The Survivability of Profound Anemia: Understanding Compensatory Mechanisms

Dr. Stephen Selinger, Chairman and Director of the Department of Medicine and Director of Critical Care Services
We’ve learned a great deal about severe anemia from animal models. For example, in a porcine model of severe euvolemic anemia, evidence of lactic acidosis—which indicates insufficient tissue oxygen utilization—did not occur until a hemoglobin of 2.7 grams per deciliter. At a hemoglobin of 4, there was no statistical evidence of anemic hypoxic injury in the brain or heart, although other organs were less tolerant.

In humans, we have information dating back several decades indicating that many patients can survive illnesses associated with severe anemia. In fact, in postoperative patients, hemoglobin values as low as 2-3 gm/dl are associated with significant survival rates. There are multiple databases that support the significant survivability of severe anemia. In one retrospective analysis of propensity-matched patients managed in a protocolized manner with hemoglobin less than 8, survival was similar in bloodless and transfused patients.

So the human body tolerates anemia even when hemoglobin is profoundly reduced. This is due to multiple compensatory mechanisms that help maintain adequate tissue oxygenation when the blood’s oxygen-carrying capacity is diminished. These mechanisms include:

- Enhanced ability of hemoglobin to unload oxygen
- Increased extraction of oxygen from the blood as it passes through capillaries
- Increased cardiac output
- And redistribution of that cardiac output

Oxygen delivery to the periphery is determined largely by cardiac output or by means of convection. By the time oxygen reaches the periphery, the partial pressure of oxygen is quite low, and diffusion to the mitochondria where oxygen is utilized occurs down a relatively narrow gradient. The ability of hemoglobin to unload oxygen becomes all the more important when the system is stressed with severe anemia.

The oxygen hemoglobin saturation curve plots the proportion of hemoglobin in its saturated form on the vertical axis against the partial pressure of oxygen in the blood on the horizontal axis. A variety of factors can shift the curve. When shifted to the right, for example, by low pH, high temperature, or high carbon dioxide, oxygen becomes easier to unload and compensates for reduced convective delivery by anemia.

Normally, 25% of the arterial oxygen content is extracted by the peripheral tissues from each milliliter of blood. A reduction in delivery from a fall in cardiac output or anemia is associated with increasing extraction, allowing the body to maintain a normal oxygen consumption.

Increased Cardiac Output & Redistribution

In the normal resting state, the heart pumps about five liters of blood every minute. When there is a greater demand for oxygen, as during exercise, the heart can increase its output many fold, to as much as 30 liters per minute.

During severe anemia, a rise in both stroke volume and heart rate contribute to an increase in cardiac output.
Vasodilation and decreased blood viscosity are important components of this response.

In addition to increasing cardiac output, the body prioritizes the brain and heart. Control of peripheral vascular tone by the nervous system and other local mechanisms allows blood to be redistributed from less vital to more vital organs.

As a response to anemia, small blood vessels in the skin contract, causing a greater resistance to the flow of blood than is present in more vital organs. The result is a partial diversion of blood from the skin to other organs. Blood is also diverted from the kidneys as part of the adaptation to anemia.

The diversion of blood flow from the skin causes one of the cardinal clinical features of anemia: pallor. Pallor is the pale color observed in the skin of a light-skinned anemic individual, and in the mucous membranes and nailbeds of all anemic individuals, regardless of skin color.

It should be noted that anemic patients are pale not because their blood is thin but because the diversion of blood means there is less blood in the skin.

**About the Author**

Dr. Stephen Selinger  
*Chairman and Director of the Department of Medicine and Director of Critical Care Services*