Cardiopulmonary Adjustments Following Single High Dosage Administration of Methylprednisolone in Traumatized Man

JEFFREY LOZMAN, M.D., ROBERT E. DUTTON, M.D.,
MARK ENGLISH, B.S., SAMUEL R. POWERS, JR., M.D.

From the Departments of Surgery and Physiology, Albany Medical College of Union University, Albany, New York

Pharmacologic doses of methylprednisolone sodium succinate were administered to 10 critically ill patients when the steroid was the only variable. Measurements of respiratory and circulatory physiologic parameters were obtained in all patients prior to injection and at 30 and 90 minutes following injection of methylprednisolone sodium succinate. A significant increase in Cardiac Index was seen ($P<.01$) which appeared to be in association with a decrease in pulmonary vascular resistance ($P<.01$) at a time when physiologic shunting of blood through the lungs increased ($P<.01$). These changes imply improved perfusion of non- or poorly ventilated portions of the lungs. Four of ten patients demonstrated removal of lactate by the lung during the control period. Following methylprednisolone sodium succinate injection, 9 of 10 patients demonstrated production or a washout of lactate from the lungs.

GLUCOCORTICOID PREPARATIONS in pharmacologic doses have been recently advocated as primary therapy for management of both medical and surgical acutely ill patients.[2,4,7,8,15,20,26-28,31-33,43-45] Beneficial effects claimed for these preparations include stabilization of lysosomal membranes, improvement in cardiac dynamics, and a decrease in peripheral vascular resistance. Much of the available literature deals with animal models and artificially controlled systems. In most instances studies in humans have included patients who received a number of other drugs, blood, and intravenous fluids in addition to steroid preparations.[4,7,8,24,26,27] Also, many authors do not discriminate between the various glucocorticoid preparations.[27,28,34,41,44] This situation severely limits one's ability to interpret the reported data.

The present study was undertaken to investigate respiratory and circulatory effects of a high dosage of one steroid preparation, methylprednisolone sodium succinate, when administered to the acutely ill patient during a time in which the action of the steroid was the only known variable.

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Method and Materials

Studies were performed on ten seriously ill patients who were admitted to the Trauma Center of the Albany Medical College. Seven patients were victims of multiple trauma accidents, one patient was in septic shock following surgery, and two patients were postoperative following repair of ruptured abdominal aneurysms. Radial artery catheters were inserted and a flow-directed triple lumen 7F Swan Ganz[55] catheter was positioned in a pulmonary artery and then advanced to a wedge position. All ten patients were intubated and ventilated with a volume cycled respirator. Pulmonary artery, pulmonary wedge and arterial blood pressures were measured by means of strain gauge transducers. Cardiac output was determined by indocyanine green dye dilution technique. Analog voltages from the densitometer and the output of selected channels of a recorder were transmitted on-line to a medium size digital computer for calculation of cardiac output, and its conversion to cardiac index based on the patient's body surface area (BSA), and for calculation of pulmonary vascular resistance determined from mean pulmonary artery pressure and pulmonary wedge pressure.[17] Mixed venous blood was obtained from the Swan Ganz catheter. Blood gases were analyzed using P_{O_2}, P_{CO_2}, and pH electrodes. Physiologic shunt fraction of blood through the lung was computed off-line using the Berggrens formula with appropriate correction for shift in the oxygen dissociation curve, hemoglobin concentration and dissolved oxygen. (Error of determination ±3%).

TABLE 1. *Patient Description, Mean Aortic Blood, Pressure and Pulmonary Wedge Pressure in Ten Patients Receiving Methylprednisolone.*

Patient	Age Sex	Diagnosis	Survival or Death	Mean Aortic Blood Pressure (mm Hg) Baseline	30 min	90 min	Pulmonary Wedge Pressure (mm Hg) Baseline	30 min	90 min
1	14/M	Trauma	Survived	112	116	115	10	10	14
2	43/F	Trauma	Survived	97*(84)	99	90	17	8	8
3	21/M	Trauma	Survived	108	98	105	10	5	5
4	62/F	Aneurysm	Survived	135	112	114	3	4	3
5	39/M	Trauma	Survived	102	96	107	13	13	13
6	37/M	Septic Shock	Survived	74	72	72	—	—	—
7	19/F	Trauma	Survived	100*(62)	86	75	9	11	14
8	29/M	Trauma	Died	102	105	108	18	20	20
9	81/M	Trauma	Died	88*(48)	84	71	6	6	6
10	69/M	Aneurysm	Died	63*(96)	54	50	10	10	8
Mean				98.1	92.2	90.7	10.7	9.7	10.1
S.E.				±6.3	±6.0	±7.1	±1.6	±1.6	±1.8
					P<.05	P-NS		P-NS	P-NS

*Change in mean aortic pressure immediately following injection of methylprednisolone sodium succinate.

Oxygen consumption was determined by the Fick equation from cardiac output multiplied by the arterial-venous oxygen content difference [[.0031 (P_{aO_2}) + Hb (1.39) (arterial saturation)] - [.0031 (P_{vO_2} Hb (1.30) (venous saturation)]]. Oxygen delivery was obtained by multiplying cardiac output by arterial oxygen content. (Error of determination ±21 ml/min).

Limb blood flow, an indication of peripheral perfusion, was obtained by the method of English *et al.*[9] using an impedance plethysmograph. The impedance of a segment of the lower extremity provides a measure of total limb volume.[5,6,23] The change in volume after sudden venous occlusion by a rapid-inflating thigh pressure cuff is proportional to blood flow.

Limb vascular resistance was determined by dividing mean aortic pressure by limb blood flow. Peripheral vascular resistance was determined by dividing mean aortic pressure by cardiac output.

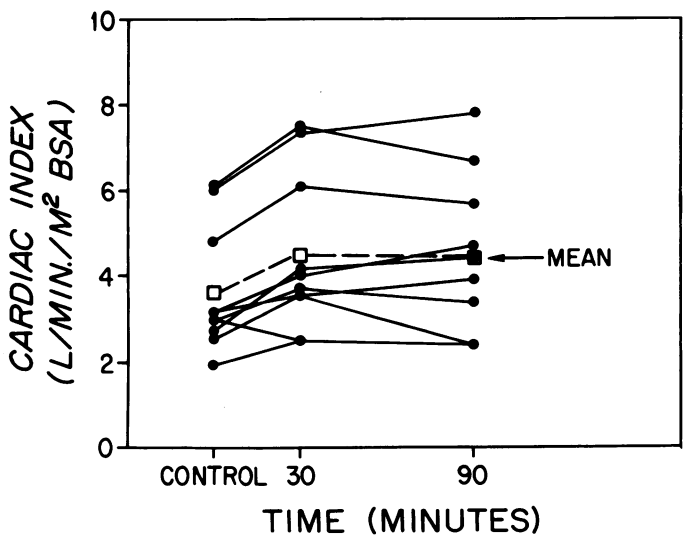

FIG. 1. Cardiac Index in L/min/m² BSA at baseline, 30 and 90 minutes after injection of methylprednisolone sodium succinate. The increase after injection was significant.

Lactate levels were determined by enzymatic reaction using a glycine buffer, lactic dehydrogenase suspension and 8% perchloric acid and spectrometer determination.*

Control measurements were made of arterial, pulmonary artery and pulmonary wedge pressures, hemoglobin concentration, cardiac index and limb blood flow. Both arterial and mixed venous bloods were analyzed for pH, P_{O_2}, and P_{CO_2} and lactate concentrations. From the time of baseline measurements and for the next ninety minutes no blood nor medications were administered. No alterations were made in the respirator settings. Following completion of the collection of the control samples, methylprednisolone sodium succinate† (30 mg/kg of body weight) was injected as a bolus into the proximal lumen of the Swan Ganz catheter. Thirty and 90 minutes after injection all of the above measurements were repeated. In four patients arterial blood pressure was recorded continuously for the entire ninety minutes.

Informed consent for the above procedures was obtained from the patient's legal guardian after the nature, purpose and risks of all procedures to be performed were explained according to the recommendations in the Declaration of Helsinki.

All statistics employ Student's T test for paired variance unless otherwise stated. All comparisons are referenced to baseline values.

Results

The ten patients studied included seven males and three females with ages ranging 19–81 years (Table 1). Eight of the ten patients developed the adult respiratory distress syndrome as evidenced by characteristic chest X-Ray changes and elevated levels of pulmonary physiologic shunting at some time early in their hospital course.

*Sigma Chemical Company, No. 826-UV, St. Louis, Missouri.
†Upjohn, Kalamazoo, Michigan.

TABLE 2. *Cardiac Dynamics, Physiologic Shunt Through Lungs, Oxygen Delivery and Oxygen Consumption in Ten Patients Receiving Methylprednisolone.*

	Cardiac Index (L/min/m² BSA)			Pulse Rate (beats/min)			Physiologic Shunt %			Oxygen Delivery (ml/min)			Oxygen Consumption (ml/min/m² BSA)		
Patient	Base-line	30 Min	90 Min	Base-line	30 Min	90 Min	Base-line	30 Min	90 Min	Base-line	30 Min	90 Min	Base-line	30 Min	90 Min
1	6.0	7.5	6.7	144	132	132	7.1	21	18	1948	2301	2023	202	192	185
2	3.2	4.0	4.7	90	90	96	10	12	18	774	941	1073	122	151	147
3	4.8	6.1	5.7	114	108	108	13	16	17	1327	1607	1499	168	157	154
4	2.7	4.2	4.4	102	102	108	12	22	21	682	1048	1074	120	152	179
5	2.6	3.6	2.5	60	63	60	10	24	20	722	889	686	85	96	86
6	3.2	3.6	3.9	102	96	90	14	21	21	924	989	1096	166	156	164
7	6.0	7.4	7.8	108	120	108	15	14	13	887	1057	1133	149	129	168
8	2.5	2.6	2.5	96	96	96	18	20	25	637	636	627	110	110	91
9	2.0	2.6	2.5	69	67	66	32	39	36	594	772	699	85	95	105
10	3.0	3.7	3.4	84	84	84	43	48	45	752	905	832	119	131	132
Mean	3.6	4.5	4.4	97	96	95	/7.4	23.7	23.4	925	1114	1074	133	137	141
S.E.	±0.5	±0.6	±0.6	±7.5	±6.8	±6.7	±3.6	±3.6	±3.1	±131	±154	±135	±12	±9.7	±11
		P<.001	P<.01		P-NS	P-NS		P<.01	P<.01		P<.01	P<.01		P-NS	P-NS

Cardiac Index

The average presteroid cardiac index was 3.6± 0.5 l/min/m² BSA (Table 2, Fig. 1). Thirty minutes after the administration of methylprednisolone sodium succinate the cardiac index increased in all ten patients to an average of 4.5± 0.6 l/min/m² BSA (P <.001). At 90 minutes the cardiac index was still elevated over baseline values in eight of the ten patients. The mean cardiac index at ninety minutes was 4.4± 0.6 l/min/m² BSA (P<.01). Thus, the rise in the cardiac index associated with the injection of methylprednisolone sodium succinate was significant.

Pressure Measurements and Pulse Rate

Pulmonary wedge pressure, a reflection of left atrial pressure, remained within 2 mm Hg of control over the ninety minute study period in five of the nine patients in whom it was measured (Table 1). Changes that did occur in the mean pulmonary wedge pressure were not statistically significant. In both patients in whom wedge pressure rose, the cardiac index was higher than baseline values. However, in two patients in whom the wedge pressure fell, the cardiac index did not fall, but rose also.

Average mean radial artery pressure was initially 98± 6.3 mm Hg (Table 1). Thirty minutes after methylprednisolone sodium succinate, it fell to a mean of 92.2± 6.0 mm Hg (P <.05). Although at ninety minutes the mean was 90.7± 7.1 mm Hg, this was not significantly below control because of the wide variability between patients.

Among four patients in whom arterial pressure was continuously recorded following methylprednisolone sodium succinate administration, an abrupt drop in blood pressure occurred in three patients from a mean of 95 mm Hg to a mean of 64.6 mm Hg within four minutes of the injection (Table 1). The period of hypotension was brief and all values approached baseline by thirty minutes after injection. The hypotension was not treated with any additional medication or intravenous fluid administration.

There was no significant change in pulse rate following injection (Table 2).

Hemoglobin Concentration and Arterial Blood Gases

Hemoglobin levels did not change during the period of study (Table 3). Inspired oxygen concentrations for the ten patients ranged from 20% to 80%. Five patients received positive end-expiratory pressure ventilation which was not changed throughout the period of study. The range of end-expiratory pressure was 5 cm H_2O to 20 cm H_2O. Mean arterial pH remained virtually constant. Arterial P_{O_2} decreased in nine of ten patients after injection of methylprednisolone sodium succinate. The drop to a mean arterial P_{O_2} of 91± 9 mm Hg at ninety minutes was significant (P <

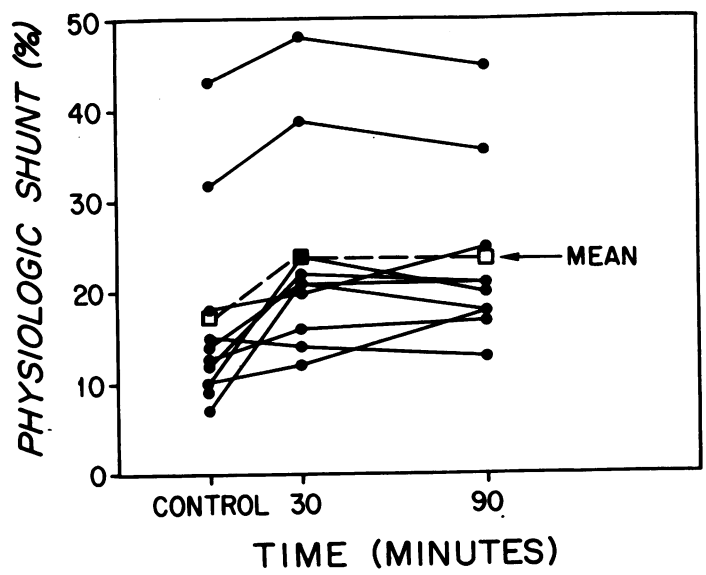

FIG. 2. Physiologic shunt through the lung at baseline, 30 and 90 minutes after injection of methylprednisolone sodium succinate. The increase after injection was significant.

TABLE 3. *Blood Gases, Inspired Oxygen Concentration and Hemoglobin in Ten Patients ReceivingMethylprednisolone*

	Systemic Arterial Blood Gases												
	Baseline			30 Min			90 Min						
Patient	pH	P_{O_2} mm Hg	P_{CO_2} mm Hg	pH	P_{O_2} mm Hg	P_{CO_2} mm Hg	pH	P_{O_2} mm Hg	P_{CO_2} mm Hg	Inspired Oxygen Fraction	Hemoglobin gm % Baseline	30 Min	90 Min
1	7.40	110	32.6	7.40	127	42.6	7.41	132	42.1	.40	11.3	10.5	10.2
2	7.41	125	35.4	7.41	109	33.9	7.38	94	43.0	.30	10.1	9.8	9.7
3	7.42	91	32.4	7.40	92	36.6	7.41	89	31.1	.20	10.7	10.3	10.4
4	7.50	123	34.0	7.51	84	32.1	7.46	82	31.8	.40	11.3	11 3	11.3
5	7.52	161	31 5	7.50	91	33.8	7.46	96	34.8	.40	10.5	9.6	10.5
6	7.41	118	28.7	7.41	94	29	7.43	95	34.1	.50	10.2	10.2	10.2
7	7.36	122	37.4	7.42	120	35.1	7.38	126	37.5	.40	10.6	10.2	10.5
8	7.49	110	31.8	7.49	94	29.9	7.49	78	36.7	.50	9.2	9.1	9.3
9	7.53	87	34 7	7.47	69	38.3	7.47	67	34.4	.80	11.0	11.8	11 5
10	7.44	54	34 6	7.41	52	36.8	7.44	51	35.7	.70	10.8	10.9	10.7
Mean	7.45	110	33.3	7.44	93.2	34.8	7.43	91.0	36.1		10.6	10.4	10.4
S.E.	±.02	±9.0	±.8	±.01	±7.1	±1.3	±.01	±7.7	±1.2		±.2	±.2	±.2
				P -NS	P<.05	P<.05	P -NS	P .05	P<.05			P -NS	P -NS

.05). Despite fixed respirator settings, arterial P_{CO_2} increased significantly from 33.3± 0.8 mm Hg to 36.1± 1.2 mm Hg at ninety minutes (P <.05).

Oxygen Delivery, Oxygen Consumption and Physiologic Shunt

Oxygen delivery increased in nine of ten patients following methylprednisolone sodium succinate injection (Table 2). Baseline oxygen delivery averaged 925± 131 ml/min. The mean at 30 minutes after injection had increased to 1,114± 154 ml/min (P<.01), and after 90 minutes the mean was 1,074± 135 ml/min (P<.01). Thus, the rise in oxygen delivery after steroid injection was statistically significant.

Control oxygen consumption averaged 133± 12 ml/min/m²BSA. Thirty minutes after methylprednisolone sodium succinate injection oxygen consumption was virtually unchanged from presteroid levels. No significant change was seen ninety minutes after injection (Table 2).

Baseline physiologic shunt of blood through the lung averaged 17.4± 3.6% (Table 2, Fig. 2). Thirty minutes after methylprednisolone sodium succinate physiologic shunt increased in nine of ten patients to an average of 23.7± 3.6% (P<.01). At 90 minutes the shunt remained significantly elevated over baseline at a mean of 23.4± 3.1% (P<.01). While physiologic shunt of blood through the lungs and cardiac index both increased significantly following the administration of methylprednisolone sodium succinate, the correlation between the two parameters was not significant (r= .28; P> .05 : Spearman rank correlation coefficient).

Pulmonary Vascular Resistance

Control pulmonary vascular resistance averaged 180 ±25 dyne-sec/cm⁵ (Table 4) (Normal 120 dyne-sec/cm⁵).

TABLE 4. *Pulmonary, Limb and Peripheral Vascular Resistances in Ten Patients Receiving Methylprednisolone*

	Pulmonary Vascular Resistance (dyne-sec/cm⁵)			Limb Flow (ml/min/gm)			Limb Vascular Resistance (dyne-sec/cm⁵)			Peripheral Vascular Resistance (dyne-sec/cm⁵)		
Patient	Baseline	30 Min	90 Min	Baseline	30 Min	90 Min	Baseline	30 Min	90 Min	Baseline	30 Min	90 Min
1	116	67	63	4.44	2.62	3.68	.238	.419	.298	1499	1242	1378
2	250	152	160	2.61	3.39	2.45	.575	.432	.534	2434	1987	1538
3	62	62	46	5.05	2.90	2.36	.332	.509	.607	1807	1290	1479
4	262	143	150	2.50	1.71	1.41	.700	.845	1.050	4015	2141	2080
5	84	84	—	2.75	4.01	2.92	.470	.306	.467	3150	2141	3437
6	125	137	134	2.84	3.35	3.74	2.160	1.780	1.600	1857	1606	1482
7	215	185	144	0.52	0.86	0.93	2.370	1.25	1.000	1338	933	772
8	195	144	211	3.35	2.55	3.90	.470	.622	.427	3276	3243	3469
9	287	241	236	1.12	0.63	1.07	1.140	1.743	.982	3533	2594	2281
10	202	154	165	1.63	1.75	1.90	.523	.467	.346	1686	1172	1181
Mean	180	137	145	2.68	2.38	2.44	.897	.832	.737	2460	1835	1910
S.E.	±25	±17	±20	±0.40	±0.40	±0.40	±.240	± 178	± 130	±303	±229	±290
		P<.01	P<.05		P -NS	P -NS		P -NS	P -NS		P<.01	P<.05

TABLE 5. *Lactate Concentrations and Arterial-Pulmonary Artery Lactate Differences in Ten Patients Receiving Methylprednisolone*

Patient	Arterial Lactate (mg %)			Pulmonary Artery Lactate (mg %)			Arterial-Pulmonary Artery Lactate Difference (mg %)		
	Baseline	30 Min	90 Min	Baseline	30 Min	90 Min	Baseline	30 Min	90 Min
1	11.2	16.1	15.3	10.8	12.8	9.20	0.4	3.3	6.1
2	26.2	4.5	19.9	18.7	1.8	13.2	7.5	2.7	6.7
3	16.5	22.3	16.8	17.4	18.8	13.9	−0.9	3.5	2.9
4	1.5	10.7	20.5	3.9	10.0	12.8	−2.4	0.7	7.7
5	18.0	24.2	10.9	23.0	18.1	9.4	−5.0	6.1	1.5
6	27.9	25.0	12.1	31.2	22.7	12.8	−3.3	2.3	−0.7
7	11.7	16.4	18.0	8.7	10.3	13.3	3.0	6.1	4.7
8	37.3	36.9	34.5	29.8	37.3	29.9	7.5	−0.4	4.6
9	20.6	10.6	24.7	14.7	8.2	17.4	5.9	2.4	7.3
10	35.0	18.4	33.6	34.1	15.7	28.2	0.9	2.7	5.4
Mean	20.6	18.5	20.6	19.2	15.6	16.0	1.9	2.9	4.6
S.E.	±3.5	±2.9	±2.6	±3.2	±3.1	±2.3	±1.4	±0.6	±0.8
		P-NS	P-NS		P-NS	P-NS		P<.001	P<.001

Thirty minutes after injection of methylprednisolone sodium succinate the pulmonary vascular resistance had decreased markedly from control levels to a mean of 137± 17 dyne-sec/cm^5 (P<.01). At the end of ninety minutes the pulmonary vascular resistance was decreased in seven of the nine patients in whom it was determined, yielding a mean of 145± 20 dyne-sec/cm^5 (P<.05).

Peripheral Vascular Resistance, Limb Blood Flow and Limb Vascular Resistance

Peripheral vascular resistance decreased significantly following the administration of methylprednisolone sodium succinate, falling from a mean control value of 2,460± 303 dyne-sec/cm^5 to 1,835± 229 dyne-sec/cm^5 following the injection (P<.01). It remained less than control at ninety minutes after injection for a mean of 1,910± 290 dyne-sec/cm^5 (P<.05) (Table 4).

Despite this significant decrease in peripheral vascular resistance the limb vascular resistance and limb blood flow did not change significantly at either thirty or at ninety minutes following injection (Table 4). In five of ten patients in whom limb vascular resistance did increase, the cardiac index was concomitantly increasing rather than decreasing.

Lactate Concentrations

Control arterial lactate levels averaged 20.6± 3.5 mg% (Table 5). Control pulmonary artery lactate averaged 19.2 ±3.2 mg%. In six patients arterial lactate exceeded pulmonary artery lactate by an average of 4.2 mg%. This positive arteriovenous difference in lactate concentrations during steady state conditions is an indication of production or washout of lactate from the lungs. However, in four patients the arteriovenous difference was negative by an average 2.9 mg% indicating possible uptake of lactate by the lung. This phenomenon of apparent lactate storage or consumption by the lung has not been previously reported in man, although a negative arteriovenous difference has been observed in dogs.[11] Thirty minutes following methylprednisolone sodium succinate injection the average systemic arterial lactate was 18.5 ±2.9 mg%, whereas the average pulmonary artery lactate was 15.6 ±3.1 mg%. In nine of ten patients at thirty minutes after injection the arteriovenous difference was positive an average of 2.9 ±0.6 mg% indicating that almost all patients were now washing out lactate from their lungs or their lungs were producing lactate. All patients with negative control arteriovenous differences became positive. By 90 minutes the apparent lactate washout or production had increased over baseline values even further for a mean arteriovenous difference of 4.6± 0.8 mg% (P<.001).

Survival

Seven patients survived and three patients died (Table 1). Only the physiologic shunt of blood through the lung and arterial lactate levels appeared to be of statistically significant value in predicting survival (P <.05). Physiologic shunts were highest in the three patients who died. They had an average presteroid shunt of 31% (range 18 - 43). Average baseline shunts of the survivors were 11.6% (range 7.1 - 15%). After methylprednisolone sodium succinate the shunts of most of the patients increased, including those of survivors as well as those who died.

The average presteroid arterial lactate concentrations for the patients who died was 31 mg% (range 20.6 - 37.3 mg%) and in the survivors the average was 16 mg% (range 1.5 - 27.9 mg%). In only one survivor was the lactate level greater than 20 mg% on more than one occasion whereas, among those who died, all three patients had lactate levels greater than 20 mg% at least twice during the study. Improvement in the cardiac index was not followed by a decrease in the blood lactate level up to ninety minutes after the injection of methylprednisolone sodium succinate.

Discussion

Significant effects of methylprednisolone observed in this group of patients included an increase in cardiac output and a fall in peripheral vascular resistance. In addition, there was a fall in pulmonary vascular resistance associated with an increased pulmonary physiologic shunt and a fall in arterial P_{O_2}.

The increased cardiac output observed in all of our patients thirty minutes after injection of steroid is consistent with the findings of a number of other investigators.[7,8,27,28,43,44] Wilson and Fisher,[44] who followed a test sequence comparable to that of the present study, found a 23% increase in cardiac output of 23 patients at 30 minutes after injection and a 19% increase at 60 minutes after injection of either hydrocortisone, methylprednisolone, or dexamethasone. However, at 90 minutes their patients' average cardiac output was lower than control. In the present study, cardiac output was lower than control in only one of ten patients at 90 minutes. The overall increase in cardiac output cannot be ascribed to an increased filling pressure of the left ventricle or an increased pulse rate, for neither pulmonary wedge pressure nor pulse rate changed significantly.[27] It is possible that methylprednisolone has a positive inotropic effect on the myocardium, although experimental support for such a hypothesis remains controversial.[13,32]

The increase in cardiac output led to an increase in oxygen delivery, but body metabolism did not change in response to the rise in delivery of oxygen since there was no increase in oxygen consumption. This is in contrast to the direct relationship found between oxygen consumption and oxygen delivery in patients receiving positive end-expiratory pressure ventilation.[22]

The above increase in cardiac output appears to be associated with increased perfusion of blood to areas other than peripheral skeletal musculature, for total peripheral resistance of these patients decreased significantly while limb vascular resistance remained unchanged. There is previous evidence that increased flow through the renal vasculature may occur following steroid administration.[34] The decreases in peripheral vascular resistance in the present study are consistent with those reported by other investigators both in experimental animals and in man.[7,8,27,28,43] However, our results differ from those of Wilson and Fisher[44] in that, following an initial decrease in peripheral vascular resistance in patients in septic or cardiogenic shock, they calculated an overall increase, rather than a sustained decrease, in peripheral vascular resistance at 90 minutes.

Resistance to blood flow through the pulmonary bed also decreased strikingly. At the same time, physiologic shunt of blood through the lungs increased. It would appear that methylprednisolone sodium succinate caused a redistribution of pulmonary blood flow by increasing perfusion to non or poorly ventilated portions of the lung. This redistribution is analogous to that found in the dog during unilateral atelectasis or hypoxia in association with systemic hypoxemia.[16,19] Thus, this drug appears to override the normal mechanism for controlling ventilation-perfusion ratios in poorly ventilated portions of the lung. The resistance changes in our patients are consistent with the drop in pulmonary vascular resistance observed by Rosenbaum *et al.*[27] in septic shock patients treated with steroids, but are not consistent with the rise in pulmonary vascular resistance they observed in cardiogenic shock patients treated with steroids.

There was a sudden drop in blood pressure in three of the four patients in whom continuous recordings were made during the injection of methylprednisolone sodium succinate. This phenomenon has been observed previously immediately after injection of steroids in both humans and dogs.[36,44] Thomas and Brockman[36] found an abrupt fall in cardiac output associated with a drop in blood pressure both of which returned to baseline within ten minutes in eight of ten dogs. Their study indicates a possible hazard of administering very large dosages of corticosteroids in that in the remaining two dogs there was no recovery from the circulatory depression following steroid injection and death resulted within 15 minutes. In all three of our patients by 30 minutes the blood pressure approached control values. However, mean blood pressure of the patients in this study remained significantly decreased at 30 minutes following injection of methylprednisolone sodium succinate. This is in contrast to the findings of several other investigators who report no significant change in blood pressure after steroid injection.[7,26,28,34]

Lactate is the final product of the metabolism of glucose in an anerobic environment. Lactate can be converted to pyruvate only in the presence of molecular oxygen in order to maintain a normal DPNH + H: DPN ratio.[3]

$$\text{Pyruvate} + \text{DPNH} + \text{H} \overset{\text{lactic dehydrogenase}}{\rightleftarrows} \text{Lactate} + \text{DPN}$$

Pyruvate may then enter into the Kreb's cycle to potentiate the breakdown of glucose into water, carbon dioxide, and energy. Net production of lactate by an organ has been interpreted to represent anerobic metabolism during periods of cellular hypoxia.

Within the literature there appears to be a controversy concerning the ability of pulmonary tissue to produce lactate. On the one hand there is evidence that during hypoxia "excess lactate" is produced which corresponds closely to the magnitude of the hypoxia.[14] Several investigators report positive arteriovenous differences in lactate concentrations across the pulmonary bed in patients with severe pulmonary disease and suggest that the lungs were adding lactate to the arterial blood.[25,33] By following glucose metabolism it has been found that approximately 30% of

this sugar was converted into lactic acid within the lung.[10,40,46] On the other hand some investigators could find no difference in lactate concentrations across the lung bed.[12,18] The present opinion is that lactate is probably produced by the lung and that this production may even occur in states other than those of hypoxia.[38,39] Furthermore, it is also believed that the lungs do not have appropriate enzymes to allow utilization of lactate.[37] Lactate levels have been found to be elevated in periods of systemic shock, being somewhat higher in hemorrhagic shock than in septic shock.[1] Steroids are reported to decrease systemic lactic acid levels several days after injection.[7,8,27,29–31] The steroids appear to have a gluconeogenic effect.[21] This decrease of lactate toward normal levels has been attributed to an initial rise associated with a washout of lactate from previously poorly perfused organs, followed by a fall as lactate production diminishes. In contrast, in this present study there was no significant reduction in lactate levels. However, there appeared to be a marked redistribution of lactate when arteriovenous differences were determined. Previously unreported in man is the finding that in at least three patients there were differences between pulmonary artery lactate and systemic arterial lactate where the former were the higher of the two values. This would indicate that as blood crossed the pulmonary vascular bed some lactate entered the lung. After methylprednisolone sodium succinate, lactate levels of all arterial samples equalled or exceeded those of pulmonary artery samples, indicating that in response to treatment, either a washout or a production of lactate from the lung occurred. A washout from the lung might occur with a redistribution of blood flow to the lung in association with the observed increase in shunt and decrease in pulmonary vascular resistance. The increase in physiologic shunting of blood through the lung, an apparently undesirable effect in patients already suffering from compromised ventilation may, in conjunction with the decrease in pulmonary vascular resistance, indicate improved perfusion of non- or poorly ventilated portions of the lung and be beneficial in the long term treatment of their adult respiratory distress syndrome.

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