in 17 of 40 (42 percent) who received doxapram infusions for greater than six hours, no tachyphylaxis developed between six and 48 hours.

As our patient had no apparent reversible cause for her repeated failures to wean, and since the patient's symptoms very closely paralleled those seen in primary alveolar hypoventilation, we empirically used doxapram. As evident from Figure 1, the change was dramatic, and the use of doxapram obviated the need to reintubate the patient. Moreover, a "recruitment" phenomenon was observed wherein each successive use of doxapram resulted in a sustained increase in respiratory rate which persisted after discontinuance of the drug. This same phenomenon has been observed when doxapram was used to facilitate weaning in brain-damaged patients.13 We could find no previous reports where doxapram had been used to assist weaning from mechanical ventilation in adults. Nor has newly developed central hypoventilation been identified as an impediment to weaning in the literature to date.

Fahey and Hyde's study identified a subgroup of COPD patients who were "won't breathers" and CO2 retainers and who, in addition, had a depressed ventilatory drive relative to nonretainers ("pink puffers"). Their patient had an amplification of this depressed ventilatory drive for reasons which remain unclear. We suspect that this condition exists in other patients requiring prolonged mechanical ventilation and may contribute to their failure to wean. It may remain unrecognized when masked by the other factors which impair weaning outlined above.

Further investigations are needed to support the existence and frequency of this problem and the potential benefits of treatment with doxapram.

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Endurance Exercise in the Presence of Heart Disease

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Although patients with heart disease have successfully completed marathon runs, the immediate cardiac effects of similar and greater distance endurance exercise competition are unknown. Two such cases are presented, demonstrating that vigorous exercise and extreme levels of fitness are not precluded in the cardiac patient.

(Chest 1989; 95:697-99)

If a cardiac patient chooses to exercise at all, the activity is usually moderate in intensity and duration, and noncompetitive. However, patients who have undergone coronary bypass grafting or myocardial infarction or who have hypertrophic cardiomyopathy have successfully completed endurance racing events such as marathons.14 While such exercise is pursued by a select few, the physician has limited scientific knowledge to draw upon in advising the increasingly common, aspiring cardiac patient-athlete.

Accordingly, we studied the immediate cardiac effects of endurance exercise competition in two patients with different forms of heart disease, one following myocardial infarction and bypass grafting, and one following receipt of a cardiac transplant.

CASE REPORTS

Case 1

At age 48, this previously healthy white man began experiencing progressive, exertional angina, culminating in an anterior myocardial infarction. Treadmill exercise stress test was positive and cardiac catheterization showed a 100 percent obstruction in the proximal left anterior descending coronary artery, with collateral flow provided by the right coronary artery. There were 50 percent lesions in both the first diagonal and the first circumflex marginal arteries. The right coronary artery was small but had a mid-90 percent

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Table 1—Results at Pre-race Baseline, within 10 minutes of Race Finish, and After 24 Hours of Recovery

<table>
<thead>
<tr>
<th>Pt No</th>
<th>BP</th>
<th>HR</th>
<th>LVDd (cm)</th>
<th>LVDs (cm)</th>
<th>PWtd (cm)</th>
<th>PWTs (cm)</th>
<th>FS (%)</th>
<th>Early (cm/s)</th>
<th>Late (cm/s)</th>
<th>Early/Late</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (2.4 mi swim, 112 mi bike, 26.2 mi run)</td>
<td>Pre-race</td>
<td>120/80</td>
<td>41</td>
<td>5.4</td>
<td>3.1</td>
<td>1.3</td>
<td>2.0</td>
<td>43</td>
<td>79</td>
<td>57</td>
</tr>
<tr>
<td></td>
<td>Finish</td>
<td>135/90</td>
<td>69</td>
<td>5.1</td>
<td>3.0</td>
<td>1.2</td>
<td>2.1</td>
<td>41</td>
<td>66</td>
<td>62</td>
</tr>
<tr>
<td></td>
<td>Recovery</td>
<td>105/80</td>
<td>71</td>
<td>4.7</td>
<td>3.0</td>
<td>1.1</td>
<td>2.0</td>
<td>35</td>
<td>62</td>
<td>50</td>
</tr>
<tr>
<td>2 (1.5k swim, 40k bike, 10k run)</td>
<td>Pre-race</td>
<td>140/150</td>
<td>92</td>
<td>5.2</td>
<td>2.6</td>
<td>.8</td>
<td>1.8</td>
<td>50</td>
<td>64</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>Finish</td>
<td>180/105</td>
<td>104</td>
<td>3.0</td>
<td>1.2</td>
<td>1.5</td>
<td>2.5</td>
<td>60</td>
<td>107</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>Recovery</td>
<td>160/100</td>
<td>86</td>
<td>5.2</td>
<td>2.8</td>
<td>.9</td>
<td>1.6</td>
<td>46</td>
<td>63</td>
<td>30</td>
</tr>
</tbody>
</table>

LVDd, LVDs = left ventricular diameter at end-diastole and end systole; PWTd = posterior wall thickness at end diastole and end systole; FS = fractional shortening.

Obstruction. The patient underwent uneventful single vessel coronary bypass grafting. Five years following surgery, he competed in the Hawaii Ironman Triathlon Race (2.4 mile swim, 112 mile bike, 26.2 mile run), for which he trained 30 hours per week. His training regimen consisted of weekly averages of six miles of swimming (38 min/mi pace; range three to eight mi/wk), 200 miles of cycling (20 mph pace; range 150 to 300 mi/wk) and 70 miles of running (7'30" min/mi pace; range 60 to 68 mi/wk). Little or no interval or high intensity training was included. On a bicycle exercise test, he achieved a maximal workload of 19 METS, with an estimated maximal oxygen consumption (VO2 max) of 66.5 ml/kg/min. At the time of the triathlon, he was asymptomatic and taking no medications.

Baseline physical examination revealed a grade 2/6 blowing apical systolic murmur. Resting M-mode and two dimensional echocardiogram showed a top normal sized left ventricle with concentric hypertrophy. He had anteropical hypokinesia but an overall normal ejection fraction (Table 1). His ECG showed left atrial abnormality, left ventricular hypertrophy, and a loss of precordial R wave voltage consistent with an anterior scar.

He successfully completed the triathlon in 14 hours and six minutes. At the finish line, he was without chest pain or excessive dyspnea or fatigue. His physical examination, echocardiogram, Doppler, and ECG were essentially unchanged from baseline (Table 1). Serum electrolyte values showed increases in K, CPK, and LDH (Table 2). Recovery studies obtained 24 hours after the race finish showed no change from pre-race or finish echo and ECG recordings other than a persistent increase in heart rate and a further increase in CPK.

Case 2

Over several years, this 45-year-old white man developed an idiopathic cardiomyopathy, and while pressor dependent, underwent cardiac transplantation. Previously inactive, he began exercise training 10 to 15 hours per week and was studied nine months postoperatively during the United States Triathlon Series National Championship Race (1.5 k swim, 40 k bike and 10 k run). At that time, he was asymptomatic although he was taking prednisone, azathioprine, cyclosporine, persantine, and hydrochlothiazide.

Baseline physical examination was remarkable only for an S4 and a brief systolic ejection murmur. Resting echocardiogram was normal (Table 1). Resting ECG showed a rightward axis, incomplete right bundle branch block, and inferior T wave abnormality. Selected serum chemistries are shown in Table 2.

He successfully completed the triathlon in four hours and 12 minutes. At the finish, his physical exam result was unchanged; however, his echocardiogram showed a marked decrease in left ventricular cavity size without a change in fractional shortening. Left ventricular filling, on Doppler echo, showed a decrease in the early to late flow velocity ratio. These changes resolved after 24 hours of recovery, although Doppler echo remained slightly elevated. The ECG showed no significant change. A Holter study obtained during the race showed sinus rhythm throughout with a mean heart rate of 144 bpm (range of 139 to 162 bpm).

Discussion

These cases document remarkable athletic achievement in two patients with different forms of heart disease. While necessarily anecdotal, they suggest that significant cardiac abnormalities do not preclude either the attainment of extreme fitness or the safe, successful completion of competitive endurance events.

Exercise training of at least moderate intensity has been embraced for its ability to modify cardiac risk factors and to improve the quality of life. However, the achievement of cardiac conditioning is controversial in the coronary pa-

Table 2—Results from Selected Blood Chemistries

<table>
<thead>
<tr>
<th>Pt No</th>
<th>Na (mg/dl)</th>
<th>K (mg/dl)</th>
<th>CPK (U/L)</th>
<th>%MB</th>
<th>LDH (U/L)</th>
<th>%LD-1</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (2.4 mi swim, 112 mi bike, 26.2 mi run)</td>
<td>Pre-race</td>
<td>140</td>
<td>4.4</td>
<td>106</td>
<td>3</td>
<td>207</td>
</tr>
<tr>
<td></td>
<td>Finish</td>
<td>143</td>
<td>5.2</td>
<td>584</td>
<td>3</td>
<td>318</td>
</tr>
<tr>
<td></td>
<td>Recovery</td>
<td>906</td>
<td>2</td>
<td>257</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>2 (1.5k swim, 40k bike, 10k run)</td>
<td>Pre-race</td>
<td>145</td>
<td>4.6</td>
<td>92</td>
<td>1</td>
<td>209</td>
</tr>
<tr>
<td></td>
<td>Finish</td>
<td>143</td>
<td>4.2</td>
<td>156</td>
<td>3</td>
<td>266</td>
</tr>
<tr>
<td></td>
<td>Recovery</td>
<td>142</td>
<td>4.6</td>
<td>213</td>
<td>&lt;1</td>
<td>220</td>
</tr>
</tbody>
</table>
tient,4,10 and exercise training in patients with a denervated, transplanted heart appears to result in an increased peripheral oxygen consumption without an increase in cardiac output.11-14 Our first patient suggests that, under some circumstances, those with extensive coronary artery disease may display remarkable endurance exercise performance beyond the previously reported completion of marathon runs.15 Of note, however, is the persistent elevation in heart rate at recovery, which suggests evidence of delayed cardiac fatigue or overwork.16 Although both fractional shortening and blood pressure were slightly reduced at recovery, these differences are small and are most likely related to the decrease in left ventricular size rather than indicative of cardiac dysfunction.

Other than these changes, the finish and recovery values for all parameters fall within the range of those previously published for other, similarly aged or even younger competitors,17 suggesting that exercise effects in our patient were indeed similar to those in healthy normal subjects. In particular, the increases in CPK at finish and recovery are consistent with those seen in other athletes completing this amount of exercise,17 and in the absence of elevation of %CPK-MB or LD-1 isoenzymes, do not suggest myocardial damage.

Our second patient demonstrates that vigorous exercise training of the denervated heart is also possible. Kavanagh et al18 have clearly demonstrated this in a longitudinal study of a large group of transplant recipients, including one who successfully completed a marathon run.19 Several features are of note in our patient. The decrease in ventricular dimensions without change in shortening seen at race finish was resolved within 24 hours. While explainable by dehydration, vasodilatation secondary to elevation in body temperature, and/or the decrease in diastolic filling time associated with an increased heart rate, others have reported a decline in LV volume at higher levels of exercise in transplanted hearts.11 The altered left ventricular filling pattern is similar to transient changes we have previously observed in ultraendurance events and may represent a transient alteration in diastolic characteristics.18 Finally, systolic blood pressure remained mildly elevated at recovery, perhaps because of adrenergic stimulation.

It is important to state firmly that our findings do not imply that endurance exercise is safe or even possible for most cardiac patients. Indeed, several recent reports suggest that myocardial contractility may be transiently impaired at the end of a marathon run.19,21 Further, it must be remembered that those with underlying organic heart disease are susceptible to the common "side effects" of prolonged exercise, such as dehydration, hyperthermia, hypoxemia, and other electrolyte abnormalities, which might have more significant consequences in those with heart disease.

Obviously, the cases presented are exceptionally motivated individuals, whose illnesses left them with adequate cardiac reserve. They demonstrate that, while not suitable for the vast majority of cardiac patients, vigorous exercise and the achievement of extreme levels of fitness are not necessarily precluded.

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