Transfusion Camp for Non-Physician Prescribers
Materials based on Transfusion Camp 2018-2022 with permission from the Transfusion Camp Steering Committee
Afternoon Seminar on Day 2

Consent and Patient Blood Management

Case 1

You are attending in the critical care unit of at a community hospital and have sought advice from a neurologist at an academic hospital regarding a patient who has presented with progressive flaccid paralysis following a viral infection. The patient is awake and clinically stable but is now completely paralyzed, ventilator-dependent, and only able to communicate through blinking. The neurologist suspects Guillain-Barre Syndrome and recommends a course of high-dose IVIG (2 g/kg administered over 2 days) .

Ask one resident to enact how they would explain the <u>risks</u> of this treatment to the patient and seek general feedback from the group

Then pose the following questions to the group using the team-based learning process

1. Who should consent be sought from in this case?
    a. Consent not required in this situation
    b. The patient
    c. The patient's next of kin
    d. The public guardian

Obtaining informed consent from this patient will be difficult and time-consuming, but is nonetheless still required because the patient retains capacity: despite being unable to move or speak, he is capable of understanding the information that is relevant to making a decision about the treatment and is able to appreciate the reasonably foreseeable consequences of a decision (or lack of decision). In this situation, the physician is obliged to utilize whatever communication tools are available, even if that is restricted to having the patient answer a series of yes/no questions by blinks or hand-squeezes. In situations where the patient is unable to sign a consent form due to impaired vision, physical impairments, or illiteracy, it is sufficient for the staff to write "patient unable to sign" on the form and document the reasons why. Although having the consent discussion witnessed is not a universal requirement by all institutions, it would be advisable in this case. However, it should be remembered that the signature of a witness to a consent discussion attests only to the identity of the patient named on the form and that the person's mental state at the time appeared to allow for an understanding of what was signed: it does attest to the adequacy of the explanations given by the individual who obtained the consent. Treatment without consent can only be initiated if the

patient's life is at immediate risk and neither patient nor their substitute decision-maker are able to provide consent; this is not the situation in the current scenario.

2. Which of the following risks should be disclosed?
    a. Acute renal failure
    b. Anaphylaxis
    c. Hemolysis
    d. Thrombosis

There are innumerable risks associated with any medical intervention, and it is not necessary or desirable to list them all. Rather, your duty as a physician is to inform your patient of the *material* risks, which are defined as risks a "reasonable person", in your patient's position, would find important when making decisions about their medical treatment. This can generally be interpreted as adverse events that are common or potentially life-threatening.

When administering high-dose IVIG, common adverse reactions include fever and chills, urticaria and headache. Rare but potentially life-threatening reactions include thrombosis and anaphylaxis. Hemolysis is both a common and potentially severe complication of high-dose IVIG and amongst non-group O patients may occur in as many as 1 in 3 infusions, although only rare cases will be severe enough to require medical intervention. Because IVIG is a fractionated plasma product which has been manufactured using pathogen inactivation technologies such as solvent-detergent treatment, the theoretical risk of contamination with bacteria (sepsis) or leukocytes (graft-versus-host-disease) is arguably too small to mention. It must be acknowledged, however, that because fractionated plasma products are manufactured from the plasma donations of tens of thousands of individual blood donors, they have historically carried a very high risk of disease transmission of cell-free pathogens such as hepatitis and HIV. This was particularly true of products such as coagulation factor concentrates that underwent relatively little processing during their manufacture (an international outbreak of hepatitis C from IVIG was documented as recently as 1994.) Currently, the manufacturing process of these products is such that a number of pathogen reduction and inactivation steps can be applied that are as of yet not routinely applied to blood components such as red blood cells, platelets and plasma. Nonetheless, given the extremely high number of donor exposures per vial of fractionated plasma product and the fact that pathogen reduction and inactivation strategies are not guarantees against the transmission of all known (and unknown) agents, a "reasonable person" is still entitled to the knowledge that receipt of a fractionated plasma product may yet result in a chronic infectious disease, even if that risk is very low. A reported case of vCJD transmission from a fractionated plasma product (a FVIII concentrate infused in the UK in 1998, with vCJD diagnosed post-mortem 11 years later) underscores this point.

Case 2

You are called to the ER to see an 80 year-old woman with hemopericardium 3 days following insertion of a pacemaker for sick sinus syndrome. Physical examination reveals a heart rate of 130 BPM, blood pressure of 90/50 mmHg with a 15 mmHg pulsus paradoxus, quiet heart sounds and distended neck veins. Laboratory investigations reveal a Hgb of 100 g/L, a WBC of 9 x 10^9/L and a platelet count of 90 x 10^9/L; her INR is elevated at 2.9, aPTT and fibrinogen are normal at 40 seconds and 3.0 g/L, respectively, and the patient's family informs you she is on long-term warfarin for atrial fibrillation. A bedside echocardiogram reveals a large pericardial effusion. A decision is made to administer prothrombin complex concentrate (PCC) while arrangements are made to perform an urgent bedside pericardiocentesis.

Ask one resident to enact how they would explain the alternatives of this treatment to the patient, and then pose the following questions to the group:

3. Which of the following individuals should obtain informed consent for PCCs?
    a. The cardiologist who prescribed the patient's warfarin
    b. The hematologist who consulted on the cause of the coagulopathy
    c. The ICU fellow who will be performing the pericardiocentesis
    d. The nurse who explained the echocardiogram results to the patient

The physician who is responsible for the patient's treatment is the most appropriate individual to obtain informed consent. While this discussion can be delegated to individuals on that physician's team, those individuals must be able to fully explain the risks, benefits and alternatives to the patient. In this case, the ICU fellow might reasonably decline to perform a bedside pericardiocentesis *unless* the patient has consented to having their anticoagulation reversed (opting instead to have the procedure performed in medical imaging, or to have their attending staff physician perform the procedure instead, both of which may be safer but which may entail delay). It would therefore be inappropriate to delegate the consent discussion to any of the other three individuals listed in the answer choices. While the fellow may seek information from the consulting services regarding the advantages and disadvantages of various interventions, and may seek the assistance of the patient's nurse in effectively communicating these issues to the patient, it is ultimately the fellow's responsibility to perform the consent process themselves (unless their attending staff obtains consent directly). The role of nursing staff in the consent process is to advocate on behalf of the patient (eg., by informing the physician if the patient has not consented to the transfusion and declining to administer a blood product without evidence that the discussion had taken place) but unless the nurse is themselves taking responsibility for the transfusion with its associated risks, benefits and alternatives (eg., has been delegated the authority to order the transfusions through either a medical directive or by virtue of being an advanced practice nurse), responsibility for consent discussions remain with the most responsible (ie., treating) physician.

4. Which of the following should <u>not</u> be offered as an alternative to PCC infusion to this patient?
   a. Plasma
   b. IV vitamin K
   c. Platelets
   d. Pericardiocentesis while fully anticoagulated

While the ordering physician would be justified in preferring PCC in this patient due to its proven efficacy, ease of administration and low risk profile, there is an obligation to offer alternative treatments, particularly if the patient expresses concerns regarding the specific risks associated with PCC (eg., thrombosis due to excessive dosing, overly-rapid administration, or history of heparin-induced thrombocytopenia). Plasma has a number of disadvantages to PCC (particularly a higher rate of adverse transfusion reactions), but in an open-label randomized controlled trial of PCC vs plasma for treatment of major bleeding in patients taking vitamin K antagonists, both treatments resulted in equivalent hemostatic efficacy. Vitamin K has a slower onset of action but will result in a complete and more durable reversal of warfarin effect than either PCC or plasma (typically within 6 hours if given intravenously) and should therefore also be offered as an alternative, although as with plasma the delay in care may place the patient at increased risk from ongoing bleeing. Although performing an emergency pericardiocentesis in a fully anticoagulated patient is likely the highest-risk alternative to offer, this potentially life-saving option should not be withheld in a patient who declines to receive blood products; indeed, withholding a pericardiocentesis in this patient unless they agree to a transfusion would arguably be coercive. According to the CMPA, “Consent obtained under any suggestion of compulsion either by the actions or words of the doctor or others may be no consent at all and therefore may be successfully repudiated.”

When discussing alternatives to the proposed treatment, the risks of each should also be disclosed and contrasted, and the physician may make plain what their preferences are and why. Once the patient has been fully informed, their choice should then be honoured. However, there is no obligation by the physician to offer an alternative treatment that they do not believe will have any therapeutic benefit simply because the patient requests it or because it would be “better than nothing”. In this situation, there is no reason to believe, from either clinical experience or theoretical reasoning, that a platelet transfusion would decrease bleeding risk in this patient, given their platelet count and absence of apparent platelet dysfunction. It would therefore be inappropriate to suggest otherwise to the patient by proposing it as a treatment option, particularly given the associated risks of this product. Similarly, offering a Jehovah’s Witness a blood product simply because they express a willingness to receive it (eg, albumin or a recombinant coagulation factor concentrate) would be inappropriate if those products were not felt to have any actual therapeutic benefit.

Case 3

A 30 year-old woman, referred for elective thoracolumbar spinal fusion with instrumentation and bone grafting for severe scoliosis, is noted on the day before surgery to have a hemoglobin of 80 g/L and an MCV of 60 fL. She reports a history of chronic anemia and menorrhagia but is otherwise well and is keen to have the surgery performed as soon as possible. The attending surgeon anticipates that there will be significant bleeding during the procedure and, given the patient's current hemoglobin is fairly certain that transfusion support will be required. In fact, he suggests that 2 units of RBCs be transfused before even taking the patient to the OR, but defers to your opinion as the anesthetist regarding the best course of action.

Ask one resident to enact how they would explain the long-term risks of transfusion to the patient

Ask another resident to enact how they would present possible alternatives to transfusion in this situation

Then pose the following questions to the group

5. Which of the following is the greatest long-term risk posed to this patient from a red blood cell transfusion?
    a. Chronic hepatitis B
    b. Iron overload
    c. **Pregnancy complications**
    d. Transplant complications

While infection with hepatitis B should be considered a material risk of transfusion (a case occurred in Ireland from a RBC transfusion just this year), the risk remains extremely low, estimated to occur at a rate of 1 in 1.7 million transfusions in Canada. Iron overload is a significant hazard to patients who are started on long-term transfusion therapy, but only occurs after 20 or more units of RBCs are transfused outside the setting of hemorrhage or apheresis therapy. Thus, while this risk should be disclosed to any patient in whom chronic transfusion therapy is being proposed (or who has already developed iron overload), it is not a relevant concern in this patient. Sensitization to antigens contained within a blood product is a relatively common complication of transfusion and should be disclosed if the resulting antibodies are likely to pose a clinical hazard to the patient. In this case, inducing the formation of an anti-RBC antibody (a consequence of approximately 5% of RBC transfusion episodes) in a woman of child-bearing age will result at a minimum in the need for more aggressive monitoring during future pregnancies and possibly for interventions aimed at decreasing the incidence and severity of hemolytic disease of the newborn (such as IVIG therapy and intrauterine transfusion support). Similarly, a patient who is awaiting an organ transplant should be informed that transfusion of cellular blood products increases the risk of HLA sensitization, which in turn decreases the likelihood of finding a compatible donor. Thus, while transmission of

infectious agents should be considered a material risk in all transfusion recipients, discussion of certain other long-term complications such as iron overload, hyperhemolysis (a very rare complication of transfusion that occurs almost exclusively in patients with sickle cell disease and arguably does not need to be disclosed to this patient unless it is found she has a hemoglobinopathy (or a history of hyperhemolysis). and antibody sensitization may be tailored towards the specific risk profile of the patient.

6. Which of the following is the best course of action in this situation?
    a. Administer IV iron and erythropoietin today for tomorrow's surgery
    b. Postpone the surgery and refer for anemia management
    c. Maximize blood sparing interventions intra-operatively, including systemic tranexamic acid and careful use of electrocautery
    d. Seek consent from the patient to transfuse 2 units of RBCs prior to taking her to the OR

A key component of an informed consent discussion is that whenever possible it be performed early enough to allow the patient to avail themselves of alternative interventions. In this case, the patient most likely has iron deficiency and would benefit from intravenous iron, although other etiologies for her microcytic anemia would need to be considered as well (for example, a hemoglobinopathy or anemia of chronic disease). Administering IV iron the day before surgery, however, even if accompanied by erythropoietin, will have very little effect on the patient's hemoglobin intra-operatively and will thus be of little benefit as a transfusion-sparing alternative. Similarly, while tranexamic acid is a valuable hemostatic adjunct in orthopedic and other surgical procedures, it is unlikely that this alone will decrease the need for transfusion in a patient who will undergoing a major surgical procedure starting with such a severe degree of anemia. Thus, while IV iron and tranexamic should be offered to this patient, it is not realistic to frame these as alternatives to transfusion in the current context. Given the established adverse effects of perioperative transfusion (including post-operative infections, a transfusion risk which the patient should also be informed of), and the likelihood that blood exposure could be avoided with proper investigation and management of the patient, the preferred course of action in this situation would be to re-book the procedure for a later date. However, the patient would need to consent to this approach if the surgical team is indeed offering immediate surgery with transfusion support as an alternative course of action.

Case 4

A 64 year old woman is being seen in preoperative clinic in preparation for an elective revision total hip arthroplasty (2020 provincial transfusion rate 32%). She has been feeling fatigued over the past 6 months.She attributes this to her worsening hip pain. Her past medical history is significant for

hypertension. Her current medications include ASA, Ramipril. Her weight is 80 kg. Her labs show the following: hemoglobin 95 g/L, MCV 75 fL, WBC 6.5 x 10^9/L, platelets 425 x 10^9/L. Her creatinine is 80 µmol/L. Her ferritin is 20 mcg/L. The surgeon has a spot for the surgery next week.

7. Which one of the following tests is indicated to investigate the cause of her anemia?

   A) **GI workup including colonoscopy**
   B) Hemoglobin electrophoresis
   C) Serum protein electrophoresis
   D) Vitamin B12

The patient has a microcytic anemia with a low ferritin. The most likely cause of her anemia is iron deficiency anemia. The definition of iron deficiency varies in the literature but a generally accepted definition of iron deficiency would include: ferritin of < 30 mcg/L or a ferritin of < 100 mcg/L with a transferrin saturation of < 20%. Other causes of a microcytic anemia include thalassemia and anemia of chronic disease. Iron deficiency anemia is very common in the preoperative setting and has been found inanywhere from 20-40% of preoperative patients in various surgical settings. Typically patients with thalassemia have a persistently low MCV usually in the 60's. A serum protein electrophoresis would be performed for suspicion of myeloma and so would not be helpful here. B12 deficiency typically presents with a high MCV (> 100 fL).

The most important question to ask in any case of iron deficiency is to determine the cause of iron deficiency. The most common causes are related to bleeding and less commonly to poor GI absorption of iron. In fact, the prevalence of colon lesions has been reported to be up to 5-10% and upper GI lesions 1- 5%. Therefore additional information that would be helpful would include obtaining a history of previousanemia, information on her previous CBCs (to see if there has been a recent drop in her hemoglobin), questioning the patient for a history of bleeding (particularly gastrointestinal bleeding (note her history ofNSAIDs) and gynecologic bleeding) and whether she has undergone any recent GI investigations (stool foroccult blood testing, OGD, colonoscopy). She should also be asked about her diet (whether she eats iron- containing foods) and any malabsorption issues (chronic GI symptoms, vomiting, diarrhea, celiac disease).

Case: Can give the residents information that the patient had a recent OGD and colonoscopy through her family doctor's office 1 month ago. Her hemoglobin has been stable over the past 6 months. Thereis no overt bleeding. She had a gastric bypass 4 years ago and has had chronic iron deficiency.

8. Which one of the following is the appropriate next step in her management?
   A) Delay surgery until investigations complete
   B) **Delay surgery until patient iron replete**
   C) Proceed with surgery next week, no interventions needed
   D) Proceed with surgery next week, start iron supplementation this week

This patient's surgery should be delayed. The risk of delaying this elective procedure is minimal. The risks of proceeding with surgery far outweigh the risks of delaying the surgery. She has a treatable and reversible cause of anemia. As the transfusion rate for this procedure is high, proceeding with the surgerywould most definitely result in transfusion, put the patient needlessly at risk for the complications of transfusion and also the potential adverse effects of the resulting anemia. The need for transfusion in thepostoperative setting has also been associated with increased infection rate and increased length of stay.The typical response to any anemia treatment is about 5-10 g/L per week and thus even if she is starting on iron supplementation this week, it is unlikely that she will have a sufficient increase in her Hb to avoid transfusion.

9. Which one of the following is an appropriate treatment for her anemia?
   A) Feramax 150mg po OD
   B) Ferrous fumarate 300 mg po OD
   C) IV iron 300-500mg
   D) **IV iron 1000-1200mg**

The etiology of her iron deficiency anemia should be determined. This may include a referral to GI or gynecology. This patient has already had GI investigations and has a clear reason for iron deficiency (gastric bypass leading to poor absorption of iron). This patient should be treated with iron supplementation. Oral iron supplementation is an option. However, because her hemoglobin is so low, fulliron replacement may take months as oral iron absorption is poor and unlikely to be effective in her case due to poor absorption from her gastric bypass surgery. Thus iv iron would be most appropriate.

In terms of dosing for iv iron, the modified Ganzoni formula can be used = subject weight in kilograms x [target Hb – current Hb g/dL] x 2.4 + 500. For this patient, weight 80 kg with a target Hb 13 g/dL (=130 g/L)and a current Hb of 9.5 g/dL (=95 g/L), the total iron deficit would be 1172 mg. Simplified dosing may also be used. For example, Ning & Zeller (ASH review 2019) suggest 300-600 mg for iron deficient, non-anemic patient, 1200 to 1500mg for Hb 80-109 g/L and 2000 to 3000mg for pts with Hb less than 80 g/L.

PROMPT: What would you tell the patient about side effects of oral iron and iv iron? What would youtell surgeon about how long it would take to optimize Hb?

Patients can have significant side effects from oral iron including constipation, diarrhea, nausea, vomitingand abdominal pain. Data suggests that oral iron salts (e.g. ferrous sulfate, ferrous fumarate) are as effective and potentially superior to newer more expensive formulations (e.g. Feramax = iron polysaccharide) (References: Powers JM et al. ferrous sulfate vs. iron polysaccharide in young children, RCT. JAMA 2017;317(22):2297-2304 and CADTH. Oral iron for anemia. 2016). A better option to consider

for this patient would be intravenous iron. Side effects include hypotension, muscle cramps, joint pain, headache, injection site swelling, chest discomfort, nausea, vomiting and/or diarrhea. Serious allergic reactions (rashes, face swelling and wheezing) are rare. In terms of timing, the reticulocyte count shouldincrease in about 3-5 days after starting iron and the expected increase is about 10g/L per week. Therefore it would be expected to take about 3-4 weeks to reach a hemoglobin of 130g/L. One could consider giving the go-ahead to book the surgery in 3-4 weeks rather than just reassessing in 3-4 weeks. Itwould also be important to discontinue her aspirin preoperatively.

Case 5

You are asked to assess a 16 year-old boy for a lung transplant for bleomycin-induced lung toxicity. The patient demonstrates an understanding of the procedure but reports that he has recently become a Jehovah's Witness and therefore does not wish to be transfused. His parents, realizing that refusal of transfusion support may delay his eligibility for surgery, wish to over-rule his wishes on the argument that he has not reached the age of majority and therefore cannot fully understand the implications of his decisions. They also recall being told that he requires "special blood" due to his history of Hodgkin's disease, but are unsure exactly what that refers to.

Ask one resident to enact how they would explain the benefits of transfusion to the patient and his family

Questions for the group:

10. In adjudicating between the conflicting wishes of the patient and his family, which of the following is the best course of action?

a. Ask the Jehovah's Witness hospital liaison and Hospital legal affairs to meet with the patient and his family in order to achieve consensus
b. Defer surgery until the patient is 18 years of age
c. Respect the parent's wishes, even if that means waiting until the patient is under anesthesia before transfusing
d. Respect the patient's wishes, even if that means cancelling the surgery

According to the CMPA, "The legal age of majority has become progressively irrelevant in determining when a young person may consent to his or her medical treatment. As a result of consideration and recommendations by law reform groups as well as the evolution of the law on consent, the concept of maturity has replaced chronological age. The determinant of capacity in a minor has become the extent to which the young person's physical, mental, and emotional development will allow for a full appreciation of the nature and consequences of the proposed treatment, including the refusal of such treatments." This position has been codified by all provincial colleges with the exception of Quebec, which maintains a fixed age of 14 as the threshold below which consent of the parent, guardian or court is required. The only exception to this approach is consent to medical assistance in dying, where current legislation still upholds 18 as the minimum age for which such a decision can be made; below this threshold a patient's parents or guardian still cannot decide on the minor's behalf.

Thus, in the current situation, in which the patient does appear capable of making informed decisions, their wishes must be respected and it is not necessary to defer the surgery until they are 18 to allow these wishes to override those of the parents.

While seeking input from the patient's religious institute and hospital administrators would be wise in this situation (particularly to determine whether a surgeon is locally available who is willing to perform the surgery without transfusion support), deferring to these two groups to convince the patient and the family to adopt the same position regarding the acceptability of transfusion is probably not realistic; even after they have provided important contextual information it is likely a conflict of opinion will remain which the treating physician will still need to adjudicate.