



International Society
of Blood Transfusion



International
Haemovigilance
Network



Advancing Transfusion and
Cellular Therapies Worldwide

Standard for Surveillance of Complications Related to Blood Donation

*Working Group on Donor Vigilance
of the
International Society of Blood Transfusion
Working Party on Haemovigilance*

in collaboration with

*The International Haemovigilance Network
The AABB Donor Haemovigilance Working Group*

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These definitions have been formally endorsed by
The European Blood Alliance



European Blood Alliance

Introduction to the 2014 revised classification

Complications related to blood donations are adverse reactions and events with a temporal relation to a blood donation. Longer term complications associated with donation, such as iron deficiency, are not all captured in this donor vigilance scheme.

The 2008 ISBT standard for surveillance of complications related to blood donation introduced a classification with descriptions of types of complications. Two problems were noted with the definitions:

1. Descriptions were not sufficiently specific to permit standard classification and comparison of different donor surveillance programs.
2. Definitions were difficult to apply because they required information not easily obtainable in many countries.

A revision group was convened in 2013 to review the 2008 definitions and propose modifications.

The goals of this revised classification system are:

1. Provide simple definitions that are easy to apply in a standardised way.
2. Provide minimal requirements for international comparison that meet the needs of a basic surveillance program.
3. Provide additional attributes that may be collected nationally if possible. This additional information may be important for process improvement by the blood centre, or lead to relevant research in donor reactions. Comparisons may be made internationally by those blood centres that are able to collect this information.
4. Align definitions with those used in the AABB Donor Hemovigilance System, to permit comparisons and entry of data into an adapted version of the donorHART software.

The revisions to the 2008 document have been made with these goals in mind.

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Definitions of adverse events

A. Complications mainly with local symptoms

These complications are directly caused by the insertion of the needle. Some of these are mainly characterized by occurrence of blood outside vessels, whereas others are mainly characterized by pain.

A 1. Complications mainly characterized by the occurrence of blood outside the vessels.

Haematoma (bruise)

Definition: A haematoma is an accumulation of blood in the tissues outside the vessels.

Mechanism: The symptoms are caused by blood flowing out of damaged vessels and accumulating in the soft tissues. For apheresis procedures, haematomas may also be caused by infiltration of the soft tissues by red cells during the return phase of the procedure. Large haematomas, particularly those in deeper layers of the forearm, put pressure on surrounding tissues and may contribute to other complications such as nerve irritation and injury and more rarely compartment syndrome.

Signs and symptoms: Bruising, discolouration, swelling and local pain. Accumulation of blood in deeper tissues may result in more serious pain and pressure syndromes listed below.

Arterial puncture

Definition: Arterial puncture is a puncture of the brachial artery or of one of its branches by the needle used for bleeding the donor.

Mechanism: Because of the rapid blood flow, the risk of a large haematoma is increased and thereby risks of more serious pain and pressure syndromes listed below.

Signs and symptoms: A lighter red colour than usual of the collected blood can be seen. The needle and tubing may appear to pulsate; the blood bag fills very quickly. There may be weak pain localized to the elbow region.

Delayed bleeding (re-bleeding) - optional category

Definition: *Leakage of blood from the venipuncture site after the initial bleeding has stopped.*

Mechanism: *Re-bleeding may be related to pressure not being applied to the correct location or for an adequate duration, or premature removal of the bandage. After the donor has left the clinic, re-bleeding may be related to heavy lifting or strain to the donor's arm. Donors on certain medications, such as autologous donors on anticoagulants, may be at higher risk to re-bleed.*

Signs and symptoms: *Spontaneous recommencement of bleeding from the venipuncture site, after pressure has been applied and the initial dressing has been removed, or leaking through the dressing.*

A 2. Complications mainly characterized by pain

Nerve injury/irritation

Definition: Injury or irritation of a nerve

Mechanism: A nerve may be hit directly by the needle at insertion or withdrawal, or there may be pressure on a nerve due to a haematoma or inflammation of the soft tissues. Include medically diagnosed cases, as well as cases reported on the basis of documented 'nerve' type symptoms.

Signs and symptoms: Radiating, often 'electrical' sharp pain moving away from the venepuncture site, and/or paraesthesias such as tingling, burning sensations in the hand, wrist or shoulder area but away from the venepuncture site. Symptoms may arise immediately when the needle is inserted or withdrawn. In cases associated with a haematoma, pain may not be apparent at the time and may start when the haematoma has reached a sufficient size, some time after insertion of the needle. Symptoms may be worse in certain positions or with certain arm motions. Rarely, weakness of the arm may develop.

Optional split by duration of symptoms:

Symptoms resolving within 12 months: Symptoms usually resolve within days, but rarely may persist for months or become permanent.

Symptoms lasting more than 12 months.

Other Painful arm – optional category

Definition: Pain in the arm is the primary symptom, without the characteristics of nerve irritation outlined above, or the presence of a large hematoma or other defined complications that may be painful.

Mechanism: Pain may be related to tissue injury, possibly due to hematoma in the deeper tissues.

Signs and symptoms: Pain in the arm, without characteristics of nerve irritation. May be described as an ache or heaviness in the arm, similar to that experienced after vaccination. Include all cases where arm pain is the main symptom, unless a diagnosis of nerve injury/irritation is suspected in the presence of nerve type symptoms recognised by trained staff.

A 3. Localised infection/inflammation

Localised infection/inflammation

Definition: Inflammation along the course of a vein, which may progress to localised infection several days after phlebotomy. There may be clotting in the vein.

Mechanism: Tissue damage and introduction of surface bacteria into the deeper tissues with venepuncture. The superficial vein itself (thrombophlebitis) or the surrounding subcutaneous tissue (cellulitis) may be predominantly affected.

Signs and symptoms: Warmth, tenderness, local pain, redness and swelling at the site of phlebotomy. The site and the vein may feel tender, firm, and warm to the touch. Fever may be present.

Optional split into 2 categories:

Thrombophlebitis: *The redness, swelling, and tenderness extend along the course of the vein.*

Cellulitis: *The redness, swelling and tenderness affect the soft tissues, and are not localised to the course of the vein.*

A 4. Other major blood vessel injury

These rare, serious conditions must always be medically diagnosed.

Deep venous thrombosis (DVT)

Definition: Thrombosis of a deep vein in the donor's phlebotomy arm.

Mechanism: Superficial venous thrombosis may progress into the deeper veins of the donor's arm. DVT may also rarely occur without previous signs and symptoms of superficial thrombosis. An additional risk factor for thrombosis, in particular, the use of oral contraceptives, may be present in these donors.

Symptoms and signs: Swelling and pain in the upper arm. May be accompanied by symptoms of superficial inflammation and thrombosis (see above).

Arteriovenous fistula

Definition: Acquired connection between the vein and artery due to venepuncture lacerations.

Mechanism: A channel forms between the lacerated vein and artery immediately post-venepuncture, or in the healing process. May be related to arterial puncture.

Signs and symptoms: Pulsating mass with a palpable thrill and associated bruit. The affected area may be warm, and the distal part of the arm may be cool if significant shunting of blood is present. The distal veins may be dilated and may pulsate.

Compartment syndrome

Definition: Increased intracompartment pressure leading to muscle and soft tissue necrosis.

Mechanism: Blood may accumulate in the frontal deep areas of the forearm, closing small blood vessels and resulting in muscle and nerve tissue necrosis. May be related to arterial puncture.

Signs and symptoms: Painful arm, particularly on movement; swelling, paresthesias and partial paralysis.

Brachial artery pseudoaneurysm

Definition: Collection of blood outside an artery, contained by adventitia or the surrounding tissues alone.

Mechanism: After a traumatic arterial puncture, blood may leak out of the artery and accumulate in the surrounding space.

Signs and symptoms: Pulsating mass in the arm. May be accompanied by pain and paraesthesias. May be preceded by a large hematoma following arterial puncture.

B. Complications mainly with generalized symptoms: vasovagal reactions

Definition: A vasovagal reaction (VVR) is a general feeling of discomfort and weakness with anxiety, dizziness and nausea, which may progress to loss of consciousness (faint). It is the most common acute complication related to blood donation.

Mechanisms: Both physiologic and psychological factors may be important. The reaction is generated by the autonomic nervous system and further stimulated by psychological factors and the volume of blood removed, relative to the donor's total blood volume.

Signs and symptoms: Usually several of the following: discomfort, weakness, anxiety, light-headedness/dizziness, nausea, chills, sweating, vomiting, pallor, hyperventilation, rapid or a slow pulse. Hypotension and loss of consciousness (LOC) may occur and can be accompanied by loss of bladder or bowel control or convulsive movements. Reactions may occur before phlebotomy (rare), during phlebotomy or immediately after phlebotomy, when the donor stands up, in the refreshment area, or after the donor has left the collection site. Most reactions occur within 12 hours of phlebotomy. Reactions accompanied by LOC carry a risk of injury, particularly if they occur once the donor has left the collection site (delayed vasovagal reactions).

Vasovagal reactions are divided in two main subgroups:

Without loss of consciousness (LOC) - the donor does not faint

With loss of consciousness (LOC) - the donor faints for a period of time

Optional subdivision for donors with LOC:

LOC < 60 seconds - without other signs and symptoms

LOC ≥ 60 seconds - or with complications of convulsive movements, urinary or faecal incontinence

Optional subdivision:

With injury - Injury caused by falls or accidents in donors with a vasovagal reaction

Without injury

Optional subdivision:

Location of reaction:

On collection facility* - Symptoms occurred before donor has left the donation site

Outside collection facility - Symptoms occurred after donor has left the donation site

*in area within which staff can observe the donor and be responsible for the care of donors with complications

C. Complications related to apheresis

Citrate reaction

Definition: Neuromuscular hyperactivity related to reduced ionized calcium levels.

Mechanism: Infusion of citrate anticoagulant during apheresis causes a fall in ionised calcium levels, leading to neuromuscular hyperactivity. If untreated, symptoms may progress to tetany and severe cardiac arrhythmias, including cardiac arrest. Operator error with mix up of saline and citrate bags may occur with some apheresis equipment, and lead to rapid citrate infusion.

Symptoms and signs: Numbness or tingling of lips, feelings of vibrations, numbness or tingling in the fingers, metallic taste, chills, shivering, light-headedness, feeling of tightness, muscle twitching, rapid or slow pulse, shortness of breath.

Symptoms may progress to carpopedal spasms and vomiting, and in severe reactions, to generalised muscle contractions (tetany), shock, irregular pulse and cardiac arrest.

Haemolysis

Definition: Donor red cells may be damaged, releasing haemoglobin.

Mechanism: There may be malfunctioning valves, kinks or obstruction of the tubing, incorrect installation of equipment, or other equipment failures affecting the extracorporeal circuit. Incompatible replacement fluids, such as dextrose D5W, may be used in error.

Signs and symptoms: Pink or red plasma, blood in lines or filter may appear dark. The donor may notice pink or red urine after collection.

Air embolism

Definition: Air bubble introduced into the donor's circulation.

Mechanism: Air may enter into the lines due to incomplete priming of lines, as a result of a machine malfunction or defective collection kits or through incorrect manipulation by staff. Air in the donor's pulmonary circulation may occlude the pulmonary arteries in the lung and cause cardiopulmonary symptoms. Air may pass to the arterial circulation through an atrial septal defect, and reduce blood flow to the brain.

Signs and symptoms: Bubbling sound or feeling at the venipuncture site. Cough, dyspnea, apprehension, sweating, chest pain, confusion, tachycardia, hypotension, nausea and vomiting.

Optional category: Infiltration

Definition: *Intravenous solute (saline solution) enters the extravascular tissues during volume replacement (generally only applicable to double red cell procedures).*

Mechanism: *The needle is no longer positioned in the intravascular space, so fluids enter the surrounding tissues.*

Signs and symptoms: *Swelling of the tissues at the venipuncture site.*

D. Allergic reactions

Allergy (local)

Definition: Red or irritated skin at the venipuncture site.

Mechanism: Reaction caused by allergens or irritants in solutions used for disinfection of the arm (such as iodine or chlorhexidine) or in manufacture of the collection set. Irritation may also occur due to application of the adhesive bandage (bandage adhesive dermatitis). An allergic reaction to latex that may be in supplies such as gloves may also occur.

Signs and symptoms: Itching and redness at the venepuncture site, the bandage site, or the entire skin disinfection area. In a true allergic reaction, there may be a raised rash or hives in these areas that may expand to cover a larger area of the arm. The reaction may occur soon after donation or in the hours to days post-donation.

Generalised allergic reaction (anaphylactic reaction)

Definition: Anaphylactic type reactions usually starting soon after the procedure is begun and may progress rapidly to cardiac arrest.

Mechanism: Extremely rare reactions, attributed to donor sensitivity to ethylene oxide gas used to sterilize some collection kits.

Signs and symptoms: Apprehension, anxiousness, flushing, swelling of eyes, lips or tongue, cyanosis, cough, wheezing, dyspnea, chest tightness, cramps, nausea, vomiting, diarrhoea, tachycardia, hypotension, and altered mentation.

E. Other serious complications related to blood donation

Major cardiovascular event (MCE)

Acute cardiac symptoms (other than myocardial infarction or cardiac arrest).

Myocardial infarction

Cardiac arrest

Transient Ischemic Attack

Cerebrovascular accident

Death

Reporting is encouraged of MCE or death from any cause up to 24 hours after donation, with an assessment of imputability. Only cases with definite, probable or possible imputability should be included in international reporting. Major cardiovascular events, including death, may occur in the hours after attending the collection centre for blood donation. This can occur without any relation to the donation (for deaths, this is described by the term actuarial deaths).

F. Other complications

Other systemic reactions or complications that do not fit into the above, such as chest pain that may have been investigated as angina, but was actually musculoskeletal, or transmission of infection to a donor through erroneous re-use of equipment.

Grading of complication severity and imputability

Grading of severity - optional

Life-threatening complications and long-term disability are thankfully extremely rare after blood donation. Grading of severity for donor reactions does not easily fit into grading systems used for adverse reactions in patients. Use of this grading system is therefore optional. The criteria for classification of a reaction as serious (severe) as derived from these systems are:

<i>Hospitalization:</i>	<i>If it was attributable to the complication. The criterion of hospital admission is applicable if a donor is kept in hospital overnight. Cases where a donor is seen, examined, and in some cases given treatment (e.g. suturing, IV fluids, treatment of a fracture) but discharged home are not automatically classified as serious.</i>
<i>Intervention:</i>	<i>To preclude permanent damage or impairment of a body function or to prevent death (life- threatening)</i>
<i>Symptoms:</i>	<i>Causing significant disability or incapacity following a complication of blood donation and persisted for more than a year after the donation (Long term morbidity)</i>
<i>Death:</i>	<i>If it follows a complication of blood donation and the death was possibly, probably or definitely related to the donation.</i>

Types and definitions of reactions:

Certain complications of donation are by their nature mild or severe.

Local reactions - Most local reactions (hematoma, arm pain syndromes) would not be considered severe. Severe consequences are separate reaction types: deep venous thrombosis, arteriovenous fistula, and compartment syndrome.

Nerve injury may rarely result in long term donor signs and symptoms. This may be captured by the duration of symptoms (optional split in nerve pain category).

Systemic reactions - Vasovagal reactions are characterised as those with or without LOC. There are two optional additional characteristics: LOC can be characterised as having additional symptoms (convulsions, loss of bowel or bladder control and/or duration of ≥ 60 seconds). Reactions can be categorised as resulting in injury or not.

Complications that are by their nature severe include generalised allergic (anaphylactic) reactions, and all major cardiovascular events.

Grading of imputability

The strength of relation between donation and complication is:

Definite or certain:	When there is conclusive evidence beyond reasonable doubt for the relation.
Probable or likely:	When the evidence is clearly in favor of a relation.

- Possible: When the evidence is indeterminate for attributing the complication to the donation or an alternative cause.
- Unlikely or doubtful: When the evidence is clearly in favor of attributing the complication to other causes.
- Excluded: When there is conclusive evidence beyond reasonable doubt that the complication can be attributed to causes other than the donation.

Imputability should only be reported for cardiovascular events leading to hospitalization or death post-donation, and only cases with imputability of possible, probable or definite should be captured.

Appendix 1 Summary table, complications of donation

Optional categories or attributes are shown in *italics and underlined*

A. Local Symptoms

A1 Blood outside vessel

- Haematoma
- Arterial puncture
- Delayed bleeding

A2 Arm pain

- Nerve injury/irritation
 - duration < 12 months
 - duration > 12 months
- Other arm pain

A3 Localized infection/inflammation of vein or soft tissues

- Superficial thrombophlebitis
- Cellulitis

A4 Other major blood vessel injury

- Deep Venous Thrombosis (DVT)
- Arteriovenous fistula
- Compartment syndrome
- Brachial artery pseudoaneurysm

B. Generalized symptoms – Vasovagal Reactions

- Vasovagal Reaction, no loss of consciousness (LOC)
- Vasovagal Reaction, loss of consciousness
 - < 60 seconds, no complications
 - ≥ 60 seconds, and/or convulsions or incontinence
- With injury
- Without injury
- On collection site
- Off collection site

C. Related to apheresis

- Citrate reactions
- Haemolysis
- Air embolism
- Infiltration

D. Allergic reactions

- Local allergic reaction
- Generalized (anaphylactic) reaction

E. Other serious complications

- Acute cardiac symptoms (other than myocardial infarction or cardiac arrest).
- Myocardial infarction
- Cardiac arrest
- Transient Ischemic Attack (TIA)
- Cerebrovascular accident
- Death

F. Other

For A-F, optional separate reporting of reactions classified as serious according to standard criteria (life-threatening or leading to hospitalisation, incapacity, chronic morbidity or death).

Appendix 2 Recommended numerator and denominator data and basic information to report

Numerator data about each reaction

1. Type of donation

- a. Whole blood
 - i. *Allogeneic (optional)*
 - ii. *Autologous (optional)*
- b. Apheresis
 - i. *RBC with or without concurrent collection of plasma and/or platelets (optional)*
 - ii. *Platelets with or without concurrent collection of plasma (optional)*
 - iii. *Plasma only (optional)*

2. Gender of donor

3. First-time vs repeat donor

Age group of donors (optional): 16-18, 19-22, 23-29, 30-69, 70 and over

4. Type of complication

Denominator data about all donors

1. Total donations (who proceeded to phlebotomy) by type of donation per calendar year

- a. Whole blood
 - i. *Allogeneic (optional)*
 - ii. *Autologous (optional)*
- b. Apheresis
 - i. *RBC with or without concurrent collection of plasma and/or platelets (optional)*
 - ii. *Platelets with or without concurrent collection of plasma (optional)*
 - iii. *Plasma only (optional)*

2. All of the above by

- a. Gender of donor
- b. First-time vs repeat donors
Age group of donors (optional): 16-18, 19-22, 23-29, 30-69, 70 and over

3. Total number of donors per calendar year (optional)

- a. *By type of donations as above*
- b. *By gender*
- c. *By first-time vs repeat*
- d. *By age group*

Basic information to report

1. Age criteria for donor eligibility (state for whole blood and apheresis)

- a. Minimum
- b. Maximum

2. **Volume of bags for whole blood collection** (may split whole blood denominator into two if very different sizes used, for example 250 ml vs. 450 or 500 ml)
3. **Minimum Estimated Blood Volume criterion (if any)**
 - a. All donors
 - b. Subset of donors
4. **Minimum weight criteria (state for whole blood and apheresis)**
5. **Methods of data capture**
 - a. On site only
 - b. On site and when donors call back
 - c. On site and when donors call back and question on record of donation (if possible, do not use information from routine questioning of donors on record of donation for statistics for international comparisons)
6. **Scope of vigilance system**
 - a. All reactions
 - b. Moderate and severe reactions
 - c. Severe reactions only