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'2025
«European Science»
Book 38. Part 3

SWorld
Germany

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INTELLEKTUELLES KAPITAL - DIE GRUNDLAGE FÜR INNOVATIVE ENTWICKLUNG

WIRTSCHAFTSWISSENSCHAFTEN, MANAGEMENT UND MARKETING, PÄDAGOGIK, PHILOLOGIE, RECHTS- UND POLITIKWISSENSCHAFTEN, GESCHICHTE, KUNSTGESCHICHTE, MEDIZIN

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Monographic series «European Science»
Book 38. Part 3.

In internationalen wissenschaftlich-geometrischen Datenbanken enthalten
Included in International scientometric databases

MONOGRAPHIE

MONOGRAPH

ScientificWorld-NetAkhatAV
Karlsruhe 2025

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Intellectual capital is the foundation of innovative development: Economics, Management and Marketing, Education, Philology, Legal and Political Sciences, History, Art History, Medicine. Monographic series «European Science». Book 38. Part 3. 2025.

ISBN 978-3-98924-084-1

DOI: 10.30890/2709-2313.2025-38-03

Published by:

ScientificWorld-NetAkhatAV
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KAPITEL 12 / *CHAPTER 12* [59]
GLOBAL AND NATIONAL EXPERIENCE OF RESUSCITATION USING FRESH WHOLE BLOOD IN MODERN MEDICINE: ANALYSIS AND PROSPECTS

DOI: 10.30890/2709-2313.2025-38-03-006

Relevance of the study

Resuscitation for hemorrhagic shock caused by critical bleeding remains one of the main areas of military medicine because massive bleeding remains one of the greatest threats to life among servicemen on the battlefield and civilians. Statistics show that 54.0%-81.0% of deaths are associated with hypovolaemic shock of the 3rd and 4th degree as a result of massive traumatic injuries from various types of modern weapons, which currently tend to have greater consequences for both military personnel and civilians. Military data from recent military conflicts underlines the importance of improving and implementing effective modern strategies for transfusion of blood and its components at the pre-hospital (stabilisation point) and hospital stages, which is a key task to increase the survival rate among injured servicemen and women. Recent studies have shown an increased survival rate of servicemen with traumatic haemorrhagic shock within 24 hours and up to one month by 13.0% who received whole blood transfusion (hereinafter - WB) compared to patients who received component therapy (hereinafter - CT) with similar severity of injury [26,33].

The analysis of data on patients with haemorrhagic shock who had a higher injury severity score on admission (ISS: 27 vs. 20; blood pressure 103 to 114; higher lactate level 4.2 vs. 3.5) who received whole blood transfusion showed a 4-fold increase in survival with a 60.0% reduction in total transfusions and a lower rate of complications (occurrence of sepsis) [14].

In recent years, and especially during military conflicts, WB resuscitation with a low group O blood titer has become commonplace in both the military and civilian

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Number of characters: *91705*
Author's sheets: *2,29*

population, which are also not protected from bombardment by modern weapons (missiles, chess pieces, drones) and may represent an ideal resuscitation intervention. According to researchers, in patients with an increased likelihood of mortality at the prehospital stage, transfusion of whole blood with a low group O titer has been shown to be safer and more effective than resuscitation of blood components: up to 48.0% reduction in 4-hour mortality, up to 30.0% reduction in 28 days after injury [64].

At the time of the full-scale war in Ukraine, the relevance of WB resuscitation is of particular importance as an ideal transfusion medium for the treatment of military personnel and civilians with severe injuries, critical bleeding accompanied by severe haemorrhagic shock. Blood transfusion is critical for providing emergency care at the pre-hospital stage ('stabilisation point'), performing surgeries and stabilising the condition of the injured. Ensuring the collection, processing, transportation, storage and safe and effective WBT is now essential in the event of massive sanitary losses.

The aim of the study is to conduct a retrospective analysis of the scientific literature on the experience of using WB and its effectiveness in comparison with CT in military personnel and civilians during modern military conflicts at various severe degrees of trauma with hypovolemic shock, taking into account the time from injury to the start of blood transfusion and to study the benefits of administering red blood cells (RBCs), plasma (fresh frozen plasma (FFP), platelet (PT) components; in different degrees of hypovolaemic shock due to traumatic injuries during the hostilities in Ukraine, taking into account the time from injury to the start of blood transfusion according to two Role 2 surgical stabilisation points and one Role 3 military hospital.

Materials and methods:

A retrospective review of 120 Ukrainian and foreign scientific papers was conducted using PubMed and Google Scholar databases. After reviewing the articles and reading their full texts, 81 sources were selected on the use of WB and CT for various degrees of severity of injury and haemorrhagic shock during military conflicts. The depth of the search was for the period 2000-2024. The study was conducted on the basis of two surgical stabilisation points (Role 1) in the most active area of combat operations and a military hospital (Role 2) in January 2024. The study used

bibliosemantic, system analysis, and statistical methods.

Key words: whole blood, erythrocytic, plasma, platelet components, resuscitation, massive bleeding, wartime traumatic injuries.

12.1. Historical aspects of transfusion of whole blood and its components in medical practice

12.1.1. Hemotransfusion: from the first attempts to scientific basis.

Blood transfusion has been practiced throughout human history from Egyptian antiquity to ancient Rome to the modern era of haematology [42]. Mentions of the first attempts at blood transfusion date back to the seventeenth century. In 1665, Richard Lower, while researching potential methods of treating bleeding, conducted an experiment on blood transfusion between dogs (from the carotid artery to the jugular vein), thus initiating the study of blood as a therapeutic agent. In 1667, Jean Denis successfully performed a xenotransfusion of animal (sheep) blood to a 15-year-old boy [8].

Later, in the XIX century, the first successful human blood transfusion took place due to James Blundell. Observing the high mortality rate of women in labour due to postpartum haemorrhage, he concluded that blood transfusion should be used at least in critical situations. Based on the results of animal experiments, in 1829, Blundell J. successfully performed the first documented blood transfusion to a woman with severe postpartum haemorrhage, using 120 ml of blood from a male donor. The scientist was the first to transfuse blood from person to person and demonstrated the value of this method in bleeding [8].

Approximately three decades after Blundell J.'s successful experiments, during the US Civil War (1861-1865), surgeons Fryer and Bentley used whole blood transfusion (WB) in clinical practice, reporting two successful cases [40]. In both situations, blood transfusion was considered as a last resort to save the lives of patients with combat sepsis and amputation, and small volumes of blood were used. Despite

the fact that Blundell demonstrated the possibility of successful use of WB, this procedure remained experimental in wartime and was characterised by unstable results [24].

After the identification of interspecies haemolysis by Landois in 1875, Karl Landsteiner initiated a series of studies to determine the compatibility of human blood. In 1900, he made a fundamental discovery by describing the existence of three blood types, which he designated as A, B and C. Further research by his students Stürli and Decastello in 1902 led to the identification of a fourth blood type, which led to the formation of the modern ABO blood group classification system. The discovery of ABO blood groups by Karl Landsteiner and his students was fundamental to the development of transfusiology and ensured the safe administration of blood transfusions [60]. This allowed Ottenberg to introduce a new procedure in 1907 - cross-checking for blood compatibility before transfusion, which significantly reduced the risk of complications [6].

Until the early 20th century, blood transfusion techniques involved surgically opening the vessels of the donor and recipient and then connecting them. A variety of devices were used for this purpose, ranging from primitive ones such as a goose feather to more complex ones such as surgically joining an artery and a vein. The latter method, known as the primary end-to-end anastomosis, was first described by Alexis Carrel in 1908 [22]. In 1909, George Crile modified the existing technique by introducing a metal cannula to connect the vein to the artery. Despite the functionality of this method, it was characterised by the transfusion of an undetermined volume of whole blood, an increased risk of vascular damage in both patients, and the need for ligation of the artery and vein after the transfusion. At the same time, advances in the processing of natural polymers have led to the creation of durable, easily cleaned and reusable tubing, which has eliminated the need for a vascular anastomosis [20].

The introduction of the heated autoclave, developed by Chamberland, Pasteur, Koch in the late 19th century, was a significant advance in the practice of sterilising surgical instruments. This invention helped to transform complex surgical procedures into safe and effective ones, in particular, through the use of a skin needle. Provision

of aseptic conditions, achieved through the use of an autoclave, created the prerequisites for the development of aseptic blood transfusion [52].

One of the key problems limiting the use of blood transfusion was the lack of effective anticoagulation and logistical difficulties associated with the need for direct and simultaneous contact between donor and recipient. However, studies conducted by Douglass and Boycott in 1909 on a rabbit model demonstrated that the addition of citrate to phlebotomised blood promotes its preservation and enables safe delayed transfusion.

In the period 1914-1915, independent studies conducted by Agote, Hustin, Lewisohn and Weil were aimed at developing methods of citrating whole blood before transfusion. Lewisohn's method was particularly widespread, involving the addition of 30 ml of 2% citrate solution to 300 ml of blood, which provided the possibility of storage and delayed transfusion of CSF. However, along with the anticoagulant properties of citrate, there was a need to provide an energy substrate to maintain the viability of red blood cells (RBCs) for a long time. In 1916, virologist Peyton Rous discovered that the addition of glucose to citrate solution (Rous-Turner solution) helps to preserve the structural integrity of blood cells for about 1 month. These achievements in blood grouping, antisepsis and preservation created the necessary prerequisites for the further development of massive blood transfusion methods [50].

The discovery of the Rh factor in 1940 by Landsteiner and Wiener was another important step in transfusion safety. During the second half of the twentieth century, significant progress was made in the development of component therapy [60]. Hess J.R. and Thomas M.J. (2003) argued that the development of anticoagulants, preservatives and specialised containers for blood storage made it possible to separate blood into separate components for use in clinical practice. At the same time, methods of testing donated blood for infectious diseases were being improved, which contributed to the safety of haemotransfusions. Despite the difficulties and obstacles, thanks to many years of research and the efforts of scientists and medical professionals, blood transfusion is now a standard procedure that plays a crucial role in saving the lives of many people [32].

12.1.2. Transformation of whole blood transfusion methods from the First World War to the current day

The First World War (1914-1918) was a catalyst for the development of mass medical care for victims of traumatic shock, including large-scale blood transfusions. Despite the fact that experimental studies on healthy humans and animals helped to substantiate the theoretical aspects of this method, the large number of severely wounded soldiers in need of help posed a challenge to scientists to improve the practice of blood transfusion to save lives.

At the beginning of the twentieth century, before and during the First World War, methods of using whole blood and its components, in especially plasma, to restore fluid volume in the body were actively researched. An important step in the development of transfusiology was the discovery of the Er isoagglutinins by Karl Landsteiner in 1900, which allowed for the identification of blood groups and cross-compatibility [60]. Due to the development of blood preservation methods, such as the use of citrate and the AB0 blood grouping system, whole blood transfusion became an important component of medical care for the wounded during the First World War.

The main problem during the transfusion was rapid blood clotting. After being collected from the donor into the collection syringe, whole blood activates the clotting cascade, which leads to the clumping of cells and platelets. This blocked the passability of the needle and cannula, making further collection or transfusion impossible. In 1914 and 1915, researchers Archibald E. and Pelis K. independently concluded that sodium citrate added to blood prevents it from clotting and does not harm the patient. Edward Archibald argues that sodium citrate is particularly suitable for safe use in the military, as it is an effective anticoagulant that prolongs the time between donation and administration [6, 54].

Canadian surgeons who served in the Canadian Army Medical Corps during the First World War were responsible for introducing blood transfusion in the treatment of military wounded in the British army [55]. In 1916, Lawrence Bruce Robertson introduced a new blood transfusion technique using a syringe-cannula for direct transfusion from donor to patient, which saved the lives of many wounded [65].

Shortly after Landsteiner's discovery, British researchers proposed using colloidal solutions based on humiarabic and acacia gum to replace blood. In 1916, Bayliss published a report on the successful use of a 6.0% humiarabic solution to treat blood loss in military personnel during World War I. This moment became a key one in the ongoing debate on the use of colloidal and crystalloid solutions in transfusion therapy [69]. Subsequently, blood plasma became the preferred choice for colloidal infusions, replacing 6.0% humiarabic solution. However, Imm A. argued that the use of plasma was also accompanied by limited access to sufficient supplies, the need to use an effective preservative solution, and the provision of proper storage conditions, including refrigeration [36].

Researcher Robertson (1918) founded the first WB storage bank and noted the problem of ensuring a sufficient volume of donor blood in wartime, which led to a limitation in the number of possible transfusions. One of the main problems of doctors in hospitals near the combat zone was the availability of whole blood for transfusion; other patients became a walking blood bank of donors, as coagulation made it impossible to create a stock of whole blood in reserve. Robertson showed that blood could be collected in advance, treated with sodium citrate, and then stored under sterile conditions at low temperatures until needed. Blood that tested negative for syphilis could be transfused quickly and safely in frontline medical units.

In order to solve this problem, Robertson proposed to use a container of considerable volume - the so-called “Winchester bottle” with a capacity of 2 liters. In this container, he added 0.5 liters of whole blood to a preservative solution developed by Rous and Turner (850 ml of 5.4% dextrose solution and 350 ml of 3.8% citrate solution) [50]. It took 4-5 days to achieve optimal hematocrit sedimentation. After that, the supernatant plasma with a high concentration of citrate was removed, and the red blood cell precipitate was restored to a volume of 1 liter using saline. On average, each recipient received from 500 ml to 1 liter of blood obtained from donors. Of all the patients, 55.0% were successfully evacuated from the battlefield, while 40.0% died as a result of gangrene. No hemolytic reactions were observed after the blood transfusion. According to Robertson, the storage time of the collected blood was about 1 month

[58].

Despite significant advances in blood transfusion, wartime transfusion practices required further improvement. In the "Winchester bottle", the only component suitable for use was reconstituted Er (0.8 - 0.9 liters), which could be transfused only after a 5-day storage period at 1-3°C. In this regard, Rous P. (1918) identified an urgent need to replace Er transfusions in case of bleeding. Furthermore, he concluded that, although transfusion of Er may be desirable, it is not necessary to supply blood cells in normal cases of acute bleeding. Rous P.'s rationale was based on a controlled bleeding model in rabbits in which 25.0% to 50.0% of their blood volume was phlebotomized. He demonstrated that the animal would survive as long as it was replaced with plasma with the return of normal blood pressure [59].

Blalock A. conducted a profound study on the importance of fluid volume and its impact on survival, becoming one of the first to emphasize the role of plasma in resuscitation. In his work on hypovolemic shock, he provided convincing evidence that hypovolemia (decreased circulating blood volume (CBV)) is the main cause of death. At the same time, relative hypovolemia caused by neurogenic vasodilation and mediator-induced vasodilation (vasogenic shock) were identified as less common causes of death. In addition, in 1930, Blalock A. experimentally proved that severe injury is accompanied by the loss of extracellular fluid, which, once in the interstitial space, becomes inaccessible to the intravascular volume. The author notes that significant fluid loss leads to impaired systemic hemodynamics and, as a result, to the development of circulatory failure [11].

The clinical demonstration of the efficacy of whole blood, as well as the safety and ease of use of blood products, has led to the widespread use and acceptance of blood transfusion during military conflicts.

12.1.3. Experience of using whole blood and blood components in World War II

After a short between-war period until 1939, the world was again involved in military conflicts in different countries. Rapid and portable transfusion became even more important as the mechanisms of warfare changed, weapons became more

sophisticated, and the consequences of combat injuries became more complicated. At the beginning of the Second World War (1939-1945), the British Royal Military Medical Service used whole blood; the US military decided to focus on lyophilized plasma and albumin to resuscitate wounded with massive bleeding [29].

In 1937, the American Red Cross launched its first blood transfusion program under the leadership of Dr. William DeKleine [61]. Blalock A. (1940) concluded that it was advisable to use blood plasma instead of whole blood for resuscitation in severe injuries with critical bleeding. This decision was based on the following arguments:

1. Hemoconcentration, which characterizes most shock conditions, needs to be corrected by restoring blood plasma volume. In this context, plasma is more effective than a similar volume of whole blood.

2. Plasma is as effective as whole blood in stopping bleeding as whole blood.

3. The conditions of storage and transportation of plasma are less demanding compared to whole blood, which facilitates its use in the field conditions of military conflicts.

4. The use of plasma does not require the mandatory determination of blood type and Rh factor, which greatly simplifies and speeds up the process of providing premedical care (National Research Council, Committee on Transfusion Procedures) [10].

In 1943. Edward Churchill, a cardiothoracic surgeon, conducted an assessment of the need for and provision of WB for the needs of the front. He came to the following conclusions:

1. WB is the optimal solution for blood loss compensation in most cases of wounds on the battlefield.

2. The use of WB is the only effective way to prepare severely wounded patients for surgery.

3. Transfusion of WB helps to reduce mortality and reduce the risk of wound infection.

4. Blood plasma can be considered as a first aid agent and serve as an adjunct to WB, but it cannot replace WB transfusion in full [38].

During this period of history, transfusiology faced both the first innovations and constant challenges. The experience of the Second World War, in particular the work of Churchill, demonstrated that the transfusion of WB is vital for resuscitation in severe hemorrhagic shock. This strategy continued to influence approaches to the treatment of wounded in the Korean and Vietnam wars [32]. Despite its effectiveness, the WB had a limited shelf life, required significant resources for preparation, and was quickly depleted in the face of massive losses. The red blood cell component (RBC), which is suitable for storage, proved to be an inconvenient option for resuscitation. Further developments, including the creation of dry plasma, partially solved the logistical problems on the battlefield, but could not completely replace the transfusion of red blood cells.

In 1945. Coller and Moyer described the fluid translocation caused by the administration of saline to postoperative patients [37]. Subsequently, Shires (1964) and Roberts (1985) established the need for crystalloids in combination with blood components for effective resuscitation. These studies centralized the current understanding of infusion therapy and played a key role in shaping the concepts of circulating blood volume replacement. Over the past decades, the issues of maintaining water and electrolyte balance in the treatment of shock, burns and other critical conditions, as well as the study of physiological mechanisms of shock development, have been the subject of active scientific research in the treatment of severe trauma with critical bleeding and hemorrhagic shock [57, 62].

The armed conflicts of the first half of the 20th century not only stimulated the development of transfusiology, but also contributed to the creation of the first prototypes of blood banks, which later became the basis for the modern medical system.

12.2. Requirements for the preparation, storage and transportation of blood and its components in the modern world

12.2.1. Features of the preparation of blood and its components

We have analyzed the regulatory documents on donor blood [74-79]: the preparation of blood and its components in inpatient and outpatient settings is carried out in the blood procurement department in accordance with the above-mentioned regulatory documents. Responsibility for the management of blood procurement and the manufacture of components lies with the head of the blood procurement department, the deputy chief physician for the organization and provision of transfusion care and the authorized person for quality.

Preservative anticoagulant solutions registered in Ukraine are used to collect blood and its components, which must be sterile and apyrogenic. These solutions contain excipients that make it possible to store blood and its components during the storage period. These solutions include:

1. CPDA-1 solution (provides storage of preserved donor blood / red blood cell components at a temperature of 2 °C - 6 °C for 35 days);

2. CPD solution (ensures storage of preserved donor blood or red blood cell components at a temperature of 2 °C to 6 °C for 21 days and is contained in the main container of the kit);

3. ACD-A solution (an agent that prevents blood clotting during automatic plasmapheresis and cytapheresis procedures), and sometimes 4% sodium citrate solution is recommended as an anticoagulant for automatic plasmapheresis;

4. Glugicir solution (provides storage of preserved donor blood and red blood cell components at a temperature of 2 °C - 6 °C for 21 days);

5. Additional solutions for red blood cells (ADSOL, AS-2, SAGM) containing sodium chloride, adenine, glucose and mannitol, some of which contain sodium citrate, sodium dihydrogen phosphate or guanosine. These substances maintain the fullness of red blood cells after the plasma is removed from the component. The volume of the additional solution to be administered is 80 to 110 ml. Their use allows to store red

blood cells at a temperature of 2 °C - 6 °C for 42 days.

6. Additional solutions for platelets contain sodium chloride, potassium chloride, magnesium chloride, sodium citrate, sodium phosphate, sodium acetate, which provide

- iso-osmoticity, pH stability and concentration of adenine nucleotides (ADP, ATP) and high-energy compounds;

- reduce the accumulation of lactic acid, stimulate glycolysis;

- prevent spontaneous platelet aggregation and activation caused by the processes of blood collection and component manufacturing.

Supplemental platelet solutions create appropriate conditions for changes in cell metabolism and thus extend the shelf life of the component beyond 5 days.

During certain component manufacturing procedures, such as washing, platelet-rich layer (PRL) removal, dose pooling, cryopreservation, etc., some process steps are performed in an open system. The use of this system is permissible only in a cabinet with laminar airflow and in compliance with all aseptic requirements. Components manufactured in an open system are recommended for transfusion within 24 hours.

Red blood cell components are produced by using centrifugation modes and cytopheresis devices. Centrifugation modes are determined in accordance with the equipment of the institution and are consistent with the instructions for centrifuges. Preserved donor blood (blood collected from a suitable donor using a sterile and apyrogenic container (container system) with a preservative solution) is used primarily as a raw material for the manufacture of blood components. The components of the blood removed from the donor's vascular bed retain their full value for a limited period of time. Preserved blood is obtained by venipuncture from donors who have been previously selected by medical examination.

12.2.2. Requirements for transportation of blood components and preparations

The organization and control of transportation of blood components/preparations to a health care facility (hereinafter referred to as the HCF) is provided by a blood service institution (hereinafter referred to as the BSI). For the transportation of blood components, a validated system is used that maintains the appropriate storage

temperature of the component for the maximum permissible time (24 hours) and temperature limits during transportation. The use of temperature indicators to monitor the temperature during transportation is desirable. When components are released at the blood service facility, their storage temperature must be checked. An electronic sensor device can be used to instantly read the temperature data from the surface of the package. If no immediate transfusion is planned, the components received should be placed in a suitable refrigerator for storage. The best solution for maintaining the required temperature during transportation is to use specially adapted refrigerated vehicles (temperature from 2 °C to 10 °C) or freezer vehicles (temperature -18 °C and below) equipped with their own cooling units and their own temperature monitoring and recording systems. For the transportation of small amounts of blood components, portable refrigerators or freezers powered by a vehicle battery can be used. If these are not available, an insulated shipping container filled with cooling pads (for red blood cell components) or stable carbon dioxide, also known as dry ice (for plasma and cryoprecipitate), should be used.

If the portable refrigeration unit is not equipped with its own temperature sensor, a thermometer should be placed in the immediate vicinity of the transported blood component and the temperature should be recorded 5 minutes after the component is placed in the isothermal container and the temperature after transportation is completed.

A protocol for monitoring the temperature of transportation should be drawn up each time. For this purpose, a form should be used, which should be filled out by both the BSI that issues blood and its components and the HCF. Red blood cells are transported at a temperature between +2 °C and +6 °C. The temperature of red blood cell containers should not fall below +1 °C and rise above +10 °C. Validated transportation systems must ensure that the temperature does not exceed +10 °C at the end of the maximum transportation time (24 hours). Platelets should be transported in insulated containers with elements that stabilize the temperature, keeping it as close as possible to the recommended storage temperature during transportation. Transportation time without mixing should not exceed 24 hours. After receiving platelets, if they are

not immediately used for therapeutic purposes, the component should be transported for storage at the recommended temperature, but with further mixing. Plasma should be transported frozen at a temperature that is consistent with the storage temperature. Frozen components must be handled with extreme care, as containers can become brittle and crack at low temperatures [74-79].

12.2.3. Storage of blood and its components

An important factor in ensuring safe and effective resuscitation is the proper storage of whole blood and its blood components at the appropriate temperature in accordance with regulatory documents (Table 1). Failure to comply with storage requirements may result in reduced transfusion efficiency, potential harm to the patient, or the component becoming unusable and being disposed of [72, 74-79].

Storage conditions for blood components must ensure cell viability and function throughout the storage period. The use of "closed systems" for fractionation and storage of blood components reduces the risk of bacterial contamination. Refrigeration equipment for storing blood components must meet the following requirements: provide a set temperature that should be evenly distributed throughout the chamber; have a temperature recording system and alarm; be accessible for cleaning and withstand the effects of strong disinfectants; be appropriately labeled; be connected to an autonomous power supply; a sensor (thermometer) for temperature monitoring should be placed in a blood container with 250 ml of 10% solution The container should be located in the upper part of the refrigerator. In large refrigerators, there should be two such sensors (thermometers).

Red blood cell components are stored in an upright position at a temperature of 2 °C to 6 °C. The shelf life of components prepared with Glugicir and CPD solution is 21 days, and that of CPDA-1 solution is 35 days. The shelf life of erythrocyte-containing media prepared with additional solutions is 42 days. Freezing allows the components to be stored for 10 years or more. The shelf life of red blood cells may vary depending on the type (cell concentration, anticoagulant composition, use of additional solutions, etc.) Red blood cells for freezing and thawing should be prepared

Table 1 - Peculiarities of storage of blood products that can be used at the pre-hospital stage

Blood product	***Storage conditions***	***Transportation conditions***	***Maximum storage conditions***
Red blood cell component	1-6 °C	1-10 °C	ACD/CPD/CP2D: 21 days, CPDA-1: 35 days, with SAGM solution: 42 days CPD: 21 days CPDA-1: 35 days
Plasma component	After defrosting: 1-6 °C.	1-10 °C	
Platelet component	Normal: 20-24 °C with continuous gentle stirring. Cold storage: 1-6 °C, stirring as desired.	Normal: as close to 20-24 °C as possible, maximum time without stirring: 30 hours. Storage in the cold: 1-10 °C	Regular: 24 hours to 5 days depending on the collection system. Cold storage: according to the manufacturer's written instructions
Low titer of group O whole blood (LTOWB)	1-6 °C	1-10 °C	After defrosting: 5 days from the date of product thawing or expiration date, whichever comes first, if released as thawed plasma

and reconstituted in accordance with the manufacturer's instructions for cryopreservation equipment. Frozen red blood cells are stored at a temperature of -60 °C to -80 °C or -150 °C to -196 °C.

Blood intended for further processing and platelet manufacturing is stored at a temperature of 20 °C to 24 °C for no longer than 4 hours before the start of component manufacturing. Platelets are stored at a temperature between +20 °C and +24 °C with constant stirring. The recommended storage conditions for fresh frozen plasma and cryoprecipitate and storage conditions for cryoprecipitate-depleted plasma are 36 months at -30 °C or below and 3 months at -18 °C to -30 °C.

Blood and its components should be classified by AB0 and Rh groups and stored in separate refrigerators according to AB0 and Rh classification. Each dose of components should be placed in an upright position to ensure free air circulation between the containers and macroassessment. The permanent storage areas for red blood cell components should be carefully separated and secured:

1) those intended for dispensing ("dispensable components"), which should be stored in areas that are permanently categorized by AB0 and Rh groups

2) unused and returned ("return area");

3) without test results ("untested blood area");

4) unfit for transfusion by the time of transfusion ("components for destruction");

5) unsuitable for transfusion - expired, disqualified due to infection or other reasons ("blood for destruction");

6) intended for autotransfusion.

All types of plasma and cryoprecipitate should be stored in a freezer at -30 °C or below. Depending on the storage temperature, these components have different shelf lives: at -30 °C and below, 36 months. These components must be classified (with a clear indication of the AB0 group and the type of component) and stored separately. Also, components without results of tests for infectious diseases, components after quarantine, components without quarantine, and components intended for dispensing should be stored separately in clearly defined places. Components intended for destruction should also be kept in separate devices, but they do not need to be frozen.

Platelet concentrate (PC) should be stored at a temperature of 20 °C to 24 °C, with constant stirring (in a rotating or horizontal shaker) in the blood and blood components collection department until blood test results are obtained, and then transferred for further storage and delivery to the expedition department. Highly purified concentrates of coagulation factors should be stored according to the manufacturer's recommendations (usually at a temperature between 2 °C and 8 °C).

Blood products (albumin and intravenous immunoglobulins) should be stored according to the manufacturer's recommendations (usually at room temperature) [26].

12.3. Meta-analysis of the positive and negative aspects of the use of whole blood transfusion and component therapy (red blood cells, platelets, plasma components) in the modern world during military conflicts.

The study of Lammers et al. (2024), Dorken-Gallastegi A. (2024), based on the study of military personnel with an average age of 33 years, 79.0% of whom were men, who received penetrating wounds in 48.0% of combat operations of the US armed forces, and who received ≥1 unit of red blood cells (RBCs). The following two groups of patients were compared: (1) WB, red blood cells and plasma, and (2) PC, who received red blood cells, plasma and platelets but not WB. The database included patients wounded in both Afghanistan and Iraq who received at least one unit of red blood cells in a Role 2 or 3 hospital. Additional variables included in the analysis were patient age, vital signs on admission, and laboratory values including individualized ocular, verbal, and motor Glasgow Coma Scores, body temperature, systolic blood pressure, heart rate, blood hemoglobin levels, and injury severity scores (Trauma score/MESS). Increased 24- and 30-day survival of patients transfused with WB for traumatic hemorrhagic shock was reported compared to patients transfused with WB for similar severity of injury. A 13.0% increase in 30-day survival was recorded when WB was used in military personnel compared to the group receiving PC [18, 41].

Of particular interest is the study by Glumcher F. (2017), which emphasizes the following advantages of using WB: greater effectiveness in correcting coagulopathy and shock, minimizing the negative effects of using long-term red blood cell transfusions. WB increases cardiac output, improves microcirculation, and oxygen uptake compared to PC. In addition, WB resuscitation helps to reduce the number of complications that arise when a large number of multicomponent blood products are infused into one patient. It was also found that the dilution effect (disturbance of the ratio of electrolyte and component composition) is mitigated when using WB in contrast to that when using crystalloid and colloidal solutions [23].

A retrospective analysis revealed that the composition of WB differs significantly from WB, which includes red blood cells, platelets, and fresh frozen plasma in a 1:1:1 ratio. This comparison allows for a deeper understanding of the functional

characteristics of each of the blood replacement fluid options and their clinical use. The analysis showed that WB provides comprehensive functional characteristics necessary to maintain homeostasis. In comparison, PC, although it allows for specific correction of deficiencies of individual components, demonstrates a decrease in the concentration of critical components, which can negatively affect the effectiveness of treatment in patients with hemorrhagic and other pathologies (Table 2) [72].

Table 2 - Comparative characteristics of whole blood and component therapy

Indicators	**Whole blood 500 ml**	**Component therapy 1:1:1 (red blood cells, platelets, plasma components)**
Volume (ml)	500	675 = 1 unit of red blood cells + 1 unit of platelets + 1 unit of fresh frozen plasma
Coagulation coefficient (%)	100	1 unit of SPP = 275 ml with 80% coagulation activity
Platelet count/thousand	150-400	88-10^9 in 1 dose of platelets
Fibrinogen/mg	1000 mg	1 unit of cryoprecipitate = 15 ml with 150 mg of fibrinogen

The hemostatic properties of WB are more effective than CT consisting of red blood cells, fresh frozen plasma, and platelets, as these components are more dilute, which reduces the overall oxygen carrying capacity. The use of WB shows great promise for reducing mortality in patients with severe trauma and critical bleeding accompanied by hemorrhagic shock [23, 35, 44, 46].

Hemostatic resuscitation has become the gold standard of treatment, but ensuring access to the necessary blood components in extreme conditions is often problematic. Red blood cell transfusion is seen as a promising method to quickly stop life-threatening bleeding. In the context of the full-scale war in Ukraine, the need for

donated blood has increased due to the large number of wounded with severe injuries from modern weapons, accompanied by massive blood loss. Blood resuscitation is vital to provide care and stabilize the condition of the injured both at the pre-hospital and hospital stages. The Ministry of Health of Ukraine reported that 60.0% of fatalities during the full-scale war could have been prevented if they had received a timely transfusion of WB. As a result, it authorized the use of WB in the prehospital stage by persons with medical education and proper training. Ensuring the transfusion of safe WB is currently very necessary and relevant in the event of massive sanitary losses [16, 73, 80, 81-83].

The analysis of data from the conflicts in Iraq and Afghanistan by Dhillon et al. (2023), as well as the review of civilian trauma by Kronstedt et al. (2022), shows the important role of WB resuscitation in the treatment of critical bleeding. The experience of countries with armed military conflicts leaves open the issue of rapid resuscitation and exacerbates the need for WB transfusion to both military and civilians with critical bleeding. During the conflicts in Iraq and Afghanistan, more than 10,000 units of WB were transfused, and outcome data have emerged showing a significant improvement in the treatment of wounded who received WB transfusions compared to CT [17, 39].

The study by Williams et al. (2020) demonstrated the US program of cold storage of whole blood during the wars in Iraq and Afghanistan and its successful use in peacetime among civilian patients with massive bleeding. In U.S. military medicine, WB is associated with a 53.0% reduction in blood transfusions in the emergency department and a twofold increase in the likelihood of survival [71].

Under the severe conditions encountered by advanced US surgical teams in Afghanistan, resuscitation including WB demonstrated a survival advantage over the use of preserved red blood cells and plasma alone. Scientific publications by Hanna et al. (2022), Malkin M. (2021), provide convincing evidence that balanced resuscitation with an approximately equal ratio of packed red blood cells, fresh frozen plasma and pooled platelets leads to better outcomes in massive transfusion resuscitation and prevents the occurrence of acute traumatic coagulopathy. Due to the growing body of evidence in favor of balanced resuscitation, there is renewed interest in the use of WB

in military medicine in Ukraine. In 2014, the Committee on Tactical Combat Casualty Care recommended WB as the optimal resuscitation product on the battlefield and in the prehospital stage. In particular, the American Association of Blood Banks supports the use of low-titer group O WB as a universal donor plasma. There is growing evidence to support the use of WB instead of CT in massive transfusion due to reduced 24-hour mortality, improved transfusion logistics, and better survival outcomes among military personnel with massive bleeding, combined severe limb injuries, pneumothorax, abdominal injuries, etc.

According to the American College of Surgeons TQIP (Trauma Quality Improvement Program) data for the period 2017-2018, a study was conducted to establish the relationship between the time of WB resuscitation and its effectiveness. Patients were stratified by the time of transfusion of the first unit of WB (first 30 minutes, second 30 minutes and second hour). The authors of the study Crowe E. (2020), Hosseinpour et al. (2023), Nouh T. (2024), Risha M. (2024) found that every 30 minutes of WB transfusion delay was associated with higher odds of in-hospital mortality. Each minute of WB transfusion delay contributed to a 1.2%-2.5% increase in the odds of 24-hour mortality among patients with hemorrhagic shock [27, 47, 53, 56].

Noteworthy is the study by Feinberg G. (2023), Aoki M. (2024), which analyzed the data of patients who received whole blood transfusions together with packed red blood cells (PRBCs) in patients with severe injuries. The main question was how the ratio between EC and WB affects patient survival. When analyzing the results, there was a significant increase in 24-hour mortality with higher PRBCs/WB ratios (WB alone - 5.2%, 1:1-10.9%, 2:1 - 11.8%, 3:1 - 14.9%, 4:1 - 20.9%, 5:1 - 34.1%. The authors of the study believe that the optimal ratio of PRBCs to WB is 3:1 or less. At higher ratios of PRBCs to WB, the hemostatic effect of using WB is reduced [4, 5, 19].

In a study conducted by the Israeli Defense Forces Medical Corps, it was demonstrated that the use of whole blood of group O rhesus negative with a low agglutinin titer is an effective method of treating hemorrhagic shock in military and civilian patients. The protocol of using whole blood as a first-class resuscitation fluid

in a combat search and rescue unit has significantly improved the survival rate of wounded with hemorrhagic shock at systolic blood pressure <90 mm Hg. The Israel Defense Forces Medical Corps decided to use whole blood on the front lines, up to the frontline medical units on the battlefield. The concept of equipping airborne, special and rear medical brigades is to have a centralized blood bank in each brigade. The personnel who transport blood supplies are experienced medical professionals with special training in the use of whole blood in the field. To overcome logistical problems (delivery of WB to the battlefield and keeping them within the temperature range), special refrigeration units were purchased and installed on armored vehicles [2, 43, 67].

Researchers [48] (2021) found in their study that the use of Rh+ low titer group O whole blood (LTO-WB) is a safe alternative for resuscitation of hemorrhagic shock in both Rh+ and Rh- patients, even in the presence of Rh- WB deficiency. The authors did not find any significant differences in the laboratory parameters of these patients, the incidence of transfusion reactions, complications, or survival between these two groups of patients. The use of LTOWB whole blood in the resuscitation of patients with severe trauma and critical bleeding has demonstrated significant benefits in both military and civilian settings. A study by Clements and colleagues (2024) confirms that whole blood resuscitation is associated with improved patient survival, more effective correction of coagulopathy, and a reduced need for additional transfusions. Despite potential risks, such as immunosuppression and infection transmission, which require careful monitoring, the benefits of LTOWB are likely to outweigh the risks [3, 9, 15, 34, 49, 51, 71].

Most studies compare LTOWB to CT, but only a few have addressed the issue of low O titer WB versus type-specific whole blood (TSWB). There is sufficient data to favor the latter. Despite the growing popularity of low O-type whole blood as a universal donor product, the authors of Milford E. (2024) argue that type-specific whole blood still has an important place in modern transfusion, especially in the setting of massive bleeding. While LTOWB simplifies transfusion logistics, there are limitations and uncertainties regarding its long-term use, such as potential

immunologic risks, optimal transfusion volumes, and impact on future transfusions. The authors recommend keeping TSWB in the arsenal of blood products, especially for patients whose blood type is known, and using LTOWB as a backup for patients with an unknown blood type. This approach will ensure optimal safety and efficacy of transfusion therapy [1, 43, 66, 68].

Understanding the life-threatening nature of traumatic coagulopathy and implementing strategies that address the full spectrum of bleeding management from the time of injury through postoperative care will lead to improved outcomes for patients with critical/massive life-threatening bleeding.

1. From a pathophysiological point of view, timely infusion of WB is an ideal transfusion medium for the treatment of hemorrhagic shock and is a universal blood product for resuscitation of civilian and military trauma patients.
2. As a balanced product, WB contains fully functional red blood cells, platelets and 100% preserved clotting factor activity, which effectively prevents the development of the fatal triad of death (acidosis, coagulopathy and hypothermia).
3. WB transfusion is an independent predictor of increased 24-hour and 30-day survival of patients with traumatic hemorrhagic shock compared to CT.

12.4. Analysis of the use of whole blood and its components in the combat conditions of a full-scale war in Ukraine

12.4.1. Analysis of the use of whole blood and component therapy at the level Role 1, Role 2 in combat conditions during a full-scale war in Ukraine

An analysis of blood transfusion during Role 1 resuscitation was conducted on the basis of two surgical stabilization points in the most intense combat zone and one Role 2 hospital, which aimed to assess the benefits of administering red blood cells (RBCs), plasma (fresh frozen plasma (FFP)), and platelet (PT) components (CT); in various degrees of hypovolemic shock due to traumatic injuries during combat operations, the time of the start of blood transfusion during resuscitation from injury. Role 1 is critically important in the medical care system, as it provides for a

comprehensive approach to the treatment of patients who have sustained traumatic injuries and require urgent medical interventions. At this stage of medical evacuation, the preference was given to transfusion of red blood cell component + plasma component (RBC+PC)-72.5% and red blood cell component alone - 27.5% (Figure 1).

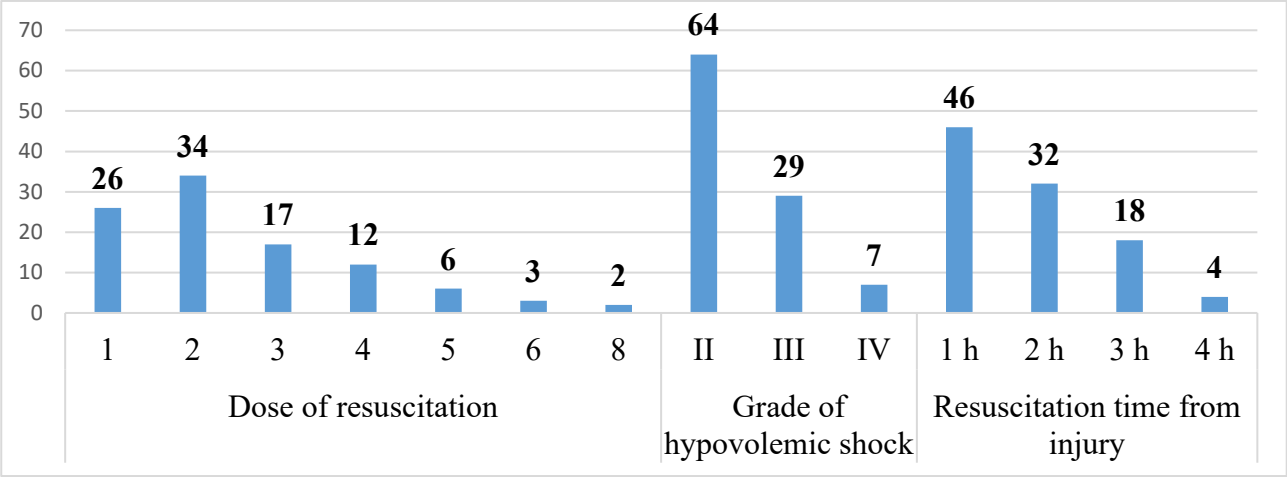

Figure 1 - Analysis of blood transfusion doses during resuscitation on Role 1 at different degrees of hypovolemic shock and time of resuscitation from injury, %.

The analysis of combat injuries revealed that the largest share of injuries (43.0%) was to the extremities, indicating their high vulnerability and the likelihood of significant blood loss. Abdominal injuries accounted for 28.0%, which is critically important because abdominal injuries are often associated with severe internal bleeding. Thoraco-abdominal injuries accounted for 17.0%, while pelvic injuries accounted for 12.0%. This distribution demonstrates the complex nature of injuries, which requires a multidisciplinary approach to treatment and timely identification of sources of hemorrhage and rapid application of appropriate surgical and resuscitation measures, which is critical for the survival of the injured.

The level of hypovolemic shock in patients indicates the seriousness of their condition: 64.0% of the servicemen had the level II shock, 29.0% - the level III, and 7.0% - the level IV. The high percentage of patients with II and III levels of hypovolemic shock indicates that most of them suffered significant blood loss, which requires urgent and adequate treatment. In 7.0% of servicemen, level IV shock was

diagnosed, which indicates a severe degree of hemorrhagic shock (decompensated).

The time elapsed from the moment of injury to the start of blood transfusion during resuscitation is an important indicator that directly affects the prognosis of treatment and prevention of fatalities. According to the study, 46.0% of wounded servicemen received blood transfusion during resuscitation within the first hour, 32.0% - within the second hour, 18% - within the third hour, and only 4% received help four hours after the injury. Timely transfusion of whole blood is critical to improving the survival of patients in Role 1 close to combat.

The analysis of blood transfusion doses during resuscitation showed that 60.0% of patients received 1-2 doses, including 26.0% who received 1 dose and 34.0% who received 2 doses. This may indicate timely and adequate medical intervention, as most patients required a moderate number of blood transfusions to stabilize their condition. At the same time, 17.0% of patients who received 3 doses and 23.0% who received more than 4 doses can be classified as high-risk, requiring constant monitoring and correction of infusion therapy during treatment.

The analysis of blood transfusion doses during resuscitation at the Role 2 military hospital indicated a high efficiency of early blood transfusion, which was performed in Role 1, which led to a significant reduction in the number of complications in servicemen in Role 2. In Role 2, the preference was given to transfusion of EC+FFP - 50.0%; EC - 43.0%; platelet components (PC) - 7.0% (Figure 2).

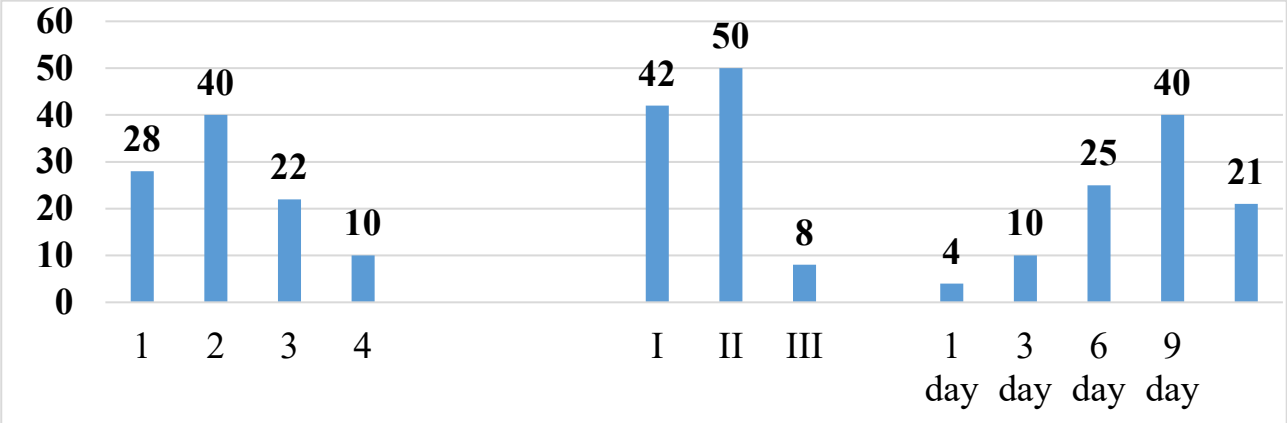

Figure 2 - Analysis of blood transfusion doses during resuscitation on Role 2 at different levels of hypovolemic shock and time of initiation of resuscitation from injury, %

The analysis of blood transfusion doses during resuscitation showed that 28.0% of patients in Role 2 received 1 dose, 40.0% - 2 doses, 22.0% - 3 doses, and 10.0% - 4 doses due to the combined trauma. This distribution structure indicates that in the vast majority of patients, the need for massive blood transfusions in Role 2 is due to timely correction of blood loss, which was performed in Role 1. Early intervention with red blood cell + plasma component transfusion allowed to achieve hemodynamic stabilization, which reduced complications after transfusion.

The level of hypovolemic shock among wounded soldiers in Role 2 was distributed as follows: 42.0% - first level, 50.0% - second level and 8.0% - third level of shock.

Particular attention was paid to the analysis of complications after blood transfusion during resuscitation on Role 2. In the majority of patients, 82.0% of complications after transfusion were not observed. Only 10.0% of patients had hyperthermia, 4.0% had acute renal failure (ARF), and another 4.0% had Quincke's edema. Such a low complication rate indicates the effectiveness of timely blood transfusion during resuscitation of the erythrocyte component + plasma component in Role 1, which helped stabilize the patients' condition and minimized the risk of post-transfusion reactions in Role 2.

The time elapsed from the moment of injury to the start of blood transfusion during Role 2 resuscitation varied significantly. Only 4.0% of patients received an infusion within the first day, while the largest number of transfusions was performed on the ninth day - 40.0%, on the sixth day - 25.0%, and on the twelfth day - 21.0%. This is explained by the fact that the most critical blood transfusions during resuscitation were performed in Role 1, where timely resuscitation was provided.

The overall results of the study indicate that timely and adequate blood transfusion during red blood cell + plasma component resuscitation at Role 1 significantly reduced the incidence of severe complications at Role 2, which confirms the key role of early hemotransfusion intervention in stabilizing hemodynamics and reducing the risk of post-transfusion reactions and severe consequences in patients with combat injuries.

The study, which covered Role 1 and Role 2, analyzed the transfusion of blood

components for transfusion therapy. The main components used were red blood cells (43.0%), which indicates that the priority task is to correct oxygen transport function in patients with significant blood loss. In 50.0% of cases, a combination of red blood cell component + plasma component was used, which indicates the need for an integrated approach to treatment aimed at simultaneous correction of hypovolemia and coagulopathy. The plasma component contains important clotting factors, which allowed for effective restoration of hemostatic function, reducing the risk of developing disseminated intravascular coagulation (DIC) and other coagulation complications that often accompany massive trauma and blood loss. Thromboconcentrate was used in 7.0% of cases, which indicates controlled hemostasis and the effectiveness of the early stages of treatment.

Thus, the predominant transfusion of red blood cell component and their combination of red blood cell component + plasma component demonstrates the effectiveness of transfusion therapy aimed at restoring oxygen transport function and coagulation status of patients, which minimized the risk of complications and helped stabilize the condition of patients with severe trauma and blood loss during warfare.

12.4.2. Comparative analysis of the goals of intensive care in the context of different transfusion fluids: whole blood and component therapy, prospects and shortcomings

The study conducted a retrospective analysis of the composition of WB and component therapy (CT), which includes red blood cells, platelets, and fresh frozen plasma in a 1:1:1 ratio. This comparison allows for a deeper understanding of the functional characteristics of each of the blood replacement fluid options and their clinical application. The analysis showed that WB provides comprehensive functional characteristics necessary to maintain homeostasis. In comparison, CT, although it allows for specific correction of deficiencies of individual components, demonstrates a decrease in the concentration of critical components, which can negatively affect the effectiveness of treatment in patients with hemorrhagic and other pathologies (Table 3).

Table 3 - Comparative characteristics of whole blood and component therapy

Indicator	**Whole blood**	**Component therapy 1:1:1 (red blood cells, platelets, plasma components)**
Volume (ml)	500	680 = 1 unit of red blood cells + 1 unit of platelets + 1 unit of fresh frozen plasma
Hematocrit, % (ml)	38-50	29
Coagulation coefficient (%)	100	65
Platelet count/thousand	150-400	200-10^9 in 1 dose of platelets
Fibrinogen/mg	1500	70 IU for plasma
Anticoagulant content/ml	63	205
Temperature ˚C	+37	+2 +6 / +20,+24 / -25ºC
Shelf life/storage conditions	21-35 days/	-erythrocyte components - at 2-6˚C shelf life 35 days (with CPDA-1 solution) or 42 days (with SAGM solution)

The results of the analysis emphasize the importance of a strategic approach to choosing between WB and CT, taking into account the individual clinical needs of the patient and the risks associated with transfusion procedures.

Intensive care is a key element in the treatment of patients with severe trauma and hemorrhagic shock. The choice of transfusion fluids is crucial to stabilize the patient and improve clinical outcomes.

In this study, we analyzed the effectiveness of different transfusion fluids - crystalloid and colloidal solutions, EC, PC, FFP, and WB - for several key goals of intensive care. The focus is on their ability to increase thrombosis, restore intravascular volume, optimize oxygen transport and electrolyte balance, and minimize side effects. Our analysis allows us to formulate more reasonable recommendations for clinical practice in the field of modern transfusion medicine (Table 4).

Table 4 - Comparative analysis of intensive care goals in the context of different transfusion fluids

Objectives.	**Crystalloid solutions**	**Colloidal solutions**	**FFP**	**Red blood cell concentrate (EC)**	**Whole blood**
1. Increase the body's ability to form blood clots in areas of active bleeding	-	-	+	-	+
2. Minimisation of adverse effects (edema and dilution of blood coagulation factors) due to iatrogenic damage from intensive care	-	+	+	+	+
3. Restoration of adequate intravascular volume and perfusion of the organ after the final surgical bleeding control	-	+	+	+	+
4. Optimisation of oxygen transport to organs and tissues	-	-	-	+	+
5. Correction of electrolyte balance and acid-base status	+	+	+	-	+

According to our research, we analysed the advantages and disadvantages of using WB.

Advantages:

1. Effectiveness in the correction of coagulopathy and shock: In our study, EC, FFP, PC was found to be highly effective in the treatment of coagulopathy and shock, providing a rapid and significant therapeutic effect.

2. Minimisation of negative effects: The use of EC, FFP, PC reduces the risk of adverse effects associated with the transfusion of long-term storage red blood cells. This is important for maintaining the patient's stable condition and preventing complications.

3. Physiological correlation of moulded elements: EC, FFP, PC provides patients with all the formative elements in the optimal physiological ratio, which allows to effectively compensate for losses during bleeding.

4. Complex composition: The study showed that EC, FFP, PC supplies all the necessary blood elements in one product, which requires only refrigerated storage, which is an advantage for use in combat or emergency situations.

5. Improved cardiac output and microcirculation: Transfusion of EC, FFP, PC can increase cardiac output, improve microcirculation and oxygen uptake, which is critical for patients in critical conditions.

6. High concentration of coagulation factors: WB contains a higher concentration of clotting factors compared to component therapy in a 1:1:1 ratio (EC, FFP, PC), which ensures more efficient blood clotting and reduces the risk of continued bleeding.

7. Effectiveness in the treatment of acute traumatic coagulopathy: WB transfusion can more effectively correct this condition in patients due to improved platelet and plasma function and concentration.

Disadvantages:

1. The need for safety testing: Safety testing may extend the time required to start a transfusion.

2. Risk of graft-versus-host disease: An increased risk of graft-versus-host reactions was noted, which requires special attention during transfusions.

Thus, the study confirms that WB is an important tool in intensive care, but its use requires a careful assessment of the benefits and risks.

12.4.3. The relevance of transfusion of whole blood, lyophilised plasma and tranexamic acid in the modern countries of the USA and Israel.

According to scientists, transfusion of whole blood of group O rhesus-negative with a low agglutinin titer showed a positive advantage in servicemen with hemorrhagic shock of the II and III degree due to traumatic injuries associated with combat operations. Hemorrhagic shock can be compensated or uncompensated and of varying severity, from mild to severe, which affects the dose of resuscitation.

According to the results of a study conducted by researchers in seven US hospitals, patients with hemorrhagic shock of varying severity who received both WB and CT (EC, FFP) resuscitation showed an improvement in 30-day survival with WB administration. WB transfusion is promising with a balanced transfusion strategy during the early resuscitation period of trauma patients and improves outcomes by reducing mortality. U.S. medical hospitals near combat operations were provided with enough WB to quickly resuscitate servicemen with severe hemorrhagic shock. In 2016, the U.S. Department of Defense proposed a program to transfuse whole blood O group Rh-negative with a low agglutinin titer [21].

Experience around the world with military conflicts has renewed interest in WB transfusion for patients with life-threatening bleeding. Ongoing analyses by the U.S. Department of Defense indicate that WB transfusion is associated with improved or similar survival for patients with traumatic injuries associated with massive bleeding compared to blood component resuscitation. Scientific evidence complements randomized controlled trials showing that platelet-containing blood products stored at +4°C have better hemostatic function, based on reduced bleeding and improved functional hemostatic parameters, compared to blood products.

Peacetime shootings in the United States today continue to result in mass casualties and the need for blood transfusions, with massive bleeding remaining the leading cause of severe hemorrhagic shock and trauma-related deaths. The reality of numerous mass shootings in the United States has led to the need for rapid resuscitation of WB and its components during these events [13].

Mass accidents in the United States continue to rise. Compared to 2019/2022, mass shootings increased by 25%. As of 2024, the country has recorded more than 400 mass shootings, which is 38% less than in 2023, when about 646 cases were recorded. Taking into account the trends of previous years, the total number of victims is steadily increasing compared to 2019/2023. Critical bleeding due to gunshot injuries is the leading cause of preventable death. The need for rapid access to life-saving WB and its components is essential to preventing deaths due to critical bleeding. It is well known that most large cities in the United States are not sufficiently prepared for such

challenges and for meeting the requirements for blood transfusion in the event of mass casualties from gunshot wounds [30].

Hemorrhagic shock remains the leading cause of death both in peacetime and during combat operations, which could be prevented despite significant advances in trauma treatment. According to scientists, early initiation of balanced resuscitation has been shown to reduce deaths in patients with critical bleeding. To eliminate restrictions on transfusions in dangerous conditions or in case of multiple losses, the principles of "walking blood bank" have been used with great success in countries with military conflicts, such as Ukraine and Israel [12].

Since 2018, the Israeli Defense Forces Medical Corps has introduced the use of WB group O rhesus negative with a low agglutinin titer as a first-class resuscitation fluid in a combat search and rescue unit during the air evacuation of both military and civilian wounded patients with hemorrhagic shock and systolic blood pressure <90 mm Hg [43].

Remote damage control resuscitation aims to apply the principles of damage control resuscitation in the prehospital setting, emphasizing early control of critical bleeding, resuscitation with balanced volume, and prevention or correction of coagulopathy, acidosis, hypothermia, and hypocalcemia [67].

Israel's military and prehospital medical organizations are investing significant resources to improve the treatment of trauma patients in order to reduce preventable deaths. The main focus is on bleeding control and resuscitation with blood components, using guidelines for remote resuscitation with damage control. The Israeli Defense Forces Medical Corps has been using tranexamic acid and lyophilized plasma as part of its damage control remote resuscitation protocol for more than a decade. Lyophilized plasma is an important medical product for treating injuries and controlling bleeding, especially in emergency situations in Israel. It is obtained by removing water from liquid plasma, which allows it to be stored at room temperature and quickly reorganized if necessary (Table 5).

Table 5 - Comparative characteristics of lyophilized plasma and tranexamic acid

Criterion	Lyophilized plasma	Tranexamic acid
Type of product	Hemotherapeutic product (lyophilized plasma)	Medicinal product (antifibrinolytic)
Mechanism of action	Enriched with clotting factors that support hemostasis	Inhibits the activity of plasminogen, preventing the dissolution of blood clots, by blocking plasmin, which leads to the preservation of platelets and fibrin
Composition	Contains coagulation factors such as fibrinogen, factors II, VII, VIII, IX and X, albumin, antibodies and electrolytes	The active ingredient is tranexamic acid, a synthetic analog of aminocaproic acid that blocks fibrinolysis
Indications for use	It is used in emergency cases for the treatment of patients with severe blood loss, in surgery, traumatology and obstetrics in case of prolonged bleeding	It is indicated for the prevention and treatment of bleeding in trauma, surgery, menorrhagia and other conditions associated with an increased risk of bleeding
Method of administration	Intravenously after recovery to a liquid state; used in critical situations	Intravenously or orally, depending on the clinical situation
Recovery time	Restored to liquid state in a few minutes by adding saline or water for injection	Tranexamic acid is rapidly absorbed, with a peak plasma concentration approximately 1-2 hours after administration
Shelf life of the product	Can be stored for up to 24 months at -20 °C to -80 °C,	Depending on the formulation; tablets can be

Criterion	Lyophilized plasma	Tranexamic acid
	which simplifies transportation and storage	stored for up to 24 months, solution for injection - 2-8°C
Safety of the product	The risk of transmission of infectious agents is minimal due to strict standards of donor blood processing; the possibility of transfusion reactions	Considered safe, but may cause side effects such as nausea, diarrhea and headache
Advantages	Provides immediate restoration of hemostasis, increases the survival rate of patients with massive bleeding; effective in extreme conditions	Reduces the need for blood transfusions, can be used in outpatient settings
Disadvantages	Need to comply with storage conditions, risk of serious transfusion reactions; limited availability in some regions	May be less effective in severe hemorrhagic conditions if coagulation is already impaired

In recent years, whole blood of group O rhesus negative with a low agglutinin titer has been integrated into Israeli Defense Forces evacuation helicopters and expanded to mobile ambulances, complementing the use of lyophilized plasma for the treatment of trauma patients in deep shock [2].

The use of EC for the treatment of anemia, FFP to replace lost or used up clotting factors, TC for thrombocytopenia and thrombocytopathies, and cryoprecipitate (Cryo) for hyperfibrinogenemia. WB contains all of these elements in a smaller volume of anticoagulant and thus provides a more concentrated product for the treatment of bleeding patients who need to replace all blood elements.

WB transfusion may be more effective than component therapy in military personnel with critical bleeding. Shivhare A. (2019) in his research noted a decrease in

the ability to deform red blood cells, changes in adhesion and aggregation of red blood cells, as well as a decrease in 2,3-diphosphoglycerate and ATP during storage and transfusion of red blood cells in CT. Bioactive compounds with anti-inflammatory effects also accumulate in the storage medium and reduce the post-transfusion viability of erythrocytes [63].

Hazelton J.P. (2022) found that during initial resuscitation, trauma patients who received 73% of a single dose of WB versus 27% were 9% less likely to have bleeding complications and 48% less likely to die than those who received CT alone. Balanced resuscitation with an equal ratio of EC, FFP, and PC units leads to better outcomes in massive resuscitation and prevents acute traumatic coagulopathy in DCR [31].

Conclusions.

1. The well-recognized therapeutic benefits of whole blood have pushed this therapy far ahead in prehospital treatment in the United States, Israel, and most recently during the Russian-Ukrainian war at the Role 1 level and beyond.

2. The effectiveness of infusion therapy: At Role 1, 60.0% of servicemen received 1-2 doses of blood, which stabilized the condition of 64.0% of patients with II degree hypovolemic shock without developing complications.

3. Reduction of shock severity: in Role 2, there was a decrease in the severity of shock, where 92.0% of patients had I-II degree of shock.

4. Minimization of complications: The number of complications after transfusions was low - 18.0%: hypertension - 10.0%, AKI - 4.0%, Quincke's edema - 4.0%, which indicates adequate selection, effective monitoring of patients and timely rescission.

5. Time to start the infusion: Timely infusion therapy, in particular within 1-2 hours after injury (78.0% of cases), played a key role in achieving positive clinical outcomes.

6. The study shows that effective infusion therapy in the early stages (Role 1) led to a significant reduction in the severity of hypovolemic shock in Role 2 and minimized the number of complications after resuscitation.

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The scientific achievements of the authors of the monograph were also reviewed and recommended for publication at the international scientific symposium

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(March 30, 2025)

Monograph published in the author's edition

The monograph is included in

International scientometric databases

500 copies

March, 2025

Published:

ScientificWorld -NetAkhatAV

Lußstr 13,

Karlsruhe, Germany

e-mail: editor@promonograph.org

https://desymp.promonograph.org

ISBN 978-3-989240-84-1