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US ARMY MEDICAL RESEARCH LABORATORY

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REPORT NO. 858

A FAIL-SAFE APPROACH TO INCOMPATIBLE BLOOD TRANSFUSIONS

(Progress Report)

by

Robert M. Nalbandian, M.D.
LTC Frank R. Camp, Jr., MSC
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9 March 1970

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UNITED STATES ARMY
MEDICAL RESEARCH AND DEVELOPMENT COMMAND

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Military Blood Transfusion Reactions
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Combat Surgery
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USAMRL REPORT NO. 858
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ABSTRACT

A FAIL-SAFE APPROACH TO INCOMPATIBLE BLOOD TRANSFUSIONS

OBJECTIVE

To develop a standard "fail-safe" system for managing incompatible blood transfusions.

METHOD

Minimum tests are specified for detection of incompatible blood transfusions. A salvage procedure is outlined and role-specific instructions are provided.

RESULTS

A cross-check for Incompatible Blood Transfusion (IBT) consists of the determination of only two parameters which will be diagnostically altered if IBT is present: positive Coombs test and an elevated plasma hemoglobin, compared to pretransfusion specimens. With a positive diagnosis of IBT, mannitol, stocked at all stations as an emergency drug, can be used instantly to salvage the patient. Thereupon, a coexistent consumption coagulopathy is investigated and managed according to a panel of coagulation parameters.

The principles of cross-checking at the operational level of the ward and the laboratory are embodied in segregated, delegated instructions, one for each member of the investigative team. Thus, role-specific sets of instructions produce a synchronous, automatic effort, accommodating all types of blood transfusion reactions. *A hospital-wide detection and salvage system for victims of IBT is thus made immediately available to the pathologist who will adopt these forms and instructions in toto.* A form (Blood Transfusion Reaction Report) is developed which protects to a great extent physician and hospital alike from litigation.

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A FAIL-SAFE APPROACH TO INCOMPATIBLE BLOOD TRANSFUSIONS

INTRODUCTION

The annual mortality rate from incompatible blood transfusions is an unknown quantity at present. Estimates vary from an incidence of 1,200 per year to over 25,000 annually (1). We believe that the methods described below will decrease the number of patients lost from this cause to an irreducible minimum (1a).

We advocate a technique for the investigation and management of the potentially lethal transfusion reaction, based on the principle of cross-checking rather than rechecking.

In this report an intricately coordinated but relatively simple and automatic investigative procedure system is discussed which is replicated in complete detail in the Supplement. It applies cross-checking principles to blood transfusion reaction problems in such a manner that each area of responsibility is delegated separately to a professional specialist for the precise and efficient completion of each area in a synchronized sequence. This system has been designed to serve two purposes: (1) the recognition of only two features of pathophysiology pathognomonic of a potentially lethal transfusion; and (2) the prompt initiation of lifesaving therapy. Only later is the offending antigen-antibody system identified. The order of priority is to determine the threat to the patient's life and to eliminate it--then other investigations may be pursued.

A Blood Transfusion Reaction (BTR), excluding late sequelae, may be defined as any adverse clinical sign or symptom occurring singly or in combinations during or shortly after a blood or blood component transfusion and the result of that transfusion. A summary of BTR's of several types is included in the Supplement. Potentially catastrophic is the Incompatible Hemolytic Blood Transfusion Disease (IHBTD) which is defined as that condition incident to a blood transfusion in which intravascular hemolysis of sensitized erythrocytes is so accelerated as to portend a possible fatality.

PRINCIPLES OF DIAGNOSIS

In analyzing data, it is infinitely preferable to confirm results by methods other than those used initially. Thus, in investigating a possible IHBTD, one must use methods other than those by which compatibility of the donor and recipient blood was originally determined. Under these circumstances rapid *cross-checking of the parameters of pathophysiology in the patient* is needed, rather than the traditional, time-consuming recheck of the entire typing and crossmatching procedure which may merely perpetuate original technical errors. In cross-check of a BTR, attention is directed only to those parameters of pathophysiology (2) *which would*

be diagnostically altered if IHBTD were present. The two diagnostic parameters which also function selectively as early indices of severity are elevated plasma hemoglobin levels and positive direct Coombs test when compared with pretransfusion specimens.

Several papers (3-5a) have emphasized the aspect of consumption coagulopathy in association with IHBTD. It is essential to investigate for consumption coagulopathy once IHBTD has been diagnosed.

It is prudent to do a gram stain on a centrifuged aliquot of plasma from the transfused unit to detect the rare case in which the transfusion reaction may be due to gross bacterial contamination of the unit of blood.

The two determinations crucial to the diagnosis of IHBTD, however, are the demonstration of elevated plasma hemoglobin levels and positive direct Coombs tests when compared with pretransfusion specimens.

PRINCIPLES OF THERAPY

Since 1953, a growing body of both evidence and opinion has supported the use of mannitol treatment in IHBTD (6-9). On the other hand, universal adoption of this therapy for IHBTD is not evident.

There is a point in time beyond which mannitol becomes progressively less effective. Thus, the interval between the offending transfusion and the initiation of mannitol therapy should be as short as possible. We recommend the classification of mannitol as an emergency drug and urge that it be stocked at all hospital stations where blood transfusions are given. At each station explicit directions for the intravenous use of mannitol should be posted (Table 1). It is important to emphasize compliance with these measures; any oversight will increase the interval between transfusion and treatment, to the patient's detriment. Time saved in our proposed cross-check detection procedure and early recourse to mannitol therapy benefits the jeopardized patient, since effective treatment can be given much earlier.

When IHBTD has been diagnosed, it follows that mannitol therapy must be instituted and diagnostic procedures for a consumption coagulopathy carried out. If a significant coagulopathy is present, appropriate therapy is also added to the regimen. Probably in every case, and in variable degree, IHBTD is accompanied by a consumption coagulopathy. Because IHBTD may be superimposed on any number of very different underlying diseases, appropriate coagulation studies should be done to determine whether the coagulopathy is: (1) primary activation of the coagulation system with a secondary fibrinolytic component; (2) primary activation of the fibrinolytic system; or (3) coequal activation of both systems. Since treatment is quite different for each type of coagulopathy and fraught with disaster if treatment regimens are interchanged, the coagulopathy must be categorized. Continuous, intravenous heparin is the indicated treatment for category (1); epsilon amino caproic acid for category (2); and

heparin with or without epsilon amino caproic acid is unacceptable for category (3), since Trasylol is no longer available by FDA edict.

The clinician should consult with the pathologist to obtain a profile of diagnostic and base line coagulation studies. *In consumption coagulopathy the basic pathophysiology is the intravascular conversion of plasma to serum. The central therapeutic principle is the titration of the patient by intravenous, indicated drug to revert the serum back to plasma as guided by the response of individual parameters in a periodically repeated coagulation profile.*

Because at present there are many different coagulation tests from among which pathologists may exercise personal preferences for the diagnosis of consumption coagulopathy, the profile of tests of coagulation parameters for diagnosis and for monitoring therapy is best left to the individual pathologist.

IMPLEMENTATION OF THE CROSS-CHECK PRINCIPLE

We now turn to the implementation of the principles of diagnosis and management of BTR and particularly IHBTD as discussed above. By segregating and separately specifying the duties and responsibilities of each member of the blood transfusion reaction investigative team (nurse, clinician, medical technologist, and pathologist), it has been possible to coordinate the *delegated activities* of several individuals located at various points in the hospital in order to detect early, and salvage effectively, victims of IHBTD. The mode of handling and recording the generated clinical and laboratory data on the Blood Transfusion Reaction Report form (Fig. 1) provides a document which, to a great extent, protects the physician and the hospital from the hazards of litigation.

There are four separate sets of instructions (see Supplement), one for each member of the professional team: (1) nurse; (2) physician; (3) anesthesiologist; (4) medical technologists. These instructions are posted at logical and appropriate stations throughout the hospital in segregated fashion such that the nursing staff only receive the nursing staff instructions; the physicians only receive the physicians' instructions, etc. (For the purpose of this report only, role-specific instructional procedures for professional personnel are attached hereto as a Supplement.

We believe that the proper role of the pathologist is one of consultation in the circumstance of a BTR. A patient with the manifestations of one or more of the several types of BTR has acquired an additional potentially lethal complication superimposed on the underlying medical problem which must be diagnosed and treated in that clinical context by a clinician. The clinician must be supported by pertinent laboratory data and by consultations with the pathologist.

A diligent perusal of the figures and sets of instructions reproduced in the Supplement clearly demonstrates that this procedure system achieves multiple ends with maximum efficiency. While each member of the investigating team receives only his role-specific instructions, the composite result of the four different sets of instructions coordinates the several independent efforts to the extent that:

(1) A BTR emergency (always a possible IHBTD) is recognized by the nurse who stops the transfusion and summons a physician. She then follows the seven instructions listed on the Blood Transfusion Reaction Report (Fig. 1).

(2) The type of BTR is diagnosed and treated by the clinician with the benefit of instructions predicated on the cross-check principle. Life-threatening emergencies can be dealt with effectively because specific instructions and drugs are at hand.

(3) There is created an historical record, the Blood Transfusion Reaction Report, which characterizes and summarizes the particular episode, and provides the hospital and involved physicians with documentary evidence in the event litigation occurs.

(4) Rechecking (retyping and recrossmatching) is done *after* the life-threatening possibility of IHBTD has been appropriately treated.

SUMMARY

In order to have maximum detection and salvage of victims of IBT, the approach must be one of *cross-checking for evidence of incompatible hemolytic blood transfusion in the patient* rather than the traditional rechecking of *in vitro* specimens. Such an approach to this serious clinical problem yields more pertinent information in much less time.

Each episode of a BTR should be approached as a potential case of IHBTD. Since it has been shown that mannitol infusion is a lifesaving measure in the treatment of IHBTD when given soon enough, a rapid, accurate diagnosis of IHBTD is imperative. Application of the *principle of cross-checking in the patient* for the presence of this clinical problem directs attention to only two easily determined parameters of pathophysiology which would be diagnostically altered if IHBTD were present. These two parameters are: (1) plasma hemoglobin levels; and (2) positive direct Coombs, when both are compared with pretransfusion specimens. If IHBTD is diagnosed, mannitol therapy is instituted immediately. Probable coexistent consumption coagulopathy must be diagnosed and treated in an appropriate manner.

We have evolved a delegated, coordinated procedure system for the investigation and management of the BTR's which is the logical implementation of the cross-check principle in the patient at the operational level of the hospital ward and at the laboratory bench (see Supplement). The

pathologist is provided with a *hospital-wide detection and salvage system*, which, if adopted *in toto* exactly as displayed in the Supplement, will: (1) detect at the earliest possible moment the existence of a BTR (including IHBTD); (2) detect a probably coexistent consumption coagulopathy; (3) mobilize swiftly lifesaving therapy in diagnosed cases of IHBTD; and (4) develop a record of the event as data are recorded on the Blood Transfusion Reaction Report. This summary record becomes part of the patient's hospital chart and to a great extent protects the hospital and physician from possible litigation. Most important of all, the death of patients from IHBTD hopefully may be eliminated.

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GENERIC AND TRADE NAMES OF DRUGS

Epsilon aminocaproic acid	- Amicar
	- Trasylol, Aprotonin
Diphenhydramine	- Benadryl
Promethazine HCl	- Phenergan
Prednisolone Phosphate Sodium	- Hydeltrasol
Levarterenol	- Levophed

SUPPLEMENT

The Supplement contains a replication of four sets of instructions for investigation and management of BTR essential to the effective application of principles discussed in the body of the report.

ATTENTION: Nursing Staff

POST AT:

1. All Nursing Stations
2. Laboratory (Blood Bank, Chemistry, Bacteriology)
3. Postanesthesia Recovery Room
4. Operating Room
5. Emergency Room

ROLE OF NURSE IN MANAGEMENT OF BLOOD TRANSFUSION REACTION

PROCEDURE:

1. Members of the nursing staff have several immediate responses in connection with the detection of a blood transfusion reaction.

   a. Stop the transfusion of blood, but leave the needle in the vein with a slow saline drip attached.

   b. Notify immediately any available house physician, intern, attending physician or anesthesiologist. The situation should be regarded as emergent and any available physician should be summoned.

   c. Check for agreement of patient's name and number with the transfusion container labels and other records.

   d. The nurse must follow seven explicit directions on the Blood Transfusion Reaction Report.

2. The nursing staff should assist the physician by carrying out any orders on a "stat" basis.

3. The nursing staff should determine that adequate supplies of mannitol are instantly available at the nursing station in case the physician should require its immediate use.

ATTENTION: Attending Physician

POST AT:

1. All Nursing Stations
2. Laboratory (Blood Bank, Chemistry, Bacteriology)
3. Postanesthesia Recovery Room
4. Operating Room
5. Emergency Room

ROLE OF PHYSICIAN IN MANAGEMENT OF BLOOD TRANSFUSION REACTION

Pages 9-11: Instructions.

Pages 12-14: Differential Diagnosis of BTR.

Page 14: Pertinent References.

A Blood Transfusion Reaction (BTR) is any adverse sign or symptom caused by blood or blood component transfusion and not related to the underlying disease of the patient manifested during or shortly after that transfusion.

An Incompatible Hemolytic Blood Transfusion Disease (IHBTD) is defined as that condition in which intravascular hemolysis of sensitized erythrocytes is so accelerated as to portend a possible fatality.

Early infusion of mannitol will save the lives of many patients with IHBTD. To test quickly for intravascular hemolysis, plasma is checked for pink or red color, a direct Coombs test is performed, and the plasma hemoglobin level is determined. Findings are compared with pretransfusion specimens, and if hemolysis is evident, mannitol is infused immediately (Table 1). The shorter the interval between the offending transfusion and the use of mannitol, the more effective the treatment. To expedite therapy, all hospital stations where blood transfusions are given stock mannitol as an emergency drug with explicit directions for its use. Also, consumption coagulopathy must be anticipated and managed if IHBTD is present.

---

1. BTR, including IHBTD, is a disease and must be diagnosed and treated by a clinician with consultative support from the pathologist.

2. Any physician must respond when summoned by a nursing staff member to attend a potentially jeopardized patient who is having a possible BTR, including IHBTD.

3. The physician shall determine whether a BTR of any type has occurred (see pages 12-14 for differential diagnosis of BTR). He must then institute appropriate therapy.

   a. Among the several types of BTR, one which is potentially lethal is IHBTD and, therefore, must be recognized forthwith. In IHBTD, the diagnostic feature of intravascular hemolysis can be easily recognized. In IHBTD there will be:

      (1) Elevated levels of plasma hemoglobin.

      (2) Increased population of sensitized erythrocytes.

   The former condition can be recognized by the determination of the plasma hemoglobin level (plasma turns pink at 20-30 mg % and above that becomes deeply red; normal plasma hemoglobin levels are 2-4 mg %); the latter condition can be recognized by the presence of a positive direct Coombs test which is quantitatively greater than the pretransfusion reaction specimen.

   b. Accordingly, the physician, after reviewing the clinical signs and symptoms, noting the pre- and posttransfusion reaction temperature readings, and the quantity of blood received by the patient, will determine the type of transfusion reaction sustained by the patient (see transfusion reaction type summary attached hereto). After instituting appropriate studies and/or treatment, the physician will complete the Blood Transfusion Reaction Report.

   c. If the physician decides there is a possibility of IHBTD, he should immediately draw a blood specimen in EDTA (purple cap, Vacutainer, #18 needle, 5 ml tube) with great care to avoid hemolysis and send this immediately to the blood bank as a "stat" specimen entitled "Possible Hemolytic Transfusion Reaction," along with data identifying the patient. At this point in the absence of laboratory data, if in the judgment of the physician there is an excellent clinical possibility of a hemolytic transfusion reaction, or if he has noticed grossly pink or red plasma, he may institute mannitol therapy in accordance with the directions attached hereto, while the laboratory data are being determined.

   d. Within a short time laboratory reports should be available which would indicate the concentration of the pre- and posttransfusion plasma hemoglobin and the pre- and posttransfusion Coombs tests. Significantly elevated plasma hemoglobin levels

above a normal value of 2-4 mg % and/or a significantly increased Coombs test are excellent evidence of IHBTD when coupled with appropriate clinical signs, symptoms, and history. Mannitol therapy should be instituted immediately (see directions attached hereto).

e. IHBTD is accompanied probably in every case and in variable degree by a consumption coagulopathy. Because the IHBTD may be superimposed on any number of very different underlying diseases, appropriate coagulation studies should be done to determine whether the coagulopathy is: (1) primary activation of the coagulation system with a secondary fibrinolytic component; (2) primary activation of the fibrinolytic system; or (3) a coequal activation of both. Since treatment is quite different for each type of coagulopathy and fraught with disaster if treatment regimens are interchanged, the coagulopathy must be categorized. Heparin, intravenously, is the indicated treatment for category (1); epsilon amino caproic acid for category (2); and Trasylol with or without heparin would be acceptable for category (3). The clinician should consult with the pathologist to obtain a set of diagnostic and base line coagulation studies. In consumption coagulopathy *the basic pathophysiology is the intravascular conversion of plasma to serum. The therapeutic principle is the titration of the patient by intravenous, indicated drug to revert the serum back to plasma as guided by the response of individual parameters in a periodically repeated coagulation profile.* Because at present there are many coagulation techniques from among which pathologists have personal preferences, the set of coagulation parameters for diagnosis and for guiding therapy is best left to the individual pathologist. As with other data in the context of the IHBTD, the results of the coagulation studies must be recorded on the Blood Transfusion Reaction Report (on the reverse blank side).

4. If the blood in the blood transfusion container appears hemolyzed and/or unusually dark or blue-black, the possibility of bacterial contamination of the donor blood (and septicemia in the patient) must be considered. The laboratory will routinely obtain a gram stain and cultural studies on the plasma from the blood transfusion container. The gram stain report will be delivered to the physician shortly after the blood transfusion container is received by the laboratory. Cultural studies will of course be available a few days later, too late to be of value in the management of the jeopardized patient.

5. *Consultation with the attending pathologist is invited at any time.*

TYPES OF TRANSFUSION REACTIONS, THEIR RECOGNITION, AND MANAGEMENT

I. Pyrogenic: Any rise in excess of 1.5° F over the pretransfusion temperature level considered significant, but not diagnostic. May be due to platelet and/or leukocyte antibodies in some cases.

Laboratory Workup: None.

Treatment: Symptomatic.

II. Anaphylactic or Allergic Reaction: Manifested by rash, pruritus, and angioneurotic edema, swelling joints. Extreme cases (anaphylaxis) may have wheezing, dyspnea, and even sudden death.

Laboratory Workup: None.

Treatment: Allergic or Hypersensitivity:

Benadryl 50 mg orally or Phenergan 25 mg orally. In more severe cases Prednisone or Prednisolone 20-40 mg daily.

Anaphylactic:

Epinephrine 1:1000, 0.3-0.5 ml/q 5 min.

Benadryl 50 mg IV or comparable dose of other antihistamine.

Hydeltrasol 20-40 mg IM or IV daily or comparable other cortical steroid.

Levophed 4 ml and 1000 ml of 5% glucose and water at 1-4 ml per min adjusted according to response for hypotension.

III. Incompatible Hemolytic Blood Transfusion Disease: This is a potentially lethal condition and rapid accurate diagnosis and expeditious treatment can save the patient. IHBTD is defined as that condition in which intravascular hemolysis of sensitized erythrocytes is so accelerated as to portend a possible fatality. Any of the signs and symptoms listed on the Blood Transfusion Reaction Report may be manifested in varying degrees and combinations.

Laboratory Workup: See instructions attached hereto.

Treatment: Mannitol and therapy for consumption coagulopathy (see instructions attached hereto).

IV. Circulatory Overload Reactions: Signs and symptoms of acute congestive heart failure are present.

Laboratory Workup: None needed.

Treatment: Individualized "standard treatment for congestive heart failure."

V. Contaminated Blood and Septicemia: Clinical manifestations of septic shock are present. This usually occurs with the administration of the first 50-100 ml of blood. There is evidence of rapid pulse, lowered or absent blood pressure, pale sweaty appearance, severe chills, feeling of impending disaster, coma, convulsions, and even sudden death.

Laboratory Workup: All that will be immediately available will be a gram stain on plasma from the blood transfusion container.

Treatment: Management for septic shock including diagnosis and treatment for consumption coagulopathy.

VI. Citrate Intoxication: Citrate intoxication is most likely in infants who have been managed with exchange transfusions, but also can be seen in adults with numerous tranfusions which have been given closely together and adults with impaired liver function. It is characterized by muscle tremors, EKG changes (prolonged ST segment, prolonged QT segment, pulsus alternans, depression of T-wave), and shock.

Laboratory Workup: As requested by attending physician.

Treatment: Ten ml of 10% calcium gluconate for each 2 liters of citrated blood (recently transfused) is prophylactic.

VII. Potassium Intoxication: Potassium intoxication is most likely to be seen in infants with exchange transfusions using bank blood from 9-21 days old. In adults, potassium intoxication may be seen in anuric patients who cannot safely tolerate increases in serum potassium levels.

Treatment: Consider use of glucose and insulin intravenously to depress the potassium level among other methods of lowering serum K level.

VIII. Other Sequelae:

a. Thrombophlebitis: Thrombophlebitis is usually seen with transfusions which have extended for more than 8 hr continuously in the same venipuncture site.

b. Air Embolism: Air embolism causes shock and dyspnea. Abnormal cardiac sounds are also auscultated.

The treatment is to place the patient on the left side, head down, feet up position.

IX. Late Sequelae:

a. Transmission of Disease: Malaria, serum hepatitis, syphilis, brucellosis.

b. Transfusional Hemosiderosis.

c. Delayed Isosensitization.

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ATTENTION: Anesthesiologists

POST AT:

1. Operating Room
2. Postanesthesia Recovery Room
3. Emergency Room
4. Laboratory (Blood Bank, Chemistry, Bacteriology)

ROLE OF ANESTHESIOLOGIST IN MANAGEMENT OF BLOOD TRANSFUSION REACTION

A Blood Transfusion Reaction (BTR) is any adverse sign or symptom caused by blood or blood component transfusion and not related to the underlying disease of the patient manifested during or shortly after that transfusion.

An Incompatible Hemolytic Blood Transfusion Disease (IHBTD) is defined as that condition in which intravascular hemolysis of sensitized erythrocytes is so accelerated as to portend a possible fatality.

Early infusion of mannitol will save the lives of many patients with IHBTD. To test quickly for intravascular hemolysis, plasma is checked for pink or red color, a direct Coombs test is performed, and the plasma hemoglobin level is determined. Findings are compared with pretransfusion specimens, and if hemolysis is evident, mannitol is infused immediately. The shorter the interval between the offending transfusion and the use of mannitol, the more effective the treatment. To expedite therapy, all hospital stations where blood transfusions are given stock mannitol as an emergency drug with explicit directions for its use. Also, consumption coagulopathy must be anticipated and managed if IHBTD is present.

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1. BTR, including IHBTD, is a disease and must be diagnosed and treated by a clinician with consultative support from the pathologist.

2. IHBTD in the anesthetized patient presents signs and symptoms somewhat different from those encountered by the clinician at the bedside of the conscious patient. In the anesthetized patient receiving an incompatible blood transfusion, the anesthesiologist will note:

a. A marked generalized bleeding and oozing at the operative site.

b. Severe shock out of proportion to the degree of blood loss.

c. An appearance of bleeding and oozing from venipuncture sites which were previously dry.

3. If such observations are made, the anesthesiologist should proceed in accordance with the instructions issued for the guidance of the attending physician and the management of blood transfusion reactions (*quod vide*).

4. If IHBTD is diagnosed and consumption coagulopathy is present, the coagulopathy can be treated during open surgery (see Rock *et al*, Transfusion, 9: 57, 1969).

ATTENTION: Laboratory Personnel:	POST AT:
Blood Bank	1. Blood Bank Laboratory
Chemistry	2. Chemistry Laboratory
Bacteriology	3. Bacteriology Laboratory

ROLE OF LABORATORY PERSONNEL IN MANAGEMENT OF BLOOD TRANSFUSION REACTION

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1. It is the function of the laboratory to generate accurate, pertinent data and to report it rapidly to the responsible physician. If the data are abnormal or pathological, it must also be reported to the attending pathologist immediately.

2. When the blood transfusion donor container is returned to the blood bank, the blood bank personnel should check for agreement of all identification on data on the container, the pilot tube and the patient. Any discrepancy must be reported to the attending pathologist "stat." The laboratory must generate and deliver data essential to the diagnosis of IHBTD as indicated below.

   a. Blood Bank: The blood bank must determine immediately the Coombs test and its intensity on the pre- and posttransfusion specimens of the patient's blood.

   b. Chemistry Laboratory: The chemistry laboratory must determine the plasma hemoglobin level on the pre- and posttransfusion specimens. Urine specimens from the patient taken at the time of the transfusion reaction and 4 hr later will be received by the chemistry laboratory and held in the refrigerator. The pathologist will indicate whether quantitative hemoglobin and a specific gravity determination will be required.

   c. Bacteriology Laboratory: The bacteriology laboratory will perform a gram stain on a centrifuged aliquot of plasma from the blood transfusion donor unit and also prepare appropriate inocula of the plasma from the blood donor container for cultural studies.

3. The laboratory reports the data from the Coombs test, the plasma hemoglobin, and the gram stain to the attending physician as rapidly as they are ready. Any abnormal values are also reported to the attending pathologist.

4. Data from the Coombs test, the plasma hemoglobin, the gram stain, and *ANY OTHER LABORATORY WORK DONE IN CONNECTION WITH THE INVESTIGATION OF THE TRANSFUSION REACTION MUST BE RECORDED ON THE BLOOD TRANSFUSION REACTION REPORT AS IT IS DETERMINED.*

5. The recheck procedure (the retyping and the recrossmatching workup) can be done at a later time during the working day in most instances. Results of this recheck procedure must also be recorded on the *Blood Transfusion Reaction Report form*. If the posttransfusion reaction specimens show a significant increase in the Coombs test and/or a significant increase in the plasma hemoglobin levels, the blood bank should automatically prepare a compatible blood transfusion unit, crossmatched with blood drawn from the patient after the transfusion reaction has occurred. This blood will remain in the blood bank on a standby basis in anticipation of need for the treatment of the jeopardized patient, according to the decision of the attending physician.

6. Deliver the Blood Transfusion Reaction Report form after all pertinent data from the initial investigation have been recorded thereon to the attending pathologist.

TABLE 1

Mannitol Infusion Treatment for Potentially Lethal Hemolytic Transfusion Reactions

Note: Mannitol is stocked at this nursing station as an emergency drug and is immediately available on request.

DIRECTIONS AND PROCEDURE OF MANNITOL TREATMENT*

Infuse intravenously 100 cc of 20 percent mannitol solution within a 15 minute period. This solution is available in 250 ml bottles at all nursing stations, including this one. This dose will initiate a diuresis of 1 to 3 ml of urine per minute in an adequately hydrated patient. The same dose may be repeated if urine flow drops below 100 ml per hour for any subsequent two hour period. Mannitol may be discontinued when the patient can maintain a urine flow of 100 ml per hour without its use. If diuresis does not occur, acute tubular necrosis may be presumed to exist and appropriate and immediate treatment for that condition is indicated.

COMMENT

Time is of critical importance in treating incompatible hemolytic transfusion reactions. The degree of injury sustained by a patient is proportional to the time interval between the offending transfusion and the onset of mannitol treatment. Therefore, the sooner mannitol is administered the less severe is the injury.

If the history, physical findings and clinical course are such that a hemolytic transfusion reaction is suspected as highly probable, mannitol infusion should be started even prior to or concurrent with laboratory investigation, since under the conditions of use prescribed above, no direct adverse sequelae from the use of mannitol will occur. The gain increment of time difference in the interval between the use of mannitol and the laboratory determinations accrues to the advantage of the patient.

These explicit instructions for the use of mannitol are instantly available to the physician as is mannitol itself at each hospital station where blood transfusions are administered.

*From: Postgrad. Med. 45: 84-89, 1969, based upon Barry, K. G. and W. H. Crosby, Transfusion, 3: 34-36, 1963.

The Blood Transfusion Reaction Report (Fig. 1) serves multiple important purposes and when completed is a most valuable document. Initially, it is used to guide the nurse's activities. Then it serves as a summary record of the salient clinical features as observed by the clinician at the time of the event. It routes and accompanies appropriate specimens to the laboratory. Data from the Coombs tests, the plasma hemoglobin tests, and the gram stain are recorded thereon.

If any of these determinations is abnormal, it is routed directly to the pathologist who may use it as a checklist for following the pertinent parameters in the jeopardized patient and for monitoring the response to therapy.

The plain, reverse page of this form can be used to record coagulation studies. The last and final function is an orderly summary record of the episode in sufficient detail to dissuade legal harassment.

In most instances, only a very few entries will be made on this record. But, since it must be adaptable to the occasion of an IHBTD, it serves as a most convenient prospective checklist for studies essential in the management and monitoring of the jeopardized patient.

BLOOD TRANSFUSION REACTION REPORT

CLINICAL DIAGNOSIS _____

HOSPITAL BLOOD UNIT NUMBER _____ AMOUNT OF BLOOD REC'D. BY PATIENT _____ ml.

ATTENTION: Nursing Staff

1. Stop blood transfusion immediately but leave needle in situ with slow saline drip.
2. Summon any available physician immediately to attend patient.
3. Check for agreement of all identifying names, numbers, and letters on pilot tubes, transfusion unit, and patient's wrist tag.
4. Obtain and record pre- and post-transfusion temperatures.
5. Obtain an immediate post-transfusion urine specimen and a second post-transfusion urine specimen 4 hours later. Forward properly labeled specimens to laboratory.
6. Request physician to complete box hereon marked Clinical Signs and Symptoms.
7. Send entire blood transfusion unit with this completed form to Blood Bank.

PHYSICIAN ONLY TO COMPLETE THIS SECTION

CLINICAL SIGNS AND SYMPTOMS CHECK (✓)

Chilly Sensation _____
Severe Shaking Chill _____
Severe Low Back Pain _____
Pulmonary Infarct _____
Nausea _____ Arthralgia _____
Hives _____ Headache _____
Angina _____ Skin Pallor _____
G.I. Hemorr. _____ Dyspnea _____
Perspiration _____ Oozing From Wound or Venipuncture _____

	PRE-REACTION	REACTION	POST REACTION
Date			
Time	(Blood Started)		(Blood Stopped)
Temp.			
Blood Press.			
Pulse Rate			

PLEASE DO NOT WRITE BELOW THIS LINE. USE REVERSE SIDE IF NECESSARY.

LABORATORY USE ONLY Time Rec'd _____ Tech _____ Date _____

RE-CHECK OF TYPING:

	Anti-Sera Reactions						Reverse				Coombs		
	A	B	A, B	D^u	D	C	A_1	A_2	B_1	B_2	Direct	Indirect	Other
Patient's Pre-reaction Blood Sample													
Patient's Post-reaction Blood Sample													
Pilot Tube-1													
Pilot Tube-2													
Donor Blood From Container													

RE-CHECK OF CROSSMATCH

	Saline	Coombs	Albumin	Immune Antibody Anti-_____			
				Titer	Day-Rx.	Day-1	Day-2
Patient's Pre-reaction Serum Sample							
Patient's Post-reaction Serum Sample							

BACTERIOLOGICAL STUDIES: **GRAM STAIN:** **CULTURE:**

BLOOD TESTS	Pre-react	Day of React	Day-1	Day-2	Day-3	Day-4	Day-5	Comments Conclusions
Hemoglobin								
Hematocrit								
Retic. Count								
Serum Plasma hemoglobin								
Bilirubin								
Methemalbumin								
Serum Haptoglobin								
URINE TESTS								
Free Hemoglo. (Quantitative)								
Free RBC								
RBC Casts								
Bile								
Albumin								
Daily Output								
Spec. Grav.								MD

ENTER CONSUMPTION COAGULOPATHY DATA ON REVERSE SIDE.

Figure 1

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13. ABSTRACT

Current methods of investigation for the detection of Incompatible Blood Transfusions (IBT) are time-consuming and, based upon rechecking, a technique which can perpetuate original errors. The efficacy of mannitol, if given in time for the treatment of this condition is well-known and poses an additional reason for the rapid, accurate detection of IBT By cross-checking patients in possible jeopardy, highly pertinent data are obtained with minimum effort. A cross-check in this context consists of the determination of those two parameters which would be diagnostically altered if IBT were present: (1) positive Coombs test; and (2) an elevated plasma hemoglobin, when compared with pretransfusion specimens. Consequently, probable coexistent consumption coagulopathy is then investigated and managed according to a panel of coagulation parameters.

The principles of cross-checking at the operational level of the ward and the laboratory are embodied in an evolved set of segregated, delegated, coordinated instructions: one for each member of the investigative team (nurse, clinician, anesthesiologist, laboratory personnel). Thus, with each member complying with instructions specific only to his role, a composite, efficient, synchronous, almost automatic effort to accommodate all types of blood transfusion reactions, but especially to detect and salvage IBT, is effected. *A hospital-wide detection and salvage system for victims of IBT is thus made immediately available to the pathologist who will adopt these principles, forms, and instructions in toto.*

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A FAIL-SAFE APPROACH TO INCOMPATIBLE BLOOD TRANSFUSIONS

by

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Page 3, line 1: ...caproic acid is unacceptable... should read

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