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1.1 Preparation

RBC concentrates are prepared from fresh whole blood or from blood processed in an automated cell separator (apheresis concentrate).

1.1.1 Types of RBC Concentrates

Licensed RBC concentrates slightly vary in contents of residual platelets, plasma and additive solution.

1.1.1.1 Leukocyte-Depleted RBC Concentrates in Additive Solution

In Germany allogeneic RBC concentrates are licensed only in the leukocyte-depleted form. Leukocyte depletion improves the quality of the RBC concentrates, strongly reduces the risk of immunization against human leukocyte antigens (HLA), and extensively eliminates the risk of infection by intracellular viruses (e.g. CMV) [51]. The plasma content is strongly reduced by employing an additive solution.

1.1.1.2 Washed RBC Concentrates

In order to particularly remove residual plasma proteins and platelets from leukocyte-depleted RBC concentrates in additive solution, the erythrocytes are washed repeatedly in isotonic solution in a closed system and subsequently resuspended in isotonic saline solution or additive solution. Washed RBC concentrates are indicated very rarely and have to be transfused immediately [7].

1.1.1.3 Cryopreserved RBC Concentrates

Prior to application, cryopreserved RBC concentrates (storage below –80 °C) are thawed, washed in a closed system using a suitable solution, resuspended, and transfused immediately [7]. Because of the high effort required, few national and international blood banks keep available a limited supply only of selected cryopreserved RBC concentrates of rare blood types.

1.1.1.4 Irradiated Leukocyte-Depleted RBC Concentrates

Irradiation is performed with a mean radiation dose of 30 Gy and must not be less than 25 Gy in any part of the product [7].

1.1.2 Quality Criteria

Immediately prior to a transfusion, each unit of RBC concentrates must be subjected to a visual quality control check by the physician performing the transfusion. In particular, attention must be paid to the intactness of the blood bag, clot formation, discoloration (a possible sign of contamination), and/or hemolysis. In addition, the proper labeling and expiration date of the blood product and its correct allocation to the recipient must be carefully controlled. Conspicuous RBC concentrates must not be used [7].

Storage and handling instructions must be strictly followed.

1.2 Active Constituents

The active constituents of RBC concentrates are morphologically and functionally intact erythrocytes. Other constituents such as plasma, platelets, anticoagulants and additive solution, the contents of which differ depending on the preparation technique used, do not have a therapeutic effect of their own and do not influence the therapeutic efficacy of the RBC concentrates.

1.3 Physiological Function, Consequences of Storage

Erythrocytes are highly specialized cells without nucleus or mitochondria, with a limited metabolism. They function as carriers of hemoglobin, the substance responsible for exchange and transport of respiratory gases in lungs, blood and tissues. 2–24 h after transfusion of 1 RBC unit, in an adult of average weight without increased erythrocyte turnover and without hemorrhage, the hemoglobin concentration can be expected to rise by about 1.0 g/dl (0.62 mmol/l) and the hematocrit by about 3–4% [79]. The survival time of erythrocytes in the blood is 110–120 days, i.e. the elimination rate is less than 1% per day. Since RBC concentrates contain erythrocytes of all ages, the mean survival time of transfused compatible fresh erythrocytes is around 58 days. Theoretically, a healthy adult must produce 12 ml of erythrocytes per day to maintain a constant hemoglobin concentration of 10 g/dl (6.2 mmol/l). In the event of complete cessation of erythrocyte production, as in severe aplastic anemia, around 1 unit of RBC (200–250 ml) per week must be transfused to guarantee a constant hemoglobin concentration of 10 g/dl (6.2 mmol/l). In the event of increased degradation a higher erythrocyte consumption is observed, especially in febrile diseases, on evidence of autoimmune antibodies and in splenomegaly.

Storage of erythrocytes outside the body leads to complex changes. Among other things, such damage includes morphological changes of the stored erythrocytes (e.g. development of spherocytes and echinocytes), functional disturbances (e.g. reduction of the 2,3-diphosphoglycerate (2,3 DPG) concentration and a resultant shift to the left of the oxygen dissociation curve, loss of deformability of erythrocytes, increased concentration of lactate, release of components (e.g. potassium, lactate dehydrogenase, hemoglobin), and decrease of the S-nitrosohemoglobin of the erythrocytes.
[3, 23, 24, 27]). To some extent these storage-related changes in erythrocytes are reversible in vivo within 48–72 h after transfusion.

At present, the clinical relevance of such storage-related changes cannot be assessed unambiguously in terms of tissue oxygenation and disease outcome in patients after transfusion. Clinical studies that were performed to determine the consequences of the duration of storage on tissue oxygenation had conflicting results [43, 70]. 2,3-DPG depletion is probably of little relevance for O₂ release from stored erythrocytes and for tissue oxygenation [74]. In some studies involving critically ill trauma patients during intensive care and postoperatively, an association was shown between the duration of storage of transfused RBC concentrates and mortality, morbidity, the occurrence of infections as well as length of stay in hospital [23, 34, 50, 54, 67, 80]. In patients who underwent heart surgery the latest data suggest that the transfusion of erythrocytes that had been stored longer than 14 days was associated with higher complication rates as well as lower survival rates [30]. This is discussed to be caused by storage-related morphological alterations and functional impairment of erythrocytes as well as the presence of cellular and bioactive components in plasma supernatant [3, 23, 27, 48]. However, it must be pointed out that the majority of these studies were performed prior to the implementation of leukocyte depletion. Therefore it is not clear whether the results can be transferred to the present situation.

### 1.4 Storage and Shelf Life

RBC concentrates must be stored at 4 ± 2 °C in a suitable refrigerator or in a cold room with continuous temperature control. RBC concentrates should also be transported at temperatures between 1 and 10 °C (cold chain!) [7].

Concerning their shelf life, the user is referred to the manufacturer’s specifications on the product label of the preparation in question.

Within the time frame of licensed storage time, it should not generally be requested to obtain RBC concentrates that were stored only briefly.

Under certain conditions briefly stored RBC concentrates should be applied in preterm infants or neonatal (e.g. replacement transfusions, massive transfusion, extracorporeal lung assist).

### 1.5 Range of Application, Dosage, Mode of Administration

#### 1.5.1 Indications

#### 1.5.1.1 General Principles

It is the therapeutic goal of erythrocyte transfusion to avoid the occurrence of an apparent anemic hypoxia. When considering a rational use of transfusion in case of anemia, due to the unspecific character of clinical symptoms in anemia additional criteria have to be taken into consideration besides the concentration of hemoglobin and/or of hematocrit measured. Among those are above all:

- cause, duration and severity of anemia
- extent and rate of blood loss
- an assessment of the individual physiological ability to compensate the reduced O₂ content in the arterial blood
- pre-existing diseases (e.g. cardiac, vascular, pulmonary) of the patient that might limit his or her ability to compensate in case of acute anemia
- the current clinical state of the patient
- symptoms that might indicate the existence of anemic hypoxia (physiological transfusion triggers)
- the intravascular volume status because in the case of lowered plasma volume (hypovolemia) the erythrocyte deficit is not reliably recognized and high concentrations of hematocrit are determined (see: acute blood loss).

In addition, the results of clinical studies on the correlation between anemia, transfusion of RBC concentrates and the clinical course of a disease must be considered in a rational decision for or against transfusion.

In any patient with acute or chronic anemia, the attending physician must attempt to identify the cause and to employ causal therapy whenever possible. An RBC concentrate transfusion is justifiable only if in all likelihood the health of the patient would be severely compromised by anemic hypoxia without the transfusion and if there is no at least equivalent therapeutic alternative.

A restrictive RBC transfusion practice avoids the exposure to a heterologous blood transfusion and is not associated with an increased mortality risk in most groups of patients [22, 40, 73].

#### 1.5.1.2 Acute Blood Loss

On principle, in the case of acute blood loss the overall oxygen delivery can be compensated without leaving permanent damage, while strictly maintaining normovolemia, with hemoglobin concentrations as low as of around 6 g/dl (3.7 mmol/l) and a hematocrit of 18% by physiologic compensatory mechanisms –

i) increase of cardiac output, ii) increase of oxygen extraction, iii) redistribution of the blood flow favoring heart and CNS – [36, 40, 73]. Clinical symptoms that may indicate anemic hypoxia (physiologic transfusion triggers) at maintained normovolemia and confirmed anemia are listed in table 1.1 [39, 61, 63, 78].
When acute blood loss occurs and when there are signs of hypoxia as well as hemorrhagic shock, the timely RBC transfusion is life-sustaining. In these situations the decision to administer RBC concentrates is made on the basis of hemodynamic parameters and symptoms of anemia as well as by considering the actual and future blood loss.

Patients with normal cardiovascular function generally tolerate isovolumetric drops in hemoglobin concentration to approximately 5 g/dl (hemoglobin 3.1 mmol/l; hematocrit 15%) without clinical signs of a critical decrease of the overall oxygen delivery [36, 77]. At hemoglobin concentrations below 6 g/dl (<3.7 mmol/l) a critical decrease of oxygen delivery that is limited to individual organ systems (e.g. splanchnicus organs) is not safely recognized on the basis of overall indices of oxygen delivery and therefore cannot be ruled out [44]. In case hemoglobin concentration drops below 6 g/dl (3.7 mmol/l), even young and healthy individuals may show ECG alterations [35], have impaired cognitive function and memory [76] as well as subjectively perceive exhaustion and fatigue [65]. These alterations were reversible by increasing hemoglobin concentration beyond 7 g/dl (4.3 mmol/l) or by transiently breathing pure oxygen [75]. The administration of oxygen is therefore recommended as an emergency procedure in cases of acute anemia [75].

Based on clinical observation and taking risk factors into account, a hematocrit value of around 15% (hemoglobin concentration 5.0–4.5 g/dl = 3.1–2.8 mmol/l) has to be assumed as critical threshold value for the absolute indication for substitution with RBC concentrates [10, 68, 77]. It must be taken into account that in hypovolemic patients the hematocrit value may be in the normal range even though the erythrocyte volume is reduced; thus the hematocrit value alone cannot be used as transfusion trigger [66].

Critically ill patients who are monitored and treated in intensive care units may profit regarding morbidity and mortality from restrictive transfusion strategies employing as target values hemoglobin concentrations of between 7 and 9 g/dl [20, 32] (table 1.2).

There are insufficient data regarding patients with cardiovascular diseases, in particular those with an established coronary artery disease, cardiac insufficiency or cerebrovascular

### Table 1.1. Clinical symptoms that may indicate anemic hypoxia (physiologic transfusion triggers) at maintained normovolemia and confirmed anemia

<table>
<thead>
<tr>
<th>Cardiopulmonary symptoms</th>
<th>Tachycardia</th>
<th>Hypotension</th>
<th>Loss of blood pressure of unknown origin</th>
<th>Dyspnoe</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG changes typical of ischemia</td>
<td>Newly occurring ST depression or elevation</td>
<td>Newly occurring rhythm disorder</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Newly occurring regional myocardial contraction disorder in ECG</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Overall indices of an insufficient oxygen delivery
- Increase of overall oxygen extraction >50%
- Drop in oxygen uptake >10% of the initial value
- Drop in mixed venous oxygen saturation <50%
- Drop in mixed venous peripheral oxygen <32 mm Hg
- Drop in central venous oxygen saturation <60%
- Lactate acidosis (lactate >2 mmol/l + acidosis)

### Table 1.2. Recommendations regarding RBC transfusion in acute anemia, taking into account the current hemoglobin concentration, the physiologic capacity to compensate the decreased oxygen content of the blood (capacity to compensate) and the presence of cardiovascular risk factors (risk factors) and clinical symptoms of an apparent anemic hypoxia (physiologic transfusion trigger)

<table>
<thead>
<tr>
<th>Hemoglobin range</th>
<th>Capacity to compensate / risk factors</th>
<th>Transfusion</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤6 g/dl (≤3.7 mmol/l)</td>
<td>–</td>
<td>yes**</td>
<td>1 C+</td>
</tr>
<tr>
<td>&gt;6–8 g/dl (3.7–5.0 mmol/l)</td>
<td>adequate compensation, no risk factors</td>
<td>no</td>
<td>1 C+</td>
</tr>
<tr>
<td></td>
<td>limited compensation, existing risk factors (e.g. coronary artery disease, cardiac insufficiency, cerebrovascular insufficiency)</td>
<td>yes</td>
<td>1 C+</td>
</tr>
<tr>
<td></td>
<td>symptoms of anemic hypoxia (physiologic transfusion trigger*: e.g. tachycardia, hypotension, ECG ischemia, lactacidosis)</td>
<td>yes</td>
<td>2 C</td>
</tr>
<tr>
<td>&gt;8–10 g/dl (5.0–6.2 mmol/l)</td>
<td>symptoms of anemic hypoxia (physiologic transfusion trigger*: e.g. tachycardia, hypotension, ECG ischemia, lactacidosis)</td>
<td>yes</td>
<td>2 C</td>
</tr>
<tr>
<td>&gt;10 g/dl (≥6.2 mmol/l)</td>
<td>–</td>
<td>no***</td>
<td>1 A</td>
</tr>
</tbody>
</table>

*See table 1.1.

**On an individual basis lower hemoglobin values may be tolerated without transfusion provided that there is adequate compensation and no risk factors.

***On an individual basis a transfusion might be indicated to increase hemoglobin values to >10 g/dl.

An individual consideration of criteria like hemoglobin concentration, capacity to compensate and risk factors of a patient is recommended in the decision for or against a transfusion of RBC.

Note:
- Hemoglobin concentration alone is no adequate measurement of oxygen supply.
- In the case of hypovolemia hematocrit does not correctly reflect erythrocyte deficiency.
- Individual factors may require an indication deviating from the recommendations.
transfusion threshold. Despite the currently limited state of knowledge, it can be concluded that hemodynamically stable patients with cardiovascular risks without symptoms of anemic hypoxia (physiologic transfusion trigger), if their hemoglobin concentration value is between 8 and 10 g/dl, do not profit from RBC transfusion in terms of mortality and morbidity [9, 25, 49]. Hemoglobin concentrations of 7–8 g/dl (4.3–5.0 mmol/l, hematocrit 21–24%) are tolerated by stable patients with cardiovascular risks without developing lasting hypoxic damage. A decrease of hemoglobin concentration below 7 g/dl (<4.3 mmol/l, hematocrit <21%) is associated with an increase in morbidity and mortality [6, 10–12, 17, 19–21, 55, 71, 72]. The impact of anemia on the quality of life, on functional capacity as well as on long-term mortality of these high-risk patients was not taken into account in the studies on acute anemia. High-risk patients with cardiovascular diseases and chronic anemia, particularly those with severe cardiac insufficiency, seem to profit from higher hemoglobin concentrations regarding survival, capacity and quality of life [16, 26, 62].

In cases of severe hemorrhage and uncontrolled bleeding (e.g. polytraumatized patient, gastrointestinal bleeding) it might be reasonable in the acute phase to administer, in addition to RBC concentrates, plasma, coagulation products and platelets according to strict regimens [31, 64].

Due to the beneficial effects of higher hematocrit levels on primary hemostasis, hemoglobin concentrations of approximately 10 g/dl (6.2 mmol/l, hematocrit 30%) should be aimed for in cases of massive uncontrolled hemorrhage (e.g. in large-volume and emergency transfusion) [19].

### 1.5.1.3 Chronic Anemias

Patients with chronic anemia (e.g. renal insufficiency, cancer-related anemia) normally undergo long-term adaptation processes that under normal conditions secure tissue oxygenation (e.g. increase of erythrocytic 2,3-DPG and a resultant shift to the right of the oxygen binding curve, increase of the left-ventricular volume as well as of the cardiac output, myocardial hypertrophy). In spite of this, chronic anemia can be detrimental to the clinical course of a disease (e.g. cardiac insufficiency) [16, 26, 29, 33, 62]. An increase of the hemoglobin value may therefore improve both subjective capacity and subjective well-being of the chronic anemia patients concerned as well as reduce the rate of in-patient treatment [14, 16, 26, 59, 62].

The decision to administer RBC concentrates should be based on an assessment of the overall clinical picture, and not on laboratory results alone (hemoglobin, hematocrit, RBC count). If acute blood loss occurs in patients with chronic anemia, the same compensation mechanisms apply as in patients without chronic anemia. Thus pre-existing chronic anemia does not imply that even lower hemoglobin concentrations might be better tolerated. In cases of additional acute decrease of hemoglobin concentration, patients with chronic anemia must be treated according to the same principles as patients without pre-existing chronic anemia.

In chronic anemia patients without cardiovascular disorders, RBC transfusions are not indicated as long as their hemoglobin levels do not fall below 8.0–7.0 g/dl (hematocrit 24–21% = 5.0–4.3 mmol/l) and the anemia does not lead to clinical symptoms.

Patients with chronic anemia due to primary or secondary bone marrow deficiency in whom a future bone marrow/stem cell transplantation cannot be ruled out with certainty should principally receive as few transfusions as possible (see sections 1.5.2 and 1.5.5). The administration of erythropoietin can lower the need for blood transfusion in patients with severe chronic diseases, with malignant diseases or in those who underwent chemotherapy [13, 53, 69]. According to the current state of knowledge, erythropoietin may have a negative impact in patients with malignant diseases, therefore its administration should be limited to patients undergoing chemotherapy [1, 52, 57]. Frequency of administration and dosage are dependent on the origin and severity of the anemia.

Patients with chronic anemia (hematocrit <24–21% and hemoglobin concentrations of <8–7 g/dl (<5.0–4.3 mmol/l) should receive RBC transfusions.

Patients with hemolytic anemia of non-immunological origin should be treated along the same principles as patients with anemias due to hematopoietic disorders.

Certain peculiarities must be considered in substitution treatment of patients with warm-type autoimmune hemolytic anemias (AIHA). The cross-match is often positive due to free autoantibodies in the patient’s serum. However, this serological incompatibility must not preclude the patient from receiving a life-saving transfusion. RBC transfusions together with the appropriate drug therapy can be life-saving in patients with potentially fatal hemolytic crises and very low hemoglobin levels [60]. Accompanying alloantibodies, which may often require difficult and time-consuming diagnostics, should be taken into account.

### 1.5.2 Indications for Special RBC Concentrates

#### 1.5.2.1 Irradiated Leukocyte-Depleted RBC Concentrates

The transfusion of blood products containing viable immunocompetent lymphocytes can lead to graft-versus-host disease (GVHD) in immunocompromized patients (see chapter 11). In the presence of a compatible HLA constellation, especially among blood relatives, GVHD can infrequently occur even in the absence of immunosuppression. In all these cases cell-containing blood products must be irradiated with 30 Gy to reliably prevent GVHD [46] (see section 11.4).
1.5.2.2 Washed RBC Concentrates

The use of washed RBC concentrates is limited to patients in whom rare transfusion-relevant antibodies against IgA or other plasma proteins have been detected, or if severe non-hemolytic transfusion reactions of unknown origin have repeatedly been observed.

1.5.2.3 Cryopreserved RBC Concentrates

Because of their limited availability and demanding storage and handling requirements, cryopreserved RBC concentrates should only be used in patients with complex antibody mixture or with antibodies against high-frequency red blood cell antigens, who cannot be managed otherwise.

1.5.2.4 CMV and Parvovirus B19

The availability of CMV-negative RBC concentrates (RBC concentrates from donors without antibodies against CMV) and of RBC concentrates tested for parvovirus B19 is limited (regarding their indication see chapter 11).

1.5.3 Selection and Dosage of RBC Concentrates

To minimize the potential risks of RBC transfusions, RBC concentrates must be carefully selected on the basis of serological testing and blood grouping. For patients in whom relevant antibodies (anti-D, anti-Kell, etc.) have been detected at any time prior to transfusion, RBC concentrates with erythrocytes lacking the corresponding antigen must always be used, even if the antibody titer has fallen or became undetectable at the time of transfusion. Girls as well as women of reproductive age should not receive RBC concentrates that could lead to immunization against clinically relevant antigens of the Rh system (Rhesus formula) or the Kell factor. Supplementary blood group and antibody testing is performed when indicated.

Immediately prior to transfusion, the ABO identity test (bedside test) is carried out for the recipient by the attending physician or under his or her direct supervision, and the results must be documented in writing [7].

RBC concentrates are transfused according to their ABO identity. In exceptional cases, ABO-dissimilar products, so-called ‘major compatible’ products, may be used for transfusion (see table 1.3). These exceptions must be documented.

Because of the scarcity of RhD-negative blood, it is sometimes impossible to avoid transfusing RhD-positive RBC concentrates to non-immunized RhD-negative patients. Nonetheless, this possibility should be considered only in life-threatening situations (e.g. in emergency and large-volume transfusions) when RhD-negative blood is not available in time and when the patient is a man or a woman of non-reproductive age. RhD-negative RBC concentrates may be transfused to RhD-positive recipients if there is no incompatibility due to Rh antibodies.

RhD-incompatible RBC transfusions must be strictly avoided in RhD-negative girls and in women of reproductive age (except for life-threatening situations). The responsible physician must determine and carefully document in writing the urgency and need for such a transfusion.

In case RhD-positive products were transfused to RhD-negative recipients, a serological follow-up examination should be performed by the subsequently responsible physician 2–4 months after transfusion to determine whether any antibody formation has occurred. On determination of corresponding antibodies, the patient concerned must be informed and receive counsel, and the fact must be documented in an emergency ID card [see section 4.2.5.8 in 7].

If a RhD-negative woman patient of reproductive age has received a transfusion of RhD-positive blood, the development of an immune reaction against the D antigen after a transfusion of RhD-positive erythrocytes can be avoided, after consultation with a clinic specializing in transfusion medicine, by the administration of anti-D immunoglobulin (cumulative dose of up to 20 µg/ml RBC concentrates in multiple partial doses i.v.) [45].

1.5.4 Mode of Administration

The responsible physician must obtain the patient’s informed consent before starting a transfusion [7].

The patient must be adequately monitored during and after the transfusion. After the transfusion, the blood bag with the remaining RBC must be sealed (e.g. through pinching-off) to prevent contamination and stored at 4 ± 2 °C for 24 h [7].

RBC concentrates are generally transfused via a peripheral vein, preferably using a separate venous access. A transfusion set with a standard filter should be used [7].

The transfusion rate has to be adjusted according to the individual needs of the patient. Hypervolemia must be avoided. Severely anemic patients with a stable circulation can receive up to 4 units of RBC (1,000 ml) over a period of 3–4 h if necessary. In patients with cardiac and/or renal failure without bleeding, the transfusion volume per unit of time should be limited to prevent cardiac decompensation.

Warming of chilled RBC concentrates is usually unnecessary. Prior warming of the RBC concentrates is indicated in large-volume transfusions of more than 50 ml RBC per minute, in patients with hypothermia already prior to transfusion, in patients with chronic cold agglutinin disease and high titers of cold antibodies, in patients who develop vasospasms

<table>
<thead>
<tr>
<th>Table 1.3. Blood group compatible RBC transfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient’s blood group</td>
</tr>
<tr>
<td>A</td>
</tr>
<tr>
<td>B</td>
</tr>
<tr>
<td>AB</td>
</tr>
<tr>
<td>O</td>
</tr>
</tbody>
</table>
when given chilled blood and in neonatal transfusions and replacement transfusions [28]. Only equipment certified for blood warming must be used.

Unsealed (‘tapped’) packs of blood components must be transfused within 6 h after opening. It is not permissible to remove blood samples for testing purposes from sealed RBC packs.

It is not allowed to add drugs or solutions for infusion when administering blood products [7].

### 1.5.5 Special Features of RBC Transfusion to Children

#### 1.5.5.1 Indications

In preterm infants, neonates and babies the number and volume of diagnostic blood sampling must be kept to a minimum, because the loss of blood caused by sampling is the most frequent reason for an RBC transfusion at this age [41]. In preterm infants the baseline hematocrit is increased by a delayed sectioning of the umbilical cord and by placing the infant lower than the placenta as well as by a manual drainage of the cord towards the infant [37]. There are only few current reviews and guidelines concerning the specification of indications and/or the determination of optimal RBC dosage [2, 4, 5, 15, 37, 38].

Preterm infants and neonates shall be given RBC concentrates as an acute therapy for a volume deficiency due to loss of blood.

Apart from that the duration and severity of the anemia, the medical history, the biological and the gestational age as well as the clinical state must be taken into account in the decision whether or not to perform an RBC transfusion (table 1.4) [37, 38, 47, 58].

In preterm infants/neonates and babies up to 4 months of age RBC transfusions shall be performed in consideration of the criteria given in table 1.4.

Combined treatment with erythropoietin, oral iron substitution, vitamin B12 and folic acid [18, 19] starting in the first week of life can decrease the need for transfusion in preterm infants [8, 42].

In children from 4 months upwards with acute blood loss and normal cardiovascular function, a decrease of hematocrit down to 20% and of hemoglobin concentration down to 7–6 g/dl (4.3–3.7 mmol/l) can be compensated by volume replacement. The transfusion threshold in children of this age group with unstable circulation is a hematocrit of 30%. Children older than 4 months with chronic anemia but without symptoms can tolerate hemoglobin values of 8–7 g/dl (5.0–4.3 mmol/l, hematocrit 24–21%) without needing treatment.

Specific recommendations arise for RBC transfusion in children from 4 months upwards.

<table>
<thead>
<tr>
<th>Age, days</th>
<th>Mean hematocrit standard value, %</th>
<th>Indication for transfusion hematocrit threshold value</th>
<th>list of indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>56</td>
<td>&lt;40</td>
<td>– mechanical ventilation, oxygen requirement (FiO₂) &gt;0.4</td>
</tr>
<tr>
<td>&lt;15</td>
<td>50</td>
<td>&lt;35</td>
<td>– life-threatening symptoms caused by anemia and/or hypovolemia</td>
</tr>
<tr>
<td>15–28</td>
<td>45</td>
<td>&lt;30</td>
<td>– intended surgical interventions</td>
</tr>
<tr>
<td>&gt;28</td>
<td>40</td>
<td>&lt;25</td>
<td></td>
</tr>
</tbody>
</table>

In children from 4 months upwards an RBC transfusion shall be performed by taking into account the following criteria:

– pre-operative anemia and hematocrit <24%
– loss of ≥ 25% of the blood volume
– symptomatic anemia and hematocrit <24%
– chemotherapy and/or radiation therapy and hematocrit <24%
– severe cardiac or pulmonary diseases and hematocrit <40%
– symptomatic sickle cell anemia or other hereditary anemias.

In children with cancer receiving chemotherapy, a weekly administration of erythropoietin can considerably lower the need for transfusion [56].

A recent randomized study of critically ill children could show that a restrictive transfusion strategy with a hemoglobin concentration threshold of 7.0 g/dl (4.3 mmol/l, hematocrit 21%) can significantly decrease transfusion requirements compared to a liberal transfusion strategy without increasing adverse outcomes. This is not applicable to preterm infants and children with hypoxemia, hemodynamic instability, active blood loss, or cyanotic heart disease [32].
1.5.5.2 Dosage

The normal volume of transfusion in children, especially in preterm infants and neonates, is 5–15 ml/kg body weight [58]. Higher dosage is required in hypovolemic shock, replacement transfusions, and surgery with extracorporeal circulation. An administration of 3 ml RBC/kg body weight increases hemoglobin concentration by approximately 1 g/dl (0.6 mmol/l).

Transfusion volume can be calculated as follows:

\[
\text{Transfusion volume (ml RBC)} = \frac{(\text{target value hemocrit}) - \text{actual hemocrit}}{\text{hemocrit of RBC (55–65)}} \times \text{blood volume (1)}
\]

Blood volume in neonates: approximately 90 ml/kg body weight.

Blood volume in older children: approximately 80 ml/kg body weight.

1.5.6 Contraindications and Restricted Application

Absolute contraindications are unknown.

Note: Potential bone marrow or stem cell recipients should never be given RBC concentrates from the transplant donor or her/his close relatives prior to the transplantation.

1.6 Adverse Reactions

See chapter 11.

1.7 Documentation

According to article 14 German Transfusion Law (Transfusionsgesetz; TFG), there is an obligation to perform a patient-as well as a product-related batch documentation for RBC concentrates.

For the particulars of documentation and quality management, see German Guide by the GMA for hemotherapy.

1.8 References


