THE EFFECTS OF AGING ON ARTERIES

“Genetics Load the Gun—Environment Pulls the Trigger”
“Genetics Predetermines Your Life Span—Environment Determines the Probabilities”

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Advancing age affects vascular structure and function. However, since the aging process varies between men and women, there must be other factors that influence aging. Extensive medical literature describes how vascular function differs in older and younger individuals. Certainly genetics have a major and defining influence on longevity. The question that begs an answer is, do environmental factors (eg, smoking, obesity, sedentary lifestyle) affect the aging process and thus the genetically predicted age?

To help define the effects of genetics and environment on aging in the vascular system, a number of questions are presented with discussions of the answers.

QUESTIONS

1. Which factor(s) confers the greatest risk for coronary artery disease (CAD), congestive heart failure (CHF), stroke, and hypertension (HTN)?
   a. hyperlipidemia
   b. diabetes
   c. sedentary lifestyle
   d. smoking
   e. genetic factors
   f. advancing age

2. The effect of aging on cardiovascular (CV) disease is explained by which theories:
   a. aging increases the exposure time to CV risk factors
   b. aging alters the underlying CV substrate, as well as the threshold for the occurrence, severity, and prognosis of disease
   c. aging increases homocysteine levels and other hormonal factors that lead to atherosclerosis

3. Which marker(s) of vascular aging may reflect subclinical arterial disease?
   a. increased large vessel lumen
   b. arterial wall thickness
   c. reduced arterial elasticity
   d. decrease in diastolic blood pressure (BP)

4. Which theory associates the increase in CV disease with aging?
   a. aging effects CV structure and function which lower the threshold for CV disease
   b. aging increases the vulnerability of the vascular system in hypertensives and hyperlipidemics
   c. hyperlipidemia is associated with aging
   d. a and b

5. A widened pulse pressure (PP), often found in the elderly, is considered to be:
   a. a precursor to postural HTN
   b. an independent predictor of risk of CAD
   c. a risk factor for arterial vasospasm

6. Which arterial change(s) in the elderly support evidence that aging provides the environment that permits vascular disease to flourish?
   a. large artery dilatation and intimal thickening
   b. endothelial dysfunction (ED)
   c. arterial stiffening
   d. wide PP
   e. all of the above

7. ED, which is associated with aging, also contributes to CV morbidity and mortality by which of the following?
   a. decreasing the release of endothelium-derived relaxing factor
   b. adversely altering arterial physiology
   c. increasing nitrous oxide release

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8. Therapeutic trends that decrease vascular aging and its complications include which of the following?
   a. leading a sedentary lifestyle
   b. exercise and a low-sodium diet
   c. controlling BP and blood lipids

ANSWERS
1. f. advancing age

The explosions in biological information, pharmaco-technological breakthroughs, and advances in primary and secondary prevention, as well as trends toward improved lifestyles, have resulted in a 60% decline in mortality from vascular diseases. However, because vascular diseases are more prevalent in the aged, the increase in longevity has resulted in a greater prevalence of arterial atherosclerotic disease. Currently in the United States, there are more than 35 million people 65 years or older, and this number is predicted to almost double by 2030. CAD and heart failure (HF) are the most common diagnoses in hospitalized patients 65 years and older and will be encountered with greater frequency as the population ages. A major goal in prevention of HF is the improvement in the treatment and prognosis of systolic HTN by strict adherence to the established guidelines.

Several risk factors for CAD, HTN, cerebral vascular accident (CVA), and CHF have been identified; however, the effects of aging on the vascular system confer the greatest risk, and this risk continues to rise steeply with age. Aging is associated with a number of anatomic and hemodynamic changes in the vascular system, including degeneration of collagen, loss of elastin, increased intima-media arterial wall thickness, and reduced vascular compliance. The result is a reduction of various degrees in the distribution and delivery of blood and thus nutrients and oxygen to all segments of the body.

2. a. aging increases the exposure time to CV risk factors
   c. aging alters the underlying CV substrate, as well as the threshold for the occurrence, severity, and prognosis of disease

Alterations in cardiac structure and function are well documented in seemingly healthy humans as they age. Many of these age-related CV changes (left ventricular hypertrophy, atrial fibrillation [AF], CHF) influence the prevalence of cardiac disease in the aging population. Several theories have been proposed to explain the effects of aging on disease; one claims that age contributes to the occurrence and severity of CV disease simply by increasing the exposure time to CV risk factors; another, that aging alters vascular structure and function. The age-disease interaction influences the threshold for the occurrence, severity, and prognosis of CV disease. The interactions between vascular aging and disease are complex, involving multiple risk factors and elusive genetic factors. However, the changes in arterial structure with aging influence function and thus may adversely affect the delivery of oxygen and basic nutrients required for optimal endothelial function as well as resistance to arterial degeneration and aging.

3. a. increased large vessel lumen
   b. arterial wall thickness
   c. reduced arterial elasticity
   d. decrease in diastolic BP

There is increasing evidence that the vascular changes once thought to be characteristic of the normal aging process actually precede clinical vascular disease and are predictive of a higher risk for CV disease (atherosclerosis, HTN, CVA). The aged population has been stratified by clinical markers to differentiate successful from unsuccessful aging. Successful aging implied the absence of signs of deleterious subclinical disease. In contrast, unsuccessful aging was considered when there were clinical manifestations of vascular aging, that is, increased large vessel lumen, wall thickening and stiffness (atherosclerosis, HTN). In this scenario, vascular aging and vascular disease are not one entity, but actually partners; each contributes specific components to a common outcome, namely, vascular disease. Thus, unsuccessful aging can be considered a risk factor for clinical disease. The same vascular changes observed in older normotensive individuals have been seen in younger, hypertensive patients. These findings may be a manifestation of unsuccessful aging in an otherwise asymptomatic person. On the other hand, the so-called “normal” vascular aging process may well be a product of the genetic background and the environment (smoking, obesity, sedentary lifestyle) and thus represent pathology rather than merely aging or accelerated aging.

4. d. a and b

Changes in CV structure and function that accompany aging alter the substrate on which CV disease is superimposed. Although these age-related changes may not overtly cause clinical cardiac disease, they can compromise cardiac reserve and lower the threshold
for disease development, thereby increasing the risk of a CV event.14 Age-related changes in coronary artery vasculovasorum in cardiac structure and function can be found throughout the vascular system. As central arteries stiffen, systolic BP rises and PP widens. Systolic HTN plus the arterial changes contribute to increased left ventricular mass, which can lead to further functional abnormalities. Of all the cardiac changes found in “healthy” aging adults, increased left ventricular wall thickness, altered diastolic filling pressure, impaired left ventricular ejection, impaired heart rate reserve, and altered heart rhythm are the most dramatic. In the absence of clinical disease, these age-related changes may explain the increased prevalence of left ventricular hypertrophy, AF, and CHF in older individuals. An age-dependent increase in left ventricular mass leads to increases in left ventricular stiffness and end-diastolic filling pressure, a manifestation of diastolic HF. Increased diastolic filling pressure often leads to left atrial dilatation, predisposing the heart to AF. The clinical features of AF (ie, tachycardia, loss of AV synchrony) further alter diastolic filling pressure and compound the evolution of diastolic HF.

5. a. a precursor to postural hypotension  
b. an independent predictor of risk of CAD

In industrialized societies, there is an age-related progressive increase in BP starting in childhood. Systolic and diastolic BPs tend to rise during the adult years, but greater increases occur in systolic BP. Systolic BP continues to rise into the eighth and ninth decade, but diastolic pressure remains constant or even declines after the fifth decade. An increase in wave reflection amplitude is seen with the loss of large artery compliance. Systolic arterial pressure rises and diastolic pressure decreases, which result in a widening PP. A widened PP, once believed to be a routine finding during the early years, and to increased large artery stiffness in later years. Large artery stiffness that occurs later in life results from intrinsic structural abnormalities related to thinning, fragmentation, fracture of elastin, increased collagen, and calcium deposition in the arterial walls.3 An increase in PP with a fixed systolic pressure occurs as a result of a declining diastolic BP that is a consequence of large artery stiffness often seen in the elderly population. In contrast, an increase in systolic BP with fixed PP occurs when there are parallel increases in systolic and diastolic BP and is probably a consequence of an elevated PVR, common in hypertensives less than 50 years old.7 Although PVR may continue to increase, the downward movement of the diastolic BP (increase in PP) is a measure of large artery stiffness and is the major hemodynamic factor in both normotensives and hypertensives.7

6. e. all of the above

Aging blood vessels provide the environment that permits vascular disease to flourish. Cross-sectional studies in humans reveal intimal wall thickening and dilatation as the major structural changes that occur in the large arteries during aging. ED, arterial stiffening, and PP widening as found in atherosclerosis are also considered to be markers of vascular aging. The question remains to be answered, are these coronary arterial changes a result of vascular aging (poor genetics that accelerate physiological aging) or due to early environmentally related changes (atherosclerosis, obesity, hyperlipidemia, sedentary lifestyle) or a combination of both?

Intimal thickening, often accompanied by luminal dilatation and reduction in compliance, results in vessel stiffness. Pulse wave velocity (PWV) uses the stiffness of the vascular wall and mean arterial pressure to index vascular stiffening. The PWV index increases with age in both genders. Increased PWV has been associated with pathologic structural alterations in the vascular media. Increased PWV, an index of large vessel stiffening, may not only be linked to structural changes in the media, but also to endothelial regulation of vascular smooth muscle tone and function. ED has been identified in early atherogenesis, diabetes, and HTN. Structural changes in the aging vessel, together with ED, lead to stiffening of the vascular wall and atherosclerosis.

7. a. decrease in the release of endothelium-derived relaxing factor  
b. adversely altering arterial physiology

Endothelial injury and dysfunction, both important factors in atherogenesis, contribute to CV morbidity and mortality by disturbing normal arterial physiology. ED is associated with aging and has been evidenced by the decreased response to flow-mediated vascular dilatation. However, ED has also been demonstrated in asymptomatic children and young adults who have strong vascular risk factors.3 The mechanism by which
Exercise conditioning improves endothelial function; diets low in sodium are associated with reduced arterial stiffening in the elderly. Pharmacotherapy with angiotensin-converting enzyme inhibitors reduced vascular aging in animals. Reduction in intramuscular thickness has been achieved with a combination of diet and medication.

**Summary**

The age association and alterations in vascular structure and function at both the cellular and molecular levels are increasingly recognized as major risk factors for CV disease. The arterial remodeling during aging that may be enhanced by the CV risk factors are supersensitive to the age-related risk factors. The aging process may well be influenced by a combination of hereditary and environmental factors. Much can be done to modify environmental risk factors, very little to genetics except for choosing your parents.

**REFERENCES**


**SELECTED REFERENCES**


The Effects of Aging on Arteries
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