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Commentary

Abstract

Diminished blood ow to the brain and other organ systems may result from an impaired microcirculation due to pathological changes in the capillaries or reduced numbers of capillaries. e former are re ected in twisting, kinking, and looping of capillaries in the cerebral cortex [1-3]. Whether these changes progress to reduced capillary numbers by cellular atrophy has not been demonstrated and is not considered further here. However, the widespread reduced capillary density (CD) found in aged animals and people has been correlated with diminished levels of angiogenic growth factors (AGFs) [4-6].

e association between CD and AGFs during old age is the focus of this essay, which advances two ideas. 1) e reduced CD of old age may be the main, primary cause of many symptoms and signs of the elderly, i.e., the 'lesser ailments of aging'. 2) A reduced CD may also be an underlying, secondary condition for other diseases associated with aging and may facilitate the action of factors postulated to cause them -- e.g. amyloid plaques, neuro brillary tangles, etc. of Alzheimer's disease (AD) or Lewy bodies, proposed malfunctioning mitochondria, etc. of Parkinson's disease (PD).

People die from accidents and major diseases. e rest live on through old age with generally two sorts of complaints: chronic a ictions and/or lesser ailments. e former involve arthritis, diabetes, atrial brillation, Parkinson's disease, or other distressing illnesses and are not a concern here. e latter, the lesser ailments, include minor symptoms, such as general muscle weakness, cold intolerance, memory lapses for names or words, and momentarily dozing, especially during the evening hours [6]. Also included are physical signs, such as wrinkled skin on the face and dorsum of the hands and the slow healing of bruises and abrasions. ese symptoms and signs may share a common etiology which is the reduced capillary density that develops throughout the body during old age.

As discussed elsewhere, a reduced CD in aged persons and animals has been described in over 40 reports and noted in many organ systems -- i.e., brain, muscle, skin, larynx, lung, colon, kidney and vasa vasorum [5,6]. Capillaries are formed and maintained by angiogenic growth factors (AGFs), whose levels are genetically programmed during early development and throughout life. A decline in AGFs in the aged has been described in seven other reports and noted in ve organ systems -- i.e., the brain, muscles, kidney, mononuclear cells, and vein wall [5,6]. Among the AGFs are vascular endothelial growth factor (VEGF), broblast growth factors (FGFs), and other such factors. For this essay, the important aspect of these AGFs is that during old age their levels decline, resulting in a reduced capillary density in the tissues. us, the lesser ailments re ect a de ciency condition of AGFs, much like the reduced testosterone levels in elderly males.

In the literature little mention has been made that the decline in the levels of AGFs in the elderly is genetically programmed. Whether amyloid plaques or other factors can also in uence capillary density is unclear.

In theory from the above analysis, the lesser ailments should be relieved or delayed by pro-angiogenic therapy -- e.g., recombinant forms of VEGF, FGF, or other angiogenic agents. is is a novel idea which must be introduced with persuasive data to be seriously considered by students of aging.

Merely listing a large number of papers sharing a common e ect does not convey so convincingly their importance as does showing the relevant data. Age-linked changes are presented here in the form of 'data pairs' -- i.e., values of CD or AGFs in adult animals or people vs. those in their aged counterparts. For example, Amenta et al. measured the capillary density in three areas of the brain of rats age 12 months vs. 18 months old and reported reduction of the CD as follows -- frontal cortex: 122 vs. 71, occipital cortex: 130 vs. 82 and hippocampus: 113 vs.

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58 [7]. Similarly, Haidet et al. compared the CD in three muscle areas of beagle dogs ages 2-3 years vs. 10-14 years and found the following -- gastrocnemius: 886 vs. 718, semitendinosus: 895 vs. 658, and triceps: 959 vs. 805 [8]. ese six sets of data are more persuasive than a generalization that papers by Amenta and Haidet show an age-linked reduce CD.

As noted above, an examination of the research literature on aging and angiogenesis has disclosed 47 studies concerning CD and levels of AGFs. ey have provided 80 data pairs showing age-linked reduced CD

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