To the Editor: The underlying issue being discussed (1a, 4) seems much broader than simply the role of venoconstriction. It is really about the regulation of the magnitude of cardiac output. Thus while the argument put forth by Hainsworth and Drinkhill is fine as far as it goes, it fails to address how it is that cardiac output can rise to four or five times its baseline level. If, as they claim, the blood volume in the splanchnic bed is flow dependent, then how can the cardiac output increase so much? Similarly, although Rothe cites evidence for volume shifts resulting from active vascular constriction, the maximal magnitude of these shifts is not nearly sufficient to account for such extreme increases in cardiac output.

Because it is axiomatic that the heart cannot pump any faster than the periphery can return blood to it, this then leaves us with the question as to how does the Pmcf increase during exercise? One possibility noted many years ago is that the heart itself can translocate sufficient volume to the periphery to substantially increase cardiac output (3). Another mechanism does not actually involve the Pmcf at all, but rather, the effective resistance to venous return. As theoretically and experimentally documented by Caldini et al. and others (1, 2), simply opening a relatively noncompliant A-V shunt (such as in a stiff contracting muscle) will significantly decrease this resistance, thereby increasing venous return and cardiac output. It is for these reasons that one needs neither much active venoconstriction nor any significant splenic contraction, to achieve substantial increases in cardiac output. Thus it seems that both sides of this pro/con debate are correct and that there really isn’t much controversy at all.

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Wayne Mitzner
Johns Hopkins University

In a modeling study (1), we demonstrated that only decreases in venous unstressed volume (15–20%) were effective in raising LVEDP to substantial levels (~25 mmHg); decreases in contractility and increases in peripheral resistance were not effective.

Finally, we suggest that changes in venous capacitance can be much more readily appreciated by the use of pressure-volume plots (5)—such studies need not be particularly invasive (3)—rather than pressure-flow plots (e.g., right atrial pressure vs. venous return). In the past, ambiguities in the concept of venous return (i.e., blood volume redistribution and/or instantaneous caval flow rate) may have obscured how venoconstriction increases end-diastolic volume and stroke volume and, thereby, modulates cardiac output (5) during exercise and orthostasis.

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To the Editor: During orthostasis, Pra falls to zero: cardiac output (CO), EDV, SV fall despite extensive vasoconstriction and, probably, hepatic venoconstriction (2a, 3). MAP is maintained until progressive rise in leg venous volume (viscoelastic creep) causes hypotension—prevented only by muscle contraction (1). Muscle veins lack noradrenergic innervation (Ref. 143 in Ref. 4). Human cutaneous veins constrict significantly when skin and core temperatures fall during heat stress (4, Fig. 30), translocating centrally large volumes that suddenly raise Pra, SV, and thoracic volume (4, Fig. 35). Such unambiguous effects of venoconstriction are not normally seen in exercise (without heating) nor orthostasis. Gwyn (2) demonstrated that muscle pumping prevented reductions in Pra normally attending increases in CO at rest (see Ref. 5). Rothe’s concept (3) of unstressed venous volume (a virtual volume calculated from a virtual pressure [Pmcf (3)—both unmeasurable], is inadequate when muscle pumping reduces a major compartment volume. Rothe’s counter to criticism that resistance increase in constricting veins would elevate pressures in compli-
ant venules upstream is that resistance of the constricting elements is small. But the effect of constriction on their resistance (radius 4) is far greater than on their volume (radius 2). Both debaters’ (2a, 3) conclusions that hepatic venoconstriction attends both stresses but that most venous volume is mobilized passively, are supported. However, in autonominously blocked dogs, normal rises in Pra and CO with exercise reveal that muscle pumping translocates enough blood volume centrally to suggest small importance of vеноconstriction in exercise as well as orthostasis (5). Finally, Hainsworth’s comment (2a) that it is “not possible to obtain accurate quantitative data from humans” overlooks precise measurements of CO, organ blood flow, intravasculare pressures, etc., from humans whose orthostatic problems are unique.

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Loring B. Rowell
University of Washington

To the Editor: We appreciate the opportunity to comment on the current discussion regarding the importance of active vеноconstriction (1, 2). While we agree with Rothe’s general conclusions, we believe his opening sentence gives the impression that active vеноconstriction only has evolved in animals that experience gravitational orthostasis (2). This may lead to unnecessary confusion.

As comparative cardiovascular physiologists, our interest in the evolution of cardiovascular systems in different animal groups has led us to recently study the role of the venous system in the overall hemodynamics of fish. Fish live in a medium with a density similar to their body fluids and therefore represent vertebrates that evolved and remain in a nearly gravity-free environment where orthostatic blood pooling is infinitesimally small. Research on fish clearly demonstrates that active venous control is an evolutionary ancient trait that evolved well before vertebrates inhabited land and became subjected to strong gravitational forces (2–5).

We have found that cardiac preload increases while venous capacitance decreases (as judged by decreased USBV and/or increased MCFP) during exercise (4), environmental hypoxia (2), and after injection of α-adrenergic agonists (3, 5). α-Adrenergic blockade fully or partially abolishes these responses and impairs the ability to increase cardiac stroke volume and output during exercise.

Thus active vеноconstriction is an integrated and important component during various cardiovascular responses to increase or maintain stroke volume, even in vertebrates as ancient as sharks. Therefore, gravitational forces were at best a secondary selection pressure for the evolution of active vеноconstriction.

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Erik Sandblom
Michael Axellson
Anthony P. Farrell
Göteborg University

To the Editor: It appears that there still is some controversy (1a, 2) concerning the role of the baroreceptor reflex system in controlling venous capacity and consequently cardiac output. Greene (1) measured the changes in vascular capacitance, resistance, the venous return curve, and cardiac function curve concurrently. They concluded that changes in vascular capacity are the primary mechanism responsible for changes in cardiac output by the reflex system. This change was ~40%, a value slightly less than reported by Shoukas (3) of 60%. The controversy today seems to be a quantitative one, namely, how important is a 40–60% change in cardiac output mediated by changes in venous capacitance. In exercise where cardiac output changes by as much as 500%, the importance of neurally mediated capacitance changes is most probably minimum and passive changes of blood flow redistribution and the muscle blood pump are extremely important. However, for the elderly suffering from orthostatic intolerance or astronauts returning from a microgravity to a gravity environment, it may be the most critically important mechanism in maintaining cardiac output and arterial pressure. It may be the appropriate time to have another symposium on vascular capacitance.

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Artin A. Shoukas
The Johns Hopkins University School of Medicine