Educational Case

Educational Case: Perioperative patient blood management

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The following fictional case is intended as a learning tool within the Pathology Competencies for Medical Education (PCME), a set of national standards for teaching pathology. These are divided into three basic competencies: Disease Mechanisms and Processes, Organ System Pathology, and Diagnostic Medicine and Therapeutic Pathology. For additional information, and a full list of learning objectives for all three competencies, see https://www.journals.elsevier.com/academic-pathology/news/pathology-competencies-for-medical-education-pcme.1

Keywords: Blood components, Concepts of blood transfusion, Diagnostic medicine, Pathology competencies, Perioperative patient blood management, Transfusion medicine

Primary objective

Objective TM1.1: Blood components. Define the blood components and blood component substitutes available for clinical use; the evidence-based indications and dosing for transfusion of these components; and how the efficacy of transfusion may be monitored.

Diagnostic findings, Part 1

The patient has a blood pressure of 126/68 mmHg, a pulse of 88 beats per minute, a respiratory rate of 16 breaths per minute, and her oxygen saturation is 98% while breathing room air. Mild conjunctival pallor is noted. Both knees show bony enlargement, crepitus, effusion, and decreased range of motion. Physical examination is otherwise normal. Standing X-rays of both knees taken prior to the visit at the orthopedic surgery clinic show significant joint space narrowing, particularly of the medial joint space as well as osteophyte formation.

Questions/discussion points, Part 1

What is the differential diagnosis for this patient’s dyspnea?

This 44-year-old woman presenting with exertional dyspnea and conjunctival pallor with a past medical history of heavy menstrual bleeding and uterine fibroids raises concern for a symptomatic anemia that should be optimized prior to surgery. Other diagnoses to consider in the differential include pulmonary disease such as interstitial lung disease and cardiac causes such as congestive heart failure.

Diagnostic findings, Part 2

Further testing is begun for this patient with a posteroanterior chest radiograph and a complete blood count (CBC). The results of the CBC are listed in Table 1. The patient’s chest radiograph is normal.

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Interpret the CBC

Generally, the diagnosis of anemia is confirmed by a low hemoglobin and hematocrit. Therefore, this patient can be diagnosed with an anemia given a hemoglobin of 10.7 g/dL, which is below 13.3 g/dL, the lower limit of normal for an adult woman.

This patient's diagnosis of anemia can also be further refined from the results of the CBC to better establish a more precise differential diagnosis of the anemia's etiology. The first step in the assessment of anemia is determining whether the anemia is macrocytic, normocytic, or microcytic based upon whether the mean corpuscular volume, which is a measure of the average volume of red blood cells (RBCs) in the sample, is low, normal, or high, respectively.

The MCV is low and means this patient has a microcytic anemia. The next step is to determine whether it is a hypoproliferative anemia (i.e., there is an issue with RBC production) or whether it is hyperproliferative (i.e., RBC production is increased but still inadequate because the cells have a decreased lifespan). This can be determined from the reticulocyte count, a measure of the percentage of immature RBCs in the sample.

The reticulocyte count is inappropriately normal for the magnitude of the anemia, which indicates the bone marrow is not responding appropriately to the anemia by increasing the rate of erythropoiesis. Additionally, the platelet count is elevated in this patient, which can be a nonspecific indicator of iron deficiency anemia. From this constellation of values from the CBC, we can conclude this patient has a hypoproliferative microcytic anemia.

What is the differential diagnosis of a hypoproliferative microcytic anemia?

Generally, the primary cause of a hypoproliferative microcytic anemia is any process that leads to impaired hemoglobin production. These can be hereditary, such as thalassemia, or acquired due to iron deficiency, exposure to certain toxins such as lead, or as a sequela of chronic disease. A thalassemia is unlikely in this patient given her active athletic history and that she does not report any family history of anemia. Toxin exposure is also unlikely given that the patient does not report any reported occupational exposure to toxins or other risk factors for exposure. Anemia of chronic disease is also possible given her history of osteoarthritis.

In addition, the red cell distribution width (RDW) is elevated. The RDW increases as the degree of RBC size variability increases. The RDW is usually increased in iron deficiency anemia, as this condition is often characterized by a larger variety of RBC sizes. In contrast, the RDW usually remains normal in anemia of chronic disease. Given this differential diagnosis, ferritin is ordered to confirm the diagnosis of iron deficiency anemia.

Questions/discussion points, Part 2

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| Laboratory values at presentation. | Value | Normal range |
|-----------------------------------|-------|--------------|
| Complete blood count              |       |              |
| Hemoglobin                        | 10.7 g/dL | 13.3–16.2 g/dL |
| Hematocrit                        | 32.1% | 38.8–46.4% |
| Red blood cell count              | 3.12 × 10^12/mm^3 | 4.30–5.60 × 10^12/mm^3 |
| Mean corpuscular volume           | 75.1 μm^3 | 79.93–93.3 μm^3 |
| Mean corpuscular hemoglobin       | 30 g/dL | 33–35 g/dL |
| Platelets                         | 450 × 10^3/mm^3 | 165–415 × 10^3/mm^3 |
| White blood cell count            | 5.2 × 10^3/mm^3 | 3.54–9.06 × 10^3/mm^3 |

Table 1

Follow-up ferritin two days after initial presentation.

| Ferritin | Result | Normal values |
|----------|--------|---------------|
| 7 ng/mL  | 10–150 ng/mL |

Table 2

Diagnostic findings, Part 3

The serum ferritin result is shown in Table 2.

Questions/discussion points, Part 3

What can be concluded from this laboratory result?

In this context, the decreased level of ferritin, the storage form of iron in the human body, confirms the diagnosis of iron-deficiency anemia. This is also consistent with her history of heavy periods as the cause of her chronic blood loss and iron depletion. If this were anemia of chronic disease, then the ferritin level would be normal or elevated.

What are the principal steps in management for this patient prior to her procedure?

In keeping with the principles of patient blood management (PBM), the patient's iron deficiency anemia should be treated to optimize this patient prior to surgery. If this were anemia of chronic disease, then treatment would be focused on treating the underlying chronic disease/inflammatory process.

What is a basic definition of patient blood management?

PBM is the appropriate use of blood transfusion for optimal patient care. This consists of both responsible, conservative use of blood products as well as measures undertaken to prevent the need for transfusion, such as preoperative optimization and minimization of perioperative blood loss. For this patient, this means a combination of preoperative optimization through addressing her anemia as well as a number of potential perioperative measures to minimize blood loss.

While the risks of transfusion are relatively small, they are not zero. Moreover, restrictive threshold strategies are usually associated with better patient outcomes compared to more liberal transfusion strategies even when controlling for demographics, clinical conditions, and disease/injury severity.

Why is detecting and treating preoperative anemia important?

Anemia is a significant predictor of requiring transfusion during surgery. Prevalences vary widely among patient populations, but a general estimate is about a third of patients have preoperative anemia.

What are the roles of erythropoietin, B12, iron, and folic acid supplementation for preoperative anemia?

Erythropoietin (EPO) is an endogenous hormone that is produced by renal peritubular interstitial cells in response to hypoxia that stimulates erythropoiesis in the bone marrow. A recombinant form of this hormone can be administered to stimulate a rapid increase in RBC production a few days to a few weeks prior to her surgery. EPO is not indicated for this patient, as there is no evidence of impaired kidney function. Intravenous iron was given to address the patient's iron deficiency. Intravenous iron was preferred over oral iron as oral iron supplementation is limited by GI side effects and poor absorption. Folate and B12 can be given if the patient is deficient, as they are sometimes relatively easily treatable etiologies of macrocytic anemia. In sum, this patient has microcytic anemia, demonstrable iron deficiency, and no suspicion or evidence of folate or B12 deficiency.
Diagnostic findings, Part 4

The patient is treated with intravenous iron, and her hemoglobin normalizes to 15.1 g/dL on a subsequent measurement. Following preoperative treatment, the patient's hemoglobin normalizes to 15.1 g/dL. The patient is scheduled for a bilateral total knee arthroplasty. She asks if she should donate blood for herself in advance, as her older brother contracted hepatitis C from a blood transfusion in the early 1980s. Her physician educates her about the safety of the blood supply and reassures her that donating for herself is not routinely necessary unless the patient has a very rare RBC phenotype.

At the time of surgery, the surgical team elects to use many measures to decrease the need for blood transfusion, including anti-hemorrhagic agents, intraoperative cell salvage, normovolemic hemodilution, and reinfusion of the blood removed during the salvage and hemodilution process.

Questions/discussion points, Part 4

What are some common indications for transfusion of various blood products?

A summary of some common indications for these blood products is shown in Table 3.

The most common blood products are RBCs, platelets, plasma, and cryoprecipitate. RBCs provide oxygen-carrying capacity. For example, RBCs are commonly transfused when a patient has signs or symptoms of anemia along with a hemoglobin of less than 7 g/dL in most patient populations. Another common indication is acute blood loss or in a massive transfusion.

Platelets provide primary hemostasis and are often transfused when a patient has bleeding due to severe thrombocytopenia. For example, platelets are commonly transfused when a patient is bleeding or undergoing surgery, and the platelet count is less than 50 k/ul. Another common indication is to prevent spontaneous bleeding in a patient with a platelet count less than 10 k/ul.

Plasma provides coagulation factors for secondary hemostasis. For example, plasma is commonly transfused when a patient has coagulopathic bleeding or ooze due to multiple coagulation factor deficiencies. An INR of greater than 1.5–2.5 is sometimes used, but the optimal INR-based threshold is not known. Another common indication for plasma is massive transfusion. Instead of plasma transfusion, an infusion with prothrombin complex concentrate (PCC; consisting of factors II, VII, IX, and X) is currently preferred for the rapid reversal of warfarin due to the decreased risks of transfusion reactions from PCC compared to plasma.

Cryoprecipitate is essentially the fibrinogen that is isolated from a unit of plasma. It is usually transfused as an adjunct to plasma in the setting of massive transfusion or for patients with coagulopathic bleeding due to hypofibrinogenemia.

What is an INR?

INR stands for international normalized ratio and is a standardized measure for assessing the extrinsic and common coagulation pathways. It is calculated from the patient's prothrombin time, which is a measure of the speed of coagulation when tissue factor and calcium are added to a sample of the patient's plasma.

What pharmacologic agents can be used to minimize perioperative blood loss and subsequently avoid blood transfusion?

Antifibrinolytics such as tranexamic acid (TXA) and aminocaproic acid have been found to reduce blood loss and the subsequent need for allogeneic RBC transfusion intraoperatively. These medications are lysine analogs that can be given intraoperatively to inhibit plasminogen activation and subsequent breakdown of clots. These merely prevent clot breakdown and do not induce clotting. As such, no significant risk of thrombosis has been demonstrated.

What is intraoperative cell salvage?

There are devices available that are able to collect bloodshed into the operative field, mix it with an anticoagulant, and store it for reinfusion later in the procedure. Using this method, approximately 50% of the blood lost during certain procedures can be recovered and reinfused. These devices typically also wash the blood to remove constituents that are not conducive to transfusion, such as free hemoglobin, contaminants, and activated clotting or immunologic factors.

What is acute normovolemic hemodilution?

Acute normovolemic hemodilution (ANH) is a strategy for the conservation of blood products, wherein blood is removed from the patient shortly after the beginning of the intraoperative period and replaced with a large volume of crystalloid or colloid. This technique decreases the effective loss of blood by decreasing the patient's hemoglobin and RBC concentration during the period where the most blood loss occurs. Following this period, the patient can then be reinfused with their own fresh whole blood. ANH may reduce transfusions, but the evidence is mixed.

What is autologous blood transfusion and why is it avoided?

Autologous blood transfusion is a blood transfusion using a patient's own blood products that were donated preoperatively in advance of the perioperative period. By using the patient's own blood products, this can theoretically decrease the risk for transfusion-related reactions and the risk of transfusion-transmitted infection. However, the preoperative donation has become much less common in the USA, as it is likely to create an anemia prior to the procedure and requires significant preoperative planning and resources despite rarely being transfused back to the patient. More importantly, the safety of the donor blood supply is dramatically better than it was in the 1980s. However, autologous donation often plays an important role in the procurement of blood with rare RBC phenotypes.

Diagnostic findings, Part 5

Using these PBM strategies, the surgical team is able to avoid blood transfusion for this patient over the course of her hospitalization. The patient does well and is discharged with the resolution of her presenting symptoms. About one year after the surgery, she continues to do well and celebrates her 45th birthday by playing 18 holes of golf at The Old Course at St Andrews in Fife, Scotland.

Questions/discussion points, Part 5

What are some other examples of PBM?

Specific practices vary among institutions and can change frequently with new data, but some common current strategies are listed in Tables 4.
Table 4

| Preoperative | Intraoperative | Postoperative |
|--------------|----------------|---------------|
| Identify anemia | Schedule surgery | Manage anemia |
| 4-6 weeks before surgery | with optimization of red cell mass | Prevent and/or manage bleeding |
| Treating iron deficiency | Balanced physiology to aid optimal coagulation and cell salvage | Minimize iatrogenic blood sampling |
| Consider erythropoietin (EPO) | Anti-thrombinics and cell salvage | |

Table 5

| Some common patient blood management strategies. |
|-----------------------------------------------|
| RBCs | Consider single-unit red blood cell transfusions for adults who do not have active bleeding |
| Platelets | Do not routinely transfuse more than a single dose of platelets |
| Plasma | Only consider plasma if clinically significant coagulopathic bleeding or oozing and not due to warfarin |
| Prothrombin complex concentrate (PCC) | Offer immediate PCC for the emergency reversal of warfarin anticoagulation instead of plasma |

and 5.16 Table 4 lists the three basic pillars of PBM: the detection and management of anemia, the minimization of bleeding and blood loss, and the improvement of tolerance to anemia. The first pillar includes the strategy of identifying anemia far enough in advance of the surgery so that the anemia can be corrected (e.g., with iron and/or EPO). Another principle is to assess the patient for bleeding risk via a bleeding history and, if necessary, refer the patient to a hematologist if the patient has a history of bleeding spontaneously or bleeding excessively when challenged. Included in this assessment is a review of medications that can cause a bleeding tendency such as anticoagulants.

The second pillar includes the strategy of minimizing iatrogenic blood loss. One aspect of this is the minimization of phlebotomy blood draws from unnecessary laboratory tests and the related Choosing Wisely campaigns to educate physicians with evidence-based recommendations for the ordering of laboratory tests.15,16 This strategy also involves intraoperative techniques, such as the use of meticulous surgical techniques to maximize hemostasis, the maintenance of balanced physiology to aid optimal coagulation, and the use of antifibrinolytics and cell salvage when indicated.

The third pillar is more indirect and involves maximizing the patient’s ability to tolerate some degree of anemia. Some aspects of this are to formulate a patient-specific plan that estimates the patient’s tolerable blood loss, optimize cardiac output, oxygenation, and ventilation, and utilize evidence-based transfusion thresholds. The latter is the result of decades of strong evidence that demonstrates that most patient populations tend to have better outcomes if they are not transfused to the normal range of the relevant laboratory parameter.17 Unlike many analytes in the blood, it is not routinely necessary to transfuse a patient’s hemoglobin, platelet count, INR, or fibrinogen level to the normal range. In fact, repeated studies have demonstrated that patients who were transfused liberally tended to have worse outcomes in randomized controlled trials compared to patient who were transfused more conservatively.20 This is a non-intuitive and critical point, as most analytes in the blood are typically maintained relatively strictly in the normal range (e.g., sodium, potassium, and glucose).

To accomplish this appropriate degree of transfusion, Table 5 lists some concrete strategies that are often recommended for transfusion indications. The context of these recommendations is that many of the evidence-based guidelines contradict popular practices from the past. For example, a common recommendation is to transfuse one unit of RBCs at a time with a post-transfusion reassessment for most patients who are not actively bleeding. The popular practice from the past that this is trying to dispel is the non-evidence-based motto of, “If you’re going to give one, then you might as well give two.” The new motto is, “Why give two when one will do?” The main concept is to view transfusions just like any other treatment and to apply the principles of evidence-based medicine and lifelong learning to transfusion decisions.20

Teaching points

- The four most common blood products are RBCs, platelets, plasma, and cryoprecipitate.
- RBCs are often given for symptomatic anemia with a hemoglobin less than 7 g/dL.
- Platelets are often given for bleeding with a platelet count less than 50 k/uL.
- Plasma is often given for coagulopathic bleeding or oozing due to multiple coagulation factor deficiency and often with an INR over 1.5–2.5. The optimal INR cutoff for plasma transfusion or the prediction of bleeding has not been established.
- Prothrombin complex concentrate is preferred for rapid warfarin reversal instead of plasma transfusion in order to minimize the risk of a transfusion reaction.
- Cryoprecipitate is often given as an adjunct to plasma to provide additional fibrinogen.
- The diagnosis of anemia and its subtypes is based upon careful assessment of complete blood count results and complementary laboratory studies.
- Patient blood management is a multi-faceted approach to optimize the responsible use of blood products.
- The overall goal of PBM is the appropriate use of blood transfusion for optimal patient care. This consists of the conservative use of blood products. Transfusion safety is at an all-time high, but the risks are not zero. Abundant evidence shows that restrictive transfusion strategies are generally associated with better outcomes than liberal strategies as an independent factor.
- Diagnosing and treating preoperative anemia is an important part of PBM, as preoperative anemia is a strong predictor of requiring transfusion during surgery.
- Common treatments of preoperative anemia include EPO, iron, folate, and B12.
- Antifibrinolytics, such as tranexamic acid and aminocaproic acid, can be used intraoperatively to decrease blood loss and the subsequent need for blood products by inhibiting plasminogen.
- Cell salvage involves the collection of bloodshed into the operative field and reinfusing later in the procedure. About 50% of the blood lost during many procedures can be saved and reinfused.
- Acute normovolemic hemodilution involves the removal of blood shortly after the beginning of the surgery and replacing it with a large volume of crystalloid or colloid. The evidence for its efficacy is mixed.
- Autologous blood transfusion uses the patient’s own blood products that were donated preoperatively. It has become much less common in the USA as the safety of the blood supply has markedly improved.
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References

1. Knollmann-Ritschel BEC, Regula DP, Borowitz MJ, Conran R, Prystowsky MB. Pathology competencies for medical education and educational cases. Acad Pathol. 2017;4. doi:10.1177/2374289517715040
2. Goodnough LT, Shander A. Patient blood management [published correction appears in Anesthesiology. 2013 Jan;118(1):224] Anesthesiology. 2012;116(6):1367–1376. doi:10.1097/ALN.0b013e3182525d1a3
3. Irving AH, Harris A, Petrie D, Higgins A, Smith J, McQuilten ZK. Impact of patient blood management guidelines on blood transfusions and patient outcomes during cardiac surgery. J Thorac Cardiovasc Surg. 2020;160(2):437–445. doi:10.1016/j.jtcvs.2019.08.102. e20.
4. Shander A, Knight K, Thurer R, Adamson J, Spence R. Prevalence and outcomes of anemia in surgery: a systematic review of the literature. Am J Med. 2004;116(Suppl 7A):S85–S95. doi:10.1016/j.amjmed.2003.12.013
5. Pagano D, Milojevic M, Meesters MI, et al. 2017 EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery. Eur J Cardiothorac Surg. 2018;53(1):79–111. doi:10.1093/ejcts/eex325
6. MacDougall IC. Strategies for iron supplementation: oral versus intravenous. Kidney Int Suppl. 1999;69:S61–S66. doi:10.1046/j.1523-1755.1999.055suppl.69061.x
7. Raval JS, Griggs JR, Reg A. Blood product transfusion in adults: indications, adverse reactions, and modifications. Am Fam Physician. 2020;102(1):30–38.
8. Cap AP, Beckett A, Benov A, et al. Whole blood transfusion. Mil Med. 2018;183(suppl.2):44–51. doi:10.1093/milmed/usy120
9. Terwindt LE, Karlss AA, Eber S, et al. Patient blood management in the cardiac surgical setting: an updated overview. Transfus Apher Sci. 2019;58(4):397–407. doi:10.1016/j.transci.2019.06.015
10. Cohen JA, Brecher ME. Preoperative autologous blood donation: benefit or detriment? A mathematical analysis [published correction appears in Transfusion. 1996;36(11–12):1036] Transfusion. 1995;35(8):640–644. doi:10.1046/j.1537-2995.1995.35895357804.x
11. Busch MP, Bloch EM, Kleinman S. Prevention of transfusion-transmitted infections. Blood. 2019;133(17):1854–1864. doi:10.1182/blood-2018-11-833996
12. Selik RM, Ward JW, Buehler JW. Trends in transfusion-associated acquired immune deficiency syndrome in the United States, 1982 through 1991. Transfusion. 1993;33(11):890–895.
13. Dodd RY, Crowder LA, Haynes JM, Nori EP, Stramer SL, Steele WR. Screening blood donors for HIV, HCV, and HBV at the American Red Cross: 10-year trends in prevalence, incidence, and residual risk, 2007 to 2016. Transfus Med Rev. 2020;34(2):81–93. doi:10.1016/j.jtcr.2020.02.001
14. Godbey EA, Thibodeaux SR. Ensuring safety of the blood supply in the United States: donor screening, testing, emerging pathogens, and pathogen inactivation. Semin Hematol. 2019;56(4):229–235. doi:10.1053/j.semhematol.2019.11.004
15. Blake JT, Clarke G. Modeling rare blood in Canada. Transfusion. 2019;59(2):582–592. doi:10.1111/trf.15027
16. Thakrar SV, Clevenger B, Mallett S. Patient blood management and perioperative anaemia. BJU Int. 2020;125(6):791–797. doi:10.1111/bju.15349
17. Baird GS. The Choosing Wisely initiative and laboratory test stewardship. Diagnosis (Berl). 2019;6(1):15–23. doi:10.1515/dx-2018-0045
18. Bishop TF, Cea M, Miranda Y, et al. Academic physicians’ views on low-value services and the choosing wisely campaign: a qualitative study. Healthc (Amst). 2017;5(1–2):17–22. doi:10.1016/j.hjdsi.2016.04.001
19. Derzon JH, Clarke N, Alford A, Gross I, Shander A, Thurer R. Restrictive transfusion strategy and clinical decision support practices for reducing RBC transfusion overuse. Am J Clin Pathol. 2019;152(5):544–557. doi:10.1093/ajcp/aqz070
20. Storch EK, Custer BS, Jacobs MB, Meintove JE, Minz PD. Review of current transfusion therapy and blood banking practices. Blood Rev. 2019;38:100593. doi:10.1016/j.bre.2019.100593