AD-A223 233

Oxygen Delivery and Demand in Conscious Pigs Subjected to Fixed-Volume Hemorrhage and Resuscitated With 7.5% NaCl in 6% Dextran

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A conscious porcine model was used to investigate the adequacy of O₂ delivery relative to O₂ demand, initially during a fixed-volume hemorrhage (37.5 ml/kg over 1 hr) and subsequently after resuscitation with 7.5% NaCl/6% Dextran 70 (4 ml/kg). Hemorrhage produced a small increase in O₂ consumption, severe lactacidemia, and a doubling of apparent O₂ demand. These effects were attributable to a behavioral compensation (periodic bouts of muscle activity) which presumably served to improve venous return. Despite enhanced ventilatory function, arterial O₂ delivery was markedly reduced by hemorrhage, an effect that was due entirely to decrements in cardiac output and hemoglobin level. The disparity between O₂ delivery and O₂ demand was lessened following resuscitation with 7.5% NaCl/6% Dextran 70, primarily by suppression of demand and secondarily by an augmentation of delivery.

Key words: swine, hypertonic saline/dextran, O₂ transport, O₂ consumption, O₂ debt, lactacidemia, ventilation, cardiac output

INTRODUCTION

The level of blood loss experienced by combat casualties and civilian accident victims is frequently so severe that death ensues in the absence of prompt and

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effective therapy. In most instances, this therapy is directed at preventing further
blood loss and implementing resuscitation procedures that reverse the life-threatening
dysfunctions associated with hemorrhagic hypotension. Efforts to improve therapy,
and thereby increase the survival incidence of hemorrhage victims, have been
commonly based on experimental data, but oftentimes this information is misleading
because inappropriate animal models have been used to study the functional effects of
hemorrhage. Ideally, an animal model should simulate the physiologic conditions
found in human hemorrhage victims, particularly when the research effort is directed
at the development of an improved resuscitation procedure. Ethical constraints, e.g.,
the extensive trauma that so often accompanies severe blood loss in humans, preclude
implementing an ideal model. At a minimum, however, the hemorrhage insult should
emulate the rate and magnitude of blood loss seen in humans after vascular rupture;
it should occur while the animal is in a conscious state to allow full and accurate
expression of the normal physiologic changes associated with blood loss; and, if
enhanced survival is an endpoint for evaluating efficacy of resuscitation, the
hemorrhage insult should be lethal if left untreated. We hope to demonstrate the
applicability of such a model in the present communication.

In several species, including pigs [1,2], sheep [3,4], and humans [5,6], small
volume resuscitation with hypertonic saline/dextran (7.5% NaCl in 6% Dextran 70)
effectively reverses many of the life-threatening dysfunctions associated with
hemorrhage. It also provides significant improvement in the survival of animals
subjected to lethal levels of blood loss [1,2]. The beneficial effects of hypertonic
saline/dextran include a return of cardiac output and arterial pressure to normal or
near normal values [1–4], an increase in blood flow to vital organs [7], and a
restoration of urine production [3]. These functional improvements are attributable, at
least in part, to fluid mobilization from the extra- to the intravascular compartment
with consequent increases in blood volume and venous return [1–4]. It is tacitly
assumed that the increases in cardiac output and tissue blood flow improve oxygen
delivery to previously ischemic tissues, thereby ameliorating the lethal effects of
hemorrhage. The validity of this assumption, however, can be questioned, at least
insomuch as conscious animals are concerned. Few data are available on the actual
levels of arterial oxygen transport or tissue oxygen demand of conscious animals
subjected to hemorrhage, and no one has investigated these variables following
resuscitation with hypertonic saline/dextran. The study reported here was directed at
these information deficits. It was a component of a much larger investigation which
compared the resuscitative effectiveness of 0.9% NaCl, 7.5% NaCl, 6% Dextran 70,
and 7.5% NaCl/6% Dextran 70 following administration to conscious chronically
instrumented pigs that had been subjected to a lethal fixed-volume hemorrhage [1].
The present study had two specific objectives. The first was to determine the effects
of this hemorrhagic insult on total body O₂ consumption, apparent O₂ demand and the
various functional components of O₂ delivery from ambient air to the body tissues.
The second objective was to determine, if possible, whether or not the resuscitative
effectiveness of hypertonic saline/dextran was attributable solely to an improvement
in O₂ delivery. Our data indicate that the lethality of the hemorrhage model is largely,
if not entirely, due to a disparity between O₂ delivery and O₂ demand. Our data also
indicate that the resuscitative effectiveness of hypertonic saline/dextran is attributable
primarily to a suppression of tissue O₂ demand and secondarily to an improvement of
O₂ delivery.
MATERIALS AND METHODS

Six immature (24.3 ± 1.11 kg, mean ± SEM) Yorkshire pigs were used to investigate the effects of hemorrhage and resuscitation with hypertonic saline/dextran. Eight pigs (23.6 ± 1.87 kg) resuscitated with an equivalent volume of 0.9% NaCl served as hemorrhage controls, and eight additional pigs (26.1 ± 0.66 kg) were used as untreated controls for another simultaneously conducted investigation [8] as well as the investigation reported here. Seven to 10 days before study the pigs were splenectomized, and were chronically instrumented with carotid and pulmonary artery catheters and an aortic sideport catheter [9], as described in detail elsewhere [1]. During this same time period, they were trained to accept a respiratory mask and physical restraint in a Pavlov sling [1]. On the day of study, after an overnight fast, each pig was brought into a quiet laboratory, placed in the Pavlov sling, and fitted with the respiratory mask to measure respiratory functions. The mask was connected to a Horizons System metabolic apparatus using a one-way Rudolph valve and 2.5 cm (O.D.) plastic tubing. The pulmonary and carotid artery catheters were connected to three-way stopcocks for blood sampling, and to pressure tubing and transducers for measurements of hemodynamic function reported in detail elsewhere [1]. The animal was allowed to rest quietly in the sling until O₂ consumption values were maintained at minimal levels for 30 to 60 min. Control measurements for all experimental variables were then made in triplicate at 10 min intervals. Immediately thereafter, the aortic sideport catheter was opened, and a fixed-volume (37.5 ml/kg) hemorrhage schedule was initiated. Over a subsequent 60 min period, blood was removed progressively on an exponential scale [10] such that successive 7.5 ml/kg increments had been withdrawn after 9, 19, 31.5, 44, and 60 min. At each of these time points all measurements were repeated. Immediately after hemorrhage, the animal received a 4 ml/kg mixture of 7.5% NaCl/6% Dextran 70, injected into the pulmonary artery over a 1-min time interval. Hemorrhage controls received 4.0 ml/kg of 0.9% NaCl. All measurements were again taken at 5, 15, 30, 60, 120, 180, and 240 min after the cessation of hemorrhage.

At each measurement point, a 30 ml blood sample was removed from the carotid artery and a 3 ml sample from the pulmonary artery; samples taken during the control and hemorrhage periods were included in hemorrhage volume. These samples were chilled in ice water and then partitioned for a variety of subsequent determinations. The latter included immediate measurement of O₂ content and hemoglobin concentration with an Instrumentation Laboratory Model 282 Cooximeter. Plasma lactate concentration was determined with a GEMSAEC autoanalyzer and Sigmasystem test kits. At all of the foregoing time points, expired ventilation was recorded BTPS, and O₂ consumption and CO₂ production STPD. On the basis of the foregoing measurements, cardiac output values were calculated by the Fick equation, and arterial oxygen delivery as the product of arterial O₂ content and cardiac output. Changes in plasma lactate concentration as a function of time were used to calculate apparent O₂ debt. In making these calculations it was assumed that 1 mol of O₂ was required to convert 2 mol of lactate to pyruvate [11]. It was also assumed that plasma lactate concentration reflected the average concentration in total body water; a value of 640 ml/kg, as determined by ³H₂O dilution [12], was chosen for the latter. The sum of O₂ consumption and O₂ debt was used to estimate apparent O₂ demand of the tissues. In addition, alveolar ventilation (Vₐ) values were calculated by the Bohr equation:
\[ V_A = \frac{(0.867) (VCO_2)}{P_aCO_2} \]

where 0.867 is a constant that converts VCO₂ from STPD to BTPS, assuming a normal porcine body temperature of 38.5°C. The shunt fraction of pulmonary blood flow (Qₕ) was calculated by a modification of the Fick equation:

\[ Qₕ = \frac{C_cO_2 - C_vO_2}{Q_T} \]

Here Qₜ is cardiac output, C_cO₂ is pulmonary end capillary O₂ content, C_aO₂ is arterial O₂ content, and C_vO₂ is mixed venous O₂ content. Temperature and Bohr factors appropriate for the oxyhemoglobin dissociation curve of porcine blood, as reported by Willford and Hill [13], were used in the calculation of C_cO₂ values. Finally, alveolar ventilation and cardiac output values were used to calculate ventilation-perfusion ratios, i.e., Vₐ/Qₜ.

Two factor (treatment, time) and single factor (time) analyses of variance were used as appropriate for within- and between-group comparisons. The single factor evaluation of pigs resuscitated with 7.5% NaCl/6% dextran was first applied to the hemorrhage period and then to the first hour of the recovery, i.e., before any of the animals had died. Changes were considered significant when \( P < 0.05 \). In addition, mean ± S.E.M. values were calculated for each time point during control, hemorrhage, and recovery periods. At 1 hr and thereafter during the recovery period, two mean values were calculated for the time point that preceded death of an animal: one mean included and the other excluded the nonsurviving animal. This double calculation was directed at minimizing data distortion that might result from changes in interanimal variance associated with a reduction in group size. Representative S.E.M. values are indicated in the figures that follow.

**RESULTS**

The responses of the control and experimental groups to hemorrhage alone were not significantly different. Resuscitation with 0.9% NaCl, however, was ineffective, and all of these controls died shortly after the resuscitation procedure was initiated [1]. Nonsurvival of these animals precluded statistical evaluation of their resuscitation data. Untreated control pigs showed only one significant functional change during a 4 hr period of continuous restraint; the respiratory exchange ratio decreased slightly (Table I). The functional data recorded in these animals were nearly identical to control (0 time) data recorded in animals subjected to hemorrhage.

Hemorrhage produced a small, progressive increase in O₂ consumption, the average values rising significantly from a control level of 6.9 ± 0.51 to 9.5 ± 0.73 ml/min/kg at the end of blood removal (Fig. 1A). This effect was associated with periodic bouts of muscle activity (leg movements and stretching). During recovery following resuscitation with hypertonic saline/dextran, O₂ consumption reverted rapidly (within 30 min) to control levels. Over the course of hemorrhage, the respiratory exchange ratio rose from 0.79 ± 0.036 to 1.06 ± 0.094, presumably as a consequence of hyperventilation.

Plasma lactate concentration (not shown), rose significantly during hemorrhage, from 0.6 ± 0.04 to 13.6 ± 1.03 mEq/L. When calculated in terms of O₂ equivalents,
<table>
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<th>Restraint time (min)</th>
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<td>30</td>
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<td>120</td>
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<td>O₂ Consump. (ml/min/kg)</td>
<td>6.7 ± 1.9</td>
<td>7.0 ± 1.5</td>
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<td>7.4 ± 2.3</td>
<td>6.4 ± 1.4</td>
<td>6.2 ± 1.0</td>
<td>8.0 ± 1.5</td>
<td>6.8 ± 1.4</td>
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<tr>
<td>Resp. exchange ratio*</td>
<td>0.79 ± 0.06</td>
<td>0.81 ± 0.03</td>
<td>0.78 ± 0.03</td>
<td>0.77 ± 0.05</td>
<td>0.78 ± 0.08</td>
<td>0.75 ± 0.08</td>
<td>0.72 ± 0.04</td>
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<tr>
<td>Expir. vent. (ml/min/kg)</td>
<td>195 ± 48</td>
<td>207 ± 24</td>
<td>266 ± 55</td>
<td>218 ± 63</td>
<td>207 ± 52</td>
<td>175 ± 38</td>
<td>217 ± 38</td>
<td>192 ± 42</td>
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<td>Resp. rate (br/min)</td>
<td>23 ± 3</td>
<td>22 ± 5</td>
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<td>Alv. vent. (ml/min/kg)</td>
<td>97 ± 22</td>
<td>100 ± 16</td>
<td>105 ± 31</td>
<td>97 ± 28</td>
<td>104 ± 31</td>
<td>79 ± 33</td>
<td>100 ± 24</td>
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<td>Card. output (ml/min/kg)</td>
<td>141 ± 36</td>
<td>150 ± 32</td>
<td>116 ± 42</td>
<td>137 ± 56</td>
<td>137 ± 45</td>
<td>117 ± 46</td>
<td>117 ± 46</td>
<td>138 ± 23</td>
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<tr>
<td>Vₐ/Qᵣ (%)</td>
<td>0.68 ± 0.11</td>
<td>0.69 ± 0.14</td>
<td>0.66 ± 0.15</td>
<td>0.72 ± 0.13</td>
<td>0.73 ± 0.18</td>
<td>0.67 ± 0.14</td>
<td>0.63 ± 0.13</td>
<td>0.67 ± 0.15</td>
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<td>Qₛ/Qᵣ (%)</td>
<td>3.8 ± 3.0</td>
<td>3.6 ± 3.0</td>
<td>5.4 ± 3.6</td>
<td>1.8 ± 1.1</td>
<td>4.1 ± 4.0</td>
<td>3.2 ± 2.3</td>
<td>6.3 ± 4.3</td>
<td>3.5 ± 2.4</td>
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<td>Hemoglobin (g/dl)</td>
<td>9.6 ± 0.9</td>
<td>9.1 ± 0.9</td>
<td>9.6 ± 0.8</td>
<td>9.8 ± 1.0</td>
<td>9.7 ± 1.1</td>
<td>9.6 ± 1.0</td>
<td>9.4 ± 0.9</td>
<td>9.9 ± 1.0</td>
</tr>
<tr>
<td>Art O₂ cont. (ml/dl)</td>
<td>12.9 ± 1.9</td>
<td>13.0 ± 2.3</td>
<td>13.0 ± 1.8</td>
<td>12.9 ± 1.7</td>
<td>12.7 ± 1.6</td>
<td>12.6 ± 1.6</td>
<td>12.1 ± 1.1</td>
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<tr>
<td>Ven. O₂ cont. (ml/dl)</td>
<td>7.8 ± 1.3</td>
<td>7.3 ± 1.4</td>
<td>6.8 ± 1.5</td>
<td>6.8 ± 1.0</td>
<td>6.9 ± 1.5</td>
<td>7.5 ± 1.2</td>
<td>6.7 ± 1.5</td>
<td>6.5 ± 1.5</td>
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<tr>
<td>Art. O₂ deliv. (ml/min/kg)</td>
<td>18.7 ± 4.7</td>
<td>20.0 ± 3.8</td>
<td>15.5 ± 4.8</td>
<td>18.6 ± 9.3</td>
<td>18.2 ± 6.5</td>
<td>15.7 ± 7.5</td>
<td>19.4 ± 8.4</td>
<td>17.7 ± 2.6</td>
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<tr>
<td>Plasma lact. (mEq/L)</td>
<td>0.60 ± 0.13</td>
<td>0.48 ± 0.19</td>
<td>0.51 ± 0.23</td>
<td>0.48 ± 0.22</td>
<td>0.45 ± 0.20</td>
<td>0.42 ± 0.18</td>
<td>0.46 ± 0.18</td>
<td>0.50 ± 0.17</td>
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†Indicated values represent the Mean ± S.D. of 8 pigs.
*Significant (P ≤ 0.05) change as a function of time.
Oxygen Delivery and Demand 211

this rise represented an absolute O$_2$ debt of approximately 100 ml/kg. When calculated as a function of time, the apparent O$_2$ debt thus rose progressively, to $8.25 \pm 0.87$ ml/min/kg at the end of hemorrhage (Fig. 1B). These changes led in turn to a significant increase in apparent tissue O$_2$ demand from a control level of $6.94 \pm 0.51$ to $15.82 \pm 2.36$ ml/min/kg (Fig. 1C). Resuscitation with hypertonic saline/dextran produced a significant reversion of O$_2$ consumption to control levels and a significant resolution of the increments in apparent O$_2$ debt and O$_2$ demand that accrued during hemorrhage.

The hemoglobin concentration of arterial blood decreased significantly during hemorrhage from $9.3 \pm 0.46$ to $6.6 \pm 0.37$ g/dl (Fig. 1D); it might be noted, incidentally, that the low control values for hemoglobin and related variables (e.g., O$_2$ content) reported here are typical of immature pigs [10]. Following administration of 7.5% NaCl/6% dextran, an abrupt further significant decrease to $5.3 \pm 0.32$ g/dl was observed at 5 min into the recovery period. Thereafter, hemoglobin concentration remained relatively stable.

Hypermetabolism during hemorrhage was supported by increased ventilation, the expired values rising significantly from $208 \pm 23.9$ to $506 \pm 61.3$ ml/min/kg (Fig. 2A). This response was accompanied by a significant rise in alveolar ventilation from $120 \pm 12.4$ to $214 \pm 32.2$ ml/min/kg (Fig. 2B). Hyperventilation was largely, if not entirely, attributable to a significant increase in respiratory rate, from $19 \pm 1.9$ to $37 \pm 4.2$ breaths/min (Fig. 2C). Thus, tidal volume (Fig. 2D) rose only slightly during hemorrhage from $10.6 \pm 0.77$ to $13.8 \pm 1.16$ ml/min/kg, a change that was not statistically significant. Expired ventilation and alveolar ventilation decreased gradually, but significantly, following resuscitation, and the values approached control levels at 4 hr into the recovery period.

The combined effects of an increase in alveolar ventilation and a decrease in cardiac output (see below) led to a marked increase in the ventilation:perfusion ratio ($V_A/Q_T$) from $0.68 \pm 0.048$ to $2.15 \pm 0.195$ (Fig. 2E). The decrease in cardiac output also caused a significant reduction in pulmonary shunt fraction ($Q_s/Q_T$) from $6.4 \pm 0.42$ to $1.4 \pm 0.28$ (Fig. 2F). Resuscitation with hypertonic saline/dextran produced an immediate and almost complete reversion of the $V_A/Q_T$ ratio toward control levels. The $Q_s/Q_T$ ratio, in contrast, was not altered significantly following resuscitation.

Hemorrhage also led to significant decrements in the O$_2$ content of arterial (from $11.7 \pm 0.64$ to $8.6 \pm 0.49$ ml/dl, Fig. 3A) and mixed venous (from $7.6 \pm 0.63$ to $0.97 \pm 0.20$ ml/dl, Fig. 3B) blood. The more pronounced change in mixed venous O$_2$ content resulted in a significant widening of the A-V difference, from $4.0 \pm 0.16$ to $7.7 \pm 0.41$ ml/dl (Fig. 3C). Resuscitation with hypertonic saline/dextran had a significant effect on all of these variables: at 5 min into the recovery period arterial O$_2$ content was further reduced to $6.8 \pm 0.40$ ml/dl, mixed
venous O$_2$ content was raised to 2.5 ± 0.50 ml/dl, and the A-V O$_2$ difference was reduced to 4.3 ± 0.39 ml/dl. The A-V difference was no different from that observed under control conditions. These acute effects of hypertonic saline/dextran were maintained with little change over the subsequent course of recovery.

A significant decrease in cardiac output during hemorrhage (from 177 ± 15.6 to 98 ± 13.9 ml/min/kg, Fig. 3D) combined with the above-indicated reduction in arterial O$_2$ content led to a significant reduction in arterial O$_2$ delivery (from 20.9 ± 2.39 to 9.3 ± 1.14 ml/min/kg, Fig. 3E). As a consequence of these changes, the ratio of O$_2$ delivery to apparent O$_2$ demand was reduced significantly from 2.96 ± 0.192 to 0.52 ± 0.055 (Fig. 3F). In short, O$_2$ delivery supported about one-half of the O$_2$ demand.

Resuscitation with hypertonic saline/dextran led to a marked and significant increase in cardiac output to 202 ± 19.0 ml/min/kg at the 5 min point during the
recovery period. This elevation, however, was not sustained, and after 30–60 min the values stabilized at about 80% of the control level. Arterial $O_2$ delivery showed only transient, and far from complete recovery following administration of 7.5% NaCl/6% dextran. During most of the recovery period the values were essentially the same as those recorded at the end of hemorrhage. The ratio of $O_2$ delivery to apparent $O_2$ demand showed a small but significant improvement following hypertonic saline/dextran administration, an effect that was sustained over the remainder of the recovery period.

**DISCUSSION**

The foregoing data show that an increasing disparity between $O_2$ delivery and $O_2$ demand presents a major threat to the survival of conscious pigs subjected to
severe blood loss. Oxygen delivery was compromised by a progressive decrease in both arterial \(O_2\) content and cardiac output. The decrements in \(O_2\) content were attributable to transcapillary refill which reduced hemoglobin concentration and blood \(O_2\) capacity. The decrements in cardiac output values were due to a progressive fall in blood volume with a consequent decrease in venous return [1]. Normal compensations were ineffective in addressing the defect in arterial \(O_2\) delivery. Hyperventilation raised arterial \(PO_2\), but the potential benefit was negated by hemoglobin dilution. Benefit from increased \(O_2\) extraction, as evidenced by a widening of the A-V difference in \(O_2\) content, was limited by venous \(O_2\) content reaching minimal values (<1 ml/dl) during the last half of the hemorrhage episode. As a consequence, apparent oxygen demand rose markedly and eventually exceeded \(O_2\) delivery by a factor of at least two. When unchecked by effective resuscitation, the disparity between \(O_2\) delivery and \(O_2\) demand became progressively more pronounced and eventually led to uncompensated acidosis, hypoventilation, myocardial failure, hypometabolism, and a consistently lethal outcome [1].

On the basis of subjective evidence, it appeared that the hemorrhage-induced increase in metabolic rate was due to physical activity (leg movements, stretching, etc.), since cyclical increases in \(O_2\) consumption coincided with periodic bouts of muscle activity; hyperventilatory work and elevated sympathetic activity may have been contributing factors. Skeletal muscle activity, in our opinion, reflected a behavioral compensation for hemorrhage and served, presumably, to enhance venous return as blood volume was reduced. Such a compensatory response has not been reported previously, insofar as we are aware, perhaps because of constraints inherent in the animal models or procedures that were used in earlier studies of energy metabolism during hemorrhage. Indeed, most [14-22] but not all [23-25] previous reports show that hemorrhage leads to an unchanged [23-25] or reduced [14-22] \(O_2\) consumption. It is perhaps significant that the majority of these investigations involved animals that were anesthetized, mechanically ventilated, subjected to a rapid and sustained reduction in blood pressure (Wiggers procedure), or a combination of these variables. One would not expect to see muscle activity with a consequent increase in the \(O_2\) consumption of chemically restrained animals, and normal compensatory responses could be overwhelmed or go unnoticed in conscious animals subjected to rapid blood loss or the Wiggers procedure. Only Nahas et al. [26] have found metabolic increments similar to those reported here. Their results were obtained with anesthetized dogs subjected to a relatively modest, fixed-volume, hemorrhage (25 ml/kg) over a 30 min period with arterial pH maintained within 0.1 unit of 7.40. They [26] attributed the hypermetabolic effect of hemorrhage to sympathetic activation, catecholamine release, and a resultant stimulation of free fatty acid oxidation. This calorigenic effect of catecholamines was observed only in the absence of acidosis [26]. Data recorded in the present study, or obtained coincidentally, are consistent with the observations and interpretations of Nahas et al. [26]. Hyperventilation and the blood buffer system effectively compensated for elevated lactic acid production (arterial pH did not change significantly) while plasma concentrations of both epinephrine and norepinephrine rose markedly [27].

It seems probable that our calculated values for apparent \(O_2\) debt underestimate the true values because one or both of two underlying assumptions were not totally valid. One of these assumptions is that lactate is uniformly distributed in total body...
Oxygen Delivery and Demand

Water. Lactate is known to be readily diffusible in body fluids [28], but it seems likely that higher concentrations would be found in tissues rendered ischemic by hemorrhage (e.g., skeletal muscle, skin, viscera) than those protected from ischemia by a preferential redistribution of cardiac output (e.g., heart, brain). If the total mass of ischemic tissue exceeds that of non-ischemic tissue, as it probably does in severe hemorrhage, then the lactate concentration of plasma would underestimate the average concentration in total body water.

The second assumption is that elevated lactic acid production is totally responsible for the $O_2$ debt associated with hemorrhage. It is now well established [11] that the reduction of pyruvate to lactate conserves $1/2$ mol (11.2 ml/mmol) of oxygen for every mole of lactate produced and, conversely, that oxidation of lactate to pyruvate requires $1/2$ mol of oxygen for every mole of pyruvate produced. This latter requirement has served as the basis for numerous studies directed at the reliability of plasma lactate, or excess lactate, as a predictor of the total body $O_2$ debt. Some workers [29] find a poor relationship between $O_2$ debt and exercise-induced lactacidemia, whereas others [30,31] report an excellent correlation. The level of lactacidemia appears to be the critical variable; the heavier the work load, the better the correlation [30,31]. Cain [32] reports similar results and conclusions when hypoxia is used to induce an $O_2$ debt. The lactate levels seen in the present study at the end of hemorrhage were comparable to those reported for heavy work by Knutten [30] and Wasserman et al. [31], hence a comparable $O_2$ debt might be anticipated. However, it is also well established [11,28,30–32] that measured values for $O_2$ debt always exceed those calculated from plasma lactate or excess lactate. The discrepancy is due to the presence of an “alactacid” debt [11,33], which includes decrements in the $O_2$ stores normally contained in the lungs, body fluids, hemoglobin, and myoglobin, a degradation of high-energy phosphates, and other as yet unidentified variables. Correction of these alactacid changes requires $O_2$ consumption over and above that predicted by plasma lactate or excess lactate alone.

The functional mechanisms responsible for the salutary effects of hypertonic saline/Dextran 70 are not totally clear, at least in terms of the factors contributing to the adequacy of $O_2$ delivery relative to tissue $O_2$ demand. On the delivery side, the improvement in cardiac output shortly after administration of hypertonic saline/dextran was consistent with the reports of others [2–4,7]. The consequent enhancement of arterial $O_2$ transport, however, was unimpressive, because fluid mobilization during resuscitation produced a sharp decrease in hemoglobin level and thus blood $O_2$ capacity.

Suppression of $O_2$ demand following hypertonic saline/dextran resuscitation appeared to be a far more important determinant of survival. It was a major factor underlying return of A-V differences in $O_2$ content to normal levels, a change that indicated adequacy of $O_2$ delivery relative to demand. The functional changes responsible for the suppression of $O_2$ demand, however, were not totally resolved in the present study. $O_2$ demand was clearly associated with a decrease in muscle activity, but other factors also may have been involved. For example, Nahas and his coworkers [26] showed that acidosis caused a reduction in $O_2$ consumption during hemorrhage and attributed this effect to an inhibition of catecholamine calorigenesis. Such effects would not be inconsistent with our observations on the actions of hypertonic saline/dextran. Accordingly, other measurements made on these pigs
showed a sharp reduction in arterial pH [29] and plasma catecholamine levels [27] shortly after the administration of hypertonic saline/dextran. The interactions of these and other related variables obviously need further investigation.

REFERENCES


The experiments described in this paper were performed in adherence to the NIH guidelines for the use of experimental animals.