Red Blood Cells

How Supplied:

All Red Blood Cell products for transfusion supplied by Versiti are leukocyte-reduced and the majority are suspended in Adsol additive with 42-day expiration from collection. Each unit is approximately 225-400 mL.

Utilization Review Guidelines:

Red blood cell (RBC) transfusion may be appropriate to improve oxygen carrying capacity. Documentation of the indication(s) for transfusion and special circumstances for transfusion that take place outside these guidelines is recommended.

Best Practice:

- Decision to transfuse should be based on **clinical assessment of the patient**, not solely on Hemoglobin (Hgb) or Hematocrit (Hct) value.[1]
- When indicated, **single unit RBC transfusions** should be the standard for non-bleeding, hospitalized patients.[1]
- A restrictive or lower transfusion threshold (Hgb ≤7.0 g/dL) is safe and indicated for most clinical scenarios when the patient is hemodynamically stable.[1]
- Patients, including neonates, can safely receive RBC units selected at any point within their licensed dating (standard issue) rather than limiting patients to transfusion of only fresh (storage length: <10 days) RBC units.[1,2]

Indications:

1. Active Bleeding (surgical or trauma-related)
    - Hgb levels in active hemorrhage often fail to accurately predict the actual RBC mass present. Surrogate markers for RBC transfusion may include:
        - Estimated acute blood loss of 30% or more of blood volume
        - Hemodynamic instability in the presence of bleeding
        - Signs/symptoms of anemia or tissue hypoxia (tachycardia, hypotension, or mixed venous oxygen saturation <55%)
        - No response to other interventions, and/or
        - Anticipated on-going bleeding[3]
    - Desired Hgb levels:
        - ≥7.0 g/dL in otherwise healthy patients
        - >8.0 g/dL in elderly patients or those with known cardiac or respiratory disease
2. Non-Bleeding Patients – Clinical Conditions and Hemoglobin Thresholds for Transfusion:
    - Hgb ≤7 g/dL
        - Hospitalized adult patients who are hemodynamically stable or asymptomatic[1]

- Critically ill (ICU) patients, including those with septic shock[3-5]
- Patients with upper gastrointestinal bleeding who are not in hypovolemic shock[3,6,7]
- Patients with traumatic brain injury, subarachnoid hemorrhage, or evidence of cerebral ischemia if patient is awake and conscious[8,9]
- Patients suffering major burn injuries[10,11]
- Patients treated with hematopoietic stem cell transplant (HSCT)[12]

- Hgb 7.1 – 8 g/dL
  - Post-operative (general, cardiac, and orthopedic) surgical patients who are asymptomatic and not bleeding[1,13,14]
  - Hemodynamically stable patients with pre-existing cardiovascular disease[1]
  - Patients with acute coronary syndrome (i.e. acute MI, unstable angina) whose symptoms have resolved after medical intervention and are now stable[16,17]
- Hgb 8.1 – 10 g/dL
  - Patients with acute coronary syndrome (i.e. acute MI, unstable angina) and on-going ischemia or unstable[16,17]
  - Patients with traumatic brain injury, subarachnoid hemorrhage, or evidence of cerebral ischemia may require higher Hgb thresholds based on oxygenation considerations and/or higher lactate levels[8,9,18]
  - Symptomatic anemia in a normovolemic patient[19]
  - For surgical oncology patients who undergo major abdominal cancer surgery, a liberal transfusion threshold (Hgb <9 g/dL) may be associated with fewer postoperative complications and lower risk of all cause mortality[15]

3. Special Patient Circumstances
   - Outpatients with bone marrow failure may need prophylactic transfusions to maintain Hgb >7.0 g/dL, and possibly >8.0 g/dL, to support quality of life.[20]
   - Patients with sickle cell disease [21,22]
     - RBC transfusion is generally performed to increase oxygen-carrying capacity by improving anemia AND to help prevent or treat complications related to hemoglobin S.
     - Patients who have an uncomplicated acute vaso-occlusive pain crisis generally do not benefit from red cell transfusion unless severely anemic.
     - For accepted indications, transfusions to increase the Hgb to 10.0 g/dL and reduce the hemoglobin S% to <30% is commonly recommended prior to major surgical procedures.
     - In the absence of symptoms, red cell transfusion is generally not indicated, even when the patient's hemoglobin is 7.0-8.0 g/dL. Keeping Hgb <10.0 g/dL prevents hyperviscosity which can contribute to red cell sickling and clinical symptoms.
     - Despite the lack of high-quality data to support the use of "fresh" red cells for transfusion in sickle cell patients, a survey of transfusion services indicated that several programs have policies that limit the storage duration of RBCs given to individuals with sickle cell disease to units less than 15 days old.[23]

4. Perioperative Surgical Patients[24,25]
    - Prior to elective surgical procedures, patients should be evaluated for anemia and appropriate management initiated (e.g. iron replacement for iron deficiency) in order to optimize the patient for best outcomes.
    - Determination of whether Hgb concentration between 6-10 g/dL justify or require RBC transfusion should be based on potential for or actual ongoing bleeding (rate and magnitude), intravascular volume status, signs of organ ischemia, and adequacy of cardiopulmonary reserve.

Dosing Recommendations:

- Single unit RBC transfusions should be the standard for non-bleeding hospitalized patients in absence of active bleeding.
- For patients with hemodynamic instability and active bleeding, refer to **Massive Hemorrhage Protocol** section for recommendations.
- For patients with risk factors for TACO (Transfusion-Associated Circulatory Overload), consider a slower rate of administration and reducing the transfusion volume. Observe patient for signs/symptoms of fluid overload.

Expected Outcomes:

- One (1) unit of RBC should raise the Hgb on average 1.0 g/dL or Hct 3% in a 70-80 kg adult. However, patients with larger blood volumes, advanced age, or higher starting Hgb may require more units to achieve a similar increment.[26]
- In non-actively bleeding patients, assessment of post transfusion Hgb may be done as early as 15 minutes after completion of the transfusion and is equivalent to one drawn at 1 hour and 24 hours following the transfusion.[27]

Comments:

- No single criterion should be used as an indication for RBC transfusion. Multiple factors related to patient's clinical status and oxygen delivery should be assessed.
  Consider:
    - rate of decline in hemoglobin level
    - intravascular volume status
    - shortness of breath
    - exercise tolerance
    - light headedness
    - chest pain
    - hypotension or tachycardia unresponsive to fluid challenge
    - patient preference.[1]
- RBC transfusions should be ordered only after appropriate alternative therapies have been considered (e.g. iron, vitamin B12, folate and erythropoietin).[28] In patients with chronic anemia

who are unresponsive to iron replacement and/or ESA (erythropoiesis stimulating agents) therapy or patients with hemoglobinopathies (i.e. sickle cell anemia), the decision for transfusion should be individualized.

- There is excellent clinical trial evidence that a restrictive policy of transfusion at a Hgb of 7 to 8 g/dL should guide transfusion decisions in most patients and is safe. Meta-analysis of several randomized control trials comparing restrictive versus liberal transfusion thresholds for hospitalized and surgical patients found that restrictive transfusion strategies did not impact the risk of 30-day mortality or other outcomes (i.e. cardiac events, myocardial infarction, stroke, thromboembolism infection).[29]

- Patients with upper GI bleeding and hypovolemic shock should be transfused based on hemodynamic status, co-morbidities, and rate of bleeding.[6,7]

- Patients with hematologic malignancies who underwent HSCT had similar transplant outcomes and HRQOL (health-related quality of life) score when following a restrictive RBC transfusion threshold.[12]

- For patients undergoing cardiovascular surgery who were at moderate-to-high-risk for death, a restrictive transfusion threshold strategy (Hgb <7.5g/dL) was not found to be inferior to a liberal strategy (Hgb <9.5g/dL) in regards to 30-day mortality, postoperative infection, acute kidney injury or acute MI with fewer RBC units being transfused.[14,30]

- Observational studies of RBC transfusion in acute coronary syndrome seem to favor a restrictive transfusion strategy. Two small randomized controlled trials comparing transfusion triggers of 8 and 10 g/dL in anemic patients with acute coronary syndrome showed conflicting results. The results from these trials support the need for a large randomized control trial (RCT) in this patient population, which is now ongoing (MINT Trial: NCT02981407 https://www.minttrial.org).[17,31]

- The optimal transfusion threshold for ambulatory (outpatient) patients has not been established.
    - Single unit RBC transfusions accompanied by restrictive threshold were found to be safe and efficacious.[32]
    - One recent large observational study revealed that ambulatory patients who were able to maintain hemoglobin (Hgb) level ≥8.0 g/dL post-RBC transfusion showed a clinically important increase in clinical function (mean walk test distance) compared to patients with Hgb level <8.0 g/dL.[20]

- Limitations of recommendations and where additional studies are needed:
    - Acute coronary syndrome/unstable angina/heart failure
    - Severe thrombocytopenia (patients treated for hematological or oncological disorders who are at risk of bleeding)
    - Chronic transfusion–dependent anemia
    - Patients with lower gastrointestinal bleeding

- Patients with coagulopathy and/or hemorrhagic shock
- Patients with traumatic brain injury/subarachnoid hemorrhage/stroke
- High risk oncology patient undergoing major abdominal surgery[15]

References:

1. Carson JL, Guyatt G, Heddle NM, et al. Clinical Practice Guidelines From the AABB: Red Blood Cell Transfusion Thresholds and Storage. *JAMA* 2016 Nov 15;316(19):2025-2035.
2. Alexander PE, Barty R, Fei Y, et al. Transfusion of fresher vs older red blood cells in hospitalized patients: a systematic review and meta-analysis. *Blood* 2016 Jan 28;127(4):400-410.
3. Long B, Koyfman A. Red cell transfusion in the emergency department. *J Emerg Med* 2016 Aug;51(2):120-130.
4. Herbert PC, Wells G, Blajchman MA, et al. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion Requirements in Critical Care Investigators Canadian Critical Care Trials Group. *N Engl J Med* 1999 Feb 11;340(6):409-417.
5. Holst LB, Haase N, Wetterslev J, et al. Lower versus higher hemoglobin threshold for transfusion in septic shock. *N Engl J Med* 2014 Oct 9;371(15):1381-1391.
6. Villanueva C, Colomo A, Bosch A, et al. Transfusion strategies for acute upper gastrointestinal bleeding. *N Engl J Med*, 2013 Jan 3;368(1):11-21.
7. Strate LL, Grainek IM. ACG Clinical Guideline: Management of patients with acute lower gastrointestinal bleeding. *Am J Gastroenterol* 2016 Apr; 111(4):459-474.
8. Lelubre C, Bouzat P, Crippa IA, Taccone FS. Anemia management after acute brain injury. *Crit Care* 2016;20(1):152. https://doi.org/10.1186/s13054-016-1321-6.
9. Boutin A, Chasse M, Shemilt M, et al. Red blood cell transfusion in patients with traumatic brain injury: a systematic review and meta-analysis. *Transfus Med Rev* 2016 Jan;30(1):15–24.
10. Palmieri TL, Holmes JH, Arnoldo B, et al. Transfusion Requirement in Burn Care Evaluation (TRIBE): a multicenter randomized prospective trial of blood transfusion in major burn injury. *Ann Surg* 2017 Oct;266(4): 595–602.
11. Curinga G, Jain A, Feldman M, et al. Red blood cell transfusion following burn. *Burns* 2011 Aug;37(5):742-752.
12. Tay J, Allan DS, Chatelain E, et al. Liberal versus restrictive red blood cell transfusion thresholds in hematopoietic cell transplantation: A randomized, open label phase III, noninferiority trial. *J Clin Oncol* 2020 May 1;38(13):1463-1473.
13. Carson JL, Terrin ML, Noyeck H, et al. Liberal or restrictive transfusion in high-risk patients after hip surgery. *N Engl J Med* 2011 Dec 29;365(26):2453-2462.
14. Carson JL, Stanworth SJ, Alexander JH, et al. Clinical trials evaluating red blood cell transfusion thresholds: An updated systematic review and with additional focus on patients with cardiovascular disease. *Am Heart J* 2018;200:96-101.
15. de Almeida JP, Vincent JL, Barbosa Gomes Galas FR, et al. Transfusion requirements in surgical oncology patients: a prospective, randomized controlled trial. *Anesthesiology* 2015 Jan;122(1):29-38.
16. Carson JL, Brooks MM, Abbott JD, et al. Liberal versus restrictive transfusion thresholds for patients with symptomatic coronary artery disease. *Am Heart J* 2013 Jun;165(6):964-971.e1.
17. Cooper HA, Rao SV, Greenberg MD, et al. Conservative versus liberal red cell transfusion in acute myocardial infarction (the CRIT Randomized Pilot Study). *Am J Cardiol* 2011 Oct 15;108(8):1108-1011.
18. Leal-Noval SR, Munoz-Serrano A, Arellano-Orden V, et al. Effects of red blood cell transfusion on long-term disability of patients with traumatic brain injury. *Neurocrit Care* 2016 Jun;24(3):371–380.
19. Carson JL, Kleinman S. Indications and hemoglobin thresholds for red blood cell transfusion in the adult. *UpToDate®* Last updated June 2020 (accessed September 2020).
20. St Lezin E, Karafin MS, Bruhn R, et al. Therapeutic impact of red blood cell transfusion on anemic outpatients: the RETRO study. NHLBI Recipient Epidemiology and Donor Evaluation Study (REDS)-III Program. *Transfusion* 2019 Jun;59(6):1934-1943.
21. Biller E, Zhao Y, Berg M, et al. Red blood cell exchange in patients with sickle cell disease-indications and management: a review and consensus report by the therapeutic apheresis subsection of the AABB. *Transfusion*. 2018 Aug;58(8):1965-1972.

22. Chou ST, Alsawas M, Fasano RM, et al. American Society of Hematology 2020 guidelines for sickle cell disease: transfusion support. *Blood Adv* 2020;4(2):327–355.
23. Karafin M, Singavi AK, Irani MS, et al. Red cell storage age policy for patients with sickle cell disease: A survey of transfusion service directors in the United States. *Transfus Apher Sci*. 2016 Feb;54(1):158-162.
24. Apfelbaum JL (Committee Chair) et al. Revised by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. Practice Guidelines for Perioperative Blood Management: an Updated Report by the American Society of Anesthesiologists Task Force on Perioperative Blood Management. *Anesthesiology* 2015:122 (2):241-275.
25. Will ND, Kor DJ, Frank RD, et al. Initial postoperative hemoglobin values and clinical outcomes in transfused patients undergoing noncardiac surgery. *Anesthesia-Analgesia* 2019; 129:819-829.
26. Karafin MS, Bruhn R, Roubinian NH, et al. The impact of recipient factors on the lower-than-expected hemoglobin increment in transfused outpatients with hematologic diseases. NHLBI Recipient Epidemiology and Donor Evaluation (REDS)-III Study. *Transfusion* 2019 Aug;59(8):2544-2550.
27. Wiesen AR, Hospenthal DR, Byrd JC, et al. Equilibration of hemoglobin concentration after transfusion in medical inpatients not actively bleeding. *Ann Intern Med* 1994 Aug 15;121(4):278-280.
28. Leung LLK, Mentzer WC. Approach to the adult with anemia. *UpToDate*® Last updated Apr 10, 2020 (accessed September-2020).
29. Carson JL, Stanworth SJ, Roubinian N, et al. Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion. *Cochrane Database Syst Rev* 2016 Oct 12;10(10):CD002042. doi: 10.1002/14651858.CD002042.pub4.
30. Mazer CD, Whitlock RP, Fergusson DA, et al. Restrictive or liberal red-cell transfusion for cardiac surgery. *N Engl J Med* 2017 Nov 30;377(22):2133-44.
31. Holst LB, Petersen MW, Haase N, et al. Restrictive versus liberal transfusion strategy for red blood cell transfusion: systematic review of randomized trials with meta-analysis and trial sequential analysis. *BMJ* 2015;350:h1354
32. Bowman Z, Fei N, Ahn J, et al. Single versus double-unit transfusion: Safety and efficacy for patients with hematologic malignancies. *Eur J Haematol* 2019 May;102(5):383-388.

Additional Resources:

33. AABB, American Red Cross, America's Blood Centers, and Armed Services Blood Program. Circular of information for the use of human blood and blood components. October 2017.

