INTRODUCTION
An important aspect of risk reduction in Transfusion Medicine is to identify physician practices that result in unnecessary transfusion. Unnecessary transfusions are transfusions in which the transfusion is prescribed and administered in the context of an absence of data with regard to efficacy (inappropriate transfusions) or in which there may be evidence or a consensus for efficacy but transfusion avoidance might have been possible if an alternative approach had been applied in a timely manner (avoidable transfusions). Although the majority of unnecessary transfusions do not result in any observed patient harm, they are wasteful of resources. If harm should ensue, unnecessary transfusions result in a substantial risk to the organization and prescribing physicians. This chapter will focus on this aspect of transfusion medicine, providing actual examples of unnecessary transfusions, some of which resulted in morbidity or mortality. The overall fraction of blood components that are prescribed unnecessarily is unknown and will likely vary from institution to institution and be different for different components. Alarmingly, it is possible that a substantial percentage of blood components are unnecessarily transfused. In the case of plasma transfusions, for example, intrainstitutional reduction in the range of 90%–95% has been achieved without any evidence of patient harm.1

Unnecessary Red Blood Cell Transfusions

Red blood cells are transfused in two clinical contexts. First, red cells are transfused to patients who are actively bleeding and exhibiting clinical features of hypovolemia. Here, the purpose is twofold: to restore normovolemia and provide hemoglobin to alleviate microcirculatory hypoxemia. The dose of red cells transfused in this situation will depend on the extent of the bleed, which will vary from patient to patient. Clinical judgment remains the most useful approach in gaging the need to transfuse in the first place and the continuing need to transfuse going forward. Attempting to assess the appropriateness or otherwise of red cell transfusion in this situation can be complicated and the default status is to consider such transfusions largely appropriate. However, there is variation in physician thresholds for transfusion. One trial of acute gastrointestinal bleeding in the context of liver cirrhosis randomized subjects presenting with acute gastrointestinal hemorrhage to a liberal versus a restrictive arm, after the administration of a single unit of red cells.2 This study was therefore a red cell dose study and enrolled 921 participants. The liberal group received red blood cells when the hemoglobin decreased to less than 9 g/dL to maintain a hemoglobin between 9 and 11 g/dL, and the restrictive arm received RBCs if the hemoglobin decreased to less than 7 g/dL, to maintain a hemoglobin between 7 and 9 g/dL. The primary outcome measure was all cause 45-day mortality, with secondary outcomes being in-hospital complications and further rebleeding. There was a statistically significant difference favoring the restrictive group (P = .02), which was evident regardless of stage of cirrhosis or site of bleeding (variceal vs. peptic ulceration). This finding, which might appear to be contra-intuitive, lacked a clear explanation but it was hypothesized that the liberal group who received more transfusions maintained higher portal pressures favoring bleeding. The conclusion is important however, as it provides data to support a conservative approach to red cell transfusion in the context of acute gastrointestinal hemorrhage: whether this finding can be generalized to acute spontaneous bleeding from other anatomic sites is unclear but in the absence of such data, a conservative approach would appear justifiable.
The second context in which RBCs are transfused involves patients who are not actively bleeding, but who have normovolemic anemia. Although by definition any hemoglobin less than 13 g/dL is anemia, this generally refers to patients with a hemoglobin less than 10 g/dL. These patients are hemodynamically stable, without evidence of bleeding. The mechanism of the anemia may be multifactorial, spanning hematinic deficiency, anemia of inflammation, acute-on-chronic or chronic blood loss anemia, hemolytic anemia, hypoproliferative anemia or anemia due to ineffective erythropoiesis. In some such patients the cause for the anemia may be apparent, in others not so. If the cause is readily identifiable, such as hematinic deficiency, that should be corrected promptly with iron, B12, and/or folate. Patients with very low levels of hemoglobin (arbitrarily <5 g/dL) are most likely to benefit from red blood cells but it is less clear whether patients with hemoglobins between 5 g/dL and 10 g/dL achieve any useful improved clinical outcome. The decision to transfuse generally takes into consideration the level of hemoglobin and any associated clinical features, although the level of hemoglobin, in itself, often may drive the decision to transfuse. This is well illustrated by a 70-year old male who developed an unexpected blood loss posthernia surgery. The surgeon was concerned and wished to transfuse, but the patient was asymptomatic and reluctant. A transfusion medicine consultation recommended observation rather than transfusion, as the pattern of hemoglobin levels suggested stabilization. In this case, the patient was discharged without transfusion (Fig. 7.1).

The controversy in these patients is the hemoglobin threshold at which an improvement in clinical outcome is achieved by transfusion. In the past 20 years, there have been numerous randomized controlled trials involving different populations of patients which have examined this threshold. The earliest trial was the Transfusion Requirements in Critical care (TRICC) study published in 1999 which equally randomized 834 patients in the Intensive Care Unit (ICU) to a restrictive arm (transfusion threshold <7 g/dL) and a liberal arm (transfusion threshold <9 g/dL). Red blood cell dosage was titrated to maintain a hemoglobin between 7 and 9 g/dL in the restrictive arm and 9–11 g/dL in the liberal arm. The outcome was 30-day mortality. Overall, there was no difference in 30-day mortality, but in a subpopulation with low Acute Physiology and Chronic Health Evaluation (APACHE) scores, a benefit was seen in the restrictive arm. Of considerable interest, Table 7.3 of the manuscript showed a difference in myocardial infarction between the two arms (0.7% for the restrictive arm and 2.9% for the liberal arm, $P = .2$). This was not commented upon, yet might be considered to be surprising. However, recent data suggests that stored red blood cells may contain prothrombotic red cell microvesicles, providing some insight into the observation. Since the TRICC trial, there have been several other randomized control trials examining the hemoglobin threshold for transfusion in different populations: the Transfusion Requirement after Cardiac surgery (TRACS) trial, a Brazilian study in postoperative cardiac surgery patients; the Transfusion requirements in Septic Shock (TRISS) trial, a study in patients with sepsis; the conservative versus liberal transfusion in acute myocardial infarction (CRIT) study in patients with acute myocardial infarction; and the Functional Outcomes in Cardiovascular Patients Undergoing Surgical Hip Fracture Repair (FOCUS) study in postoperative hip fracture surgery patients. These studies have shown that restrictive policies to transfuse at a threshold of 7 g/dL (in patients without cardiac disease) or 8 g/dL (in patients with cardiac disease) are appropriate and may be associated with a better outcome, as supported by a recent meta-analysis. There is ongoing controversy regarding acute myocardial infarction (AMI) and a two-arm randomization to hemoglobin thresholds of 8 g/dL or 10 g/dL is ongoing. Furthermore, a restrictive policy was shown to be inferior in oncology patients undergoing surgery and in oncology patients in the ICU. It may be that a threshold of 8.0 g/dL, or even higher, is appropriate in these populations. It should be emphasized that, in general, a single-unit red cell transfusion should be the dose prescribed in nonbleeding patients, with reevaluation of the clinical situation and posttransfusion hemoglobin performed prior to a second or third unit. This is well illustrated in Fig. 7.1 (Fig. 7.2) in which a low weight recipient with a pretransfusion hemoglobin less than 8 g/dL received a single unit of red cells containing a red cell mass of approximately 190 mL. A postransfusion hemoglobin of greater than 10 g/dL is evident 8 h posttransfusion and a repeat sample 12 h later verified the hemoglobin increase (Fig. 7.2).

Avoidable red blood cell transfusion

Red blood cell substitutes have never become a clinical reality despite decades of research. However, the availability of erythrocyte stimulating agents (ESAs) has
impacted transfusion in a few clinical areas, mostly the management of anemia in patients with chronic renal failure (CRF) and to some extent in oncology. Iron deficiency is the most common cause of anemia worldwide and timely correction with iron repletion can frequently avoid a red cell transfusion. Included in this category are younger women with iron loss from menorrhagia or older patients scheduled for elective surgery. Younger females who develop severe iron deficiency due to menorrhagia may present to the emergency room with fatigue and are not infrequently transfused. The use of intravenous iron in this context can result in
red cell transfusion avoidance but requires education of both Obstetricians and Emergency Department physicians. Another scenario is elective surgery in elderly patients, especially orthopedic surgery. Anemia is common (20%–30%) in elderly patients (>65 years) and related to impaired iron absorption due to reduced gastric acidity. This is illustrated in Fig. 7.3, which shows preoperative hemoglobin levels in 268 patients scheduled for elective hip or knee replacement. The probability of transfusion is determined mostly by the preoperative hemoglobin, and a hemoglobin of less than 11 g/dL was associated with a 60% chance of postoperative red cell transfusion in this cohort. A substantial number of preoperative patients have such a low hemoglobin level, and correction preoperatively could greatly mitigate red blood cell transfusion in this population.

Another strategy in orthopedic surgery is the use of tranexamic acid, either intravenously at induction or intracapsular during the operation, or both. This approach has been shown to reduce blood loss and the likelihood of red cell transfusion.

**Unnecessary Plasma Transfusion**

*Inappropriate plasma transfusion*

Plasma is transfused in two clinical situations: prophylactically, prior to an invasive procedure in patients with evidence of clotting factor deficiency; and therapeutically, in patients who are actively bleeding with a known coagulopathy or who develop a hemodilutional coagulopathy after a large volume red blood cell transfusion. The coagulation test most commonly used to determine the presence and extent of a coagulopathy is the prothrombin time (PT), often resulted as its derivative, the International Normalized Ration (INR). The problem is that the prothrombin time was originally described as an assay of prothrombin, although we now know it measures a number of clotting factors in the extrinsic system. It is especially sensitive to FVII, although FVII deficiency is not, in general, associated with clinical bleeding. Many retrospective observational studies and one randomized control trial have failed to see any relationship between clinical bleeding and the PT or INR. The transfusion of plasma justified on the basis of a prolonged PT or elevated INR has come under considerable criticism. Despite this, plasma continues to be prescribed in this context and guidelines continue to use this test as a justification for prophylactic plasma transfusion. Consider the following patient: A 56-year old female with endometrial carcinoma was scheduled for a radical hysterectomy. A preoperative INR was 1.4. The anesthesiologist was concerned that such an INR could be associated with clinical bleeding and transfused five units of plasma.

![Pre-Operative Hemoglobin](image)

**FIG. 7.3** Preoperative hemoglobins in a cohort of 268 patients scheduled for elective hip or knee replacements.
preoperatively (day 0). Approximately 30 min later, the patient developed fever, with chills and facial flushing. One to 2 h later, she developed increasing dyspnea and surgery was cancelled. She was transferred to the ICU. Three of the five donors were multiparous females. The dyspnea improved over a few days. She returned for surgery 7 days later. No plasma was given and surgery was performed uneventfully. The sample from the initially intended day of surgery (day 0) was not available for clotting factor assays, but the sample on day 7 (day of surgery) was available. As is seen in the table, there was no change in the INR and there is no clotting factor deficiency. Hence, the rationale for plasma transfusion (clotting factor deficiency) is erroneous, the transfusion of plasma was inappropriate and furthermore, the patient suffered a nonfatal TRALI reaction as a result of the inappropriate plasma transfusion (Table 7.1).

The mechanism of the elevated INR in this patient is likely the increase in D-dimer associated with the malignant condition. Inappropriate plasma transfusion appears particularly common in patients with liver disease. An elevated INR is typical of patients with advanced liver disease and is generally due to a low FV and/or hypofibrinogenemia or dysfibrinogenemia. However, patients with liver disease have a high FVIII and a low antithrombin III and a low protein C. Hence, on balance, these patients may be hypercoagulable, not hypocoagulable. Furthermore, patients with a mildly elevated INR do not respond to plasma transfusion with a material shortening of the INR. This is well illustrated (Fig. 7.4) in a series of 46 patients with an INR of <2.0 who received plasma and had measures of the INR within 6 h of plasma infusion. The mean (±1SD) pre-INR is 1.55 ± 0.3 and post-INR is 1.43 ± 0.3. This poor response of the INR to plasma transfusion has also previously been reported.

Whether patients with very high INRs (>3.0) benefit from plasma transfusion is unclear. However, retrospective studies even in this population give no support to the practice of prophylactic plasma transfusion, and

| TABLE 7.1 Clotting Tests in a 56-year Old Female With Endometrial Carcinoma Who Received Plasma (Day 0) and Had a TRALI Reaction |
|-----------------|-----------------|
|                | Day 0 | Day 7 |
| PT (s) | 15.3  | 15.3  |
| INR   | 1.4   | 1.4   |
| aPTT (s) | 27    | 25    |
| Fibrinogen (mg/dL) | 696   |       |
| D-dimer (μg/mL)  | >4    | >4    |
| FII (%) | 80    |       |
| FV (%) | 85    |       |
| FVII (%) | 58    |       |
| FX (%) | 102   |       |

**FIG. 7.4** Joined dot plot of 46 patients with an INR of <2.0 pretransfusion. The post-INR was within 6 h of the plasma transfusion.
many patients with such INRs have vitamin K deficiency or are taking a vitamin K antagonist, which should be managed with intravenous vitamin K, restricting the use of 4-factor prothrombin complex concentrates for the most urgent cases.\textsuperscript{31}

**Avoidable plasma transfusion**

There are many situations in which prophylactic plasma transfusion can be avoided if the cause of the prolonged INR is understood and potentially can be reversed or does not need to be reversed. Consider the following scenario: A request is received at 2320 h for 1 unit of FFP for a patient with an INR of 2.4 prior to surgery on the following day. A preoperative INR of <2.0 is desired. The technologist calls the surgeon and suggests giving vitamin K intravenously. The surgeon responds that the patient has liver disease and that vitamin K would not be helpful. Regardless, she agrees to administer 5 mg vitamin K intravenously that was given at 2345 h. At 0545, the INR has declined to 1.5. However, the surgeon fails to note the new test result and 1 unit of FFP is issued at 0645 immediately prior to surgery. The samples from the evening before surgery (day 0) and immediately pre-surgery (day 1) were available for clotting factor assays that are shown in Table 7.2:

As is evident, the patient has vitamin K deficiency that responded to intravenous vitamin K. This could have been predicted from the fibrinogen level, as patients with vitamin K deficiency have normal to high fibrinogen levels while patients with liver disease have low normal or low fibrinogen levels.

Another scenario is a request from the Emergency Department for two units of plasma for a 30-year old male with headache and fever prior to a lumbar puncture (LP). There is no personal or family history of a bleeding or clotting. However, the aPTT was 30 s (normal: 24–37) and the INR was 2.1. The physician is reluctant to perform the LP. Clotting factor assays to clarify the elevated INR revealed a selective FVII deficiency and a mixing study corrected the INR to 1.1. The LP was performed without plasma and without any bleeding complications (day 0). Infusion of vitamin K on the following day showed no responsiveness in the vitamin K dependent factors, confirming heterozygous FVII deficiency, an hereditary disorder not considered to be associated with clinical bleeding.\textsuperscript{24} In this case, the transfusion of plasma was avoided.

The failure to administer vitamin K in a timely manner prior to an invasive intervention can also have dire consequences, as illustrated by the following case: A 78-year old female on warfarin for atrial fibrillation required endoscopy for rectal bleeding. The INR is 4.3. Two units FFP are requested. The chronology of events is shown in Table 7.4.

Both of these units were from female donors. The first unit was from a multiparous female who returned for testing. No HLA antibodies were present in the plasma. The second unit was from a female who had a single live pregnancy in 1981 and was transfused with one unit of red blood cells. This donor returned for testing and had class I and class II anti-HLA antibodies (anti-A\textsubscript{2}, anti- A\textsubscript{68}, anti-B\textsubscript{44}, anti-B\textsubscript{45}). The recipient was DNA typed as A\textsubscript{2}, B\textsubscript{44}, DRB1*0401, confirming the TRALI mortality.

### Table 7.2

**Response to Intravenous Vitamin K**

<table>
<thead>
<tr>
<th></th>
<th>Day 0</th>
<th>Day 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
<td>1756</td>
<td>0545</td>
</tr>
<tr>
<td>Fibrinogen (mg/dL)</td>
<td>552</td>
<td>479</td>
</tr>
<tr>
<td>FV (%)</td>
<td>144</td>
<td>138</td>
</tr>
<tr>
<td>FVIII (%)</td>
<td>&gt;200</td>
<td>&gt;200</td>
</tr>
<tr>
<td>FVII (%)</td>
<td>25</td>
<td>55</td>
</tr>
<tr>
<td>FX (%)</td>
<td>18</td>
<td>48</td>
</tr>
</tbody>
</table>

### Table 7.3

**Confirmation of Hereditary Heterozygous FVII Deficiency and Avoidance of Plasma Transfusion**

<table>
<thead>
<tr>
<th></th>
<th>Time</th>
<th>INR</th>
<th>aPTT (s)</th>
<th>Fibrinogen (mg/dL)</th>
<th>FVII (%)</th>
<th>FX (%)</th>
<th>FV (%)</th>
<th>FVIII (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 0</td>
<td>0100</td>
<td>2.0</td>
<td>30</td>
<td>19</td>
<td>106</td>
<td>87</td>
<td>&gt;200</td>
<td></td>
</tr>
<tr>
<td>Day 1</td>
<td>0308</td>
<td>1.8</td>
<td>31</td>
<td>23</td>
<td>99</td>
<td>78</td>
<td>&gt;200</td>
<td></td>
</tr>
<tr>
<td>Day 1</td>
<td>1030</td>
<td>1.9</td>
<td>30</td>
<td>464</td>
<td>22</td>
<td>91</td>
<td>72</td>
<td>&gt;200</td>
</tr>
</tbody>
</table>
These cases illustrate patients with an elevated INR in which the diagnosis is unclear (heterozygous FVII deficiency), not suspected because of the context (erroneously considered to be due to liver disease) or known but not managed correctly (failure to administer vitamin K intravenously on the evening before endoscopy). In each case, plasma was prescribed in doses that would be considered ineffective. Physician education by Transfusion specialists in this area of coagulopathy is critical to avoid plasma transfusion.

Intravenous vitamin K has an important role in management but there has been a bias against the use of vitamin K based on certain myths (Table 7.5).

Of particular concern is the myth that intravenous vitamin K takes at least 6 h to decrease the INR to approximately 2.0 or less. Fig. 7.5A and B demonstrates that intravenous vitamin K successfully achieves such an INR in less than 4 h. The rapid response of FVII is evident in Fig. 7.6, which is the main driver of the decrease in INR. Importantly, these changes are achieved at doses of 5 mg IV, which would not be expected to complicate the reintroduction of warfarin postprocedure.

Plasma is also used as an exchange fluid in thrombotic thrombocytopenic purpura (TTP) and in tertiary care centers, this can account for a significant fraction of all plasma transfused. The pathophysiology of sporadic TTP is a deficiency of ADAMTS13, a metalloprotease involved in the cleavage of ultra-large multimers of von Willebrand factor. Implementation of an ADAMTS13 assay with rapid turnaround time has been shown to be extremely useful in separating TTP from other thrombotic microangiopathies thus avoiding the unnecessary use of plasma in this context. Taken together, avoidance of plasma transfusion in patients with mild (<2.0) or moderate (<3.0) elevation of the INR, careful

---

**TABLE 7.4**  
**Chronology of Events in a Patient With a Fatal TRALI Reaction**

- 1143: Specimen received in the Blood bank and types as Group O Rh (D) positive
- 1222: 1st unit FFP dispensed and transfused
- 1245: 2nd unit FFP dispensed and transfused
- 1315: Arrives in endoscopy suite
- 1320: Complains of slight dyspnea
- 1330: Procedure cancelled; more severe dyspnea; CXR shows bilateral pulmonary edema
- 1330–1400: O₂ saturation declines progressively over 30 min as follows: 86%, 77%, 66%, 32%
- Patient expires at 1404

**TABLE 7.5**  
**Myths Regarding Intravenous Vitamin K**

- Oral vitamin K acts as rapidly as intravenous vitamin K
- Subcutaneous vitamin K is more rapid in onset of action and more consistent in lowering the INR than oral vitamin K
- Intravenous vitamin K has a high risk of an anaphylactoid reaction
- Intravenous vitamin K does not lower the INR for at least 6 h
- Intravenous vitamin K will cause difficulty in reestablishing anticoagulation with warfarin

---

**FIG. 7.5** (A and B) Rapid response to intravenous vitamin K in two patients requiring urgent partial warfarin reversal.
Risk Management in Transfusion Medicine

assessment of the cause of any elevated INR, correction of an elevated INR with vitamin K where appropriate, and timely diagnosis of patients with TTP can greatly impact plasma use.\textsuperscript{1,54}

**Unnecessary Platelet Transfusion**

Inappropriate platelet transfusion

Platelets are transfused in three clinical situations: prophylactically, to prevent spontaneous bleeding; prophylactically, prior to an invasive diagnostic or therapeutic procedure; and therapeutically, in thrombocytopenic patients or patients with thrombocytopenia who are actively bleeding. Most of the platelet transfusions are administered to thrombocytopenic patients to prevent spontaneous bleeding. These patients have a hypoproliferative thrombocytopenia due to a marrow disorder (acute leukemia, myeloproliferative neoplasm, myelodysplastic syndrome, or chemotherapy or radiation therapy). In general, there is reasonable agreement regarding appropriate platelet transfusion to prevent spontaneous bleeding for this category of recipients.\textsuperscript{55–57} Platelet transfusions are appropriate for stable patients with single digit thrombocytopenia (platelet count < 10 × 10\(^9\)/L); unstable patients with clinical evidence of an inflammatory process with a platelet count < 15 × 10\(^9\)/L; patients with platelet counts of 10–20 × 10\(^9\)/L who are exhibiting a rapid decline in the platelet count in association with chemotherapy; patients with a de novo venous thrombosis requiring full anticoagulant therapy with heparin and a platelet count of < 30 × 10\(^9\)/L. Stable autologous adult bone marrow transplant patients are now managed with therapeutic only transfusions,\textsuperscript{58–60} reserving prophylactic transfusion for those patients who are unstable. The dose is considered a standard adult dose\textsuperscript{61} or approximately 2.5–4.0 × 10\(^11\). Transfusing platelets outside of these guidelines should be rare, as they are based on good data.\textsuperscript{62}

There are a few clinical scenarios where platelet transfusion to this category of patients can be questioned: (1) Patients with stable single digit thrombocytopenia who are not on any treatment. These patients typically are out-patients with MDS or aplastic anemia and despite the severe thrombocytopenia have long bleeding-free intervals without transfusion. It may be appropriate not to transfuse such patients prophylactically as there are always risks of transfusion.\textsuperscript{60} Consider the following: A 68-year old male with MDS, not on any treatment nor any overt bleeding, was transfused as an out-patient with a pretransfusion platelet count of 14 × 10\(^9\)/L. The patient was Group O, Rh negative and received prepooled whole blood derived platelets, all Group O, Rh negative. The pool was 5 days old. The transfusion occurred in clinic without any adverse event observed and he was discharged. About 1–2 h later, he stared to experience chills, followed by dry wrenching. Approximately 3 h after discharge, he returned to clinic where he was noted to be febrile. A reaction was called and the container, which had been discarded, was retrieved. The gram stain showed

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{image.png}
\caption{Changes in clotting factors in response to 5 mg vitamin K.}
\end{figure}
numerous gram positive coagulase negative cocci. He was admitted and started on intravenous cefazolin 2 G every 8 h. He was discharged 3 days later, to continue the intravenous antibiotics for another week. In retrospect, a decision to not transfuse this patient could have been a better overall approach. (2) Patients who are refractory due to broad spectrum HLA alloimmunization. These patients should be left untransfused until a suitable high grade HLA match is available, unless a life-threatening bleed ensues. This is illustrated by the following: A 69-year old female underwent allogeneic bone marrow transplant for MPN. She developed lower gastrointestinal bleeding requiring red cell transfusion. Despite the HLA alloimmunization, non-HLA matched platelets were transfused, as shown (Fig. 7.7), without any benefit as measured by platelet increments, and the clinical bleeding continued. The treating physician desired a platelet count of $30 \times 10^9/L$, which was largely unattainable with non-HLA matched platelets. After HLA matched platelets were procured, better increments were seen and the bleeding ameliorated.

(3) Overdosing. In stable patients with very severe single digit thrombocytopenia (platelet counts $<5 \times 10^9/L$), there may be a request for a double adult dose on the basis that this will protect further against spontaneous bleeding. There is no evidence that such a treatment strategy decreases the risk, if any, of clinical bleeding. Consider this 36-year old patient with AML undergoing induction therapy who developed neutropenic sepsis. The course of platelet transfusions is shown in Fig. 7.8. Noteworthy is the double dose of platelets given when the platelet count was approximately zero. While this achieved a higher increment, the increment was short lived and likely represents unnecessary overdosing.

(4) Patients with immune thrombocytopenia. These patients have severe single digit thrombocytopenia and are frequently transfused in the emergency department. Such transfusions are largely futile as the platelet increment is short lived. Platelet transfusion in this context is only appropriate for life-threatening bleeding.

(5) Lastly, patients with thrombotic microangiopathy (TMA) or posttransfusion purpura (PTP). Platelet transfusions are largely considered to be contra-indicated in these clinical situations.

The second prophylactic use of platelets is to prevent bleeding in association with an invasive diagnostic or therapeutic intervention. Regrettably, there are no randomized controls in this setting, only retrospective observational reports which neither support nor refute any specific platelet threshold. It is commonly believed that the bleeding risk in this scenario is higher than the risk of spontaneous bleeding, but no predetermined

**FIG. 7.7** Changes in the post transfusion platelet count after transfusion of non-HLA matched and HLA-matched platelets.
threshold can be justified based on good data. However, guidelines are available, and it has become a common practice to transfuse prophylactically when the platelet count is \(<50 \times 10^9/L\). However, some recent data would support a lower threshold for central line placement and also lumbar puncture for diagnostic purposes or intrathecal therapy. This is an important area for study. Consider an 84-year old patient with a platelet count of \(41 \times 10^9/L\) requiring paracentesis. The interventional radiologist insisted on a prophylactic platelet transfusion. The platelets were administered as shown. No meaningful change occurred in the platelet count as would be anticipated (Fig. 7.9).

A slightly different case is a 23-year old male newly diagnosed with B-Cell ALL. A diagnostic LP was planned and a target platelet count of \(50 \times 10^9/L\) arbitrarily desired. His pretransfusion platelet count was \(14 \times 10^9/L\). He was prescribed two apheresis doses of platelets with the intention of performing the LP after the second dose. The first dose was dispensed at 1400 h and was uneventful. The second dose was dispensed at 1800 h and the administration commenced at 1805 h. At 1835 h, after 111 mL of a 162 mL product had been transfused, the patient complained of difficulty breathing, which became progressively worse over the next hour. The respiratory rate increased to 44/min and oxygen saturation was 88% on room air. The LP was not performed and he was transferred to ICU, intubated and ventilated. He slowly improved over the next 24 h, was extubated and transferred out of the ICU. Fig. 7.10 shows the chest
X-ray shortly after the second dose and several days later. This is an example of overdosing prior to an invasive procedure and illustrates the undesired consequences of a well-intentioned but unsubstantiated policy.

These cases illustrate the problems confronting the blood bank with regard to prophylactic platelets prior to an invasive procedure. It is unlikely that randomized controlled trials will be performed as the sample size required to reach a conclusion would be large, and the bleeding risk is low. In practice, a large number of participants would have to be enrolled. Furthermore, patient heterogeneity would likely raise confounders in interpretation. Therefore, a patient registry approach might be more suitable. Given the uncertainty, identifying “inappropriate” platelet transfusions in this context is difficult. The recent ASCO guidelines are helpful in this respect but evidence to justify the guidelines is lacking.60

The third indication for platelet transfusion is therapeutic platelet transfusions in thrombocytopenic patients or patients with thrombocytopenia who are actively bleeding. With regard to thrombocytopenia, no threshold can be defined: as a practical matter, a threshold of 50 × 10^9/L is commonly used, but this has no empiric justification and may be unnecessary, even with intracranial hemorrhage (ICH). In this respect, an interesting retrospective observational study was reported from MD Anderson of ICH in patients with leukemic or MDS over a 3-year period between 2007 and 09.63 A total of 76 adult patients with ICH were reported: 42 with subdural hematoma, 9 subarachnoid bleeds, 18 intraparenchymal bleeds, and 7 intraventricular bleeds. The median platelet count at presentation was 17 × 10^9/L (range 0–178). Moreover, 8 of 76 patients had platelet count >50 × 10^9/L and 3 had platelet count >100 × 10^9/L. The management objective was to achieve and maintain a platelet count >50 × 10^9/L. Only 24/68 achieved a platelet count >50 × 10^9/L (responders). Evaluation was performed at 72 h and 30 days. At 72 h, mortality (15/76, 20%) was related to Glasgow Coma Score (GCS) score <10, but not initial platelet count, achievement of platelet count >50 × 10^9/L, or the number of platelet transfusions administered. Death due to ICH at 30 days was related to age and platelet responsiveness but not to GCS, the peak platelet count achieved, or number of days with a platelet count >50 × 10^9/L. This study indicates that the outcome of ICH in these patients is determined by factors other than the platelet count, and platelet transfusions, early platelet transfusion responsiveness, or achievement of a platelet count >50 × 10^9/L did not influence clinical outcome at 72 h or 30 days. This report casts doubt on the use of any platelet threshold or target in ICH and calls into question the use of large doses of platelets in the management of these patients.

There is some better data on the use of platelet transfusions in patients on antiplatelet therapy. The recent Platelet Transfusion Versus Standard Care After Acute Stroke due to Spontaneous Cerebral Haemorrhage Associated with Antiplatelet Therapy (PATCH) study is a randomized control study in which patients on antiplatelet therapy (APT) with spontaneous (nontrauma) intracranial bleeding were randomized to either receive platelet transfusion or placebo.64 This study involved 60 hospitals in the UK, Netherlands, and France. Patients were randomized within 6 h of the bleed to receive therapeutic platelets or
standard of care. Outcomes were death-or-dependence, measured by a modified Rankin score adjusted for stratification variables, and clinical hemorrhagic score. There were 190 participants: 97 received platelet transfusion and 91 received standard of care. The odds of death-or-dependence were 2.05 in the platelet transfused group. Furthermore, 42% of the platelet transfused group had an adverse event and 24% died. In the standard of care group, 29% had an adverse event and 17% died. The conclusion was that platelet transfusion did NOT favorably affect clinical outcome in this population. The use of therapeutic platelet transfusions in patients on APT has not been advocated by the AABB Guidelines.

**Avoidable platelet transfusion**

As yet, there is no substitute available as an alternative to platelet transfusion. The general approach has been to attempt to use agents that could augment or work in concert with platelets to promote better hemostasis. A general list is given in Table 7.6. The subject has been reviewed elsewhere but there is no consensus that these agents are efficacious.

**Conclusion:** Inappropriate transfusions are commonplace in-hospital and occur on account of the continuation of outdated, nonvidence-based practices. Avoidable transfusions occur because patient management is not optimized. Addressing intranstitutional inappropriate practices and promoting good transfusion management can be a highly effective risk reduction strategy.

### REFERENCES


CHAPTER 7 Patient Blood Management


50. Sahai T, Tavares MF, Sweeney JD. Rapid response to intravenous vitamin K may obviate the need to transfuse prothrombin complex concentrates. *Transfusion.* 2017;57:1885–1890.


