BIOMÉRIEUX

PLATELET SAFETY

Impact, Prevention & Control of Bacterial Contamination

PIONEERING DIAGNOSTICS

CONTENTS

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INTRODUCTION

Transmission of bacteria in blood components is a serious threat to patient safety. Before the practice of routine bacterial culturing of platelets for transfusion was implemented, transmission of bacteria in blood components was the highest risk of transfusion-transmitted infectious disease.

Bacterial contamination of platelets is one of the leading causes of morbidity and mortality associated with transfusion.[1] Therefore, pre-transfusion detection of contamination in platelet units is an important safety measure.[2]

Near the end of the twentieth century, astounding progress was made in the reduction of viral risk (e.g., HIV, Hepatitis B and C) from allogeneic blood transfusion.[3] For example, HIV transmission was reduced from a 1 in 100 risk per unit transfused to approximately 1 in 2 million. Given the reduction in the viral risk, at the end of the 20th century, transfusion-transmitted bacterial infections and the resulting septic transfusion reactions have emerged as the greatest threat of transfusion-transmitted disease and the leading cause of transfusion-related fatalities.[4]

This practical booklet is intended to be a useful reference tool for blood bank and transfusion services professionals involved in the preparation of platelet concentrates, and the prevention and detection of bacterial contamination.

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Platelets are smaller than red and white blood cells. They play a role in blood coagulation and wound healing. When a blood vessel ruptures, platelets combine with fibrin to form a clot.

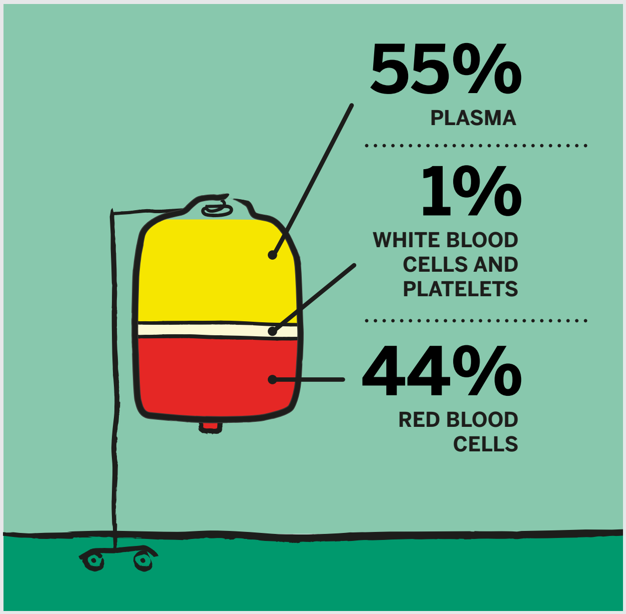


Illustration adapted from https://www.hema-quebec.qc.ca/sang/savoir-plus/composants.en.html

For easy reading and reference, look for the colored boxes highlighting the key points in each chapter.

1 WHAT ARE PLATELETS FOR TRANSFUSION?

Platelets are small cell fragments produced from the cytoplasm of large precursor cells (megakaryocytes) found in the bone marrow. These cell fragments circulate in the blood stream and assist the body to form clots and stop bleeding.

The goal of platelet transfusions is to stop or prevent bleeding in thrombocytopenic patients (patients with low platelet counts) and patients whose platelets do not function properly (e.g. as a consequence of drug exposure, chronic disease, or congenital abnormality). Thrombocytopenia (platelet counts less than the normal range of 150,000 to 450,000 platelets per microliter of blood) requiring transfusion is most commonly seen in cancer patients receiving therapy.

Platelets are collected from healthy blood donors through either:

- a **whole blood donation** which is typically separated into red cells, platelet and plasma products,
- or a donor who is connected to an **apheresis machine** which "skims" the platelets from the blood.

The platelet products are collected in a plastic, gas-permeable, storage bag and suspended in either plasma or a combination of plasma and a platelet additive solution. The platelets are then stored at room temperature until transfused or until expiration.

While most contaminating bacteria fail to grow in the collected components or in the recipient, some do and may cause severe, sometimes fatal infection.

Platelets are particularly prone to contamination since they are stored at room temperature.[22] Therefore, routine testing for bacterial contamination is important to detect those units that are contaminated and could potentially cause harm to transfused patients.

2 THE IMPACT OF BACTERIAL CONTAMINATION OF PLATELETS

Each year, about 10 million platelet transfusions are administered to patients worldwide with marked differences in usage between regions depending on the socio-economic development of the countries.[5]

In the United States, approximately 2.4 million dose-equivalent platelet units are distributed and 2 million transfused annually. The 2015 National Blood Collection and Utilization Survey revealed that platelet products in the U.S. were either obtained by apheresis (92%), or derived from whole blood (8%).[6] This equates to approximately one platelet product being transfused every 10.5 seconds in the United States.[7]

A therapeutic dose of platelets typically contains 3 x 10^{11} platelets. An apheresis donation can result in 1-3 therapeutic doses. Whole blood-derived platelets are typically transfused as a pool of 4-6 individual units.

Plasma and red cell products are stored refrigerated (1-6°C) or frozen. Platelet products are stored at **room temperature (20-24°C)** to maintain their ability to circulate; however, such a temperature range provides optimal conditions for bacterial proliferation for a wide variety of organisms. Prior to the introduction of methods to minimize bacterial contamination (diversion and detection), multiple aerobic culture surveillance studies found that **1-2 per 1000 platelet products were bacterially contaminated**.[4]

Cancer patients are the patients who receive the most platelets. However, because of their therapy, they are immunosuppressed and therefore the least able to handle a bacterial infection.[8] **Minimizing bacterial contamination of platelets is particularly critical for this patient population.**

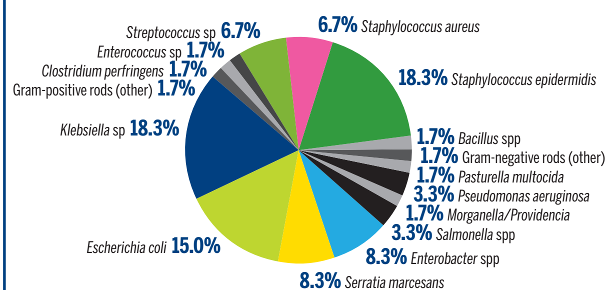
Sepsis rate, source and implicated organisms

Historically, **bacterial contamination of platelet products** has been reported to be a **significant cause of post-transfusion fatalities**. A fatality rate of 1 in 17,000 for pooled platelet-rich plasma whole blood-derived platelets (PRP-WBPC) and 1 in approximately 61,000 for single-donor apheresis units were reported from the Johns Hopkins hospital.[9] Similarly, the University Hospitals of Cleveland (from 1991-2004) reported a fatality rate of 1 in 84,108 for PRP-WBPC, and 1 in 48,067 for single-donor apheresis units.[10] However, it is widely thought that **sepsis due to platelets containing bacterial contamination is often unrecognized and thus is under-reported**.

From October 1, 1995 to September 30, 2004, 60 post-transfusion fatalities due to infections arising from contamination of platelets were reported to the FDA **(Figure 1)**.[11] Notably, 38 of the 60 (63.3%) cases were Gram-negative organisms. Similarly, other reports have found that Gram-negative organisms account for the majority of post-transfusion bacterial fatalities (United States bacterial contamination).

Figure 1. Transfusion fatalities due to bacterial contamination of platelet products reported to the FDA (1995-2004, 10 yrs, 60 cases).[11]

Adapted from Niu MT, et al. *Transfus Med Rev*. 2006;20(2):149-157



In a compilation of reports from the United States, the United Kingdom and France, Gram-negative organisms accounted for 34.4% of cases of observed sepsis but 81.8% of the fatalities **(Table 1)**.[4, 12-14] Gram-positive organisms comprised 65.6% cases of sepsis but only 18.2% of the fatalities. **As shown in Table 1, 45% of patients with Gram-negative sepsis died, compared to only 10% of patients with Gram-positive sepsis.**

Table 1. Organisms implicated in infections associated with platelet transfusions (BACON, SHOT and BACTHEM studies).[4, 12, 13.14]

Adapted from Brecher ME, Hay SN. *Clin Microbiol Rev.* 2005;18(1):195-204

Organism	No. of contaminated units in:			Total no.
	United States	United Kingdom	France	
Gram-positive				
Bacillus cereus	1	4 (1)	2	7 (1)
Coagulase-negative staphylococci	9	6 (1)	5	20 (1)
Streptococcus spp.	3 (1)	2		5 (1)
Staphylococcus aureus	4	2 (1)		6 (1)
Propionibacterium acnes			3	3
Subtotal	17 (1 or 6%)	14 (3 or 21%)	10 (0 or 0%)	41 (4 or 10%)
Gram-negative				
Klebsiella spp.			2 (1)	2 (1)
Serratia spp.	2 (2)		1 (1)	3 (3)
Escherichia coli	5 (1)	2 (1)	1	8 (2)
Acinetobacter spp.			1	1
Enterobacter spp.	2 (1)	1 (1)	1	4 (2)
Providencia rettgeri	1 (1)			1 (1)
Yersinia enterocolitica	1			1
Subtotal	11 (5 or 45%)	3 (2 or 67%)	6 (2 or 33%)	20 (9 or 45%)
Total	**28** (6 or 21%)	**17** (5 or 29%)	**16** (2 or 13%)	**61** (13 or 21%)

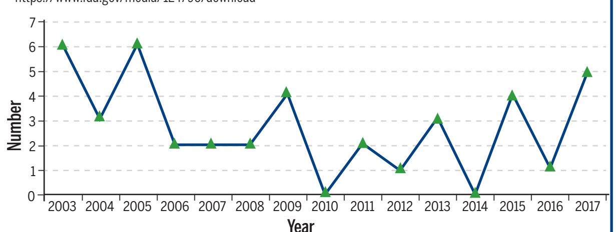
Actual numbers and percentages of fatalities are given in parentheses.

This contrasts with the observation that the majority of organisms isolated from contaminated platelet bags are Gram-positive organisms (thought to originate predominately from the venipuncture site with skin saprophytes).[15]

With the introduction of early bacterial detection, the observed rate of bacteria-related fatalities has substantially decreased **(Figure 2)** and virtually all cases of Gram-negative contamination can be prevented.[16, 17] In those rare cases of Gram-negative sepsis that occur despite an early bacterial detection step, human error is frequently identified as the cause.[18]

Figure 2. Bacterially Contaminated Apheresis Platelets 2003 - 2017.[17]

Adapted from Fatalities Reported to FDA Following Blood Collection and Transfusion Annual Summary for FY2017
https://www.fda.gov/media/124796/download



Risk of sepsis without bacterial detection and the use of diversion.*

- 1-2 per 1000 platelet units were bacterially contaminated.[4]
- Fatality rates ranged from 1/17,000 to 1/84,000 per platelet product.[9]
- Gram-negative organisms were the cause of contamination in approximately 1/3 of septic transfusion reactions but 4/5 of the fatalities.[4, 12-14]

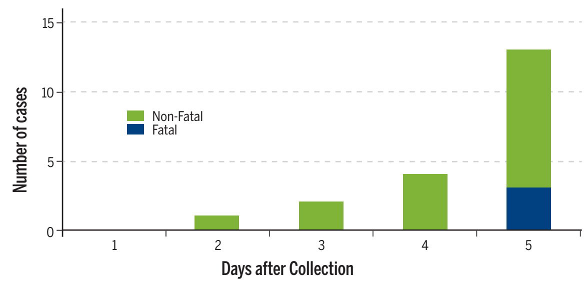
* Bacterial detection and the use of diversion (by diverting the first few milliliters of blood from the collection into a pouch to reduce the quantity of skin contaminants) are thought to have reduced the risk of sepsis and death by 70-80%.[15]

Risk of sepsis and platelet storage time

While Gram-negative organisms grow rapidly within a platelet bag during storage, it is known that some Gram-positive organisms which grow at a slower rate (e.g., *Staphylococcus sp*.) frequently reach clinically significant concentrations only after several days of storage.[19, 20] In addition it has been shown that the **age of platelets** appears to be related to the **risk of sepsis or death (Figure 3)**.

Figure 3. Relation between age of platelets and risk of sepsis (American Red Cross Experience - 2004-2006).[21]

Adapted from Eder AF, Kennedy JM, Dy BA, et al. *Transfusion*. 2007;47(7):1134-42



It is this concern of **bacterial overgrowth over time** that is the basis for **limiting the shelf life of platelet concentrates**. However, the differential growth seen in different types of organisms is an over-simplification. Differential extended lag times could also be a function of the specific donor plasma used during storage.

In one study of 48 platelet concentrates inoculated with the same isolate of *Staphylococcus epidermidis,* bacterial growth was seen in 91.7% of platelet concentrates 3 days after inoculation and in 98.0% by Day 4. However, one platelet unit (2.1%) had demonstrable growth only on Day 7.[19] Similarly, Murphy et al., found that when one isolate of *Staphylococcus capitis* was inoculated into platelet concentrates, quantitative cultures performed using 1 mL samples taken on Days 2, 3, 4, 5, 6 and 7 showed no growth in any unit until Day 4 in 3 units, Day 5 in a fourth unit and Day 7 in the remaining 2 units.[20]

The second rationale for the heightened concern associated with longer storage of platelets is the **apparent increasing risk of sepsis and/or death observed following transfusion of older platelet units** (particularly with 4 or 5 days of storage). For example, the American Red Cross reported an increasing number of cases of platelet transfusion-associated sepsis (fatal and non-fatal) by days after collection: Day 1 = 0, Day 2 = 1, Day 3 = 2, Day 4 = 4, Day 5 = 13 (with 3 of these cases associated with a fatality) **(Figure 3).**[21]

However, **several blood bank organizations worldwide have already implemented screening protocols, extending platelet storage up to 7 days.**[22,23]

In the UK, the the NHS Blood and Transplant screening protocol has been shown to effectively reduce the number of clinically adverse transfusion transmissions.[22] Furthermore, 7-day storage protocols are part of the recommended strategies contained in the final FDA guidance (released September 2019).[24]

Accreditation

> **In many countries, national standards exist to limit and detect bacterially contaminated platelets.**

For example, in 2003 in the United States, both the College of American Pathologists (CAP) and the American Association of Blood Banks (AABB) introduced guidelines to limit and detect bacterial contamination of platelet products.[25, 26]

3 STRATEGIES TO CONTROL BACTERIAL RISK AND DETECT CONTAMINATION OF PLATELETS

A number of different strategies have been developed to limit the risk of contaminating platelet products with bacteria.

Donor site skin preparation

Topical disinfection results in a reduction in the bacterial bioburden of the phlebotomy site. Organisms harbored in sebaceous glands and hair follicles may remain viable and contaminated skin fragments can be drawn up into the collection bag during the initial phase of donation.[27, 28]

Iodine and chlorhexidine solutions (both of which may be combined without isopropyl alcohol) have been shown to be the most effective disinfectants in reducing the donor skin bacterial bioburden (Table 2).

"Green soap" has been alternatively used with iodine-sensitive donors. However, in the context of blood donations, this method does not result in an adequate reduction in the skin bioburden. Notably, in one series of experiments, 13 of 30 donors had more bacteria after cleansing with green soap than before the arm preparation.[29]

Table 2. Percentage of donors with bacterial growth after skin disinfection.[29]

Adapted from Goldman M, et al. Evaluation of donor skin disinfection methods. *Transfusion*. 1997;37:309-312

Bacterial colonies per plate	0	1 - 10	11 - 100	>100	P-value compared to povidone iodine
Povidone iodine	34 - 49	35 - 43	10 - 14	0 - 13	
Isopropyl alcohol and iodine tincture	63	34	2	1	<0.001
Chlorhexidine glucomate	60	25	12	3	>0.3
Green soap and isopropyl alcohol	0	17	47	36	<0.001

Diversion

Studies have shown that **initial diversion of the first few milliliters of whole blood from the collection reduces the amount of bacterial contamination from the skin** entering the blood collection bags.[30, 31]

One study performed in the Netherlands on 18,257 blood donations using standard collection techniques found that 0.35% were contaminated. However, when the first 10 mL were diverted, only 0.21% were contaminated. (n = 7,087; comparison, $p<0.05$).[30]

In a French study of 3,385 collections, the first 15 mL of the collections showed 76 were contaminated (2.2%) compared with just 21 (0.6%) in the second 15 mL.[31]

While diversion is most effective at decreasing contamination with skin flora, it is important to note that the majority of bacteria-related fatalities involve Gram-negative organisms which are not minimized by diversion.

Therefore, diversion alone is not sufficient to control the risk of bacterial contamination of platelets.

Single-Donor Apheresis *versus* Whole Blood-Derived Platelet Concentrates (WBPC)

Pooled platelets obtained from multiple donors are at higher risk of bacterial contamination (as a result of the multiple venipunctures and donors which contributed to the pool).

Johns Hopkins Hospital increased the use of single-donor apheresis platelets from 51.7% in 1986 to 99.4% in 1998 and saw a 70% reduction in septic transfusion reactions involving platelets, from 1 in 4,818 transfusions to 1 in 15,098 transfusions.[9]

In practice, many institutions consider culturing of individual WBPC to be impractical, however the use of sterile connection devices to create a closed pool allows the pre-storage pooling of WBPC which can then be tested for contamination in the same way as that of a single-donor apheresis platelet unit.

Culture-based bacterial detection method

Automated liquid culture-based systems for bacterial detection in platelets use broth bottles with a colorimetric sensor, which changes color as a consequence of increasing CO_2 produced by bacterial proliferation. The instruments monitor both the rate of change of the colorimetric sensor and the absolute color change of the sensor. The method **reliably detects contamination of platelets inoculated to 10 colony forming units per milliliter (CFU/mL) and in many cases ≤ 5 CFU/mL** (e.g., *B. cereus, S. marcescens, C. perfringens, S. epidermidis, S. pyogenes, E. coli, K. pneumoniae, S. aureus*, and viridans streptococci) in 12 to 26 hours.[32-38]

Utility of anaerobic cultures

Although platelet products are generally thought of as an aerobic environment, cases of anaerobic contamination have been documented and the need for anaerobic cultures has been questioned.[39-41]

The following points should be considered.

- Anaerobic organisms, such as *Clostridium perfringens*, have been implicated in platelet-related bacterial sepsis.[40, 41]
- Platelets are stored in plastic bags that are typically described as capable of gaseous exchange rate with the external atmosphere. However, the gaseous exchange rate in these bags is slow. The pO_2 during storage drops significantly with bacterial proliferation.[42] Therefore, the stored platelets may, at times, actually be in-between an aerobic and anaerobic environment.
- The broths used in aerobic and anaerobic culture bottles are often different. It has been shown that certain organisms (e.g. *Streptococcus* sp.) will grow faster in an anaerobic bottle.[33-38]
- **Manufacturers recommend the use of at least two different types of culture bottles: aerobic and anaerobic.**[43, 44]

Global best practices and scientific experts strongly support the use of both aerobic and anaerobic culture bottles.[22, 23]
Adding an anaerobic culture bottle allows for an increase in detection yield due to increase in platelet volume cultured and for detection of strict anaerobes (e.g. *Clostridium perfringens*). It may also provide faster detection of aerobes and fastidious organisms.

Timing of Sampling

Until recent changes were introduced to improve safety, **platelets were held for at least 24 hours post-collection** (to allow bacteria time to grow, so that a small sample of the product would be likely to contain organisms), sampled, cultured, and variably held for a further period of 0-24 hours before then being distributed as "**culture-negative to date".**

A number of enhanced protocols have been reviewed and implemented to further improve platelet safety. These include:

Large Volume Delayed Sampling (LVDS*)

- **This enhanced primary culture strategy enables extension of dating to seven days.**
- In this protocol, platelet components are held for a minimum of 36 hours before taking and culturing an 8 mL sample in both an aerobic bottle and an anaerobic bottle.[22, 23]

Primary culture followed by secondary culture

- **A primary culture** is performed no sooner than 24 hours post collection with a sample volume of 8-10 mL in both an aerobic and an anaerobic culture bottle.
- **Secondary testing** no sooner than Day 3 can be used to extend platelet storage up to Day 5. When performed no earlier than Day 4, the secondary testing may be used to extend shelf life to 7 days.[24, 45]
- While feasible at some large transfusion services, implementation of a secondary culture may be operationally difficult at many smaller institutions.
- Relatively low cost compared to pathogen-reduction technologies or secondary rapid testing.[46]
- This is another way to extend the shelf life of platelet units to 7 days.

Primary culture followed by secondary rapid testing

- In this case, a primary culture is performed after 24 hours of collection with a sample volume of 8-10 mL in both an aerobic and anaerobic culture bottle.
- A secondary rapid test is then performed close to the time of transfusion.
- This is a third possible way to extend the shelf life to 7 days.

* At the time of publication there are no FDA-cleared, culture-based methods for LVDS in the U.S.

Rapid detection assays

Rapid tests screen for bacterial antigens or bacterial peptidoglycan. They are intended to be an **adjunct test after the use of a bacterial culture method**. These tests take approximately 25 minutes to perform and are optimally performed after at least 72 hours of platelet storage.[47] Analytical sensitivity is between 10^4 and 10^5 CFUs/mL for common bacterial contaminants.[48]

Pathogen Reduction Technologies

Several pathogen reduction technology (PRT) methods have been developed, including solvent/detergent treatment, light treatment (with or without a photosensitizer), and chemical treatment. All methods are designed for unspecific pathogen reduction, but the mode of action of each technology influences the pathogens that can be efficiently reduced, the specific blood components that can be treated, and the effect on the components.[63]

Current pathogen-reduction systems are largely successful in eliminating bacteria, viruses and parasites and are expected to mitigate both known and unknown infectious disease risk.[49-54] Although treated platelets may have decreased recovery and circulation compared with untreated platelets "when patients are supported with comparable doses of platelets, the mean number of platelet transfusions is similar".[49, 55, 56]

As of the date of this platelet safety informational pamphlet, barriers to broad implementation of pathogen reduction in the United States include:[57]

- Stringent process guard bands (which preclude the treatment of all collections),
- Lack of approval for all platelet products (e.g., for triple collections or whole blood derived platelets),
- Lack of approval for seven-day storage,
- Pathogen reduction costs and reimbursement for inpatients.

In conclusion, each of the strategies described in this section has demonstrated enhanced platelet safety, but they have different economic profiles and a different set of operational challenges that need to be taken into account by blood centers and transfusion services before implementation.

A simulation model representing the supply chain managed by Canadian Blood Services showed that, following implementation of an LVDS strategy, extended-shelf-life platelets could potentially reduce wastage within a blood supply chain.[58] For example, by extending shelf life to 7 days, a 38% reduction in wastage could be expected, with outdates being equally distributed between suppliers and hospital customers.

Recent analyses have suggested that extending platelet shelf life to 7 days may reduce discards of outdated platelets, increase platelet availability for patients and facilitate inventory management.[58, 59]

Table 3. Overview of best practices used to screen apheresis platelets for bacteria.[45]

Adapted from Kamel H and Goldman M. *Transfusion*. 2018;58:1574-1577

	Primary testing				Secondary testing			
	Delay before sampling (hr)	Aerobic (mL)	Anaerobic (mL)	Shelf life (days)	Day	Aerobic (mL)	Anaerobic (mL)	Shelf life (days)
Early practice	≥24	4		5	Secondary testing not performed			
Prevailing practice in United States	≥24	8		5	Secondary testing not performed			
Pathogen reduction				5	Secondary testing not performed			
NHSBT	≥36	8	8	7	Secondary testing not performed			
Blood Systems, Inc.	≥24	10-28		5	Secondary testing not performed			
Hema-Quebec	≥48	10	10	7	Secondary testing not performed			
Australian Red Cross	≥24	7-10	7-10	5	Secondary testing not performed			
CBS	≥36	8-10	8-10	7	Secondary testing not performed			
Germany				4	Secondary testing not performed			
Irish Blood Services	≥12	7.5-10	7.5-10	5	4	7.5	7.5	7
Rapid secondary test	≥24	8		5	4, 5, 6			+24 hr
Culture-based secondary test	≥24	8		5	≥4	8	8	7
Johns Hopkins Hospital	≥24	8		5	3	5		5

4 PRACTICAL CONSIDERATIONS FOR THE ROUTINE ASSESSMENT OF PLATELET PRODUCT STERILITY

Maintaining the sterility of the platelet product

When sampling a platelet product to assess sterility, **it is of paramount importance not to introduce bacteria**.

Optimally, this can be achieved by either having an **integral sample bag with collection set** or with the **use of a sterile connection device**. Such a device forms a heat weld with the attached tubing creating a closed system.

To minimize false-positive results when inoculating a culture device (e.g. a bottle or plate), an aseptic technique must be employed. Many laboratories choose to use a laminar flow hood for such inoculations.

"Negative to date"

Cultures of the platelet product should optimally be maintained for the duration of the storage time of the product. Platelet products will be **released to inventory as "negative to date"** when on-going monitoring of the culture occurs.

Key points and actions[62]

Interpretation of sterility monitoring tests

Units are interpreted as bacterially contaminated if at least one of the following conditions is observed:

- Both the Gram stain and the culture yield a bacterial species with the same characteristics.
- The same bacterial species is obtained from both the cultured platelet sample and an additional repeat sample from the implicated bag(s).
- Susceptibilities or other tests to confirm the identity of the two isolates (e.g., RFLP* or sequencing) should match.

Test result notification

- All (initial and repeat) positive results indicative of bacterial contamination should be reported immediately from the microbiology laboratory to the transfusion service and updated as additional results become available.
- The transfusion service should immediately communicate this information to the clinical service if co-components have been transfused.
- The blood donor service should be notified of both positive and negative results so that donor investigation can be initiated if warranted and other components can be discarded or released from quarantine.
- Regional and national reporting must be completed as required by the microbiology laboratory, the transfusion service and the blood donor center.

Blood Center actions

- Retrieve and quarantine any remaining co-components. These remaining co-components should be cultured if the implicated blood bag is found to be bacterially contaminated.
- Assess the occurrence of transfusion reactions from any co-components transfused.
- Determine the distribution and use of co-components.
- Facilitate reporting of any transfused co-components.

*RFLP: restriction fragment length polymorphism

5 PRACTICAL CONSIDERATIONS FOLLOWING A SEPTIC TRANSFUSION REACTION

Clinical presentation

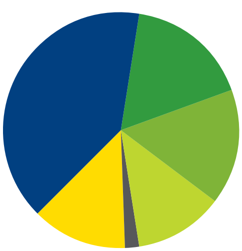
The clinical presentation of sepsis resulting from a bacterially contaminated platelet unit can be quite variable, ranging from asymptomatic to mild fever (which may be indistinguishable from a non-hemolytic transfusion reaction) to acute sepsis, hypotension, and death.

> **Sepsis due to transfusion of contaminated platelet units is vastly under-recognized and under-reported.**

As previously noted, the majority of platelet units tend to be transfused to patients who are immunosuppressed **(Figure 4)** and are thus most at risk of sepsis.[8] Further complicating the clinical picture is the fact that an immunosuppressed patient's fever may be misattributed to other infectious causes. Broad-spectrum antibiotics should be considered for any patient who develops fever within 6 hours of platelet infusion.[60, 61] The time from transfusion to clinical sepsis can range from immediate to over 1 week.

Figure 4. Categories of immunosuppressed patients receiving platelet transfusions.[8]

Adapted from Cummings JP et al. University Health System Consortium. 1998



40%	Adult medicine/oncology
17%	Pediatric hematology/oncology
16%	Hemopoietic progenitor cell (HCP) transplant
12%	Adult hematology
2%	Cardiopulmonary bypass
13%	Other

Identifying septic transfusion reactions

A recent study of platelet-related septic transfusion reactions found that the American Association of Blood Banks (AABB) criteria **(Table 4)** for the recognition of transfusion reactions arising from suspected bacterially contaminated platelet units showed the highest diagnostic sensitivity of a number of published criteria reviewed.[62]

In this study, all 5 patients who developed reactions after receiving bacterially contaminated platelet units, met the AABB criteria. However, none of the 5 septic transfusion reactions had been reported to the transfusion service and cases were only documented as a result of an active prospective platelet culture surveillance program.

This underscores both the underreporting and lack of recognition of septic transfusion reactions and the need for further education of clinicians who are transfusing patients.

Table 4. AABB criteria for the investigation of a possible septic transfusion reaction (over a 24-hour observation period).[62]

Adapted from AABB Association Bulletin 2014;#14-04

1 Fever defined as temperature ≥ 38°C (100.4°F) with a rise of ≥ 38°C (1.8°F) PLUS any of the following signs and symptoms:

- Rigors
- Hypotension
- Shock
- Tachycardia (rise of >40 beats/minute from the pre-transfusion value)
- Dyspnea
- Nausea/vomiting

And/or

2 Any change in the clinical condition leading to a suspicion of sepsis, even in the absence of fever or other typical signs and symptoms of sepsis.

Fever may not occur in immunosuppressed patients, particularly in patients pre-medicated with antipyretic and antihistaminic agents before transfusion. In particular, syncope and hypotension in the absence of other features of sepsis have been reported in patients transfused with bacterially contaminated platelets.

Note: All findings may be delayed for up to 48 hours.

Key points and actions[62]

Bedside actions in response to a suspected septic transfusion reaction

- **Immediately STOP the transfusion**.
- Provide fluids and pharmacologic support to maintain adequate blood pressure.
- Provide antibiotic coverage in support of sepsis therapy.
- Notify the transfusion service and return the blood bag to the transfusion service (per facility policy).
- **Immediately draw blood cultures from the patient (aerobic and anaerobic x 2).**
- Alert the patient's physician.

Laboratory Management Transfusion Service / Microbiology

- Search, obtain and quarantine any co-components. The supplying blood center should be notified to aid in the tracking of co-components.
- Test implicated component for bacterial contamination (direct stain and culture, optional use of rapid assays). In the absence of residual volume in the bag, the bag can be rinsed with 10-20 mL of sterile broth prior to sampling. Cultures (aerobic and anaerobic) should be incubated for a minimum of 5 days.
- Microbiology laboratories should save all bacterial isolates from the patient and the bag(s) in anticipation of establishing the relatedness of the bacterial isolates.
- Retain the implicated bag at 4°C in case additional testing is required.
- Retain the bacterial isolates from the patient and the bag) at -70°C for possible further study.

Note: Septic transfusion reactions are typically associated with bacterial loads >10^5 CFU/mL.

Interpretation of tests following a suspected septic transfusion reaction

Units are interpreted as bacterially contaminated if any of the following conditions are observed:

- Both the Gram stain and the culture yield a bacterial species with the same characteristics.
- The same bacterial species is obtained from both the patient (obtained shortly after the transfusion) and the implicated bag. Susceptibilities or other tests to confirm the identity of the two isolates (e.g., RFLP* or sequencing) should match.

Test result notification

- All positive results indicative of bacterial contamination should be reported immediately from the microbiology laboratory to the transfusion service and updated as additional results become available.
- The transfusion service should immediately communicate this information to the clinical service.
- The blood donor service should be notified of both positive and negative results so that donor investigation can be initiated if warranted and other components can be discarded or released from quarantine.
- Regional and national reporting must be completed as required by the microbiology laboratory, the transfusion service and the blood donor center.

Blood center actions

- Retrieve and quarantine any remaining co-components. These remaining co-components should be cultured if the implicated blood bag is found to be bacterially contaminated.
- Assess the occurrence of reactions from any transfused co-components.
- Discard co-components appropriately.
- Facilitate reporting of any transfused co-components.

* RFLP: restriction fragment length polymorphism.

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