THE TRANSFUSION TRIGGER:
INDICATIONS FOR RED CELL THERAPY

Introduction. Red cell transfusions augment oxygen-carrying capacity. Since transfusion therapy can result in transmission of infectious disease and immunologic, allergic, alloimmune and other adverse events, clinicians reserve red cell transfusions for patients at risk for inadequate oxygen delivery to tissues related to low hemoglobin concentrations. The “transfusion trigger” or minimal hematocrit or hemoglobin level at which adult patients require transfusions has been the subject of clinical investigation and controversy. Some transfusion medicine specialists dispute the concept of a “transfusion trigger,” and instead, advise careful monitoring for evidence of inadequate tissue oxygen delivery on a case-by-case basis. Many physicians consider a minimum hemoglobin concentration of 7g/dL (21% hematocrit) as an indication for red cell transfusions and a 10g/dL hemoglobin concentration (30% hematocrit) as a level at which transfusion therapy usually is unnecessary.

Physiological adaptive (compensatory) mechanisms for anemia. Cardiac output increases in response to anemia, thereby routing more oxygenated red cells to tissues. Cardiac output is augmented by an increased heart rate and/or an increase in stroke amount (the amount of blood pumped per heartbeat). Anemia also can trigger redistribution of blood from parts of the body with low oxygen requirements to those with higher demand, e.g., shunting blood away from intestinal tissues to extremity muscles during physical activity. Increasing the amount of oxygen transferred from red cells to tissues is another adaptive mechanism. Patients with chronic anemia benefit from an increase in the red cell enzyme, 2,3 DPG, which aids red cell oxygen off-loading by up to 18%.

In combination, these physiologic mechanisms help patients compensate for lower than normal hemoglobin concentrations and reduce the need for red cell transfusions, until the hemoglobin concentration approaches one-half to one-third of the patient’s normal level. Compensation for anemia in patients with clinically significant coronary artery disease may be less efficient. Coronary artery narrowing can limit increases in coronary blood flow from increased cardiac output. The shortened time for cardiac filling at increased heart rates, during which blood flows through the coronary arteries, can limit heart muscle oxygen delivery.

Clinical observations in anemic patients. Several published reports involving patients suffering blood loss during surgery, treated in intensive care units, refusing blood transfusions for religious reasons, or anemic for other reasons provide evidence that judicious transfusion-avoidance strategies do not increase morbidity and mortality.

In a randomized study involving patients undergoing coronary artery bypass surgery, no clinical differences were seen between patients whose hematocrits were maintained at 25% compared to 32%. The group transfused at 25% received one unit of blood compared to 2.05 for the other group. In another study involving patients undergoing similar procedures, patients received red cell transfusions either when hemoglobin fell below 12g/dL or below 7g/dL. Mortality, morbidity, and exercise tolerance evaluations did not differ between the two groups. However, myocardial oxygen deficiency was detected in the group transfused at the lower level. Another randomized study involved trauma patients assigned to receive transfusions when the hematocrit was 40% or 30%. Oxygen delivery was adequate in both groups. Patients transfused at 40% hematocrit levels received five more units of red cells than patients receiving transfusions when the hematocrit fell to 30%.

Hébert et al enrolled critically-ill intensive care unit patients with normal blood volumes into a study in which they were assigned randomly to (1) a restrictive transfusion strategy (red cells transfused if the hemoglobin concentration dropped below 7g/dL with subsequent maintenance of the hemoglobin between 7 and 9 g/dL) or (2) a liberal strategy (transfusions when the hemoglobin concentration was less than 10g/dL with maintenance at 10 to 12 g/dL). Overall 30-day mortality was similar (18.7% and 23.3%) but lower in less severely ill restrictive group patients (8.7% versus 16.1%) and in those less than 55 years of age (5.7% versus 13.0%). No 30-day mortality differences were detected among patients with clinically significant cardiac disease in either group (20.5% versus 22.9%). The overall hospital mortality rate was lower in the restrictive transfusion group (22.2% versus 28.1%). The authors concluded that a restrictive red cell transfusion strategy is at least as effective—and possibly superior—to the liberal strategy in critically ill patients, with the possible exception of those with significant cardiac disease. Restrictive group patients received 54% less blood than those in the liberal group; 33% of those in the restrictive group received no transfusions.

Descriptive reports provide additional information. One study of outcomes in patients refusing red cell transfusions on religious grounds found few deaths attributed to anemia if the hemoglobin concentration remained above 5g/dL. Another study found a 1.3% 30-day mortality rate in Jehovah’s Witness patients with preoperative hemoglobin concentrations greater than 12 g/dL compared to 33% if the preoperative level was
less than 6g/dL. The death rate was 4.3-fold higher in patients with cardiovascular disease. This finding was not replicated when the same investigators evaluated consecutive patients undergoing surgical repair of fractured hips. However, almost all patients in the latter study received transfusions when the hemoglobin concentration fell below 8g/dL, making valid comparisons with the earlier study impossible.

Phlebotomy (with concomitant albumin administration to maintain intravascular volume) was used in volunteers and surgical patients to decrease the hemoglobin concentration to 5g/dL (isovolemic hemodilution). In these subjects, who were at rest in the supine position, oxygen delivery to tissues was maintained at hemoglobin levels of 5g/dL. This study, however, does not provide information about situations requiring increased oxygen consumption.

Of note, quality of life measurements in chronically ill patients with anemia, such as those with end stage renal disease and AIDS, show improvement in subjective and sometimes objective measurements as the hemoglobin concentration increases to 10g/dL and above. This implies a variance between the minimal hemoglobin levels needed to maintain oxygen carrying capacity and those needed for many daily activities. However, concern about adverse consequences of transfusion relegates most guidelines to focusing on minimal hemoglobin levels for achieving adequate tissue oxygenation.

**Clinical Guidelines.** The 1988 National Institutes of Health Consensus Development Conference noted that some chronically anemic patients tolerate hemoglobin levels below 7g/dL. The Consensus Statement concluded that the decision to transfuse should be based on consideration of the duration of anemia and the presence of conditions that affect oxygen delivery, such as impaired pulmonary function, cardiac disease, or cardiovascular disease.

In 1992, the American College of Physicians issued a statement suggesting that transfusions be administered on a case-by-case basis as signs and symptoms of anemia occur (syncope, dyspnea, tachypnea, tachycardia, angina, postural hypotension, transient ischemic attack). The statement indicated that hemoglobin concentrations of 7 to 10 g/dL generally are tolerated.

A 1996 American Society of Anesthesiology report indicated that oxygen delivery is maintained in most patients at hemoglobin levels of 7g/dL, that red cell transfusion is rarely needed if the hemoglobin concentration is greater than 10g/dL, and almost always needed when the level is less than 6g/dL.

The Canadian Expert Working Group reiterated the belief that few patients have signs or symptoms of anemia when the hemoglobin concentration is greater than 7 to 8 g/dL. They stated that weakness occurs when the hemoglobin drops to 6g/dL. Symptoms at rest occur at 3g/dL, and congestive heart failure occurs at 2 to 2.5g/dL. They suggested the following strategies for meeting on-going transfusion needs: (1) assessing anemia-related symptoms; (2) determining whether signs or symptoms of anemia are alleviated by transfusion; (3) specifying the minimal hemoglobin level at which patients function satisfactorily; and (4) evaluating the risk: benefit ratio for transfusion—taking into account the patient’s lifestyle, other medical conditions, and prognosis.

The College of American Pathologists’ guideline indicates that red cell transfusions should be given to minimize symptoms of anemia. Such symptoms usually occur at hemoglobin concentrations of 5 to 8 g/dL.

In a 1997 survey of its member institutions, the University Health System Consortium found that 59% used a hemoglobin concentration of 8g/dL in consideration with other clinical factors as the level for ordering transfusions, 25% used 7g/dL, and 16% used 9g/dL. Overall, only 11% used hemoglobin levels alone as a justification for transfusion.

**References**