The Response of the Normal and Abnormal Heart to Exercise
A Functional Evaluation

By Albert G. Bickelmann, M.D., Eugene J. Lippschutz, M.D., and Leonard Weinstein, M.D.

For many years physiologists and clinicians have sought means of assessing the functional capacity of the human heart. Universal agreement, however, has not been achieved in such fundamental principles as the role played by stroke volume in augmenting cardiac output in the normal subject. In cardiac disease consistent patterns of abnormal behavior of the heart, excluding pressure measurements, have not been fully documented.

This investigation was undertaken with the premise that, in the final analysis, cardiac output represents the only role of the heart, and that an integral part of this role is to increase its output proportional to tissue demands, at least within certain limits. With use of graded exercise as a mechanism of stress, the response of the cardiac output and related measurements was characterized in normal human beings and compared with the results of identical studies of people with unselected heart disease. Derived from our data are concepts relating to the performance of the normal and failing human heart.

Methods and Procedures

The major portion of this investigation is comprised of 32 complete studies on 29 subjects, 15 of whom had no evidence of cardiovascular or pulmonary disease. A history and physical examination, electrocardiogram, and routine posteroanterior chest x-ray were obtained in each case to permit adequate clinical evaluation.

Studies were performed in the laboratory with the subject in the supine position on an examining table, at the foot of which was mounted a generator bicycle ergometer. This ergometer is so designed as to permit varying the work load of exercise by means of an external switch, which changes the internal resistance to pedaling. The rate of pedaling was kept constant. The intensity of work performed was calculated from a previously constructed calibration curve which relates electrical current generated to energy expended for each resistance used. Both the subject and an observer ascertained that the ammeter needle was kept at a constant and predetermined point during each entire exercise period.

Cardiac output was determined by a modification of the Hamilton dye-dilution technic with use of a Colson cuvette densitometer to monitor arterial dye concentration. Approximately 5 mg. of dye, indocyanine green (Cardiogreen®), were delivered rapidly into an anteceubital vein for each determination by the method of flushing 10 to 15 ml. of normal saline through a specially constructed volume-calibrated glass cartridge filled with dye. A continuous record of dye concentration in arterial blood was obtained by constant withdrawal of blood via a Riley needle placed in the radial artery, through the cuvette densitometer by means of a motor-driven syringe. The output of the densitometer was led into an appropriate galvanometer, and the curve was recorded on photographic paper. Heart rate was monitored simultaneously by continuous electrocardiographic recording of a single lead.

Cardiac outputs were determined at rest and during the last minute of each of three 4-minute periods of graded exercise separated by 15-minute rest periods. Work loads arbitrarily chosen were 1,800 foot pounds per minute (200 Kg. M./min.) for "low exercise," 2,900 foot pounds per minute (400 Kg. M./min.) for "medium exercise," and 4,500 foot pounds per minute (625 Kg. M./min.) for "high exercise."

Recently, cardiac outputs have been determined at rest, and at 1, 3, 5, 7, and 9 minutes of continuous exercise at each work load. Twenty minutes of rest were allowed between exercise periods.
more than 200 ml. of blood were withdrawn during each complete study. Stroke volume was calculated by dividing the cardiac output in milliliters by the electrocardiographically determined heart rate. Calibration curves were constructed each time on whole blood, to which known increments of dye were added by means of lambda pipettes.

Attention was given to the dead space between the arterial needle and the cuvette, the character of calibration curves done on undyed and dyed blood, and to the question of early recirculation. The dead space was determined to be less than 0.3 ml.; calibration curves were linear (although occasionally the zero point was not intersected) and showed no difference in value before and after each study.

It has been our practice to inject dye into a peripheral vein for the determination of cardiac output. Care has been taken to ensure rapid and complete delivery of the dye by a specially devised method whereby the dye is simultaneously delivered and flushed by 10 to 15 ml. of saline within 2 seconds. Since a long pathway from injection to sampling site may allow recirculating dye to distort or alter the descending limb of the curve, particularly during exercise, injection was made through a cardiac catheter (NIH no. 7) placed into the superior vena cava in two individuals, and compared with the results of peripheral injections. On multiple injections the mechanical resistance offered by the catheter system was considerably greater than with peripheral injection, and rate of delivery was slower. The arrival time of the dye for both methods of injection was virtually identical, but the calculated cardiac output for the catheter studies was lower by as much as 4 liters per minute. These observations suggested that rapid simultaneous delivery and flushing of dye into a peripheral vein carries it to the portals of the heart almost instantaneously. Furthermore, in all normal subjects increasing magnitudes of exercise consistently resulted in smaller dye curves, indicating that increased cardiac output was reflected by use of a peripheral injection. The effect of early recirculation due to shortened pathways on the dye curve would be to increase its area. The downslope of the semilogarithmic plots of these curves was always linear and was abruptly interrupted by evident recirculation. Although a straight line semilogarithmic plot provides evidence against unapparent recirculation altering the curve of first circulation, it does not constitute absolute proof of its absence.24 The method is subject to this potential although controversial source of error, but, in our hands, use of a cardiac catheter has magnified the difficulty due to the resistance offered to rapid injections.

Results

Investigation of cardiac output and related functions by dye-dilution methods has been carried out in this laboratory for the past 5 years and has totaled 792 satisfactory determinations. Results obtained have been highly reproducible. Analysis of duplicate or triplicate determinations of cardiac index at rest on 78 consecutive patients revealed the standard error of the method to be 0.09 L/min./M.2 in normal subjects and 0.14 L/min./M.2 in those whose cardiac index was below 2.45 L/min./M.2 (the lower limit of resting normal for this laboratory). During exercise, the physiologic variations to stress and the inconstant emotional response of the subject probably precluded the same degree of reproducibility of cardiac index determined at a specific time for a specific work load. Results obtained, however, on the same subject at different times (table 1, subject A.B.; table 2, H.P.) have shown reasonable agreement.

Tables 1 and 2 summarize the results of the present study. A typical example of a dye-curve series obtained on a normal subject (W.W.) and its graphic representation are shown in figure 1. It is apparent that the area under each dye curve diminishes with increasing work load, indicating a progressive rise in cardiac output. In figure 2, similar individual graphic analysis of the variations of cardiac index, stroke volume, and heart rate with increasing work load are plotted for another normal subject (A.B.) and three patients with different degrees of disability as a result of cardiovascular disease, J.R. (mild), H.P. (moderate), and O.F. (severe). Subject A.B. (upper left) demonstrated an almost linear rise of all three measures through the entire study; this is in marked contrast to the performance of any of our abnormal patients. Typical of the exercise response of an asymptomatic cardiac patient is J.R. (upper right), who was unable to increase his cardiac output from medium to high exercise: whereas there was a suboptimal rise in stroke volume from low through medium exercise, no further increase occurred during the high-
Table 1
Cardiodynamics at Rest and during Three to Four Minutes of Exercise, Normal Subjects

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age</th>
<th>B.S.A.</th>
<th>Cardiac index (L./min./M²)</th>
<th>Stroke volume (ml./beat)</th>
<th>Heart rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Rest</td>
<td>Low</td>
<td>Medium</td>
</tr>
<tr>
<td>D.J.</td>
<td>23</td>
<td>1.80</td>
<td>3.91</td>
<td>6.20</td>
<td>7.65</td>
</tr>
<tr>
<td>L.W.</td>
<td>30</td>
<td>1.93</td>
<td>3.81</td>
<td>5.71</td>
<td>6.48</td>
</tr>
<tr>
<td>R.W.</td>
<td>21</td>
<td>1.98</td>
<td>4.30</td>
<td>5.93</td>
<td>6.50</td>
</tr>
<tr>
<td>W.R.</td>
<td>46</td>
<td>1.99</td>
<td>2.47</td>
<td>5.30</td>
<td>5.32</td>
</tr>
<tr>
<td>D.P.</td>
<td>28</td>
<td>1.66</td>
<td>5.08</td>
<td>8.05</td>
<td>8.66</td>
</tr>
<tr>
<td>P.I.</td>
<td>30</td>
<td>2.22</td>
<td>3.35</td>
<td>5.14</td>
<td>6.06</td>
</tr>
<tr>
<td>R.F.</td>
<td>20</td>
<td>1.84</td>
<td>2.90</td>
<td>..</td>
<td>5.68</td>
</tr>
<tr>
<td>T.F.</td>
<td>25</td>
<td>2.19</td>
<td>3.34</td>
<td>5.61</td>
<td>5.00</td>
</tr>
<tr>
<td>B.D.</td>
<td>32</td>
<td>2.14</td>
<td>3.04</td>
<td>4.99</td>
<td>5.93</td>
</tr>
<tr>
<td>A.B.</td>
<td>35</td>
<td>2.04</td>
<td>4.38</td>
<td>6.18</td>
<td>6.48</td>
</tr>
<tr>
<td>A.B.</td>
<td>35</td>
<td>2.06</td>
<td>3.27</td>
<td>5.19</td>
<td>6.69</td>
</tr>
<tr>
<td>J.J.</td>
<td>27</td>
<td>2.03</td>
<td>2.57</td>
<td>5.25</td>
<td>6.10</td>
</tr>
<tr>
<td>W.W.</td>
<td>45</td>
<td>2.04</td>
<td>2.58</td>
<td>4.66</td>
<td>5.20</td>
</tr>
<tr>
<td>C.W.</td>
<td>26</td>
<td>1.62</td>
<td>2.98</td>
<td>9.00</td>
<td>8.11</td>
</tr>
<tr>
<td>J.C.</td>
<td>39</td>
<td>1.84</td>
<td>2.85</td>
<td>5.06</td>
<td>5.42</td>
</tr>
<tr>
<td>B.W.*</td>
<td>26</td>
<td>1.76</td>
<td>5.06</td>
<td>7.64</td>
<td>8.01</td>
</tr>
<tr>
<td>Mean</td>
<td>1.96</td>
<td>3.39</td>
<td>5.87</td>
<td>6.39</td>
<td>8.08</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>±0.76</td>
<td>1.22</td>
<td>1.03</td>
<td>0.85</td>
<td>11.5</td>
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<tr>
<td>Fractional increment</td>
<td>1.00</td>
<td>1.73</td>
<td>1.88</td>
<td>2.38</td>
<td>1.00</td>
</tr>
</tbody>
</table>

*This subject's response to insertion of the needles was that of mild clinical shock. Although his blood pressure was maintained at normotensive levels he remained diaphoretic throughout the study, and his heart rate and stroke volume response to exercise were atypical. This subject’s results were omitted in calculating mean values.
Table 2
Cardiodynamics at Rest and during Three to Four Minutes of Exercise, Abnormal Subjects

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Diagnosis</th>
<th>Age</th>
<th>B.S.A.</th>
<th>Cardiac index (L./min./M.²)</th>
<th>Stroke volume (ml./beat)</th>
<th>Heart rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Rest</td>
<td>Low</td>
<td>Medium</td>
</tr>
<tr>
<td>J.R.</td>
<td>Hypertension, emphysema</td>
<td>56</td>
<td>2.00</td>
<td>2.55</td>
<td>4.28</td>
<td>5.21</td>
</tr>
<tr>
<td>C.B.</td>
<td>Hypertension</td>
<td>26</td>
<td>1.91</td>
<td>2.54</td>
<td>3.78</td>
<td>5.08</td>
</tr>
<tr>
<td>F.B.</td>
<td>Emphysema, cor pulmonale</td>
<td>61</td>
<td>2.07</td>
<td>2.24</td>
<td>2.80</td>
<td>3.32</td>
</tr>
<tr>
<td>M.B.</td>
<td>Mitral stenosis</td>
<td>38</td>
<td>1.70</td>
<td>3.43</td>
<td>4.72</td>
<td>4.30</td>
</tr>
<tr>
<td>C.D.</td>
<td>Emphysema, Polycythemia</td>
<td>57</td>
<td>1.84</td>
<td>2.68</td>
<td>3.17</td>
<td>3.37</td>
</tr>
<tr>
<td>R.H.</td>
<td>Con. pulmonic stenosis, mild</td>
<td>19</td>
<td>1.92</td>
<td>2.59</td>
<td>4.11</td>
<td>4.71</td>
</tr>
<tr>
<td>O.F.</td>
<td>Hypertension, emphysema</td>
<td>62</td>
<td>1.80</td>
<td>2.76</td>
<td>3.73</td>
<td>3.25</td>
</tr>
<tr>
<td>E.P.</td>
<td>Mitral insufficiency &amp; stenosis</td>
<td>58</td>
<td>1.58</td>
<td>2.97</td>
<td>3.93</td>
<td>3.70</td>
</tr>
<tr>
<td>H.P.</td>
<td>Aortic stenosis</td>
<td>23</td>
<td>1.85</td>
<td>1.52</td>
<td>3.92</td>
<td>4.97</td>
</tr>
<tr>
<td>H.P.</td>
<td>Aortic stenosis</td>
<td>23</td>
<td>1.85</td>
<td>1.57</td>
<td>3.63</td>
<td>3.29</td>
</tr>
<tr>
<td>H.P.</td>
<td>Aortic stenosis</td>
<td>23</td>
<td>1.85</td>
<td>1.52</td>
<td>4.69</td>
<td>4.13</td>
</tr>
<tr>
<td>B.A.</td>
<td>Diabetes ST-T changes</td>
<td>51</td>
<td>2.14</td>
<td>1.81</td>
<td>3.05</td>
<td>3.14</td>
</tr>
<tr>
<td>G.R.</td>
<td>Emphysema</td>
<td>61</td>
<td>1.83</td>
<td>2.20</td>
<td>3.03</td>
<td>4.58</td>
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<tr>
<td>H.S.</td>
<td>Pul. sarcoidosis</td>
<td>59</td>
<td>1.74</td>
<td>1.89</td>
<td>3.77</td>
<td>3.66</td>
</tr>
<tr>
<td>K.S.</td>
<td>Aortic insufficiency, mild</td>
<td>17</td>
<td>1.70</td>
<td>3.24</td>
<td>4.40</td>
<td>4.62</td>
</tr>
<tr>
<td>J.T.</td>
<td>Emphysema</td>
<td>49</td>
<td>2.22</td>
<td>2.80</td>
<td>3.66</td>
<td>3.46</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td></td>
<td>1.88</td>
<td>2.39</td>
<td>3.79</td>
<td>4.05</td>
</tr>
<tr>
<td>Standard deviation</td>
<td></td>
<td></td>
<td>±1.90</td>
<td>0.57</td>
<td>0.73</td>
<td>0.81</td>
</tr>
<tr>
<td>Fractional increment</td>
<td></td>
<td></td>
<td>1.00</td>
<td>1.58</td>
<td>1.69</td>
<td>2.18</td>
</tr>
</tbody>
</table>
Cardiodynamics at rest and during 3 to 4 minutes of exercise at each of three work loads (low, medium, high). Normal subject W.W. Top. Original dye curves and electrocardiogram. Bottom. Graphic analysis of derived responses of cardiac index (CI), stroke volume (SV), and heart rate (HR).

Individual variation was seen in the response of the cardiac index, stroke volume, and heart rate to increasing work load in both the normal and the abnormal groups. That a virtually complete separation exists between the groups in response to increasing work load, however, is apparent from the data itself as well as in figures 3 and 4. Figures 5 and 6 demonstrate individual responses of normal and abnormal subjects without specific reference to the time or magnitude of work performed.

Preliminary investigation of cardiodynamic variations during prolonged exercise at each work load has been carried out on five normal subjects and on one patient with moderately severe pulmonary emphysema and cor pulmonale. Their 3-minute responses are reported together with the others in the present paper. Figure 7 illustrates the results obtained on a normal individual (D.J.) who demonstrated steadiness of the cardiac index and heart rate from 3 through 9 minutes at the highest and to a degree during the lowest level of work but not during medium exercise. The other five subjects showed a progressive
rise of cardiac index at each of the three work loads. Four other individuals in the normal group were studied at both 3 and 5 minutes of exercise at each level. No predictable "steady state" existed between 3- and 5-minute determinations. In these 10 individuals cardiac output tended to rise progressively with time, and the "steady state" was an inconstant finding.

Discussion

Work Done by Others

In their classic article, Donald and his co-workers1 demonstrated that cardiac output and heart rate increase with increasing levels of work. The importance of the work intensity in testing was emphasized as well by Holmgren,2 who also demonstrated that in the upright position at rest, cardiac output, stroke volume, and heart volume are lower than in the supine position and that the heart rate is increased.3,4 During exercise, the magnitude of response of these functions varies as well with body position. Reeves et al.5 suggested that circulatory dynamics during treadmill and supine exercises are so different as to be not comparable.

The wide variation in experimental conditions is probably a great factor in the divergence of opinion regarding the importance of the stroke volume during exercise. Chapman and his group,6 for example, showed that one third to one half of the increase in cardiac output during severe treadmill exercise can be attributed to the increase in stroke volume. On the other hand, Donald et al.,1 Barratt-

![Figure 2](https://circ.ahajournals.org/doi/fig/10.1161/01.CIR.28.1.243.f2)

**Figure 2**

*Responses of cardiac index, stroke volume, and heart rate to graded exercise in four subjects.*

*Circulation, Volume XXVIII, August, 1963*
Boyes and Wood, Holmgren et al., and Rushmer and Smith tended to disparage the part played by the stroke volume. In recent studies on normal and abnormal subjects with the Fick principle and with leg-raising exercise designed to evoke oxygen consumption of "two- to threefold over resting values," 35 per cent of normal subjects failed to show a significant rise in stroke volume.

The method of determination of cardiac output and its related functions must be considered critically. Most reported studies have employed the direct Fick analysis of oxygen consumption and arteriovenous oxygen difference during exercise at a "steady state," based upon the conclusion of Donald and his co-workers, that a "steady state" is present normally from 2 to 5 minutes of exercise at a given work load. A careful perusal of the individual results in this study, though, will reveal that, in at least one of the four subjects

RESTING AND 3-4 MINUTE EXERCISE STUDIES

<table>
<thead>
<tr>
<th>Normal</th>
<th>Abnormal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>Medium</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td></td>
</tr>
</tbody>
</table>

Cardiac index vs. work: normal individuals and subjects with heart disease at rest and at 3 to 4 minutes of exercise.

Figure 3

EXERCISE LOAD

Figure 4

Stroke volume vs. work: normal subjects and individuals with heart disease at rest and at 3 to 4 minutes of exercise.

for each work load, the minute-to-minute variation of the cardiac index was great and unpredictable. Thus, at least 25 per cent of the time, there was no "steady state" and unless this condition is fulfilled, the Fick principle is invalid. Lack of a "steady state" during exercise has also been pointed out by Holmgren and Pernow and by Levy and his co-workers.

The problem of achieving a "steady state" in patients with heart disease is more complex than it is in normal subjects. Data of minute-to-minute supine exercise determinations reported by Donald and his co-workers do not support the contention that a "steady state" usually occurred in 2 to 3 minutes in patients with mitral stenosis. Ferrer et al. in 1952 showed that for the mild variety of
Individual variations of cardiac index with heart rate at rest and during exercise at each work load (normals, solid lines; abnormals, dotted lines). Some responses in normal subjects are included at 5 to 6 minutes of each exercise here and in figure 6.

Individual variations of cardiac index with stroke index at rest and during exercise at each work load (normal, solid lines; abnormal, dotted lines).

Circulation, Volume XXVIII, August, 1963
supine exercise performed, a minimum of 5 minutes was required for the individual with rheumatic heart disease to reach a steady state, and that the only consistent hemodynamic variation with exercise was aggravation of resting pulmonary hypertension.

By means of the cardiac catheter and the Fick equation, the natural history of specific types of cardiac disease has been explored. These studies correlate clinical patient evaluation with intracardiac and intravascular pressure measurements both at rest and during some form of exercise. In mitral stenosis and hypertensive cardiovascular disease, for example, clinical deterioration is associated with the development of pulmonary arterial hypertension and increase in pulmonary capillary wedge pressure, at first only during exercise but later also at rest. The behavior of the cardiac output and stroke volume in these investigations correlates poorly with progression of disease. There is much overlap among individuals in different functional classes with respect to these measurements both at rest and during exercise. Lewis, Houssay, Haynes, and Dexter, however, found that with the development of severe congestive heart failure, stroke index consistently either did not change or tended to decrease on exercise.

It has been customary for investigators who employ Fick methods studying exercise cardiology to equate oxygen consumption with work. Donald and his co-workers demonstrated a distinctly linear relationship between the two. The more recent work of Huckabee and Judson, however, raises doubt as to the validity of this equation. They demonstrated that in patients in congestive heart failure, 20 to 50 per cent of the energy required for the performance of very mild exercise was supplied anaerobically. Thus, oxygen

Figure 7
The response of the cardiac index and heart rate of a normal subject (D.J.), periodically determined during extended exercise at low, medium, and high work loads.
consumption could not indicate the amount of work performed. Even in normal individuals some 5 per cent of this work was accounted for by anaerobic metabolism. Moreover, no data are available on aerobic versus anaerobic contributions during more severe exertion by subjects with or without heart disease. Therefore, at least in normal individuals and class I cardiac subjects, final judgment of the validity of measuring work performed in terms of oxygen consumption must be reserved. Furthermore, it seems inappropriate to justify correlation of cardiac output with oxygen consumption as a measure of work, when the results of the former, as derived from the Fick equation, are directly dependent on the latter.

The Present Study

The results of the present study show that the behavior of the stroke volume during increasing grades of exercise clearly distinguishes normal individuals from even mild cardiac patients. It is evident that under the conditions of this experiment the ability of the cardiac patient to increase his stroke output is impaired.

Increasing levels of exercise characteristically evoke increases in cardiac output and heart rate. The magnitude and slope of rise of cardiac index with respect to heart rate, however, are decidedly limited in patients with heart disease. The separation of normal and abnormal subjects on the basis of cardiac index and stroke volume response becomes increasingly widened with increasing magnitudes of work. Analysis of the over-all responses of the individual to varying degrees of exercise allows a functional assessment of the capacity of his heart.

Prior to the actual exercise determinations, no attempt was made to assess scientifically the degree of physical conditioning of any subject. Nevertheless, former college athletes in the normal group show the steepest rises of cardiac index for small increments of heart rate, and the few abnormal individuals who are interspersed with the lowest normal persons are actively engaged in high school ath-

**Figure 8**

The mean fractional increments of cardiac index, stroke output, and heart rate in normal subjects are plotted against work.

*Circulation, Volume XXVIII, August, 1963*
The observed mean increment of cardiac output as compared to a hypothetical state in which increments of output were calculated from the product of heart rate at each work load and resting stroke volume.

Figure 9

The effects of physical conditioning are even more apparent among the normal subjects when stroke index is plotted against cardiac index-hearterate curves, whose magnitude, however, was generally greater than those of athletic individuals with heart disease. This implies that for given heart rate, a poorly conditioned normal individual tends to have a higher cardiac index than does a well-conditioned cardiac patient.

The effects of physical conditioning are even more apparent among the normal subjects when stroke index is plotted against cardiac index-heart rate curves, whose magnitude, however, was generally greater than those of athletic individuals with heart disease. This implies that for given heart rate, a poorly conditioned normal individual tends to have a higher cardiac index than does a well-conditioned cardiac patient.

All sedentary normal subjects demonstrated relatively flatter cardiac index-heart rate curves, whose magnitude, however, was generally greater than those of athletic individuals with heart disease. This implies that for given heart rate, a poorly conditioned normal individual tends to have a higher cardiac index than does a well-conditioned cardiac patient.

The effects of physical conditioning are even more apparent among the normal subjects when stroke index is plotted against cardiac index-heart rate curves, whose magnitude, however, was generally greater than those of athletic individuals with heart disease. This implies that for given heart rate, a poorly conditioned normal individual tends to have a higher cardiac index than does a well-conditioned cardiac patient.

No abnormal person achieved a stroke volume of more than 83 ml./beat for any exercise determination between 3 and 4 minutes. In fact, with more severe cardiac impairment, stroke volume tended to decrease significantly with increasing levels of work.

When mean values of our data from normal subjects are expressed as fractional increments of the resting values (fig. 8), it is evident that the output of the heart is augmented in a linear fashion with respect to work, and that increments of heart rate and stroke volume each contribute to this rise. A similar analysis of the mean data from the abnormal group reveals a qualitatively similar response, with identical increments of the two groups with respect to heart rate, but with smaller increments of both stroke volume and cardiac output in the abnormal subjects. Considered as a group, therefore, the patients with cardiovascular disease in this study had lower resting cardiac outputs and stroke volumes, and failed to augment these to some degree as did the normal persons.

Increments of heart rate and stroke volume contributed to the rise of cardiac output in response to exercise in all normal individuals. To illustrate the relative importance of these
two dependent variables the observed mean increment in cardiac output in normal individuals was compared to a hypothetical state in which stroke volume was assumed to be fixed at the resting value, and increments of cardiac output were calculated from the product of the heart rate at each work load and resting stroke volume (fig. 9). While rate-dependent minute-output increments may be sufficient to meet the needs of the human body during mild stress, they are incapable of doing so at even moderate work loads, where the necessity for a rise in stroke volume to augment cardiac output is readily apparent. It must be emphasized here that it is the actual level of stroke volume achieved, rather than its percentage increase alone, that appears to underlie the efficiency of cardiac function.

The controversy in the literature regarding the significance of increments of stroke volume in the normal individual under stress may be resolved through the technic of determining his cardiac response at rest, and at the same moment during several periods of consistent but different exercise loads. By the use of these methods in our laboratory we believe we have established that increments of stroke volume assume a significant role in augmenting cardiac output.

Summary and Conclusions

With use of dye-dilution methods for the determination of cardiac output in conjunction with multiple, graded-exercise loads, normal and abnormal human subjects were studied.

In normal individuals the response of the cardiac output and stroke volume to the stress of graded exercise may be utilized to assess the functional capacity of the heart; increments of cardiac output under the stress of exercise are governed by stroke volume as well as heart rate.

In subjects with heart disease there is a definite limitation in the response of the cardiac output to graded exercise; this limitation is conditioned by an inadequacy of stroke volume. Progressively severe dysfunction is associated with progressive diminution in the capacity of stroke volume to rise during exercise; with severe impairment, stroke volume tends to fall during even mild exertion.

References


William Withering

William Withering was born March 17, 1741, at Wellington in Shropshire, England. The name was originally Witherings and also Witherington and Widdington. Whittington belongs to this same name group, a fact of interest as Dick Whittington of cat and Lord Mayor of London fame came from the West Country. Thomas Witherings was the first postmaster-general of England, appointed by King Charles I on July 31, 1635. The name, Withering, is probably of place or of occupational origin, a withering floor being the term applied to the drying floor of a malt house.

The great-grandfather of William Withering was James Witherings of Cheswardine. His grandfather was also William Withering. His father, Edmund, was born December 30, 1712. His mother was Sarah Hector, born November 18, 1708, so she was somewhat more than four years older than her husband, whom she outlived twenty years, dying at the age of eighty-one. They had three children: Mary, who died in infancy, William, and Sarah, the youngest, born February 12, 1750.

Withering's father, Edmund Withering, was a physician and his mother belonged to a well-known medical family. She was a sister of Dr. Brooke Hector of Lichfield. Her father, Dr. George Hector, had delivered Samuel Johnson so that could have claimed the distinction of having ushered one of the greatest of men into the world. Another of her brothers, George Hector, and a cousin, Edmund Hector, both of whom became physicians, went to school with Johnson. Withering's mother was also distantly related to Bishop Hurd of Worcester.

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Circulation. 1963;28:238-250
doi: 10.1161/01.CIR.28.2.238

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/28/2/238.citation

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