AN EDUCATIONAL TOOL FOR UNDERSTANDING
THE CARDIOPULMONARY CHANGES ASSOCIATED WITH AGING

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Normal aging is associated with cardiac, vascular, and pulmonary adaptations that significantly affect the individual's ability to maintain homeostasis. To understand the changes associated with aging, we developed a laboratory exercise that compares and contrasts the cardiopulmonary responses to exercise in a young and an older individual. We also developed this interactive tool because it is our experience that learning is better facilitated when students are encouraged, and required, to become an active and integral part of the educational process. This exercise provides a unique opportunity to analyze, integrate, and interpret the changes associated with aging because more is learned about how a system operates when it is forced to perform than when it is idle. In this laboratory exercise, basic anatomical and physiological data about aging are provided. Subsequently, figures are presented that illustrate the responses of specific cardiopulmonary variables during exercise (e.g., heart rate, cardiac output, blood pressure), and the students are challenged to analyze and assimilate information from the figures, answer questions, make calculations, and plot graphs. The laboratory does not require equipment or software, only rulers and pencils. Questions, and answers to them, are provided in the appendix. The emphasis is on the application of basic science principles, interpretation of pictorial or tabular material, and problem solving skills. In addition, an evaluation instrument was developed to assess the effectiveness of this instructional tool in an academic setting. Specifically, the evaluation instrument addressed four major components, including aims and objectives, content of materials, components and organization, and summary and recommendations.

Key words: aging, cardiopulmonary responses, teaching tool, education, evaluation

Aging is a logical extension of the physiological processes of growth and development that begin at birth and end at death. In 1988, 24% of the population was over 65 years of age. By the year 2000, it is predicted that nearly 30% of the population will be over 65 and there will be a dramatic increase (30–35%) in the number of individuals over the age of 80. Interestingly, the fastest growing age group is the centenarians, those over 100 years old.

Understanding the fundamental processes of aging is essential not only to establishing the causes of aging but also to developing interventions that might postpone or even slow the aging process. The dramatic increase in life expectancy is only of value if the quality of life is endurable. Therefore, significant effort is now being directed toward maintaining health and postponing the onset of debilitating disease as long as possible (referred to as the compression of morbidity).
The largest and most highly publicized cohort in the United States is the “baby boomers” (those born between 1946 and 1954), who are now at midlife and requiring gradually increasing amounts of health care. If the incidence and duration of morbidity in this population cannot be compressed, the baby boomers could potentially collapse the health care system as they pass retirement age.

Cardiovascular disease continues to be the leading cause of death in the United States. This occurs despite the fact that, in recent years, gains in life expectancy have been achieved in the elderly population by reducing mortality due to cardiovascular disease, which in turn may actually increase the cardiovascular morbidity rate. Thus an understanding of the cardiopulmonary changes associated with aging is of considerable importance to facilitate evaluation of cardiopulmonary dysfunction, for diagnosis of pathophysiological conditions, and for initiating interventions directed at prevention against, or rehabilitation from, cardiopulmonary morbidity.

We developed an educational tool to help students understand the cardiopulmonary changes associated with aging. This interactive tool encourages, and requires, the student to become an active, integral part of the educational process. By following a more traditional teaching style, one that involves a strictly lecture-based format, students become vessels, passively waiting to be filled with a predetermined body of knowledge. However, by becoming actively involved in the learning process, the students enhance their level of understanding and ability to integrate and synthesize materials. In addition, the students’ conceptualization of functions and mechanisms and, ultimately, their level of retention are superior. This process demands a high level of personal investment in learning, in which students take responsibility and actively participate in the process.

PROCEDURE

Protocol. To understand the changes in the cardiopulmonary systems associated with aging, we developed an educational tool that compares and contrasts the responses of the cardiopulmonary system during exercise in a 20-yr-old and a 70-yr-old individual. The tool presents basic anatomical and physiological information about each individual. Subsequently, a figure is presented that illustrates the response of a specific cardiopulmonary variable during exercise. Students are challenged to analyze the cardiovascular changes that occur during exercise, keeping in mind the limitations and adaptations present in each individual. The students answer questions, make calculations, and plot data related to that figure. The answers to all the questions are provided.

Students were presented with the educational tool as part of the syllabus in the Geriatric Module of the Principles of Medicine course required of the second-year medical students. (Textual materials are reproduced in the Appendix). Students were asked to work through the tool on their own and subsequently to come to lecture prepared to discuss and answer questions relevant to the materials.

During the class, a slide was presented that illustrated the response of a specific cardiovascular variable (e.g., heart rate) during exercise in the young and older individuals. The subsequent slide presented questions concerning the previous figures. Students then responded to the question in writing or verbally. The third slide in the sequence contained the answers to the previous questions. Thus students had immediate feedback for their answers.

Evaluation. Having developed this laboratory exercise, we considered it necessary to evaluate the effectiveness of this instructional tool in an academic setting. An evaluation instrument was developed to address specific elements of our educational tool (Table 1). Specifically, the evaluation instrument addressed four major components: aims and objectives, content of materials, components and organization, and summary and recommendations. The medical students were asked to complete this evaluation form after finishing this exercise.

Statistical analysis. Results from the evaluation instrument (Table 1) were analyzed using descriptive statistics and are expressed as means ± SE.

RESULTS

The evaluation instrument used to determine the effectiveness of the educational tool and the re-
TABLE 1
Evaluation of instructional materials on the cardiopulmonary changes associated with aging

<table>
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<td>$4.3 \pm 0.20$</td>
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Goals and objectives
1. The purpose and rationale behind the materials are fully explained.
2. The goals and objectives of the materials are clearly identified.
3. The content of the materials is directed to the achievement of the stated goals and objectives.
4. The assessment techniques that measure student achievement of the goals and objectives are included in the materials.

Content of materials
5. Contains challenging and motivating materials for this subject matter.
6. Teaches basic information which must then be integrated to understand broader concepts and mechanisms.
7. Concepts are well developed and sequentially presented.
8. The materials are free of confusing and/or conflicting concepts.
9. The materials clearly identify major points of understanding.
10. The materials follow a thematic organization to help develop concepts and skills.
11. The materials are appropriate for students in this course.

Components and organization
15. The materials were clear, concise and easily understood.
16. The materials were not too lengthy or complex in their format.
17. The structure and layout of material facilitated learning and did not distract from the information being presented.
18. An opportunity to assess an individual's understanding through questions and answers was provided.

Summary and recommendations
19. These materials fulfill the goals and objectives as stated in the introduction.
20. This method of presenting material was as effective as any other I have encountered.
21. These materials were educationally attractive due to the novelty of their style and format.
22. The interactive nature of these materials facilitated my learning of this content area.
23. I would recommend the development and utilization of similar materials for other content areas.

General comments
Please comment on any aspect of this educational tool that you feel may contribute to its improvement.

Evaluation instrument designed to assess the educational tool, including results expressed as means ± SE. Students responded to the following direction: The following statements evaluate specific components of the materials on a scale of 1 to 5. Circle the number that most accurately defines the way you feel regarding each statement. Scale: 1, strongly disagree; 2, tend to disagree; 3, neither agree nor disagree; 4, tend to agree; 5, strongly agree.

Responses of the students are presented in Table 1. Thirty medical students returned the evaluation form. This represented a ~30% response rate. The evaluation instrument was divided into four general categories, and the mean responses for each of these categories are presented in Fig. 1. Each general category was divided into several specific questions, for which the students reported that basic information was integrated to understand broader concepts (statement 6, $4.3 \pm 0.18$), the thematic organization helped to develop higher levels of thinking (statement 12, $4.2 \pm 0.22$), the students had an opportunity to assess their understanding through questions and answers provided (state-
ment 18, 4.3 ± 0.21), and the materials fulfill the goals and objectives as stated in the introduction (statement 4, 4.3 ± 0.18). Students responded most negatively to the following statements: the materials were too lengthy and complex in their format (statement 16, 3.3 ± 0.29), the materials were not educationally attractive due to the novelty of their style and format (statement 21, 3.6 ± 0.24), and the method of presentation was not as effective as other methods they had encountered (statement 20, 3.7 ± 0.26). Finally, the general comments were very favorable.

DISCUSSION

This educational tool was a component of the Geriatric Module in the Principles of Medicine Course for the second-year medical students. The students received the tool in advance, with the understanding that they would complete the materials before class. Many students had taken advantage of this opportunity; however, it was obvious that a significant number of students waited until after the classroom presentation. The class was conducted with a question, answer, and discussion format. The students were required to answer questions, make calculations, plot data, and discuss answers. The evaluation forms were returned over a period of the next two weeks, as many students did not return the evaluation until after they had completed the laboratory exercise.

In general, the students reported that they found the educational tool extremely useful, well presented, thorough in its content, and valuable in the mechanisms it reinforced from their prior course in Physiology. What they appeared to value most was that it reinforced information they had previously learned but required them to review and apply those concepts in another context. Having to rethink and apply the information by responding to questions, making calculations, and plotting data was a valuable means of assessing their actual level of understanding.

These verbal and written comments were substantiated by the high level of agreement reported in the evaluation instrument. The students reported that the goals and objectives had been clearly identified and satisfactorily achieved in the instructional tool. The students were also pleased that there was a vehicle to assess the attainment of those goals and objectives. With respect to the actual content of the tool, students consistently reported that the materials were sufficiently challenging and required integration and a conceptual understanding. Finally, the students agreed that the materials emphasized the major concepts and were appropriate for students at this level.

The majority of students seemed to appreciate and value the interactive nature of this instructional tool.
The opportunity to learn and then evaluate their own level of understanding was educationally appealing and unique in its approach. There were those students, however, who felt that the need to interact with the text and the questions served more as a distractor from than a facilitator to learning. This minority opinion suggests that the process was emphasized at the expense of comprehension.

The major criticism of this instructional tool was, as we had anticipated, the time required for completion of the laboratory exercise. The laboratory exercise requires at least four hours of concentrated effort, which the students considered excessive. There will always be a certain number of students who prefer a very traditional style of teaching and will object to change or innovation on the part of an educator. Our goal was to introduce an alternative educational tool for teaching the cardiopulmonary changes associated with aging that would facilitate student learning. We think that the goals and objectives that we set out to achieve have been accomplished to the satisfaction of both the students and ourselves.

**APPENDIX**

**Background Information, Figures, and Questions**

Normal aging is associated with anatomical and physiological changes that significantly affect the organism’s adaptability to internal and external stimuli. Normal anatomical changes associated with aging include cardiac and arterial stiffness due to proliferation of connective tissue, subendothelial layer thickening, elastin fragmentation, increased wall thickness, and calcification in the media. These anatomical changes result in decreased vascular and cardiac compliances and increased peripheral resistance. The proliferation of connective tissue also reduces the compliance of the chest wall, decreasing elastic recoil of the lungs. This results in increased respiratory muscle work, ventilation-perfusion imbalance, and decreased respiratory muscle strength and endurance. In addition, aging is associated with decreases in bone mineral density, connective tissue elasticity, range of motion in joints, lean body mass, muscle fiber mass, and increases in fat mass.

Physiological changes associated with aging include reduced pulmonary function (decreases in vital capacity, forced expired volumes), impaired cardiovascular function (decreased cardiac output, stroke volume, maximal heart rate, exercise capacity, and baroreceptor function), compromised nervous function (decreased nerve conduction velocity, reaction time, visual acuity), and numerous metabolic/hematologic changes (decreased BMR, glucose tolerance, insulin sensitivity, red cell mass, and increased cholesterol levels).

**Heart rate.** Heart rate (HR) is under the control of the autonomic nervous system. Vagal efferent fibers release acetylcholine onto muscarinic (M2) receptors located on the sinoatrial (SA) node to decrease HR. Cardiac sympathetic efferent fibers release norepinephrine onto β1-adrenergic receptors located on the SA node to increase HR. At rest, vagal efferent activity dominates and is predominately responsible for the resting HR.

At the onset of exercise, there is a centrally generated signal that activates the cardiopulmonary and motor centers (Central Command), causing an initial rapid rise in HR due to the withdrawal of parasympathetic (vagal) activity. The vagus nerve acts as a tonically active brake on cardiac acceleration (HR). Withdrawal of the vagus (releasing the brake) results in an increased HR. Once HR has risen to ~100 beats/min, HR increases linearly with oxygen consumption (VO2) up to ~70% of maximal VO2 (VO2max) due to sympathetic efferent activation. Sympathetic nerves function like the accelerator (gas pedal) on a car: increasing their activity increases HR.

Aging is associated with a decline in both parasympathetic withdrawal and β-adrenergic responsiveness. A reduction in

**FIG. 2**

Heart rate at rest and during exercise on an absolute (l/min, A) and a relative (percent maximal consumption [%VO2max], B) scale in 20- and 70-yr-old individuals.
parasympathetic tone (less restraint) with age results in an increased resting HR and an attenuated initial response to exercise because there is a delay in the withdrawal of vagal activity. Sympathetic efferent responses are also decreased with age. There does not appear to be a reduction in sympathetic drive; rather, the decrease in response appears to be due to an attenuated sympathetic responsiveness of the β-adrenergic receptors.

Intrinsic HR (the heart’s inherent capacity to beat independently of the autonomic nervous system) is also attenuated. This decrease in the intrinsic HR is most likely due to proliferation and infiltration of connective tissue into the myocardial wall. These changes in myocardial collagen also result in increased passive stiffness, and thus a decrease in compliance (ΔV/P).

1. Compare resting HR. What contributes to the slightly higher resting HR in the older individual?

2. Compare the rate of increase in HR with increasing workloads. What accounts for the reduced slope in the older individual?

3. Why is the maximal HR lower in the older individual?

4. If circulating catecholamine concentrations are higher in an older individual, what mechanism accounts for the decrease in maximal HR?

**Stroke volume.** Stroke volume (SV) is a measure of the volume of blood that is ejected from the ventricle with each beat of the heart. SV is a function of venous return (preload), contractility, and afterload. SV increases as a result of changes in ventricular volume that result from an increased venous return, which invokes the Frank-Starling (F-S) mechanism or length-tension (L-T) relationship. This mechanism allows for an increased force of contraction due to the lengthening of the ventricular myocardial fibers. As well, a change in the inotropic state of the myocardium (contractility) increases SV due to sympathetic activity and circulating catecholamines. Finally, increases in afterload oppose the increase in SV. During ejection, the aortic semilunar valve opens, and blood is rapidly ejected into the aorta. For this to occur, the pressure in the left ventricle must be greater than the pressure in the aorta. Therefore afterload is the aortic pressure the heart must pump against during ejection. If, however, the aortic pressure is increased, the heart must generate a greater pressure to eject a given blood volume.

With exercise, SV can increase approximately twofold up to 35–40% of VO₂max, where a leveling off occurs. End-diastolic volume (EDV), the volume of blood contained in the ventricle at the end of diastole, increases because of an increased venous return resulting from the muscle pump. Skeletal muscles of the legs serve as effective pumps to drive blood back to the heart, thereby increasing venous return. The increased EDV stretches the myocardial fibers, which increase their force of contraction in accordance with the F-S mechanism or L-T relationship. Sympathetic activity increases myocardial contractility, consequently strengthening each ventricular contraction, resulting in a decreased end-systolic volume. SV is limited, however, by the tachycardia associated with exercise, thus reducing the filling time. A small increase in mean arterial pressure increases the afterload and opposes the increase in SV.

Associated with aging, there is a slower HR response during exercise (Fig. 2) that allows for ventricular filling. This results in an increased EDV, allowing for an increased SV (F-S mechanism and L-T relationship). Despite an initial increase in SV, several factors limit its potential in the older heart. An increase in afterload (resulting from a stiffening in the arterial system), a diminished response to β-adrenergic agonists that attenuates the increase in contractility, and a decreased ventricular compliance that limits the increase in EDV will all result in an attenuated SV response during exercise. SV is attenuated because the aging heart and vasculature result in an increased end-systolic volume and, therefore, an ejection fraction that does not increase.

5. Compare the initial SV response. What contributes to the slightly greater SV in the older person?

6. Compare the flat portions of each curve. How do they differ? What accounts for this difference?

7. What contributes to the failure of SV to increase after ~40% of VO₂max?
**Cardiac output.** Cardiac output (CO) is the volume of blood pumped by the heart in 1 min. It is the product of HR and SV and is highly correlated with VO₂. Changes that affect HR and SV will therefore affect CO. Increases in SV contribute to a greater extent to an increase in CO up to ~40% of an individual's VO₂max. Subsequent increases in CO are a result of increases in HR. CO declines with age because of the smaller increments in HR and SV observed in older individuals.

8. CO is the product of HR and SV. Using Figs. 2 and 3, calculate the CO response during exercise in the two individuals. Plot these results in Fig. 4.

9. CO at rest is slightly higher in the older individual. What accounts for this difference?

10. Compare the CO response in the old and young individuals. How are they different? What contributes to these differences?

11. As workloads increase, the difference in CO between the two individuals also increases (see Fig. 5). What accounts for this increasing difference in CO?

12. Compare the CO curves at VO₂max. How are they different, and what effect might this have on blood pressure and blood flow?

**Systolic blood pressure.** Systolic blood pressure (SBP) is the pressure exerted against the walls of the arteries by the blood ejected into the aorta during ventricular systole. SBP is a function of ventricular stroke volume, the compliance of the aorta, and the peak ejection rate. At higher workloads, CO (not SV alone) and vascular compliance are the major determinants of SBP. When blood is ejected into the aorta, the vessel expands and absorbs much of the energy. If the vessel is unable to expand (decreased compliance), the energy is not absorbed, and SBP increases. With aging, there is a decreased vascular compliance due to proliferation and infiltration of connective tissue into vascular smooth muscle. The decreased compliance increases SBP because the energy of ventricular systole is not absorbed by the aorta. The SV ejected with each ventricular contraction is pushed into this rigid arterial network, causing an increased systolic pressure.

At the onset of exercise, there is an initial rapid rise in SV, which increases because of an increase in EDV and an increased myocardial contractility that strengthens each ventricular contraction. The increased myocardial contractility increases the rate of ejection and therefore contributes to the rise in SBP. In addition, the SV response causes a rapid rise in systolic pressure up to ~35–40% of VO₂max. In the older heart, this increase in SBP will be augmented by the decreased compliance in the aorta. As exercise continues, the SV response levels off and the increase in cardiac output is not maintained; thus, despite the less compliant arterial system, SBP increases at a much slower rate in the older person. The total volume of blood contained in the arterial system no longer continues to increase because of the leveling off of CO. This lower SBP also occurs despite the increased sympa-
Systolic blood pressure at rest and during exercise on an absolute (l/min, A) and a relative (%VO₂max, B) scale in 20- and 70-yr-old individuals.

Diastolic blood pressure. Diastolic blood pressure (DBP) is the pressure exerted by the volume of blood that remains in the arteries after the peripheral runoff of blood during the relaxation phase of the cardiac cycle. DBP is a function of the compliance of the vasculature, the peripheral vascular resistance, and the amount of rest afforded the heart (as a function of HR).

Compliance affects DBP, because if the vessel has a high compliance, it expands during systole and rebounds during diastole. The rebound imparts energy (Windkessel effect) into the vascular system and increases DBP. A decreased compliance reduces the rebound, and therefore DBP is lower. An increase in HR, leading to a decrease in relaxation time between each contraction, will reduce the time during which the outflow of blood occurs through the resistance vessels and will increase the volume of blood injected into the arteries. Therefore DBP increases.

Peripheral resistance is regulated by sympathetic efferent tone, local metabolic products, and circulating hormones (e.g., catecholamines, vasopressin, and angiotensin). Normally, DBP remains the same or decreases only moderately during exercise, because although HR increases, peripheral vascular resistance decreases. With exercise, as soon as HR increases > 100 beats/min, the sympathetic nervous system becomes activated and attenuates the fall in total peripheral resistance (TPR). DBP will decrease slightly because of the opposing influence of vasodilator mechanisms (autoregulation, local metabolites, flow-mediated release of nitric oxide). An increase in HR, leading to a decrease in relaxation time between each contraction, will reduce the time during which the outflow occurs through the resistance vessels.

13. Compare SBP at rest. What contributes to the slightly elevated resting SBP in the older individual?

14. The older individual has an initial rapid rise in SBP that subsequently levels off. What accounts for this response?

15. Examine the SBP responses to increasing workloads. How do they differ between individuals? What accounts for the difference?

16. In the older individual, SBP fails to increase to the same extent as in the younger individual. What factor accounts for this failure to increase?
During exercise, perfusion pressure is monitored and maintained by the arterial baroreflex and muscle metaboreflex. If cardiac performance is not adequate enough to maintain perfusion pressure, the arterial baroreflex and muscle metaboreflex reflexly increase TPR. As previously discussed, cardiac performance is compromised in the elderly, which would suggest an augmented metabo- and baroreflex response to compensate for the decline in CO. If baroreceptor sensitivity is attenuated in the elderly, this would compromise the sympathetic nervous system's ability to adjust for the decline in cardiac output. At the same time, with a reduced baroreceptor response and increased sympathetic drive, there are elevated levels of circulating norepinephrine. A resultant vasoconstrictor effect will be present, leading to an increase in TPR.

17. Compare the DBP response at rest. What accounts for the higher pressure in the older individual?

18. How does arterial compliance affect DBP?

19. Compare DBP values during exercise. In the elderly individual, what does the rise in DBP with exercise signify?

Mean arterial blood pressure. Mean arterial pressure (MAP) is the average pressure throughout the cardiac cycle. Because systolic is shorter than diastolic, MAP is slightly less than the value halfway between systolic and diastolic pressures. This is often described as the perfusion pressure, or the pressure necessary to maintain adequate tissue blood flow. MAP is calculated by the formula

\[
\text{MAP} = \text{Diastolic pressure} + \frac{1}{3} \times \text{Pulse pressure}
\]

\[
\text{(Pulse pressure} = \text{SBP} - \text{DBP})
\]

20. Using Figs. 6 and 7, calculate the MAP response during exercise in the old and young individuals. Plot these results in Fig. 8.

MAP is the average pressure in the arterial system over time. It is determined by the average blood volume contained within the arterial system throughout the cardiac cycle. Any factors that impact the inflow and/or outflow from the arterial system will therefore influence MAP. CO and TPR have direct influence on inflow and outflow, respectively. Under normal conditions, MAP rises with increasing workloads as a result of the increases in CO despite decreases in TPR.

In the older individual, TPR is higher at rest and during exercise. With exercise, MAP increases as a result of increases in CO. Despite a lower absolute CO in the older individual, TPR is significantly elevated, and therefore MAP continues to increase throughout the increasing workloads.
21. What accounts for the higher MAP at rest in the older individual?

22. SBP at the higher workloads is significantly reduced in the older individual, yet MAP continues to rise. What accounts for this response?

23. Compare the MAP response to increasing workloads between the two individuals. What factors account for these responses?

Splanchnic and renal blood flow. Blood flow to any region is a function of perfusion pressure and resistance as expressed by the relationship Flow = Pressure/Resistance. Thus blood flow is directly proportional to pressure and inversely proportional to the cross-sectional area of the resistance vessels. Splanchnic and renal vascular beds can change their resistance through several different mechanisms, including autoregulation, local metabolic regulation, endothelium-derived relaxing factors, sympathetic nervous system activation, and hormonal regulation (including renin angiotension and vasopressin).

Blood flow to skeletal muscle must increase enormously during exercise of increasing intensity. Reductions in blood flow to regional vascular beds facilitate an increase in blood flow to the working skeletal muscle by redistributing CO. Splanchnic and renal circulations make the greatest contribution to redirecting CO to skeletal muscle.

Splanchnic and renal blood flows begin to decrease near a HR of 100 beats/min. This represents the point at which sympathetic control begins to dominate and plasma norepinephrine levels rise with increasing workloads. This suggests that an increased sympathetic activity to the heart to increase its rate is accompanied by an increased sympathetic vasomotor outflow to regional vascular beds. Decreases in regional flows and elevated NE levels occur in a similar fashion but at different absolute levels of O₂ uptake. (There is a significant inverse relationship between splanchnic blood flow and plasma NE concentrations.)

24. To what extent does blood flow in nonexercising regions decrease during maximal exercise? What mechanism mediates this vasoconstriction?

25. Why do both the young and older individuals have the onset of vasoconstriction occurring at the same relative Vo₂?

26. Compare the decreases in splanchnic and renal blood flow between the young and older individuals. What would explain the difference in their vasoconstrictor responses?

![FIG. 10](image_url) Splanchnic and renal blood flow at rest and during exercise on an absolute (L/min, A) and a relative (%Vo₂max, B) scale in 20- and 70-yr-old individuals.

![FIG. 11](image_url) Skeletal muscle blood flow at rest and during exercise on an absolute (L/min, A) and a relative (%Vo₂max, B) scale in 20- and 70-yr-old individuals.
Muscle blood flow. Skeletal muscle blood flow is under the control of neural, local, and humoral mechanisms. At rest, local regulatory mechanisms dominate. Neural control mediated by the sympathetic nervous system modulates local regulating mechanisms.

Muscle arterioles contain both α- and β-adrenergic receptors. Sympathetic nerves release norepinephrine (NE), which binds to α-adrenergic receptors to begin a cascade of events that cause constriction, thereby reducing blood flow. β₂-adrenergic receptors respond to hormonal stimuli, primarily adrenally released epinephrine, which acts to vasodilate blood vessels.

At the onset of exercise, there are locally produced metabolites that act to vasodilate the muscle’s vasculature, resulting in a rapid increase in blood flow. Autoregulatory mechanisms and flow-mediated release of nitric oxide also serve to vasodilate the vasculature at the onset of exercise. Once HR is elevated > 100 beats/min, sympathetic activation releases NE, which in turn vasoconstricts the vessels. This response maintains blood pressure by matching CO and TPR. At maximal exercise, the metabolic demand exceeds supply, resulting in a rapid accumulation of vasoactive metabolites, which exert a powerful vasodilatory stimulus. As the metabolic rate and the level of vasodilation increase, the effect of neural vasoconstriction is enhanced. In fact, sympathetic adrenergic nerves exert powerful vasoconstrictor effects in active skeletal muscle despite the metabolically induced vasodilation.

In the older individual, when CO fails to meet the metabolic demands of increasing workloads, there will be an increased activation of the sympathetic nervous system (unloading of the baroreceptors). This happens because vasodilation occurs faster than CO increases. The baroreflex matches CO and TPR. Active skeletal muscle must be reflexly vasoconstricted during maximal exercise; otherwise blood pressure would fall.

Aging appears to be accompanied by changes in certain neurally controlled responses. The constrictor response to α-adrenergic agonists appears to remain intact in the older individual. Adrenergic modulation of isolated blood vessels, particularly β-adrenergic-mediated vasodilation, however, has been found to decrease with aging.

27. Compare the initial muscle blood flow response to exercise in the young and older individuals. What accounts for the response at the onset of exercise?

28. How does the blood flow response to increasing workloads differ between the young and older individuals?

29. At higher workloads, which mechanisms are exerting an influence on muscle blood flow? What mechanism exerts the greatest influence on blood flow?

Total peripheral resistance. TPR is a measure of the resistance to blood flow and reflects the state of constriction/dilation in the peripheral vasculature. The radius of the vessel is the single most important parameter affecting TPR, as can be seen from Poiseuille’s law (Poiseuille’s law is expressed as Resistance = 8 η length/r² radius⁴). Therefore, TPR is finely controlled by changes in arteriolar diameter that directly impact blood flow and arterial pressure. Very small changes in the arteriolar radius can have a dramatic effect on blood flow because resistance varies inversely with the fourth power of the radius. There are numerous factors that control arteriolar diameter through increasing workloads. Vasodilation is stimulated initially by locally produced metabolites, autoregulation (the tissue’s ability to control its own blood supply), and flow-dependent release of endothelium-derived relaxing factors. Adrenal release of epinephrine also functions in a vasodilatory capacity. As TPR falls due to these vasodilatory mechanisms, a restraint on vasodilation is initiated by the arterial baroreflex, which functions to maintain MAP. The counterbalancing vasoconstrictor mechanism includes sympathetic nerve activity, adrenally released NE, and various hormones, including renin-angiotensin and vasopressin. However, the major mechanisms appear to be local metabolites and sympathetic nerve activity.

At the onset of exercise, local metabolites trigger vasodilation, which increases blood flow and causes a drop in perfusion pressure. This drop in pressure causes upstream vasodilation by autoregulatory mechanisms. The increased flow resulting from the autoregulatory mechanisms stimulates the release of endothel-
innovations and ideas

lium-derived relaxing factors. The vasodilatory response may lead to a decrease in arterial blood pressure. The decrease in arterial blood pressure unloads arterial baroreceptors, which reflexly increases sympathetic nerve activity. This increased sympathetic activity attenuates the metabolic vasodilatory response and functions to attenuate the fall in TPR and to maintain MAP.

The peripheral vasculature’s main function is to control MAP whenever there are alterations in CO. (MAP is the product of CO and TPR.) The two reflexes that control peripheral resistance are the arterial baroreflex and the muscle metaboreflex. When CO and/or MAP falls, the arterial baroreflex and muscle metaboreflex activate sympathetic adrenergic activity to vasoconstrict and thereby increase arterial pressure.

TPR appears to increase with aging. This phenomenon may be explained by structural and/or functional changes in the resistance vessels of skeletal muscle and increased sympathetic nerve activity. In the older individual, CO fails to meet the demands of increasing workloads during exercise. In this situation, the arterial baroreflex is unloaded and functions to maintain MAP by attenuating the decrease in TPR.

As discussed previously, aging appears to be accompanied by changes in certain neurally controlled responses. Sympathetic adrenergic constrictor responses appear to remain intact in the older individual and may even be increased because of the increased circulating catecholamines that result during exercise. An attenuated vasodilatory response may occur with aging, particularly in response to β-adrenergic stimulation. Both of these mechanisms would result in an increased peripheral resistance, particularly in response to exercise.

30. Compare the initial peripheral resistance responses in the young and older individuals. What factors account for these responses?

31. Peripheral resistance levels off after ~40% VO₂max in both individuals. What accounts for this response?

32. How does the peripheral resistance response to increasing workloads differ between the young and the older individuals?

33. Compare the peripheral resistance responses at the highest workload between these two individuals. How do they differ, and what accounts for this difference?

Arteriovenous O₂ difference. VO₂max is the product of maximal CO and maximal arteriovenous (a-v) O₂ difference (i.e., the maximal extraction of O₂ from the blood). The a-v O₂ difference refers to the difference between the O₂ content of blood on the arterial and the venous side of the vascular bed. At rest, arterial and venous O₂ contents are ~20 and 15 ml O₂/100 ml blood, respectively. This results in an a-v O₂ difference of ~5.0 ml/100 ml blood. [Resting arteriovascular O₂ difference is calculated from blood hemoglobin (Hb) concentrations × O₂-carrying capacity of the blood, i.e., in males 15 g Hb/100 ml blood × 1.34 ml O₂/g Hb – 20.1 ml O₂/100 ml blood. Venous a-v O₂ difference results from the metabolizing tissues extracting ~4.0 ml O₂/100 ml blood at a normal resting CO, i.e., 20.1 ml O₂/100 ml – 4.0 ml O₂/100 ml = 16.1 ml O₂/100 ml]. During maximal exercise, this a-v O₂ difference can increase up to 15 ml O₂/100 ml blood and is not normally considered to be a limiting factor to VO₂. (When metabolism increases, active tissues have a built-in mechanism for releasing more O₂ from Hb. This mechanism is known as the Bohr Effect and describes how a decrease in pH and increases in CO₂ and temperature result in a rightward shift in the O₂/Hb dissociation curve). The a-v O₂ difference is influenced by a variety of factors, including muscle mass, the capacity of arterial blood to transport and relinquish O₂, and the capacity of the tissues to take up and utilize O₂.

In the older individual, there is a decrease in skeletal muscle oxidative capacity. A lower capillary-to-muscle fiber ratio results in a reduced ability to extract O₂ from the blood. Other potential mechanisms that may affect the a-v O₂ difference are a decline in blood flow to the active skeletal muscle and a smaller ratio of muscle mass to total body mass. These mechanisms could result in a reduced transport and utilization capacity of muscle for VO₂. However, despite these potential limitations, a-v O₂ difference in the older individual increases in a manner similar to that in the younger individual. (On a relative scale, the a-v O₂ differences are virtually the same when expressed as a percentage of their

VOLUME 12 : NUMBER 1 – ADVANCES IN PHYSIOLOGY EDUCATION – DECEMBER 1994

S28
When CO fails to meet the energy demands of the higher workloads, a-v O₂ difference appears to increase even further in an effort to satisfy the higher energy requirements.

34. Compare the a-v O₂ difference between the young and older individuals. What factors account for this difference?

35. Does a-v O₂ difference limit the VO₂ max?

Tidal volume. Tidal volume is the volume of air inspired or expired on each respiratory cycle. Tidal volume can increase to ~ 50% of the lung's total vital capacity and thus will be influenced by changes in this ventilatory parameter. With increasing workloads, minute ventilation increases, initially by changes in tidal volume up to ~ 40% of VO₂ max, where maximal tidal volumes begin to level off. Resting tidal volumes are ~ 30% higher in the older individual as a result of the increases in compliance and the decrease in elasticity of the lung. The resultant widening of the airways increases the lung's dead space and thus increases resting tidal volumes.

Vital capacity decreases linearly ~ 4-5% per decade in the average population. Vital capacity decreases as a result of the physiological changes that occur with aging. The increased residual volume, the increased compliance of the lungs and rigidity of the lung and chest wall, and the increased physiological dead space all lead to a diminished vital capacity. As tidal volumes can only increase up to ~ 50% of vital capacity, a decrease in vital capacity will necessitate an attenuated response in tidal volumes.

36. Compare tidal volumes at rest between the young and older individuals. What accounts for this difference?

37. Compare the tidal volume responses between the old and young individuals. How do they differ and what effect will this difference have on minute ventilation?

Respiration rate. Respiration rate refers to the total number of breaths per minute. Resting respiration rate ranges between 10 and 16 breaths/min. As workloads increase, the respiratory rate initially remains fairly constant until tidal volumes have approached ~ 50% of the vital capacity (a measure of the maximal amount of air that can be exhaled after a maximal inhalation). At this point, respiration rate sharply increases, which functions to increase minute ventilation. Maximal respiration rate is attenuated in the older individual, although its response to increasing workloads is such that the rate will increase at earlier workloads to compensate for the limitation on increasing tidal volume.

Respiration rate also increases in response to an increased reliance on anaerobic metabolism with increasing workloads.

![FIG. 14](image)

Tidal volumes at rest and during exercise on an absolute (L/min, A) and a relative (%VO₂ max, B) scale in 20- and 70-yr-old individuals.

![FIG. 15](image)

Respiration rate (frequency of breathing) at rest and during exercise on an absolute (L/min, A) and a relative (%VO₂ max, B) scale in 20- and 70-yr-old individuals.
38. Compare the respiration rates between the young and older individuals with increasing workloads. Why does respiratory frequency increase to a greater extent at lower workloads in the older individual?

39. What accounts for the difference in the maximal respiratory rate?

Minute ventilation. Minute ventilation is the volume of air inspired each minute and is the product of tidal volume and respiration rate. At the onset of exercise, the increase in minute ventilation is mainly due to an increase in tidal volume. An increase in respiratory rate contributes more to the increase in minute ventilation at higher workloads.

Minute ventilation is the product of tidal volume and respiration rate. Using Figs. 14 and 15, calculate the minute ventilation response during exercise in the two individuals. Plot these results in Fig. 16.

Respiratory minute ventilation is the volume of air inspired each minute and is the product of tidal volume and respiration rate. Minute ventilation can increase 15- to 20-fold with increasing workloads up to maximal exercise. These large increases in ventilation result initially from increases in tidal volume up to ~40% of $V_{O_2\text{max}}$, where tidal volume levels off. Thereafter, increases in ventilation occur as a function of increases in respiratory rate (i.e., breaths/min). This is similar to the relationship between HR, SV, and CO. At the onset of exercise, CO increases mainly by an increase in SV up to ~40% of $V_{O_2\text{max}}$ (Fig. 5), where SV levels off. Subsequent increases in CO are a result of increases in HR (Fig. 2). As with HR, where a too rapid increase will preclude adequate filling time, respiration rate must increase at a sufficiently moderate rate to allow for adequate time for the lungs to fill with air.

Minute ventilation increases linearly at the onset of exercise because of "central command" and afferent signals from the working muscle. Central command is the concept whereby signals from the cerebral cortex initiate changes in the cardiopulmonary systems and in skeletal muscle motor systems. With increasing workloads, there is an increased reliance on anaerobic metabolism, which is accompanied by an increased production of lactic acid in the muscle. Lactic acid will stimulate muscle and respiratory chemoreceptors, which in turn activate the MRC. This produces an enhanced respiratory drive at higher workloads as a
result of the increased lactic acid. This is particularly noticeable at workloads > 90% \( \text{VO}_{2\text{max}} \), where there is a dramatic increase in respiration rate. This hyperventilatory response function to offset the acidification due to a rapid accumulation of lactic acid at higher workloads \( (\text{H}_2\text{O} + \text{CO}_2 = \text{H}_2\text{CO}_3 = \text{H}^+ + \text{HCO}_3^-) \)

At lower workloads, the ventilatory equivalent for \( \text{O}_2 \) (the ventilatory volume of air required to obtain one liter of \( \text{O}_2 \)) is ~25 liters of air per liter of \( \text{O}_2 \) consumed. This value can increase up to ~40–50 liters of air/liter \( \text{O}_2 \) consumed as individuals approach their maximal work capacity. This ventilatory equivalent increases with age.

The chest wall is stiffer because the cartilaginous tissues of the rib cage become calcified. The lung’s compliance increases because lung elasticity decreases. As lung compliance increases and elasticity decreases, there is an enlargement of the trachea and airways, which results in an ~30% increase in dead space and tidal volume. The older individual respires at a much higher percentage of total lung capacity, which leads to a greater amount of air trapping. Residual volume is increased because of the increased diameter of the airways, and the lung no longer resists expansion because of the loss of elasticity. Thus tidal volume must increase to fill the extra dead space so that the physiological volume (that volume of inspired air that is available for gas exchange) remains the same.

In the older individual, the diaphragm becomes flattened. The lung’s compliance increases because lung elasticity decreases. As lung compliance increases and elasticity decreases, there is an enlargement of the trachea and airways, which results in an ~30% increase in dead space and tidal volume. The older individual respires at a much higher percentage of total lung capacity, which leads to a greater amount of air trapping. Residual volume is increased because of the increased diameter of the airways, and the lung no longer resists expansion because of the loss of elasticity. Thus tidal volume must increase to fill the extra dead space so that the physiological volume (that volume of inspired air that is available for gas exchange) remains the same.

Respiration is itself an energy-consuming activity. The respiratory cost for a given workload increases ~3–5% yr in older individuals. As aerobic capacity is already compromised in the elderly, respiration consumes a greater proportion of the total energy available to perform work and thus limits the older individual’s total work capacity.

40. Compare minute ventilation at rest and during the lower initial workloads in the two individuals. How does it differ and what accounts for this difference?

41. Compare minute ventilation at the higher workloads. What accounts for the lower minute ventilations in the older individual?

Answers

Heart rate. 1. The older individual has decreased vagal tone, which normally acts as a brake on HR. You might expect then to see a much higher resting HR; however, because of a lower intrinsic HR, the resting HR will be only slightly elevated.

2. After the initial response, in which central command mediates parasympathetic withdrawal of the tonic restraint on HR, sympathetic efferent activity increases. Above a HR of ~100 beats/min, there is a linear increase in HR with workload up to ~75% of \( \text{VO}_{2\text{max}} \). This increase is due to sympathetic activation of the SA node (NE released onto \( \beta \)-adrenergic receptors). In the older person, the \( \beta \)-adrenergic response is attenuated; thus there is a diminished HR response (i.e., a lower slope) to increasing workload. Again, attenuated sympathetic responses are principally the result of decreased receptor responsiveness.

3. The maximum HR is lower in an older individual because of the effects of diminished sympathetic activation. \( \beta_1 \)-adrenergic receptors have an attenuated responsiveness to NE released from the cardiac sympathetic nerves and circulating catecholamines from the adrenal medulla. Resting NE concentrations are not age related, but resting epinephrine (E) concentrations are elevated with age (for the 60–77-yr-old individual, an NE range of 300–350 pg/ml and an E range of 30–60 pg/ml). Plasma catecholamines (NE and E) are higher in the older individual both at submaximal and maximal efforts. The maximum HR is also lower in an older individual because of a decreased exercise tolerance.

4. If concentrations of circulating catecholamines are high in the older individual, then the attenuated HR response cannot be a result of decreased sympathetic drive. Rather, it would appear that there is a diminished responsiveness of \( \beta \)-adrenergic receptors in the presence of adequate catecholamines. This could suggest a downregulation of the \( \beta \)-adrenergic receptors. Downregulation is the concept whereby exposure of target cells (receptors) to high concentrations of hormones results in subsequent decreases in the sensitivity of those cells.

Stroke volume. 5. With diminished vagal withdrawal and attenuated responses to sympathetic activation, there is a slower HR response at the onset of exercise. This allows for an increased time for ventricular filling (increased diastolic time) and increased reliance on the \( F-S \) mechanism or L-T relationship and thereby an increase in SV. At submaximal workloads, because of the reduced HR, the ventricle can increase \( SLV \) sufficiently to raise SV. In this context, higher SV values have been reported for even young subjects under \( \beta \)-adrenergic receptor blockade. This effect occurs as a result of an attenuated HR response due to blockade of sympathetic accelerator effects on HR. The reduced HR allows for increased filling time and increased reliance on the \( F-S \) mechanism to increase SV. This example illustrates the role of HR in mediating the SV response during exercise.

6. The older individual’s SV levels off sooner and at lower volumes. The apparent early failure to increase SV with increasing workloads is misleading. Relative to any individual’s \( \text{VO}_{2\text{max}} \), SV reaches its maximum at approximately the same relative workload. Failure of SV to increase further occurs at ~35–40% of each individual’s respective \( \text{VO}_{2\text{max}} \).
The lower absolute values for SV are a result of several factors. The older individual has an increase in afterload, an attenuated response of β-adrenergic receptors, and a decreased ventricular compliance. At higher workloads, these mechanisms offset any increase in SV by decreasing ejection fraction.

7. The energy demands of increasing workloads are met (but not solely) by an increase in both HR and SV. The larger relative increase in HR suggests that it may have the dominant role in meeting the energy demands. With exercise, SV is limited by afterload and the reduced filling time that results from the exercise-induced tachycardia. SV will therefore increase to its maximum relatively early.

Cardiac output. 9. CO is the product of HR and SV. As seen in Fig. 2, HR in the older individual is slightly elevated because of a decrease in vagal tone. SV at rest is the same for these two individuals. The slightly elevated CO at rest in the older individual results then from the slightly elevated HR.

10. The initial response to exercise is very similar between the young and old individuals. The older individual depends slightly more on SV than on HR to meet the initial demands due to the diminished HR response. At 40% of the older individual’s V02max, there is an attenuated increase in CO with increasing workloads. This change in the slope of the CO curve results from the diminished abilities of HR and SV to keep pace with the energy demands of increasing workloads. Ultimately, CO is reduced in the older individual.

11. Figure 2 illustrates that the slope of the increase in HR is much lower for the older than the younger individual. Figure 3 illustrates a similar initial increase in SV between the two individuals, but the older individual’s SV levels off at a lower absolute value. Because CO is the product of HR and SV, the HR response will be primarily responsible for the increasing difference in CO between the two individuals with increasing workloads.

12. The maximum CO values are significantly different between the two individuals at maximum workloads. CO is a major factor in providing blood flow to the working muscles and in maintaining blood pressure. Therefore, as we will see later, the two individuals will have very different blood pressures and blood flow responses during exercise as a result of the difference in CO.

Systolic blood pressure. 13. Resting SBP is elevated in the older individual most likely because of stiffening of the aorta, resulting in a reduced compliance and a resultant decreased ability to absorb the energy of ventricular systolic. This increased stiffening of the arterial tree does not appear to alter systolic cardiac function at rest despite the reduced ability of the arteries to expand. Although SV is not altered at rest in the older individual, the reduced compliance of the arteries results in a higher SBP.

14. SV and arterial compliance are the major determinants of SBP. The older individual begins exercise with an elevated SBP because of the reduced compliance of the arteries. Figure 2 illustrates an early rapid rise in SV up to 40% V02max. SBP responds in a similar fashion, demonstrating a failure to increase after 40% V02max. The SBP response to increasing workloads up to 40% V02max appears to be primarily determined by SV in the older individual. Low arterial compliance most likely accounts for the increase in SBP in the older individual after 40% V02max, because SV fails to increase, and even begins to decrease, by the final workload.

15. The younger individual has a similar early rise in SBP, but it continues to increase through the higher workloads. This increase in SBP at the higher workloads results from the continued increase in CO that is seen in this individual (see Fig. 5). As well, the arterial stiffness that results from the increased sympathetic activity will also facilitate this increase in SBP. Thus the higher SBP response seen in the younger individual is a result of the continued increase in CO and the increased vascular stiffness.

16. The failure of SBP to increase in the older individual at the higher workloads is due to the failure of CO to increase. CO cannot continue to increase because SV levels off at 40% V02max, and the HR response is attenuated because of a decreased responsiveness of the β-adrenergic receptors. Accompanying this failure of CO to increase, there will be an increased sympathetic nervous activity due to the unloading of the baroreceptors, which in turn causes an increased vascular rigidity. This increase in sympathetic activity is not sufficient to offset the effect of declining CO; thus SBP will not increase to the same extent as seen in the younger individual.

Diastolic blood pressure. 17. Resting DBP is slightly elevated in the elderly individual because of an increase in TPR. If TPR is elevated, the rate of outflow of blood after systole is reduced, resulting in a greater blood volume contained within a more rigid vascular system. Peripheral resistance is controlled by the resistance vessels (arterioles), which will show similar changes in rigidity and lack of compliance. These vessels will be more resistant to dilation, resulting in elevated TPR under resting conditions. The lack of distensibility and increased impedance to flow will reduce the rate of blood flow out of the arterial network, resulting in an increased DBP. However, the major influence on the resistance vessel is an increased sympathetic activity, which is elevated at rest in the older individual.

The slightly elevated resting HR also increases CO slightly, which further increases the volume of blood in the arterial system. The elevated resting HR reduces the time in diastole, thereby reducing the time for peripheral runoff of blood.

18. Arterial compliance in the older individual is reduced because of proliferation and infiltration of connective tissue into the vascular smooth muscle. This decreased compliance reduces rebound, which imparts energy into the vascular system (windkessel effect). Therefore, without the rebound, DBP is lower. However, DBP is in fact elevated in the older individual both at rest and during exercise. This suggests that TPR and HR contribute to a greater extent to DBP and that the contribution of lower arterial compliance to DBP is relatively small.
19. There is an increase in DBP in the older individual because of a smaller reduction in TPR (Fig. 12). In the older individual, DBP rises in response to increasing workloads because of impaired cardiac performance (Fig. 4). This decreased cardiac performance results in a reduced SBP response, which in turn unloads the arterial baroreflex. Unloading the arterial baroreceptors reflexly increases sympathetic nerve activity and TPR. This response is the body’s attempt to maintain perfusion pressure. As the primary determinant of DBP, an attenuation of the fall in TPR in response to exercise will produce an elevated DBP. If cardiac performance fails to meet the demands of increasing workloads, DBP may even rise to greater levels. (During a stress test to evaluate cardiac function, a sudden rise in DBP would signal the heart’s inability to meet the energy demands of the exercise and would be a criterion for ending the test).

The slight decrease in DBP in the younger individual results from the effects of local vasodilatory substances, autoregulation, and endothelium-derived nitric oxide to decrease TPR and thus decrease DBP. Myocardial performance in the young heart is not compromised, so CO can keep up with the metabolic demands of the exercise. As a result, the sympathetic nervous system will not be activated to the same extent as in the older heart (unloading of baroreceptor reflex leads to vasodilation and an increased DBP).

**Mean arterial pressure.**

1. The higher MAP at rest in the older individual results from both a slightly greater CO and an elevated peripheral resistance. CO is elevated because of the slightly higher resting HR. TPR is elevated because of an increased level of sympathetic activity and an increased rigidity in the resistance vessels. This results in a slightly greater inflow yet a simultaneously reduced rate of outflow from the arterial system. The net result is an elevated MAP due to the greater volume of blood contained within the arterial system.

2. Although SBP is reduced at higher workloads in the older individual, MAP continues to rise. This rise in MAP occurs despite a smaller rate of increase in CO in this individual. The increase in MAP is maintained as a result of the increase in DBP. This increase in DBP occurs when arterial baroreceptors are unloaded during exercise and reflexly increase sympathetic nerve activity. A decrease in cardiac performance results in the reduced SBP response, which in turn unloads the arterial baroreflex that functions to increase TPR. As demonstrated in the equation MAP = DBP + 1/3 (SBP + DBP), an increase in DBP results in an increase in MAP. Therefore, to maintain perfusion pressure at the higher workloads in the older individual, MAP will increase by an increase in DBP.

23. The slopes of the increases in MAP are fairly similar through increasing workloads. However, the factors that contribute to the gradual increases in MAP are very different. In the younger individual, the MAP rises as a result of gradually increasing CO and decreasing TPR. SBP continues to rise as DBP slowly decreases with increasing workloads. The older individual’s MAP rises partially from the increase in CO but primarily from an attenuation of the decrease in TPR initially. SBP accounts for the rise in MAP, and once SBP levels off, DBP increases and maintains the gradual rise in MAP.

The elderly individual must maintain this higher MAP, which functions to maintain perfusion pressure. This higher perfusion pressure produces the force to supply O2 and nutrients to the working cells. An attenuated response to local metabolic vasodilation and an augmented vasoconstrictor response to sympathetic efferrnts from the arterial baroreflex and muscle metaboreflex all function to increase the MAP response in the older individual.

From these results, it appears that MAP is the regulated variable. That is, MAP is the response most important to maintaining homeostasis. The physiological systems will elevate MAP by whichever mechanisms are available to the specific individual. Thus there is an obligatory increase in MAP.

**Peripheral blood flow.**

24. Blood flow to nonexercising vascular beds can be reduced by 75–80% during maximal exercise. This restriction in flow and subsequent shunting of blood to the working skeletal muscle will facilitate meeting the increased energy demands of the muscle during exercise of increasing severity.

25. If you refer back to Fig. 2, you will notice that both individuals have a HR of 100 beats/min at approximately the same VO2 (0.75 L/min). There is a marked increase in sympathetic activity once HR has reached 100 beats/min and this sympathetic activation stimulates vasodilation in the regional vascular beds. The decrease in regional flows occurs concurrently with increased NE levels that result from this increase in sympathetic activation.

26. The vasoconstrictor response after a HR of 100 beats/min has been achieved is actually similar when expressed relative to each individual’s percentage of VO2max (see Fig. 10). The total reduction in blood flow occurs over a smaller increase in VO2; however, the absolute amount of decrease in blood flow is the same.

Blood flow to these regions is determined by perfusion pressure and vascular resistance. With increasing workloads, sympathetic nerve activity increases and causes marked vasoconstriction in the extremal and splanchic vascular beds. At the same time, CO is increasing with increasing workloads, and this results in increasing perfusion pressure. The perfusion pressure cannot increase proportionately with the increase in resistance, and blood flow will therefore decrease to these regions (Flow = Pressure/Resistance). In the older individual CO increases at a slower rate and to a lesser extent, so the decrease in blood flow will occur at a greater rate.

**Skeletal muscle blood flow.**

27. The young and older individuals respond in similar fashion to the onset of exercise. There is an early rapid rise in muscle blood flow, most likely as a result of the release of vasoactive metabolites early in exercise, causing marked vasodilation. Autoregulatory mechanisms and flow-mediated release of nitric oxide also serve to vasodilate the vasculature at the onset of exercise.

28. After the initial rapid rise in blood flow, sympathetic adrenergic activity increases, stimulating vasoconstriction. Although the metabolically induced vasodilation dominates during exercise, the sympathetically activated vasoconstriction will slow the rate.
vasoconstriction attenuates the metabolite, autoregulation, and total peripheral resistance. There is an early rapid decline in the metabolically induced vasodilation, which has the greater impact on muscle blood flow.

The blood flow response differs between the young and old individuals in two ways. First, because of the limitations of increasing CO, the maximal blood flow response will be reduced in the elderly individual. As the heart fails to maintain an increasing CO, the baroreflex and metaboreflex will increase sympathetic activation. As sympathetic adrenergic activation increases, blood flow is reduced and blood pressure is maintained. This vasoconstrictor response will increase, resulting in a reduced muscle flow. The muscle’s vasodilatory response may also be attenuated because of a diminished β-adrenergically-mediated vasodilation.

**Total peripheral resistance.** There is an early rapid decline in TPR in both the young and older individuals. This decrease in TPR results from the production of local metabolites that are a powerful stimulus for vasodilation. Autoregulatory mechanisms and flow-dependent release of endothelium-derived nitric oxide (EDNO) also contribute to vasodilation. This vasodilation allows for a rapid increase in muscle blood flow (Fig. 11) to meet the increased metabolic demands of the working muscle. The increase in blood flow also serves to help clear the metabolic by-products as the energy requirements increase with increasing workloads.

**31.** Once HR has reached 100 beats/min at ~40% VO2max, sympathetic nervous activity increases. This increased sympathetic activity causes an attenuation of the decrease in peripheral resistance through vasoconstriction of the arterioles. This function to maintain perfusion pressure in the muscle bed. Thus vasoconstriction attenuates the metabolite, autoregulation, and EDNO-induced vasodilation, which is illustrated by the leveling off of TPR.

32. Although TPR decreases at approximately the same relative rate in the older individual, it starts at a slightly higher level and remains elevated through increasing workloads compared with that of the younger individual. This increase in TPR in the older individual occurs as a result of a number of different mechanisms. The structural changes that occur with aging are associated with a decreased compliance that will impact the resistance vessels in skeletal muscle. With increasing workloads, CO fails to increase, which will stimulate an increase in sympathetic nerve activity to vasoconstrict, and thus increase, TPR. There is also an attenuated vasodilatory response to β-adrenergic stimulation that will also function to increase TPR.

33. At the highest workload, TPR increases slightly in the older individual. Figure 5 illustrates that CO has started to decrease and muscle blood flow is beginning to fall off (Fig. 11). As CO fails to meet the metabolic demands of this final workload (the inability of HR and SV to increase), the baroreceptor will be unloaded, which increases sympathetic nerve activity. This increased sympathetic activity vasoconstricts the arterioles, which function to maintain perfusion pressure.

34. a-v O2 difference. a-v O2 difference between the young and older individuals differs very little at rest and with increasing workloads. Despite the changes that occur with aging with respect to decreased muscle oxidative capacity, decreased capillary-to-fiber ratio, lower muscle blood flow with exercise, and a decrease in the muscle mass-to-total body mass ratio, it appears that a-v O2 difference is not compromised in the older individual. This is most likely a result of the fact that, under normal circumstances, the potential a-v O2 difference is never actualized in that there is a far greater potential for O2 extraction than is utilized.

The only time when young and older individuals differ is at the highest workload, when the older individual’s a-v O2 difference appears to go up slightly. This most likely occurs in an attempt to compensate for the failure of CO to increase by widening the a-v O2 difference to raise VO2 as workload increases.

**35.** a-v O2 difference is not the limiting factor to the VO2max in the older individual. Even at the higher workloads, a-v O2 difference is continuing to increase with no indication of a leveling off even as the energy requirements continue to increase. From the equation \( VO_2 = CO \times a-v O_2 \), it is clear that CO is the limiting factor to VO2 in the older individual.

**Pulmonary responses**

**Tidal volume.** Tidal volume at rest is higher in the older individual. As lung compliance increases and elasticity decreases, there is an enlargement of the trachea and airways which results in an ~30% increase in dead space and tidal volume. The older individual respires at a significantly higher percentage of total lung capacity, which leads to a greater amount of air trapping. Therefore significantly more air must be inspired to fill the increased space. Residual volume increases because of the increased diameter of the airways, and the lung no longer resists expansion because of the loss of elasticity. Thus tidal volume must increase to fill the extra dead space so that the physiological volume (that volume of inspired air that is available for gas exchange) remains the same.

37. Once exercise begins, there is an attenuated response of tidal volume in the older individual. This response is due to the physiological changes that occur with aging and the effect that they have on vital capacity. This attenuated tidal volume response is the major contributing factor to the decrease in minute ventilation that is observed in the older individual.
Respiration rate. 38. Respiration rate increases at much lower workloads in the older individual because of the lower tidal volume. If minute ventilation is to be maintained and tidal volumes are limited, the respiration rate will be forced to compensate by increasing at lower workloads than are seen in the younger individual. There will also be an increased respiratory drive by the MRC, which will increase respiratory rate so as to offset the acidification due to increased lactate formation during anaerobic metabolism at increasing workloads.

39. Physiological limitations experienced by the aging pulmonary system will affect the maximal respiration rate. The increased metabolic cost of breathing will be most apparent as the respiratory rate increases with increasing workloads. The rigidity of the chest wall, the weakness of the respiratory muscles, and the increased energy requirements as a proportion of total aerobic capacity will all limit the ability of the respiratory rate to keep pace with the increased energy costs of the higher workloads.

Minute ventilation. 40. At any given percentage of VO2max, the minute ventilation for the young and old individuals is the same. Yet at each percentage of VO2max, the older individual is working at a much lower absolute VO2. The ventilatory equivalent is much higher in the older individual, in that he must work much harder at any given workload. Because the older individual's lungs are already filled (i.e., higher residual volumes), it will require greater ventilatory work to fill the lungs further. Work is being performed at the limit of the lung's compliance curve, thus a greater ventilation is required per liter of O2 consumed.

41. Minute ventilation in the older individual is occurring at a much greater percentage of that individual's total lung capacity. This results from the changes in lung compliance and elasticity and from the stiffening of the chest wall. In both individuals, at lower workloads, minute ventilation increases linearly with VO2. On reaching the anaerobic threshold (that level of VO2 above which blood lactate levels show a systematic increase above resting levels, signaling metabolic acidosis resulting from increasing contribution of anaerobic metabolism), minute ventilation increases dramatically, which functions to offset the acidic effects of increasing lactate. The older individual, however, is already breathing at a much greater percentage of total lung capacity, and there is little room for increasing ventilation as much as is required. At this point the younger individual continues to increase his minute ventilation, thereby blowing off increasing amounts of CO2 and enabling him to continue exercise for a longer period of time. The older individual will be limited in exercise capacity by this inability to increase minute ventilation any further.

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