Basics of Blood Management
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Much has been done in blood management since the first edition. This is not only true for the many scientific studies that elevate blood management out of the low plains of experience-driven action into the realms of evidence-based medicine. Many of the things that blood managers over the decades have observed have now been proven in randomized clinical trials. Other things in blood management that may have been driven by tradition and belief have come into question. These developments contribute greatly to the maturation of this new specialty of blood management.

It is interesting, though, to note that the definition of blood management is still not accepted by all who claim to practice blood management. Some use the term blood management to efficiently distribute the ever more scarce resource of banked blood to those patients who are deemed to be in the greatest need. Others consider blood management as the outcome-oriented part of transfusion medicine that delivers allogeneic blood products in an evidence-based manner. Still others see blood management as a mix of transfusion medicine and hematology. And another group of medical practitioners consider blood management to be a religiously motivated restriction of modern medicine. However, blood management is none of these. At the core of blood management are two foci: one is the patient’s own blood as a precious, live-saving, and potentially finite resource; and the other is the patient’s outcome. To manage the patient’s resource “blood” skillfully to optimize his or her outcome is the philosophy that drives blood management.

Practically speaking, blood management is a multidisciplinary, multimodality concept that focuses on the patient by improving his/her outcome. Every medical specialty, from neonatology to geriatrics, from anesthesiology to urology, and including all clinical specialties as well as laboratory-based specialties such as diagnostic laboratory medicine, can contribute to a successful blood management program.

As in the first edition, the book introduces the reader to blood management and explains how to improve medical outcomes by avoiding undue blood loss, enhancing the patient’s own blood, and improving tolerance of anemia and coagulopathy until any of the underlying conditions are successfully remedied. While the first edition considered transfusion avoidance as a very important outcome improvement, the second edition shifts its focus from this aspect of improving outcomes to the even more important reduction of morbidity and mortality. This does not mean that transfusion avoidance is not a noble goal. But it means that–lacking good (scientific) reasons to transfuse–there is no point in trying to avoid something that has no proven value in itself. It should be self-evident that such non-proven therapies should be let go. Mounting evidence shows that the outcomes of patients treated by current principles of transfusion medicine are not superior to those obtained in transfusion-free environments, and that in some subgroups even the contrary might be the case. Therefore, it seems timely to advance patient care beyond this point and focus attention on interventions that have proven value in improving patient outcome. We therefore again invite you cordially to continue your efforts to improve your patient’s outcome by optimal blood management.

Petra Seeber and Aryeh Shander
March 2012
The benefit-to-risk ratio of blood products needs constant evaluation. Blood products, as therapeutic agents, have had the test of time but still lack the evidence we expect from other medicinals. Blood, an organ, is used as a pharmaceutical agent by the medical profession, due to the achievements in collection, processing, banking, and distribution. The fact that the most common risk of blood transfusion is blood delivery error supports the notion that blood must be handled as a pharmaceutical agent. Over the last few decades, the risk of blood transfusion and associated complications has raised concerns about the safety of blood by both the public and healthcare providers. At the same time, experience with patients refusing blood and data on blood conservation have brought to light the real possibility of other modalities to treat perisurgical anemia and to avoid it with blood conservation methods. In addition to risks and complications, data have become available that demonstrate the behavioral aspect of transfusion practice versus an evidence-based practice. In this book, we address many aspects of modern transfusion medicine, known blood conservation modalities, and new approaches to the treatment of perisurgical anemia, as well as special clinical considerations. This approach, now termed “blood management” by the Society for the Advancement of Blood Management (SABM, www.sabm.org), incorporates appropriate transfusion practice and blood conservation to deliver the lowest risk and highest benefit to the patient. In addition, it brings all these modalities to the patient’s bedside and above all is a patient-centered approach. Blood management is a multidisciplinary, multimodality concept that focuses on the patient. Patient outcome is improved, making this one of the most intriguing and rewarding fields in medicine.

Blood management requires an understanding of all elements of blood and transfusions. It includes the philosophy, biology, physiology, and ethical considerations, as well as demonstrating the practical application of various techniques. This publication introduces the reader to blood management and explains how to improve medical outcomes by avoiding undue blood loss, enhancing the patient’s own blood, and improving tolerance of anemia and coagulopathy until any of these underlying conditions are successfully remedied.

This introduction to blood management is intended for training and early practicing clinicians. It is meant to be both informative and practical, and spans many of the medical specialties that encounter blood and transfusions as part of their daily practice. It will aid in tailoring individual care plans for different patients. Finally, it addresses the structure and function of a blood management program, a novel approach to blood conservation, and improved patient outcome.

In this book, blood management is considered from an international perspective, so attention is paid to conditions encountered in developing as well as industrial countries. Techniques such as cell salvage are performed differently in economically deprived countries; HIV, hepatitis, and malaria may or may not be a threat to the blood supply, depending on geographical location; oxygen, intravenous fluids, and erythropoiesis-stimulating proteins may be readily available in some countries or inaccessible in others. The book is intended to broaden the readers’ horizons, discussing working conditions encountered by blood managers around the world. Many of the clinical scenarios and the exercises that follow are intended to allow the reader to adapt the information to the prevailing circumstances in their location.

This book is unique in the fact that it is the first dedicated in its entirety to the concept of blood management. The authors hope that this book will stimulate its readers to further advance blood management through shared experience and research. It is intended to be informative, practical, enjoyable, and hopefully will stimulate debate and discussion as well as help patients in need.

Petra Seeber and Aryeh Shander
March 2007
Blood management has evolved from humble beginnings into a viable, rapidly-developing medical specialty. Its development was initiated by the wish of Jehovah’s Witnesses for a transfusion-free treatment and has been shaped by influences coming from transfusion medicine and the military’s experiences. Blood management has today been introduced into mainstream medicine. The vivid history of blood management is described in this chapter.

Transfusion-free medicine and surgery: Since “bloodless medicine” is something of a misnomer, the term “transfusion-free medicine” was coined and is used instead.

Blood conservation: “Blood conservation is a global concept engulfing all possible strategies aimed at reducing patient’s exposure to allogeneic blood products” [1]. This concept does not exclude the use of allogeneic blood entirely.

Blood management: Blood management is the philosophy to improve patient outcomes by caring for and managing the patient’s own blood as a precious, life-saving resource. It is a patient-centered, multidisciplinary, multimodal, planned approach to patient care. Blood management is not an “alternative” to allogeneic transfusions; it is the standard of care.

Patient blood management: In order to clarify that blood management is not confused with an outcome-oriented transfusion therapy, the term “patient” is added, denoting that it is not the blood in the blood bank that is managed but the patient’s own blood that is taken good care of and managed in accord with the philosophy of blood management.
blood transfusion. The essence of bloodless medicine, and lately, blood management, however, is not restricted to the beliefs of a religious group. To get a better understanding as to what bloodless medicine and blood management mean, let us go back to the roots of these disciplines.

One is not completely wrong to attribute the origin of the term “bloodless medicine” to the endeavor of Jehovah’s Witnesses to receive treatment without resorting to donor blood transfusion. Their attitude toward the sanctity of blood greatly influences their view of blood transfusion. This was described as early as 1927 in their journal The Watchtower (December 15, 1927). Although the decision to refuse blood transfusion is a completely religious one, the Witnesses have frequently used scientific information about the side effects of donor blood transfusion to convince their physicians that their decision is a reasonable one and is corroborated by scientific evidence. The booklet entitled Blood, Medicine and the Law of God (published in 1961) explained the Witnesses’ religious stand, but also addressed issues such as transfusion reactions, transfusion-related syphilis, malaria, and hepatitis.

Refusing blood transfusions on religious grounds was not easy. Repeatedly, patients were physically forced to take donor blood, using such high-handed methods as incapacitation by court order, strapping patients to the bed (even with the help of police officers), and secretly adding sedatives to a patient’s infusion. In the early 1960s, representatives of Jehovah’s Witnesses started visiting physicians to explain the reasons why transfusions were refused by the Witness population. They often offered literature that dealt with techniques that were acceptable to Witness patients, informing physicians of the availability of so-called transfusion alternatives. In 1979 the governing body of the Jehovah’s Witnesses announced the formation of Hospital Liaison Committees (see Chapter 20). These continued to “support Jehovah’s Witnesses in their determination to prevent their being given blood transfusions, to clear away misunderstandings on the part of doctors and hospitals, to establish a more cooperative spirit between medical institutions and Witness patients (our italics)” and to “alert hospital staff to the fact that there are valid alternatives to the infusion of blood”. Occasionally, the Witnesses even went to court to fight for their rights as patients. In a great number of cases, the Witnesses’ position was upheld by the courts.

Although many physicians had difficulty with the concept of bloodless medicine, some took up the challenge to provide the best possible medical care without the use of blood transfusions. These were in fact the earliest blood managers. As their experience in performing “bloodless” surgery increased, more complex procedures, such as open heart surgery, orthopedic surgery, and cancer surgery, could be performed. Even children and newborns could successfully be treated without transfusing blood. Before long, these pioneering physicians published their results with Witness patients, thereby encouraging other doctors to adopt the methods used in performing such surgical interventions.

Among the first to rise to the challenge was the heart surgeon Denton Cooley of Texas. In the early 1960s, his team devised methods to treat Witness patients. He described the techniques in an article, “Open heart surgery in Jehovah’s Witnesses,” published in 1964 in The American Journal of Cardiology. In 1977, Cooley reported his experiences with more than 500 patients [2].

Cooley’s example was followed by many other courageous physicians. For instance, in 1970 Dr Pearce performed bloodless open heart surgery in New Orleans. His efforts did not go unnoticed. Newspapers reported on these spectacular cases. Perhaps out of curiosity or out of the earnest desire to learn, many colleagues visited Dr Pearce’s team in the operating room to learn how to do “bloodless hearts.” Jerome Kay, from Los Angeles, also performed bloodless heart surgery. In 1973 he reported that he was now performing bloodless heart surgery on the majority of his patients. The call for bloodless treatments spread around the whole world. Sharad Pandey, of the KEM Hospital in Mumbai, India, adopted bloodless techniques from Canada and tailored them to Indian conditions. Centers in Europe and the rest of the world started adopting these advances as well.

It is understandable that Witness patients preferred to be treated by physicians who had proven their willingness and ability to treat them without using donor blood. The good reputation of such physicians spread and so patients from far away were transferred to their facilities. This laid the foundation for organized “bloodless programs.” One of the hospitals with such a program was the Esperanza Intercommunity Hospital in Yorba Linda, California, where a high percentage of patients were Witnesses. Herk Hutchins, an experienced surgeon and a Witness himself, was known for his development of an iron-containing formula for blood-building. Among his team was the young surgeon Ron Lapin, who was later famed for his pioneering work in the area of bloodless therapies. Critics labeled him a quack. Nevertheless, he continued and was later honored for opening one of the first organized bloodless centers in the world, as well as for publishing.
the first journal on this topic, and for his efforts to teach his colleagues. During his career, he performed thousands of bloodless surgeries.

The pioneers of blood management had to rise to the challenge of using and refining available techniques, adjusting them to current needs, and individualizing patient care. They adopted new technologies as soon as was reasonable. Much attention was paid to details of patient care, thus improving the quality of the whole therapy. They also fought for patients’ rights and upheld those rights. Many involved in the field of blood management confirm the good feeling that comes from being a physician in the truest sense. There is no need to force a particular treatment. Such an attitude is a precious heritage from the pioneers of blood management. Now, at the beginning of the 21st century, this pioneering spirit can still be felt at some meetings dedicated to blood management.

Currently, strenuous efforts are being made to incorporate blood management further and deeper into mainstream medicine. This elicits various responses. Transfusionists, who are actually well suited to spearhead blood management, sometimes insist that their current realm of activity defines blood management. However, transfusion medicine so far is a discipline in itself and defines only certain aspects of blood management, such as cell salvage or the rare provision of specific, purified blood products, e.g., fibrinogen concentrates. Other aspects of blood management include surgical techniques, pharmacological hemostasis, diagnostic procedures, etc. At the core of blood management, however, is the patient’s own blood as a precious, life-saving commodity. To emphasize this further, recently the term blood management has been replaced by the term patient care, thus improving the quality of the whole therapy. Such an attitude is a precious heritage from the pioneers of blood management. Now, at the beginning of the 21st century, this pioneering spirit can still be felt at some meetings dedicated to blood management.

Military use of blood and blood management

Over the centuries, the armies of different nations have contributed to the development of current blood management, but not on religious grounds. Instead, the military made many crucial contributions to blood management by taking care of the thousands of wounded operated on before transfusions became feasible, thereby actually performing “bloodless surgery.” It was on the battlefield that hemorrhage was recognized as a cause of death. Therefore, it was imperative for military surgeons to stop hemorrhage promptly and effectively, and to avoid further blood loss. To achieve this, many techniques of bloodless medicine and blood management were invented. The experience of the early surgeons serving near the battlefield is applicable in today’s blood management schemes. William Steward Halsted, a surgeon on the battlefield, described uncontrolled hemorrhage [3] and later taught his trainees at Johns Hopkins the technique of gentle tissue handling, surgery that respects anatomy, and meticulous hemostasis (Halstedian principles). His excellent work provides the basis of the surgical contribution to a blood management program.

Since war brought a deluge of hemorrhaging victims, there was a need for a therapy. As soon as transfusions became practical, they were adopted by the military, but experience from the First and Second World Wars also showed their drawbacks, such as storage problems and transfusion-transmissible diseases. So, while the world wars propelled the development of transfusion medicine, they simultaneously spurred the development of alternative treatments. Intravenous fluids had been described in the earlier medical literature [4, 5], but the pressing need to replace lost blood and the difficulties involved in transfusions provided a strong impetus for military medicine to change its practice. In this connection, the following comment in the Providence Sunday Journal of May 17, 1953 is pertinent: “The Army will henceforth use dextran, a substance made from sugar, instead of blood plasma, for all requirements at home and overseas, it was learned last night. An authoritative Army medical source, who asked not to be quoted by name, said ‘a complete switchover’ to the plasma substitute has been put into effect, after ‘utterly convincing’ tests of dextran in continental and combat area hospitals during the last few months. This official said a major factor in the switchover to dextran was that use of plasma entails a ‘high risk’ of causing a disease known as serum hepatitis—a jaundice-like ailment. Not all plasma carries this hazard, he emphasized, but he added that dextran is entirely free of the hazard. ‘We have begun to fill all orders from domestic and overseas theaters with dextran instead of plasma.‘”

The military readily adopted other promising products in blood management. For example, the surgeon Gerald
Klebanoff, who served in the Vietnam War, introduced a device for autotransfusion in military hospitals. Another example is “artificial blood.” Efforts to develop a “blood substitute” were intensified by the US military in 1985, with major investments supporting research at either contract laboratories or military facilities [6]. The driving force for this was not the search for a plasma expander but the search for an oxygen carrier. A third example is the recombinant clotting factor VIIa. Although officially declared to be a product for use in hemophiliacs, the Israeli army discovered its potential to stop life-threatening hemorrhage and therefore used it in the treatment of injured soldiers.

After the attack on the World Trade Center in New York on September 11, 2001, physicians of the US military approached the Society for the Advancement of Blood Management for advice on blood management. Consequently, specialists in the field of blood management met with representatives of the US military, the result of which was an initiative named STORMACT® (Strategies to Reduce Military and Civilian Transfusion). The consensus of this initiative was a blood management concept to be used to treat victims of war and disaster as well as patients in a preclinical setting.

Recently, the military has spearheaded research in the management of massive bleeding and coagulopathy in polytraumatized patients. This research has addressed the immediate application of a tourniquet to a bleeding extremity and the use of hemostatic combat dressings. Military research is even challenging deeply entrenched mnemonics, changing the ABCDE algorithm for trauma care into cABCDE, highlighting the c for catastrophic bleeding as being even more important than airway management.

### Transfusion specialists support blood management

Interestingly, right from the beginning of transfusion medicine, the development of blood transfusion and transfusion alternatives was closely interwoven. “Alternatives” to transfusion are as old as transfusion itself.

The first historically documented transfusions in humans were performed in the 17th century and their aim was to cure mental disorders rather than the substitution of lost blood. However, the first transfusion specialists were in fact also the first to try infusions that were later called transfusion alternatives: it was reported that Christopher Wren was involved in the first transfusion experiments as well as being the first to inject asanguin-ous fluids, such as wine and beer. After two of Jean Baptiste Denise’s (a French transfusionist) transfused patients died, transfusion experiments were prohibited in many countries. Even the Pope condemned those early efforts and transfusions ceased for many years.

At the beginning of the 19th century, the physician James Blundell was looking for a method to prevent the death of women due to profuse hemorrhage related to childbirth. His excellent results with retransfusion of the women’s shed blood rekindled the interest of the medical community in transfusion medicine. Due to his work with autotransfusion, he was named in the list of the “fathers of modern transfusion medicine.” Other physicians followed his example, giving new impetus to transfusion medicine. However, in 1873 Jennings published a report of 243 transfusions in humans, of which almost half of the cases died [7]. Frustration around this situation led some researchers to look for alternative treatments in the event of hemorrhage. Barnes and Little suggested normal saline as a blood substitute [8] and this was introduced into medical practice. Hamlin tried milk infusions [9]. The use of gelatin was also experimented with. One of the advocates of normal saline, W.T. Bull, wrote in 1884 [10]: “The danger from loss of blood, even to two-thirds of its whole volume, lies in the disturbed relationship between the caliber of the vessels and the quantity of blood contained therein, and not in the diminished number of red blood corpuscles; and this danger concerns the volume of the injected fluids also, it being a matter of indifference whether they be albuminous or containing blood corpuscles or not.”

In the early 1900s, Landsteiner’s discovery of the blood groups was probably the event that propelled transfusion medicine to where it is today. Some 10–15 years later, when Reuben Ottenberg introduced routine typing of blood into clinical practice, the way was paved for blood transfusions. About that time, technical problems had been solved with new techniques and anticoagulation was in use. Russian physicians (Filatov, Depp, and Yudin) stored cadaver blood. The groundwork for the first blood bank was laid in 1934 in Chicago by Seed and Fantus [11], and as already mentioned, the wars of the first half of the 20th century brought about changes in transfusion medicine. Following the two world wars the medical community had a seemingly endless and safe stream of blood at their disposal. Adams and Lundy suggested that the threshold for transfusion should be a hemoglobin level of 10 mg/dL and a hematocrit of 30% [12]. For nearly four decades thereafter, physicians transfused to their
liking, convinced that the benefits of allogeneic transfusions outweighed their potential risks.

Over time reports about the transmission of blood-borne diseases increased. In 1962, when the famous article of J.G. Allen [13] again demonstrated a connection between transfusion and hepatitis, an era of increased awareness about transfusion-transmissible diseases began. However, the risk of hepatitis transmission did not concern the general medical community, and it became an acceptable complication of banked blood. It was not until the early 1980s that the medical community and the public became aware of a transfusion-transmissible acquired immunodeficiency syndrome, and the demand for safer blood and “bloodless medicine” increased. Other problems with allogeneic transfusions, such as immunosuppression, added to the concerns. Lessons learned from the work with the Jehovah’s Witnesses community were ready to be applied on a wider scale. In the United States, the National Institutes of Health launched a consensus conference on the proper use of blood. Adams and Lundy’s 10/30 rule was revised, and it was agreed that a hemoglobin level of 7 mg/dL would be a better transfusion threshold in otherwise healthy patients.

With time, the incentives for effective blood management changed. The immunomodulatory effects of allogeneic blood came to the fore and offered compelling reasons for carefully handling the patient’s own blood. The incremental increase of the costs of blood products is another compelling reason for blood management. Lastly, the experience with tens of thousands of patients treated successfully without allogeneic blood transfusions has led some physicians to see allogeneic transfusions having the same fate as the ancient blood-letting.

**Blood management today and tomorrow**

Currently, there are more than 100 organized bloodless programs in the United States. Many are transitioning to become blood management programs. This is not unique to the United States, since many more programs have been established worldwide. Most were formed as a result of the initiatives of Jehovah’s Witnesses, but a growing number now realize the benefits that all patients can receive from this care. The increasing number of patients asking for treatment without blood demonstrates a growing demand in this field. Concerns about the public health implications of transfusion-related hazards have led government institutions around the globe to encourage and support the establishment of these programs. Private and government initiatives have been taken so far that in 2011, the first state-wide blood management program was launched in Western Australia.

The growing interest in blood management is reflected by the activities described below. Major medical organizations (see Appendix B) now include blood management issues on the agenda of their regular meetings. Many transfusion textbooks and medical journals have incorporated the subject of blood management. A growing body of literature invites further investigation (see Appendix B). In addition, professional societies dedicated to furthering blood management have been founded throughout the world (see Appendix B). It is their common goal to provide a forum for the exchange of ideas and information among professionals engaged in the advancement and improvement of blood management in clinical practice and by educational and research initiatives. Clearly, from humble beginnings as an “outsider” specialty, blood management has evolved to be in the mainstream of medicine. It improves patient outcome, reduces costs, and brings satisfaction for the physician—a clear win–win situation. Blood management is plainly good medical practice.

What are the future trends in blood management? As long as there is a need for medical treatment, blood management will develop. Many new drugs and techniques are on the horizon. There are already many techniques available to reduce or eliminate the use of donor blood. It is the commitment to blood management that will change the way blood is used. The authors of this book hope that the information provided by its pages will be another piece in the puzzle that will eventually define future blood management by a new generation of physicians.

**Blood management as a program**

The organized approach to blood management is a program. These programs are named according to the emphasis each places on the different facets of blood management, such as bloodless programs, transfusion-free programs, blood conservation programs, or global blood management programs. Recently, some programs have been renamed “patient blood management programs.” No matter what a hospital calls its program, some basic features are common to all good quality programs, as described below. The step-by-step approach to the development of an organized blood management program is described in Chapter 19.