Influence of Age on the Hemodynamic Response to Exercise

By Stevo Julius, M.D., Sc.D., Antoon Amery, M.D., Leigh S. Whitlock, Ph.D., and James Conway, M.D., Ph.D.

SUMMARY

Respiratory and hemodynamic measurements were made on 54 sedentary subjects during progressive exercise on a bicycle ergometer up to the point of maximal voluntary effort. The age range of the group was from 18 to 68 years.

The maximum tolerated exercise, as indicated by the highest achieved level of oxygen consumption (\(V_{O_2}\)), diminished with age. Older subjects had a lower resting cardiac output (\(Q\)) than normal subjects, but an identical increase in \(Q\) with \(V_{O_2}\). There was no evidence of flattening of this curve as the older subjects approached highest exercise loads. Consequently, the arteriovenous oxygen difference did not increase abnormally on high loads, and the cardiac response to exercise in older subjects appeared to be adequate. The relationship between inspired air volume and heart rate with \(V_{O_2}\) at submaximal loads was not influenced by age.

Systolic pressure increased progressively with exercise and showed a greater change in older subjects. Total peripheral resistance at rest increased with age; but with increasing exercise, this difference progressively diminished.

Additional Indexing Words:
Cardiac output Arterial pressure Total peripheral resistance
Heart rate Oxygen consumption Pulmonary ventilation

With advancing age, there is a gradual reduction in physical strength and the ability to sustain strenuous physical exercise.\(^1\)\(^\text{-}\)\(^4\) The mechanism responsible for this has not been elucidated, and studies of it have usually been concentrated on certain areas, such as maximum aerobic capacity and heart rate.\(^1\),\(^2\) In the hemodynamic studies which have been made, there have been limitations in the age range of the subjects studied.\(^5\)\(^\text{-}\)\(^11\) Consequently, hemodynamic data are limited, especially the data on middle-aged subjects. In the present study, an unselected group of normal working subjects has been investigated in order to determine the changes that occur with age in the ability to undertake physical exercise. Since cardiac disease is so prevalent in older subjects, and the resting cardiac output falls with age, particular care has been taken to determine whether the exercise limitation is caused by a failure of the heart to meet the demands placed on it by exertion.

Group Studied

Fifty-four subjects (35 males and 19 females) were investigated. The subjects were classified into three groups according to age: 18 to 34 (group I), 35 to 49 (group II), and 50 to 69 (group III). Each group contained 18 subjects. For the purposes of this study, the sexes were not analyzed separately since they have shown only minimal differences in their responses, and the distribution was not radically different among the groups studied. The subjects were recruited by public advertisement for the most part from employees of the University...
of Michigan. They were all of sedentary occupation, and the groups did not differ in habitual levels of exercise as revealed by a questionnaire. None of the subjects undertook regular competitive sports, and only 15 engaged in strenuous exercise at least once each week. Six of these were from group I, five from group II, and four from group III. None had experienced any major illnesses in the past year or had knowledge of any physical handicap or heart disease. Each was known to have normal blood pressure and also to have had a normal resting 12-lead electrocardiogram. None of the subjects had had previous experience with this type of laboratory test.

**Methods**

The exercise selected for this study was performed on a mechanically braked cycle-ergometer (Monark, Sweden), with the subjects pedaling at a rate of 50 cycles per minute as indicated by a metronome. A progressive exercise test was used: it started at 300 kg/min and increased in steps of 150 kg/min every 4 minutes until the patient felt unable to exercise further. The electrocardiogram was monitored continuously by means of a bipolar lead placed at the anterior axillary line on each side and a ground lead over the sternum.

During exercise, respiratory data were recorded automatically by methods similar to those described by Mostyn and associates\(^1\) (fig. 1). Subjects breathed through a high velocity Rudolph valve, and inspired air volume \(V_i\) was measured by a dry gas meter (Parkinson-Cowan D4) adapted for the electrical recording of the rate of air flow. Expired air passed through a mixing box and drying column, and the fractional concentration \(F_{CO_2}\) was measured by an infrared analyzer (Capnograph, Instrument Associates) and \(FeO_2\) by a recording paramagnetic oxygen analyzer (Beckman, F3). The apparatus was calibrated with gases of known composition before each test, and the output was recorded every 3 to 4 seconds by a Honeywell multipoint recorder. All gas volumes have been reduced to STPD. Pressure measurements from the respiratory valve during exercise showed oscillations not exceeding 3 cm of water at any time.

Systemic arterial pressure was recorded from the brachial artery through an 18 or 19-gauge Teflon needle (Becton-Dickinson). This was connected by approximately 20 cm of polyethylene tubing (PE280) to a Statham strain gauge (P23G), the zero reference level of which was maintained at the sternal angle in both the recumbent and sitting positions. The transducer

**Figure 1**

Apparatus used for the collection of respiratory data.

was calibrated statically before and after each test, and the entire assembly gave a frequency response which was flat from 0 to 17 cycles per second. Mean pressure was obtained by electrical damping of the pressure tracing. Cardiac output was measured by the indicator-dilution technique\(^1\) using a Gilford densitometer. Injection of indocyanine-green (Cardio-Green) (3 mg in 1 ml of fluid) was made through a polyethylene catheter (PE50) which had been passed through a thin-walled 18-gauge needle from the antecubital vein to a point high in the axillary vein. The dye curves were calibrated after each test by the addition of known quantities of dye to aliquots of blood which were then drawn through the densitometer at the same rate as that used for the injection of the initial curves (31.5 ml/min). The hemodynamic data were recorded on a Gilson Polygraph, the servo-channel of which gave a resting dye curve approximately 25 cm in height. Recirculation of dye during the exercise tests and at rest was not evident because the curves had fallen below 30% of their maximum height. Since oxygen consumption was measured during the injection of the dye curves, calculations have been made of the arteriovenous (A-V) oxygen difference using the Fick equation. The peripheral resistance has been calculated by dividing the cardiac output into the mean blood pressure and conversion to dynes cm\(^{-5}\).

**Procedure**

The subjects entered the laboratory at least 1½ hours after a light meal. They completed a questionnaire regarding their usual physical activity and were instructed in the procedure of the
Table 1

Mean ± Standard Error of Cardiopulmonary Data at the Voluntary Maximal Exercise Level in Fifty-four Normal Subjects Grouped According to Age

<table>
<thead>
<tr>
<th>Age group &amp; BSA (m²)</th>
<th>( \dot{V}_{O_2} ) (ml/min)</th>
<th>( V_I ) (L/min)</th>
<th>R</th>
<th>Pulse rate (beats/min)</th>
<th>Arterial blood pressure (mm Hg)</th>
<th>Cardiac output (L/min)</th>
<th>Calculated</th>
<th>( O_2 ) difference (ml/100 ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Systolic</td>
<td>Diastolic</td>
<td>Mean</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>2.0</td>
<td>2172.8</td>
<td>53.8</td>
<td>1.05</td>
<td>169.8</td>
<td></td>
<td></td>
<td>173.3</td>
</tr>
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<td></td>
<td>±0.1</td>
<td>±128.0</td>
<td>±3.28</td>
<td>±0.017</td>
<td>±4.7</td>
<td></td>
<td></td>
<td>±5.22</td>
</tr>
<tr>
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<td>2.0</td>
<td>1638.5**</td>
<td>39.4**</td>
<td>1.02</td>
<td>158.7**</td>
<td></td>
<td></td>
<td>181.4</td>
</tr>
<tr>
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<td>±0.1</td>
<td>±66.7</td>
<td>±2.44</td>
<td>±0.022</td>
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<td></td>
<td>±4.19</td>
</tr>
<tr>
<td>III</td>
<td>2.1</td>
<td>1379.9**</td>
<td>34.5***</td>
<td>1.06</td>
<td>139.6***</td>
<td>202.8**</td>
<td>97.1</td>
<td>135.4*</td>
</tr>
<tr>
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<td>±0.029</td>
<td>±4.74</td>
<td></td>
<td></td>
<td>±6.34</td>
</tr>
</tbody>
</table>

* to *** Significant differences refer to differences from age group I: * = \( P < 0.05 \); ** = \( P < 0.01 \); *** = \( P < 0.001 \).

Abbreviations: BSA = mean body surface area in square meters; \( \dot{V}_{O_2} \) = volume of oxygen per unit of time; \( V_I \) = volume of inspired air; and R = respiratory exchange ratio.
AGE AND HEMODYNAMIC RESPONSE

Cardiac output response to exercise in three age groups. In figures 2 to 7 the level of exercise has been indicated by the oxygen consumption. Mean values (± se) obtained in the resting recumbent position (RR) are given followed by resting sitting (RS) and then curves have been constructed from the data for each subject with increasing oxygen consumption of 200 ml/min. As the exercise test was a progressive one, the number of subjects decreased toward the maximal level. All curves have been drawn to the point at which there were six subjects remaining. Significant differences between the curves of the two older groups as compared to those of the youngest have been indicated by asterisks (*): * = P < 0.05; ** = P < 0.01; *** = P < 0.001.

Exercise. These measurements were made with the Astrup technique.*

Analysis of the data has been made from three main points of view: (1) maximum achieved exercise level, (2) changes in respiratory and cardiovascular parameters with increasing oxygen consumption, and (3), the interpretation of the ECG findings. Throughout, the statistical differences between the youngest and the older two groups have been determined by analysis of variance.

Results

Findings at Maximally Achieved Level of Exercise

The maximum tolerated exercise level as indicated by the level of oxygen consumption diminished with increasing age (table 1), and it was clear during the performance of the tests that the older subjects were less willing to accept, or less capable of accepting, the degree of discomfort tolerated by younger ones.

*Radiometer, Copenhagen, Denmark.

*Circulation, Volume XXXVI, August 1967
Nevertheless, the respiratory exchange ratio (R) in each group of subjects at the point of maximum exercise demonstrates that the degree of anaerobic metabolism was approximately the same and it may be inferred, therefore, that the subjects were well motivated. Likewise, the maximum pulse rate, although lower in the older subjects, was as close (15%) to the maximum levels reported by others\textsuperscript{1, 14} as that of the younger subjects. At the point of maximal effort, the cardiac output was lower in the older subjects, and analysis of the individual data showed that this was a linear decline over the age span ($r = 0.47$, $P < 0.001$). Systolic arterial pressure and total peripheral resistance were higher at the maximum level of exercise, and these were also linear over the age span studied.

None of the 11 subjects tested (six were in the oldest group) showed arterial desaturation at the point of maximum exercise. The mean value for the Pa$_{O_2}$ was 87 mm Hg at rest while sitting on the bicycle and 92 mm Hg at the final load of exercise. The Pa$_{CO_2}$ increased by 2.9 mm Hg and arterial pH fell by 0.08 units, indicative of metabolic acidosis. The vital capacity measurements did not show a decline of more than 200 ml in any subject after exercise; in fact, most subjects showed a small increase after exercise.

**Observations According to Levels of Oxygen Consumption**

The illustrations (figs. 2 to 7) summarize most of the data obtained in the performance of the exercise tests. They give means (± SEM) of the cardiorespiratory data obtained in each age group, at rest in the supine and sitting positions, and during exercise for each increment in oxygen consumption of 200 ml/min.

There were no differences between groups in oxygen consumption in relation to the work loads, and the respiratory data demonstrated that the curve for pulmonary ventila-

**Figure 5**

Changes in respiratory exchange ratio with exercise in three age groups.

**Figure 6**

Effect of exercise on arterial blood pressure in the youngest and the oldest groups of subjects.
AGE AND HEMODYNAMIC RESPONSE

Effect of exercise on the calculated total peripheral resistance in three age groups.

Figure 7

AGE AND HEMODYNAMIC RESPONSE

...tion which increased in a curvilinear fashion up to the maximal load, was practically identical for the three groups. Likewise, there was no difference in the resting values and in the relation between pulse rate and oxygen consumption between groups. The data for these, therefore, have not been given.

As others also have found, the mean cardiac output at rest in the recumbent position was lower in the oldest group. This difference was maintained in the sitting position and at the lower levels of exercise, giving parallel curves of increasing cardiac output with oxygen consumption, but in the two younger groups, there was some evidence of leveling off in the cardiac output response to increasing exercise when the oxygen consumption exceeded 1,000 ml/min (fig. 2). It must be appreciated, in passing, that since the older subjects had a lower resting cardiac output, the increase observed during exercise was proportionately greater than that seen in the youngest group. This has a bearing on the changes in calculated peripheral resistance recorded below.

For the youngest subjects, stroke volume increased with exercise up to oxygen consumption of 800 ml/min and then leveled off as described by others for exercise in the upright position; however, there was a further rise as maximum levels were approached as reported by Chapman and associates. The oldest subjects showed a progressive increase in stroke volume up to an oxygen consumption of 1,200 ml/min which was their maximum level. The middle group showed the same general increase with exercise and subsequent leveling off, but the leveling off was at a greater level of oxygen consumption than that of the youngest group (fig. 3).

Since there were no differences between groups in oxygen consumption and heart rate with exercise, the calculated A-V oxygen difference and stroke volume reflected the differences in cardiac output. The A-V oxygen difference at rest was greater in the older subjects (fig. 4). For all subjects it increased with progressive exercise but leveled off as the maximum was approached.

The greatest change in respiratory exchange ratio (R) at all levels of exercise was in the oldest group; the middle and the youngest age groups were identical up to oxygen consumption of 800 ml/min; thereafter, there was a greater increase in R in the middle-aged group (fig. 5). The variability in the data, however, does not allow a demonstration of statistical significance at any level of exercise, but the data are given here to illustrate the trends with increasing exercise in the three age groups.

Though the change in cardiac output with exercise appeared to be approximately the same for the three groups, the same could not be said for blood pressure. At rest in the recumbent position, the diastolic blood pressure was alike in the three groups and the systolic was slightly higher in the oldest group. On assumption of the sitting position on the bicycle, the rise in both systolic and diastolic pressures was greater for the oldest group than for the youngest (fig. 6). With exercise, the rise in systolic pressure was greater in the older subjects than in the younger. For the diastolic pressure, there was a small rise in pressure on exercise, but this was approximately the same for the three...
age groups. The rise in systolic pressure on exercise has been reported by the earliest workers who used indirect methods of measuring pressure and by others who used direct recordings. For the younger subjects, our results are close to those reported by Grimby,8 though they are greater than those found by Holmgren in physically fit young men. For the older subjects our findings concur with those of Strandell.11

Calculated peripheral resistance was higher at rest in the older subjects, and the differences increased substantially on sitting. With exercise, however, the disproportionate increase in cardiac output in the older groups more than compensated for the greater rise in mean pressure so that the difference in peripheral resistance between the groups progressively diminished (fig. 7).

Electrocardiographic Abnormalities

No serious electrocardiographic abnormalities were seen in this study. Minor arrhythmias, mainly ventricular extrasystoles, emerged during exercise in six subjects, and junctional ST depression was seen in seven. These were not considered to be of sufficient importance to merit further study. Five subjects showed ischemic ST depression exceeding 0.1 mv. Two of these were seen in age group II and three in group III. When their individual data for \( V_1 \), heart rate, and cardiac output were compared with those of the others in their age groups, no deviations were observed, and their maximal voluntary exercise level was close to the mean for their group.

Discussion

Aging is a complex process involving subtle changes in function of many systems, but in man the most frequent failure is in the cardiovascular system. It is important, therefore, to determine the possible mechanisms which lead to the decline in the ability to exercise with age and, in particular, to determine whether these mechanisms are of cardiac origin.

The maximum voluntary level of oxygen consumption obtained by the tests used in this study is, of course, not equivalent to the true maximum aerobic capacity, but it does indicate the level to which these subjects were willing to exercise. Since they were all volunteers, their motivation was good, and the changes in \( R \) and the maximum pulse rate indicate that the level of motivation in the three age groups was approximately the same. It should be noted that the maximum voluntary oxygen consumption in all groups was much lower than the levels to be expected from subjects in a reasonably fit condition. The maximum values are, however, very close to those reported by Bruce and associates who also used a progressive exercise test.

The lower cardiac output in the older subjects is unexplained. It is not related to a lower metabolic rate, and the increase with oxygen consumption appears to be normal. Although cardiac output and stroke volume are lower in the older subjects and the maximal values are also lower, the limitation in oxygen uptake cannot be attributed to cardiac disability, since there is no evidence of a leveling off in the response at the higher grades of exercise. Observations similar to these have also been made by Strandell, although others, using the nitrous oxide method, have found a higher cardiac output during exercise in older subjects. For the oldest subjects, likewise, the A-V oxygen difference did not increase excessively as they approached their maximum exercise; in fact, it leveled off. The cardiac response to exercise, therefore, appears to be adequate. The leveling off and the low maximum A-V oxygen difference indicate either a poor distribution of blood flow or an inability of the muscles to extract oxygen. The early rise in the respiratory exchange ratio in older subjects would be consistent with this. The absence of change in vital capacity and arterial oxygen saturation, moreover, confirm the adequacy of the respiratory system at the point of maximum exercise. Likewise, the fact that the ventilatory response to exercise was the same in all groups speaks against
excessive respiratory stimulation in older subjects, such as might be expected with early pulmonary congestion. The present evidence, therefore, together with the findings of others strongly suggests that the cardiac or respiratory systems are not responsible for the decline in the capacity for physical work with age. Since motivation of each group appeared to be adequate, the cause of the limitation should be sought either in the central nervous system or in the peripheral tissues. It may well be that the ability of the muscles to extract oxygen may be an important factor limiting oxygen uptake.

Looking at the overall circulation as reflected in the calculated peripheral resistance, older subjects undergo greater degrees of vasodilatation than younger ones. The reduction in resistance must be, in part, a passive reflection of the greater rise in mean arterial pressure with exercise, but inefficiency in the distribution of blood may also play a part. Alternatively, muscle weakness in older subjects may require the use of larger groups of muscle fibers and hence may produce active dilatation in a wider vascular bed.

In conclusion, therefore, the gradual decline which occurs with age in the capacity to undertake strenuous physical exercise does not appear to result from cardiac or pulmonary disability, and there is no evidence that these systems are maximally stressed during exercise in the type of test used in this study. The control of pulmonary ventilation and of the heart is unaffected by age apart from the fact that the cardiac output is set at a lower level in relation to oxygen consumption in the older subjects. Local circulatory or neuromuscular factors, therefore, must be sought as responsible for the decline in ability to exercise.

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