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Guideline for Investigation of Suspected Transfusion Transmitted Bacterial Contamination

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Guideline for Investigation of Suspected Transfusion Transmitted Bacterial Contamination

Transfusion Transmitted Injuries Section
Blood Safety Surveillance and
Health Care Acquired Infections Division

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Background

This Guideline was developed by a Working Group formed by the Public Health Agency of Canada (PHAC) to provide standardized instructions for investigation of suspected bacterial contamination related to the transfusion of blood components that will be useful to hospitals and practical in terms of implementation. The group was created as the result of numerous requests from hospitals that participate in the Transfusion Transmitted Injuries Surveillance System (TTISS) in Canada as well as from the National Working Party for Data Review, which reviews the national data from TTISS for the PHAC.

The Working Group consists of the following:

Dr. Gilles Delage, Héma-Québec

Dr. Mindy Goldman, Canadian Blood Services

Ms. Nancy Heddle, McMaster University

Ms. Nancy McCombie, Public Health Agency of Canada

Dr. Pierre Robillard, Public Health Agency of Canada

The Guideline has also been reviewed by experts in the fields of Transfusion Medicine, Medical Microbiology and the Transfusion Safety Officers in Canadian hospitals. In addition, comments were also provided by representatives from the Canadian Society of Transfusion Medicine, Association of Medical Microbiology and Infectious Disease Canada, the National Working Party for Data Review and the Provincial/Territorial TTISS Working Group.

Introduction

The purpose of this Guideline is to standardize the identification, the handling and storage of blood component bags and the sampling and culture of recipient and blood components when bacterial contamination of transfused blood components is suspected. The recommendations contained in this document will help hospitals develop appropriate policies and procedures for the management of suspected bacterial contamination of blood components.

The targeted blood components are: whole blood, red blood cell concentrates, platelet concentrates (whole blood derived or by apheresis), plasma for hospital transfusion, cryoprecipitate and cryosupernatant plasma.

This Guideline applies to reactions where rapidly growing bacteria are suspected. In cases where other microorganisms are involved (such as Q fever, Lyme disease, syphilis), the investigation must be tailored to the specific organism.

An algorithm has been provided in Appendix 'A' to show the flow for each step in the process.

Guideline

Clinical Triggers for Investigation of Suspected Bacterial Contaminations

A bacterial contamination should be suspected and an investigation undertaken if the following appear during or within 4 hours of the end of transfusion:

1) Fever defined as a rise in T° ≥ to 1° C from pre-transfusion value and T° ≥ 38° C PLUS Any of the following signs and symptoms:
    - Rigors
    - Hypotension
    - Shock
    - Tachycardia (rise > 40 beats from pre-transfusion value)
    - Dyspnea
    - Nausea/vomiting

OR

2) Fever defined as a rise in T° ≥ 1° C from pre-transfusion value and T° > 39° C even in absence of other signs or symptoms

OR

3) Fever not responding to antipyretics

OR

4) A high suspicion of sepsis even in the absence of fever

NB: If you suspect bacterial contamination, you should conduct an investigation even if the above criteria have not been met.

At the Bedside

Since investigation of possible bacterial contamination requires culture of the residual blood component, it is preferable to keep the platelet and red cell concentrate bags after transfusion, either in the laboratory or on the ward. If possible the open port should be covered (cap, clamp, etc…), to decrease contamination post-transfusion and stop leakage from the bag. The empty blood component bag may be placed in a sealed plastic bag to contain leakage. Most reactions occur during or up to 4 hours post-transfusion; therefore a storage period of 4 hours post-transfusion is adequate.

When bacterial contamination is suspected as the cause of an adverse event, the transfusion of blood components should be stopped immediately if still ongoing. All bags (with or without residual blood components) of transfusions given within the last 4 hours should be sent to the laboratory for testing. **The bag should be inspected to detect any visible anomaly.**

At least one set of blood cultures (aerobic and anaerobic bottles) should be obtained from the patient before administering antibiotic therapy.

N.B.: Individual platelet bags that were pooled in the transfusion service laboratory should be kept for a minimum of 4 hours post-transfusion.

In the Laboratory

Management of Co-components* in Suspected Bacterial Contamination

*Co-components are defined as:

All blood components prepared from one donation.

Example: If whole blood derived platelets were transfused and are the implicated component, the possible co-components may be red cell concentrates, plasma for hospital transfusion, cryoprecipitate and cryosupernatant plasma.

It is important that the Blood Supplier be notified immediately in cases where bacterial contamination is highly suspected, since co-components from the involved donation may also be contaminated. Highly suspected bacterial contamination cases include those in which there are preliminary positive laboratory results (e.g. positive gram stain on blood component, preliminary positive culture results) and those in which clinical symptoms are highly suggestive of post-transfusion bacterial sepsis (e.g. shock, hypotension).

Once the Blood Supplier is notified they will take the appropriate action on co-components in their inventory. When co-components have already been distributed to hospitals the Blood Supplier will inform the hospital transfusion service laboratories involved. If co-components have already been transfused at the hospital, the recipient should be assessed for possible post-transfusion sepsis. If there is any remaining blood component, such as a retained pooling bag or initial blood component bag, it should be cultured. If co-components have not been transfused, the Blood Supplier will provide instructions to the hospital to return them to the Blood Supplier, or to discard or quarantine them. These units might be quarantined at the hospital, pending more information about the transfusion reaction. This might be appropriate, for example, when the likelihood of the reaction being due to bacterial contamination is low, and when the unit is difficult to replace, such as a red blood cell unit from a rare blood group.

Samples

Samples should be obtained from all components using an aseptic technique (usually with needle and syringe). If no blood component remains in the bag, 10 to 20 cc of trypticase soy broth or other culture broth (sterile saline may be substituted) should be aseptically injected into the bag, the bag shaken, and the broth reaspirated and used for inoculation. **Never use segments for bacterial culture: due to the small volume of blood in the segment it is unlikely to contain the initial inoculum of bacteria (high risk of false negative result), and due to the difficulty of obtaining the sample there is likely to be contamination of the specimen (high risk of false positive result).** For pooled platelets, both the bag in which the pool was placed and the individual blood component bags should be sampled.

Inoculation

Blood Culture Bottles

All blood components should be inoculated aseptically (preferably under a Class II Biological Safety Cabinet) into a set of both aerobic and anaerobic blood culture bottles after alcohol disinfection of the rubber stoppers. Volume inoculated should be according to manufacturer's instructions.

Bottles should be incubated for 5 to 7 days at 35° C to 36° C.

If a manual blood culture bottle system is used, blind subcultures to solid media should be done at 18 and 48 hours.

Direct Examination

A slide should be prepared from all bags, including those into which nutrient broth has been added for staining (Gram or Acridine orange) and microscopic examination. Direct examination of a stained specimen allows for rapid diagnosis for patient management purposes and also helps in interpretation of culture results.

Solid Media

If bacteria are seen on direct examination, solid media should be inoculated for incubation at 35° C. Blood agar plates and chocolate agar plates should be inoculated and incubated for 4 days (aerobic) and 6 days (anaerobic).

Irrespective of direct examination results, solid media can be inoculated for incubation at 35° C. If growth occurs, the laboratory will gain more rapid access to the causative organism for purpose of further testing (identification, antibiotic susceptibility testing), and for interpretation of positive blood culture results.

Positive Blood Culture Bottles

If macroscopic examination of the bottles indicates growth, or if the automated detection system gives a positive signal, subculture onto blood agar and chocolate agar plates (aerobic incubation at 35° C) and blood agar plate (anaerobic incubation at 35° C). Also, a slide should be prepared for Gram stain.

All isolated colony types should be identified according to procedures in place in the laboratory. Antibiotic susceptibility testing should be carried out. If final identification is impossible, the strain should be forwarded to a reference centre (usually the public health laboratory) for further study.

All strains should be kept for further characterization.

If bacteria are isolated from both blood component and patient, further characterization to establish relatedness of the strains may be indicated (e.g. molecular typing, serotyping). Contact your reference laboratory to make the necessary arrangements.

Growth on Solid Media

If there is growth of bacteria on inoculated solid media, proceed as above for identification, antibiotic susceptibility testing, and further characterization.

Determination of Endotoxin Levels

If available, this test can also be carried out according to manufacturer's instructions.

Reporting of Culture Results

All results should be reported to the transfusion service laboratory. The transfusion service laboratory should report to the Blood Supplier all positive results and all culture results (positive or negative) for cases previously reported to the Blood Supplier.

All preliminary positive results on a suspected case should be sent before final results are obtained, to ensure that co-components are removed from inventory in a timely fashion.

If the organism could be related to donor bacteremia or donor pathology, such as *Streptococcus bovis*, the Blood Supplier may notify the donor and advise them to be seen by their physician. If the organism involved is one that may be involved in nosocomial outbreaks, such as *Serratia marcescens*, the Blood Supplier will perform an environmental investigation and may also quarantine or investigate other blood donations from the same clinic or bag lot number.

A copy of the reports with final interpretation should also be placed in the patient's file.

Classification of Bacterial Contamination Cases in the Canadian Hemovigilance System

Results will be interpreted taking into account culture results (Gram or acridine orange staining); relatedness of strains from patient and blood component if appropriate; and the Transfusion Transmitted Injuries Surveillance System (TTISS) definitions:

Possible

Bacterial contamination is considered "Possible" if it meets the following criteria:

- The recipient's blood culture is positive.
- Contamination of the blood sample or laboratory contamination is not suspected.
- The recipient presents signs and symptoms of sepsis (nothing else explains it).
- A blood, blood component, or blood product (plasma derivative) cultures was not done.
  - No specimen was available
  - A blood culture was not ordered

Probable

Bacterial contamination is considered "Probable" if it meets the following criteria:

- Positive blood, blood component, or blood product (plasma derivative) culture.
- Contamination of the blood sample or laboratory contamination is not suspected.
- The recipient presents signs and symptoms of sepsis (nothing else explains it).
- The recipient's blood culture was not done.
  - No specimen was available.
  - A blood culture was not ordered.
- The recipient's blood culture is negative.
  - The recipient is already taking antibiotics.

Definite

Bacterial contamination is considered "Definite" if it meets ALL of the following criteria:

- The same bacteria are found in the recipient and the blood, blood component, or blood product (plasma derivative).
- Contamination of the blood sample or laboratory contamination is not suspected.

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Appendix 'A'

An Algorithm for Laboratory Investigation of Suspected Bacterial Contamination