

## TRIP Definitions of Transfusion reactions (February 2008 version)

### **Non-hemolytic transfusion reaction (NHTR)**

Rise in temperature of  $\geq 2^{\circ}\text{C}$  (with or without rigors) during or in the first two hours after a transfusion, OR rigors in the same period, without other relevant symptoms or signs; normalization within 24 hours of transfusion.

Investigations: 1,2,3,4 all negative and there is no other likely explanation.

### **Mild non-hemolytic febrile reaction**

Rise in temp.  $>1^{\circ}\text{C}$  ( $<2^{\circ}\text{C}$ ) during or in the first two hours after a transfusion with no other relevant symptoms or signs; *optional reporting to TRIP*

Investigations: 1, 2,3,4 all negative if done and there is no other likely explanation.

### **Acute hemolytic transfusion reaction**

Increased destruction of red blood cells within a few minutes of starting to 24 hours after a transfusion with signs such as: fall in blood pressure  $\geq 20$  mm Hg systolic and/or diastolic, rise in temperature /rigors, nausea /vomiting, backache, dark or red urine, ool or no Hb increment or unexpected drop in Hb.

Investigations: 2 positive; 3 may be positive, 4 negative

### **Delayed hemolytic transfusion reaction**

Symptoms / signs of increased destruction of red blood cells occurring any time from 24 hours to 28 days after a transfusion: unexplained fall in hemoglobin, dark or red urine, rise in temperature / rigors.

Investigations: 2 and 3 positive, 4 may be done if clinically relevant.

**If new antibodies are found without biochemical confirmation of hemolysis, report as 'new allo-antibodies'**

### **TRALI (transfusion-related acute lung injury)**

Symptoms / signs of acute lung injury such as dyspnoea and hypoxia, occurring within 6 hours of a transfusion, with bilateral fine patchy shadowing on the chest X-ray

Investigations: 2,3,4 all negative

Investigation 5: chest X-ray consistent with TRALI (immune-mediated or non-immune).

### **Transfusion-associated circulatory overload (TACO)**

Symptoms / signs of circulatory overload such as dyspnoea, orthopnoea, cyanosis, tachycardia  $>100/\text{min.}$  or raised central venous pressure within six hours of transfusion.

Investigation 5 (chest X-ray) consistent with TACO

### **Anaphylactic reaction**

Rapidly developing reaction occurring within a few seconds to soon after the end of transfusion, with features such as in- and expiratory stridor, fall in blood pressure  $\geq 20$ mm Hg systolic and/or diastolic, nausea or vomiting or diarrhoea, backache, skin rash.

Investigations: 2,3,4 all negative, investigation 6 may be positive.

### **Other allergic reaction**

Allergic phenomena such as itching, redness or urticaria but without respiratory, cardiovascular or gastrointestinal features, arising from a few minutes of starting transfusion till a few hours after its completion.

Investigations: 2,3,4 all negative if done

**Development of new antibody against blood cell antigens**

After a transfusion, demonstration of clinically significant antibodies against blood cells (irregular antibodies, HLA antibodies or HPA antibodies) which were previously absent (as far as is known in that hospital).

**Post-transfusion bacteremia/sepsis**

Clinical features of bacteremia / sepsis during, soon after or a longer time after a transfusion, with a relevant positive blood culture in the patient and sometimes with confirmation of a causal link with a transfused blood component.

Investigations: 4 positive

**Post-transfusion viral infection**

Any viral infection which can be related to a transfused blood component, with typing of the virus and demonstration of identical strains in the recipient and the donor or (related) blood component and with no other likely source of infection.

**Hemosiderosis**

Iron overload resulting from frequent transfusions, with a ferritin level of 1000 microgrammes or more, with or without organ damage.

**Post-transfusional purpura (PTP)**

Serious self-limiting thrombocytopenia possibly with bleeding manifestations 1-24 days after transfusion of a red cell or platelet concentrate.

Investigations: HPA antibodies and HPA typing of the patient

**Transfusion-associated graft versus host disease (TA-GVHD)**

Clinical features of graft versus host disease such as erythema which starts centrally, watery diarrhoea, fever and rise in liver enzymes 1-6 weeks (usually 8-10 days) after transfusion of a T-cell containing (non-irradiated) blood component.

Diagnosis can be supported by skin biopsy (and liver biopsy)

**Other transfusion reaction**

Transfusion reactions which do not fit in one of the above categories.

**Incorrect blood component transfused (IBCT)**

All cases where the patient is transfused with a blood component which did not meet all the requirements for a suitable transfusion for that patient, or that was intended for another patient.

TRIP requests reporting of these incidents, even if there are no consequences for the patient. Please indicate where the error arose, any further errors or failed checks, and how the error was discovered.

**Positive bacteria screening**

Any case where the blood service finds an initial positive result on a blood component but bacterial contamination is not confirmed on culturing the material or another component derived from the same donation(s). (*optional reporting to TRIP*).

**Bacterially contaminated blood component**

Using aseptic sampling and appropriate laboratory methods, demonstrating a relevant quantity of bacteria in a (remnant of a) blood component, material used for bacteria screening of platelets or a blood component derived from the same donation as a unit with an initial positive screening result; preferably with confirmatory typing of the bacterial strain.

**Look back**

Information from the blood service concerning a possibly contaminated donation, where the recipient is tested and is found not to have the infection in question.

**Virally contaminated blood component**

Any case where subsequent additional laboratory testing demonstrates viral contamination in a blood component which previously screened negative and has been transfused'.

**Near miss**

Any mistake or error which, if undetected, could have led to a wrong blood group result or to issuance or administration of a wrong blood component, and which was detected before transfusion (*optional reporting to TRIP*).

Please indicate where the error arose, any further errors or failed checks, and how the error was discovered.

**Hemolysed product**

Occurrence of clinical signs / symptoms in a patient associated with the presence of free hemoglobin in a transfused product (from recovered blood)

**Heparinisation**

Clotting problems associated with incomplete removal of added heparin during automated blood recovery method

**Other incident**

Errors / incidents in the transfusion chain which do not fit in the above categories, for instance patient transfused whereas the blood was supposed to be kept in reserve, transfused unnecessarily on the basis of a wrong Hb result or avoidable loss of a blood component.

**IMPORTANT**

When reporting an incident please indicate (if known) during which step or procedure the first error occurred; additional errors or failed checks; explain how the incident was discovered and what the consequences for the patient were.

## Recommended testing

### 1. Exclude administrative error

Check correct identification of patient (at the bedside)

Check correct bag

Check identification of patient at collection of blood sample(s) and check identification of sample tubes

Check correct selection of blood component

### 2. Hemolysis testing (biochemistry)

Examine plasma colour + urine colour

Hemolysis:

after 24 to 48h LDH 1,5x baseline value or 1,5x upper limit of normal

bilirubin (unconj.) 1,5x baseline value or 1,5x upper limit of normal

haptoglobin reduced

### 3. Blood group serology investigations after transfusion reaction

Repeat ABO and Rhesus D blood group, antibody screening using indirect antiglobulin test, direct antiglobulin test (look for mixed field) and full cross-match using patient samples from before and after transfusion.

(If applicable) antibody identification, in any case exclusion of other antibodies (CBO recommendations) before and after transfusion.

Check ABO and Rhesus D blood group and direct antiglobulin test on all donor erythrocytes administered before or during the transfusion reaction.

If hemolysis shown biochemically, test eluate with sensitive technique (even if DAT is negative). Type patient for the antigen against which antibody has been found (look for mixed field); type donor blood for the antigen against which antibody has been found.

If hemolysis has been confirmed biochemically but above tests are negative, consult reference laboratory.

### 4. Bacteriological investigation

Take blood cultures (aerobic/anaerobic) from patient.

Take cultures (anaerobic/anaerobic) from remnant of unit and all blood products administered before or during the transfusion reaction.

If the same bacteria are found in the patient as in the bag (providing this has been appropriately taken down and conserved) contamination is 'certain'; preferably further testing will be carried out to confirm identity of the strains.

### 5. Investigation in patient with difficulty in breathing/suspicion of TRALI

Chest X-ray TRALI: bilateral patchy appearance

Circulatory overload: enlarged heart, Kerley B lines, lung oedema

Exclude other pathology

Further investigations if clinical picture and X-ray appearances fit TRALI: HLA- and granulocyte antibodies in donor(s) and patient in concert with Sanquin Bloedbank -> subclassification

Immune mediated

Non-immune (idiopathic).

### 6. Further investigation following anaphylactic reaction

Titre of IgA and anti-IgA; consider IgA subclass investigation if total IgA normal.

## Severity of a reaction

Assessment of the severity is separate from the rating of imputability.

Example: Patient is admitted from day care unit because of fever and features suggesting infection which arose during transfusion. Patient recovers completely. Severity = grade 2; time course, results of investigations and presence or absence of other possible causes will be considered in judging whether there is a link with transfusion.

<b>Grade 0</b>	no morbidity (no symptoms); applicable when a reaction is detected only through laboratory investigation.
<b>Grade 1</b>	minor morbidity, not life-threatening
<b>Grade 2</b>	moderate to serious morbidity, may or may not be life-threatening; also any case necessitating hospitalisation, where illness and/or hospitalization is prolonged and/or where chronic invalidity or functional impairment ensues.
<b>Grade 3</b>	serious morbidity with immediate threat to life.
<b>Grade 4</b>	death as outcome after a transfusion reaction.

## Imputability

**Assessment of the relation to the blood transfusion**  
(not applicable for reports of errors without clinical consequences)

<b>Certain</b>	<b>(tekst uit EU RL)</b>
<b>Probable</b>	
<b>Possible</b>	
<b>Unlikely</b>	
<b>Excluded</b>	
<b>Not yet known:</b>	Further investigations under way, reassessment when results available.

### Imputability assessment tool

Clinical features during/after transfusion (starting score)	= +1
Add: Appropriate time course appropriate for the suspected reaction	= +1
Appropriate findings in investigations (see descriptions)	= +1
Other causes excluded	= +1
Demonstration of a probable alternative explanation	= -1

Total score gives the imputability:

<b>Certain</b>	score 4
<b>Probable</b>	score 3
<b>Possible</b>	score 2
<b>Unlikely</b>	score 1
<b>Excluded:</b>	Another cause has been conclusively demonstrated.