Optimal hematocrit: a Procrustean bed for maximum oxygen transport rate?

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Physiological systems are characterized by multiple interdependent components that collectively subserve various processes and functions. In seeking better understanding of the performance of such complex systems, we must identify and evaluate alternative ways and operating schemes, comparing their predicted performance with goals or objectives of interest. Optimization entails selecting a better or best alternative from among a number of candidates. Such alternatives are defined by the values of pertinent properties and operating physiological variables. Once physiological performance objectives (measures) and various alternatives for achieving proposed levels of these objectives have been identified, mathematical models can be developed and used to help identify specific alternative ways that best meet them. Constrained optimization together with simulation modeling is the primary approach we have for estimating the values of the physiological variables that will best achieve specified performance objectives (5, 13, 14, 20).

An intriguing problem in physiology and hemorheology is to evaluate the hematocrit that satisfies the optimality criterion of maximum transport rate of oxygen to the systemic microcirculation. With modern laboratory equipment, the hematocrit is determined by an automated analyzer, by multiplying the red cell count by the mean cell volume, rather than directly measured. It is slightly more accurate than the conventional packed cell volume that includes small amounts of blood plasma trapped between the red blood cells. A reduced hematocrit can be caused by either overhydration, which raises the plasma volume, or a diminution in the number of red blood cells caused by blood loss or various anemias. An increased hematocrit can be brought about by loss of fluids, such as in dehydration, diuretic therapy, and burns, or by an overproliferation of red blood cells, such as occurs in cardiovascular and renal disorders, polycythemia vera, and chronically impaired ventilation.

Hematocrit is a primary determinant of blood viscosity, viscosity decreasing (thixotropy) as shear rate rises (1, 18, 19). Blood viscosity and blood flow in the microcirculation change in opposite directions with hematocrit level; they are also affected by erythrocyte and platelet aggregability and rouleaux formation, erythrocyte deformability, and plasma viscosity. Effective microcirculatory blood viscosities are also modified by the Fåhraeus-Lindqvist effect, causing viscosity reduction in capillary tubes of a diameter below 0.3 mm (8), and its inversion as vessel diameter approaches 5–7 µm (6). Anemia and hypervolemic hemodilution decrease not only the oxygen content of blood, but also blood viscosity, thus raising regional blood flow and cardiac output (4, 9). Inversely, hemococoncentration and hyperviscosity syndromes can—by positive feedback mechanisms—limit the ability of autoregulatory processes to augment blood flow, resulting in compromised organ perfusion and even thrombosis (17). Thus hematocrit variations are only weakly correlated with maximal oxygen uptake (3, 7). Moreover, there are other confounding factors, such as that the amount of oxygen normally taken from arterial blood is only about 20% of that available. Although the oxygen content of blood decreases with declining hematocrit, the reduced viscosity allows the relative oxygen transport capacity to increase as the hematocrit is lowered to 30–33% (12, 15). Then again, recombinant human erythropoietin increases red blood cell mass and the maximal oxygen carrying capacity of blood as well and augments maximal oxygen consumption (10, 11).

The ratio of hematocrit divided by blood viscosity epitomizes the theoretical ability of blood to deliver oxygen in the microcirculation; when plotted as a function of hematocrit, it yields a parabolic concave curve concave to the hematocrit axis (2), akin to an inverted U, with a broad maximum signifying an optimal hematocrit range for oxygen delivery. This maximum is physiologically important because it indicates an advantageous steady-state coming about between moderately low blood viscosity and relatively high oxygen binding capacity; it coincides with the species-dependent normal range of hematocrit values. Deviations from this range lead to reduced oxygen transport capacity, attributable to either a suboptimal hemoglobin concentration or a seriously augmented blood viscosity ensuing from the increased hematocrit.

The intriguing problem of the hematocrit that best satisfies the optimality criterion of maximum transport rate of oxygen to the systemic microcirculation is considered in the elegant and parsimonious paper by Drs. Stark and Schuster in this issue of the Journal of Applied Physiology (16). The authors consider theoretical optimal values of hematocrit in vertebrates and collect, from the literature, experimentally observed values for 57 animal species to critically assess the power and limitations of optimal hematocrit theory. They nicely achieve their goal, namely, to provide a systematic overview of different approaches in optimal hematocrit theory geared to their above mentioned optimality criterion.

There is, nonetheless, an inherent qualification in this sort of investigation: the collection of complete information and the consideration of all alternatives is seldom possible for most complex physiological systems with multiple interdependent components and regional spatiotemporal inhomogeneity. We should always determine and bear in mind the scope and limitations of the model. Deviations from the optimal value of any controlled physiological parameter, including optimal hematocrit, can result from changes in the internal and external environments. In principle, a receptor system monitors the value of the parameter to maintain, and conveys it to a regulatory module via an afferent information pathway (14). Accordingly, restraints must be placed on extrapolations and generalizations, which might be contemplated by some without due attention to applying conditions pertinent to specific applications. Or, as the authors put it, “Different models can be built for the same process, and it is decided by the practical
application which one works best.” In other words, the optimal hematocrit cannot be a Procrustean bed for maximum oxygen transport rate.

Depending on the purpose of the analysis, a given physiological process or phenomenon may be explainable by sets of laws or mechanisms having different degrees of generality. There are important comparative and evolutionary physiology insights from the 30,000-ft., global view of the hematocrit provided by Drs. Stark and Schuster. Understandably, however, none of these generalizations applies to the microenvironment of patient encounter. What is the optimal hematocrit for a sick patient? When do you intervene? Heavy cloud cover mars the answers to such pedantic but critical questions. Just like most questions arising in a clinical context, the answer has to be individualized. A thorough understanding of germane factors and their interrelationships, well-founded in science, should provide a foundation for improving clinical practice guidelines and may help to characterize the advantages of individual as against population-based hematocrit targets. In this context, the comprehensive study by Drs. Stark and Schuster should play an important role to our better comprehension of hematocrit regulation and is intellectually appealing.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author.

AUTHOR CONTRIBUTIONS

Author contributions: A.P. conception and design of research; A.P. performed experiments; A.P. analyzed data; A.P. interpreted results of experiments; A.P. prepared figures; A.P. drafted manuscript; A.P. edited and revised manuscript; A.P. approved final version of manuscript.

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