Cardiovascular response to severe head injury

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The cardiovascular, pulmonary, and metabolic responses to severe head injury were studied clinically in the acute phase after severe head injury with the object of determining if a common response was present and, if so, its significance in the management of the patients' intracranial and systemic physiological states. Cardiac output, pulmonary capillary wedge pressure, arterial blood pressure, arterial and mixed venous blood gases, and arterial and mixed venous epinephrine (E) and norepinephrine (NE) levels were measured serially in 15 patients during the first 3 days after injury. A hyperdynamic state was found, characterized by increased cardiac output, cardiac work, moderate hypertension, tachycardia, decreased or normal systemic and pulmonary vascular resistance, increased pulmonary shunting, and increased oxygen delivery and utilization. Arterial E and NE levels correlated well with the cardiac output, cardiac work, blood pressure, heart rate, oxygen delivery, and oxygen utilization but not with vascular resistance or pulmonary shunt. The magnitude of the hyperdynamic state did not correlate with intracranial pressure, Glasgow Coma Scale score, or computerized tomography findings. It is concluded that a hyperdynamic cardiovascular state occurs after severe head injury, and that it is mediated in part by sympathetic nervous activity. The significance of this state for systemic management of patients with head injury is discussed.

KEY WORDS • head injury • cardiac output • blood pressure • vascular resistance • epinephrine • norepinephrine • cardiovascular system

CARDIOVASCULAR abnormalities in severe head injury have long been recognized. Elevations of blood pressure (BP) over 160 mm Hg have been found in one-fourth of patients with severe head injury, and elevation of pulse greater than 120 beats/min and tachypnea have been found in one-third.8 The mortality rate in patients with severe head injury increases proportionally with the age of the patient. Patients over 50 years of age may die of myocardial infarction after severe injury without elevation of intracranial pressure (ICP). In an autopsy study of 50 patients who died of severe head injury, 50% of the patients had subendocardial hemorrhage.5 Similar cardiac pathology can be produced in animals by infusion of epinephrine (E) or norepinephrine (NE).18 In a study of 48 head-injured patients with Glasgow Coma Score (GCS) scores of 4 to 15, venous NE levels were elevated in those with low GCS scores and correlated with the mean arterial pressure (MAP), heart rate (HR), and GCS scores in those without multiple trauma.6 This finding of a hyperadrenergic state characterized by moderate elevation of BP and cardiac index with decreased systemic vascular resistance (SVR). Others have documented decreased cardiac output and increased vascular resistance.3,4,17 However, many of the findings may have been influenced by hypovolemia and the inclusion in the series of neurologically moribund patients.3,4,17

The recognition in head-injured patients of a hyperdynamic cardiovascular response could have important implications for management of cerebral blood flow and fluid and electrolyte balance. For these reasons, plasma E and NE values and the cardiovascular state have been studied in detail during the first 3 days after injury in 15 patients with severe head injury so as to define the cardiovascular response to severe head injury.

Clinical Material and Methods

Patient Population

The patients studied came from a group of 115 patients with severe penetrating and nonpenetrating head injury who were admitted to the Neurosurgery
Definitions of Abbreviations

\( \text{avDO}_2 \) = arteriovenous oxygen difference  
BP = blood pressure  
CaO\(_2\) = arterial oxygen content  
CBF = cerebral blood flow  
CI = cardiac index  
CVP = central venous pressure  
CW = cardiac work  
E = epinephrine  
HR = heart rate  
ICP = intracranial pressure  
MAP = mean arterial pressure  
NE = norepinephrine  
O\(_2\)Av = oxygen availability  
O\(_2\)ER = oxygen extraction  
PAP = pulmonary artery pressure  
PCWP = pulmonary capillary wedge pressure  
PVR = pulmonary vascular resistance  
QS/QT = pulmonary venous admixture  
SI = stroke index  
SVR = systemic vascular resistance  
VO\(_2\) = oxygen consumption  
VSW = ventricular stroke work

Service at Ben Taub General Hospital from June 1, 1981, to June 1, 1982. The GCS scores of these patients were less than 8. Seventy-nine of these patients had closed head injuries and 36 sustained gunshot wounds (GSW). The mortality rate of the 79 patients with closed injuries was 40%, and 29% of these patients died within the first 48 hours. The mortality rate of patients with GSW was 94%; 80% of this group died within 48 hours. Of the 41 patients with closed injuries and the seven patients with penetrating injuries who survived the first 48 hours, 15 patients (31%) who had no major systemic injuries were selected randomly for detailed cardiovascular study. Tables 1 and 2 give the demographic characteristics, primary diagnosis, GCS scores, and outcome at 3 months after injury of the patients studied.

**Patient Management**

Mean time from injury to neurosurgical evaluation was 2 hours. Patients were intubated upon admission to the emergency department and treated with volume ventilation and supplemental oxygen. All patients underwent computerized tomography (CT) scanning within 45 minutes of admission. Patients with intracranial hematomas underwent craniotomy and removal of the hematoma. Those with GSW had surgical debridement and ICP monitoring. Mannitol (1 gm/kg), dexamethasone (4 mg), and a loading dose of phenytoin (18 mg/kg) were given intravenously. Arterial \( pO_2 \) was maintained at 100 mm Hg or greater by supplemental oxygen and volume ventilation, and \( PaCO_2 \) was maintained between 27 and 30 mm Hg. Morphine and pancuronium bromide were used when necessary to control ventilation. All patients had a Swan-Ganz catheter, a subarachnoid bolt or ventriculostomy tube, and a radial or femoral arterial catheter placed within a few hours after admission. All patients received the following medications intravenously during the first 7 days: phenytoin 100 mg/6 hrs; dexamethasone 4 mg/6 hrs; and cimetidine 300 mg/6 hrs. For systolic blood pressure sustained at over 160 mm Hg, either hydralazine or propranolol was administered. Spontaneous posturing was blocked by morphine or pancuronium bromide.

Elevated ICP was treated first by hyperventilation to a \( PaCO_2 \) of 25 mm Hg and by optimal head positioning. If ICP was not controlled, patients were given 5 to 10 mg of morphine intravenously and pancuronium bromide. Ventricular drainage was also used. If hyperventilation, head elevation, morphine, paralysis, and ventricular drainage did not control ICP, mannitol was given intravenously in a dose of 0.25 gm/kg every 4

**TABLE 1**

Characteristics of patients studied

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Diagnosis</th>
<th>GCS Score*</th>
<th>Intracranial Pressure</th>
<th>Outcome†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Day 1</td>
<td>Day 7</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>16, M</td>
<td>epidural hematoma</td>
<td>4</td>
<td>4</td>
<td>normal</td>
</tr>
<tr>
<td>2</td>
<td>24, M</td>
<td>diffuse brain injury</td>
<td>4</td>
<td>4</td>
<td>normal</td>
</tr>
<tr>
<td>3</td>
<td>23, M</td>
<td>subdural hematoma</td>
<td>4</td>
<td>4</td>
<td>normal</td>
</tr>
<tr>
<td>4</td>
<td>21, M</td>
<td>diffuse brain injury</td>
<td>7</td>
<td>12</td>
<td>normal</td>
</tr>
<tr>
<td>5</td>
<td>21, M</td>
<td>subdural hematoma</td>
<td>7</td>
<td>11</td>
<td>normal</td>
</tr>
<tr>
<td>6</td>
<td>52, M</td>
<td>diffuse brain injury</td>
<td>6</td>
<td>6</td>
<td>normal</td>
</tr>
<tr>
<td>7</td>
<td>24, F</td>
<td>diffuse brain injury</td>
<td>4</td>
<td>6</td>
<td>normal</td>
</tr>
<tr>
<td>8</td>
<td>30, M</td>
<td>diffuse brain injury</td>
<td>4</td>
<td>6</td>
<td>normal</td>
</tr>
<tr>
<td>9</td>
<td>42, M</td>
<td>intracerebral hematoma</td>
<td>6</td>
<td>5</td>
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<td>10</td>
<td>31, M</td>
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<td>7</td>
<td>10</td>
<td>normal</td>
</tr>
<tr>
<td>11</td>
<td>26, M</td>
<td>diffuse brain injury</td>
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<td>6</td>
<td>elevated</td>
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<tr>
<td>12</td>
<td>40, M</td>
<td>epidural hematoma</td>
<td>5</td>
<td>3</td>
<td>elevated</td>
</tr>
<tr>
<td>13</td>
<td>22, M</td>
<td>epidural hematoma</td>
<td>6</td>
<td>10</td>
<td>normal</td>
</tr>
<tr>
<td>14</td>
<td>30, M</td>
<td>gunshot wound</td>
<td>7</td>
<td>10</td>
<td>normal</td>
</tr>
<tr>
<td>15</td>
<td>28, M</td>
<td>gunshot wound</td>
<td>7</td>
<td>6</td>
<td>normal</td>
</tr>
</tbody>
</table>

*GCS = Glasgow Coma Scale.
†Outcome classified according to the Glasgow Outcome Scale.
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hours. A major goal of therapy was to maintain the pulmonary capillary wedge pressure (PCWP) at greater than 8 mm Hg. Fluid that was excreted in the urine over the 4-hour interval after mannitol administration was replaced intravenously. Most patients were maintained at an intravenous fluid rate of 100 cc/hr.

Physiological Measurements

A total of 67 cardiovascular measurements were made one to three times daily during the first 3 days after injury. Sampling was begun within 24 hours of admission for all patients, but not within 12 hours of anesthetic administration or volume expansion. The thermodilution technique was used to measure cardiac output. Reported values are a mean of three determinations using 10 cc of iced saline. Plasma volume was measured by an isotope dilution technique using radiiodinated serum albumin. Mean PCWP was 9.2 ± 5.6 mm Hg during sampling, and plasma volume was normal or increased on each of the days of sampling for five patients. Based on PCWP, plasma volume studies, and serum sodium concentration, no patient was dehydrated. Sampling was done while patients were still and when they had not been turned, submitted to suctioning, or stimulated for at least 15 minutes. When necessary, morphine and, in one patient, pancuronium bromide were used to stop spontaneous movement. Mean temperature was 37.6°C and was elevated (higher than 38.3°C) during sampling on six occasions in three different patients. Acetaminophen was used in some patients and some were placed on cooling blankets. In no case was culture-proven infection present during the period of study. Some cardiovascular samples were taken during spontaneous posturing and after administration of antihypertensive drugs, but these data were analyzed separately. The following parameters were recorded at each sampling: MAP, pulmonary artery pressure (PAP), PCWP, HR, temperature, ICP, central venous pressure (CVP), mixed venous and arterial blood gases, epinephrine (E) and norepinephrine (NE) levels, and hemoglobin. Parameters calculated from these directly measured values were: arteriovenous oxygen differences (avDO₂), oxygen consumption (VO₂), and oxygen availability (O₂Av), cardiac index, stroke index, systemic vascular resistance (SVR), pulmonary vascular resistance (PVR), left and right cardiac work (CW), left and right ventricular stroke work (VSW), and pulmonary venous admixture (QS/QT). Standard 12-lead electrocardiograms (EKG's) were recorded daily for the first 3 days after injury.

Arterial and mixed venous E and NE levels were measured in plasma taken from the arterial catheter and the Swan-Ganz catheter just prior to each cardiovascular sampling. When the first 35 samples were analyzed, mixed venous E and NE levels were found to correlate with cardiovascular parameters much less closely than did arterial values, and only arterial E and NE values were analyzed thereafter. Samples of blood for E and NE analysis were collected in a chilled solu-

<table>
<thead>
<tr>
<th>Parameters</th>
<th>No. of Cases</th>
</tr>
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<tbody>
<tr>
<td>sex</td>
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<tr>
<td>male</td>
<td>14</td>
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<tr>
<td>female</td>
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</tr>
<tr>
<td>age (yrs)</td>
<td></td>
</tr>
<tr>
<td>15–24</td>
<td>7</td>
</tr>
<tr>
<td>25–34</td>
<td>5</td>
</tr>
<tr>
<td>35–44</td>
<td>3</td>
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<td></td>
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<tr>
<td>diffuse brain injury</td>
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</tr>
<tr>
<td>epidural hematoma</td>
<td>3</td>
</tr>
<tr>
<td>intracerebral hematoma</td>
<td>2</td>
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<tr>
<td>subdural hematoma</td>
<td>2</td>
</tr>
<tr>
<td>gunshot wound</td>
<td>2</td>
</tr>
<tr>
<td>Glasgow Coma Scale scores: Day 1</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>4–5</td>
<td>6</td>
</tr>
<tr>
<td>6–7</td>
<td>9</td>
</tr>
<tr>
<td>Glasgow Coma Scale scores: Day 7</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>4–5</td>
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<td>6–7</td>
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<td>8–10</td>
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<td>11–15</td>
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<td>outcome*</td>
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<td>good recovery</td>
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<td>moderate disability</td>
<td>2</td>
</tr>
<tr>
<td>severe disability</td>
<td>1</td>
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<tr>
<td>persistent vegetative state</td>
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</tr>
<tr>
<td>dead</td>
<td>3</td>
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<tr>
<td>intracranial pressure (mm Hg)</td>
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<tr>
<td>&gt; 20</td>
<td>2</td>
</tr>
<tr>
<td>≤ 20</td>
<td>13</td>
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</table>

* Outcome classified according to the Glasgow Outcome Scale.
### Table 3

**Cardiovascular profile of head-injured patients**

<table>
<thead>
<tr>
<th>Parameters Measured</th>
<th>Formula</th>
<th>Normal Values</th>
<th>Mean Values For This Series*</th>
<th>Therapeutic Goals†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Volume-Related Variables</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean arterial pressure (MAP) (mm Hg)</td>
<td>MAP = diastolic + ( \frac{\text{systolic} - \text{diastolic}}{3} )</td>
<td>82–102</td>
<td>108 ± 11</td>
<td>&gt; 84</td>
</tr>
<tr>
<td>central venous pressure (CVP) (mm Hg)</td>
<td>direct measurement</td>
<td>0–8</td>
<td>7 ± 5</td>
<td>&gt; 2.5</td>
</tr>
<tr>
<td>blood volume (ml/sq m)</td>
<td>direct measurement</td>
<td>1780–2840</td>
<td>2634</td>
<td>500 ml more than normal</td>
</tr>
<tr>
<td>stroke volume indexed (SI) (ml/sq m)</td>
<td>SI = ( \frac{\text{CI}}{\text{HR}} )</td>
<td>35–45</td>
<td>47.2 ± 12.4</td>
<td>—</td>
</tr>
<tr>
<td>mean pulmonary arterial pressure (MPAP) (mm Hg)</td>
<td>MPAP = diastolic + ( \frac{\text{systolic} - \text{diastolic}}{3} )</td>
<td>15</td>
<td>15.7</td>
<td>&gt; 19</td>
</tr>
<tr>
<td>pulmonary capillary wedge pressure (PCWP) (mm Hg)</td>
<td>direct measurement</td>
<td>5–12</td>
<td>9 ± 6</td>
<td>&gt; 9.5</td>
</tr>
<tr>
<td><strong>Flow-Related Variables</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cardiac index (CI) (liter/min·sq m)</td>
<td>CI = ( \frac{\text{cardiac output}}{\text{body surface area (sq m)}} )</td>
<td>2.5–3.5</td>
<td>4.38 ± 1.46</td>
<td>&gt; 4.5</td>
</tr>
<tr>
<td>LVSW = SI × MAP × 0.0136</td>
<td></td>
<td>51–61</td>
<td>69 ± 21</td>
<td>&gt; 55</td>
</tr>
<tr>
<td>LVSW (g/min·sq m)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Bodily Response</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>systemic vascular resistance index (SVR) (dynes·sec·cm²·sq m)</td>
<td>SVR = ( \frac{79.96}{\text{CI}} ) (MAP - CVP)</td>
<td>1900–2200</td>
<td>2051 ± 621</td>
<td>&gt; 1446</td>
</tr>
<tr>
<td>pulmonary vascular resistance index (PVR) (dynes·sec·cm²·sq m)</td>
<td>PVR = ( \frac{79.92}{\text{CI}} ) (MPAP - PCWP)</td>
<td>150–250</td>
<td>116 ± 70.8</td>
<td>&lt; 226</td>
</tr>
<tr>
<td>heart rate (HR) (beats/min)</td>
<td>direct measurement</td>
<td>60–90</td>
<td>95 ± 25</td>
<td>&lt; 97</td>
</tr>
<tr>
<td><strong>Oxygen Transport-Related Variables</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>arterial oxygen content (CaO₂) (ml/100 ml)</td>
<td>CaO₂ = (Hgb × 1.39 × SaO₂) + (PaO₂ × 0.0031)</td>
<td>19–20</td>
<td>16.54 ± 2.18</td>
<td>—</td>
</tr>
<tr>
<td>oxygen consumption (VO₂) (ml/min·sq m)</td>
<td>VO₂ = CI × avDO₂ × 10</td>
<td>115–165</td>
<td>173 ± 71</td>
<td>&gt; 167</td>
</tr>
<tr>
<td>oxygen availability (O₂Av) (ml/min·sq m)</td>
<td>O₂Av = CaO₂ × 10 × CI</td>
<td>550–650</td>
<td>685 ± 232</td>
<td>&gt; 556</td>
</tr>
<tr>
<td>oxygen extraction (O₂ER) (%)</td>
<td>O₂ER = avDO₂/CaO₂</td>
<td>22–30</td>
<td>26 ± 8</td>
<td>&lt; 31</td>
</tr>
<tr>
<td>arteriovenous oxygen difference (avDO₂) (ml/dl)</td>
<td>avDO₂ = CaO₂ - CvO₂‡</td>
<td>4–6</td>
<td>4.18 ± 1.23</td>
<td>—</td>
</tr>
<tr>
<td><strong>Pulmonary</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent shunt (QS/QT)</td>
<td>QS/QT = ( \frac{\text{CeO}_2 - \text{CaO}_2}{\text{CeO}_2 - \text{CvO}_2} )</td>
<td>0–8%</td>
<td>13 ± 6</td>
<td>—</td>
</tr>
</tbody>
</table>

* Data are given for 67 samples obtained from the 15 head-injured patients in this series.
† Therapeutic goals for critically ill postoperative patients as proposed by Shoemaker, et al.21
‡ CeO₂ = (Hgb × 1.39) + (PaO₂ × 0.0031); CvO₂ = (Hgb × 1.39 × SvO₂) + (PvO₂ × 0.0031).

samples in the same patient. Table 3 gives the mean values for the patients studied as well as the range of normal and the derivation of each value. Also included for comparison are the monitoring goals recommended by Shoemaker21 for critically ill postoperative patients with systemic injury. The intensity of the hyperdynamic response varied among patients so that a metabolic profile could be established for each patient. Three patients were in a sustained hyperdynamic state requiring antihypertensive therapy. One of these patients had sustained a systolic BP of over 200 mm Hg. Only one patient had cardiac indices in the normal range and, because of elevated cardiac enzymes, he was suspected of having sustained a myocardial contusion. In those patients not in an extreme hyperdynamic state (sustained systolic BP greater than 160 mg Hg) values varied in intensity but were always above the normal range. In a larger series it will perhaps be possible to correlate neuropathology with the extent of the hyperdynamic response, but in this group no correlations were found between CT findings, GCS scores, and the extent of the response. Within the 3-day period studied, no consistent trend could be discerned for changes in the hyperdynamic response over time.

The abnormality most consistently found was moderate to severe hypertension with either normal or decreased SVR. The measured values were compared to those listed as normal in Table 3 and are expressed as means ± standard deviation. Cardiac index (4.38 ± 1.46 liter/min/sq m) was increased in 47 (72.3%) of the
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65 samples. Systemic vascular resistance index (2050 ± 621 dynes-sec/cm²-sq m) was decreased in 33 (51%) and normal in 14 (21.5%) of the 65 samples. One patient had a myocardial contusion and this accounted for most of the samples with decreased cardiac index and increased SVR. Heart rate (95 ± 25 beats/min) was increased in 31 (48%) of the 65 samples. Mean arterial pressure (108 ± 11 mm Hg) was increased in 47 (70%) of 67 samples. Increased MAP correlated with increased cardiac index (r = 0.49, p < 0.01 in 57 samples, Fig. 1), and with increased HR (r = 0.463, p < 0.01 in 57 samples), but not with SVR. The QS/QT (12.7% ± 5.6%) was increased in 58 (89%) of 65 samples and did not correlate with the cardiac index or with PVR.

Pulmonary vascular resistance (116 ± 70.8 dynes-sec/cm²-sq m) was decreased in 44 (66%) and normal in 19 (28%) of 67 samples. Oxygen consumption measured by arterial and venous blood gases was increased in 25 (50%) of 50 samples. Arteriovenous oxygen difference was normal in 18 (36%) and narrowed in 26 (52%) of 50 samples. Oxygen availability, which is an index of oxygen delivery to the tissues, was elevated in 29 (57%) of 51 samples. Plasma volume was measured a total of 15 times in five patients daily for the first 3 days after injury. The mean values for each day were greater than normal (Table 4). Urinary fluid losses were elevated. Mean daily urine output for the period of study was 3422 ± 1404 cc.

Cardiac output increased to provide the oxygen needed for elevated systemic metabolism. In several cases, the elevation of the cardiac index was in excess of tissue oxygen needs. Oxygen availability (O₂Av), as seen in Table 3, depends upon arterial oxygen content and the cardiac index. Mean hemoglobin was 12 ± 1 gm, with a lowest level of 9 gm. Mean oxygen saturation was 99% ± 1% and the lowest level was 95%. Arterial oxygen content (CaO₂) was, therefore, seldom decreased and relatively constant, so that the primary determinant of oxygen delivery was the cardiac index. In many samples, avDO₂ was normal, reflecting an appropriate cardiac index for tissue oxygen needs. In five samples from four patients, the cardiac index was low relative to tissue oxygen needs, causing a widened avDO₂. In 26 samples avDO₂ was narrowed, suggesting an elevation in cardiac index inappropriate to tissue oxygen needs.

Two patterns of hypertension (systolic BP greater than 160 mm Hg) were seen: sustained hypertension and labile hypertension. During posturing, spontaneous movement, or suctioning, patients usually became transiently hypertensive, sometimes to a marked degree. In some resting patients, BP would spontaneously vary without visible stimulation of the patient. Most patients demonstrated a marked cardiovascular lability which diminished with time and with neurological improvement. The cardiovascular response of one patient to spontaneous extensor posturing is shown in Fig. 2.

Three patients developed sustained hypertension requiring antihypertensive therapy. Data presented in this section contain only five data points from the patients with sustained hypertension, and the measurements...
were made prior to antihypertensive therapy or before barbiturate administration. The ICP was increased at the time of sampling in two of these three patients, and the rise in BP could be considered to be a Cushing response. The other patient (Case 1), who had markedly increased BP and arterial E levels but normal ICP, clinically had signs of a brain-stem injury. This patient exhibited an extreme hyperdynamic response (Table 5). The patient was a 16-year-old boy who was involved in a motor vehicle accident, sustaining an epidural hematoma. His GCS score was 4, and he had bilateral third nerve palsies. After evacuation of this hematoma, he was neurologically unchanged. The ICP was less than 10 mm Hg, but 24 hours after surgery his BP continuously rose to 199/107 mm Hg, and his HR was 146 beats/min, not modified by sedation or paralysis. Data from the 2nd day after injury are shown in Table 5. Cardiac index ranged from 6 to 8 liters/min/sq m (2 to 2.5 times normal) with widened avDO₂ and markedly increased VO₂. Electrocardiographic changes with ST elevations were noted. U-waves, peaked T-waves, inverted T-waves, and premature atrial contractions were found. Creatinine phosphokinase was increased, but isoenzyme analysis did not suggest myocardial damage.

Sixty-seven samples (n) of each cardiovascular parameter were plotted against either arterial E or NE values and 39 against arterial or mixed venous E or NE levels. Arterial NE correlated with HR (r = 0.5, n = 57, p < 0.01), MAP (r = 0.44, n = 58, p < 0.01), cardiac index (r = 0.41, n = 57, p < 0.01), VO₂ (r = 0.43, n = 49, p < 0.01), and left CW (r = 0.48, n = 57, p < 0.01). Arterial E correlated with HR (r = 0.44, n = 57, p < 0.01), MAP (r = 0.45, n = 58, p < 0.01), cardiac index (r = 0.45, n = 57, p < 0.01), O₂Av (r = 0.4, n = 50, p < 0.01), VO₂ (r = 0.45, n = 49, p < 0.01), and left CW (r = 0.53, n = 57, p < 0.01). Neither arterial E nor NE correlated with stroke index, SVR, PVR, left or right VSW, QS/QT, avDO₂, or oxygen extraction. The relationship of VO₂, left CW, cardiac index, and MAP to arterial E is shown in Fig. 3.

Thirty-nine samples of mixed venous E or NE correlated only with MAP, cardiac index, and left CW. Arterial E levels were on the average 2.6 times normal whereas the mean arterial NE levels were 2.0 times normal. Mixed venous E and NE samples were initially drawn from the right atrium or superior vena cava (22 samples). Because of the possibility of not obtaining truly mixed blood from both superior and inferior vena cavae, subsequent samples were drawn from the distal port of the Swan-Ganz catheter in the pulmonary artery. Regression analysis of 39 paired samples of arterial NE and venous NE obtained simultaneously from the pulmonary artery or the right atrium showed no significant differences. Epinephrine values were, however, significantly higher in arterial than in mixed venous blood, when compared by Student’s t-test.

**Discussion**

Sympathetic nervous hyperactivity as measured by plasma and urinary E and NE levels has been documented in head injury and in many other medical conditions. An essential question is whether the hyperdynamic response to head injury is adaptive or maladaptive. A hypermetabolic response is not unique to head injury, and data suggest that it may be an adaptive response in major systemic trauma. Shoemaker, et al., found that in post-resuscitated shock patients, increased cardiac index, increased O₂Av, and increased VO₂ were strongly predictive of survival, whereas failure to achieve these goals was strongly predictive of death. The therapeutic monitoring goals which Shoemaker has found optimal for survival in post-resuscitated shock patients are similar to the cardiovascular parameters found in head-injured patients.
Cardiovascular response to severe head injury

(Table 3). Traumatized patients without shock have shown elevated cardiac index and elevated VO₂. In the initial stages of sepsis, there are increased tissue oxygen needs and a cardiovascular profile similar to that found in head injury and trauma. These changes have been associated with elevated urinary E and NE levels. Burned patients have been found to have a hypermetabolic response characterized by markedly increased VO₂ with elevated levels of E and NE in plasma. Failure of the cardiovascular system to meet increased tissue oxygen needs in burns, sepsis, and trauma, whether due to inadequate cardiac function, anemia, or hypoxemia, is fatal. In these conditions, the hyperdynamic response appears to be a neurally mediated response to injury which is adaptive in providing for increased oxygen and metabolic needs. The cardiovascular response to head injury may also be adaptive unless it is extreme.

In some head-injured patients, the intensity of the hyperdynamic state exceeds levels reported in burns, sepsis, or trauma, and may be maladaptive. There is evidence that the hyperdynamic response, if extreme, may damage the myocardium. The finding of subendocardial hemorrhages in 50% of autopsied patients with severe head injury suggests myocardial damage from the hyperdynamic state. Myocardial infarction may be the cause of death in older patients with head injury. The EKG abnormalities of head-injured patients have been extensively documented and are probably the result of sympathetic nervous hyperactivity. Fatal arrhythmias have been reported in otherwise healthy head-injured patients. In patients who have sustained hypertension or who frequently posture, cardiac work may be markedly elevated for long periods of time. The amount of cardiovascular stress in these patients may reach that of an exercising adult, with cardiac index elevated to twice normal for sustained periods. Treatment with beta-adrenergic blocking agents may be necessary to prevent myocardial damage.

Recognition of the hyperdynamic response may allow more physiological management of hypertension and fluid status. Langfitt, et al., found that elevation of MAP by NE infusion after experimental head injury in baboons increased cerebral blood flow and also ICP. Because in some patients arterial hypertension may result in increased cerebral blood flow, the recommendation has been made that elevated BP in head-injured patients be controlled below 160 mm Hg systolic. The drugs most often recommended for treatment of hypertension are vasodilators. However, these drugs may not be appropriate for patients who are already vasodilated and are hypertensive from elevated cardiac output, with increased levels of plasma E and NE. Use of propranolol in several patients in this study normalized the cardiovascular abnormalities, whereas hydralazine worsened them. This subject is discussed in a companion study.

The large urine output frequently seen in patients with head injury, and documented in this group of patients, may be related to elevated renal blood flow since blood flow is systemically elevated. An increased rate of maintenance fluid replacement is required to prevent severe dehydration from large urinary fluid losses. Because of systemic vasodilation, head-injured patients are relatively hypervolemic if PCWP is kept in

![Graphs showing relationship to arterial epinephrine of oxygen consumption, left cardiac work, cardiac index, and mean arterial pressure.](J Neurosurg. Volume 59 / September, 1983)
a normal range. Fluid restriction may result in very rapid and severe dehydration. In animals, hypovolemia may decrease cardiac output without a fall in arterial pressure by increasing SVR through reflex sympathetic action. To the extent that hypovolemia impairs oxygen delivery to tissues, it may be deleterious systemically and to the injured brain in brain-injured patients. It is recommended, therefore, in order to avoid decreased oxygen delivery due to a fall in cardiac output, that fluid losses from osmotic diuretics be replaced, that maintenance fluid administration be kept at a normal or elevated level, and that a Swan-Ganz catheter be used for monitoring cardiovascular parameters.

Elevated plasma epinephrine was associated with increased oxygen consumption as well as increased cardiac output. In some cases, even though cardiac output was markedly elevated, VO₂ was elevated beyond the ability of the heart to provide oxygenated blood, and oxygen extraction was increased to compensate. The metabolic profile of Case 1 (Table 5) illustrates this situation. However, a widened avDO₂ was found in only a few samples. In 90% of samples, the cardiac index was sufficient or in excess of tissue oxygen needs. Since oxygen consumption was elevated in 50% of samples, appropriate treatment of hypertension would require a decrease in tissue oxygen utilization as well as cardiac output to avoid inadequate oxygen delivery. Since both responses are related to sympathetic nervous hyperactivity, beta-adrenergic blocking agents should decrease cardiac work and tissue oxygen needs as well.

Further improvements in the management of brain injury depend upon the establishment of the relationship between the hyperdynamic state and cerebral blood flow and cerebral metabolism.

References


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