Effects of Training on the Distribution of Cardiac Output in Patients with Coronary Artery Disease

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SUMMARY

In nine patients with coronary artery disease, cardiac output distribution was evaluated at rest and during exercise by measurement of cardiac output and regional blood flow parameters (hepatic and muscle blood flow). In seven patients repeated values were obtained after a physical training program of 4 to 10 weeks' duration. After training, cardiac output was reduced at moderate work loads (13.1%) causing a change of the relation between oxygen uptake and cardiac output from hyperkinetic to normal. During heavy exercise the cardiac output was increased (5.5%) after training. Similar changes were observed in muscle blood flow, which was reduced at submaximal loads (14.9%) and increased at maximal (8.6%). Hepatic blood flow showed in contrast a less pronounced reduction at both work loads after training (difference, 7.2%). These effects of training could be explained as peripheral regulatory alterations without implying primary improvement in myocardial performance. They are consistent with the view that local changes in the trained muscles are important for the reduction in myocardial pressure-work caused by physical conditioning.

Additional Indexing Words:
Hepatic blood flow  Muscle blood flow  Tension-time index

Previous investigations have suggested that the immediate beneficial effects of physical conditioning on symptoms related to chronic coronary artery disease (CAD) could be explained by hemodynamic alterations which reduce myocardial pressure work. The finding of a more hypokinetic circulation at a given submaximal work load after training indicated that redistribution of cardiac output might be of importance for this economizing effect on the heart. The mechanism responsible for the observed reduction in cardiac output was, however, unclear. Some investigators ascribed such decrement to a more effective sympathetic vasoconstriction in the "nonworking" tissues favoring the blood supply to the working muscles. This assumption disagrees, however, with the observation that the perfusion of abdominal viscera is less reduced during exercise in trained subjects as compared to untrained. In a previous study we observed that muscle blood flow during exercise was reduced after training. Hence we suggested that the reduction in cardiac output after training may be secondary to the reduced flow in the working muscles. In the present investigation the effect of training on the distribution of cardiac output to working as well as "nonworking" tissues was studied. Muscle blood flow and hepatic blood flow were measured in patients with CAD before and after a physical conditioning program.
Methods

Group Studied
Nine male patients with CAD were examined. Their clinical data are given in Table 1. The mean age was 53 years (range, 46 to 59 years). The patients were treated in the outpatient clinic and were admitted to the training program not earlier than 4 mo after myocardial infarction. None of the patients was in cardiac failure or had serious persistent rhythm disturbances. All had sedentary habits, and none had participated in athletic activities during the last 10 years. The aim of the study and the experimental procedure was explained to the patients to obtain their informed consent.

Procedures
Prior to the training the patients underwent a physical examination including a working capacity test on bicycle ergometer with registration of the electrocardiogram. Fasting values for hemoglobin, erythrocyte sedimentation rate, serum creatinine, serum transaminases (GOT and GPT), serum lactic dehydrogenase, and serum cholesterol were obtained. Chest x-rays and respiratory function tests were also performed. These clinical routine determinations were repeated after the training program.

Hemodynamic Measurements
The blood flow in the vastus lateralis muscle (MBF) was determined during bicycle ergometer tests at several submaximal and at the maximal work load. The determinations were performed three to four times with an interval of at least 6 days in order to avoid a pronounced training effect. The MBF measurements were repeated three to four times within a week immediately after the training.

Determination of cardiac output (CO), hepatic blood flow (HBF), ventilation (VE), oxygen uptake (VO2), heart rate (HR), intra-arterial blood pressure, blood oxygen content, and blood lactate concentration at rest and during exercise at two submaximal work loads were performed once before and once after the training. The investigation took place in the morning. The subjects were allowed a light breakfast, and no premedication was administered. With the subjects in the supine position three catheters were inserted at the antecubital fossae. One arterial catheter (Odman-Ledin no. 6) was placed in the brachial artery and advanced to the subclavian artery. The tip of a venous catheter (Intracath) was placed in the superior vena cava. A second venous catheter (Goodale-Lubin no. 6-8) was inserted in the contralateral arm. The tip was...

Table 1

<table>
<thead>
<tr>
<th>Subject</th>
<th>Initials &amp; symbol</th>
<th>Occupation</th>
<th>Age (yr)</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
<th>History</th>
<th>Chest x-rays</th>
</tr>
</thead>
<tbody>
<tr>
<td>L.T.</td>
<td>◇ Provision dealer</td>
<td>47</td>
<td>168</td>
<td>72.0 (70.1)*</td>
<td>Infarct 14 mo before</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>G.J.</td>
<td>♦ Clerk</td>
<td>57</td>
<td>175</td>
<td>70.3 (70.0)</td>
<td>Angina at severe exertion for 6 mo (mild)</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>V.B.</td>
<td>▲ Driver</td>
<td>59</td>
<td>170</td>
<td>72.0 (72.5)</td>
<td>Infarct 10 mo before</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>S.B.</td>
<td>▼ Clerk</td>
<td>54</td>
<td>172</td>
<td>68.5 (66.8)</td>
<td>Infarct 12 mo before; angina for 12 mo (mild)</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>P.J.</td>
<td>◇ Electrician</td>
<td>48</td>
<td>173</td>
<td>81.0 (76.5)</td>
<td>Arterial hypertension (moderate) for 3 yr; infarct 13 mo before; angina for 13 mo (mild)</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>H.T.</td>
<td>♦ Workman</td>
<td>58</td>
<td>176</td>
<td>88.0 (84.2)</td>
<td>Infarct 15 mo before</td>
<td>Heart slightly enlarged</td>
<td></td>
</tr>
<tr>
<td>K.S.</td>
<td>♦ Post office employee</td>
<td>51</td>
<td>181</td>
<td>87.7 (86.2)</td>
<td>Infarct 7 mo before; mild angina on exertion since</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>H.J.</td>
<td>♦ Clerk</td>
<td>46</td>
<td>165</td>
<td>69.3 (68.1)</td>
<td>Infarct 4 mo before</td>
<td>Heart slightly enlarged</td>
<td></td>
</tr>
<tr>
<td>R.H.</td>
<td>◇ Dairyman</td>
<td>58</td>
<td>180</td>
<td>78.0 (-)</td>
<td>Angina pectoris on exertion (severe) for 3 yr</td>
<td>Heart slightly enlarged</td>
<td></td>
</tr>
</tbody>
</table>

*Figures in parentheses are post-training values.
wedged into a right hepatic vein under fluoroscopic guidance and then retracted just sufficiently to allow free withdrawal of blood. After a 30-min rest the different above-mentioned determinations were carried out with the subject still resting supine. When these were completed, the subject assumed the sitting position, the placement of the hepatic catheter was checked again with the fluoroscope, and then he was transferred to an arm chair placed in front of a bicycle ergometer (Elema-Schönander A 308). Thereafter the hemodynamic examinations were repeated during leg exercise in the sitting position first at a work load of approximately 60% of the pretraining maximum and then, after a 5 to 10-min rest, at the highest load the subject could tolerate before training for the 12 to 15 min necessary to perform the measurements. These two submaximal work loads were identical (in kpm/min) before and after training and will be referred to hereafter as “moderate” and “heavy” loads, respectively. A warm-up period lasting 5 and 3 min preceded the respective exercise measurements. Lastly it was ensured that the hepatic catheter had not been displaced during the investigation. The protocol outlined above was repeated after the training program using identical time intervals. No patients complained of precordial pain during these exercise studies. One patient (K.S.) had a vasovagal syncope after the first exercise period and therefore did not perform the second work load. Technical difficulties prevented measurement of cardiac output at the first level in patient H.J. Furthermore in this patient we failed to insert two venous catheters, and the determinations were therefore performed omitting measurement of HBF.

Technics

Hepatic Blood Flow (HBF)

To determine hepatic blood flow during rest, constant intravenous infusion of indocyanine green was used. Prior to the start of the infusion an initial dose of 18 mg was given. The infusion was administered at a constant rate (average, 0.5 mg/min) through the caval catheter by an electrically driven pump. After 30 min of infusion at rest four pairs of blood samples for determination of dye and oxygen saturation were simultaneously drawn from the arterial and the hepatic catheters at intervals of 5 min, each sampling lasting approximately 30 sec. Concentrations of indocyanine green were determined spectrophotometrically. HBF was calculated from the dye infusion rate and the arteriohepatic venous dye difference.

Due to the difficulties in using the constant infusion technic during short-term exercise, HBF during exercise was calculated by using the actual arteriohepatic venous oxygen difference and the estimated resting hepatic oxygen consumption. Blood sampling was started after 3 min of work with three pairs of blood samples being collected thereafter at intervals of 3 min. The repeated determinations of arteriohepatic venous oxygen differences showed a good reproducibility within the same investigation both at rest and during exercise (sn, 0.64 vol%).

Cardiac Output

Cardiac output (CO) was determined immediately after the HBF measurements by the indicator-dilution technic with collection at 1-sec intervals of multiple samples of arterial blood by means of an automatic sampling apparatus after injection of 10 to 20 μc of 131I-labeled o-iiodohippuric acid* in 1 ml of isotonic saline solution through the caval catheter. The radioactivity in the blood samples was counted to 10,000 counts in a well-type scintillation counter using a conventional scaler. CO was calculated from the injected amount of tracer and the area under the outflow time-concentration curve.

Other Determinations

Intra-arterial blood pressure (BP) and heart rate (HR) were continuously recorded during each study. Peripheral vascular resistance (PVR) was calculated in mm Hg/L/min as the arterial mean blood pressure divided by CO. The tension-time index (TTI) was calculated in mm Hg·sec/min during 30-sec periods as the product of HR and the area under the systolic arterial pressure curves obtained by planimetry (paper speed, 50 mm/sec).

The oxygen content (ml/100 ml) in the blood samples was calculated from the spectrophotometrically measured oxygen saturation and the hemoglobin concentration. Arterial blood lactate concentrations were measured enzymatically (Boehringer kit:TC-B no. 15972).

The hemotocrit in the arterial and hepatic venous blood samples was determined by centrifugation in a modified Wintrobe tube (3,000 rpm, radius, 15 cm ~ 1500 g, for 30 min). The correction factor for trapped plasma was 0.96.

Ventilation, oxygen consumption, and carbon dioxide elimination were determined as earlier described.

The muscle blood flow (MBF) during exercise was measured in both vasti laterales by the 133Xenon local clearance technic. In each test the outwash from two to four individually intramuscularly injected 133Xe depots was followed by the same number of light weight

*Farbwerke Hoechst, Frankfurt, Germany.
**Table 2**

*Training Program: Individual Data*

<table>
<thead>
<tr>
<th>Subject</th>
<th>Days of training</th>
<th>Work load (kpm/min)</th>
<th>Difference</th>
<th>Heart rate during training work</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Initial</td>
<td>Final</td>
<td>kpm/min</td>
</tr>
<tr>
<td>L.T.</td>
<td>37</td>
<td>640</td>
<td>800</td>
<td>160</td>
</tr>
<tr>
<td>G.J.</td>
<td>30</td>
<td>720</td>
<td>940</td>
<td>220</td>
</tr>
<tr>
<td>V.B.</td>
<td>36</td>
<td>650</td>
<td>940</td>
<td>290</td>
</tr>
<tr>
<td>S.B.</td>
<td>16</td>
<td>600</td>
<td>760</td>
<td>160</td>
</tr>
<tr>
<td>P.J.</td>
<td>23</td>
<td>540</td>
<td>600</td>
<td>60</td>
</tr>
<tr>
<td>H.T.</td>
<td>21</td>
<td>650</td>
<td>720</td>
<td>70</td>
</tr>
<tr>
<td>K.S.</td>
<td>17</td>
<td>600</td>
<td>900</td>
<td>300</td>
</tr>
<tr>
<td>H.J.</td>
<td>47</td>
<td>600</td>
<td>975</td>
<td>375</td>
</tr>
<tr>
<td>(R.H.)</td>
<td>(2)</td>
<td>(430)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

scintillation crystals strapped to the thigh. Only curves showing a monoexponential washout of at least 75% of the initial counting rate were used. This procedure was followed to minimize the random experimental error. An average of eight to 11 MBF determinations were obtained from each patient at each work level.

**The Training Program**

This consisted of intermittent bicycle ergometer work 5 days a week for 4 to 10 weeks. The initial and final work loads and the number of training days for each subject are shown in table 2.

**Results**

Eight of the nine patients examined in the untrained state completed the training program. No serious complications were seen during the training, but one patient (R.H.) discontinued after only 2 days due to a severe attack of angina pectoris at rest during the evening of the second day of training. No signs of myocardial infarction were found, but the patient preferred to withdraw from the

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**Figure 1**

Heart rate in relation to oxygen uptake at supine rest and during upright exercise at two work loads. Individual data before and after training and group means before (o—o) and after (e—e) training. (Symbols explained in table 1.)
training. Another patient (K.S.) went through the entire training program but did not want to participate in the investigations after the training.

The clinical effect was similar to that observed earlier. All patients enjoyed the daily exercise sessions and reported increased general well-being during the training. The patients studied here were initially extremely untrained but in none of the patients who were trained, was physical activity limited by severe angina pectoris. Two patients (G.J. and K.S.) complained of discomfort in the chest at severe exertion in the untrained state but not after training. Two other patients (S.B. and P.J.) suffered from moderate anginal pains during exercise. Attacks of pain during the training work were only seen the first few days. After training they still had attacks of anginal pain occasionally during daily activities involving other types of physical exercise. The attacks were, however, less frequent and less severe than before.

**Physical Working Capacity**

A direct measurement of the maximal oxygen uptake was not performed in the present study. The maximal work load was defined as the work load on bicycle ergometer which the patients could sustain for just 5 min. The group mean value before training was 633 kpm/min corresponding to an estimated oxygen uptake of approximately 20 ml/kg/min. After training the maximal work load was increased 32% to an average of 830 kpm/min or approximately 26 ml O₂/kg/min (N = 8). Before training two patients (S.B. and P.J.) had anginal pain at the end of the determination of maximal work load. After training no patients had precordial pain during this test.

**Hemodynamic Studies**

Individual values and group averages for the most important respiratory and circulatory
The oxygen uptake at rest was within normal limits in all patients before training (mean, 255 ml/min, sd = 16, N = 9). The increase in relation to the work load corresponded well to that reported in other studies involving exercise on the bicycle ergometer, the mechanical efficiency being about 20%. The training caused no significant changes in the oxygen uptake at rest or during exercise (table 3).

The ventilatory equivalent (VE/V\textsubscript{O\textsubscript{2}}) during exercise was reduced at both work loads after training from 28.1 L/min to 25.6 L/min and from 29.8 L/min to 26.4 L/min, respectively (P < 0.05 and < 0.0125).

The heart rate (fig. 1, table 3) at rest supine was normal in all patients but one. This patient (R.H.) had marked sinus tachycardia (120 beats per min) and his circulatory response to exercise was essentially different from that observed in the other patients. In the eight patients who completed the program, the training reduced heart rate both at rest (diff., 7.1%) and at the two work loads (diff., 12.7% and 10.3% respectively). After training in the patient (K.S.) who did not participate in the hemodynamic investigation, the decrease in heart rate was assessed from the values obtained during the daily training sessions.

Before training the relation between cardiac output (fig. 2, table 3) and oxygen consumption was normal at rest but clearly hyperkinetic during moderate submaximal work for the majority of patients. In seven patients cardiac

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**Table 3**

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>Exercise: Submaximal load</th>
<th>Exercise: Heavy load</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(\dot{V}\textsubscript{E} (L/min))</td>
<td>(\dot{V}\textsubscript{O\textsubscript{2}} (L/min))</td>
<td>(\text{CO} (L/min))</td>
</tr>
<tr>
<td>Mean Before</td>
<td>7</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Value</td>
<td>5.60</td>
<td>0.255</td>
<td>6.60</td>
</tr>
<tr>
<td>diff.</td>
<td>-0.41</td>
<td>-0.014</td>
<td>0.32</td>
</tr>
<tr>
<td>ns = d</td>
<td>1.07</td>
<td>0.016</td>
<td>1.30</td>
</tr>
<tr>
<td>P</td>
<td>NS*</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Exercise: Submaximal load</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Before</td>
<td>6</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Value</td>
<td>30.32</td>
<td>1.078</td>
<td>13.13</td>
</tr>
<tr>
<td>diff.</td>
<td>-3.03</td>
<td>-0.015</td>
<td>-1.72</td>
</tr>
<tr>
<td>sd = d</td>
<td>1.89</td>
<td>0.132</td>
<td>1.50</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.01</td>
<td>NS</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Exercise: Heavy load</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Before</td>
<td>7</td>
<td>6(^\dagger)</td>
<td>6</td>
</tr>
<tr>
<td>Value</td>
<td>44.57</td>
<td>1.489</td>
<td>12.99</td>
</tr>
<tr>
<td>diff.</td>
<td>-5.89</td>
<td>-0.027</td>
<td>0.72</td>
</tr>
<tr>
<td>sd = d</td>
<td>5.80</td>
<td>0.126</td>
<td>2.04</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.05</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

*NS = not significant \(P > 0.05\).
†The mean difference 7.2% for all exercise values taken together (24 determinations) is significant (\(P < 0.05\)).
†The patient (H.J.) who only performed one work load is not included.
CO for this patient was 11.53 (L/min) both before and after training (compare fig. 6).
output was determined at two exercise levels. All had higher heart rates and oxygen uptakes at the heavy submaximal work load compared to the moderate, but a concomitant increase in cardiac output occurred in only two (G.J. and V.B.). In accordance, the group mean stroke volume, which was greater during moderate submaximal work than at rest supine, decreased significantly on transition to the heavy work load (diff. 20 ml, P < 0.013) (fig. 3).

After training, the stroke volume at rest supine increased 12.5%, corresponding to the reduction in heart rate while the cardiac output was essentially unchanged. The training caused marked alterations of the circulatory regulation pattern during exercise in the six patients who worked at two loads both before and after training. The relation between cardiac output and oxygen uptake was changed from hyperkinetic to normal due to a significant decrease of cardiac output at the moderate load and a minor insignificant increase at the heavy load (fig. 2). The group mean stroke volume was not altered at the moderate work load (fig. 3) and thus the reduction of cardiac output at this work level was explained solely by the lower heart rate. In contrast a significant increase of the stroke volume was seen after training at the heavy work load, where the cardiac output was higher despite a lower heart rate.

Following training the systolic arterial blood pressure (table 3) decreased at rest, whereas the diastolic pressure and the mean blood pressure were unchanged. The increase in systolic, diastolic, and mean arterial blood pressures during exercise was less pronounced at both work loads after training (table 3). The calculated TTI (table 3) was reduced after training both at rest and during exercise. The total peripheral vascular resistance was unchanged at rest and during moderate submaximal work, but was significantly lower at the heavy work load (table 3).

Hepatic blood flow at rest supine (fig. 4 and table 3) was within normal limits in all patients examined in the untrained state. The group mean value was 1421 ml (sd, ± 261 ml, N = 8). During exercise HBF was reduced in proportion to the work intensity in all patients. This reduction was most pronounced (to 30% of the resting value) in the patient...
(R.H.) who was unable to increase cardiac output during exercise. Apart from this patient the interindividual variations in the per cent reduction of HBF were only small. The training did not change HBF at rest (table 3). During exercise an increase of HBF was observed compared to the pre-training values at both work loads (table 3). In absolute terms these differences are, however, not statistically significant, but after training HBF expressed as a percentage of the value at rest was increased 7.2%, for all exercise determinations taken together, and this difference is significant (N = 24; P < 0.05).

Muscle blood flow (MBF) in vastus lateralis muscle during exercise increased almost linearly with the work intensity up to an average 70% (range, 64 to 75%) of the maximal work load. Beyond this level no further increase of MBF was seen (fig. 6). This plateauing of MBF before maximal work load is reached was observed both before and after training. However, the training displaced the curve relating blood flow to the absolute work load to the right (fig. 6). Thus MBF was reduced at two submaximal work levels while MBF was increased at maximal work loads (table 4).

Blood lactate concentration increased less at both work levels after training (table 3). The respiratory quotient (RQ) at rest was 0.68 before and after training. RQ during exercise was reduced after training from 0.82 to 0.78 (P < 0.05) and from 0.91 to 0.82 (P < 0.01) at the moderate and heavy work loads, respectively.

Other Measurements

The mean hemoglobin concentration was 15.4 g/100 ml (sd, ± 2.4 g/100 ml) and was not altered by the training. Mean arterial oxygen saturation was 94% at rest and 97% during exercise both before and after training.
The training caused a slight improvement of the forced expiratory volume in 1 sec (diff., 4.5%, $P < 0.05$) whereas all other pulmonary function tests were unchanged. The fasting serum transaminases, lactic acid dehydrogenase, serum creatinine, and serum cholesterol were identical at both occasions. A slight weight reduction was observed in most patients (mean diff., 1 kg).

**Discussion**

The question whether physical conditioning changes the distribution of cardiac output during submaximal work arises from observations of a reduced cardiac output after training.\textsuperscript{14} Also in the present study a decrement of cardiac output was seen at moderate work intensities, whereas the cardiac output was unchanged or even increased during heavy exercise. Three previous studies of the hemodynamic response to training in patients with CAD are available.\textsuperscript{1-3} The results from these studies differ somewhat with respect to the effect on cardiac output.

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**Table 4**

**Blood Flow in the Vastus Lateralis Muscle During Exercise in Six Patients**

<table>
<thead>
<tr>
<th>Work load</th>
<th>% of max.</th>
<th>N</th>
<th>Before</th>
<th>After</th>
<th>Mean Difference in MBF</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (ml/100g/min)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
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</tr>
</tbody>
</table>

*L.T., G.J., V.B., S.B., P.J., and H.T.*
Hepatic blood flow (HBF) as a percent of the value at rest. Group means ± SEM at supine rest and during upright exercise at two work loads before (○—○), after training (●—●).

cannot be excluded that real variations in the hemodynamic reaction to training occur in CAD patients depending on their initial fitness and degree of cardiac disability. Some of the observed variations are, however, obviously explained by the different experimental procedures used in the respective investigations. Exercise at several work loads was only performed in one of these studies.² The changes in cardiac output after training corresponded to those found here although the decrease at moderate submaximal loads was less pronounced. This difference is probably due to the fact that the patients in the present study exercised in the upright position whereas the patients in the former study were examined in the supine position. In the two remaining studies the patients exercised in the upright position, but cardiac output was only measured at one work level in each patient.¹,⁵ In one of these investigations a significant decrease of the mean cardiac output was seen¹ while in the other study the results varied among the patients, probably due to differences in the individual relative work loads.³

The primary purpose of the present investigation was to evaluate eventual changes in the distribution of cardiac output between the working muscles and the “nonworking” tissues following training. Hepatic blood flow was chosen as the quantitatively most important single representative for the “nonworking” tissues. The mean values for HBF at rest obtained here agreed well with the values reported in the literature¹⁵ and were not changed after the training program. The coefficient of variation for the repeated HBF measurements was at rest 19.7% and thus was a little greater than the day-to-day variation (15%) observed by Winkler and Tygstrup.¹⁶

In the estimation of HBF during exercise we were obliged to rely on the assumption that the oxygen uptake in the splanchnic area and the liver is not changed on transition from rest to exercise, an assumption which finds support in the literature.⁶,¹⁷ The reduction of HBF seen during exercise both before and after training in our study was somewhat smaller than that reported by Rowell and associates⁶ at comparable relative work loads. This is probably due to the different types of work and the difference in body position used in the two studies. Our patients performed bicycle exercise sitting in an armchair, while the subjects examined by Rowell’s group⁶ walked on a treadmill. The day-to-day experimental error of the method used for measurement of HBF is rather great. We have therefore attached greater importance to a comparison of the per cent reduction of resting HBF caused by exercise before and after training, than to a comparison of the absolute HBF values. The per cent reduction of HBF during exercise was significantly less pronounced after training, all exercise HBF values taken together (P < 0.05). We therefore find it justified to conclude that hepatic blood flow at a given work load was increased after training. This accords well with the finding in previous studies that the reduction

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of hepatic and renal blood flow during exercise is proportional to the relative work load.6,7 The hepatic flow and the renal flow during exercise are controlled by the sympathetic vasoconstrictor system. It is assumed that the vasoconstrictor system during exercise acts en masse.18 The results obtained in studies of blood flow to the abdominal viscera are therefore probably valid also for other “non-working” tissues supplied with sympathetic vasoconstrictor nerves. It can thus be expected that at a given submaximal work load after training a greater fraction of the cardiac output is directed to these regions.

The skeletal muscles performed the same submaximal work with a lower blood flow after training. In the present study this reduction (15%) was somewhat lower than that found in the previous investigation (21%).8 Varnauskas and co-workers9 reported an even greater decrement of 30% in MBF in seven young normal subjects after 6 weeks of strenuous training. The more moderate decrement seen in the present study might be ascribed to the fact that the two patients earlier studied by us were younger and more trainable than the majority of the patients examined here. The mechanism responsible for the decrease in MBF is not clear, but the results from a study by Linderholm and associates20 may give an important clue. In a group of patients with a hereditary abnormal muscle metabolism, hyperkinetic circulation during exercise was caused by an abundant blood flow through the working muscles. According to these authors this could be explained by an abnormally large accumulation of vasodilator metabolites in the active muscles resulting from decreased oxidative capacity of the muscle mitochondria. A similar regulatory pattern, although less pronounced, may exist in the untrained CAD patient, who

Figure 6
Blood flow in m-vastus lateralis (MBF) during exercise in relation to the work load (kpm/min). Group means ± SEM before (o—o) and after (e—e) training. Relative work load (% of max.) is shown above. Q↓ indicates the load at which cardiac output was determined.
can be expected to have a low oxidative metabolic capacity in the skeletal muscles. Physical conditioning is known to increase the capacity of oxidative enzymes in the trained muscles.19, 21 This might limit the release of vasodilator metabolites and thus cause a reduction of muscle blood flow.

In a qualitative sense the changes in MBF and cardiac output observed after training were in good agreement. Both parameters decreased at the moderate work load and increased at the heavy work level (compare fig. 2 and fig. 6). The calculated absolute decrease in MBF of 4.7 ml/100 g/min, however, can hardly account for the 1.72 L/min reduction in cardiac output at the moderate load since it would imply an active muscle mass of 37 kg, that is, a value probably exceeding the total muscle mass of a patient. It is discussed elsewhere that the \(^{133}\)Xe-clearance method probably somewhat underestimates absolute MBF values.22 This however, does not influence the evaluation of the flow in a qualitative sense and does not invalidate the statement made above that MBF is decreased during submaximal work after training. Thus, according to our findings the change of the circulatory regulation from hyperkinetic to normal induced by training could be related to a reduction in the blood flow through the working muscles, which overshadowed inversely directed changes in the perfusion of "nonworking" tissues.

Before training at the heavy work load it was found that despite a normal increase of the heart rate cardiac output failed to increase due to a marked decrease of the stroke volume. A similar abnormal hemodynamic response to exercise has been described earlier in a selected group of extremely untrained middle-aged subjects.28 After training the circulatory regulation was normalized due to an increase in cardiac output provided by a greater stroke volume and a lower heart rate.

In normal subjects the lower heart rate induced by training occurs together with an increased stroke volume.24 In consequence the deceleration of the heart rate during submaximal exercise is generally considered to be secondary to a direct improvement of myocardial function. It is therefore interesting, that a reduction in heart rate could be observed in these CAD patients at the moderate work load without a concomitant increase of the stroke volume (compare figs. 1 and 3). This finding suggests that peripheral factors contribute to the training effect on the heart rate. We have tested this hypothesis in a training study of normal subjects.25 Two groups were trained daily during 4 weeks by maximal dynamic exercise on bicycle ergometer. The one group performed the training work with the arms, the other group trained their legs. The reduction in heart rate obtained by training the arm muscles could not be transferred to exercise performed with the leg muscles; nor did leg training cause significant reduction of the heart rate during dynamic arm work. Thus it was concluded that local changes in the trained muscles are of importance for the effect of training on heart rate.*

The myocardial pressure work expressed as the tension-time index was reduced after training at both work loads.† The decrease in the heart rate and in the systolic blood pressure contributed to this reduction. In the previous studies concerning the hemodynamic effects of training in CAD patients, the blood pressure was also reduced during exercise when measured in the upright position1, 3 but not during supine exercise.2

The results presented herein seem to indicate that physical conditioning in addition to eventual direct improvement of respiratory and cardiac performance causes alterations in

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*In a study now in progress we trained a cardiac patient with complete atroventricular block treated with a fixed-rate artificial pacemaker (72 beats/min). Two weeks of bicycle training caused a marked reduction of the atrial rate (P-wave frequency) from 146 to 115 beats/min (work load, 300 kpm). This preliminary result seems to confirm the above conclusion that peripheral factors are important for the reduction in heart rate found after short-term physical training.

†The justification of using peripheral blood pressure tracings for evaluation of left ventricular work has previously been discussed.3
the trained muscles which are essential to the general circulatory regulation. When emphasizing the importance of local training effects in skeletal muscle we are in agreement with the results recently presented by Kajser. In an extensive study of the limiting factors for aerobic muscle performance in normal man, he concluded that the upper limit normally is determined by the maximal metabolic rate of the muscles and not by cardiac output or the local perfusion. The assumption that the training effect on cardiac performance in patients with CAD is to a large extent restricted to exercise performed with the trained muscles has important implications for the planning of training programs for these patients. To be beneficial for the patients in their daily activity the training must namely include types of exercise normally performed by the patients at work and at leisure. Exercise on a bicycle ergometer makes the patient a competent ergometer cyclist but hardly increases his tolerance for exercise performed with the arms, for example.

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Editor’s Dilettantism

Cardiac Glycosides, Blue Jays, and Butterflies

Monarch butterflies Danaus plexippus, when reared on tropical asclepiads and apocynads, contain cardiac glycosides which make them unpalatable to avian predators. . . .

Glycosides were extracted from seeds [of the plants] . . . and insect tissue . . . purified on a Florisil column . . . and their identity was verified by thin-layer chromatography on silica gel G, by spectrophotometry, and by biological assay (inotropic response in rat heart, and antagonism of this by aldosterone). . . .

The blue jay Cyanocitta cristata bromia is the major avian predator employed in studies of palatability. . . . We do not know whether Danaus feeding on Asclepias simply accumulates glycosides according to the type and concentration in the plant, or if it has specific selective or concentration mechanisms.


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Effects of Training on the Distribution of Cardiac Output in Patients with Coronary Artery Disease

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