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### *Strategies to minimize the transfusion of two units of RBCs for an anemic but euvoletic non-actively bleeding patient without measuring the patient's hemoglobin level after giving the first of two units*

**A physician working at a blood collection center in a southern US state** reports that his institution is **trying to influence the practice of community doctors** who **routinely order the transfusion of two units of RBCs** for an anemic but euvoletic non-actively bleeding patient without measuring the patient's hemoglobin level after giving the first of two units. For instance, the kind of patient being referred to is an otherwise stable post-operative patient or a heme/onc patient on a regular medical floor, etc. In the inquiring physician's experience, clinicians will see a patient's hemoglobin is in the justified range for transfusion (between 7 and 8 g/dL, though frequently > 8 g/dL) and order two RBC units 'up front' rather than order one unit, assess the hemoglobin increment and clinical response, and then order a second unit, if needed. The inquiring colleague has been asked to speak to medical and surgical groups within his blood center's distribution network, and he is **trying to find some good references** on the aforementioned issue. He already has several references on blood management, more restrictive transfusion guidelines, etc but he cannot seem to find anything **specifically addressing the suggestion of only ordering one RBC unit, to be followed with a hemoglobin determination, and then ordering a second RBC unit if needed** based on clinical and laboratory response/increments. He was wondering if anyone has advocated this approach and if they have references they would be willing to share.

**ADDENDA** June 19, 2008

- The Chairman of a Hospital Transfusion Committee and Blood Bank Director at a community Hospital in Massachusetts** reports that he has become interested in the practice of routine two-unit transfusions, particularly influenced by the **Canadian TRICC Trial published in 1999** (Hébert PC et al. NEJM 1999;340:409-417. This trial, in his opinion, is the **best evidence-based support** for refuting a practice of automatically ordering two units of RBC at a time. There have also been some **relevant editorial comments** in the CAP TODAY; in particular [this story](#) from December 2005. Specifically, to quote Dr. Bruce Spiess: "I believe most one- and two- unit transfusions are absolutely unnecessary and probably not in the patient's best interest. There's good data that they make patient outcomes worse." and Dr. Susan Roseff: "There is a related folklore among clinicians that if you need to transfuse red cells, you need two units, because if you gave only one that meant you didn't need any cells. That's not true. One of the things we review for is patients automatically getting two units without any clinical or laboratory check in between. If a person needs one unit, then give them that. It's also best to give them one and then see how they do. They may not need a second one."

Another [relevant reference](#) is from May 2007. At his Hospital, their Meditech system allows them to **identify two-unit transfusions** and they **look at all with a resultant hematocrit of > 35**, which is quite liberal, and it seems there are a usual few repeat practitioners. When one was queried, the reply was, "So what's the problem"? One of their reviewers has commented these are probably occurring in small patients, so they now look up the **Body Mass Index and Body Surface Area**, easily obtained from the Electronic Medical Record, and this is **part of the Transfusion Review**. Just last week, the Director of the responding physician's Hospitalist program has taken an active interest in this practice to discourage it. He commented in their recent Departmental minutes, "It was further discussed that the thinking about the number of units to be transfused has shifted to 'one unit at a time, with subsequent checks of hematocrit to ensure that further transfusions are required.'" So we'll see how this helps. The responding Blood Bank Director concludes saying "I think discouragement of this practice is probably **one of the most fertile grounds to reduce unnecessary transfusions** and I look forward to other comments."

2. **According to Dr. Irwin Gross** (attribution used with permission), who is the **Medical Director of the Transfusion Services at Eastern Maine Medical Center (EMMC)**, over a three month period beginning in March, 2007, their medical center implemented a program to reduce the number of multi-unit red cell (RBC) transfusion orders. This included the following measures:

- The hospital's transfusion committee **made it clear** that **single unit transfusion was not a criterion for retrospective transfusion review**.
- A **newsletter** was circulated that questioned the need for multiple unit RBC transfusions in hemodynamically stable patients without active bleeding.
- The **red cell transfusion order** in their **computerized physician order entry (CPOE)** system was divided into Red Cells, Patient Actively Bleeding and Red Cells, **Patient Not Actively Bleeding**. The **computer permits only a single unit per order** when Red Cells, Patient Not Actively Bleeding is used. (Multiple units may still be requested with a single order if the "actively bleeding" option is used).
- A **requirement that a post-transfusion hematocrit** be performed after **each unit** of RBCs in non-bleeding patients
- A **monthly report**, arranged by physician and clinical service, of the percentage of all RBCs (patients actively bleeding and not actively bleeding) ordered as individual units.
- **Prospective transfusion review** of orders for more than one unit at the same time (though entered individually as required by our CPOE system), in non-bleeding patients.

Dr. Gross reports that from January through March, 2007, orders for **single RBC units** made up **59%** of all RBC orders, **increasing to 82%** by May, 2008. At the same time, overall RBC use was declining. **Average monthly RBC transfusions** at EMMC for the three month period beginning December, 2006, compared to the three month period beginning December 2007 **decreased** from 609 to 362 (**40.6%**). (Other blood conservation initiatives were also implemented during that time period).

This process has contributed to a culture in which **each RBC transfusion** is seen as an **independent clinical decision**. This is one of several factors that have contributed to an overall decrease in the number of units and the number of patients transfused.

Dr. Gross acknowledges that he does not have references specific to this issue, but there are many references that address the "dose response" relationship between number of red cells transfused and adverse consequences, i.e. the incremental risk associated with each red cell transfusion.

**ADDENDA** June 20, 2008

3. **According to Dr. Harvey G. Klein, Chief, Department of Transfusion Medicine at the Clinical Center of the National Institutes of Health** (attribution used with permission), "good medical practice requires that physicians measure the outcome of therapeutic interventions. In the case of transfusion, these measurements often involve a surrogate outcome measure such as platelet increment in the case of platelet transfusion and hemoglobin increment following red cell transfusion. The frequency and timeliness of these measurements depends on the patient, the patient's clinical status, and the desired outcome. **For a patient who is chronically transfused with red cells**, such as a patient with thalassemia, it is **hardly necessary to measure hemoglobin increment after each red cell transfusion**. One can **estimate the increment based on the patient's size** - a unit of red cells ordinarily raises hemoglobin concentration 1 g/dL in the average adult - and transfuse 2-3 red cell units per outpatient visit. Measurement of the hemoglobin concentration at the end of a transfusion episode is certainly sufficient and accurate enough for this purpose."

Dr. Klein continues saying, "When the **intent is to minimize red cell transfusion** (maximize benefit/risk) for a **stable, anemic patient** who is deemed to require transfusion, the **measurement should be taken at the conclusion of the transfusion episode**. If it is predicted that the patient will require one unit of red cells because the target level is "x", then that is the conclusion of the treatment and a measurement confirms that "x" has been achieved. One must bear in mind that **measurement soon after termination of transfusion may not be accurate because of fluid shifts**. This too will vary depending upon the patient. If the inquiring physician is concerned that the ordering physician requests two units when only one is needed - increasingly the case since one-unit transfusions are often audited and considered (erroneously) by some reviewers as poor practice, the measurement of hemoglobin after one unit is appropriate. However, if one **estimates that two units (or more) will be required**, and an **elevation of 2 g/dL is the desired outcome**, it is **unnecessary and potentially counterproductive** to interrupt the transfusion episode to determine a value which in itself will really be no more than an estimate and will likely only confirm that one is approaching the desired and predicted endpoint. Too much of a good thing can be too much of a

good thing."

**ADDENDA** June 22, 2008

4. **A transfusion medicine physician at an academic medical center in North Carolina** reports that at his institution the practice of only transfusing a **minimum of 2 red cell units without checking the hemoglobin increment between units has been passé for over 10 years**. He would suggest the following references:

- The AABB *Technical Manual* states "In the past, there was some concern that transfusions of a single RBC unit were unlikely to represent unnecessary intervention. However, if transfusion of a single unit will achieve the desired clinical outcome, then only one unit should be transfused. Transfusion additional units in this setting will increase the risk of transfusion without any additional benefit." Brecher MB, Editor. *Technical Manual* 15th edition, page 487. AABB Press 2005.

Additional pertinent references might include:

- Grey DE, Finlayson J. *Red cell transfusion for iron-deficiency anaemia: a retrospective audit at a tertiary hospital*. *Vox Sang*. 2008 Feb;94(2):138-42.
- Gupte SC, Shaw A. *Evaluation of single unit red cell transfusions given to adults during surgery*. *Asian Journal of Transfusion Science* 2007;1:12-15.

**ADDENDA** June 28, 2008

5. **A transfusion medicine physician in Chicago** comments that in the context of a euvolemic, **non-bleeding, anemic patient**, who has an indication for RBC transfusion (such as either symptomatically anemic or at risk for deficits in organ perfusion or oxygen-delivery [e.g., coronary or cerebral ischemia]), he **advocates an approach** of ordering and transfusing **one unit of RBC at a time**. In his experience, **"stable" patients are neither acutely losing blood nor hemolyzing**, and they may logically be expected to appropriately increment their hemoglobin and hematocrit values with RBC transfusion. The clinical goal of RBC transfusion is either to relieve symptoms or decrease risk factors attendant to the anemia. **"Treating the laboratory value" is not the goal of RBC transfusion**. Therefore, older and current practice guidelines (i.e., recommendations) for RBC transfusion do not explicitly require that a repeat H & H be determined after each and every unit transfused. On the assumption, which has been questioned, that RBC transfusions actually benefit recipients, **individualized clinical assessment using some measure of patient improvement is the outcome and goal to be sought**. [Interim laboratory testing is reasonable if one were transfusing an appropriate dose of plasma and / or cryoprecipitated AHF to a patient with a consumptive coagulopathy. Checking post-transfusion coagulation times and fibrinogen levels would be logical and good practice. In this instance, wherein the levels of coagulation proteins may be transient or evanescent, using repeat or serial laboratory measures to assess adequacy of treatment is often necessary.]

He adds that "In stable, euvolemic, non-bleeding anemic patients, one unit of RBC (or at least 1 at a time) may be all that is necessary to relieve signs, symptoms, and decrease risks of ischemia. The questionable practice of ordering two RBC units 'up front' may partly be a holdover of an **historical artifact**. Fifteen or 20 years ago, The Joint Commission (then known as The Joint Commission on the Accreditation of Hospitals, later Healthcare Organizations) promulgated a **blood utilization monitor on single-unit transfusions**. At that time, single-unit transfusions were **actively discouraged**, apparently because it was thought that only patients needing  $\geq 2$  units should be transfused; or if any RBC's were needed, use of  $\geq 2$  was somehow preferred. This was **wrong-minded thinking** that missed the point and caused a backlash that I observed. Hounded by Transfusion Committee letters regarding single-unit transfusions, individual **physicians subsequently began ordering only 2 units of RBC at a time, to avoid falling victim to a faulty auditing criterion** that ignored reality. Certainly, there are times when transfusion of 1 unit of RBC is both necessary and sufficient. Presumably, few institutions now use this outmoded monitor as part of blood utilization review activities."

If the inquiring Blood Center physician has recent articles on blood management, many publicized by the *Society for the Advancement of Blood Management (SABM)*; articles on the randomized clinical trials in critical care, where more restrictive transfusion was convincingly shown to be associated with improved outcomes; and /or older articles on minimizing donor exposure, then these references should suffice. To the Chicago physician's knowledge, there are no freshly-minted articles, case-control studies or new guidance documents that require or recommend interim hemoglobin determination, if a second unit is indicated based on clinical evaluation and criteria. **Bottom line: Blood component therapy requires clinical judgment.**

6. A **surgeon who is very experienced in transfusion medicine therapy and blood avoidance practices** comments that he certainly understand the inquiring physician's concern about overuse of blood caused by inappropriate ordering practices. The following is the surgeons referenced comments:

"These practices are based on the received knowledge about blood transfusion that has been passed on verbally from one generation of physicians to the next. The teaching of "If you are ordering one unit of blood, order two instead because two are better than one " has never been proven to be of benefit.<sup>1</sup> Taken at face value, it quite clearly does not make sense. Since we all know that **blood transfusion carries risk, why double the risk if there is no expected benefit?**

The other "myth" of current blood ordering practice defines "need" for blood transfusion by hemoglobin or hematocrit. It has been over 10 years since an NIH consensus panel strongly recommended that RBC transfusion be used only in patients with a demonstrated oxygen need and only after other therapies, such as increasing inspired O<sub>2</sub>, have been tried and failed.<sup>2</sup> Although a number of subsequently published guidelines have made recommendations for transfusion based on a stratified hemoglobin level, they all include the advice to **evaluate the patient's clinical condition BEFORE relying on hemoglobin or hematocrit in the transfusion decision.**<sup>3-6</sup> Reliance on hemoglobin or hematocrit alone can lead to unwarranted and potentially dangerous transfusions. Consider the patient who has just returned from major surgery, has had minimal blood loss, is awake and stable, has a pulse-ox measurement of 96% but has a measured hematocrit of 26%. The knee jerk reaction would be to transfuse two units of RBCs to raise the hematocrit. Transfusion would be "treating" only the physician's anxiety, not the patient's clinical status.

The appropriate response would be to determine how much blood loss has occurred during surgery and to evaluate the patient's fluid status. Many patients come out of surgery volume overloaded from crystalloid infusion, regardless of the amount of blood loss. We tend to forget that **hematocrit is a volume-based measure**, that is, the percent of RBC mass in a given volume. This patient's RBC mass may not have decreased much but his hematocrit has fallen because the red cells are distributed in more intravascular volume. Transfusing two units of RBCs will increase the intravascular volume, add pre-load to the heart and may lead to transfusion-associated circulatory overload (TACO). This most common of transfusion complications is vastly under-recognized.<sup>7</sup> What can be done to change these practices? Controlling maximum surgical blood ordering schedules (MSBOS) and use of computer-based systems have helped both to reduce the amount of inappropriate blood use in surgical patients and to foster single unit transfusion.<sup>8-12</sup> **Educational programs targeting the goal of single-unit transfusion that are reinforced with compliance monitoring have been successful in reducing RBC use.**<sup>13-15</sup> They have also shown that **single-unit transfusion is a safe practice**.<sup>16-18</sup>

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