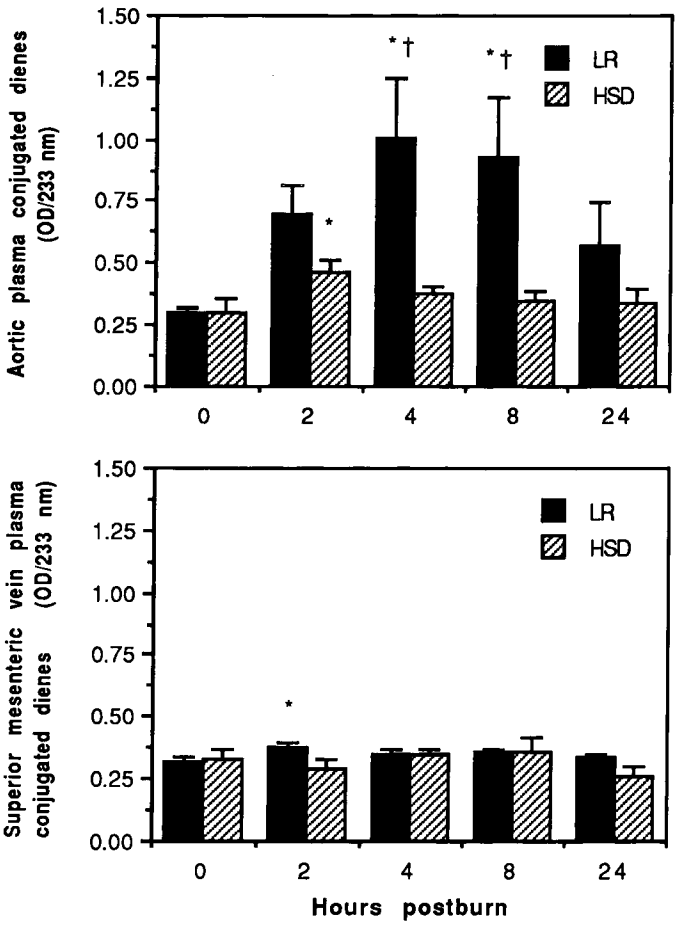

FIG. 5. Aortic and superior mesenteric vein plasma conjugated diene levels. Aortic plasma conjugated diene levels were elevated four fold in the LR group at four and eight hours postburn. In the HSD group these changes were of a significantly less magnitude and of shorter duration. Superior mesenteric vein plasma conjugated diene levels were unchanged in the HSD group and only modestly increased at two hours in the LR group. LR, lactated Ringer's; HSD, hypertonic saline dextran; * $p < 0.05$ vs. baseline; † $p < 0.05$ LR vs. HSD group.

ologic responses to the increased load of sodium and dextran caused the differences between the two groups.

The ability to preferentially dilate the mesenteric vascular bed after hemorrhagic shock has been reported by Rocha-e-Silva et al.[50] It was shown that mesenteric vascular blood flow was increased out of proportion compared with femoral and renal blood flows. Behrman et al. reported that microcirculatory blood flow in intestinal mucosa was higher after administration of HSD compared with an equivalent volume of LR.[51] Gut ischemia is a frequent finding after all kinds of circulatory shock. If the early use of HSD consistently increased mesenteric blood flow, then the potential to attenuate the rate of bacterial translocation should be examined. Our data did not show a statistical reduction in translocation with HSD (3 of 8 animals) compared with LR (5 of 8 animals). The trend, however, suggests further research is needed to fully delineate this process.

Although HSD resuscitation increased the postburn cardiac output significantly more than LR, systemic O_2 delivery was not increased to the same extent and was similar in both groups. This is in contrast to the findings of Wade et al.[52] and Allen et al.,[53] who reported increased O_2 delivery with HSD resuscitation in hemorrhagic and gastric dilatation-volvulus shock, respectively. Hannon et al., however, stressed that increased O_2 delivery will not keep pace with increased cardiac output because of hemodilution resulting from fluid mobilization during HSD resuscitation.[8] We think this also was the case in our study, because the blood hemoglobin level decreased significantly from 11.2 to 9.3 g/100 mL in two hours in the HSD group, whereas it was unchanged in the LR group during this time period.

More important than O_2 delivery is O_2 consumption; HSD resuscitation increased systemic O_2 consumption significantly more than LR resuscitation. Increased O_2 consumption, in the absence of increased delivery, suggests that HSD optimizes the utilization of O_2 by the tissues. This may happen by relieving the so-called metabolic blockade at the mitocondrial level,[46,54] by reducing microcirculatory O_2 diffusion distances, or by increasing nutrient capillary flow through redistribution of blood in the microcirculation.[35,55,56] Mazzoni et al. reported that HSD re-establishes capillary hemodynamics by decreas-

ing hydraulic resistance through osmotically induced shrinkage of endothelium.[57,58] Behrman et al., using laser Doppler flow analysis, showed that HSD restores blood flow to the microcirculations of the intestinal mucosa and renal cortex more rapidly and effectively than LR.[51]

The beneficial effects of HSD resuscitation on microcirculation were also reflected in our data showing significant early decreases in the resistance of the systemic, splanchnic, and renal vascular beds. Our results are consistent with those of Maningas et al., who reported increased blood flow to the myocardium, kidneys, liver, small intestine, and pancreas with HSD resuscitation but not with LR resuscitation of hemorrhagic shock in swine.[11] Other investigators also reported increased perfusion of the kidneys[6,51] and the gut[51] with HSD resuscitation after hemorrhagic shock and septic shock.[59]

There is ample evidence in the literature that oxygen-derived free radicals may be produced after thermal injury and may play an important role in the subsequent tissue damage that results in the local burn wound or other systemic tissues.[22,39,47,60–63] Although the mechanism underlying the post-ischemic injury is not completely understood and oxidant-induced damage may encompass many cell components, peroxidative decomposition of membrane lipids has been considered as the basis of cell injury.[21,26] According to Tribble et al., lipid peroxidation is important in oxidative injury because it increases the number of free radical chain reactions, compromises detoxification systems, and causes direct deleterious effects, since lipid peroxidation products themselves are toxic.[26] Nishigaki et al., using a rat model, showed that lipid peroxidation products in burned skin were elevated significantly one hour after injury and were released into the systemic circulation, causing parallel increases in serum lipid peroxide levels. These investigators linked postburn dysfunction of organs such as the spleen, liver, and kidneys to this circulating "burn toxin."[22] The association between postburn local and systemic oxidant release and lipid peroxidation locally in the wound and in distant tissues and organs was shown in other animal[61] and human studies.[62] The formation of burn edema,[61,63] burn-induced gastric mucosal lesions,[64] and the postburn activation of serum complement and consequent intravascular hemolysis,[25] neutrophil activation,[65] and acute lung injury[24,66] were all associated with burn wound-related, H_2O_2-dependent oxygen radical formation.

Since conjugated diene levels in the systemic circulation are considered an index of postburn oxidant-induced injury,[22,61,62] our finding of decreased plasma lipid peroxidation products suggests that HSD is beneficial in reducing the postburn reperfusion injury seen with LR resuscitation. Menger et al. reported that hemodilution provides better conditions for capillary reperfusion after ischemia and reduces microvascular reperfusion failure.[67] Behrman et al. thinks that reduced reperfusion injury with HSD resuscitation may be the result of dextran's oxygen free-radical scavenging and anti-neutrophil plugging properties.[51]

At two hours postburn in the burn group resuscitated with LR alone, we also found a significant increase in superior mesenteric vein plasma conjugated diene levels. However, this elevation was not as large as that observed in the aortic plasma and was not significantly different from the levels found in the HSD resuscitation group. Since the postburn level of conjugated dienes in the SMV was so much lower than that observed in the arterial blood, these data suggest that the gut is not a major source of the oxygen free radicals and in fact may be responsible for clearance of the conjugated dienes. The radicals could have their origins from a number of organs: the liver, burned skin, the lung, etc. This is an area that certainly will require further clarifications.

The modest increase in conjugated dienes in the superior mesenteric venous plasma may reflect minimal intestinal lipid peroxidation, which may result from the mesenteric reperfusion after early postburn mesenteric vasoconstriction. Probably because of the small number of animals studied, this minimal reperfusion injury in the LR group, or the lack of it in the HSD group, did not translate to a significant change in the bacterial translocation rate in either group.

In conclusion, hypertonic saline dextran resuscitation rapidly and effectively restored postburn cardiac output. Concomitantly, postburn vasoconstriction in the mesenteric, celiac, and renal vascular beds was prevented by HSD. Despite higher early postburn cardiac output with HSD resuscitation, O_2 delivery was not significantly improved because of hemodilution. However, more important than O_2 delivery is O_2 consumption, which was increased both systemically and in the mesenteric circulation. Additionally, postburn oxidant-induced systemic and mesenteric lipid peroxidation was ameliorated. The postburn bacterial translocation rate tended to be less with HSD resuscitation, but this difference was not statistically significant. Our findings suggest that there may be a use for hypertonic saline dextran in the early treatment of burns.

REFERENCES

1. Bitterman H, Triolo J, Lefer AM: Use of hypertonic saline in the treatment of hemorrhagic shock. *Circ Shock* 21:271, 1987
2. Gunn ML, Hansbrough JF, Davis JW, et al: Prospective, randomized trial of hypertonic sodium lactate versus lactated Ringer's solution for burn shock resuscitation. *J Trauma* 29:1261, 1989
3. Luypaert P, Vincent JL, Domb M, et al: Fluid resuscitation with hypertonic saline in endotoxic shock. *Circ Shock* 20:311, 1986
4. Nerlich M, Gunther R, Demling RH: Resuscitation from hemorrhagic shock with hypertonic saline or lactated Ringer's (effect on the pulmonary and systemic microcirculations). *Circ Shock* 10:179, 1983
5. Peters RM, Shackford SR, Hogan JS, et al: Comparison of isotonic and hypertonic fluids in resuscitation from hypovolemic shock. *Surg Gynecol Obstet* 163:219, 1986
6. Sondeen JL, Gonzaludo GA, Loveday JA, et al: Hypertonic saline/dextran improves renal function after hemorrhage in conscious swine. *Resuscitation* 20:231, 1990
7. Hannon JP, Wade CE, Bossone CA, et al: Blood gas and acid-base

status of conscious pigs subjected to fixed-volume hemorrhage and resuscitated with hypertonic saline dextran. *Circ Shock* 32:19, 1990
8. Hannon JP, Wade CE, Bossone CA, et al: Oxygen delivery and demand in conscious pigs subjected to fixed-volume hemorrhage and resuscitated with 7.5% NaCl in 6% dextran. *Circ Shock* 29:205, 1989
9. Holcroft JW, Vassar MJ, Perry CA, et al: Use of a 7.5% NaCl/6% Dextran 70 solution in the resuscitation of injured patients in the emergency room. *Prog Clin Biol Res* 299:331, 1989
10. Kramer GC, Perron PR, Lindsey DC, et al: Small-volume resuscitation with hypertonic saline dextran solution. *Surgery* 100:239, 1986
11. Maningas PA: Resuscitation with 7.5% NaCl in 6% dextran-70 during hemorrhagic shock in swine: Effects on organ blood flow. *Crit Care Med* 15:1121, 1987
12. Mattox KL, Maningas PA, Moore EE, et al: Prehospital hypertonic saline/dextran infusion for post-traumatic hypotension. The U.S.A. Multicenter Trial. *Ann Surg* 213:482, 1991
13. Wade CE, Hannon JP, Bossone CA, et al: Resuscitation of conscious pigs following hemorrhage: Comparative efficacy of small-volume resuscitation. *Circ Shock* 29:193, 1989
14. Horton JW, White DJ, Baxter CR: Hypertonic saline dextran resuscitation of thermal injury. *Ann Surg* 211:301, 1990
15. Onarheim H, Missavage AE, Kramer GC, et al: Effectiveness of hypertonic saline-dextran 70 for initial fluid resuscitation of major burns. *J Trauma* 30:597, 1990
16. Dantzker DR, Foresman B, Gutierrez G: Oxygen supply and utilization relationships. A reevaluation. *Am Rev Respir Dis* 143:675, 1991
17. Rackow EC, Astiz ME, Weil MH: Cellular oxygen metabolism during sepsis and shock. The relationship of oxygen consumption to oxygen delivery. *JAMA* 259:1989, 1988
18. Demling RH, LaLonde C, Fogt F, et al: Effect of increasing oxygen delivery postburn on oxygen consumption and oxidant-induced lipid peroxidation in the adult sheep. *Crit Care Med* 17:1025, 1989
19. Shoemaker W, Appel PL, Kram HB, et al: Prospective trial of supranormal values of survivors as therapeutic goals in high risk surgical patients. *Chest* 94:1176, 1988
20. Shoemaker WC, Appel C, Czer L, et al: Pathogenesis of respiratory failures (ARDS) after hemorrhage and trauma: Cardiorespiratory patterns preceding the development of ARDS. *Crit Care Med* 8:504, 1980
21. McCord JM: Oxygen-derived free radicals in postischemic tissue injury. *N Engl J Med* 312:159, 1985
22. Nishigaki I, Hagihara M, Hiramatsu M, et al: Effect of thermal injury on lipid peroxide levels of rat. *Biochem Med* 24:185, 1980
23. Demling RH, LaLonde C, Liu Y, et al: The lung inflammatory response to thermal injury: Relationship between physiologic and histologic changes. *Surgery* 106:52, 1989
24. Ward PA, Till GO, Hatherill JR, et al: Systemic complement activation, lung injury, and products of lipid peroxidation. *J Clin Invest* 76:517, 1985
25. Hatherill JR, Till GO, Bruner LH, et al: Thermal injury, intravascular hemolysis, and toxic oxygen products. *J Clin Invest* 78:629, 1986
26. Tribble DL, Aw TY, Jones DP: The pathophysiological significance of lipid peroxidation in oxidative cell injury. *Hepatology* 7:377, 1987
27. Till GO, Morganroth ML, Kunkel R, et al: Activation of C5 by cobra venom factor is required in neutrophil-mediated lung injury in the rat. *Am J Pathol* 129:44, 1987
28. Carter EA, Tompkins RG, Schiffrin E, et al: Cutaneous thermal injury alters macromolecular permeability of rat small intestine. *Surgery* 107:335, 1990
29. Ziegler TR, Smith RJ, O'Dwyer ST, et al: Increased intestinal permeability associated with infection in burn patients. *Arch Surg* 123:1313, 1988
30. Deitch EA: Intestinal permeability is increased in burn patients shortly after injury. *Surgery* 107:411, 1990
31. Deitch EA, Winterton J, Berg R: Thermal injury promotes bacterial translocation from the gastrointestinal tract in mice with impaired T-cell-mediated immunity. *Arch Surg* 121:97, 1986
32. Maejima K, Deitch E, Berg R: Promotion by burn stress of the translocation of bacteria from the gastrointestinal tracts of mice. *Arch Surg* 119:166, 1984
33. Maejima K, Deitch EA, Berg RD: Bacterial translocation from the gastrointestinal tracts of rats receiving thermal injury. *Infect Immun* 43:6, 1984
34. Deitch EA: The role of intestinal barrier failure and bacterial translocation in the development of systemic infection and multiple organ failure. *Arch Surg* 125:403, 1990
35. Siegel JH, Greenspan M, Del Guercio LR: Abnormal vascular tone, defective oxygen transport and myocardial failure in human septic shock. *Ann Surg* 165:504, 1967
36. Deitch EA, Bridges W, Baker J, et al: Hemorrhagic shock-induced bacterial translocation is reduced by xanthine oxidase inhibition or inactivation. *Surgery* 104:191, 1988
37. Deitch EA, Ma L, Ma WJ, et al: Inhibition of endotoxin-induced bacterial translocation in mice. *J Clin Invest* 84:36, 1989
38. Granger DN, Shah AK, Parks DA: Oxygen radicals: Effects on intestinal vascular permeability. *Am J Physiol* 247:G167, 1984
39. Ma L, Ma JW, Deitch EA, et al: Genetic susceptibility to mucosal damage leads to bacterial translocation in a murine burn model. *J Trauma* 29:1245, 1989
40. Jones WG, Minei JP, Barber AE: Angiotensin converting enzyme inhibition decreases bacterial translocation after burn injury. *FASEB J* 4:A953, 1990
41. Herndon DN, Morris SE, Coffey JA, et al: The effect of mucosal integrity and mesenteric blood flow on enteric translocation of microorganisms in cutaneous thermal injury. *Prog Clin Biol Res* 308:377, 1989
42. Morris SE, Navaratnam N, Herndon DN: A comparison of effects of thermal injury and smoke inhalation on bacterial translocation. *J Trauma* 30:639, 1990
43. Morris SE, Navaratnam N, Townsend CM, et al: Decreased mesenteric blood flow independently promotes bacterial translocation in a chronically instrumented sheep. *Surg Forum* 40:88, 1989
44. Saydjari R, Beerthuizen GI, Townsend CM, et al: Bacterial translocation and its relationship to visceral blood flow, gut mucosal ornithine decarboxylase activity, and DNA in pigs. *J Trauma* 31:639, 1991
45. Tokyay R, Traber DL, Herndon DN: Thromboxane synthetase inhibition prevents the increased mesenteric vascular resistance seen after major thermal injury in a chronic porcine model. *Surg Forum* 41:47, 1990
46. Duff JH, Groves AC, McLean AP, et al: Defective oxygen consumption in septic shock. *Surg Gynecol Obstet* 128:1051, 1969
47. Till GO, Hatherill JR, Tourtellotte WW, et al: Lipid peroxidation and acute lung injury after thermal trauma to skin. Evidence of a role for hydroxyl radical. *Am J Pathol* 119:376, 1985
48. Dunnett CW: New tables for multiple comparison with a control. *Biometrics* 20:482, 1991
49. Snedecor GW, Cochran WG: *Statistical Methods.* Ames, The Iowa State University Press, 1980
50. Rocha-e-Silva M, Negraes GA, Soares AM, et al: Hypertonic resuscitation from severe hemorrhagic shock: Patterns of regional circulation. *Circ Shock* 19:165, 1986
51. Behrman SW, Fabian TC, Kudsk KA, et al: Microcirculatory flow changes after initial resuscitation of hemorrhagic shock with 7.5% hypertonic saline/6% dextran 70. *J Trauma* 31:589, 1991
52. Wade CE, Hannon JP, Bossone CA, et al: Superiority of hypertonic saline/dextran over hypertonic saline during the first 30 min of resuscitation following hemorrhagic hypotension in conscious swine. *Resuscitation* 20:49, 1990
53. Allen DA, Schertel ER, Muir W, III, et al: Hypertonic saline/dextran resuscitation of dogs with experimentally induced gastric dilatation-volvulus shock. *Am J Vet Res* 52:92, 1991
54. Wilson RF, Christensen C, LeBlanc LP: Oxygen consumption in critically-ill surgical patients. *Ann Surg* 176:801, 1972
55. Hooper TL, Jones MT, Thomson DS, et al: Hypertonic citrate solution as an alternative to modified Euro-Collins' solution for lung preservation. *Transplantation* 51:1043, 1991
56. Siegel JH, Greenspan M, Del Guercio LR: Myocardial failure, vascular tone, and oxygen transport in septic shock in a human being. *Surg Forum* 17:5, 1966
57. Mazzoni MC, Borgstrom P, Arfors KE, et al: Dynamic fluid redistribution in hyperosmotic resuscitation of hypovolemic hemorrhage. *Am J Physiol* 255:H629, 1988
58. Mazzoni MC, Borgstrom P, Intaglietta M, et al: Capillary narrow-

ing in hemorrhagic shock is rectified by hyperosmotic saline-dextran reinfusion. *Circ Shock* 31:407, 1990
59. Kreimeier U, Frey L, Dentz J, et al: Hypertonic saline dextran resuscitation during the initial phase of acute endotoxemia: Effect on regional blood flow. *Crit Care Med* 19:801, 1991
60. Demling RH, LaLonde C: Systemic lipid peroxidation and inflammation induced by thermal injury persists into the post-resuscitation period. *J Trauma* 30:69, 1990
61. Friedl HP, Till GO, Trentz O, et al: Roles of histamine, complement and xanthine oxidase in thermal injury of skin. *Am J Pathol* 135:203, 1989
62. Thomson PD, Till GO, Woolliscroft JO, et al: Superoxide dismutase prevents lipid peroxidation in burned patients. *Burns Incl Therm Inj* 16:406, 1990
63. Till GO, Guilds LS, Mahrougui M, et al: Role of xanthine oxidase in thermal injury of skin. *Am J Pathol* 135:195, 1989
64. Yoshikawa T, Naito Y, Ueda S, et al: Role of oxygen-derived free radicals in the pathogenesis of gastric mucosal lesions in rats. *J Clin Gastroenterol* 12(Suppl 1):S65, 1990
65. Till GO, Lutz MJ, Ward PA: Hydroxy radical as autotoxin in chemotactically activated neutrophils. *Biomed Pharmacother* 41:349, 1987
66. Ward PA, Johnson KJ, Till GO: Animal models of oxidant lung injury. *Respiration* 50 (Suppl 1):5, 1986
67. Menger MD, Sack FU, Barker JH, et al: Quantitative analysis of microcirculatory disorders after prolonged ischemia in skeletal muscle. Therapeutic effects of prophylactic isovolemic hemodilution. *Res Exp Med (Berl)* 188:151, 1988

DISCUSSION

DR. TIMOTHY C. FABIAN (Memphis, Tennessee): I would like to begin with a couple of methodologic questions.

The data that Dr. Zeigler presented in his manuscript demonstrated some interesting differences of base line between the two groups of animals. Specifically, the mesenteric flows were 300 versus 250 in the lactated Ringer's versus the hypertonic saline group. The celiac flows were 360 versus 260, again with more in the lactated Ringer's group. And the renal blood flow was 250 versus 200. I realize that they were comparing changes from base line, but it makes one wonder how this experiment was set up. These are fairly significant differences.

Ideally the study should have been done on one animal in each group each day. Clearly that is labor intensive and perhaps equipment is not available to do such. But a second option is to do an animal in each group on alternating days to eliminate the many variables that can occur with different batches of animals, different anesthetics from day to day, and a myriad of other things. So I would like to know precisely how was this done to tighten up the data?

The second methodologic question is relative to diene levels, which were used as a marker of reperfusion injury. I wonder if this is a sensitive estimate of such. These are products of oxygen radicals reacting with polyunsaturated fatty acids and releasing hydrogen. A double bond is formed and it results in an increased spectrophotometric absorbance at 233 nm. I think that's correct, but how specific is the analysis? In other words, are there other products from burned skin, subcutaneous fat, muscle, and the like that also could absorb at 233 nm? Therefore, could this not really reflect burn damage rather than reperfusion injury?

Those are relatively minor methodologic questions. Now I would like to shift to a more significant and fundamental issue dealing with experimental design. I must admit I feel a little bit like Natalie Wood discussing this at this time, because the results satisfy my bias. What I'm referring to is in the film *The Miracle on 34th Street,* when, if you remember, little Natalie was torn between her anal-retentive mother and Kris Kringle on deciding whether Santa Claus really existed. She kept saying, "I want to believe, I want to believe, I want to believe." Well, I want to believe this, too, but I think there are some problems.

First, I would like to begin with a brief review of prior laboratory investigations with 7.5% saline and 6% dextran in which a vast majority of this work until very recently has been done in hemorrhagic shock and not burn resuscitation. Multiple studies have shown that it increases the cardiac index. Some of the earliest and best work has been done by George Kramer from the authors' laboratory.

Most people have found that it's most effective as an "internal" versus "external" resuscitation, if you will, by mobilizing intracellular and extracellular fluid rather than giving external fluids. Many have also demonstrated decreased systemic vascular resistance. Dr. Gann has shown a decreased catecholamine response. And very interesting data from Mazzoni and colleagues have demonstrated increased microcirculation by shrinking the endothelial cells, and thus improving capillary flow and organ nutrition, which goes along with some of the data that were demonstrated by the authors today. In fact, I think one of the most interesting findings they demonstrated was in light of decreased oxygen delivery; in fact there was increased oxygen consumption, suggesting perhaps that maybe the microcirculation is improved, although it could also reflect increased cardiac utilization of oxygen by increasing cardiac index.

But now I would like to emphasize that nearly all investigators in the past have compared hypertonic saline with lactated Ringer's, which brings us to the major problem with this study. Both groups had equal lactated Ringer's resuscitation but one had the addition of 10 mL/kg hypertonic saline dextran. This is a huge bolus of fluid, with an osmolality of 2,400 for hypertonic saline versus 300 for lactated Ringer's. If this were extrapolated to a clinical equivalent of a 70-kg man, the 10 mL/kg would have been osmotically equivalent to 5.5 L extra fluid that the hypertonic saline group received. So I don't think it's too surprising that they had better perfusion, had improved cardiac outputs, and the like. Perhaps, in fact, you have created the classic straw man and went ahead and destroyed him relative to the experimental design.

I think that adding hypertonic saline to the Parkland formula in this model certainly is better than the Parkland formula alone, but what about also adding more lactated Ringer's? I believe that you really need at least one other group with a large initial bolus of lactated Ringer's so that more equal resuscitation in fact can be compared.

In summary, I really do want to believe, but I think the data are very difficult to interpret with this inequality of fluid resuscitation.

DR. JANICE MENDELSON (San Antonio, Texas): It has long been known that dextran improves circulation both by increasing the blood volume and by its effect on microcirculation. I wonder why you didn't just use dextran with normal saline or with lactated Ringer's without using the hypertonic saline. Might the results be even better?

DR. STEVEN SHACKFORD (Burlington, Vermont): My question is more ideological than methodological.

The addition of dextran or colloid to hypertonic solutions was done to hold that fluid which had been extracted from cells in the capillary space; in other words, it required an intact capillary membrane, since colloids generally have a high capillary reflectance. In a burn patient, however, capillary permeability is increased and the advantage of adding colloid to the solution seems to me to be sort of a waste of money.

My question to the authors is why not just 7.5% hypertonic saline alone and forget the dextran, which increases astronomically the cost of the solution and the resuscitation?

DR. STEVEN STEINBERG (New Orleans, Louisiana): I have two questions for the author.

First, how did you choose the dose of hypertonic saline dextran? I, along with Dr. Fabian, am a little bit troubled by that. You gave a very large dose relative to what has been reported elsewhere in other animal models.

Second, I am troubled even more by the fact that the hemodynamic data that you report in the presentation are significantly different than what is in the abstract, particularly as it pertains to the cardiac output. This alteration in the data required that one of your conclusions from the abstract be changed; and that is that there is no late increase in cardiac output in the Ringer's lactate group. Please address these concerns.

DR. ERNEST E. MOORE (Denver, Colorado): I have a couple of simple methodologic questions. The standard bolus of HSD for profound hemorrhagic shock has been 4 mL/kg, larger volumes have been associated with apparent toxicity. How did you select the 10 mL/kg dosage? The second issue is distinguishing the positive, or potentially negative, effects of dextran versus sodium. Our previous work with a Langendorff preparation suggested that ionic hyperosmolar solutions; e.g., sodium, depress myocardial function; whereas, dextran improves function via scavenging hydrogen peroxide generated during reperfusion. Did you administer the saline and dextran in separate groups and did you find evidence of attenuated lipid peroxidation? Finally, you enticed us in your abstract to believe that HSD would reduce bacterial translocation following burn injury. Did you examine your animals with respect to bacterial content in the mesenteric lymph nodes or systemic endotoxin levels?

DR. CUTHBERT SIMPKINS (Baltimore, Maryland): I was impressed with the large and consistent differences that you had with respect to oxygen consumption. Do you have an explanation for this?

DR. STEPHEN T. ZEIGLER (Closing): First, I would like to thank Dr. Fabian and everyone for their discussions and questions. There were no statistically significant differences seen between groups using the unpaired *t* test. The experiments were done such that one animal from each group was done weekly in order to lessen group-to-group variability. The data were also analyzed as a percentage of baseline in order to normalize the groups and thus lessen intergroup variations.

The second question concerning the differences in volumes of fluid received during the first hour postburn addresses whether the effects seen in these experiments were merely a bolus phenomenon. While our current study does not answer this question definitively, we have additional data that would suggest these phenomena are not a bolus effect. All our pigs weighed approximately 20 kg. In a previous experiment we gave the Parkland resuscitation plus 2 mL/kg/hour of Ringer's solution as maintenance fluid. At 20 kg for each animal, the HSD group, the Parkland group, and the Parkland plus maintenance group received 200 mL, 100 mL, and 130 mL of volume, respectively, over the first 30 minutes of resuscitation. The Parkland group and the Parkland plus maintenance group showed similar significant decreases in mesenteric blood flow following thermal injury, whereas, this decrease in mesenteric blood flow was prevented in the HSD group. Similar results are seen when looking at cardiac index. The HSD group showed no decrease in cardiac index relative to the Parkland or Parkland plus maintenance groups. There appears to be a real difference between the HSD group which is not related to an exogenous volume infusion. Our data are supported by other investigators studying hemorrhagic models in which it has conclusively been shown that the effects seen with HSD infusion are not an exogenous bolus effect (Maningas et al. *Ann Emerg Med,* 1986).

The questions as to whether the effects seen in our experiments are from the hypertonic saline, the dextran, or both remains to be elucidated completely. The literature has clearly shown that the combination of hypertonic saline with dextran has far superior benefits in the resuscitation of hemorrhagic shock when compared with single drug therapy. Our study does not answer the question of which is better, but we are in the process of investigating the effects of 7.5% hypertonic saline, 6% dextran, and a volume control of Ringer's solution on their ability to prevent postburn changes in gastrointestinal homeostasis. Again, the cardiovascular effects are probably maximized by the combination of HSD as seen in the hemorrhagic shock model.

Dr. Shackford's question regarding the use of a colloid compound early in the resuscitation of thermal injuries in face of known capillary permeability changes is a good question. Again, we intend to clearly define each component's role with regard to resuscitation of a thermally injured animal. However, the use of HSD initially in the resuscitation may prevent a vicious cycle of initial hypovolemia followed by systemic and mesenteric vasoconstriction. The effects of the dextran component may be short lived, but its oncotic effect on the expanded intravascular volume induced by hypertonic saline may last long enough to prevent the beginning of the cycle of vasoconstriction.

In regard to the dose of HSD used, it has been shown that the standard 4 mL/kg used in thermal injury showed improved cardiovascular function transiently (Onarheim, et al., *J Trauma,* 1990). Dr. Fabian recently showed that 10 mL/kg 7.5% hypertonic saline can be used safely to improve hemodynamics following hemorrhagic shock in a pig model (Fabian, et al., *J Trauma,* 1989). Therefore, we chose 10 mL/kg infusion of HSD given that 4 mL/kg was not adequate and 10 mL/kg appeared to be safe.

The use of conjugated dienes is accepted as an indicator of reperfusion injury. However, there are controversies regarding which test best indicates a true ischemia-reperfusion injury. It is known that dextran has oxygen radical scavenging properties, and it may be these properties that actually attenuate the rise in conjugated dienes seen in the Parkland resuscitated group.

As Dr. Fabian mentioned, Mazzoni has shown capillary swelling following hemorrhagic shock which is reversed with HSD infusion (Mazzoni et al. *Circ Shock,* 1990). Therefore, it is appealing to think that HSD caused its effects by decreasing this endothelial swelling in this thermal injury model, thereby improving systemic and mesenteric microcirculation with attenuation of potential ischemic insults as a result of thermal injury. By improving microcirculation, oxygen delivery and consumption may be improved.

Dr. Moore, we are very interested in bacterial translocation and have shown previously that the degree of mesenteric ischemia seen in the Parkland resuscitated group is associated with significant translocation. In this study in which portal vein catheters were placed, translocation occurred in five of eight animals in the Parkland resuscitated group and two of eight in the HSD resuscitated group.

The discrepancies seen between the data in the abstract and the presentation are because the abstract represented n = 4 animals and the presentation represented n = 8 animals.