



Advancing Transfusion and
Cellular Therapies Worldwide

ASSOCIATION BULLETIN

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Date: January 24, 2005
To: AABB Members
From: Paul D. Mintz, MD - President
Karen Shoos Lipton, JD - Chief Executive Officer
Re: Guidance on Management of Blood and Platelet Donors with Positive or Abnormal Results on Bacterial Contamination Tests

Summary

This Bulletin is intended to provide general guidelines for medical decision-making in managing donors with a positive result on a test for bacterial contamination in donated platelets. This guidance supplements the information provided in Association Bulletin #04-07.

Background

Under Standard 5.2.2 of the 22nd edition of *AABB Standards for Blood Banks and Transfusion Services*, blood collection facilities must notify donors if any medically significant abnormality is discovered during the interview or detected as a result of laboratory testing. Deferral criteria are established by the Food and Drug Administration (FDA), the applicable State Department of Health (or regulatory agency), and/or by guidelines from the facility medical director.

The notification of a donor whose platelet unit has an initially positive result from a bacteria detection test is a complex issue. Before the performance of confirmatory assays, initial-positive test results include both true- and false-positive results. The initial test may be a false-positive result because surrogate tests have poor specificity (eg, pH, glucose) or, for culture tests, because contamination was introduced at the time of culturing.

The initial test may be a true-positive result due to detection of a wide variety of organisms. While some positive results are of little or no clinical significance to the donor, others may be significant. A true-positive test result is most often caused by skin flora (resulting from incomplete skin decontamination or a skin plug). However, a true-positive test result can also be the result of bacteremia caused by organisms that may be of clinical significance to the donor and the recipient. Organisms presumed to originate from donor bacteremia have, in fact, been implicated in the majority of fatal posttransfusion sepsis cases. Confirmatory testing (by culture methods) and organism identification are both needed in order to make

rational donor management decisions. Furthermore, in cases with a confirmed positive test result, it is important to consider the need for further investigation to identify the manner in which bacteria entered the platelet unit. A thorough investigation is important for the health of the donor, future recipients of components collected from that donor, and possibly other donors (eg, if the source of contamination is related to a defect in the transfusion set). In some circumstances, the investigation must be followed by notification and counseling of the donor. Rarely, the investigation also may uncover data of public health importance.

Donor Management Guidelines

The following discussion provides guidance with regard to initial-positive, false-positive, and true-positive test results.

- 1) **Initial-Positive:** *Initial-positive test result – positive or abnormal (out-of-range) initial test.* Actions based on an initial-positive test result will be determined by both of the following:

- a) The source of the donor platelets (eg, apheresis or whole-blood-derived platelets).
- b) The initial testing method used (eg, culture-based methods, surrogate tests, Gram's stain).

Culture. An initial-positive result from a culture-based test on an apheresis donation should result in the implementation of a procedure to ensure that the donor is not allowed to donate until confirmatory testing has been completed. Collection facilities should follow their own internal procedures to ensure that this occurs. One acceptable method would be a prompt, albeit preliminary, notification of the donor to refrain from any subsequent donation while confirmatory testing (ie, repeat culturing) is conducted. This will prevent the donor from presenting for another apheresis donation before completion of the investigation. In contrast, immediate contact and notification is not necessary for an initial-positive culture test result for a whole blood donor, because the interval between donations is much longer. This longer interval allows the investigation to be completed and the confirmatory tests results to be obtained before the donor is eligible to donate again. Performance of a Gram's stain or similar staining method on the initial culture positive test may provide immediate information that may be beneficial in the investigation and evaluation of the donor, particularly when a gram-negative organism is found. Notification of donors with an identified gram-negative organism should be considered even before obtaining a confirmatory culture result because gram-negative organisms generally indicate the presence of bacteremia.

Gram's stain. When a Gram's stain or similar staining method is used as the initial test method, the same approach should be used for notification of the donor as described above.

Surrogate Test. Surrogate tests such as pH or glucose lack specificity. Accordingly, notification of donors with an initial-positive surrogate test result should not occur until after a confirmatory culture test is performed.

- 2) False-Positive: *False-positive test result – positive on initial test, negative on confirmatory test.* If confirmatory culture results are negative and the donor has been previously notified of the initial-positive test result for the same donation, the collection facility should contact the donor to inform him/her that further blood donations are acceptable. If the donor has not been previously notified of the initial-positive result, there is no need to contact the donor.
- 3) True-positive: *True-positive test result – positive on both initial test and confirmatory test.* The determination of whether to notify and/or counsel a donor with a true-positive test result depends on the identification of the organism, because the type of organism may help to identify the source of bacteria. The source may be categorized as environmental/skin contamination or endogenous bacteremia. Gram-negative organisms (eg, *Escherichia coli*) are likely to be from occult bacteremia of donor origin (endogenous bacteremia). Gram-positive organisms (eg, *Staphylococcus epidermidis*) are likely to be either skin commensals or environmental contaminants (environmental/skin contamination). However, some gram-positive organisms (eg, *Staphylococcus aureus*, *Streptococcus pneumoniae*) may be from endogenous bacteremia in the donor. Table 1 categorizes organisms that can frequently be identified in cultures from donated platelets.
 - a) Environmental/skin contamination. If the contaminating organism is likely to be a skin contaminant, it is important to consider whether the phlebotomy itself was traumatic, and whether the donor has scars at the venipuncture site, either from the most recent phlebotomy or from a previous one, that could have prevented effective disinfection. Resolution of this question may involve a review of the phlebotomy records, discussion with the staff and/or the donor, and inspection of the phlebotomy site. Table 2 provides guidelines for potential process investigation, but not all suggestions will be applicable in every case.
 - Donor deferral beyond the conclusion of the investigation identifying skin flora in a contaminated unit is not warranted. However, when extensive pitting or scarring at the venipuncture site is observed or when subsequent positive results are obtained from the same donor, the medical personnel of the collection facility should determine if a deferral may be warranted.
 - The identification of skin flora in a contaminated unit should be regarded as an opportunity to engage the institution's self-assessment process. This should lead to improvements in phlebotomy operations, collection processes, or staff training.
 - b) Endogenous bacteremia.

Donor management. All gram-negative organisms should be considered potentially significant for the donor's health (see Table 1). As noted above, some gram-positive organisms result from endogenous bacteremia, and can be

clinically significant. For example, an organism such as *S. aureus* may originate from bacteremia in a patient whose osteomyelitis was incompletely treated. Moreover, some organisms may have low pathogenicity, but may indicate a significant underlying disease (eg, *Streptococcus bovis* bacteremia associated with colon cancer).

Donor notification is indicated for any suspected bacteremia with a possible pathogenic organism. This notification should follow the principles for notification of donors with confirmed viral infections. Specifically, the donor should be informed of the results, counseled about their potential medical significance (eg, possible occult infection), and given the recommendation to see a physician. With the donor's permission, the donor's results and their possible significance should be communicated by the blood center to the donor's physician. Information provided to the physician should emphasize the need to perform a thorough clinical history and a physical examination and should suggest the possibility of follow-up investigations including blood cultures, other body-site cultures, and additional tests as appropriate to search for occult infection. Alternatively, the medical director of the blood center may elect to provide some of this follow-up directly to the donor.

Donor deferral should be based on medical judgment and must be considered when confirmed culture results are obtained and the organism identified could be potentially harmful to the donor or the recipient or the organism has been detected previously in the same donor. Deferred donors should be notified of their deferral status. If deferred, the donor should not be accepted again for donation until a physician has cleared him or her. This decision could be based on the donor's successful completion of any recommended treatment.

Public Health Considerations

Certain organisms that result in bacterial contamination of a unit are of important public health significance, regardless of the effect on the donor's health, and require additional consideration. (See Table 3.) The identification of an organism of public health significance will most likely trigger state and/or local health department reporting requirements, summarized below. Further, it is recommended that isolates of all such organisms be saved for a reasonable length of time in accord with regulations, standards, and guidelines. Public health authorities should be consulted as appropriate.

- **Bacterial Category A - Agents of Bioterrorism (Table 3).** Certain organisms may be potential agents of bioterrorism. Category A agents are the highest priority agents for identification and immediate reporting because they can be disseminated or transmitted easily from person to person (including in the laboratory setting); result in high mortality rates and have potential for major public health impact; and require special action for public health preparedness. For these agents, an immediate report is requested. An immediate report means to report to state or local health authorities within 24 hours of organism identification according to state or local requirements. A routine report also should be filed according to usual regulations (see below). In addition, for organisms classified as Bacterial Category A Agents of Bioterrorism, blood

collection facilities are requested to call the Centers for Disease Control and Prevention (CDC) hotline at 888-246-2675.

- For other selected bacteria associated with nationally notifiable diseases (Table 3), reporting should proceed through routine mechanisms set forth by local, regional, or state public health authorities. The most current information on procedures for reporting the occurrence of communicable diseases nationally can be found in the *Manual of Procedures for Reporting Nationally Notifiable Diseases to CDC*. Note that the list of notifiable diseases (Table 3) varies by state, as reporting is mandated only at the state level. The list of nationally notifiable infectious diseases for the current year and recent previous years is available at the following site: <http://www.cdc.gov/epo/dphsi/PHS/infdis.htm>.
- Other nonreportable organisms may be of epidemiologic interest, including *S. aureus* and all gram-negative organisms, for the purpose of detecting clustering or unusual organism characteristics. Expert consultation with CDC on organisms of epidemiologic significance can be arranged through the Assistant Director for Blood Safety, CDC, 404-639-2775.

Table 1. Examples of Organisms that Can Be Identified in Blood Cultures			
Pathogenic Organisms		Organisms Frequently of Lesser Clinical Significance	
Name	Gram's Stain Result	Name	Gram's Stain Result
<i>Staphylococcus aureus</i>	Gram-positive cocci in pairs and clusters	<i>Coagulase-negative staphylococci</i>	Gram-positive cocci in pairs and clusters
<i>Streptococcus pneumoniae</i>	Gram-positive cocci in pairs	<i>Alpha hemolytic streptococci</i>	Gram-positive cocci in pairs and chains
Beta hemolytic streptococci	Gram-positive cocci in pairs and chains	<i>Propionibacterium acnes</i>	Pleomorphic gram-positive rods
<i>Enterococci</i>	Gram-positive cocci In pairs and short chains	<i>Bacillus</i> spp. (except anthrax)	Gram-positive rods
<i>Enterobacteriaceae</i>	Gram-negative rods		
<i>Serratia</i> spp.			
<i>Klebsiella pneumoniae</i>			
<i>Escherichia coli</i>			
<i>Pseudomonas aeruginosa</i>	Gram-negative rods		
<i>Listeria monocytogenes</i>	Short gram-positive rods		
<i>Bacteroides fragilis</i> group	Gram-negative rods		
<i>Clostridium</i> spp.	Gram-positive rods		
<i>Streptococcus bovis</i>	Gram-positive cocci in pairs and short chains		

Table 2. Guidelines for Possible Process Investigation

Process	Potential Considerations for Evaluation
Equipment/Supplies	<ul style="list-style-type: none"> • Was a diversion pouch system used? • What skin preparation method was used? <ul style="list-style-type: none"> ○ Is this a new arm prep method? ○ Is in-house validation documentation available? • What is the method to obtain a sample for inoculation/testing? (Sterile connecting device) • What solution(s) (alcohol/iodine) were used to clean the bottle before inoculation? <ul style="list-style-type: none"> ○ Were nonsterile swabs or pads used to clean the bottles before inoculation? • Is additional information available from the manufacturer regarding the collection kit? <ul style="list-style-type: none"> ○ Recall/adverse event reports? • Was there a deviation in the pooling process? • Was this an aliquot of a parent unit? <ul style="list-style-type: none"> ○ How was the aliquot prepared? <ul style="list-style-type: none"> ▪ Sterile connecting device? ▪ Open system?
Collection	<ul style="list-style-type: none"> • Was this a traumatic draw/collection? • Was there manipulation of the needle during collection procedure? • Was the needle changed during the procedure? • Was this associated with kit breakage or other potential issues related to the collection kit? • Was the venipuncture site palpated?
Staff	<ul style="list-style-type: none"> • Has this staff member been involved in previous cases of a potentially contaminated unit? • Is this a new staff member? Is he/she currently in training? • Is there direct observation documentation available for this staff member?
Donor	<ul style="list-style-type: none"> • Has the donor been implicated in another case of suspected contamination? <ul style="list-style-type: none"> ○ Were pathogenic or potentially pathogenic organisms identified? • Is the organism identified as a public health concern? • Interview donor for medical/donation history <ul style="list-style-type: none"> ○ Evaluate donation frequency ○ Arm inspection – Does there appear to be pitting or scarring present at venipuncture site? ○ Refer to primary care physician <ul style="list-style-type: none"> ▪ Urinary track infection (UTI) ▪ Upper respiratory infection (URI) ▪ Prior diagnosis ▪ Recent medical/dental treatment
Organism	<ul style="list-style-type: none"> • Is the organism identified as gram-negative or gram-positive? • Has this organism been implicated in another recent case of suspected contamination? • Is the organism identified as a public health concern? • Is the organism a common pathogen? • Is the organism of questionable clinical significance but frequently associated with other diseases?

Table 3. Examples of Organisms of Public Health Significance*

Bacteria	Action	
Bacterial Category A Agents of Bioterrorism		
<i>Bacillus anthracis</i>	Immediately report to public health authorities (Save isolates for confirmatory identification and further action)	
<i>Yersinia pestis</i>		
<i>Francisella tularensis</i>		
<i>Clostridium botulinum</i>		
Other selected bacteria associated with nationally notifiable diseases**		
<i>Listeria monocytogenes</i>	Report to public health authorities (Save isolates for confirmatory identification and further action)	
<i>Salmonella</i> spp. (all spp.)		
<i>Shigella</i> spp. (all spp.)		
Group A streptococci		
<i>Streptococcus pneumoniae</i>		
<i>Neisseria meningitidis</i>		
<i>Neisseria gonorrhoeae</i>		
*Reporting requirements may vary by state; follow reporting criteria set forth by local authorities.		
** See http://www.cdc.gov/epo/dphsi/PHS/infdis.htm for complete list.		