How do I get an emergency civilian walking blood bank running?

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The shift toward using a transfusion strategy in a ratio to mimic whole blood (WB) functionality has revitalized WB as a viable option to replace severe blood loss in civilian health care. A military-civilian collaboration has contributed to the reintroduction of WB at Haukeland University Hospital in Bergen, Norway. WB has logistical and hemostatic advantages in both the pre- and in-hospital settings where the goal is a perfectly timed balanced transfusion strategy. In this paper, we describe an event leading to activation of our emergency WB collection strategy for the first time. We evaluate the feasibility of our civilian walking blood bank (WBB) to cover the need of a massive amount of blood in an emergency situation. The challenges are discussed in relation to the different stages of the event with the recommendations for improvement in practice.

We conclude that the use of pre-screened donors as a WBB in a civilian setting is feasible. The WBB can provide platelet containing blood components for balanced blood resuscitation in a clinically relevant time frame.

The term walking blood bank (WBB) describes a setting where fresh WB is drawn from a pre-tested "walking" donor pool for immediate use in bleeding casualties. Typically, blood component therapy is either unavailable due to logistical reasons or the available blood components are not adequate to resuscitate the patients.[1] Fresh WB from WBBs has been used in military conflicts since World War I. From 1915, when Oswald Hope Robertson introduced citrate as an anticoagulant, until the end of the Vietnam War, cold-stored WB was the backbone of hemorrhagic shock resuscitation.[2]

The use of fresh and cold-stored WB in civilian care gradually declined from the early 1970s due to the widespread introduction of blood component therapy. In developed countries, WB was nearly abandoned after the HIV epidemic.[3] For decades, the shock resuscitation strategy combined packed red blood cells (pRBC) with excessive use of crystalloids and/or colloids. Current guidelines point to replacing severe blood loss with a balanced transfusion strategy using all three components in a ratio mimicking whole blood functionality.[4] The shift toward using a 1:1:1 blood component therapy has revitalized

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WB as a viable option in civilian health care.[5,6] WB offers logistical and hemostatic advantages both in pre- and in-hospital settings where the goal is a perfectly timed balanced transfusion strategy.[7] During events of depleted inventory or inadequate surgical hemostasis, both cold-stored WB and freshly drawn WB from a WBB are options.[8]

Haukeland University Hospital is a regional level 1 trauma center for the city of Bergen and western Norway and a national burn center, with approximately 900 beds, serving a population of 1.1 million and 5.3 million, respectively. The annual average pRBC usage is 22,000 blood units per year. Our average blood bank inventory is 8 units WB, >500 units pRBC, >600 units frozen plasma, >50 units freeze-dried plasma (FDP) and 30 (10–40) units of platelet concentrates. The hospital covers an area of 43,500 km^2 including fjords, mountains, and large areas with lack of ground transportation possibilities.

In 2010, we started a military-civilian collaboration between the Norwegian Naval Special Operation Commando and the Department of Immunology and Transfusion Medicine at Haukeland University Hospital. In collaboration, a research, training, and implementation program named Blood Far Forward, was established.[9] The goal was to implement WB and FDP as far forward as possible in military settings. In our civilian health care services, the collaboration resulted in a contingency plan for our hospital in case of a mass casualty event (MCE).[10] This includes the use of freshly drawn WB from established or pre-tested blood group O donors with a low titer of anti-A and anti-B (LTOWB). In our civilian helicopter emergency medical service (HEMS) we have progressively introduced advanced storage and deployment of FDP (2013), pRBC (2014), and LTOWB (2015),[11] followed by in-hospital use of cold-stored LTOWB (2017) for patients with massive bleeding.

In this paper, we describe an event in which our whole blood preparedness strategy was activated for the first time. We evaluate the feasibility of our civilian WBB to cover the need of a massive amount of blood in an emergency situation. The challenges are discussed in relation to the different stages of the event.

A critically injured young man was admitted to our hospital after a single-vehicle accident on an early Sunday morning. He was trapped in the deformed car for about 25 minutes before he was extricated. At HEMS arrival, he had insufficient respiration, weak carotid pulses, and a heart rate of 35–40 beats per minute. He was unconscious and unresponsive with no obvious signs of external injuries to the head. Trauma exam by HEMS-physician revealed clinical signs of pneumothorax, distended abdomen, open pelvic fracture, and fracture of the left femur. The progress of the patient throughout the care pathway is shown in Fig. 1.

Identification of hemorrhagic shock and the indication for prehospital transfusion

Based on the mechanism of injury and initial clinical examination, the patient was assessed to be in a severe hemorrhagic shock. Immediate transfusion was prioritized, and two units of LTOWB were started on-scene, with additional one unit of FDP and 1 g tranexamic acid during the 45 minute transfer to the hospital. He was intubated and received bilateral chest drains on-scene. The pelvis was stabilized with a sling and the femur repositioned.

Hemostatic control - the anaesthesiologist's and surgeon's perspective

On arrival, the core temperature was 35.0°C and lactate 14.8 mmol/L, indicating a significant risk of coagulopathy. TEG® (Hemonetics) on presentation showed a decreased maximum amplitude of 46.9 mm (RR 51–69 mm), otherwise within the reference range. Blood-based resuscitation was continued using the massive hemorrhage protocol.

In a bleeding trauma patient, hemostatic control is dependent on both mechanical hemostasis and the trauma-associated coagulopathy. The latter is a self-propagating cycle enhanced by the acidosis and hypothermia associated with hypo-perfusion, collectively termed the lethal triad of trauma. For this reason, patients in severe hemorrhagic shock often require rapid damage control surgery with a limited surgical intervention to control hemorrhage, contamination, and reduction of temperature loss. Patients are then stabilized in an intensive care unit until definitive surgery is possible.

The Blood Bank inventory of LTOWB was emptied early in the resuscitation phase, and the therapy was changed to component-based massive transfusion packages consisting of 6 units of pRBC, 6 units of plasma, and 2 platelet concentrates, see Fig. 1. *At hospital arrival, the patient was taken to the operating theater for damage control surgery. Emergency laparotomy was preformed, revealing bleeding in the mesentery of the small intestine which was sutured. Profound bleeding from multiple fractures in the pelvis could only partially be controlled with packing. The pelvic fracture was stabilized with a C-clamp and external fixation of the femur fractures was done. Visually the surgeon observed poor blood clotting with oozing from all bleeding sites. After surgery, the patient was transferred to the intensive care unit for warming and adjunctive supportive therapy.*

What should trigger the initiation of an emergency WBB?

The transfusion medicine physician on call (at home because of weekend work hours), was informed about a low platelet inventory and high blood consumption 3 hours and 35 minutes after the injury. On the understanding that all available resources were being activated to save the patient's life, she initiated the emergency WBB to cover the patient's need. The WBB initiation was based on multiple factors. We had a traumatized patient in hemorrhagic shock needing ongoing hemostatic resuscitation. WB is, in our opinion, the ideal product to cover this need.[7] As both our LTOWB and platelet inventory were running low, drawing fresh WB from a pre-prepared walking donor pool was considered the fastest way

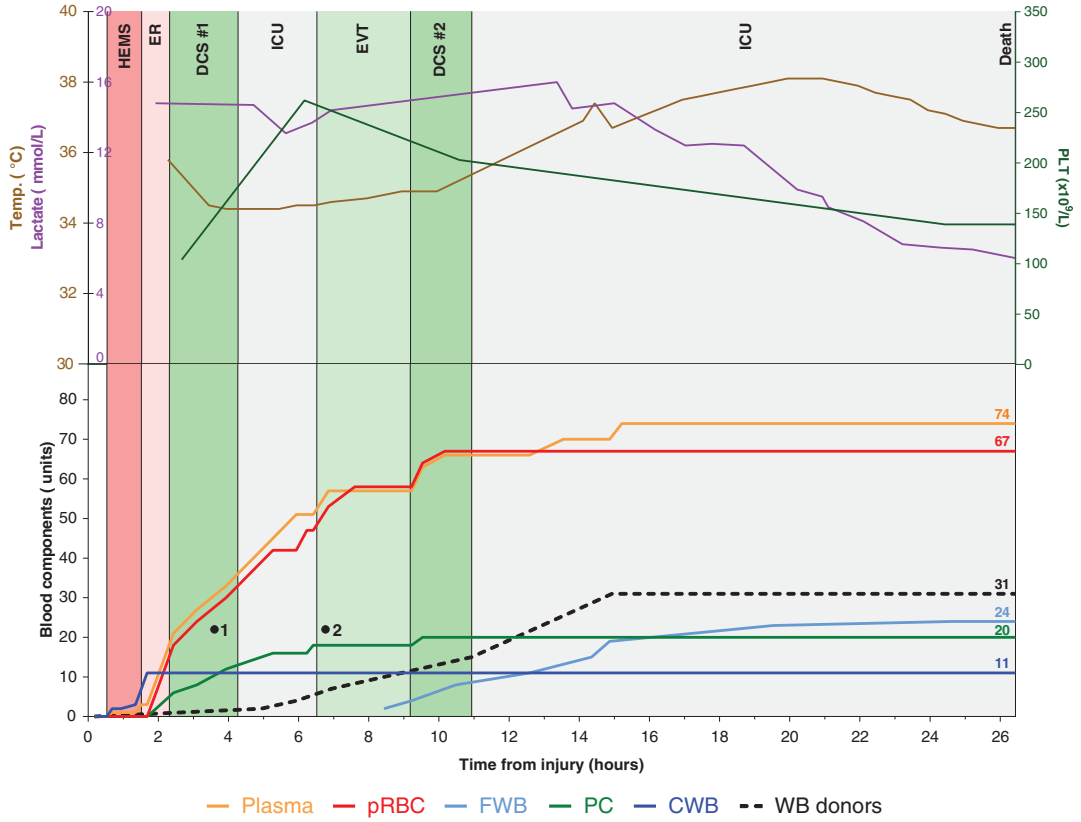

Fig. 1. Illustration of the patient's consumption of blood products and laboratory results in the different stages of treatment. Stages of treatment: HEMS = helicopter emergency medical service. ER = emergency room. DCS = damage control surgery. EVT = endovascular treatment. ICU = intensive care unit. Blood products: pRBC = packed red cells. FWB = fresh whole blood. PL = platelets. CWB = cold-stored whole blood. Highlighted points: •1 = walking blood bank initiation. •2 = first unit of fresh WB ready.

to make a platelet-containing blood product available for immediate use. Alternatively, we could have ordered platelet concentrates from other blood banks. However, the transport time from the nearest blood banks with adequate stores of platelet concentrates is at least 5 hours by road. Transport of blood products by HEMS would shorten the transport time to 1 and 2 hours from our closest larger blood banks in Stavanger and Oslo, respectively, see Fig. 2. However, the availability of HEMS is unpredictable for this kind of assignment and this approach might lead to platelet shortage in these Blood Banks as well.

Estimate the need of blood products

The high consumption of blood products in a short period of time and the uncontrolled bleeding indicated a further need for transfusion support. Our goal in the Blood Bank is to intervene at the right time to maintain a sufficient amount of blood products in storage and provide optimal blood transfusion therapy for each patient. We started by drawing WB from 10 donors and subsequently conducted 3 platelet apheresis procedures. This number was based on clinical evaluation of the patient, blood consumption up to this point, and to cover the further surgical intervention to stop the bleeding. Retrospectively, we could have drawn from more donors at this point. The key point is, however, to be prepared for ongoing changes in the patient's needs. Frequent communication between the transfusion medicine physician and the anaesthesiologists was crucial to coordinate blood bank activity.

To get resources quickly on a weekend

It is crucial to have donors available close to the donation site for quick recruitment whenever fresh WB is needed. As our Blood Bank was opened on a Sunday, the first donors (contacted by telephone) were ready to answer the questionnaire 1 hour and 20 minutes after WBB initiation. This quick response was possible because the person responsible for recruitment of blood donors invited two family members, already established blood donors, to donate WB immediately.

Having sufficient blood donors titrated for anti-A and anti-B

Only donors considered to have a low titer of anti-A and anti-B on a previous donation are included in our WBB. We have defined the low titer cut off for IgM to be 250 and

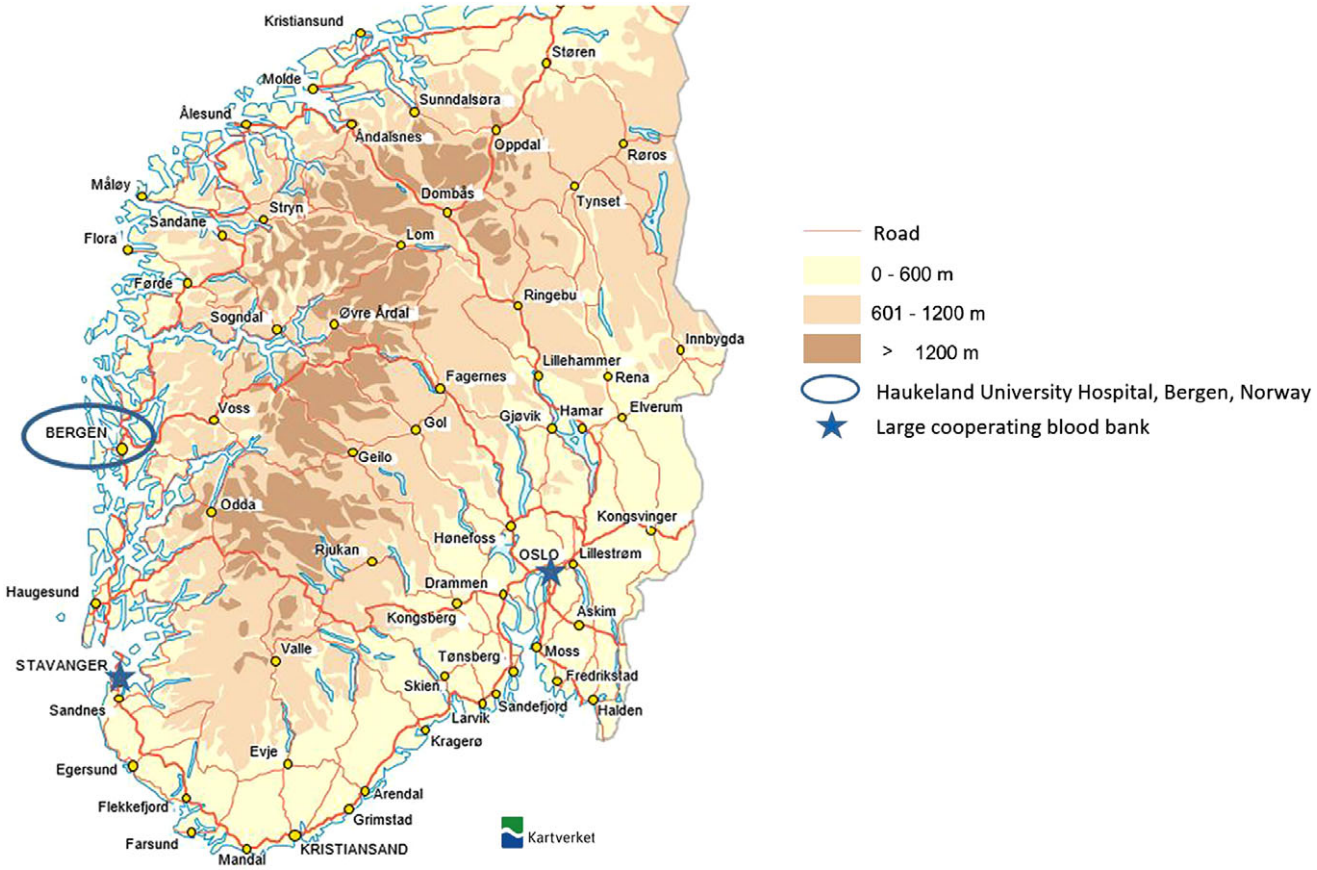

Fig. 2. Map illustrating geographical conditions around Bergen (pop. 300,000), the second largest city in Norway (pop 5.3 mil) and distance to the closest cooperating large blood banks.

IgG to be 500 using a gelcard-based analysis. As anti-A and anti-B titers show minimal variation over time,[12] our standard is to repeat titration of donors after pregnancy, vaccination, or transfusion. Among our group-O WB donors (active-last-2 years), 72% are titrated, and of them, 79% are classified "low titer donors."

Production of whole blood - need to save time?

Our emergency strategy goal is to have LTOWB available within a period of 1–4 hours depending on time of day/weekday. For WB production, we use the IMUFLEX® wb-sp blood bag system with integral WB leukocyte reduction filter with diversion blood sampling arm® cpd/optisol® solution (Terumo). After a 2-hour rest at room temperature the WB is filtered according to manufacturer's instructions. The filtration step takes 40 minutes. Importantly, 80–90% of platelets go through the filter yielding a platelet-containing WB product.

Our WB products meet all Norwegian quality requirements, and neither omitting the 2-hour benchtop resting time nor the leukocyte filtration will infringe on this. Omitting filtration will however significantly reduce the production time.[13] Although universal leukocyte reduction is required in Norway, the filtration step may be omitted following a risk assessment. The decision as to whether or not to filter has to be made before donation, as only our WB collection bag without a filter has ports to be spiked for direct transfusion. For fresh WB, irradiation is desirable,[14,15] but this is dependent on the degree of emergency. Cold-stored WB is not irradiated in our hospital. However, for our patient, the fresh WB was filtered and irradiated. The first unit was ready 3 hours and 10 minutes after activation of the WBB. The next two units were ready after 4 hours and 5 minutes. If the resting time, leukocyte filtration, and irradiation were omitted, the time from donation to release of WB could be reduced to 55 minutes including routine virus testing, which would be the time-determining factor. We omitted the resting period for the first 4 units of fresh WB. Unfortunately, virus serology (HIV, Hepatitis B, and hepatitis C) was unavailable due to technical problems at our microbiology facility. After waiting for results of viral serology in 1 hour and 40 minutes, we decided to transfuse the non-virus tested WB on a vital indication because these were established donors and the risk of infection is low. The risk of seroconversion in our national regular donor pool in the previous 3 years is 1:100,000 for hepatitis B and hepatitis

C in total and none for HIV. Based on the patient risk of exsanguination compared to the risk of transfusion transmitted infections, we found this justifiable.[16] The virus testing was performed later the same day, and all tests results were negative. Based on our experiences, appropriately selected rapid virus testing could be considered as a resilience measure in scenarios like this.

Running out of platelets while waiting for WB

While collecting and preparing fresh WB from our emergency WBB, the patient was supplied with blood components in a 1:1:1 ratio. From WBB initiation until the WB was ready, 58 pRBC, 54 units of plasma, and 18 platelet concentrates (with mean platelet count per bag >200 x 10∧9/L) were transfused. Simultaneously, the Blood Bank had several requests for platelet concentrates for other patients needing transfusion due to hypoproliferative thrombocytopenia. We were facing a rapid-falling platelet inventory, falling to only two units of platelets. We conducted a second blood donor session. During the next hours, we performed 20 emergency WB collections and 5 platelet apheresis collections, yielding a total of 10 platelet concentrates. Retrospectively, we should have recruited more apheresis platelet donors earlier to reduce the risk of total depletion of platelet inventory.

Transfusion logistics

The logistics of physically transfusing massive transfusions is a demanding task. The use of WB delivered a 57% reduction in number of units transfused (6 pRBC: 6 plasma: 2 platelets versus 6 units WB) and represents a perfectly balanced transfusion as all 3 components enters the patients circulation simultaneously. For our patient, at least two nurses were needed continuously to administer the transfusions, and at least one physician to prescribe the next units, trying to keep a balanced ratio. Unfortunately, our IT systems lack functionality to keep a real-time overview of the inventory at the Blood Bank and the balance in transfused products for the patient. We solved this problem with handwritten notes and manually counting our inventory.

Six hours after the injury, our patient was still hypovolemic, indicating active bleeding. He required continuous transfusion of blood products. A bleeding from the distal internal iliac artery was angiographically revealed, and endovascularly plugged. One leg was getting ischemic with a clinical compartment syndrome. The abdomen was getting distended and leaking fluids through the midline incision. A second surgical intervention revealed ongoing bleeding from the pelvis, which was packed again, and a fasciotomy of the leg was performed. No further surgery was considered possible because of several sources of bleeding in the fractured pelvis.

Preserving body temperature

Preserving body temperature is difficult in the exsanguinated trauma victim. Fluid warming systems are not permitted during helicopter transport due to flight regulations in Norway. Therefore LTOWB was transfused at 4°C prior to arrival at the hospital. To preserve the patient's temperature, the room temperature was increased, and warming blankets were used. LTOWB, pRBC, and plasma were transfused using pneumatic pressure bags through blood warmers. Despite this, the temperature of the patient dropped to 34.5°C at the lowest during the first surgery, slowly increasing to normal during the next hours. Using fresh room-temperature WB contributed positively to maintain an adequate body temperature.

Around midnight, approximately 18 hours after the injury, the situation seemed irreversible. Blood pressure was still too low, the lactate levels remained high, there was no urine production, and the patient was still bleeding. As the decision to de-escalate treatment efforts was made, the situation suddenly changed. The blood pressure increased, lactate levels dropped to 5–6 mmol/L, and transfusion requirements fell. The decision to continue resuscitation was reconsidered. Continuous renal replacement therapy was initiated mainly because of increasing serum-potassium. During the next 8 hours, only 5 units of WB were given, and he was considered more clinically stable.

Early next morning, however, the blood pressure suddenly dropped, and the patient had a sudden cardiac arrest (asystole). Cardiopulmonary resuscitation was provided for a short period of time, but considered futile and withdrawn. The patient died in the intensive care unit 27 hours after the injury.

Replacing the inventory after the incident

After one patient using 35 units of WB, 67 units pRBC, 74 units of plasma, and 20 units of platelets in about 24 hours on a Sunday, our inventory was rather scarce on Monday morning. Operating at normal capacity, hospital requests for blood products were undiminished, but could be met. In order to replace our inventory after the incident we needed to increase the number of donors coming for the following weeks and our inventory level was back to normal after 17 days.

DISCUSSION

After the event, we reviewed the activation process of the WBB. The main lesson identified highlighted the importance of close interaction between the clinicians and the transfusion medicine physician on call. The overall management of this event was considered satisfactory and in accordance with our pre-planned procedures for initiation of a WBB. Upscaling of effort was considered possible if the number of casualties involved had been higher. The time to achieve shock reversal and hemostasis has impact on mortality. Treatment including transfusion, should not be delayed.

The recruitment of donors takes time and must be initiated as early as possible. Recruitment of blood donors from health personnel working in our hospital is encouraged, as they are more readily available. Donors should be pre-tested with titration of all group-O donors to reduce the response time.

The short storage time of 7 days for platelet concentrates is a major obstacle for having a sufficient inventory without a high discard rate. Thus, options for longer storage as well as other platelet sources preserving hemostatic function are needed. Presently, clinical studies to explore the ability of cold-stored platelets to control bleeding in cardiothoracic surgery are being conducted in our hospital.[17] Cold storage of platelet concentrates might allow storage with preserved hemostatic function for 14–21 days. Otherwise, Thrombosomes® (Cellphire), which are lyophilized platelet fragments, are under clinical evaluation and might serve as a viable option together with cryopreserved platelets.[18–23]

The presented case illustrates that even a Norwegian level 1 trauma center with the second-largest integrated blood center in Norway, can be forced to trigger the mass casualty preparedness plan due to one single trauma patient. Transfusion of about 200 units of blood products in a short period of time is challenging when it comes to administration, and to keep record of the ratio between red cells, plasma, and platelets. By using WB, the number of blood products needed to maintain a balanced transfusion simplified the delivery process both for the clinicians and the Blood Bank. Importantly, fresh WB (at room temperature by the time of transfusion), contributes significantly to avoid hypothermia.

Neither National nor European transfusion guidelines determine the minimum requirements for the safety acceptable for MCE when the blood inventory is running low or platelets are unavailable. This case raises a number of questions: What do we do if virus testing cannot be performed? Do we have time to do leukocyte filtration of our WB? Should irradiation be performed on the fresh WB? Basically, the main response is: "What is acceptable risk" in scenarios where immediate balanced transfusion is considered lifesaving?

Norway has a decentralized hospital system with local hospital-based blood banks ensuring proximity to qualified emergency care. Many of our smaller hospitals, however, have a limited inventory of blood components, especially platelets. Even hospitals dedicated to have damage control surgery and resuscitation capability do not have platelets in stock at all. The supply is planned to be airborne or by ground transportation from the nearest blood bank. In our opinion, hospitals having damage control resuscitation capability should have immediate access to platelets in some form.

Norwegian trauma and transfusion guidelines recommend early balanced blood transfusion in life-threatening bleeding.[24,25] A robust physician-staffed HEMS available 24/7/365 has been developed for primary emergency care with a goal that 90% of the population can be reached within 45 minutes.[26] Even though the goal is to have all massive bleeding patients transported to a level 1 trauma center, delaying factors like weather conditions, road blocks due to avalanches, or air space lockdown represent possible challenges.

Further development of robust contingency plans for all hospitals at risk of exhaustion of the blood supply need to be considered. The advantage of the Norwegian hospital-based Blood Bank system is that blood collection facilities exist, with few exceptions, in every hospital. By use of an emergency plan to collect fresh WB from local blood donors, an early balanced hemostatic resuscitation also can be maintained in remote local hospitals. In this case, untested blood was transfused. Even though this was performed after risk analysis, this is an unwanted situation. Thus, there is a need to develop and implement a rapid testing back-up system for use in critical situations.

In our opinion, fresh WB from a WBB is the most feasible solution for the emergency supply of platelets in massive bleedings. Changes in the national regulations need to be considered to allow contingency plans including use of fresh WB in civilian and military emergencies.

CONCLUSION

We conclude that a preplanned WBB using established group-O low-titer donors in a civilian setting is feasible. A prerequisite is that a sufficient number of eligible group-O low-titer donors should be available in the donor pool and available to donate in a timely fashion. The manufacturing response time is dependent on a number of process variables which can be modified after risk assessment. Close communication and coordination between the blood bank and the clinical ward is paramount for success.

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CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

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