Editorial

In this issue of *Vascular Medicine*, Shaffer and Mohler describe the effects of vascular disease and aging on the regulation of circulating endothelial progenitor cells.¹ This study is of interest because aging, cardiovascular risk factors, and cardiovascular diseases are all associated with reductions in endothelial function. Previous studies in healthy subjects without cardiovascular disease have shown a correlation between the number of circulating endothelial progenitor cells and the overall risk of subsequent cardiovascular events, as well as a correlation between circulating progenitor cells and endothelial function.² In patients with established cardiovascular disease, circulating progenitor cells at baseline are associated with a subsequent risk of cardiovascular events.³ Thus, normal endothelial function is in part maintained by circulating endothelial progenitor cells that can interact with vascular endothelium. Impairment of endothelial function and subsequent clinical outcome is associated with decreased numbers of circulating progenitor cells.⁴ In addition, acute exercise is known to modulate endothelial function,⁵ possibly by mobilizing progenitor cells.

In the study by Shaffer and Mohler, several progenitor cell populations were measured at rest and in response to exercise in healthy control subjects and in patients with peripheral arterial disease (PAD). The results demonstrated that healthy resting younger subjects had higher progenitor cell numbers than the older or PAD groups, but the overlap in individuals was considerable. Graded exercise in young healthy subjects was associated with an increase in several progenitor cell populations, but patients with PAD and older subjects had no change or variable changes in these cell lines with exercise. The authors concluded that in addition to aging, muscle ischemia induced by exercise in patients with PAD was an insufficient stimulus to mobilize endothelial progenitor cells. Their findings may relate to loss of endothelial function in these populations.

Understanding the effects of endothelial progenitor cells on endothelial function may provide information on several potential pathways that relate to claudication therapy. For example, exercise training improves walking distance in patients with PAD, and this clinical improvement is not associated with any changes in calf blood flow.⁶ Several effects of training may account for this improvement, including alterations in the biomechanics of walking, adaptations in muscle metabolism and improvements in endothelial function as assessed by the activity of nitric oxide.⁵ Whether changes in circulating endothelial cells with training

relate to the clinical improvement that results from exercise training will require further study.

While the findings of Shaffer and Mohler are of considerable interest, several questions remain. In particular, this study found increases in endothelial progenitor cell numbers in healthy young subjects who were tested at higher work loads than the older or PAD subjects. Therefore the exercise stimulus was not equivalent between groups. Further investigation is warranted to more critically look at the dose-response relationships between exercise duration, intensity, and mobilization of different cell lines in healthy subjects.

Despite those limitations, alterations in the number and/or function of circulating endothelial progenitor cells may have clinical ramifications for vascular health and functional capacity. Greater understanding of the role of progenitor cells in the regeneration of the endothelial lining may have therapeutic implications, particularly as it pertains to exercise training.

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