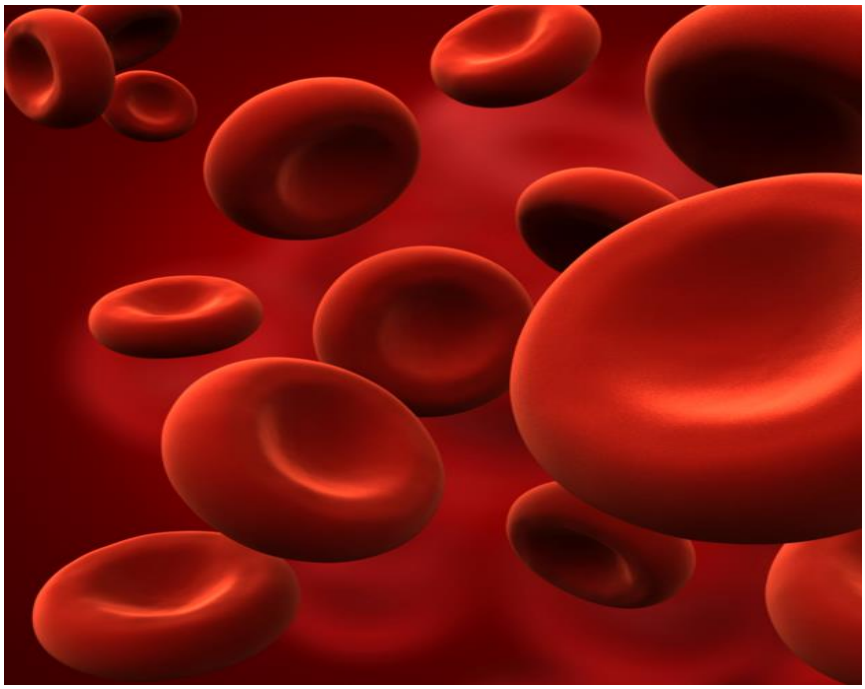
Patient Blood Management



Essentials for non-health professionals

Jean-François Hardy, M.D.

Professor Emeritus

Département d'anesthésiologie
et de médecine de la douleur
Faculté de médecine

Université de Montréal

Updated November 2024

Table of Contents

Glossary of the main terms used

Anemia	Decrease in the number of red blood cells in the blood. This decrease is measured by the hemoglobin content of red blood cells, which is expressed in grams per litre (g/L). The normal concentration is 120 g/L or more in women and 130 g/L or more in men.
Packed RBC	Unit of red blood cells (RBC) obtained after fractionation of a blood donation into red blood cells, plasma and platelets.
Erythropoietin	A natural hormone secreted by the kidney that stimulates the production of red blood cells.
Hematinic	A substance that helps in the formation of red blood cells (iron, vitamin B12, folic acid).
Hemoglobin	A protein containing iron, contained in the red blood cells to which it gives its color, and which carries oxygen in the blood.
Bone marrow	A soft, fatty substance that fills the medullary canal and alveoli with the spongy substance in the center of the various bones, responsible for the production of all the figurative elements (cells) of the blood.
Morbidity (or complications)	All the effects following an illness or trauma (such as an operation), often referred to as sequelae. These are mainly harmful and long-lasting repercussions on health, for medium to long-term periods.
Perioperative	Before, during and after the operation
Platelets	Platelets prevent blood loss. When a blood vessel is damaged, platelets adhere to it to form a plug that stops bleeding.
Plasma	A liquid component of the blood in which three types of cells are bathed: red blood cells, white blood cells and platelets.
Preoperative	Before the operation
Elective	Refers to a non-urgent operation that can be put on the operating schedule at any time.

A brief history of Patient Blood Management (PBM)

First, what is PBM?

The principle behind PBM is very simple. In patients scheduled for major hemorrhagic surgery (i.e., surgery with a significant risk of bleeding; defined below), preoperative anemia and blood transfusions have been shown to be associated with increased perioperative morbidity (complications) and mortality. Thus, in the context of PBM, the hospital team uses best practices to correct preoperative anemia, control bleeding during and after the procedure and minimize blood transfusions, with the primary objective of improving the patient's outcome. That's what PBM is all about!

But how did we get there?

The Pre-Transfusion Era

Before the first blood bank, founded in 1935, clinicians caring for patients at risk of bleeding meticulously tried to prevent bleeding and conserve the patient's blood. Indeed, at that time, blood transfusions simply did not exist.

The arrival of transfusions

With the emergence of transfusion medicine at the beginning of the 20th century and the development of blood banks, blood transfusion has increased considerably in medicine. Thus, blood transfusion has become one of the most widely used procedures in hospitals. As we have been told so often, transfusion "saves lives." Of course, transfusion has led to important developments in medicine (bone marrow transplants, for example) and during a major operation such as heart surgery. It is, without a doubt, essential to treat massive bleeding secondary to a road accident or other major trauma. On the other hand, it has often been abused by targeting arbitrarily chosen (high) hemoglobin levels, unrelated to the patient's condition and symptoms. However, it is now known that moderate anemia is most often well tolerated and that transfusions are not necessary. It is these unnecessary or misguided transfusions that are dangerous (see below: The Risks of Transfusions).

Reviewing our ways of doing things

Jehovah's Witnesses, refusing transfusions of blood products on religious grounds, led us to review our practices. Multidisciplinary teams have combined many therapeutic modalities to allow these patients to benefit from major interventions without the need for transfusion. But other patients have also benefited from this approach, for example those with a rare blood type for whom blood is not always available.

In addition, with the aging of the population, the blood supply is becoming increasingly problematic in some countries. The elderly population is the one who consumes the most care – and transfusions – and who is the least able to donate blood. This situation is likely to lead to shortages of blood products essential to the survival of some patients.

The risks of transfusions

The arrival of the acquired immunodeficiency syndrome (AIDS) in the early 1980s made the medical profession and patients more suspicious of transfusions. Although in rich and advanced societies the risk of transmission of the AIDS virus through transfusion has become infinitesimal, other viral risks have emerged, such as the Zika virus, not to mention those that are not yet known.

Transfusions are also associated with a range of complications such as infectious complications (e.g., pneumonia), respiratory, cardiac and renal complications, increased length of hospital stay and short- and long-term mortality.

And the costs in all this?

Transfusions are associated with significant costs. For a unit of red blood cells, this cost has been estimated at $600 (2006) but is more of the order of $900 according to more recent estimates (2010) if we take into account the cost of production by Héma-Québec, storage, laboratory analyses (compatibility) and administration (equipment for the IV, nurse's time).

Patient Blood Management: why?

Several studies have shown that preoperative anemia, regardless of all other pre-existing conditions/diseases of the patient, is associated with increased complications after surgery. Preoperative anemia, even when it is mild, is associated with a 30 to 55% increase in surgical morbidity and mortality.

Based on the principle that blood is a precious resource, we must do everything possible to increase the patient's reserves (correct anemia before the operation), reduce blood loss during the operation, and avoid transfusions as much as possible. The adoption of a lower (also called "restrictive") transfusion threshold (the level of hemoglobin at which a transfusion is administered) is well tolerated and allows several transfusions to be avoided.

We have therefore moved from the pre-transfusion era during which clinicians practiced blood conservation to the transfusion era for which transfusion has become the universal answer to all problems of anemia and bleeding. Today, we are in the era of Patient Blood Management, a direct reference to the patient who is at the center of the process. The primary goal is not to reduce transfusions (albeit an important effect of PBM), but to improve patient outcomes by reducing perioperative complications and mortality.

In 2010, the World Health Organization recommended to its members the implementation of Patient Blood Management programs. In 2020, the WHO renewed its call for PBM programs to ensure universal access to safe, quality blood products.

Anemia and its treatment before surgery

Definition of anemia

In women, the average hemoglobin level varies between 130 and 139 g/L and, in men, between 140 and 149 g/L. According to the World Health Organization, anemia is defined as a hemoglobin level of less than 120 g/L in women, 110 g/L in pregnant women and 130 g/L in men. This definition of anemia is not universal, but it is the most widely used and is therefore the one we have adopted in this text. For several reasons, some consider that the 130 g/L threshold is valid for both men and women.

How common is anemia?

Anemia is a very common medical condition in the population, affecting nearly 33% of the world's population.

As for the surgical population (i.e., all patients who benefit from an operation), according to various publications, the incidence of preoperative anemia varies from 24% in gynecological surgery to 52% in cardiac surgery. At the CHUM, an audit conducted in 2013 showed that, on average, 32% of patients who had undergone orthopedic, cardiac, vascular, thoracic or neurosurgical surgery were anemic before the operation. These patients were more transfused, they had more complications, and their mortality rate was higher.

What causes anemia?

Iron deficiency

The most common cause of anemia is iron deficiency, being responsible for about 50% of cases. This proportion varies by sex, age, and geographic region, but iron deficiency remains the leading cause of anemia in both men and women. Iron deficiency occurs either because of insufficient intake or is due to blood loss (see table: Main causes of iron deficiency).

Meat is the main source of dietary iron. For those who do not eat meat (vegan or vegetarian diet), foods such as molasses, lentils, tofu, spinach, chickpeas, and other iron-rich foods should be consumed to prevent iron deficiency.

Main Causes of Iron Deficiency

- Menstrual discharge
- Pregnancy and childbirth
- Inadequate intake of iron in the diet
- Gastrointestinal loss
    - Cancer
    - Gastritis (inflammation of the stomach)
    - Helicobacter pylori: a bacterial infection that causes gastritis or a duodenal ulcer
    - Taenia (tapeworm) and other parasites
    - Meckel's diverticulum: malformation (small sac) in the small intestine that can bleed or become infected
    - Vascular malformations
- Obesity and Bariatric Surgery (Obesity Surgery)
- Celiac disease or inflammatory bowel disease (e.g., Crohn's)
- Hematuria (blood loss in the urine)
- Repeated blood donation (3 to 4 times per year) over an extended period

Other causes of anemia

Other causes of anemia are inflammatory anemia, vitamin B12 deficiency anemia, and folic acid deficiency anemia.

How is anemia treated?

Treatment of iron, vitamin B12 or folic acid deficiency anemias is treated with an oral or intravenous supplement of these hematinics. In the case of inflammatory anemia, treatment with intravenous iron will be necessary, but insufficient. It will be necessary to stimulate the production of red blood cells with a synthetic hormone, recombinant erythropoietin. Erythropoietin can be administered in hospitals, out-patient clinics, doctors' offices, or as a self-administration.

Anemia, transfusions, and bleeding procedures: what are the risks?

What is a procedure at risk of bleeding?

We speak of an operation with bleeding potential when the expected blood loss exceeds 500 mL (in comparison, 450 mL of blood is collected when blood is donated to Héma-Québec) or when the risk of transfusion exceeds 10%. However, this definition does not consider the differences between men and women. On average, a woman will have a smaller blood volume (4 to 5 L) due to her weight, compared to a man's blood volume (5 to 6 L). Therefore, a loss of 500 mL is, proportionally, much greater in a 50 kg woman than in an 80 kg man. Women are therefore more at risk of being transfused than men, even if their hemoglobin level is normal (120 g/L). For this reason, some recommend that women reach a hemoglobin of 130 g/L before the day of the operation, the same hemoglobin level as in men.

What are the risks associated with anemia and transfusions?

It is not always easy to distinguish the effects of preoperative anemia from the effects of transfusions or the effects of the underlying disease. Several studies suggest that anemia and transfusions are independent risk factors for increased morbidity and mortality. In any case, the fact remains that pre-existing anemia increases the risk of transfusion during and after surgery. Both factors are linked to an increase in complications and mortality. It is therefore necessary to try to correct preoperative anemia in order to reduce the risk of transfusion and optimize the patient's outcome. In other words, the non-treatment of preoperative anemia is a suboptimal clinical practice.

The clinical benefits of PBM

PBM reduces transfusions

Numerous studies have shown that the interventions advocated by PBM reduce transfusions. A first systematic review, published in 2019, showed that, all types of operations combined, PBM reduces the incidence of transfusion by 39%. The largest decrease was in orthopedics, with a decrease of 55%, followed by cardiac surgery with 50%.[1]

Another meta-analysis, published in 2020, clearly showed that it decreased the incidence of red blood cell transfusion by 40%. PBM also decreased the incidence of transfusion of fresh frozen plasma and platelets, by 26% and 12%, respectively. The decrease in the number of packed RBC transfused averaged 0.83 units of red blood cells per patient.[0]

These results are important for several reasons. First, as we have seen previously, transfusions carry risks and, logically, reducing exposure to transfusions improves the patient's outcome. Secondly, the decrease in the number of transfusions helps us to cope with the current demographic context and the decrease in the availability of blood products.

In fact, the over-65 age group is constantly increasing and consuming an increasingly large share of blood products, compared to the 18 to 64 age cohort in which the majority of donors are found. The pressure on the availability of blood products is therefore increasing, which is the main reason why Italy has made PBM mandatory. Finally, in times of pandemic, the availability of blood products and the demand for these products varies considerably depending on the phases of the global epidemic. PBM, by minimizing the use of transfusions, helps to maintain the delicate balance between availability and demand.[0]

PBM decreases morbidity, length of stay and mortality

The systematic review published in 2019, mentioned above, did show a statistically significant decrease in morbidity and mortality when a comprehensive PBM program was implemented. The total number of complications decreased by 20%, with the largest reduction reported in cardiac surgery (27%), followed by orthopedics and vascular surgery

[1] Althoff FC, et al. Multimodal Patient Blood Management Program Based on a Three-pillar Strategy: A Systematic Review and Meta-analysis. Ann Surg. 2019 May; 269(5):794-804.
[0] Roman MA, et al. Patient blood management interventions do not lead to important clinical benefits or cost-effectiveness for major surgery: a network meta-analysis. Br J Anaesth. 2020 Jun 30:S0007-0912(20)30342-1.
[0] Shander A, et al. Essential Role of Patient Blood Management in a Pandemic: A Call for Action. Anesth Analg. 2020 Jul; 131(1):74-85.

with 22% and 17% respectively. PBM also reduced the length of hospital stay by 0.45 days, with the largest decrease being in cardiac surgery with 1.34 days. Overall, PBM decreased mortality by 11%, with the largest decrease observed in orthopedics at 27%.

The experience of Western Australia is particularly interesting. In 2008, the Ministry of Health implemented a universal PBM program in the state's four adult specialty hospitals. The results of their experiment were published in 2017. The authors reported a significant reduction in the use of blood products, a decrease in mortality by 28%, length of stay by 15%, infections by 21%, and myocardial infarction by 31%.[0]

It therefore appears that PBM, through its integrated, multidisciplinary and interprofessional approach, allows for better overall patient care. This approach not only reduces blood loss and transfusions, but above all, reduces complications and mortality after surgery. PBM is a comprehensive ensemble of care whose elements will be applied to the patient, according to his or her particular needs, before, during and after the operation.

PBM lowers costs

PBM reduces costs by reducing transfusion and complication treatment expenses. With respect to transfusions, the National Advisory Committee on Blood and Blood Products (Canada) estimates that the cost of a transfusion in 2022 is approximately $775 (acquisition of the product, verification at the blood bank, administration, etc.).[0] Thus, at the CHUM, we have calculated that PBM could eventually generate savings of about $1.7 million and thus largely reimburse the expenses related to its implementation, i.e., at most, $1.3 million.

In addition, the savings related to the reduction of complications, length of stay and mortality are much greater and have been documented in several studies. For example, on average, the average cost of hospitalization for a given *Diagnosis Related Group (DRG*) was 1.83 times higher in transfused patients. Transfusion of a single unit of red blood cells was associated with a 1.57-fold increase in hospitalization costs, rising to 4.89-fold for transfusion of 10 or more units.[0] Using these figures, the excess transfusion expenses are in

[0] Leahy MF, et al. Improved outcomes and reduced costs associated with a health-system-wide patient blood management program: a retrospective observational study in four major adult tertiary-care hospitals. Transfusion. 2017 Jun; 57(6):1347-1358.

[0] NAC position statement on patient blood management. V20220622. https://nacblood.ca/en/resource/nac-patient-blood-management-statement

[0] Trentino KM, Farmer SL, Swain SG, Burrows SA, Hofmann A, Ienco R, Pavey W, Daly FF, Van Niekerk A, Webb SA, Towler S, Leahy MF. Increased hospital costs associated with red blood cell transfusion.

the order of $4,700 per transfusion (including the cost of the transfusion). Applied to the CHUM, this amount would generate savings of nearly $13 million per year. Even if not all transfusions can be avoided, the savings made are still major for the health system.

In the context of the transition of hospital funding (based on historical funding) to a DRG based funding,[0] such savings are significant, even vital, for each hospital. The reduction of complications and length of stay associated with PBM will optimize the efficiency of the health care system by being able to treat more patients at a lower cost while increasing the quality of care provided.

Transfusion. 2015 May; 55(5):1082-9.

[0] Francis Vailles. Revolution in the financing of hospitals. https://www.lapresse.ca/affaires/chroniques/2022-05-09/revolution-dans-le-financement-des-hopitaux.php

The experience of the Centre Hospitalier de l'Université de Montréal

In this section, we review the PBM program from the patient's point of view, in a time sequence.

The Preoperative Clinic (POC) and the Preoperative Anemia Clinic (PAC)

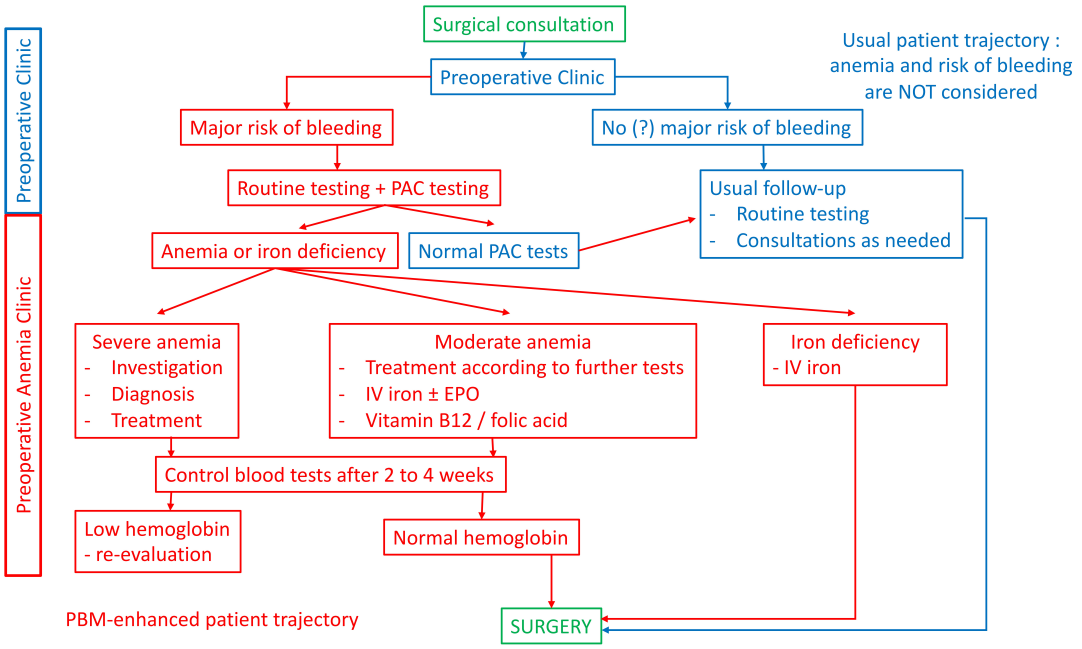
It all starts with the patient's meeting with his surgeon. The surgeon sends an operative request to the surgical program. The latter schedules an appointment at the preoperative clinic (POC) and notifies the patient. If the operation is on the list of surgeries at high-risk of bleeding, the nurse adds a "PAC workup" (a set of additional tests requested by the Preoperative Anemia Clinic) to the basic laboratory tests ordered by the surgeon. These tests will determine whether the patient is anemic or not and detect iron deficiency.

On the day of the preoperative visit, the patient meets with the POC nurse who performs the blood tests requested by the surgeon and the "PAC workup" (if required). If necessary, the patient meets with the consulting specialist requested by the surgeon, such as the internist, cardiologist, or nephrologist. Finally, the patient meets with the POC nurse who completes his or her assessment and provides the relevant education for the planned intervention. The patient can then go home.

After leaving, the nurse checks the blood test results when available, usually the same day. If the PAC workup is normal, i.e., if the hemoglobin is normal and if the patient does not lack iron, the preoperative follow-up follows its usual course without intervention by the PAC. On the other hand, if the patient is anemic or has an iron deficiency, his file is then transferred to the PAC nurse for care.

The PAC nurse takes note of the patient's file and communicates with the patient to inform him or her that he or she is being cared for by the PAC for the treatment of his or her preoperative anemia. She then checks whether the operation is urgent, such as surgery for cancer or certain heart surgeries for example, or elective (non-urgent). An elective operation can be delayed or cancelled without danger to the patient. It is not necessarily a minor or trivial operation, but the underlying medical problem does not jeopardize the patient's vital prognosis. In the context of PBM, total hip or knee replacements, for example, are elective operations and the PAC has time to correct preoperative anemia. If the operation is not

urgent, the patient is put on a "non-availability list". However, if the surgery is urgent, the patient's status is not changed. The PAC must act within the time available (whatever it may be) between the preoperative visit and the date of the operation. It should be remembered that even if the deadlines are short, a beneficial intervention is always possible.



This diagram describes, in broad strokes, the patient's journey from his or her encounter with the surgeon to the operation. Blue squares: usual trajectory where anemia and risk of bleeding are not considered. Red boxes: pathway through the preoperative anemia clinic. See text for details.

Based on the results of the initial laboratory tests, the PAC nurse orders additional laboratory tests and follows up on them. Depending on the results, several treatment options can be considered.

If we simplify a little, three scenarios are possible.

Scenario 1

The patient has "severe" anemia, which is immediately worrying, as his hemoglobin level is less than 100 g/L. The PAC physician is notified. He consults the results of the additional analyses, and the case is discussed with the PAC team. Anemia is a symptom; it is not a disease. It is therefore imperative to properly investigate and diagnose the pathology

responsible for anemia. Subsequently, the patient will be treated to correct the anemia before the operation.

Scenario 2

The patient has mild to moderate anemia. Various additional tests are requested, and the treatment will be administered as soon as possible at the CHUM's day care unit or in an outpatient clinic. In cases of inflammatory anemia, additional treatment with erythropoietin should be considered by the PAC physician.

Follow-up tests are requested 2-4 weeks after treatment. If the hemoglobin level has returned to normal, then the surgeon is notified, and the patient becomes "available" for the procedure again. Since the effectiveness of the treatment is temporary (4 to 8 weeks), the operation is planned as soon as possible.

Scenario 3

The patient is not anemic, but his iron stores are insufficient. Intravenous iron will be administered at the CHUM's day care unit or in an outpatient clinic. Once the patient has received IV iron, the procedure will be scheduled within two weeks.

For all scenarios, once the patient has been operated, the file is closed at the PAC. A letter is sent to the patient instructing him to contact his family doctor to follow up on his anemia. A similar letter is sent to the family physician, asking him or her to contact the patient to follow up on the anemia and ensure continuity of treatment.

Indeed, the PAC's intervention is a one-time intervention and only aims to correct the anemia before the operation. Long-term follow-up and final diagnosis should be done by the family physician or the physician who referred the patient to the surgeon.

Measures taken during the operation

We have put a lot of emphasis on the PAC because the clinic is being developed at the CHUM and is changing everyone's habits. But PBM is not limited to correcting preoperative anemia. It is a global approach that involves all hospital stakeholders and patients.

Therefore, during the operation, both the surgical team and the anesthesiology team contribute to the preservation of the patient's blood by minimizing blood loss.

During the procedure, the anesthesiologist should tailor the transfusion strategy to the clinical situation (slow, controlled bleeding or massive bleeding) to minimize exposure to blood transfusions to the extent possible. In all cases, the anesthesiologist aims to avoid transfusions that are not essential and contribute to increasing the risk of complications and mortality.

After the operation: what do we do?

After the procedure, the patient may or may not be anemic. If the patient is symptomatic of his or her anemia and these symptoms are potentially serious, blood transfusion should be considered, one unit at a time until symptomatology is controlled. If symptoms are less severe but affect the patient's quality of life, intravenous iron therapy, with or without erythropoietin, should be considered to correct the anemia as soon as possible.

The clinician must discuss the situation with the patient and ensure free and informed consent before prescribing a transfusion.

Conclusions

Unfortunately, it happens that we or a loved one requires a major operation at high risk of bleeding. Surgical techniques have made enormous progress in recent years and more and more operations are being performed using a minimally invasive approach. However, many procedures still involve large openings, such as in the chest or abdomen, and a significant risk of perioperative bleeding. It is in these circumstances that the principles of PBM must be applied.

Let us recall the main principles of PBM:

- Patient Blood Management is a patient-centered, systematic approach based on best practices. PBM aims to improve the outcome of patients by managing and conserving their own blood.
- Anemia and blood transfusions are independently associated with increased complications and mortality after surgery.
- Anemia must be diagnosed, investigated, and corrected before any major intervention with a high risk of bleeding.
- Anemia is a contraindication to a major elective (i.e., non-urgent) procedure at high risk of bleeding.
- Even if the operation is urgent, there is always a way to do something to correct the anemia before or after the surgery.
- Anemia is a symptom; it is not a disease. It is therefore necessary to find the cause and treat it appropriately.
- The PAC intervention is one-time and only aims to correct the anemia before the operation. The final diagnosis and long-term follow-up should be done by the family physician or the physician who referred the patient to the surgeon.
- Before, during and after the procedure, everything must be done to optimize the patient's blood mass and reduce perioperative blood loss, as if transfusions were not available.
- When a transfusion is necessary, it should be administered with the patient's free and informed consent in a judicious, gradual, and prudent manner. The clinician should

therefore seek to avoid non-essential transfusions that contribute to an increased risk of complications and mortality.

The management of preoperative anemia involves expenses, but these are more than offset by the reduced costs associated with transfusions, treatment of complications (during and after hospitalization) and prolonged length of stay; not to mention the dramatic consequences of death for the patient and his family.

Excellence is therefore the approach chosen by the CHUM. The implementation of a complete PBM program will be conducted in stages over the next few years. This program will be applied, progressively, to all major interventions with a high risk of bleeding, for the well-being of patients and for the overall improvement of the health system.

Helpful Resources

In French

Book « La Gestion Personnalisée du Sang - Visons l'excellence dans la qualité des soins - De la théorie à la pratique » par Jean-François Hardy, M.D.

Available free of charge at Bibliothèque et Archives nationales du Québec: http://collections.banq.qc.ca/ark:/52327/bs4365587

Handbook « La Gestion Personnalisée du Sang - Tous unis pour l'excellence des soins - Un manuel à l'intention du personnel soignant » par Jean-François Hardy, M.D.

Available free of charge at Bibliothèque et Archives nationales du Québec: http://collections.banq.qc.ca/ark:/52327/bs4366205

In English

Miscellaneous Internet links

Network for the advancement of patient blood management (NATA), European learned society, https://nataonline.com/

Society for the advancement of patient blood management (SABM), an American learned society, https://sabm.org/

International Foundation for Patient Blood Management (IFPBM), Swiss learned society, https://ifpbm.org/

About the Author

Dr. Hardy received his medical degree from the University of Montreal in 1974, practiced family medicine and subsequently obtained his specialty degree in anesthesiology in 1983. For more than 30 years, he taught in the Department of Anesthesiology at the University of Montreal. He was appointed Full Professor in 1998. He retired from the Université de Montréal in 2018 and was named Professor Emeritus in June 2019.

Since 1990, his main area of research has been focused on transfusion and strategies to reduce bleeding and transfusion use. In 2005, Dr. Hardy founded the " Chaire de médecine transfusionnelle Fondation Héma-Québec – Bayer de l'Université de Montréal " at the Université de Montréal, a chair he held until 2015.

Although he is retired from clinical practice and the University, Dr. Hardy actively participated in the implementation of Patient Blood Management at the CHUM until 2021. If the CHUM's pilot project proves to be a success, the PBM could be extended to all of Quebec in the future.