Comparative Exercise-Cardiorespiratory Performance of Normal Men in the Third, Fourth, and Fifth Decades of Life

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SUMMARY
The circulatory and respiratory responses to five levels of treadmill exercise were recorded for 75 normal males divided equally in the age groups 20 to 29, 30 to 39, and 40 to 49 years. Parameters studied included heart rate, cardiac output, stroke volume, intra-arterial blood pressure, minute ventilatory volume, oxygen uptake, and carbon dioxide elimination. Values for peripheral vascular resistance, left ventricular work, and stroke work indices were calculated. Intergroup and intragroup differences were analyzed by modified covariance technique using oxygen uptake per square meter of body surface area as the concomitant variable reflecting a specific midrange work level. Significant differences were observed between groups in cardiac output, stroke volume, systolic, diastolic, and mean arterial blood pressure as well as pressure-related variables with regard to absolute values and trend over the exercise spectrum. The results indicate that normal untrained males in the fourth and fifth decades of life react to moderate and heavy upright exercise with statistically significant systemic pressure elevations as compared to 20-year-olds. A tendency toward initially high cardiac output and stroke volume during light exercise was observed in the older men. Relatively small subsequent increments in cardiac output with resultant low absolute values during heavier work were also characteristic for this group as reflected in their decreasing stroke output at submaximal loads.

Additional Indexing Words:
Aging and exercise Cardiac output Exercise cardiodynamics
Intra-arterial pressure Treadmill exercise

During the past 30 years numerous isolated data have been published comparing the exercise responses of young and old, supposedly normal men. Only recently1-5 have integrated hemodynamic studies in fairly broad age categories described alterations of circulatory and respiratory responses to exercise associated with aging. The present study expands to a three decade interval this laboratory’s observations of age-related exercise performance with uniform and systematic testing procedure. For more meaningful interpretation of intergroup and individual intragroup differences, results have been analyzed by the usual statistical methods and also by a refined variance analysis technique and age-correlated polynomial curve

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fitting. Within the inherent inadequacies of a cross-sectional study of this type, the data define significant differences in circulatory parameters between the ages of 20 and 50 years.

Methods

Groups I (age range, 20 to 29 years), II (30 to 39 years), and III (40 to 49 years) each comprised 25 male volunteers. No strict selection was made on the basis of previous or current exercise and dietary habits or body size. However, none of the subjects was obese as judged from height and weight. Members of group I, although obviously more active physically than their older counterparts, were in no sense "athletes." Analysis of the heart rates, oxygen uptake, and other aspects in the three groups, and comparison of these factors with data obtained on true, highly trained athletes\(^6\) indicate a random subject selection in regard to state of training for groups I, II, and III. Therefore, the differences in exercise response between groups reported here are not related to a high degree of physical conditioning in one group.

Composition of group I was primarily university undergraduate and graduate students and hospital personnel. Groups II and III were largely composed of faculty members and businessmen. A monetary incentive was offered all participants, but its payment was not dependent upon successful completion of any prescribed amount of work.

Medical histories and physical examinations were obtained on all subjects. Candidates with any previous history or current physical findings which conceivably could affect exercise performance were excluded. Although some degree of pre-selection is implicit in arbitrary setting of allowable upper limits for resting systolic and diastolic pressure, particularly in older individuals, an upper limit of 150/90 mm Hg was applied for selection of the older subjects.\(^8\)

Detailed methodology has been presented in earlier reports.\(^9\)\(^,\)\(^10\) Cardiac output was estimated by dye-dilution technique using both the Waters 250-A and 300 densitometers and indocyanine green (Cardio-Green). The right forearm rested passively on a support at waist level while the left arm was allowed to move normally at the subject's side. At no time was a subject permitted to support himself by grasping the treadmill siderails. Intra-arterial pressure was measured with a Statham P23Db transducer and this signal was amplified in the Electronics for Medicine DR-8 recorder. Minute volume of ventilation, oxygen uptake, carbon dioxide elimination, and oxygen ventilatory equivalent were measured and calculated by standard methods from expired gas collections. Peripheral vascular resistance was estimated from cardiac output and mean arterial pressure. Left ventricular work index and stroke work index were calculated as the products of cardiac and stroke indices, respectively, mean arterial pressure, and the constant 13.6/1000.

Measurement and calculation of these parameters were made with each subject recumbent at rest, standing at rest, walking at 3 miles per hour on the level treadmill and at treadmill elevations of 4\(^\circ\), 8\(^\circ\), 12\(^\circ\), and 14\(^\circ\). The exercise program was thus identical for all subjects. Determinations and collections were initiated after 4 minutes of exercise for the level, 4\(^\circ\), and 8\(^\circ\) walks, and after 2 to 3 minutes for the 12\(^\circ\) and 14\(^\circ\) walks. Between exercise periods subjects were allowed to rest sitting down until their heart rates approximated the original resting recumbent values, thus avoiding variations in results secondary to prolonged work periods.\(^11\)\(^,\)\(^12\)

Statistical Analysis

For each variable group mean, standard deviation of the mean and standard error were calculated according to accepted statistical methods. Intergroup mean differences were tested for significance by standard t-tests. Adherence to the following P values was followed: \(P < 0.05 = \text{probably significant}; \quad < 0.01 = \text{significant}; \quad < 0.001 = \text{highly significant.} \) To define more exactly significant intergroup differences taking cognizance of intragroup variations for all levels of exercise, a modified covariance analysis was applied to the work data. Performance differences between groups were tested with oxygen uptake per square meter of body surface area as concomitant variable. Statistical significance of these differences is expressed on the basis of a group's rate of variable change (slope) for the entire exercise spectrum and also as the absolute group mean value at the selected analysis point of 900 ml/min/m\(^2\) of oxygen uptake (intercept). A complete description of the theoretical basis for this analysis is provided in "Appendix I.”

All statistical examination of data was carried out on an IBM 1130 Computing System. The graphs depicting trends in variables with age were plotted by a California Computer Products CalComp Plotter.

Results

Mean values and ranges for subjects' age, height, weight, and body surface area are presented in table 1. It should be noted that the group mean ages are almost exactly
Anthropometric Data

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Age (yr)</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
<th>BSA (m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I: n = 25</td>
<td>Mean</td>
<td>23.2</td>
<td>176.3</td>
<td>77.2</td>
<td>1.92</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>2.2</td>
<td>8.9</td>
<td>9.2</td>
<td>0.14</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>(20-29)</td>
<td>(145-188)</td>
<td>(58-94)</td>
<td>(1.59-2.12)</td>
</tr>
<tr>
<td>Group II: n = 25</td>
<td>Mean</td>
<td>33.1</td>
<td>176.1</td>
<td>79.6</td>
<td>1.96</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>2.7</td>
<td>8.6</td>
<td>9.3</td>
<td>0.15</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>(30-39)</td>
<td>(159-200)</td>
<td>(66-97)</td>
<td>(1.70-2.28)</td>
</tr>
<tr>
<td>Group III: n = 25</td>
<td>Mean</td>
<td>44.0</td>
<td>173.8</td>
<td>74.2</td>
<td>1.88</td>
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<td></td>
<td>SD</td>
<td>2.4</td>
<td>6.7</td>
<td>8.1</td>
<td>0.13</td>
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<tr>
<td></td>
<td>Range</td>
<td>(40-48)</td>
<td>(161-188)</td>
<td>(62-92)</td>
<td>(1.69-2.13)</td>
</tr>
</tbody>
</table>

decade-separated and that the physical characteristics are closely matched. The mean body surface area of group III is lower than that of the other groups, but not significantly so. Because of the close agreement in weight, the mean work load performed at each exercise level was comparable for all groups. The comparison of mean values for all parameters measured at rest and during exercise (table 2) can, therefore, be made with the realization that physical characteristics and work loads for all groups are nearly uniform.

With regard to the ability of individual subjects to perform the highest work loads, there was a considerable variation between groups. At the 12° treadmill elevation 24 members of both groups I and II and all members of group III successfully completed the exercise. However, at the 14° treadmill elevation all men in group I, 19 in group II, but only 15 in group III were able to exercise. The disparity in ability to perform the highest work load, therefore, means that the group III men completing the full study represent a fairly highly selected group, comparable in exercise ability to the younger men and, as seen from their responses at this work load, indistinguishable from the younger men. Had the other 10 older subjects been pushed to the highest load, it is almost certain that responses of group III as a whole would be significantly different from those listed in table 2 under 14°.

Heart rate was essentially uniform for all three groups while recumbent, resting, and at work loads up to 900 kg-m/min. Group III men evidenced a highly significant lower rate while standing at rest, however, and at the two highest exercise levels.

Although little variation is apparent in level-by-level group means for cardiac output (table 2), analysis of individual performances reveals a distinctly different trend in the oldest subjects. Thus, 16 group III men had outputs of 14 L/min or greater at the lowest work load, and 11 of these did not significantly augment the output value which they had attained at level or 4° treadmill walking. This contrasts sharply with the vast majority of subjects in groups I and II who evidenced stepwise output increments with increasing exercise.

As mentioned, only 15 of the 40-to-49-year-old subjects completed the greatest work load. Examination of this subgroup's responses as well as those of the 10 men of the same age who did not perform the 14° treadmill walk reveals two markedly different trends across the entire exercise spectrum. The latter subjects demonstrated relatively high cardiac output at the start of exercise and then maintained this flow level basically unchanged throughout. Six of the mean completing all exercise also had initially high outputs, but they were able to increase this with progressive exertion, although not as adequately as do the younger groups.

The individual 12° results showed that
### Table 2

<table>
<thead>
<tr>
<th>Exercise Level</th>
<th>Group</th>
<th>Resting</th>
<th>Recumbent</th>
<th>Standing</th>
<th>Resting</th>
<th>Exercise 4°</th>
<th>Exercise 8°</th>
<th>Exercise 12°</th>
<th>Exercise 14°</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>HR (bpm)</td>
<td>CO (L/min)</td>
<td>CL (L/min)</td>
<td>SV (L/min)</td>
<td>CO (mL/min/m²)</td>
<td>CL (mL/min/m²)</td>
<td>SV (mL/min/m²)</td>
<td>CO (mL/min/m²)</td>
</tr>
<tr>
<td></td>
<td>I</td>
<td>72</td>
<td>8.03</td>
<td>4.20</td>
<td>12.00</td>
<td>3.40</td>
<td>2.40</td>
<td>1.40</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>70</td>
<td>7.76</td>
<td>3.90</td>
<td>9.00</td>
<td>3.20</td>
<td>2.40</td>
<td>1.40</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>74</td>
<td>8.63</td>
<td>4.30</td>
<td>10.00</td>
<td>3.50</td>
<td>2.50</td>
<td>1.50</td>
<td>1.10</td>
</tr>
</tbody>
</table>

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**Abbreviations:**
- HR = heart rate
- CO = cardiac output
- CL = cardiac index
- SV = stroke volume
- MV = minute volume of ventilation
- VO₂ = oxygen uptake
- CO₂ = carbon dioxide elimination
- WL = work load
- PVR = peripheral vascular resistance
- O₂V = oxygen ventilatory equivalent
- LVWI = left ventricular stroke work index
- RVWI = right ventricular stroke work index
the subgroup of 10 men had a low mean output value of 17.85 L/min as opposed to 19.37 L/min for their 15 group III partners and 22.57 and 20.52 L/min for groups I and II, respectively. The mean cardiac output for group III as a whole was also different to a highly significant degree from that of all younger subjects at 12°. At 8° the subgroup differences were: 18.74 L/min for the nonfinishers (identical to group II) and 19.49 L/min for the others (identical to group I). For the level and 4° treadmill walks the smaller subgroup had elevated outputs compared to younger men.

Therefore, the present sample of 25 men, 40-to-49-years old, clearly exhibits two types of cardiac output response to exercise: (1) high initial output at minimal exercise with maintenance of essentially the same level up to heavy work load; and (2) initial high output with increments at each added load, but with comparatively low output at highest load. The overall net effect for the oldest group, as mirrored in the mean values, is therefore a relatively high cardiac output with low exercise, a midrange value comparable to the younger groups, and a lower output during heavy work. In addition, only 60% of group III could finish the entire exercise program, and even this subgroup had reduced cardiac output level at highest load. Since the midrange value for oxygen uptake of 900 ml/min/m² was chosen for statistical analysis and corresponds to the point at which all groups had closely similar cardiac output values, no significant intergroup differences in cardiac output intercept at this point were seen. Similarly, group slopes were not significantly at variance statistically due at least partially to the influence of the selected nature of group III subjects able to perform 14° exercise.

Correlations of cardiac output with other physiological variables are shown in figures 1 and 2. Regressions of output on oxygen uptake for groups I and II show the same trend during exercise but at different flow levels. Group III is characterized by its different trend compared to the other groups.

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**Figure 1**

Regression of cardiac output on oxygen uptake for subjects aged 20 to 29 years (I), 30 to 39 years (II), and 40 to 49 years (III).

**Figure 2**

Relationship between exercise responses of intra-arterial blood pressure and cardiac output in different age groups. Initial values are for standing at rest.
It may also be seen from the groups’ mean values at 12° and 14° (table 2) that the older men are not only unable to maintain cardiac output but have lower oxygen uptake than groups I and II. The large group III reductions in both these parameters are such, however, that cardiac output per liter of oxygen uptake is almost identical to that of the younger men. When related to systolic, diastolic, and mean blood pressure, cardiac output shows a similar clear differentiation of groups (fig. 2). It is obvious that for any given level of cardiac output, group II is performing at higher levels of systolic, diastolic, and mean arterial pressure than group I, and that this is also true for group III compared with group II. The tendency of the oldest men to achieve relatively high cardiac output during minimal stress but comparatively lower output at high loads is again well illustrated.

Figure 3, employing heart rate as an indicator of exercise severity, demonstrates that all three groups maintain approximately the same level of stroke volume following initiation of treadmill walking. The data indicate that group III manifests a slight but gradual decline of stroke volume for work beyond the 4° treadmill level, culminating in a marked fall for 12° exercise. The subsequent rise at 14° is again undoubtedly related to the group’s selected composition at this work load. With the exception of group III’s marked drop, all groups maintained stroke volume within a 10% range of their respective highest exercise values, and the maximal mean exercise variation of this variable was only 14 ml. For resting and early exercise determinations group III stroke volume was significantly higher than that of the other men according to t-testing. At 8° and 12° exercise, the stroke volume of the oldest group was significantly lower than that of the youngest group, and at 12° also lower than that of the 30 to 40-year-olds.

The most significant intergroup differences in the present study are those of intra-arterial blood pressure and pressure-related parameters. Three of the oldest men developed exordial diastolic hypertension (>90 mm Hg) compared to only one subject in the 30-to-40-year-old group and none of the youngest subjects. For systolic, diastolic, and mean pressures group II had higher values than group I, and group III higher than group II. Although the former differences were greater, a general stepwise progression of pressures with age is seen (fig. 4). By the covariance analysis employed, it is apparent that the
Mean intra-arterial pressure related to age group and exercise level.

The trend (slope) of all three pressure increases is the same for groups II and III but both are different from group I. This is also the case for the absolute systolic pressure at a common oxygen uptake of 900 ml/min/m² (intercept). All intergroup exercise differences in absolute values of diastolic and mean pressures were highly significant according to either covariance analysis or t-test. Systolic pressure variances between groups I and III were also significant throughout, and between groups II and III standing at rest, during mild exercise, and at 14°.

The mean arterial pressure variances are graphically illustrated in figure 5. Also seen here is the fact that the oldest men, in contrast to those younger, did not have a pressure drop standing at rest, and this is correlated with a significantly lower standing heart rate for group III. Up to and including 12° exercise, each group evidenced a general widening of arterial pulse pressure, but no further increase was seen at 14°. All ages had similar values for moderate exertion, the older sub-
III's decline in stroke work at 12° and subsequent rise at 14° reflect the apparent heterogeneity of the group and its exercise capabilities. The group response rates for stroke work were not significantly different, but all three groups were statistically distinguishable with regard to mean values.

Although a clear delineation of ages on the basis of stroke work indices was obvious, the same cannot be said for left ventricular work index. Group I does differ from group III regarding mean values at upper work rates, but other significant intergroup variances are lacking in either this respect or relative to response trends.

Examination of respiratory parameters indicates that the two older groups tend to develop larger minute volumes of ventilation for a given load. The 30- to 40-year-olds did not differ significantly from the younger or older men, but groups III and I were obviously different. In terms of oxygen uptake, the two older groups during early work were performing at an almost identical level which, however, was greater than that of the youngest subjects. Group III then exhibited comparatively smaller increments of uptake at 8° exercise and above. By virtue of these simultaneous changes in volume of ventilation and oxygen extraction from this volume, oxygen ventilatory equivalent becomes progressively higher with advancing age at any given load for all but mildest exercise. The responses of carbon dioxide elimination closely parallel those of oxygen uptake as is reflected in the fact that respiratory quotients for all three groups are almost identical at each exercise point.

Figure 8 presents the trends with age of six variables for resting and exercise measurements of this study. Four-year age intervals from 20 to 48 were selected for data averaging at each point. The curves represent the best-fit lines of a fifth degree polynomial equation for each parameter at each exercise level.

Discussion

As has been emphasized before,13, 14 cross-sectional studies of age-related changes in

![Figure 7](image)

*Figure 7*

Relationship of left ventricular stroke work to heart rate at rest and with increasing work loads.

- objects developing comparatively elevated values at 8° and above.
- The decade-to-decade "trepp" effect of pressure elevation is reflected in the increasing level with age of peripheral vascular resistance at a given exercise intensity. As seen in figure 6, there was no significant difference in the group trends, that is, the response rate of the three groups was the same and independent of work load. However, significance was established for the distinction in means between group I and the other men at the selected midrange exercise level, and by t-test all intergroup differences were highly significant. Both groups II and III appeared to approach an asymptote of resistance starting at the 8° treadmill elevation, little significant change occurring beyond this point.

- Due to the similarity of group mean stroke volumes but markedly disparate corresponding mean arterial pressures, a clear separation of age categories is obtained from values for stroke work indices (fig. 7). Each group attains a relatively stable stroke work at lowest exercise which is maintained throughout subsequent work loading. Once again, group
Figure 8
Age-related trends of cardiac output, stroke volume, arterial pressure, and left ventricular work at rest and during five levels of exercise. R, S, L, and so forth as in figure 4.

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physiological functions are not ideal. Despite random selection of subjects, those of older age necessarily represent a mortality-selected group who have maintained relatively good clinical health despite advancing years. Also, it is impossible to delineate whether a recorded functional decline in any one individual is due to structural changes or what has been termed the aging trend and its related alterations. Ideally, large numbers of healthy subjects should be examined longitudinally, that is, over periods of many years. With perhaps one notable exception, this has not proved feasible in the past, and relatively sparse information has been gained from such studies of exercise responses. Indeed, most cross-sectional studies have also used small subject groups without strict regard to age categorization, work loads have often been nonuniform, and until relatively recently the effects of body position have been largely ignored. Surprisingly few studies have made simultaneous observations of many interrelated parameters. The most recent of these employed both male and female subjects reacting to uninterrupted, progressive work loading which is known to produce significant time-related alterations in physiological responses.

In examining the 75 men reported on herein, we have attempted to illuminate some of the many problems still existing in exercise physiology with regard to aging trends. The investigation was designed to compare reactions of several interrelated variables in a significant number of men performing a standardized program of work based on treadmill walking. We have done this although fully cognizant of a cross-sectional study’s theoretical deficiencies, such as the fact that a 50-year-old man may perform identically to a 20-year-old one. Emphasis has, therefore, been directed away from sole reliance on group mean values by analyzing individual and subgroup responses and through covariance statistical application. The individualized nature of the analysis is stressed in the age trend graphs of figure 8. To our knowledge, this is the first available illustration of age-associated changes in physiological responses to exercise covering three age decades and with significant numbers of subjects performing standardized exercise.

Although the three groups had similar heart rates at submaximal work, the well-known and oft-described lower exercising pulse rates in older men performing heavy work became evident in 40-year-old men at loads of 1,300 and 1,500 kg/m/min. There is little doubt that the majority of these subjects were performing maximal work at the 12° and 14° treadmill elevations, as attested to by the completion rate for the latter exercise and also as judged by oxygen uptake at these levels. The ultimate effect of this may be appreciated in measurements of flow when the lower heart rate and stroke volumes result in significantly decreased cardiac output. The physiological factors underlying this progressive decrease of heart rate with age are far from fully understood, but the practical implications seem clear. Foremost of these is the realization that fitness testing of middle-aged and older men cannot be conducted or evaluated employing standards, such as the physical working capacity at heart rate 170/min, which have been developed from observations in young subjects.

In the oldest subjects (group III) a definite differentiation was obtained from the younger men with regard to cardiac output, not only during strenuous exertion but also during minimal and moderate physical effort. This is clear from figures 1 and 2 where the tendency toward initially higher output and subsequent considerably lower output characterizes the response of the oldest subjects during progressive work loading. In addition, only 60% of 40-year-olds completed the full exercise program, thus once more substantiating the decline of maximal work possible in older men.

Expressed as liters per liter of oxygen uptake, cardiac output differs, although not greatly, from group to group in the present subjects. It is probable that the 30-year age span represented here embodies performance capabilities antedating establishment of a
truly hypokinetic circulatory response. However, cardiac output differences are manifest and may well represent the initial evidence for such hypokinesis. This is certainly suggested by the asymptotic cardiac output response of group III at treadmill levels 8°, 12°, and 14°. It is also consistent with the finding that this older group actually comprises two distinct subgroups: (1) those subjects responding to minimal exercise with relatively high cardiac output and very little subsequent augmentation during heavy work, and (2) those men with initially high output which is augmented but to a lesser degree than that of the younger men. It is of particular interest that the former type of cardiac output response to exercise has been recorded in several young labile hypertensives.24

Prior studies25-30 have recorded that resting recumbent cardiac output declines at the rate of approximately 1% per year and that the absolute level of exercising output will gradually decrease with age for any given work load. We have not been able to define such resting decrements over three decades, either in recumbent or standing resting positions. Likewise, as has been pointed out, cardiac output was generally higher at low exercise levels in our oldest men, falling off only at quite heavy exertion. It has also previously been suggested15 that exercise causes comparable increases in cardiac output regardless of age when output is viewed as a function of the corresponding oxygen uptake. This has been confirmed in studies comparing old with young men,4 but the results in the present age ranges are not entirely in agreement (fig. 1). We cannot definitely state the reason for this, but it may well lie in the fact that there are marked differences in physiological responses to stress dependent on the type of ergometry employed.31-34 Most earlier investigations giving data which can be compared with present results have been performed with bicycling, and as has been pointed out,25 a significant increase in the muscle mass activated will take place at high work loads on a bicycle. This undoubtedly affects oxygen intake and cannot be strictly comparable to treadmill walking where participation of trunk, shoulder, and arm musculature is not a major factor.

Only two previous reports35, 36 have defined the tendency toward a greater exercising cardiac output with age. Despite the possibility of methodological error in the nitrous oxide rebreathing technique employed37 and large standard deviations of group mean values, the study of Becklake and associates35 involved three work loads up to 550 kg-m/min, which are comparable to our own mild-to-moderate exertion. In examination of middle-aged athletes Grimby and associates36 also reported high cardiac output values for work of 600 kg-m/min, but these men also developed large output during maximal exertion. National differences in exercise habits may partially explain discrepancies in published observations, Scandinavians of most ages being athletically inclined. It is tempting to speculate that in these middle-aged sedentary Americans such high output response to relatively moderate exertion represents an "overshoot" phenomenon and reflects an uneconomical tendency in terms of cardiac and stroke work. In mechanical terms this could be characterized as an undamped response of the physiological servo-systems subserving exercise needs. Although the mean resting cardiac output of the group III subgroup not finishing all exercise was considerably higher than that of the other 15 men of this age (9.24 L/min versus 8.22 L/min), there is no evidence from heart rate or oxygen uptake to suggest that apprehension was a factor contributing to this finding. It is most unlikely that these men represent examples of the "hyperkinetic heart syndrome"38 since all subjects were clinically normal without symptoms, murmurs, or cardiac enlargement. More important, no manifestations of an "enhanced cardiac contractility" were present as witnessed by normal values for ejection time and ejection rate.

Transition from standing rest to exertion involved an approximate doubling of stroke volume at all ages, but thereafter little mean intergroup or intragroup variation exists until

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high degrees of exercise are reached. At this point the older men evidence significant and rapid falloffs which are consistent with previous observations. Group mean values, however, obscure the fact that the relative contributions of stroke volume and heart rate to cardiac output increases during exercise can vary considerably from subject to subject. Although each group contained subjects who at submaximal loads increased either rate or stroke volume or both, the majority of men in this study increased output wholly through elevation of heart rate. The evidence, therefore, confirms that augmentation of stroke volume is neither a constant nor a necessary factor in the cardiac output adaptation to exercise.

General agreement exists that advancing age may be equated with rising blood pressure levels at a given degree of exertion. Resting pressure data have revealed that age changes involve a greater rate of systolic increase than diastolic with a resultant widening of pulse pressure. The present results indicate decade-by-decade increments of systolic, diastolic, and mean pressures at all work loads, the absolute and percentage increases being approximately equal for all ages. Pulse pressure was also significantly higher in the older men when performing strenuous exercise. Although no significant difference in the pressure response trends of 30- and 40-year-old subjects was observed, the latter exhibited uniformly elevated values across the exercise spectrum (fig. 2).

Despite recognized differences in centrally and peripherally recorded arterial systolic pressure, it is clear that the present three groups are distinctly separate population samples on the basis of pressure responses to exercise. These age-related alterations may be attributed to "decreased volume distensibility of central vessels," an associated partial obliteration of peripheral vascular beds with resultant increase of peripheral resistance, and a relatively small decline in flow. Since pulmonary artery wedge and right ventricular end-diastolic pressures have been found elevated in old men, decreased compliance of the heart itself has also been implicated as part of the related aging process. The net result is, therefore, an increase in ventricular work and stroke work. Since this represents "pressure work" rather than kinetic or "flow work," it is very expensive in terms of energy consumption.

With regard to heart rate, cardiac output, and arterial pressure, the group III reaction to standing at rest is of particular interest. It is essential to differentiate between passive tilting studies and having a subject stand, but certain similarities of response in the two conditions exist. The tachycardia subsequent to standing is less pronounced in the oldest men, and conversely, fall of cardiac output is considerably greater. Similar responses to tilting have been recorded. Stroke volume decrement is, therefore, much the same from 20 to 50 years. However, blood pressure changes are quite different in tilting versus standing and vary according to age. The oldest men in our study maintained virtually identical pressure while standing compared to the recumbent measurements, while those in groups I and II had significant decreases. Age differences were reflected in increasingly elevated peripheral vascular resistance for older subjects. Since measurements of these parameters involving the extent of change and the restitution to original recumbent levels are often used as indicators of circulatory "competency," the present findings are pertinent.

Age-related differences in respiratory variables were generally not significant. On performing comparable moderate exercise, older men tend to have larger minute volumes of ventilation but also slightly higher oxygen uptake than young subjects. The relatively greater hyperventilation, however, results in increased oxygen ventilatory equivalents for the more elderly. With heavy work loading the disparity of minute ventilation persists, but older subjects' oxygen uptake increases are not as great. Since respiratory quotient changes in each group are comparable, parallel alterations of carbon dioxide elimination.
are also taking place. These observations correlate well with others made during submaximal exercise, and indicate that deficiencies of ventilation or oxygen uptake are not present at these ages. There is thus no reason to suspect that these functions are influencing the subjects' exercise capabilities or the hemodynamic results.

Thus, determinations of flow, resistance, pressure, and cardiac work indices have defined the primary reactions to aging in this investigation. To maintain adequate flow and have the oxygen pump satisfy peripheral exercise needs, the aging organism compromises by augmenting pressure and the work performed against a steadily increasing resistance (fig. 8). Various adjustments in vascular capacitance and resistance circuits, neural and neurohumoral mechanisms, and cardiac mechanical characteristics accommodate to this end. What finally limits maximal cardiac output at any age or for any degree of physical exertion is still undefined. Present evidence indicates that study of central and not peripheral mechanisms will ultimately provide the solution.

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Appendix I

Analysis of Covariance Technique

By David B. Hill, Ph.D.*

Only data from exercise measurements were examined. No statistical procedures were applied to the resting recumbent or standing resting data due to the inter-subject variability observed at these levels. It was felt that this variability is the result of factors such as apprehension which were not of interest in this study.

The following technique was employed for the exercise results: let $x_{ijkl}$ be the measurement of the $j^{th}$ variable at the $j^{th}$ exercise level on the $k^{th}$ subject in group I. Consider the linear model

$$x_{ijkl} = \alpha_{il} + \beta_{il} (W_{jkl} - W^o) + e_{ijkl}$$

where $W$ is a variable directly related to the work done at level $j$ by the subject. The model suggests that the observation $x_{ijkl}$ is composed of a constant term $\alpha_{il}$ which is dependent on the particular variable in question and the group to which the subject belongs; a linear term $\beta_{il} (W_{jkl} - W^o)$, where $\beta_{il}$ is the slope and is again a function of the variable and group, $W_{jkl}$ is related to the work done by subject $k$ at level $j$, and $W^o$ is some fixed value of the quantity $W$; $e_{ijkl}$ is a random term assumed to be $N(0, \sigma^2)$.

For each variable of interest there are then two hypotheses of major import. They are:

1. $\alpha_{i1} = \alpha_{i2} = \alpha_{i3}$

that is, the group means for variable $i$ at $W^o$ are equal, and

2. $\beta_{i1} = \beta_{i2} = \beta_{i3}$

that is, the rate of change of variable $i$ with respect to work load is the same for all groups.

The figures 9 to 11 illustrate various ways in which these hypotheses may be violated.

Case 1: Hypothesis (1) is false; hypothesis (2) holds true.

Case 2: Hypothesis (1) is true; hypothesis (2) is violated.

Case 3: Neither hypothesis holds true.

The interpretation of the various cases is clear. In case 1 there is a difference between groups which is not exercise dependent. In case 2 the groups are equivalent at a moderate exercise level but exhibit different response rates to the exercise regimen, and in case 3 the groups are different with respect to variable $i$ at this moderate level, and the degree of difference is a function of the exercise level.

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Estimates of $\alpha_{il}$ and $\beta_{il}$ were obtained by standard regression techniques for each subject and each variable of interest. Denoting these individual estimates by $\hat{\alpha}_{ik}$ and $\hat{\beta}_{ik}$, respectively (that is, $\hat{\alpha}_{ik}$ is the estimator of $\alpha_{il}$ obtained by considering the measurements on subject $k$), the estimators $\hat{\alpha}_{il}$ and $\hat{\beta}_{il}$ are obtained as

$$
\hat{\alpha}_{il} = \frac{1}{25} \sum_{k=1}^{25} \hat{\alpha}_{ik} \quad \text{and} \quad \hat{\beta}_{il} = \frac{1}{25} \sum_{k=1}^{25} \hat{\beta}_{ik}.
$$

Estimates of the variance of $\hat{\alpha}_{il}$ and $\hat{\beta}_{il}$ are obtained in standard fashion from the $\hat{\alpha}_{ik}$ and $\hat{\beta}_{ik}$ observations. For all variables under consideration the homoskedasticity assumption appeared well justified.

Hypothesis (1) and (2) were then tested by Tukey's procedure\textsuperscript{43} that is, the range of the three estimated values of group intercept (or slope) was compared with a pooled variance estimator. The resulting statistic had the "Studentized" range distribution and hence significance levels of intergroup differences could easily be obtained.

References


In order to proceed with the analysis, a meaningful variable $W$ must be selected. Previous studies\textsuperscript{6, 7, 9-11} show that oxygen uptake is highly correlated with workload, and a preliminary analysis of the data reported here indicated that oxygen uptake/m$^2$ of body surface area has a surprisingly consistent range over all subjects in the study. Hence, $W_{jk}$ is defined as oxygen uptake/m$^2$ of body surface area for subject $k$ of group $l$ at level $j$. $W^0$ was taken at 900 ml/min/m$^2$, a figure which closely approximates the midrange value of $W$ for all subjects.


Spurs That Force Us Toward Medicine and Specialization

Most of us engaging in the practice of a profession never analyze our reasons for selecting it. Some acknowledge accident and circumstance as the chief movers. To oversimplify a very complex problem, we become physicians from a mixture of motives compounded of altruism, curiosity and the search for power. Each is solving his own problems, satisfying his needs, and is driven by many forces never reaching the level of conscious motives.

The profession of medicine and its practice encompass the practical arts, basic science and applied science. The practical arts of medicine are nourished by altruism, the basic sciences are supported and embellished by curiosity, and the applied sciences live on power and feed it. Such motives govern our lives. In varying combinations they guide us in our choice of life work, and in doing it. The satisfactions of practicing a humane profession and the intellectual pleasures of exercising and sometimes satisfying curiosity are its real rewards. We must never lose them in a drive for power.—WILLIAM BENNETT BEAN: Careers in Medicine: Some Inquiry into "Why We Study Medicine?" and "Why We Specialize?" The Pharos 20: 15, 16, 1957.
Comparative Exercise-Cardiorespiratory Performance of Normal Men in the Third, Fourth, and Fifth Decades of Life
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