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Epinephrine as an inotropic agent in septic shock: A dose-profile analysis

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Objective: **To characterize the acute actions and physiologic dose profile of epinephrine, as a single inotrope, in patients with septic shock.**

Design: **Prospective clinical study. The relationship between epinephrine dose and cardiovascular variables was analyzed using repeated-measures analysis of variance.**

Setting: **ICU in a university teaching hospital.**

Patients: **Eighteen patients with septic shock, mean age 64 ± 8 (SD) yrs, and with a mean admission Acute Physiology and Chronic Health Evaluation (APACHE II) score of 23 (range 14 to 35).**

Interventions: **Initial volume loading and the measurement of a baseline hemodynamic profile were followed by the administration of an epinephrine infusion at 3 μg/min with subsequent increments of 3 μg/min and the determination of a hemodynamic profile after each dose increment. Therapy was titrated to clinical goals of perfusion and restoration of premorbid systolic arterial BP.**

Measurements and Main Results: **After volume loading, mean hemodynamic indices were as follows: mean arterial pressure (MAP) 62 ± 7 mm Hg; cardiac index 3.8 ± 1.1 L/min/m²; left ventricular stroke work index 25 ± 11 g·m/m²; oxygen delivery ($\dot{D}o_2$) index 460 ± 168 mL/min/m²; and oxygen consumption ($\dot{V}o_2$) index 165 ± 64 mL/min/m². In the dose range of 3 to 18 μg/min, epinephrine produced linear increases in average heart rate, MAP, cardiac index, left ventricular stroke work index, stroke volume index, $\dot{V}o_2$, and $\dot{D}o_2$. No effect was noted on pulmonary artery occlusion pressure (PAOP), mean pulmonary arterial pressure, or systemic vascular resistance index.**

Conclusions: **Epinephrine increases $\dot{D}o_2$ in septic shock by increasing cardiac index without an effect on systemic vascular resistance index or PAOP. (Crit Care Med 1993; 21:70–77)**

KEY WORDS: epinephrine; septic shock; inotrope; dose profile; intensive care unit; hemodynamics; systemic vascular resistance; oxygen consumption; cardiac output; catecholamines; critical illness

Septic shock is associated with an unacceptably high mortality rate. The cardiovascular dysfunction in septic shock may be conceptualized as having "central" and "peripheral" components; the central being a biventricular myocardial depression with reduction of ejection fraction and chamber dilatation (1) and the peripheral being a collapse of vascular tone (2).

Therapeutic approaches in septic shock include appropriate vascular volume "loading," the administration of antibiotics, and inotropic drugs (3, 4). Considerable interest, if not controversy, has attended the question of which inotropic agent(s) to use (5, 6). More recently, the focus has been directed toward oxygen transport principles in both describing septic shock pathophysiology and directing therapy (7, 8).

With these insights in mind, we sought to prospectively determine the acute initial effects and the physiologic dose profile of epinephrine alone in septic shock.

We hypothesized that epinephrine would produce systematic change in cardiorespiratory variables in septic shock. To test this hypothesis, we performed a prospective study of septic shock patients having dose increments, from baseline, of epinephrine. We analyzed the effect on these cardiorespiratory variables using repeated-measures analysis of variance.

MATERIALS AND METHODS

Patients. The study involved the prospective assessment of patients with septic shock. Septic shock was defined as a clinical syndrome of inadequate tissue perfusion, along with the following characteristics

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Table 1. Clinical characteristics of patients

Patient	Age (yr)	Sex	Outcome	APACHE II Score	Epinephrine Dose, Maximum (μg/min)	Diagnosis
1	74	F	Died	30	15	Biliary sepsis
2	75	M	Died	14	3	Postoperative pneumonia
3	75	M	Survived	24	3	Postoperatve peritonitis
4	65	F	Survived	24	27	Septicemia/multiple myeloma
5	54	F	Survived	19	6	Liver abscess and empyema
6	60	M	Died	20	3	Legionella pneumonia
7	71	M	Survived	14	12	Urinary tract infection
8	62	M	Survived	35	18	Pneumonia
9	61	F	Survived	29	12	Urinary tract infection
10	70	F	Survived	27	9	Postoperative peritonitis
11	53	F	Survived	19	9	Urinary tract infection
12	59	M	Died	24	9	Pneumonia
13	73	M	Survived	22	6	Pneumonia
14	61	F	Died	18	15	Aspiration pneumonitis
15	58	M	Survived	28	15	Pneumonia
16	73	F	Survived	18	12	Urinary tract infection
17	49	M	Survived	18	18	Pneumonia
18	66	F	Died	23	12	Infectious arthritis

APACHE , Acute Physiology and Chronic Health Evaluation.

Table 2. Number of patients vs. epinephrine dose

Epinephrine dose (μg/min)	3	6	9	12	15	18	21	24	27
Number of patients	18	15	13	9	6	3	1	1	1

systolic arterial BP of ≤90 mm Hg; oliguria of <20 mL/hr; evidence of a septic focus or positive blood cultures; fever or hypothermia (temperature >37.5°C or <36.5°C); and leukocytosis or leukopenia (WBC count >10 × 10^9/L or <4 × 10^9/L) (3).

Patients in the ICU were included in the study if they had a) a clinical diagnosis of septic shock, and b) a complete "baseline" hemodynamic profile performed before the beginning of inotropic therapy. Patients with ongoing inotropic therapy or those patients in whom inotropic therapy was begun before hemodynamic profiles were obtained, were excluded. Thus, the series was not consecutive.

The study was approved by the Hospital Ethics of Research Committee.

Protocol. All patients were studied in the ICU. Upon establishing a diagnosis of septic shock, a radial arterial cannula and pulmonary artery flow-directed catheter (93A 831 7.5F VIPTM, Baxter Edwards Critical-Care, Irvine, CA) were inserted. Intravascular pressures, mean arterial pressure (MAP), right atrial pressure, pulmonary artery occlusion pressure (PAOP), mean pulmonary arterial pressure, and heart rate (HR) were recorded via transducers (60-800, Trantec®, Bentley, Irvine, CA) and a monitoring system (404-1, Sirecust®, Siemens, Erlangen, FRG) and were measured at end-expiration, using a four-channel strip-chart recorder (1400, MFE, Honeywell, Salem, NH). Cardiac output measurements were performed in triplicate, using a cardiac output cartridge (2261, Siemens), with 10 mL of 5% dextrose at a temperature of <5°C. Blood gas analysis of arterial and mixed venous blood samples were made using a blood gas analyzer (ABL3, Radiometer, Copenhagen, Denmark).

The following derived variables were calculated using standard formulas (7): cardiac index, stroke volume index, systemic vascular resistance index, left ventricular stroke work index, oxygen delivery ($\dot{D}o_2$), oxygen consumption ($\dot{V}o_2$), pulmonary shunt fraction, and oxygen extraction ratio.

Fluid resuscitation with colloid and/or blood was performed to a PAOP of ≥15 mm Hg. Supplemental oxygen was administered to maintain an arterial oxygen saturation of ≥90% and patients were mechanically ventilated according to clinical indication. A baseline hemodynamic profile was performed and those patients who did not sustain a systolic arterial BP of ≥90 mm Hg with volume therapy were begun on epinephrine and entered into the trial. No other inotrope (e.g., neither low-dose dopamine nor digoxin [9]), was prescribed during the study.

Epinephrine was infused at a rate of 3 μg/min iv via a central vein at a dilution of 10 mg/500 mL of 5% dextrose in water. After a steady state was achieved (at 20 mins [10]), a repeat hemodynamic profile was

Table 3. Hemodynamic data and blood gas values (mean ± SD) at baseline (dose = 0) and during epinephrine infusions

Dose (μg/min)	HR (beats/min)	MAP (mm Hg)	RAP (mm Hg)	MPAP (mm Hg)	PAOP (mm Hg)	CI (L/min/m²)	SI (mL/m²)
0	96 ± 22	62 ± 7	15 ± 6	30 ± 7	19 ± 5	3.8 ± 1.1	42 ± 20
3	104 ± 20	70 ± 14	16 ± 3	32 ± 9	20 ± 6	4.2 ± 1.2	43 ± 13
6	106 ± 22	71 ± 13	15 ± 4	30 ± 8	21 ± 6	4.7 ± 1.6	47 ± 21
9	106 ± 25	72 ± 9	15 ± 3	31 ± 6	18 ± 3	4.5 ± 1.3	46 ± 22
12	107 ± 19	72 ± 12	15 ± 4	33 ± 9	19 ± 5	4.7 ± 1.4	45 ± 14
15	111 ± 22	78 ± 15	15 ± 6	31 ± 7	19 ± 7	4.1 ± 1.1	38 ± 11
18	122 ± 23	81 ± 22	14 ± 5	35 ± 11	22 ± 8	4.3 ± 1.5	36 ± 16
p Value	.002	.0001	.89	.07	.5	.0001	.0001

Dose, epinephrine infusion rate; HR, heart rate; MAP, mean arterial pressure; RAP, right atrial pressure; MPAP, mean pulmonary index; SVRI, systemic vascular resistance index; $\dot{V}O_2$, oxygen consumption; $\dot{D}O_2$, oxygen delivery; $\dot{Q}sp/\dot{Q}t$, shunt fraction; O_2 Extr, oxygen *p* refers to the test of significance for zero slope in the equation E (variable) = a + b × dose, where E is the expected or predicted average

performed. The rate of epinephrine was then increased by increments of 3 μg/min with a hemodynamic profile being measured 20 mins after each inotropic increment. Ongoing fluid losses were replaced with appropriate fluid infusion.

The therapeutic end-points of inotropic therapy were primarily clinical: improvement in tissue perfusion; return of urine output to >0.5 mL/kg/hr; and restoration of systolic arterial BP to a minimum of premorbid levels. Secondarily, these end-points were goal directed to objective indices. In particular, an attempt was made to achieve certain hemodynamic and oxygen transport indices associated with improved outcome (7, 8, 11): a cardiac index >4.5 L/min/m²; $\dot{D}O_2$ >600 mL/min/m²; $\dot{V}O_2$ >170 mL/min/m².

Statistical Analysis. The relationship between epinephrine dose and the various cardiovascular variables was subjected to statistical analysis using an unbalanced, repeated-measures analysis of variance with autoregressive error structure, with allowance for the possibility of a quadratic relationship to exist between response and drug dose. Patient weights were included in the analysis as a covariate. The analysis was done marginally, no attempt being made to treat it as a multivariate problem, i.e., each variable was analyzed separately for a relationship with epinephrine dose. The analysis was performed using a computer program (5V, BMDP, UCLA, Los Angeles, CA). Data are presented as mean ± SD values, unless otherwise noted.

We adopted this approach, cognizant of the problem of multiple comparisons of group means. This problem has recently been the subject of review (12, 13). Thus, the inherent statistical inferential difficulties associated with, for example, multiple *t*-tests between different dose levels, was avoided. Moreover, the approach used would appear to overcome the recent critique (14) of the consequences of inappropriate analysis of data due to "pooling," where no account was taken of significant "interpatient" relationships.

RESULTS

The clinical characteristics of the 18 study patients are shown in Table 1. There were nine males and nine females with a mean age of 64 ± 8 yrs. The mean admission Acute Physiology and Chronic Health Evaluation (APACHE II) score was 23 with a range of 14 to 35. Of 18 patients, 17 were studied on the day of admission; patient 7 (Table 1) was studied on the second day after admission. The survivors (n = 12) had a mean admission APACHE II score of 23 (range 14 to 35); the nonsurvivors (n = 6) had a mean score of 23 (range 14 to 30). Patients who survived were discharged from the ICU at a mean time of 15 days after the study (range 1 to 50); patient deaths occurred at a mean of 5 days after the study (range 0.7 to 10). Death was due to a combination of multiple system organ failure and recalcitrant hypotension. Eleven patients were mechanically ventilated and the overall mortality rate was 33%. Six patients had severe, longstanding coexistent disease processes: chronic renal failure (n = 2); diabetes mellitus (n = 1); alcohol-induced cirrhosis (n = 1); intractable angina pectoris (n = 1); and rheumatoid arthritis (n = 1).

The mean volume of resuscitation fluid prescribed before inotrope infusion was 1.9 ± 0.8 L.

The dose range of epinephrine prescribed in the study was 3 to 27 μg/min. The number of patients receiving different infusion rates of epinephrine infusion is shown in Table 2. As only one patient received ≥21 μg/min of epinephrine, our results are given for a dose range of 3 to 18 μg/min.

The baseline and subsequent hemodynamic variables of the study patients are shown in Table 3. A linear, but not curvilinear relationship betw

Table 3 *(continued)*

LVSWI (g·m/m²)	SVRI (dyne·sec/ cm⁵·m²)	Arterial pH	$\dot{V}O_2$ (mL/ min/m²)	$\dot{D}O_2$ (mL/ min/m²)	$\dot{Q}sp/\dot{Q}t$ (%)	O_2 Extr (%)
25 ± 11	1079 ± 429	7.31 ± 0.11	165 ± 64	481 ± 132	22 ± 13	35 ± 12
30 ± 13	1084 ± 432	7.28 ± 0.14	173 ± 56	547 ± 132	23 ± 10	32 ± 10
30 ± 12	1039 ± 460	7.27 ± 0.13	198 ± 81	589 ± 156	19 ± 9	35 ± 12
33 ± 18	1118 ± 476	7.25 ± 0.12	198 ± 74	570 ± 137	17 ± 7	36 ± 13
31 ± 7	1091 ± 516	7.24 ± 0.1	234 ± 78	615 ± 174	20 ± 9	39 ± 11
29 ± 8	1356 ± 604	7.23 ± 0.11	175 ± 46	522 ± 38	22 ± 9	33 ± 7
26 ± 6	1448 ± 876	7.21 ± 0.17	193 ± 24	531 ± 4	9 ± 4	37 ± 5
.0005	.8	.11	.016	.0003	.96	.27

arterial pressure; PAOP, pulmonary artery occlusion pressure; CI, cardiac index; SI, stroke volume index; LVSWI, left ventricular stroke work extraction ratio.
value, a is the interupt, and b is the slope of the line.

infusion rate (dosage) and the analyzed variables was found for HR, MAP, cardiac index, stroke volume index, left ventricular stroke work index, $\dot{V}O_2$, and $\dot{D}O_2$. The significance of these relationships is shown in Table 3. Those variables for which there was a significant dose relationship are shown in Figures 1 and 2, where the lines describing the predicted average values are drawn according to the following general model equation: E (variable) = a + b × dose, where E is the expected or predicted average value, a is the intercept, and b is the slope of the line.

There was no demonstrable effect of patient weight on the relationship between epinephrine dose and the cardiovascular/oxygen transport variables.

The epinephrine infusions were well tolerated, with no clinically important ventricular or supraventricular dysrhythmias during the course of the study.

DISCUSSION

Critique of Methodology. Our study demonstrated that in the dose range of 3 to 18 μg/min, epinephrine is vasoactive in patients with septic shock to the extent that there were increases in key cardiovascular variables. However, some cautions may apply to this study.

First, although it was a prospective study, the patients were not consecutive, and thus severely hypotensive patients may have been selected out. Our mean baseline MAP was 62 ± 7 mm Hg, which is higher than that value in recent studies (15–17), although it was similar, or lower, in other studies (18–21). A number of the latter studies (18–20), which investigated a single or a combination of agents, provided no systolic arterial BP definition of septic shock and baseline MAP values showed considerable variation: 69 ± 27 (SEM) mm Hg; 63 ± 15 mm Hg; and 61 ± 21 mm Hg (18, 19, and 20, respectively).

Second, although our mean initial cardiac index (3.8 ± 1.1 L/min/m²) was similar to values in other studies (15, 17, 21), the initial PAOP, at 19 ± 5 mm Hg, was higher and the systemic vascular resistance index was 1079 ± 429 dyne·sec/cm⁵·m², which would appear to be in the middle range (15–21). This high PAOP may have been due to the fluid-loading regimen or to myocardial disease. However, Rackow et al. (3) were unable to demonstrate a difference in the PAOP after fluid loading between those patients with and without cardiovascular disease (16 vs. 15 mm Hg).

Third, although the mean predicted $\dot{D}O_2$ at an epinephrine infusion rate of 18 μg/min was 700 mL/min/m², the ability of epinephrine alone to achieve $\dot{D}O_2$ values of, for example, 843 ± 27 mL/min/m², as in the study of Edwards et al. (15) where a combination of agents was used, has not been demonstrated. Furthermore, as lactate concentration values were not measured, we are unable to speculate as to whether the parallel increases in $\dot{V}O_2$ and $\dot{D}O_2$ with epinephrine were associated with increased lactate concentration, when $\dot{V}O_2$ is supply (i.e., on $\dot{D}O_2$) dependent (22, 23), or due to an effect of the inotrope per se (24).

Epinephrine as an Inotrope. With the above caveats in mind, what may we say regarding epinephrine as an inotrope? As an inotrope for use in acute circulatory failure, epinephrine receives mention in reviews (25, 26), but usually to reiterate well-documented effects in "normals" (24, 27–30), or in the context of effects in cardiopulmonary resuscitation (31) and postcardiopulmonary bypass (32, 33). Studies on the effects of epinephrine alone in septic shock appear to be rare (34, 35).

Effect in Normals. In normal humans, iv infusions of epinephrine, in dose ranges of ≤20 μg/min, produce increases in the following variables: a) cardiac output of ≤2 × the baseline value; b) systolic arterial BP; c) HR

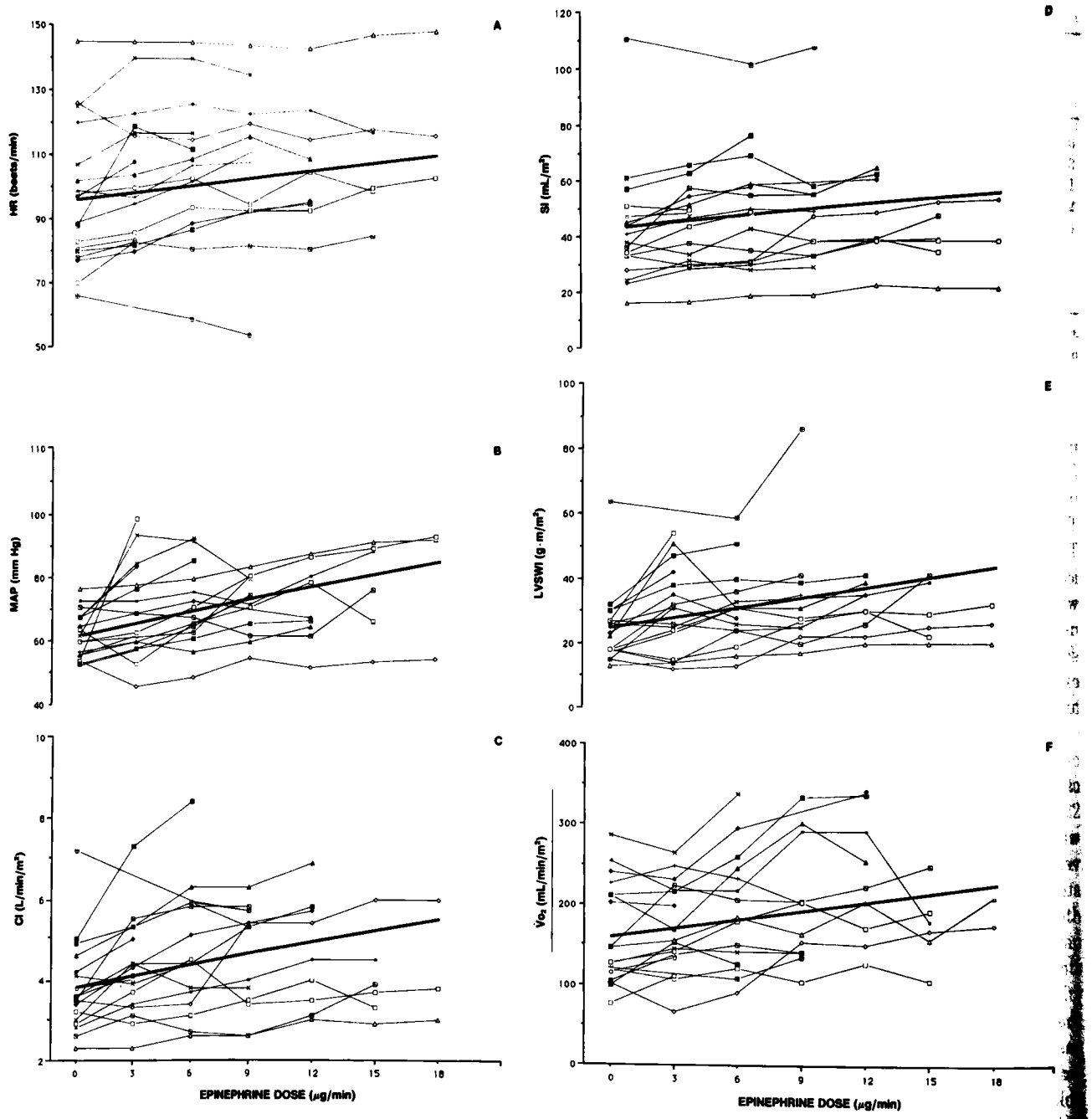

Figure 1. Relationship between epinephrine dose and heart rate (*HR*), mean arterial pressure (*MAP*), cardiac index (*CI*), stroke volu index (*SI*), left ventricular stroke work index (*LVSWI*), and oxygen consumption ($\dot{V}o_2$) (graphs *A* through *F*, respectively). The *bold* shows the fitted model mean response of the variables to epinephrine dose according to the following equations (as determined repeated-measures analysis of variance): E (HR) = 96.4 + 0.79 × dose (p = .002); E (MAP) = 63.2 + 1.19 × dose (p = .0001); E (CI) = + 0.01 × dose (p = .0001); E (SI) = 43.3 + 0.62 × dose (p = .0001); E (LVSWI) = 25.1 + 1.02 × dose (p = .0005); E ($\dot{V}o_2$) = 166.2 + 3.3 × (p = .016). E is the expected or predicted average value.

of "moderate" degrees (20); d) mean pulmonary arterial pressure; and e) $\dot{V}o_2$ and metabolic rate. At 10 μg/min, total peripheral resistance decreases, which is associated with a large (2×) increase in muscle blood flow (36), while diastolic and MAP values show varia effects (no change, decrease, or increase).

Postcardiac Bypass. The effects of epinephri alone have been reported in two series

postcardiopulmonary bypass patients. At 4 μg/min (32), significant increases in HR, cardiac index, stroke volume index, and a decrease in systemic vascular resistance were noted, with no significant difference between epinephrine dosage rates of 4 and 8 μg/min, except for cardiac index (2× the effect). At low dose (0.04 μg/kg/min), immediately after cessation of bypass, epinephrine produced significant increases (20% to 30%) in cardiac index and MAP with no significant changes in stroke volume index, HR, or systemic vascular resistance (33). In both these studies (32, 33), patients had baseline variables (MAP >80 mm Hg, cardiac index >2.0 L/min/m^2) that were not consistent with a diagnosis of shock.

Effect in Septic Shock. Two studies (34, 35) reported the effects of epinephrine alone in septic shock. MacKenzie et al. (34), in 13 patients studied after fluid resuscitation, at a mean dose of 11 μg/min (range 3.5 to 29), showed significant epinephrine-induced increases in MAP, cardiac index, $\dot{D}o_2$, and left ventricular stroke work index and a variable effect on systemic vascular resistance. There was no effect on HR or $\dot{V}o_2$. No adverse side-effects of the epinephrine infusion were reported. Runciman (35), using epinephrine doses of 3 to 12 μg/min in 44 patients, reported epinephrine as a "drug of first line," with epinephrine-induced increases in BP in 68% of patients and urine output in 74%, and no change in HR in 73% or a decrease in 25% of patients.

Previous studies (37, 38) of inotropes in septic shock found various effects of single agents. Winslow et al. (37), studying norepinephrine, dopamine, and isoprenaline, found significant increases in MAP, HR, and cardiac index with norepinephrine and dopamine, but no significant change in MAP or left ventricular stroke work index with isoprenaline, which also caused substantial increases in HR (20%) and cardiac index (47%). Isoprenaline has found recent advocates (16) for its use in septic shock. Similar inotropic effects of these agents were also described by Loeb et al (38). Systemic vascular resistance was substantially greater with norepinephrine therapy, being unchanged with dopamine and decreased with isoprenaline. This effect on systemic vascular resistance has mandated the reintroduction of norepinephrine into the drug armamentarium of septic shock in the context of achieving objective goals, i.e., systemic vascular resistance >700 to 800 dyne·sec/cm^5 (15, 17, 39). Few recent studies (17) have used norepinephrine as an initial agent, and although concomitant improvements in urine output have been reported with the combined use of norepinephrine and other agents, the consequences of manipulating systemic vascular resistance need to be further explored. Hussain et al. (40), in a canine septic shock model, could

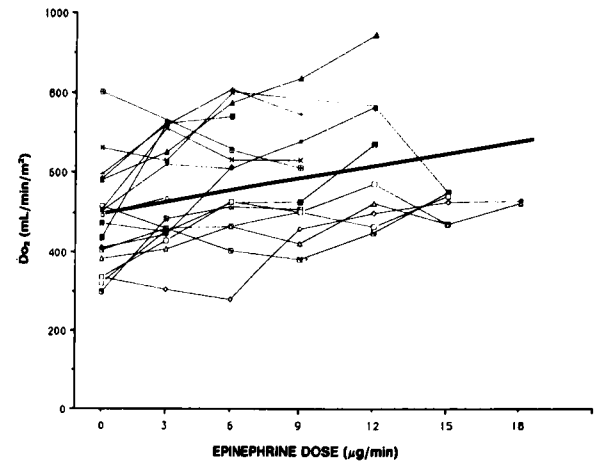

Figure 2. Relationship between epinephrine dose and oxygen delivery ($\dot{D}o_2$). The *bold line* shows the fitted model mean response of $\dot{D}o_2$ to epinephrine dose according to the equation (as determined by repeated-measures analysis of variance): E ($\dot{D}o_2$) = 503.5 + 11 × dose (p = .0003). E is the expected or predicted average value.

not demonstrate improved vital organ blood flow with norepinephrine.

The particular actions of dopamine and dobutamine, used as sole agents in septic shock, have been assessed (16–21). Both agents have been shown to do the following: a) increase MAP and cardiac index; b) variably affect PAOP (increase [16] or no change [19, 20] with dopamine and a decrease [18, 19] with dobutamine); c) lower or maintain systemic vascular resistance (16, 18, 19); and d) consistently increase HR and shunt fraction.

Effects in the Current Study. Epinephrine, at doses of ≤18 μg/min, had favorable effects to the extent that substantial increases were produced in cardiac index, MAP, left ventricular stroke work index, and stroke volume index. Based on our analysis, at 18 μg/min, such epinephrine-induced increases would be predicted to be 46%, 34%, 73%, and 26%, respectively. Over the whole dose range, no significant changes in PAOP, mean pulmonary arterial pressure, shunt fraction, or systemic vascular resistance index were obtained. An increase in HR of 15%, which would occur at 18 μg/min, is disadvantageous, as chronotropy is the major contributor to total myocardial oxygen demand (41), although global ischemia is not a mechanism of cardiac depression in septic shock (42). Moreover, in a canine model of acute ischemic heart failure, Haider and co-workers (43) found improved hemodynamics and survival with epinephrine as the inotropic agent.

The predicted epinephrine-induced increase in stroke volume index at 18 μg/min in our study was comparable with increments in stroke volume index

found in the studies above; norepinephrine at 13% to 15%, dopamine at 15% to 26%, and dobutamine at 15% to 28%. However, the concomitant increase in left ventricular stroke work index induced by all the agents must be balanced against an increase in left ventricular filling pressures induced by norepinephrine and dopamine, which effect is not seen with epinephrine. Loeb et al. (38) commented that an increase in left ventricular stroke work index associated with an increase in ventricular filling pressure does not necessarily indicate improved cardiac function. Dopamine would also appear to consistently increase mean pulmonary arterial pressure (16, 20, 21) and, combined with the tendency to increase both PAOP and shunt fraction, would have a spectrum of potentially adverse effects that are not demonstrated with epinephrine.

All inotropes, as sole agents, have a combination of advantageous and potentially deleterious effects. Epinephrine, an inexpensive agent, within the dose range of 3 to 18 μg/min, increases cardiac index and $\dot{D}o_2$ without any effect on systemic vascular resistance index or PAOP. Such action merits further study of epinephrine as an inotrope in septic shock; in particular, the effect of doses >18 μg/min and in combination with other agents.

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Erratum

In the article, "Fellowship Programs in Critical Care Medicine: 1992/1993," *Crit Care Med* 1992; 20:1346–1354, the following corrections (in italics) should be noted:

A. ADULT PROGRAM

- Type of ICU: M, S, B, NS with other rotations in Anesthesia, Nutrition, Pulmonary, Research
  Specialty restriction: IM

Univ. of Miami/VA Medical Center
1201 N.W. 16th Street
Miami, FL 33125
Director: R. M. Schein, MD, FCCM†

B. PEDIATRIC PROGRAMS

- *The program is currently not offered.* Resumption of the program will be announced in a subsequent issue of *Critical Care Medicine.*

Rush-Presbyterian-St. Luke's Medical Center
1753 W. Congress Parkway
Chicago, IL 60612
Director: G. M. Goldman, MD†

- *Accredited by the Accreditation Council for Graduate Medical Education.*

Baylor College of Medicine/
Texas Children's Hospital
6621 Fannin Street, 4-218
Houston, TX 77030
Director: L. S. Jefferson, MD, FCCM†

The Society of Critical Care Medicine regrets the inconvenience caused by these oversights.

†Society of Critical Care Medicine member.