Redistribution of Regional and Organ Blood Volume and Effect on Cardiac Function in Relation to Upright Exercise Intensity in Healthy Human Subjects

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To determine the effect of relative exercise intensity on organ blood volume and its relation to cardiac function, changes in relative blood volume and cardiac function were monitored with radionuclide techniques in 14 healthy volunteers. After labeling the subject's red cells with technetium 99m, we acquired data at rest, zero-load cycling, and at 50%, 75%, and 100% of maximal oxygen uptake. From rest to zero-load cycling, leg blood volume decreased 32±2% (mean±SEM), whereas relative end-diastolic blood volume increased 9.6±1.2%, and lung blood volume increased 18±2%, suggesting that the lungs may act as a blood volume buffer during periods of acutely increased venous return. With relative increasing exercise, leg blood volume stabilized, and then the blood volume in the abdominal organs decreased, further augmenting cardiopulmonary blood volume; leg blood volume and abdominal blood volume decreased by 23±2% and 19±2% from baseline, respectively, whereas thoracic blood volume increased 38±4%. In the abdomen, large decreases in blood volume were observed in the spleen (46±2%), kidney (24±4%), and liver (18±4%). In contrast, lung blood volume increased 50±4%, with the upper lung fields increasing more than the lower. Blood sampling revealed an increase in the hematocrit level by 4.3±0.4 units at peak exercise that paralleled the decrease in splenic blood volume ($r^2 = -0.64, p < 0.001$), suggesting a role for the spleen in augmenting cardiovascular performance by the release of concentrated red blood cells into general circulation. We conclude that upright exercise results in marked blood volume shifts from the legs and abdominal organs to the heart and lungs in a dynamic process correlating closely with oxygen consumption. (Circulation 1990;81:1550–1559)

In addition to increasing cardiac output, exercise increases cardiopulmonary blood volume.\(^1\)\(^-\)\(^5\) The source of this additional blood volume, however, is unknown. $\alpha$-Adrenergically mediated responses to exercise cause vasoconstriction of inactive regions that participates in redirecting blood flow to the working muscles and an increase of cardiac output that is closely coupled to systemic oxygen demand.\(^6\)\(^-\)\(^9\) These changes in regional blood flow should elicit an alteration in the regional distribution of blood volume to maintain flow in areas of muscle bed vasodilation. Two potential “donor” areas for this blood volume are the veins of the lower extremities and the vessels of the abdominal viscera.

The human splanchnic blood pool decreases in volume during exercise,\(^1\)\(^0\)\(^,\)\(^1\)\(^1\) and splanchnic blood flow declines in proportion to the relative cardiovascular stress imposed by exercise.\(^1\)\(^2\) This observation is consistent with the hypothesis that this region represents a significant reservoir for redistribution of blood to the heart and lungs. There is, however, a paucity of data identifying the contributions of specific splanchnic organs. Particularly intriguing is the potential contribution of the spleen, which, in animals such as dogs, sheep, and horses, is an important source of red blood cells for increasing the capacity to transport oxygen.\(^1\)\(^3\)\(^-\)\(^1\)\(^5\) In contrast, the role of the spleen in humans undergoing exercise has not been determined.

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Monitoring a years Subjects body (Technicare front of the subject’s body). Also, a standard field-of-view camera equipped with an 8-mm pinhole collimator was positioned 1.3 m in front of the subject to monitor activity from the whole body (Technicare 420/550) (Figure 1). Each gamma camera’s pulse-height analyzer was set at 140 keV with a 20% window. Data were acquired for serial 60-second frames into 64×64-pixel matrices and recorded in dedicated nuclear medicine computers.

An ambulatory cardiac function monitor (VEST, Capintec Ramsey, New Jersey) continuously monitored and recorded beat-to-beat left ventricular time-activity curves and a modified V-1 electrocardiogram lead on a modified Holter recorder worn by the subjects. Parameters calculated included heart rate (HR), ejection fraction (EF), relative end-diastolic volume (rEDV), relative end-systolic volume (rESV), relative stroke volume (rSV), and relative cardiac output (rCO). The description and validation of this device have been previously published.16–18

Oxygen consumption (VO₂) was measured continuously with a pulmonary function analyzer (model 2000, Medical Graphics, St. Paul, Minnesota). A bicycle ergometer (Philbin model 600, James Wright, Jewett, Connecticut) was used for the exercise procedure.

Procedure

Pretesting. One to 2 days before the experiment, we tested the subjects to familiarize them with the protocol and laboratory environment and to establish their maximal VO₂. During graded exercise on the cycle ergometer, VO₂ was monitored continuously with methods described below. The work load was increased 30 W every 3 minutes until exhaustion. The last completed work load was taken as the point of maximal exertion and used to establish work load settings corresponding to 50%, 75%, and 100% of maximal VO₂ for the experiment.

Testing. The subjects fasted for at least 3 hours and had no caffeine for at least 6 hours before testing. The protocol is summarized in Figure 2. The subject’s red blood cells were labeled with 740 MBq technetium 99m with the technique of Callahan et al19 and were reinjected. After equilibration, a multi-gated acquisition cardiac blood pool scan was
obtained in the left anterior oblique position that had the best separation of right and left ventricles. While the subjects were sitting, the data were recorded with a standard field-of-view gamma camera through an all-purpose parallel-hole collimator at the 140-keV photopeak with a 20% window. Six-minute acquisitions were divided into 16 frames/heart beat to acquire approximately 250,000 counts/frame.

The VEST detector was positioned over the left ventricular blood pool as previously described.\textsuperscript{16,17} The microprocessing unit and recorder were started, and the subject sat quietly on a chair for 15 minutes so that resting values could be recorded.

Subjects were then moved to the cycle ergometer and connected to the pulmonary function analyzer (Figure 1). The large field-of-view gamma camera was placed parallel to the subject's back to include the entire thorax and abdomen. Positioning images were obtained to ensure that the apexes of the lungs were within the field of view, and then two stabilizing straps were secured diagonally across the chest and hips to minimize subject motion.

The standard field-of-view camera with pinhole collimator was positioned 1.3 m in front of the subject to obtain whole body images. This geometry produced approximately a sixfold reduction of the subject image onto the detector of the gamma camera. Care was taken to ensure that the field of view included the subject's feet throughout each pedal revolution of the cycle ergometer.

Serial blood pressures were recorded by sphygmomanometry, and nine subjects had venous blood samples drawn from indwelling 18-gauge intravenous catheters, placed antecubitally, for complete blood count and differential at each stage of exercise.

At time zero, both gamma cameras and the pulmonary function analyzer were started, and the event marker of the VEST was activated to note the beginning of the protocol. For the first 2.5 minutes (baseline), the subject rested on the cycle ergometer while blood pressure was measured and a blood sample was obtained. For the next 2.5 minutes, the subject cycled without applied resistance to the ergometer flywheel (zero-load cycling). A pedaling speed of 60 rpm was maintained throughout exercise with the aid of an audible metronome. At the start of the sixth minute, the ergometer work load was increased to that calculated to elicit 50% of maximal \( V_o_2 \) (based on pretesting) and maintained for the next 5 minutes. At 10 minutes, the work load was increased to 75%, and at 15 minutes, the work load was increased to the predetermined 100% of maximal \( V_o_2 \). At 20 minutes, which was the end of the maximal work load, the resistance was gradually reduced to zero during a 20-second period, and the subject then continued cycling for 15 minutes.

Data Analysis

VEST. The recorded data were reviewed for technical adequacy. Electrocardiographic data were then evaluated, and R waves were identified to permit interval summing of the nuclear count data for 30-second intervals so that \( E_F \), \( r_E_S \), \( r_E_D \), and \( r_C_O \) could be calculated. The graphic trendgram (Figure 3) and numeric data were evaluated.

Relative EDV was expressed as 100% at the beginning of the protocol (baseline), and \( r_E_S \) was expressed as a percentage of the \( r_E_D \). Relative SV was calculated as the difference between \( r_E_D \) and \( r_E_S \), and \( r_C_O \) was the product of \( r_S \) and \( H_R \). \( E_F \) was calculated by dividing \( r_S \) by \( r_E_D \). A background subtraction of 70% of the raw \( r_E_D \) counts was used before calculating the above parameters, and this provided optimal correlation with multiparameter acquisition blood pool (MUGA) scan-derived resting\textsuperscript{16,17} and exercise\textsuperscript{18} \( E_F \) values as previously described.

Large field-of-view gamma camera. The sequence of images was reviewed to detect significant movement within the field of view. Lateral motion typically was limited to 2 pixels (approximately 1.1 cm), and vertical motion was limited to 1 pixel. Regions of interest were drawn, after correction for body motion, over the 1) lungs, both total and divided into upper and

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure2}
\caption{Schematic protocol. Squares and circles indicate time of data collection for blood pressure (BP) and blood sampling (Blood), respectively. ZLC, zero-load cycling; PFA, pulmonary function analyzer; LFOV, large field-of-view gamma camera; SFOV, standard field-of-view gamma camera.}
\end{figure}
lower lung fields, 2) heart, 3) spleen, 4) liver, 5) right kidney (the left kidney was excluded because of greater activity superposition from the spleen), and 6) "bowel" (the remainder of the abdomen, exclusive of the great vessels). The decay-corrected counts for each region of interest during each minute of imaging were analyzed for changes in activity. Baseline was defined as the first minute of the protocol; counts collected during the final minute of each work load and at 5 and 15 minutes of recovery were expressed as a percentage of the baseline value.

Pinhole collimated standard field-of-view gamma camera. Images from the standard field-of-view camera were evaluated similarly to those from the large field-of-view camera. The regions of interest were created over 1) the thorax, 2) the abdomen, and 3) the legs, encompassing the entire range of bicycle pedal excursion and excluding the hip and groin region.

Pulmonary function analyzer. Oxygen consumption was averaged every 15 seconds and recorded.

Blood samples. At each sampling point, 5 ml blood was drawn into a glass tube with liquid EGTA, kept on ice, and then analyzed for hemoglobin level, hematocrit level, white blood cell count and differential, and platelet count.

Statistical Analysis
The effect of relative exercise intensity on relative blood volume change, cardiovascular responses, and hematological parameters was assessed by a one-way analysis of variance (ANOVA). When a significant F value was obtained, a Newman-Keuls multiple-comparison test was used to delineate specific differences in means for each variable at each relative work load. A least-squares linear regression was performed to determine the relation between relative work load and relative blood volume change. This was followed by an ANOVA to determine the significance of the slope and fitness of the regression. Correlations were determined using Pearson's correlation matrix test. Statistical significance for all analyses was defined as a p value of 0.05 or less.

Results
Baseline values (mean±SD) for HR, systolic and diastolic blood pressures, and VO₂ were 79±14 beats/min, 119±10 mm Hg, 78±7 mm Hg, and 5.8±2.4 ml/kg/min, respectively. HR, systolic blood pressure, and VO₂ rose to maximal values of 188±7 beats/min, 199±16 mm Hg, and 39.0±9.3 ml/kg/min (all p<0.01) at peak exercise.

Cardiac Parameters
With zero-load cycling, rEDV rose 9.6±1.2% (mean±SEM) (p<0.01) from baseline, but rESV, EF, HR, and rCO did not change significantly (Table 1). Initially, rESV decreased by 7.0±1.8% from baseline (p<0.05) at the 50% work load and then

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**Figure 3. Trendgram presentation of VEST (ambulatory cardiac function monitor) data for a typical subject.** Upper graph: Heart rate (solid line) and ejection fraction (dotted line). Lower graph: End-diastolic volume (solid line) and end-systolic volume (dotted line) as a percentage of the initial end-diastolic volume. Vertical lines identify the beginning of each protocol segment. BPM, beats/min; EDV, end-diastolic volume.
TABLE 1. Cardiovascular Responses

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Zero-load cycling</th>
<th>50%</th>
<th>75%</th>
<th>100%</th>
<th>IMPEX 5 min</th>
<th>Recovery 15 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min)</td>
<td>79±4</td>
<td>86±3</td>
<td>134±4**††</td>
<td>169±3**††</td>
<td>188±2**††</td>
<td>136±4**††</td>
<td>125±3**††</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>119±3</td>
<td>131±6</td>
<td>153±5**††</td>
<td>175±3**††</td>
<td>199±5**††</td>
<td>145±6**††</td>
<td>127±6**††</td>
</tr>
<tr>
<td>VO₂ (ml/kg/min)</td>
<td>5.8±0.9</td>
<td>8.0±1.3</td>
<td>20.7±2.1**††</td>
<td>31.5±2.3**††</td>
<td>39.0±3.8**††</td>
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<td>...</td>
</tr>
<tr>
<td>rCO</td>
<td>1.00</td>
<td>1.28±0.04</td>
<td>2.19±0.10**††</td>
<td>2.70±0.16**††</td>
<td>2.82±0.19**</td>
<td>2.41±0.14**†</td>
<td>2.01±0.11**††</td>
</tr>
<tr>
<td>rEDV</td>
<td>100</td>
<td>109.6±1.2**</td>
<td>109.1±2.7**</td>
<td>109.9±1.4**</td>
<td>110.4±1.7**</td>
<td>103.6±2.0**†</td>
<td>102.6±1.8</td>
</tr>
<tr>
<td>rESV</td>
<td>40.3±2.9</td>
<td>41.3±2.8</td>
<td>33.3±3.8†</td>
<td>35.9±4.5</td>
<td>40.1±4.9</td>
<td>19.6±3.7**††</td>
<td>25.3±3.6*</td>
</tr>
<tr>
<td>%rSV</td>
<td>...</td>
<td>14.5±2.4*</td>
<td>27.7±3.8**††</td>
<td>24.1±3.7**</td>
<td>17.2±4.6**</td>
<td>40.7±4.5**††</td>
<td>30.0±4.3**</td>
</tr>
<tr>
<td>EF</td>
<td>59±2</td>
<td>62±2</td>
<td>70±3**††</td>
<td>68±4**†</td>
<td>64±4*</td>
<td>81±4**††</td>
<td>76±3**††</td>
</tr>
</tbody>
</table>

All values are mean±SEM.
IMPEX, immediately postexercise; HR, heart rate; SBP, systolic blood pressure; VO₂, oxygen consumption in ml/kg/min; rCO, relative cardiac output; rEDV, relative end-diastolic volume; rESV, relative end-systolic volume; %rSV, percent change in relative stroke volume (from baseline value); EF, ejection fraction; ††p<0.01 from previous level.

*p<0.05 from baseline, †p<0.05 from previous level, **p<0.01 from baseline, ††p<0.01 from previous level.

increased modestly with increasing exercise. The interaction of rEDV and rESV resulted in a maximum exercise rSV and EF at the 50% work load, which then gradually decreased with increasing exercise but remained above baseline, whereas rCO continually rose with increasing exercise.

During recovery, rEDV rapidly approached baseline values. Two to 4 minutes immediately after peak exercise (IMPEX), relative ESV reached a minimum, resulting in maximum values for rSV and EF. These values slowly returned to baseline as the HR slowed.

Whole Body Gamma Camera Images

Leg blood volume decreased to 68±2% of baseline (p<0.01) with zero-load cycling, thoracic blood volume increased 16±2% (p<0.01), whereas the abdominal blood volume remained unchanged (Table 2). The transition from zero-load cycling to 50% maximum work load initiated a slight increase in leg blood volume to 76±3% of baseline (p<0.01), which then remained constant at the two higher work load levels. Abdominal blood volume progressively declined to 81±2% of baseline (p<0.01) at peak exercise intensity as thoracic blood volume increased to 138±4% (p<0.01). During recovery, all values rapidly approached baseline.

Large Field-of-View Gamma Camera Images

These images provided a detailed view of the changes in individual thoracic and abdominal organs. With zero-load cycling, kidney, liver, and spleen blood volumes were not significantly changed from baseline, whereas blood volume in the bowel region increased 6±1% (p<0.05) (Table 3). Both the upper and lower lung zones had appreciable increases in blood volume (to 120±3% and 118±1% of baseline, respectively; both p<0.01), whereas the heart region increased to 113±1% (p<0.01).

At peak exercise, spleen, liver, and kidney blood volumes decreased to 54±2%, 82±4%, and 76±4% of baseline, respectively (all p<0.01), whereas the bowel blood volume was not significantly different from baseline. Complementary changes were seen in the thorax as total lung blood volume increased to 150±4% and the heart region increased to 124±2% at peak work load (both p<0.01).

An example of the changes in blood volume described above from a typical subject are illustrated in Figure 4. The four images, acquired with the large field-of-view gamma camera, are from baseline and the 50%, 75%, and 100% work load intervals, which in this subject corresponded to 100, 150, and 200 W of bicycle exercise.

During freewheeling recovery, heart and lung blood volumes rapidly approached baseline. However, the abdominal organs recovered slowly; the spleen and liver blood volumes had only recovered to 85±5% (p<0.01) and 86±6% (p<0.05), respectively, at the end of the no-load cycling recovery period.

Blood Samples

Blood sampling demonstrated an increase in hematocrit levels from 44.0% to 48.3±0.4% from baseline to peak exercise, respectively. White blood

TABLE 2. Blood Volume Changes, Standard Field-of-View Gamma Camera

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Zero-load cycling</th>
<th>50%</th>
<th>75%</th>
<th>100%</th>
<th>IMPEX 5 min</th>
<th>Recovery 15 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thorax (%)</td>
<td>100</td>
<td>116±2**</td>
<td>120±3**</td>
<td>128±4**</td>
<td>138±4**††</td>
<td>127±2**††</td>
<td>103±2**††</td>
</tr>
<tr>
<td>Abdomen (%)</td>
<td>100</td>
<td>102±2</td>
<td>96±2†</td>
<td>88±2**††</td>
<td>81±2**††</td>
<td>89±2**††</td>
<td>94±2*</td>
</tr>
<tr>
<td>Legs (%)</td>
<td>100</td>
<td>68±2**</td>
<td>76±3**††</td>
<td>78±3**</td>
<td>77±2**</td>
<td>88±3**††</td>
<td>83±3*</td>
</tr>
</tbody>
</table>

All values are mean±SEM.
*p<0.05 from baseline, †p<0.05 from previous level, **p<0.01 from baseline, ††p<0.01 from previous level.
The cell concentration increased to 173±5% of baseline at peak exercise and increased to a maximum of 181±6% of baseline at 5 minutes of recovery (both p<0.01). The differential count indicated that the absolute number of all types of white blood cells increased, but the relative increase in lymphocytes (141%) and monocytes (167%) was greater than that of granulocytes (51%). The platelet count increased to 130±4% (p<0.01) of baseline at 5 minutes of recovery, which is similar to the pattern of increase in white blood cells.

Discussion

Increasing relative intensity of upright bicycle exercise causes marked changes in the regional distribution of blood volume. The physiological rationale for these changes is the requirement for enhanced preload to maintain cardiac output. The use of individually determined exercise work loads at fixed percentages of maximal VO2 minimized interindividual variability21 and permitted comparisons at equivalent relative cardiovascular stress. During the adjustment from baseline to zero-load cycling, the blood volume of the legs decreased, whereas pulmonary blood volume and left ventricular EDV increased. With increasing exercise work load, there was a decline in the blood volume of the abdomen, which was associated with an increase in the blood volume of the thorax. These findings confirm the significance of the skeletal muscle pump and the splanchnic system in redistributing blood volume to the cardiopulmonary system during upright exercise.

Thoracic, Abdominal, and Leg Blood Volume Redistribution

Images of the whole body from the standard field-of-view gamma camera demonstrated gross redistribution of blood volume from the legs and abdomen to the thorax. As zero-load cycling was started, the blood volume of the lower extremities decreased, most likely reflecting the effective action of the skeletal muscle venous pump, whereas the blood volume of the abdomen and thorax increased. At exercise work loads from 50% to 100% of maximal VO2, leg blood volume increased slightly and then stabilized despite the remarkable increase in blood flow.22 Simultaneously, abdominal blood volume decreased, and thoracic blood volume increased. These data suggest that the primary augmentation of cardiopulmonary blood volume at low work loads occurs by redistribution of leg blood volume, and at moderate-to-high work loads, abdominal blood volume is redistributed to facilitate the increased cardiac output required by the increased systemic oxygen demand.

Cardiac Blood Volume and Function

In the present study, EF increased maximally at the 50% work load and then gradually decreased with an increasing work load but remained above baseline. While rEDV increased modestly, the major changes in EF were due to the initial decrease in rESV early in exercise and the gradual increase in rESV late. These findings differ from those previously reported for conventional radionuclide ventriculographic stress testing in which increasing exercise

### Table 3. Organ Blood Volume Changes, Large Field-of-View Gamma Camera

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Zero-load cycling</th>
<th>Work loads</th>
<th>Recovery</th>
<th></th>
<th></th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>50%</td>
<td>75%</td>
<td>100%</td>
<td>5 min</td>
</tr>
<tr>
<td>Thorax</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td>100</td>
<td>113±1**</td>
<td>115±2**</td>
<td>119±2**</td>
<td>124±2**</td>
<td>109±3**††</td>
</tr>
<tr>
<td>Lungs (total)</td>
<td>100</td>
<td>118±2**</td>
<td>127±3**</td>
<td>139±3**†</td>
<td>150±4**††</td>
<td>120±6**††</td>
</tr>
<tr>
<td>Upper half</td>
<td>100</td>
<td>120±3**</td>
<td>132±4**</td>
<td>149±4**††</td>
<td>166±6**††</td>
<td>123±8**††</td>
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<td>Lower half</td>
<td>100</td>
<td>118±1**</td>
<td>124±3**</td>
<td>133±3**††</td>
<td>140±4**</td>
<td>118±4**††</td>
</tr>
<tr>
<td>Abdomen</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spleen</td>
<td>100</td>
<td>105±2</td>
<td>92±3††</td>
<td>71±3**††</td>
<td>54±2**††</td>
<td>65±3**††</td>
</tr>
<tr>
<td>Liver</td>
<td>100</td>
<td>104±3</td>
<td>94±4</td>
<td>88±4*</td>
<td>82±4**</td>
<td>85±3**</td>
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<tr>
<td>Kidney</td>
<td>100</td>
<td>102±2</td>
<td>92±2††</td>
<td>84±3**††</td>
<td>76±4**††</td>
<td>91±3††</td>
</tr>
<tr>
<td>Bowel</td>
<td>100</td>
<td>106±1*</td>
<td>102±2†</td>
<td>99±2</td>
<td>98±3</td>
<td>98±2</td>
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</table>

All values are mean±SEM. *p<0.05 from baseline, †p<0.05 from previous level, **p<0.01 from baseline, ††p<0.01 from previous level.

### Table 4. Hematological Parameters

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Work loads</th>
<th>Recovery</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>50%</td>
<td>75%</td>
<td>100%</td>
<td>5 min</td>
</tr>
<tr>
<td>Hematocrit level</td>
<td>44.0</td>
<td>45.3±0.4*</td>
<td>46.3±0.3**†</td>
<td>48.3±0.4**††</td>
<td>47.0±0.4†</td>
</tr>
<tr>
<td>White blood cell (%)</td>
<td>100</td>
<td>126±3**</td>
<td>143±4**</td>
<td>173±5**††</td>
<td>181±6*</td>
</tr>
<tr>
<td>Platelets (%)</td>
<td>100</td>
<td>115±2</td>
<td>111±1*</td>
<td>124±2**††</td>
<td>130±4**</td>
</tr>
</tbody>
</table>

All values are mean±SEM. *p<0.05 from baseline, †p<0.05 from previous level, **p<0.01 from baseline, ††p<0.01 from previous level.
intensity was associated with increasing EDV in concert with a decreasing ESV, resulting in a rise in SV and EF. Our data also indicate that there is no decrease in cardiac filling with increasing exercise, as evidenced by a stable rEDV with increasing exercise work loads, despite the high HR and resultant decreased diastolic filling time. The principal rise in rEDV occurred in concert with the marked decrease in leg blood volume, suggesting that redistribution of leg blood volume is the primary source for augmentation of EDV when exercising in the upright position.

In our study, rSV reached maximum at the 50% exercise work load and then decreased by 10.5% at peak exercise. This is in contrast to some studies using exercise-gated scans in which rSV continued to rise throughout exercise. Our data agree with those of Boucher et al who noted that EF consistently increased up to the anaerobic threshold (approximately 60% of maximum VO₂) and then changed variably with further increases in exercise intensity. In addition, the review of angiographically acquired data by Astrand and Rodahl suggested that maximal SV is reached at a work load corresponding to 40% of maximum VO₂, without any further significant changes in SV. We believe that the observed decrease in rSV is due to increased afterload resulting in increasing limitation to systolic emptying with peak exercise.

At 3 minutes after exercise, a transient nadir in rESV occurred as rEDV neared baseline, resulting in a maximal rise in EF (22.0±1.8% above baseline, p<0.01). This phenomenon, reported previously, may be due to two factors: 1) As the work load ceased, the skeletal muscle venous pump partially disengaged, reducing venous return and thus cardiac filling (rEDV returned nearly to baseline). 2) The HR and systolic blood pressure declined resulting in increased ventricular systolic emptying, as catecholamine-stimulated myocardial contractility persisted, further reducing rESV and resulting in the maximal rise in EF.

**Lung Blood Volume**

A significant increase in total lung blood volume occurred with zero-load cycling (18±2% above baseline, p<0.01) that was reciprocally related to decreased leg blood volume (−32±2% from baseline, p<0.01) but was out of proportion to the nonsignificant changes in HR, rCO, and VO₂. Thus, when blood is redistributed from the lower extremities, the pulmonary vasculature may act as a transient blood volume reservoir or “buffer,” which may be an important adaption for maintenance of constant left
ventricular filling pressure in the face of acutely increased venous return. At maximum exercise pulmonary blood volume increased to 150±4% of baseline (p<0.01). Blood volume increased more in the upper than in the lower half of the lungs throughout exercise and was likely the result of pulmonary capillary distension and recruitment, with the latter more pronounced in the upper lung fields.27

Although there is general agreement that supine exercise produces little or no increase in lung blood volume,28,29 our results are to be contrasted with other reports of upright exercise where lung blood volume increased only slightly or remained unchanged. Giuntini et al4 observed an increase in pulmonary blood volume of 9% at low levels of exertion. Nichols et al30 noted no change in lung blood volume, possibly because of elution of his tracer,11 carbon monoxide, from the red blood cells during the interval of measurement.

**Splanchnic Organs**

Liver blood volume increased 4±3% above baseline (p=NS) with zero-load cycling, then declined to 82±4% of baseline (p<0.01) at peak exercise, similar to the findings of Brown et al31 who reported a 25% decrease in liver blood volume in subjects undergoing supine exercise. Blood volume of the kidney decreased to 76±4% of baseline (p<0.01) at peak exercise, followed by a rapid return of blood volume during recovery. A decline in kidney blood volume during exercise has not been reported previously, but renal blood flow may decrease to 25% of resting values during severe exercise,32 which, alone, may result in mild diminution of renal size. Our visual inspection of sequential images of kidney is in agreement, because the decrease in blood volume appeared greater in the cortex than in the medulla. Although the initial renal concentration of tracer may be elevated due to excretion of poorly bound tracer activity, it is unlikely that this value would change after equilibration during the protocol period. The insignificant difference in bowel blood volume between baseline and peak exercise suggests that in the 3-hour fasted state the blood volume of the bowel is at a physiological minimum, without the ability to further redistribute blood.

**Spleen Blood Volume**

Blood volume in the spleen decreased to 54±2% of baseline (p<0.01) during maximal upright exercise, similar to the findings of Sandler et al.33 Previously, only the spleens of animals such as dogs and horses13,15 were felt to expel concentrated red blood cells into circulation during exercise, thereby causing an increase in the hematocrit level and total circulating red blood cell volume. The present observation identifies an important new hemodynamic function of the human spleen that can be added to its previously known immunological and filtering functions. The mechanism for the decrease in splenic blood volume is uncertain. Animals have muscular splenic capsules that may physically squeeze the splenic contents,12 but the human spleen has not been thought to possess a significantly muscular capsule to cause a decrease in splenic volume. Recently, however, Pinkus et al,34 using antibodies to smooth muscle, noted an extensive network of smooth muscle elements throughout the spleen, suggesting the presence of a mechanical mechanism for splenic contraction akin to that in animals.

**Hemoconcentration**

The hemoconcentration observed in humans during exercise generally has been explained by a shift in plasma volume from the intravascular space to the interstitium of active skeletal muscle.35 Data from the present study suggest an alternate mechanism, autotransfusion from the spleen, as a mechanism for the increase in hematocrit levels, white blood cell count, and platelet count. Red blood cell autotransfusions from other splanchnic organs should have little effect on the hematocrit level because their blood is believed to be isoconcentrated. In contrast, the spleen is believed to contain concentrated red blood cells (hematocrit levels of 70–80 have been measured), which, if released or expelled, would increase the circulating blood volume hematocrit level. We found a significant correlation in our subjects between the exercise-associated decrease in splenic blood volume and increase in hemoconcentration (r²=−0.64, p<0.001), which lends support to this hypothesis.

The increases in platelet and white blood cell counts were similar to those of Schaffner et al,36 who demonstrated a 50% reduction in the spleen blood volume in response to an intravenous infusion of epinephrine in hypersplenic subjects with an associated granulocytosis. The rise in hematocrit levels may be purely passive, because peak hematocrit levels occurred at the 100% work load. The change in white blood cell and platelet counts, however, may be mediated by other factors, such as catecholamines, because these cells had their maximum concentration at 5 minutes into recovery.

**Critique of Method**

Radiolabeling of red blood cells is an accepted method to measure the total intravascular red blood cell volume and relative changes in organ blood volume. These measurements assume that the labeled red blood cells are uniformly distributed within the intravascular space37 and that regional changes in externally detected radioactivity reflect regional changes in blood volume correlations that have been demonstrated for the heart38 and lungs.39 Remaining sources of error with this technique, however, include damage to the red blood cells during the labeling process, movement of the organ relative to the region of interest, and background contamination from tissue adjacent to the region of interest. In an attempt to minimize our error we 1) used the in vitro red blood cell labeling technique of...
Callahan et al., which minimizes cellular damage and reduces extraneous, free tracer to negligible levels, 2) secured our subjects to the gamma camera to avoid motion error, and 3) chose regions of interest conservatively to minimize adjacent tissue overlap so that the measured changes err, if at all, on the side of underestimation. Also, we did not calculate absolute blood volume in each region, because of variation in count rate for similar blood volumes caused by attenuation. These values could be approximated from the recorded data but with an error of greater than 30%. As a result, all data were expressed as relative changes in blood volume, values that could be calculated with an error of less than 5%.

From our data on regional and organ blood volume changes in relation to percentage of maximal VO2, regression equations were developed to predict blood volume changes representative of healthy individuals during increasing exercise intensity. The regression equations are depicted graphically in Figure 5. All regression slopes were significant (p<0.05 level) except for that of bowel blood volume.

Conclusion

This study indicates that upright bicycle exercise causes a complex sequence of changes in organ blood volume. Initially, blood volume from the lower extremities is mobilized to the thorax and abdomen; increasing exertion causes progressive loss of blood volume from the splanchnic bed, whereas the blood volume in the thorax increases.

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