TRANSFUSION REACTIONS

Dr. Soudabeh Haddadi

Associate Professor of Anesthesia

GUMS

Dec. 2022

IN THE NAME OF GOD

1- عوارض حاد تزریق خون:

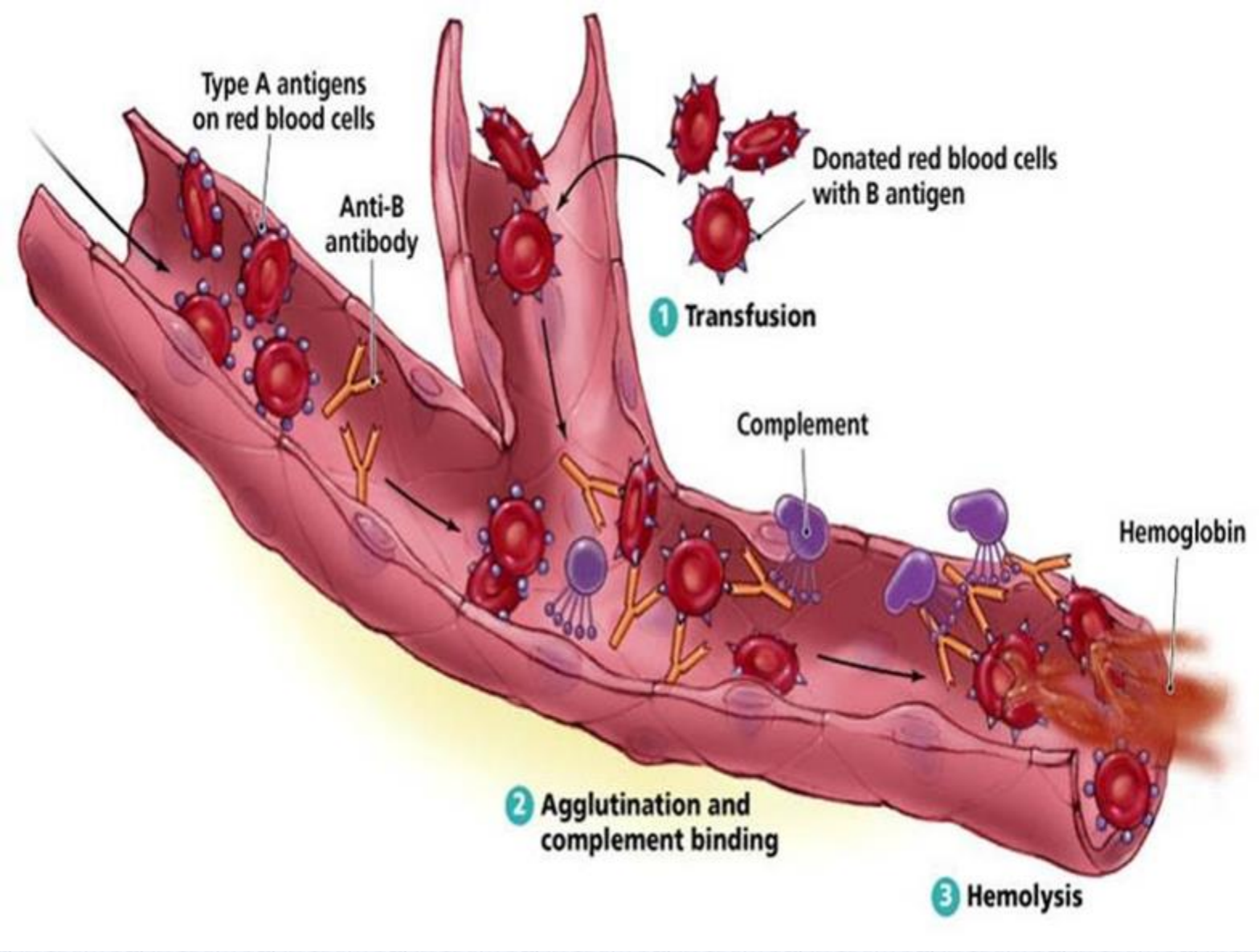
- **واکنشهای خفیف:**
  - واکنشهای کهیری آلرژیک
- **واکنشهای متوسط:**
  - واکنشهای کهیری شدید
  - واکنشهای تب زای غیر همولیتیک
  - تماس احتمالی با عوامل باکتریایی
- **واکنشهای تهدید کننده حیات:**
  - همولیز داخل عروقی حاد
  - شوک سپتیک ناشی از عوامل باکتریایی
  - افزایش حجم مایع
  - واکنشهای آنافیلاکتیک
  - آسیب های ریوی وابسته به تزریق

۲- عوارض تاخیری تزریق خون:

- **عفونت های منتقله توسط تزریق خون** (هپاتیت ، ایدز ، شاگاس، مالاریا، سایتومگالوویروس، سیفلیس)
- **سایر عوارض تاخیری:**
  - واکنش همولیتیک تاخیری
  - پورپورای بعد از تزریق خون
  - GVHD
  - افزایش تجمع آهن

HEMOLYTIC TRANSFUSION REACTION

- In 2011 the incidence of an acute hemolytic transfusion reaction resulting from ABO incompatibility was 1:1200 to 1:190,000
- Intravascular hemolysis occurs when there is a direct attack on transfused donor cells by recipient **Ab** and **complement**
- Such reaction can occur from infusion of as little as 10 ml of blood

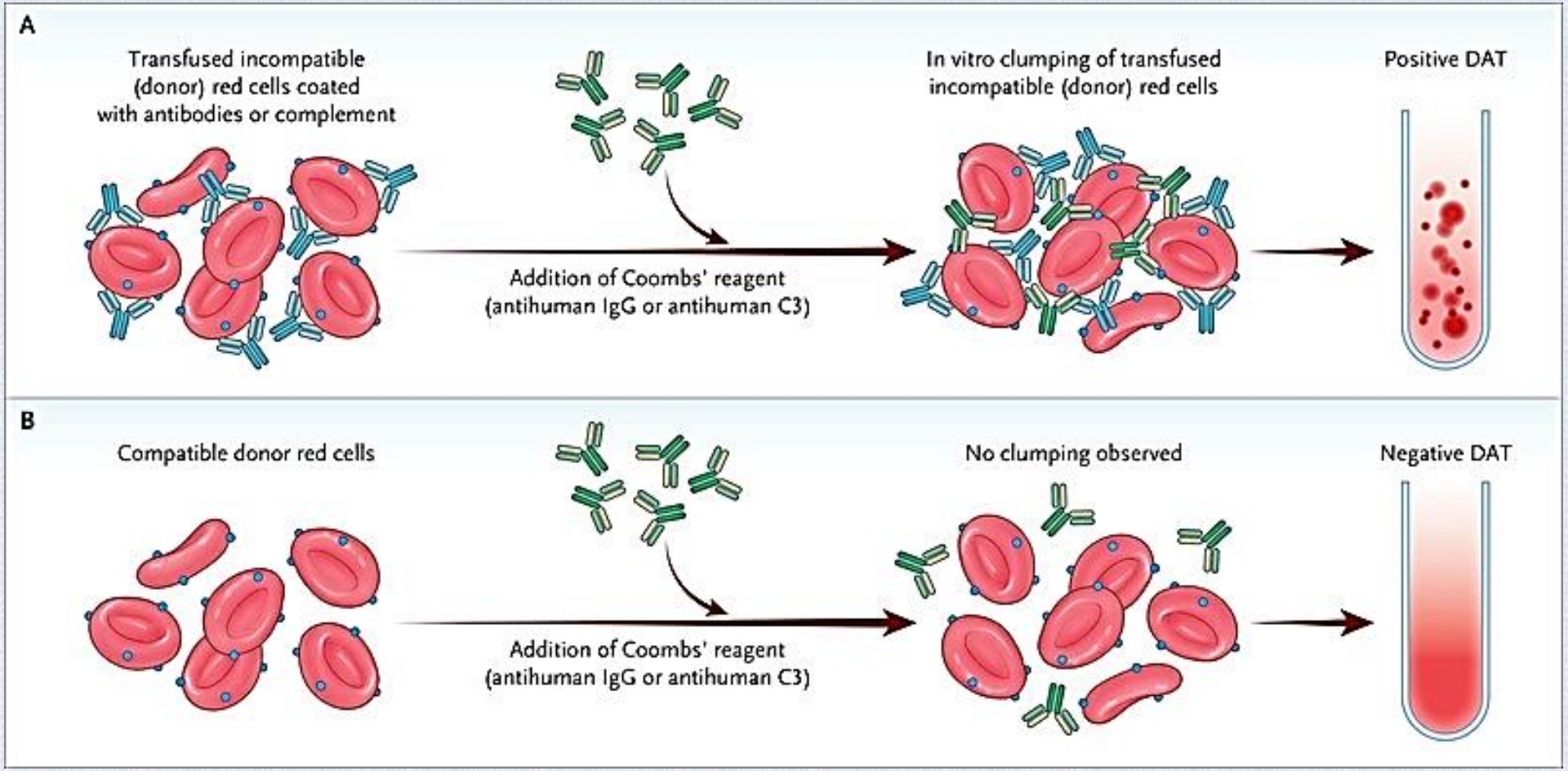

Type A antigens
on red blood cells
Anti-B
antibody
Donated red blood cells
with B antigen
1 Transfusion
Complement
Hemoglobin
2 Agglutination and
complement binding
3 Hemolysis

Signs and Symptoms

- The clinical consequences are very serious but quite variable.
  Factors include :
  1- volume of transfused blood
  2- number of antigenic sites on the cell membrane
  3- activity of the reticuloendothelial system
  4- properties of the Ab (concentration & ability to activate complement)
- A sample of plasma that contains 2 mg/dl of Hb is faintly pink or light brown. When reaches to 100 mg/dl the plasma is red and when reaches to 150 mg/dl hemoglobinuria is occurs.
- **Lab tests** :
  serum haptoglobin
  plasma & urine Hb
  bilirubin
  direct antiglobulin (can confirm the presence of hemolysis)

FREQUENCY AND SIGNS AND SYMPTOMS OF HEMOLYTIC TRANSFUSION REACTIONS IN 40 PATIENTS

Sign or Symptom	No. Patients
Fever	19
Fever and chills	16
Chest pain	6
Hypotension	6
Nausea	2
Flushing	2
Dyspnea	2
Hemoglobinuria	1



direct antiglobulin test

Treatment

- Blood & urine samples should be sent to the laboratory
- Blood bank should check all paperwork & lab tests should be performed :
  - direct antiglobulin test
  - repeat compatibility testing
  - repeat other serologic tests
  - U/A for hemoglobinuria
- **Renal** & **coagulation system** are affected
- **ARF** : Hb in the form of acid hematin precipitate in the distal tubule and is inversely related to the volume of urine flow & its PH
- Maintain U/O > 75 ml/h by IV fluid & diuretics
- Crystalloid to maintain the CVP between 10-15 cm H2O + 12.5 – 50 g manitol or diuretics (furosemide)
- Alkalinization of the urine
- **DIC**: RBC stroma is severed releasing erythrocytin , which activates the intrinsic system of coagulation
- Lab tests: Plt , PT , PTT (baseline values for subsequent compare)
- **Hypotension** : result from activation of the kallikrein system (plasma kininogen is converted to bradykinin , a potent vasodilator)

Steps in the Treatment of a Hemolytic Transfusion Reaction

1. STOP THE TRANSFUSION.
2. Maintain the urine output at a minimum of 75 to 100 mL/hr by the following methods:
   a. Generously administer fluids intravenously and possibly mannitol 12.5 to 50 g, given over 5 to 15 minutes.
   b. If intravenously administered fluids and mannitol are ineffective, administer furosemide (20 to 40 mg) intravenously.
3. Alkalinize the urine; because bicarbonate is preferentially excreted in the urine, only 40 to 70 mEq of sodium bicarbonate per 70 kg of body weight is usually required to raise the urine pH to 8, whereupon repeat urine pH determinations indicate the need for additional bicarbonate.
4. Assay urine and plasma hemoglobin concentrations.
5. Determine platelet count, partial thromboplastin time, and serum fibrinogen level.
6. Return unused blood to blood bank for repeat crossmatch.
7. Send patient's blood and urine sample to blood bank for examination.
8. Prevent hypotension to ensure adequate renal blood flow.

TRANSFUSION-RELATED ACUTE LUNG INJURY (TRALI)

- The common cause of transfusion-related fatalities
- TRALI is a noncardiogenic pulmonary edema
- Clinically appear 1-2 hours after transfusion & are in force within 6 hours
- Fever, dyspnea, fluid in the ETT , severe hypoxia
- All blood components , especially FFP
- **Treatment** : stopping the transfusion & critical care support
- Most patients recover within 96 hours
- **Risk factors**: higher IL-8 ,liver surgery, chronic alcohol abuse, shock, higher peak airway pressure during M.V, smoking, positive fluid balance

TRALI vs. Normal Lung

TRANSFUSION-RELATED FATALITIES IN THE UNITED STATES, 2008 THROUGH 2012

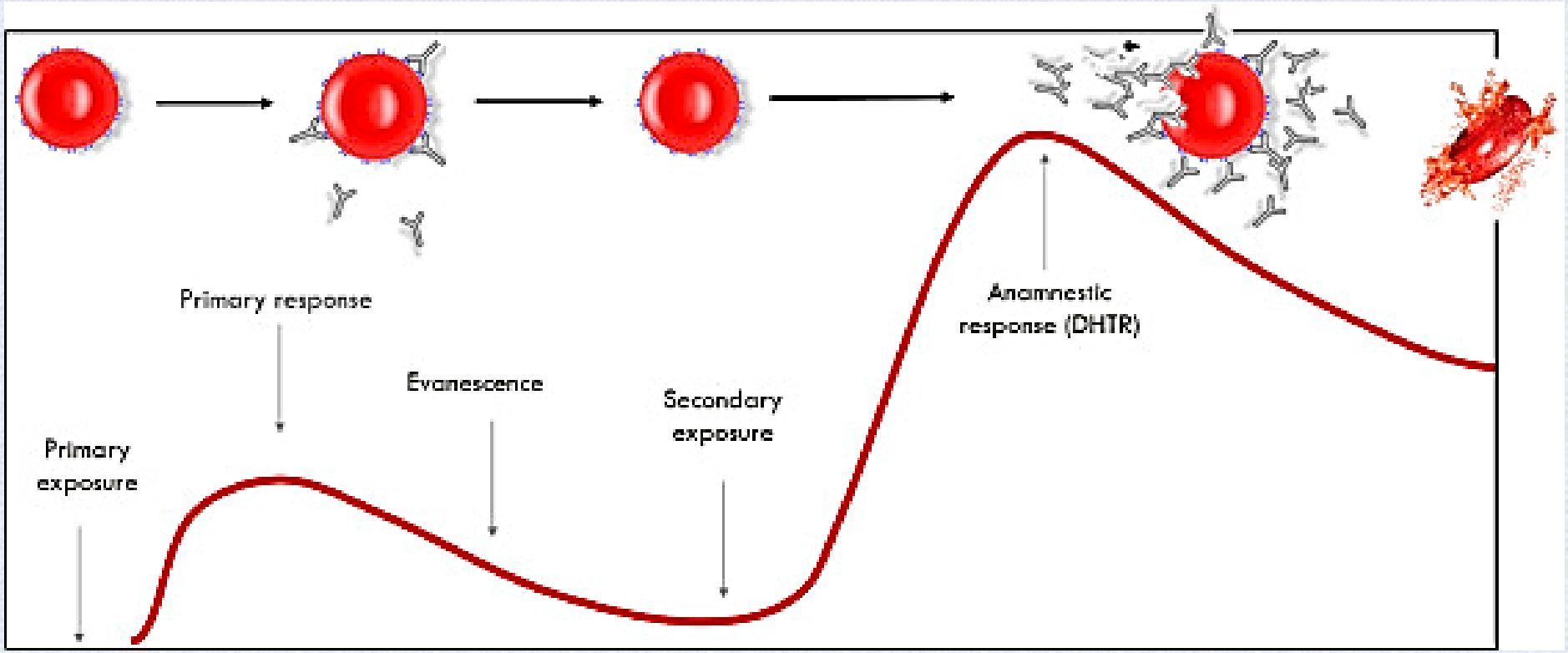
Cause of Fatality	2008 to 2012	2012
TRALI	74	17
Other reactions (non-ABO hemolytic therapy, anaphylaxis)	53	8
Bacterial contamination	21	3
ABO hemolytic transfusion therapy	22	3
Transfusion not ruled out	99	27

From Fatalities Reported to FDA following blood collection and transfusion: annual summary for fiscal year 2012. These reports are available online. at http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/ReportaProblem/TransfusionDonationFatalities/ucm346639.htm

TRALI, Transfusion-related acute lung injury.

DELAYED HEMOLYTIC TRANSFUSION REACTION

- The transfused donor cells may survive well initially, but after a variable delay (2-21 days) they are hemolysed.
- Occurs in recipients sensitized to RBC Ag by previous blood transfusions or pregnancy
- In which the level of Ab at the time of transfusion is too low & RBC destruction occurs only when the level of Ab is increased after secondary stimulus
- Often manifested only by a decrease in the post transfusion Hct
- **Jaundice** & **hemoglobinuria** can occur and can cause impairment in renal function, but only rarely lead to death
- Are in the **Rh & kidd systems** rather than the ABO system
- Not be preventable, because pre transfusion testing is unable to detect very low level of Ab


Primary response
Evanescence
Secondary exposure
Anamnestic response (DHTR)
Primary exposure

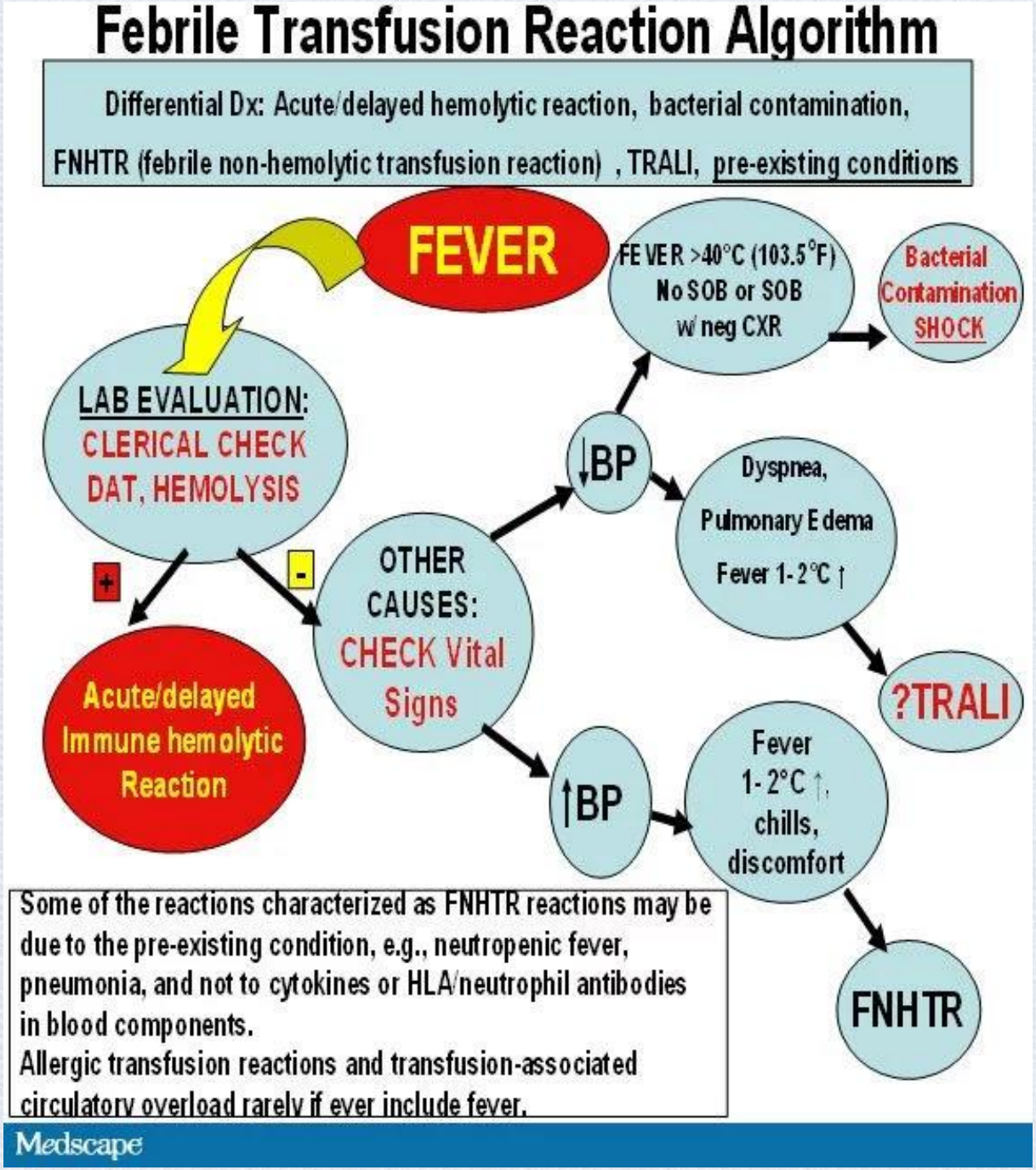
NONHEMOLYTIC TRANSFUSION REACTIONS

- Usually are not serious and are **febrile** or **allergic**
- Fever may be the first sign of a **hemolytic reaction** or of **bacterial contamination**

1- Febrile reactions

- **Symptoms** : chills, fever, headache, myalgia, nausea, nonproductive cough, (less common :) hypotension, chest pain, vomiting, dyspnea , pulmonary infiltration in CXR
- Caused by pyrogenic cytokines & intracellular contents released by donor leukocytes
- Use of leukoreduced blood lowerd the incidence of febrile reaction
- **Direct antiglobulin test** can differentiates a hemolytic reaction from a febrile reaction
- No clear consensus exist on whether the transfusion should be determinated

Febrile Transfusion Reaction Algorithm



2- Allergic reactions

- Can be minor **anaphylactoid** or **anaphylactic**
- An anaphylactoid reaction is clinically similar to anaphylaxis, but it is not mediated by IgE

A- anaphylactoid reaction

- Most are minor & caused by the presence of foreign protein in the transfused blood
- **Symptoms:** urticaria with itching (most common)
  facial swelling (occasionally)
- Transfusion does not need to be discontinued
- **Treatment:** antihistamines

B- anaphylaxis

- **Symptoms:** dyspnea, hypotension, laryngeal edema, chest pain, shock
- caused by the transfusion of IgA to patients who are IgA deficient & have formed anti-IgA
- Occurs very rapidly, after transfusion of only a few ml of blood or plasma
- Patients who experience these anaphylactic reactions can be given transfusion with washed RBC

OTHER NONINFECTIOUS RISKS

- The term **NISHOT** (non infectious serious hazards of transfusion) includes all noninfectious complication

1- transfusion-associated circulatory overload (TACO)

- Refers to an excessive administration of blood
- Risk factors :
  - cardiopulmonary dis.
  - renal failure
  - extremes of age (especially infants)
- Decrease the rate of transfusion & diuretics may be helpful

TRALI *vs.* TACO

LOYOLA UNIVERSITY HEALTH SYSTEM

TRALI	TACO
Signs & Symptoms • Respiratory distress • Tachypnea • Hypoxemia • Hypotension • **Noncardiogenic** pulmonary edema • Fever • Onset within 6 hours of transfusion **Supporting Data** • B/L pulmonary infiltrates on CXR • Decreased WBC count • *Associated with* HLA and/or Neutrophil Antibodies	**Signs & Symptoms** • Respiratory distress • Tachypnea • Hypoxemia • **Hypertension** • **Cardiogenic** pulmonary edema • Improves with diuretics **Supporting Data** • B/L pulmonary infiltrates on CXR • Pretransfusion **fluid overload** • **Elevated BNP** • Increased heart size • Vascular congestion • Pulmonary wedge P > 18 mm Hg

LOYOLA UNIVERSITY HEALTH SYSTEM

2- transfusion-related immunomodulation (TRIM)

- Blood transfusion can suppress the immune system because of circulating lymphocytes

3- microchimerism

- Refers to more than one cell line in an individual organism
- Donor lymphocytes may persist in a patient
- It is associated with **pregnancy** , **transplant** , and **trauma**
- Out-come is not known

4- post transfusion purpura

- Refers to recipient alloantibodies attacking donor **platelet Ag**
- Treated with IV immunoglobulin

5- hypotensive transfusion reaction

- Activation of the coagulation pathway activates production of **bradykinin** & **allergic reaction**

6- transfusion-associated graft-versus-host disease (TA-GVHD)

- Refers to transfusion into an immunocompromised host
- Is an extremely serious & fatal problem

Transfusion Associated Graft-vs-Host Disease (TA-GVHD)

- Incidence: Rare
- Etiology: Donor lymphocytes engraft in recipient and mount an attack on the host tissues
- Presentation: Rash, erythroderma, maculopapular rash, anorexia, nausea, vomiting, diarrhea, hepatitis, pancytopenia, fever, bone marrow fibrosis and failure
- Lab testing:
  - Skin biopsy
  - Bone marrow biopsy and HLA typing

8- alloimmunization

- Only 2-8% of recipients who are chronically transfused develop RBC alloantibodies

9- iron overload

- It is the results of chronic transfusion therapy
- Iron deposits into vital organs
- Fatal **liver** or **heart** dysfunction , or both , can occur

Iron Overload

- 1 unit of PRCs has ~ 250 mg of Iron

  Removed by body 1 mg / day

accumulate iron → Hemosiderosis

iron accumulate in tissue → Hemochromatosis

TABLE 61-9 NONINFECTIOUS HAZARDS OF TRANSFUSION

Transfusion Reaction	Incidence (per 10^5 Transfusions)	Etiology	Therapy	Prevention
Febrile	All components: 70-6800	Storage-generated proinflammatory cytokines Patient antileukocyte antibodies bind to donor leukocytes	Stop transfusing Give antipyretics Supportive care	Prestorage leukoreduction
TACO	All components: 16.8-8000 Practice-dependent	Circulatory overload Patients with cardiac or renal disease, infants, and the critically ill are at increased risk	Stop transfusing Give diuretics Oxygen	Identify patients at high risk Transfuse slowly
TRALI	Erythrocytes: 10-20 Platelets/plasma: 50-100	Passive transfusion of donor antibodies Storage-generated toxic lipids	Supportive care	Remove high-risk donors from the donor pool
Allergic	All components: 3000 mild, 2 anaphylactic	Mild reactions: Transfusion of soluble antigens in donor plasma Anaphylaxis: IgA deficiency or other recipient protein deficiency	Stop transfusing ASA monitors Large-bore IV access Epinephrine Antihistamines Supportive care	Pretransfusion antihistamine use remains common practice despite limited evidence
Hemolytic	Erythrocytes: 1.1-9.0	Donor antibodies bind to patient erythrocytes Patient antibodies bind to donor erythrocytes	Stop transfusing Repeat matching Supportive care Treat DIC	Standard operating procedures
TRIM	Unknown	The mechanism is unknown but may depend on the presence of donor leukocytes	Treat complications (e.g., infection, malignancy)	Prestorage leukocyte reduction may be beneficial, but this approach is controversial
Microchimerism	All components: 5000-10,000 massive transfusion	Permanent residence of donor cells in recipient	Unknown	Unknown
Posttransfusion purpura	All components: 2	Recipient alloantibodies attack donor platelet antigens	IVIG	Avoid units positive for implicated HPA antigens in patients with a history of PTP
Hypotensive	Unknown	Production of kinins by the activation of the contact system Patients on ACE inhibitors are at increased risk	Stop transfusing ASA monitors Large-bore IV access Supportive care	Avoid the use of negatively charged leukocyte reduction filters
Graft-versus-host	Varies by patient population	Transfusion into immunocompromised host Transfusion of donor cells closely matching HLA type	No consensus exists Consider bone marrow transplant	Gamma irradiation of cellular products

TRANSFUSION-TRANSMITTED INFECTION

- The use of more sensitive screening tests and changes in transfusion medicine practices has made these infectious risks quite rare

PERCENTAGE RISK OF TRANSFUSION-TRANSMITTED INFECTION WITH A UNIT OF SCREENED BLOOD IN THE UNITED STATES*

Infection	Risk	Window Period (Days)
Human immunodeficiency virus-1 and -2	1:1,476,000	5-6
Human T-lymphotropic virus (HTLV-II)	1:2,993,000	51
Cytomegalovirus (CMV)	Infrequent with leukocyte-reduced components	
Hepatitis C virus (HCV)	1:1,149,000	3-4
Hepatitis B virus (HBV)	1: 280,000	24
Hepatitis A virus (HAV00)	1:1,000,000	
Bacteria red blood cells	1:1,000 with septic reaction in 1:500,000	
Pheresis platelets (with early aerobic culture)		
Parasites: Babesia and malaria	<1:4,000,000	7-14
West Nile virus (WNV)	1/1,100,000	?
Acute hemolytic transfusion reactions	1:38,000-1:70,000	

Infectious Disease Testing for Blood Transfusions: 1998

1. Discontinue serum alanine aminotransferase testing
2. Hepatitis C antibody testing
3. Antibody to hepatitis B core antigen
4. Human immunodeficiency virus (HIV) type 1
5. HIV-2
6. HIV Ag (p24 antigen)
7. Human T-cell lymphotropic virus (HTLV) types 1 and 2
8. Serologic test for syphilis

بررسی نشانه های مهم عوارض حاد مرتبط با تزریق خون

(دستورالعمل سازمان انتقال خون)

تب

تعریف : افزایش ۱ درجه سانتی گراد یابیشتردردمای پایه بدن در طی تزریق خون و یا در طی ۲ -۱ ساعت بعد از اتمام تزریق خون

آیا علائم مهم زیر برای بیمار مطرحند ؟

افزایش دمای بدن بیش ازیک درجه سانتی گراد

افت فشارخون، شوک، تاکی کاردی، لرز، اضطراب، دیس پنه، درد پشت

هموگلوبینوری، الیگوری، خونریزی در محل رگ گیری

تهوع ، استفراغ

اگر هیچکدام از علائم فوق مطرح نباشد :

دادن مسکن استامینوفن

پیگیری وتحت نظر گرفتن شدید بیمار

(ادامه تزریق (البته پس از قطع اولیه تزریق خون)درFNHTR مورد بحث می باشد وبستگی به نظر پزشک معالج- وضعیت بالینی بیمار و نتایج آزمایشات انجام شده ازجمله ردواکنش همولیتیک داشته ودرصورت ادامه تزریق باید با نظارت دقیق و شدید پزشک معالج و پرستار انجام شود.)

تب

علل :

Bacterial contamination

AHTR

FNHTR

TRALI

Other Causes

اقدامات مورد نیاز:

گرفتن نمونه خون ونمونه ادرار مجدد از بیمار و ارسال به بانک خون

ارسال کیسه خون وست تزریق به بانک خون

انجام سایر آزمایشات با توجه به تشخیص افتراقیهای مورد نظر

تنگی نفس

علل :

TRALI

TACO

Anaphylaxis

Other Causes

کهیر

سایرعلائم احتمالی همراه : ادم صورت، ادم راه های هوایی، علائم ونشانه های سیستم تنفسی تحتانی ، افت فشارخون، شوک

آیا نشانه های جدی زیر مطرحند ؟

۱- افت فشار خون- فلاشینگ – اضطراب

۲- تنگی نفس – سرفه

۳- تاکی کاردی

۴- کهیر ژنرالیزه بیش از دو سوم بدن

۵- تهوع – استفراغ

۶- راش منتشر

اگر جواب مثبت است :

تزریق خون را آغاز نکنید.

سریعا به پزشک اطلاع دهید.

سریعا به بانک خون اطلاع دهید.

علل :

آنافیلاکسی **Anaphylaxis**

ترالی **TRALI**

Other Causes

اگر جواب منفی است :

تشخیص واکنش آلرژیک خفیف است.

اقدامات مورد نیاز :

-تجویز آنتی هیستامین مانند دیفن هیدرامین

ادامه تزریق خون با نظارت دقیق وشد ید پرستاروپزشک معالج در صورتی که کهیرپوستی کمتر از ۲/۳ سطح بدن باشد و بیمارعلامت دیگری نداشته باشدو کهیر بیماربه درمان جواب داده وفروکش کرده باشد.

توجه: در صورتی که کهیر تمام سطح بدن را فراگرفت و یا با سایر علائم سیستمیک همراه شد بایستی بلافاصله تزریق خون مجددا قطع و اقدامات حمایتی – درمانی آغاز گردد.

افت فشار خون

تعریف :کاهش واضح فشار خون سیستولیک و یا دیاستولیک

- * در کم فشاری مرتبط با تزریق خون بیمار علائم ونشانه های عوارض دیگر انتقال خون مانند تب-لرز-تنگی نفس و..ندارد. درجه کاهش فشار خون که برای تشخیص لازم است مورد بحث بوده ودر کل کاهش
- ۳۰-۱۰میلی متر جیوه را در فشار سیستول یا دیاستول خون شریانی به نسبت مقدار پایه قبل از تزریق در نظر می گیرند.
- کاهش فشار خون در خلال تزریق آغاز شده وبا قطع تزریق خون بلا فاصله بر طرف می گردد.
- *چنانچه افت فشار خون تا۳۰دقیقه بعداز قطع تزریق خون برطرف نگردد قطعا تشخیص دیگری مطرح می باشد.

افت فشار خون

علل :

-Bradykinin mediatedHypotension

-Sepsis

-AHTR

-TRALI

-Other Causes

avoidance of unnecessary transfusions will be the most effective way to reduce complications of blood transfusions !


Thank You