عوارض حاد مرتبط با تزریق خون

عوارض حاد

در زنجیره درخواست خون تا تزریق، در هر یک از مراحل امکان اشتباه وجود دارد که در صورت عدم دقت و سهل‌انگاری برای بیمار بسیار مخاطره‌آمیز است.

Transfusion reactions

- **Acute:** presenting during or within 24 h
- **Delayed:** presenting anytime after 24 h

Transfusion Reactions

- **Infectious**
  - Viral
  - Bacterial
- **Noninfectious**
  - **Reaction to RBC Antigens**
    - Acute Hemolytic Transfusion Reactions (AHTR)
    - Delayed Hemolytic Transfusion Reactions (DHTR)
  - **Reactions to Donor Proteins**
    - Minor Allergic Reactions
    - Anaphylactic Reactions
  - **White Cell-Related Transfusion Reactions**
    - Febrile Reactions
    - Transfusion-Related Acute Lung Injury (TRALI)

عوارض حاد

حدود ۱۰٪ دریافت کنندگان خون یا فرآورده ها یک واکنش زیان بار را تجربه می کنند.

تعریف : هر نوع نشانه یا علامت ناخواسته یا نامساعدی که درحین و یا به فاصله ۲۴ساعت از انتقال یک واحد خون یا فرآورده رخ میدهد، ناشی از تزریق خون است مگر خلافش ثابت شود.

نشانه های یک واکنش مرگ آفرین(مثل واکنش همولیتیک حاد) و یک واکنش نسبتاً خفیف ممکن است در ابتدای امر کاملا شبیه به هم باشند (*تب و لرز*).

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علایم و نشانه های عوارض حاد مرتبط با تزریق خون در بیماران هوشیار

❊ علایم عمومی :

-تب

-لرز

-درد قفسه سینه

-درد کمر

-درد عضلانی

-سردرد

-احساس گرما در محل تزریق یا در طول رگ

احساس درد در محل تزریق

❊ علایم سیستم عصبی:

- گزگز اندام ها

❊ علایم سیستم تنفسی :

-تاکی پنه

-آپنه

-تنگی نفس

-سرفه

-ویز

* علایم قلبی – عروقی :

-تغییرات ضربان قلب(تاکیکاردی،برادیکاری)

-افت فشار خون یا افزایش فشارخون

-خونریزی

* علائم جلدی:

-راش

-کهیر

-خارش

* علایم گوارشی:

-تهوع

-استفراغ

-کرامپ شکمی

-اسهال خونی

*علائم کلیوی:

-تغییرات در حجم ادرار(الیگوری،آنوری)

- تغییر دررنگ ادرار

علایم در بیمار غیر هوشیار

- -نبض ضعیف، - تاکی کاردی - برادیکاردی
- تب
- - افت فشار خون یا افزایش فشارخون
- -تغییر در رنگ ادرار، الیگوری - آنوری
- -افزایش خونریزی در محل جراحی

فراموش نکنیم

واکنش های حاد تزریق خون در ابتدای امر ممکن است تظاهرات یکسان داشته باشند بنابراین هر نشانه ای باید جدی گرفته شود و تزریق خون متوقف تا علت مشخص گردد.

بررسي نشانه هاي مهم عوارض حاد مرتبط با تزريق خون

تب

تعریف : هنگامی تب را به عنوان علامتی از بروز عارضه می پذیریم که ۱- درجه حرارت نسبت به قبل از تزریق یک درجه یا بیشتر افزایش پیدا کرده باشد.

۲- در صورتی که درجه حرارت قبل کمتر از ۳۸ درجه باشد و درجه حرارت بعد از بروز عارضه حداقل نیم درجه سانتی گراد افزایش نشان دهد به شرطی که به ۳۸ یا بالاتر برسد

شیوع ۱٪

و در ۲۰٪ تزریق پلاکت

- **Mild**: unexplained fever ≥38°C and a temperature rise of at least 1°C but <1.5°C from pre-transfusion baseline, occurring in the absence of chills, rigors, respiratory distress and haemodynamic instability
- **Moderate**: unexplained fever ≥38°C and a temperature rise of at least 1°C but not meeting criteria for either mild or severe FNHTR
- **Severe**: unexplained fever >39°C and a temperature rise ≥2.0°C from pre-transfusion baseline and chills/rigors .
- **STOP TRANSFUSION**
- **Check label and recipient identity**
- **Slow the transfusion if reaction is mild and MO elects to continue transfusion**
- **Antipyretic Paracetamol 1g po and monitor closely**

- تب میتواند به دلیل
  - عفونت باکتریایی
  - واکنش تب زای غیر همولیتیک
  - ناسازگاری ABOایجاد شود
  - TRALI

تب می تواند علامت واکنش حاد همولیتیک باشد و به همین دلیل است که پس از افزایش درجه حرارت 1 درجه سانتیگراد ، تزریق متوقف می شود.

این امر از تزریق خون ناسازگار اضافی در صورت واکنش همولیتیک جلوگیری می کند

لرزیدن و تب بیش از 2 درجه سانتیگراد اغلب هنگام تزریق محصول خون به بیمار حاوی اندوتوکسین باکتریایی و سایر محصولات جانبی میکروبی مشاهده می شود

.

از آنجا که پلاکتها مانند RBC در یخچال قرار ندارند ، احتمال رشد باکتریها بیشتر است

آزمایش باکتریایی پلاکت ها در طی فرآیند تولید اکنون یک روش استاندارد است ، بنابراین میزان آلودگی باکتریایی کاهش یافته است.

واکنش تب زای غیر همو لیتیک

- در 3تا۷درصد موارد تزریق گلبول قرمز ایجاد می شود

- ۲۰-۳۰درصد تزریق پلاکت ایجادمی شود
- معمولا در انتهای تزریق اتفاق می افتد
- به دلیل آنتی بادی علیه آنتی ژن های گلبول سفید اتفاق می افتد
- یا به دلیل آزاد شدن سیتو کین ایجاد می شود

- علایم شامل

- آنفلونزا
- احساس لرز
- سرما
- سردرد
- تهوع
- بدن درد

تب

اقدامات فوری :

قطع تزریق خون وباز نگاه داشتن مسیر وریدی با نرمال سالین

چک مجدد علایم حیاتی

تایید هویت بیماربا توجه به مستندات موجود(کیسه خون – فرم درخواست خون و...) به جهت کسب اطمینان از

تزریق فرآورده مورد نظر به بیمار مورد نظر

اطلاع به پزشک معالج

اطلاع به بانک خون

ارسال کیسه و ست تزریق خون-نمونه خون و ادرارجدید ازبیماربعد ازوقوع عارضه به بانک خون

انجام سایر آزمایشات با توجه به تشخیص افتراقیهای مورد نظر

در چه صورت تب مهم است

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) در افزایش درجه حرارت کمتر از ۱/۵ درجه

بستگی به نظر پزشک معالج

وضعیت بالینی بیمار و

نتایج آزمایشات انجام شده

رد واکنش همولیتیک داشته

ادامه تزریق باید با نظارت دقیق و شدید پزشک معالج و پرستار انجام شود

Non-Hemolytic reactions

Bacterial Contamination

- Onset typically rapid, occurring within 30 minutes of completion of transfusion
- More common in components stored at RT
- Examine returned unit for abnormal appearance (brownish or purple discoloration, clots, muddy appearance)
- Gram’ s stain and Culture of blood bag contents should be performed if clinical presentation suggests bacterial sepsis

Bacterial Contamination

Bacterial sepsis;

Rate of bacterial infection/contamination is higher with platelets is because they are stored at room temperature and the units are generally pooled between 6 and 10 donor units.

Bacterial Contamination

Presentations:

Fever

Chills

Tachycardia

Hypotension

Shock

* **The patient may also develop DIC and acute renal failure.**

Laboratory evaluation in Bacterial Contamination

***1-Visual examination returned component:**

-COLOR CHANGE

-BUBBLES

***2-Gram's stain on returned component**

***3-Cultures on returned component & post transfusion specimen**

Bacterial contamination management

***Stop transfusion & maintain IV access**

***Take patient vital signs**

***Recheck identification of & blood products**

***Notify physician**

***Notify transfusion service:**

Other products from the same donor can be quarantined

***Return clamped blood unit& tubing attached for culture**

Collect blood samples for blood culture

Broad spectrum antibiotic therapy

Prevention of bacterial Contamination

*Inspect all blood products for visual evidence of contamination

*The first 40 ml of blood collected is diverted in a pouch to reduce risk of transmitting organisms from skin

تنگی نفس

- تنگی نفس، یک علامت نگران کننده است
- علت تنگی نفس، مستقیماً مربوط به خود فرآورده خون خاص نیست ، بلکه به دلیل بیماری زمینه ای بیمار و افزایش مایعات در یک بیمار حساس است.
- افراد مسن بیماران مبتلا به نارسایی قلبی ، کم خونی مزمن یا بیماری کلیوی مستعدابتلا به اضافه حجم هستند.

تنگی نفس می تواند ناشی از واکنش آنافیلاکتیک است

آنافیلاکسی یک واکنش آلرژیک شدید است که منجر به تنگی نفس و افت فشار خون می شود
.

علل ایجاد تنگی نفس

TRALI

TACO

Anaphylaxis

Other Causes

Transfusion-Related Acute Lung Injury (TRALI)

- **TRALI presents as sudden onset of respiratory difficulties during or shortly after transfusion.**
- **Hypoxemia and lung infiltrates are detected on chest X-rays in almost all patients with TRALI**
- **half of patients show a pinkish, frothy sputum**
- **Tachypnea, tachycardia, and elevated airway pressure are frequently observed.**

Transfusion-Related Acute Lung Injury (TRALI)

- The most common cause of transfusion-related death

- Pathophysiology of TRALI:

- Recipient neutrophils are activated against an antigen in donor blood product →neutrophils become sequestered in lung capillaries →Capillary leak →Pulmonary edema

Transfusion-related acute lung injury

Incidence :

1/5000-1/190,000 blood and blood components transfused

***Packed red cells**

Cryoprecipitate

FFP

can cause TRALI

*** 15ml of blood component are sufficient to cause TRALI**

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Transfusion-related acute lung injury (TRALI)

Prognosis :

*Most patients recover within 48–96hr

*Hypoxemia and radiological evidence of pulmonary infiltration can persist for 7 days in 20% of patients

*70% patients require mechanical ventilation

*In-hospital mortality: 5–10%

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- Fever, hypotension, and cyanosis occur in less than one-third of patients with TRALI.

- Confirming hypoxemia
- obtaining a chest X-ray
- evaluating vital signs
  - are required to diagnose TRALI.

- No laboratory test is specific for diagnosing TRALI.

- Blood bank should investigate associated donors for presence of anti-human leukocyte antigen (HLA) and
- possibly man neutrophil antigen (HNA) antibodies
- Goal is to find donors should be deferred from future donations.

TRALI versus TACO

	TRALI	TACO
Blood pressure	Low-normal	Normal-high
Body temperature	Normal-elevated	Normal
CXR	No vascular congestion	Vascular congestion, pleural effusion
BNP	Low (< 250 pg/ml)	High
PAOP	Low-normal	High
Ejection fraction	Normal function	Abnormal function
Response to diuretics	Inconsistent	Improved
Edema fluid	Transudate	Exudate

Diagnostic Criteria

- Acute onset of hypoxemia (within 6 hours of conclusion of transfusion)
- Bilateral CXR infiltrates consistent with ALI
- Absence of evidence of left atrial hypertension
- Absence of temporally related causes of ALI

Additional laboratory evaluation in TRALI

1-WBC Ab screening in donor & recipient If positive antigen typing may be indicated

2- WBC cross match

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Treatment

- Largely supportive
- Transfusion should be stopped
- Supplemental oxygen and ventilation support if necessary
  - Use low tidal volume settings like in ARDS
- No diuretics
- Glucocorticoids have been administered but no evidence supporting their administration

Prevention :

Transfusion-related acute lung injury (TRALI)

No universally agreed approach to donor management

1-It is suggested that donors implicated in TRALI and who have demonstrable antibodies should be permanently disqualified from the donor pool

2-Deferring multiparous female

3-Using male donor plasma

4-Washed blood products

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Non-Hemolytic reactions

Circulatory overload

- Usually seen in patients with compromised cardiac or pulmonary status
- Difficulty breathing, cough, cyanosis, tachycardia, hypertension, headache, congestive heart failure
- Symptoms usually improve when infusion is stopped and patient is placed in sitting position

Transfusion-Associated Circulatory Overload (TACO)

- Risk factors
  - Patients with limited cardiopulmonary reserve (very young and elderly)
  - High volume transfusion
  - History of cardiac or renal disease
- Onset: within 1-2 hours after transfusion

Circulatory Overload

Treatment:

Stop transfusion
Upright posture
Oxygen therapy
IV diuretic (furosemide)
Phlebotomy

Prevention:

*** Administer transfusion slowly (1ml/kg/hr)**
Use of diuretics

- **Prevention:**
- **slow administration of blood**
- **pretreatment with diuretics**
- **blood administration with dialysis**

تنگی نفس

اقدامات فوری :

قطع تزریق خون وباز نگاه داشتن مسیر وریدی با نرمال سالین

چک مجدد علایم حیاتی

تایید هویت بیماربا توجه به مستندات موجود(کیسه خون – فرم درخواست خون و...) به جهت کسب اطمینان از

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واکنش های آلرژیک

- واکنش های آلرژیک در کمتر از 2 %گیرندگان خون و به علت واکنش های آنتی ژن آنتی بادی ناشی از تزریق پروتئین های پلاسما رخ می دهند.

- علایم و نشانه های آن از تظاهرات جلدی (کهیر، خارش و گاهی تب مختصر)تا واکنش های آنافیلا کتیک سیستمیک از جمله برونکواسپاسم متفاوت است.

- شدت یک واکنش آلرژیک معمولاً به میزان خون تزریق شده ارتباطی ندارد.
- اکثر واکنش های آلرژیک مختصر هستند، تکرار نمی شوند و به آنتی هیستامین های خوراکی یا تزریقی پاسخ می دهند.

اولین پاسخ به خارش و کهیر همیشه باید توقف تزریق خون باشد.

اگر علائم فقط به خارش محدود شود میتواند انتقال خون از سر گرفته شود.

ادامه تزریق خون با نظارت دقیق پرستار و پزشک معالج

- مصرف فیلترهای خونی نسل سوم کاهش دهنده لکوسیتی ارزش ندارد

Mild

- Urticaria
- Itching
- Flushing

Severe

- Wheezing
- Dyspnea
- Bronchospasm

ایا کهیر مهم است؟

- ~~افت فشار خون~~
- اضطراب
- تنگی نفس
- سرفه
- تاکی کاردی
- کهیر ژنرالیزه بیش از دو سوم بدن
- تهوع ،استفراغ
- راش منتشر

اگر جواب مثبت است :

تزریق خون را آغاز نکنید.

سریعا به پزشک اطلاع دهید.

سریعا به بانک خون اطلاع دهید.

علل :

Anaphylaxis آنافیلاکسی

TRALI ترالی

Other Causes

- اگر جواب منفی است :
- تشخیص واکنش آلرژیک خفیف است.

- اقدامات مورد نیاز :
- -تجویز آنتی هیستامین مانند دیفن هیدرامین طبق دستور پزشک
- در صورتی که کهیرپوستی کمتر از 6/1 سطح بدن باشد و بیمارعلامت دیگری نداشته باشد و کهیر بیمار به درمان جواب داده و فروکش کرده باشد.
-
- * در صورتی که کهیر تمام سطح بدن را فرا گرفت و یا با سایرعلایم سیستمیک همراه شد
- بایستی بلافاصله تزریق خون مجددا قطع و اقدامات حمایتی – درمانی آغاز گردد

anaphylactic Reactions

- Can occur very quickly, with only a small amount of transfusion usually within 50 mls
- Hypotension, SOB, Tachycardia, Shock
- Loss of consciousness
- Facial or laryngeal edema
- Dizziness, Chest tightness, abdominal cramping
- Get order for epinephrine corticosteroids

افت فشار خون

تعریف : کاهش ۳۰-۱۰میلی متر جیوه واضح فشار خون سیستولیک و یا دیاستولیک نسبت مقدار پایه قبل از تزریق

- ❊ در کم فشاری مرتبط با تزریق خون بیمار علائم ونشانه های عوارض دیگر انتقال خون مانند تب-لرز-تنگی نفس و..ندارد. .
- 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.

علل افت فشار خون

-Bradykinin mediatedHypotension

-Sepsis

-AHTR

-TRALI

-Other Causes

افت فشار خون

اقدامات فوری :

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Anaphylactic Reactions

This occurs in :

***Pts with hereditary IgA deficiency**

***Ab against C4-Haptoglobin-Ethylene Oxide**

Incidence:

1/20,000-1/50,000 of transfusions

Reactions include:

Dyspnea, Bronchospasm, Hypotension, laryngeal edema, Wheezing, stridor, and shock

Anaphylactic Reaction

Rare (1/150000 transfusions)

Severe, can occur with very small amounts of blood.

Typically in IgA deficient patients with IgA antibodies (1 of 600-800 patients in the general population)

Treatment :

a- epinephrine

b- fluids

c- corticosteroid

b- supportive measure

Washed packed RBC or deglycerolized frozen RBC or IgA free blood units.

Laboratory evaluation in Anaphylaxis

***-Perform quantitative IgA test**

***-Perform Anti IgA**

Therapeutic/Prophylactic Approach

***Trendelenberg position**

***Epinephrine(Adult dose :0.2-0.5 ml of 1/1000 solution SC IM , in sever cases 1/10000 IV**

***Antihistamines,corticosteroids,**

beta-2 agonists

Prevention:

***Transfusion of IgA –deficient components or Washed cellular components**

- کیسه ای که تزریق آن قطع شده حداقل باید سی دقیقه بین قطع و شروع مجددش فاصله زمانی رعایت شود.

- در صورتی که با چک مجدد متوجه اشتباه تزریق کیسه شویم نباید تزریق ادامه یابد.

- تنها در صورتی اجازه ادامه تزریق همان کیسه را داریم که علامت بیمار **فقط تب کمتر از یک و نیم درجه سانتی گراد** باشد یا **فقط خارش و راش در کمتر از دوسوم بدن**باشد.

Acute Hemolytic Transfusion Reactions (AHTR)

Pathophysiology:

-Transfusion of ABO incompatible RBC

-Other antibodies:Kell,Rh,Kidd,Duffy

-Transfusion of ABO incompatible Plasma

Incidence:

Acute Hemolytic: 1/6000-1/20,000

Fatal: 1/100,000-1/600,000

CAUSES OF TRANSFUSION REACTIONS

- Clerical errors:
  - Inadequate labeling
  - Wrong blood issued
- Technical errors:
  - Error in blood grouping & cross matching
  - Incorrect interpretation of test results
- Others:
  - Blood contamination during phlebotomy
  - Blood infusion thr' small bore needle
  - Blood cooler to -30^{o}C or warmed to > 42^{o} C
  - Concomitant administration blood & drugs thr' common set

علایم واکنش حاد همولیتیک

تب
-لرز
-درد قفسه سینه
-درد کمر
-درد عضلانی
درد در محل تزریق
-کاهش فشار خون
-احساس گرما در محل تزریق یا در طول رگ
تغییر رنگ ادراریا پلاسما
خونریزی
نارسایی کلیه

Clinical features

- Inflammatory:
  - Fever/chills
  - Pain at infusion site
- Circulatory:
  - Blood pressure changes
  - Shock
  - Hemoglobinemia/uria
- Pulmonary:
  - Dyspnea, orthopnea, wheezing
- Coagulation:
  - Unexplained increase in bleeding
  - DIC
- Psychological:
  - Sense of unease or impending "doom"!

- Assume all suspected reactions are hemolytic, and work to disprove your assumption
- A high index of suspicion is much better than low
- You will be wrong in your assumption almost every time,
- **But the one time that you are right, will be life-saving!**

Acute Hemolytic Transfusion Reactions (AHTR)

Activation of the complement system results in the release of histamine and serotonin from mast cells resulting in bronchospasm.

DIC

Renal damage occurs for several reasons

blood flow is reduced because of hypotension and renal vasoconstriction

free hemoglobin can cause a mechanical obstruction

DIC occurs fibrin thrombi can be deposited in the renal vascular

Management of a transfusion reaction

Immediately STOP the transfusion once a reaction has been dentified.
Disconnect the tubing from the patient but leave the bag and tubing attached. Do not discard the blood.
Immediately take the patients vital signs.
Maintain venous access with normal saline.
Call the patients physician.
Continue to monitor the patients vital signs.
Recheck the information on the blood container,the requisition and the patients armband.

1. **the physician suspects a transfusion reactionNotify the Blood Bank.**
2.Complete an Unusual Occurrence Report and return to the Blood Bank with completed information on the amount of blood product transfused into the
patient.
3.Collect, label and send the appropriate blood samples to the Blood Bank.
4.Return the unit of blood involved in the transfusion reaction along with all the tubing
attached to the Blood Bank.
5.Continue to monitor the patients vital signs as ordered, until stable.
6.Record the vital signs and any other necessary
pertinent information on the Blood Products Administration flow sheet.
7.Record the amount of the blood transfusion absorbed on the Transfusion Flow Sheet.

- **Clerical check** to ensure right unit went to right patient.
- **Inspection of the unit** for discoloration or obvious issues
  - Darkened color in unit: Suspicious for bacterial contamination
  - Check for clots, aggregates, or anything out of the ordinary
- **Visible hemoglobinemia check**
- Spin a post-transfusion EDTA sample and examine visually for a pink-red color change indicative of free hemoglobin in the plasma
- Best to use EDTA because the same sample can be used for the DAT
- Compare to pre transfusion sample.

- False-positive visible plasma hemoglobin:
  - Poor phlebotomy technique (traumatic stick, drawing through IV line)
  - Nonimmune hemolysis (infusion with 0.45 NS, faulty blood warmers, etc.)
  - Autoimmune hemolysis
  - G6PD deficiency and hemoglobinopathies
- False-negative visible plasma hemoglobin:
  - Delay in drawing sample (with functioning kidneys, hemoglobin may be cleared in several hours)
  - Sample collected from IV line (dilution of blood)

- Repeat ABO/Rh testing
- Check both pre- and post-reaction specimens
- **Additional testing for suspected hemolysis:**
- Repeat antibody screen (on both pre- and post-transfusion samples); consider different enhancement (PEG, LISS, cold/warm incubation, etc) or platform
- Repeat crossmatch with pre- and post samples
- if computer crossmatch used, do serologic cross match
- Best done with tube technique including
  - immediate spin
  - IAT phase readings
  - 37 C reading (gel does not necessarily detect ABO incompatibility)

DAT

- Demonstrates coating of RBCs with antibody and/or complement in-vivo
- Most commonly done with polyspecific method (IgG + C3d)
- If positive, must compare to pretransfusion DAT
- **Positive DAT does not prove an acute hemolytic reaction**
  - Nonspecific positives in hospitalized patients (20%),
  - Autoantibodies, drugs, passive administration of other things like RhIG or IVIG
- **A negative DAT does not disprove an acute hemolytic reaction**
  - If donor RBCs are completely destroyed by brisk hemolysis, DAT will be negative

- Elution studies if DAT is positive to determine specificity of the antibody
- Serum Haptoglobin
  - Haptoglobin binds to free hemoglobin molecules, facilitating their clearance from the circulation by monocytes and macrophages in the RE system
  - This interaction prevents iron from escaping through the kidneys
  - Levels decrease sharply in acute intravascular hemolysis
  - Long turnaround time and acute phase reaction make for limited usefulness in acute setting.
- Direct and indirect bilirubin
  - Both will rise quickly, peak in less than 10 hours, may be normal within 24 hours

- Lactate dehydrogenase (LDH)
  - LDH is abundant in RBCs (especially LDH 1 and LDH2 isoenzymes)
  - Not specific for intravascular hemolysis (+/- in extravascular, too)
- Urine hemoglobin
  - Not as sensitive or as fast as hemoglobinemia for intravascular hemolysis
  - Remember that hematuria is not same as hemoglobinuria!

- Blood product bag sent for culture if contamination is suspected or if any of the following clinical indicators are present:
  - shock
  - hypertensive (systolic rises > 30mm Hg)
  - hypotensive (systolic falls > 30mm Hg)
  - fever (2°C or 3.5°F rise in temperature)
  - rigors (shaking chills)
  - tachycardia (heart rate is > 120/min, or rises > 40/min above pre-transfusion rate).
- Both patient and product must be evaluated
  - Patient: Blood cultures; both aerobic and anaerobic
  - Consider culture of all intravenous fluids running at the time of reaction if clinically suspicious of sepsis
  - Product: Gram stain and culture of actual residual product in the bag (don't culture a segment)

Classification of reactions

- Based on the timing of the reaction
- Acute : during or < 24 hrs after transfusion,
- Delayed : > 24 hrs after transfusion

Acute hemolytic transfusion reactions (AHTRs)

- Symptoms:
  - Fever and chills: Most common presenting symptom (> 80%)
  - Back or infusion site pain
  - Hypotension/shock
  - Hemoglobinuria (may be first indication of hemolysis in anesthetized patients)
  - DIC/increased bleeding (also important in anesthetized patients)
  - Sense of "impending doom"
- Lab findings
  - Hemoglobinemia (pink or red serum/plasma); lasts several hours in those with adequate renal function
  - Hemoglobinuria (typically clears by the end of one day)
  - Positive DAT (unless all donor cells destroyed); may be "mixed field

- Elevated indirect and direct bilirubin
- Peripheral smear:
  - Schistocytes: Intravascular hemolysis
  - Spherocytes: Extravascular hemolysis
- Pathophysiology
- ABO antibodies fix complement well, leads to membrane attack complexes and rapid RBC lysis
- Other antibodies (especially Kidd) may also fix complement and lyse RBCs
- Seen much less commonly with incompatible donor plasma (e.g., platelet transfusions from group O donor with high-titer anti-A to group A recipient)

- Hemolysis leads to a complex chain of events, including:
  - Release of free HGB and HGB-free RBC stroma into circulation
  - Stimulation of intrinsic coag pathway and bradykinin via Ag-Ab complexes
  - C3a and C5a generation ("anaphylatoxins")
  - Production of several very important cytokines:
    - • Tumor necrosis factor (TNF-α)
    - • Interleukin-1β (IL-1β)
    - • Interleukin-6 (IL-6)
    - • Interleukin-8 (IL-8)

- Inflammation: TNF-α, IL-1β, and IL-6 strongly promote fever
- Coagulation: Activation of intrinsic pathway by Ag-Ab complex interaction with factor XII
- Circulatory consequences:
  - Increased C3a/5a, IL-1β, and TNF-α stimulate increased nitric oxide (NO) levels, which leads to systemic vasodilation,
  - Bradykinin promotes transient systemic hypotension
- Renal consequences:
  - Sympathetic response to hypotension leads to renal vasoconstriction
  - Free hemoglobin scavenges renal NO, promoting vasoconstriction
  - Renal microthrombi from diffuse coagulation also decrease renal blood flow
  - Hemoglobin-free RBC stroma also damages renal tubules directly
  - All of above contribute to risk for acute tubular necrosis, with resultant oliguric renal failure in about 1/3 of confirmed acute HTRs

- Respiratory consequences:
  - Anaphylatoxins promote bronchoconstriction, with resultant wheezing/dyspnea
  - Aggressive hydration during resuscitation gives pulmonary edema risk
- Extravascular hemolysis (e.g., Rh/Kell/Duffy, etc.) is usually but not always less severe due to lack of systemic complement and cytokine activation
- Treatment
  - Hydration and diuresis are critical early components for hypotension treatment and renal function preservation
  - Maintain urine output > 1 mL/Kg/hr with saline +/- furosemide
- Prevention possibilities
  - Training and careful attention to phlebotomy, labeling, issue, and administration
  - two separate ABO/Rh types before transfusion
  - Advanced methods (RFID, bar codes, etc) will likely be helpful in future

INITIAL MEASURE BEFORE THE INVESTIGATION TEST.

Stop the transfusion

An intravenous line with normal saline should be maintained

The patient should then be assessed and supported as necessary while the patient's physician and the transfusion service are notified

A responsible physician will need to evaluate the patient and determine appropriate clinical care

The unit and all tubing should be returned to the blood bank, along with post-infusion blood and urine samples as clinically indicated

The reaction should be documented in the patient's chart

The role of lab for hemolytic transfusion reaction(HTR)

Acute HTR

Delayed HTR

Immediate procedures

- Check for clerical errors
- Check for visual hemolysis
- Test the post-transfusion sample: Redo ABO grouping and perform direct antiglobulin test (DAT)

- compare the positive post-transfusion DAT to pre-transfusion DAT
- Post antibody screen to identify antibody, elution of DAT (+) cells
- Re-do pre antibody screening.

TRANSFUSION REACTION LABORATORY INVESTIGATION

- After the initial measure , the 3 basic preliminary test

- Purpose : to determine the likelihood the occurrence of hemolytic transfusion reaction.
- If there is evidence of hemolysis or if the clinical situation suggests something severe and unusual, the additional test such as TRALI and TACO must be performed.

Clerical check

- To identify any possibilities of ABO incompatibility.
- Compare the component bag, label, paperwork with patient sample and look for errors.
- If an error is found, the physician must be notified.
- Most common errors:
  - Misidentification of patient when pre-transfusion sample drawn.
  - Mix up of samples in the lab.
  - Not enough incubation time.

Visual check

- What's checked:
  - ✓ Plasma or serum post-reaction & compare with pre-transfusion
- This step is done to examine the presence
- The destruction of red cells and releasing hemoglobin will resulting a pink to red su
- The pink or red colored serum indicate int hemolysis
- Thus the ABO testing must be repeated o post-transfusion specimen
- An urine examination of a post-reaction helps in diagnosis of an acute hemolysis.
- The free hemoglobin in the urine indicates the intravascular

LABORATORY INVESTIGATION

Component	Delayed HTR result	Normal value
Lactate dehydrogenase (LDH)	Elevated	-
Bilirubin	Elevated	0.3 to 1.9 mg/dL
Serum haptoglobin	Low	41 - 165 mg/dL
Free hemoglobin in urine	Present in urine	-
D-dimer	Elevated (may be)	-
Prothrombin test (PT),	Elevated (may be)	12-14 s
Partial thromboplastin time (PTT)	Elevated (may be)	18-28 s

* D-dimer, prothrombin test (PT), and partial thromboplastin time (PTT) may be elevated, particularly

Management has 3 main objectives:

1-Maintenance of systemic blood pressure

2-Preservation of renal function

3-Prevention of DIC

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LABORATORY INVESTIGATION:

- After initial measures, there are three basic preliminary test are done. They are:
  - Clerical check
  - Visual check
  - Serology check

خطاهای دفتری

بررسی کیسه ی خون
لیبل روی کیسه
مچ بند شناسایی
گروه خونی روی فرم درخواست
گروه خونی روی پرونده بیمار

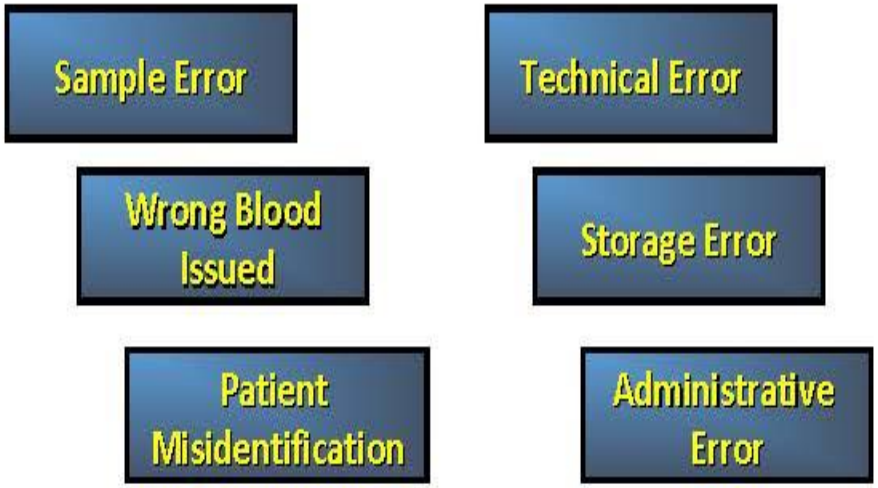
1. عدم شناسایی بیمار هنگام نمونه گیری
2. جابجایی نمونه در آزمایشگاه
3. مدت زمان انکوباسیون نا کافی
4. انتخاب کیسه ی اشتباه جابجایی یا اماده کردن کیسه ی اشتباه
6. خطای آ زمایشگاهی یا تفسیر غلط گروه خونی
7. نگه داری ناصحیح کیسه ی خون
گروه خونی اشتباه بر روی کیسه
عدم شناسایی بیمار هنگام تزریق

Checking for Clerical Errors

- Was the blood transfused to the intended recipient?
- Was the correct unit tagged?
- Was the correct unit issued?
- Was the correct sample used for testing?

How to Prevent Errors in the Transfusion Chain

- Where in the process do errors occur?



- Who is making the errors?
- Why are the errors occuring – which elements of good transfusion practice are failing

Clerical Errors

- The risk of getting the wrong unit of blood exceeds all transmissible disease risks combined.
- 1990-1999 data: 1 in 19,000 units was administered to other than the intended recipient
  - 51% errors at patient care area
  - 29% errors in Blood Bank
  - 15% multiple, sequential errors

Linden JV, Wagner K, et al. Transfusion 2000

The greatest risk from transfusion is that somebody will make a mistake

Not just in transfusion practice:

1GM Wednesday December 24 2014 | THE TIMES

Thousands of patients killed by drug and equipment errors

Safe as Planes

The NHS has a lot to learn from airlines about avoiding unnecessary risk

'Official figures show that at least 8000 patients a year are killed or severely harmed needlessly by drug errors' - a report by Jane Reid

'We should design errors out of the system by making them much harder or impossible to commit' - Leading article

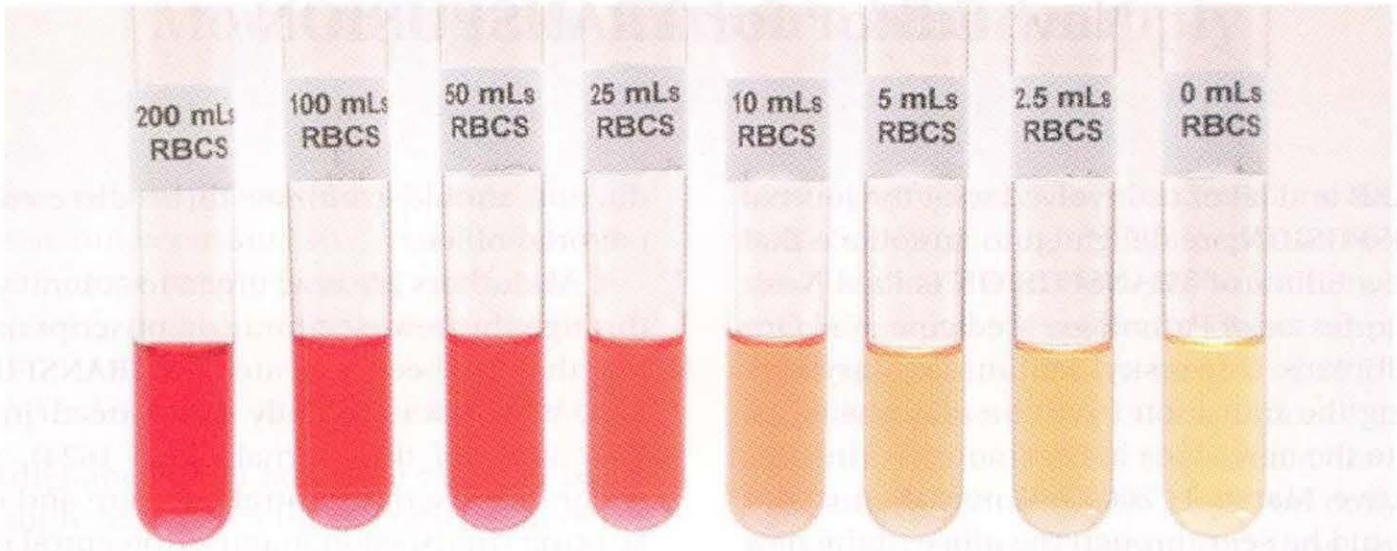
Incident investigation and feedback is very important

- Why did it happen?
- What can be learned from it?
- Corrective and preventative actions to reduce likelihood of recurrence

- پلاسما قبل و بعد از تزریق برای وجود همولیز مقایسه می شود

- در صورت لیز گلبول قرمز رنگ پلاسما صورتی تا قرمز می شود
- رنگ پلاسما قرمز تا قهوه ای نشانه تبدیل هموگلوبین به بیلی روبین است
- افزایش بیلی روبین از یک ساعت بعد از تزریق شروع میشود در عرض 5-7 ساعت زیادشده و در ظرف 24 ساعت ممکن است نرمال شود
- آزمایش برای شناسایی بیلی رئبین در 24 ساعت اول مهم است
- ازمایش گروه بندی بر نمونه بیمار بعد از تزریق تکرار می شود
- آزمایش ادرار برای شناسایی همولیز

Visual Inspection for Hemolysis



Visualizing the hemolytic transfusion reaction

Kathryn Elliott, Jack Sanders, and Mark E. Brecher

- If any of these three test above have positive and suspicious results, REDO test done before blood transfusion which are:
  - ABO &Rhesus grouping.
  - Antibody screening.
  - Repeat crossmatch.

تکرارآزمایش کومبز مستقیم

اگر در نمونه بعد از تزریق مثبت بود آزمایش بر نمونه قبل از تزریق تکرار می شود اگر ازمایش کومبز مستقیم بعد از

- تزریق مثبت و قبل منفی نشانه ی همولیز است

Antibody screening

- Antibody screening is valid for 72 hr if it is negative and patient needs repeated transfusion , patient only need immediate spin crossmatch and ABO /Rh typing .
- Antibody screening valid for one week in patient have no history of transfusion or pregnancy in the last three months .

LIMITATION OF ANTIBODY SCREENING TEST

- This test cannot detect all antibodies of potential clinical significance
- Antibody may be reactive with low incidence antigen absent on screen cells
- If antibody is exhibiting “dosage” it may be missed. Duffy (Fy), Kidd (Jk) and Rh antibodies may only be detected with homozygous cells. It will influence decision to use 2 or 3 cell screen

If antibody screening is positive, additional tests to specifically identify antibody using the antibody identification panel and red cell antigen typing must be performed.

3) REPEAT COMPATIBILITY TESTING

- The compatibility testing or cross-match procedure is done again for confirmation to determine whether blood donor is compatible with recipient blood.
- This test involve 3 phases which are Immediate spin, 37°C, and AHG.
- The 2 main function of the repeating cross-match test are:
  - It is the final check of ABO compatibility between donor and patient.
  - It may detect the presence of an Ab in the patient's serum that was not detected in the Ab screening because the corresponding Ag was lacking from the screening cell.
- There are two types of crossmatch :

Major cross-match

- The major cross-match involves testing the patient's serum with donor cells.
- To determine whether the patient has an antibody which may cause HTR or decreased cell survival of donor cells.

Minor Cross-match

- This test involves testing the patient's cells with donor plasma.
- To determine whether there is an antibody in the donor's plasma directed against an antigen on the patient's cells.

The cross-match has many limitations. A compatible cross-match during pretransfusion will not:

- Guarantee normal survival of transfused RBCs
- Prevent immunization of the recipient
- Detect all unexpected RBC antibodies in the recipient serum
- Prevent delayed hemolysis due to an amnestic antibody response to antigens against which the patient has previous but undetectable immunization
- Detect all ABO grouping errors either in donor or recipient
- Detect most group D grouping errors in the donor or recipient

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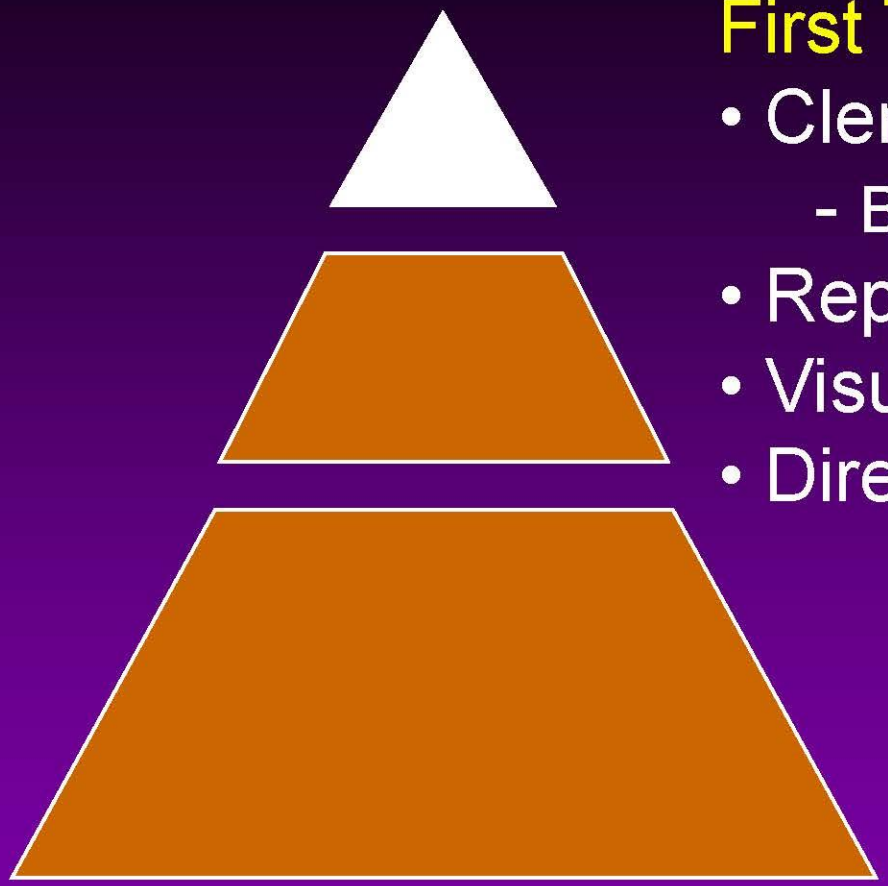
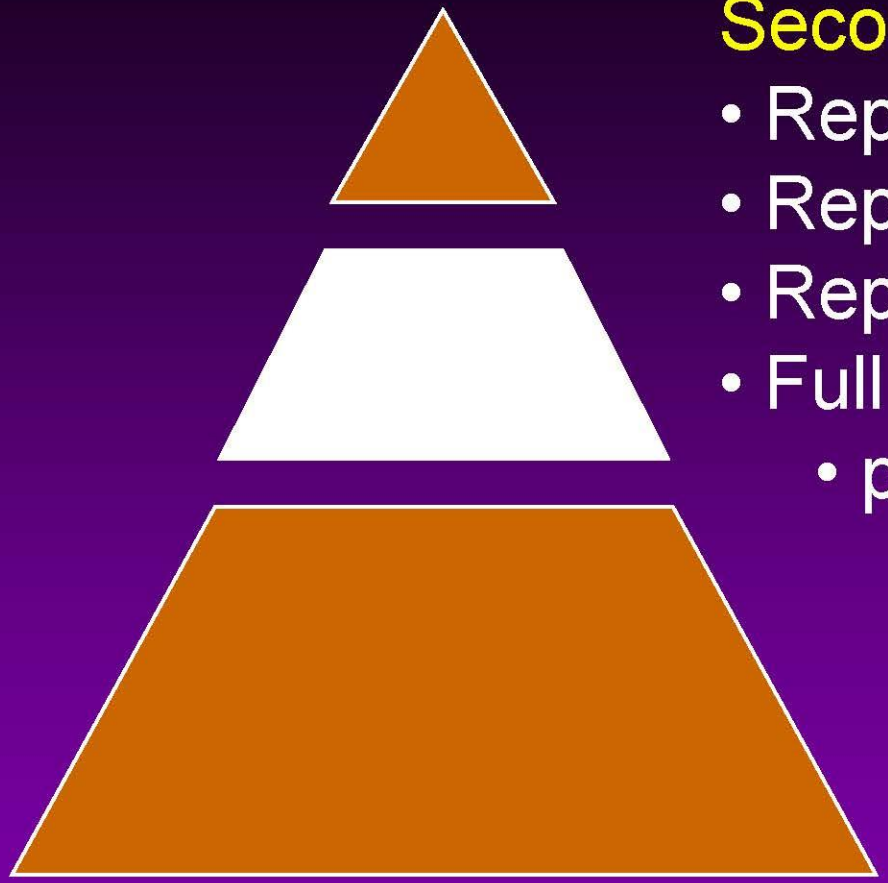


First Tier

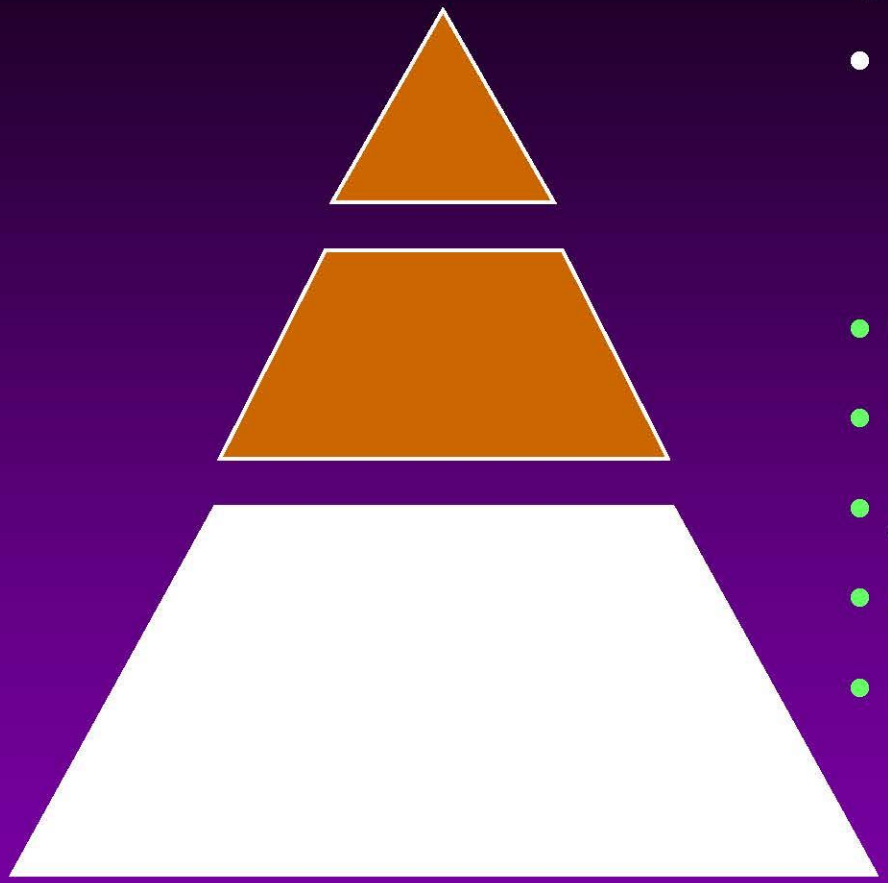
- Clerical Check
  - Bedside and Laboratory
- Repeat ABO/Rh (pre/post)
- Visual Check for Hemolysis
- Direct Antiglobulin Test*

** may be pos or neg with immune hemolysis due to RBC destruction*



Second Tier

- Repeat ABO/Rh units
- Repeat antibody screen
- Repeat special antigen typing
- Full crossmatch
  - pre/post-reaction specimens



Third Tier

- "Blood Bank Voodoo"
  - enhanced techniques

- Clinical findings/history
- Contributing factors
- Ancillary tests-hemolysis
- Other pertinent testing
- Monitoring and treatment

Direct Antiglobulin Test

- Used as serologic check for incompatibility
- Perform on post-transfusion specimen; test pre-transfusion DAT for comparison
- DAT is likely to be positive if incompatible rbcs *or* incompatible plasma was transfused

- Perform DCT on the pre- and post transfusion sample.
- A positive DCT test usually indicates the presence of recipient ab's on the surface of donor red cells, however if all the cells have been already destroyed , the test may be negative.
- check urine (post-transfusion) 1st sample

LABORATORY INVESTIGATIONS

- Examine the patient pre-transfusion & post-transfusion plasma from EDTA sample for evidence of free Hb or increased bilirubin.
- Pink or red discolouration in post-transfusion plasma indicates the presence of free Hb due to red cell destruction.
- Yellow discoluration of the sample drawn 6-8 hr after transfusion indicates increased blirubin.

Direct Antiglobulin Test

- Incompatible red cell transfusion:
  - DAT may have a mixed-field appearance
  - If transfused cells were rapidly destroyed, post-reaction DAT may be negative
  - Time sample drawn is important, should be collected ASAP after reaction occurs
  - Type of AHG employed may affect results

Additional Evaluation – When?

- If any of initial checks and tests give positive or suspicious results
- Clinical presentation is consistent with a Hemolytic Transfusion Reaction (HTR)

Repeat ABO grouping

- Standard 7.4.2.1 [26th edition]

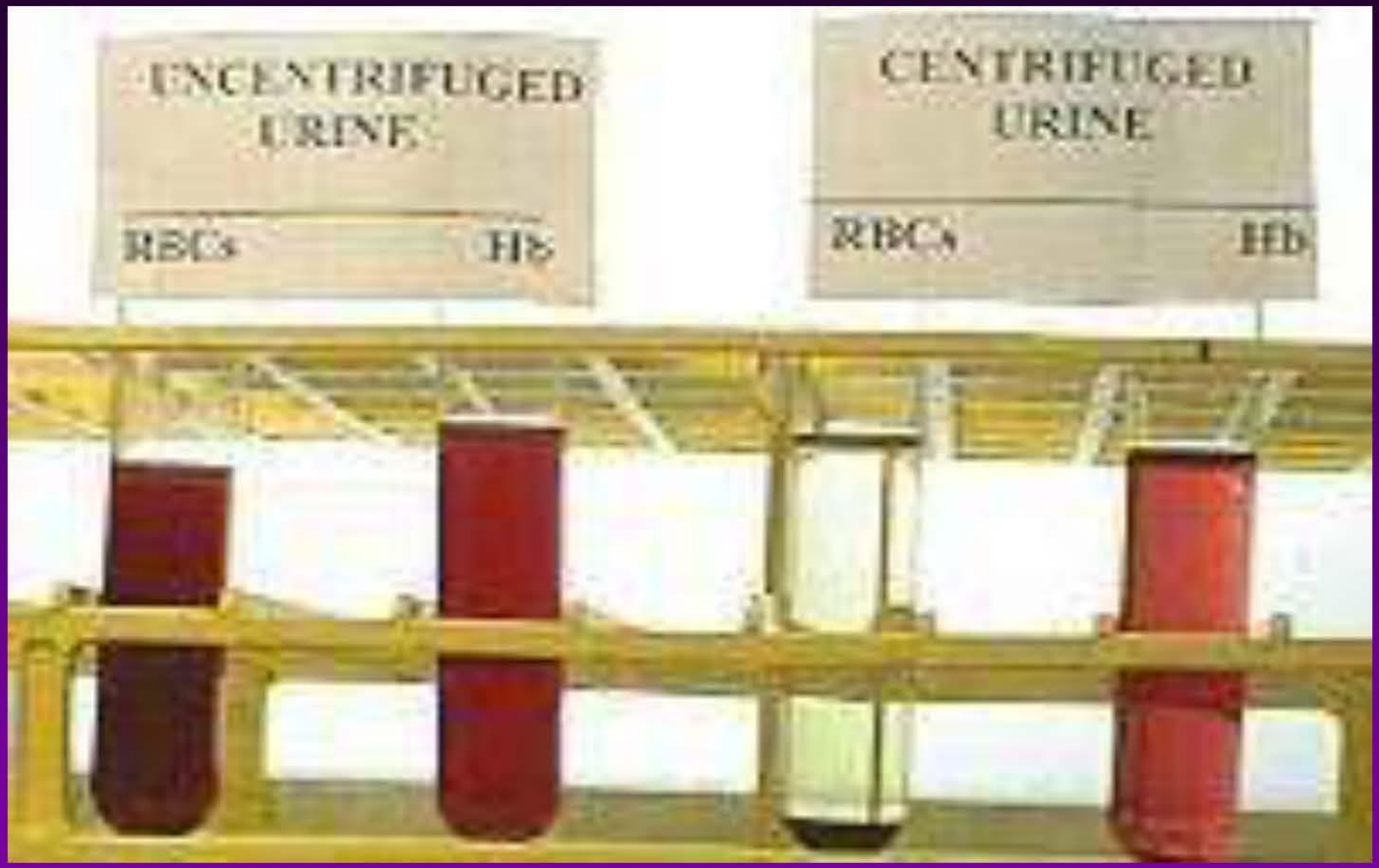
  "For suspected hemolytic transfusion reactions…, a repeat ABO group determination shall be performed on the post-transfusion sample."

- Also repeat ABO testing on pre-transfusion sample and blood from transfused unit or attached segment.

ABO grouping discrepancies

- Error in patient/sample identification
  - Pretransfusion sample mislabeled
  - Sample mix-up in the laboratory
  - Transfusion given to wrong patient
- Error in original ABO-group interpretation
  - Recording error
  - Problem solving incorrect
- Error in blood product labeling

Hemoglobinuria vs Hematuria



S.G. Sandler, D.A. Sandler. Emedicine.com 2003

Hemolysis: Laboratory Evidence

Acute Hemolysis

- Plasma/serum free hemoglobin
- Haptoglobin
- Lactate dehydrogenase (LDH)
- Bilirubin
  - Direct < Indirect Bilirubin
- Urinalysis

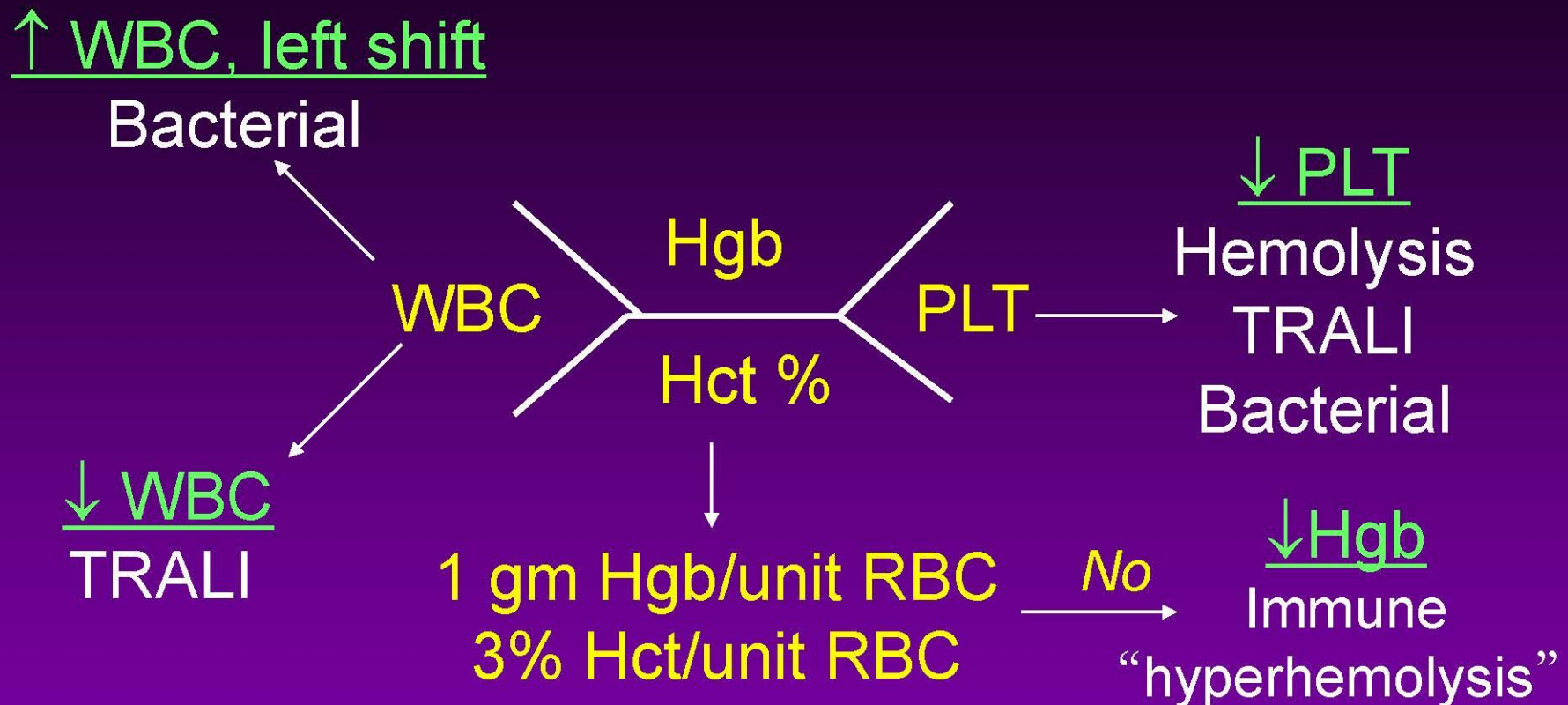
} Interpreted relative to overall liver function

Coagulation Studies

Monitor for Disseminated Intravascular Coagulation (DIC)

- Platelet count
- Fibrinogen
- PT and aPTT
- D-dimer

Complete Blood Count with WBC Differential



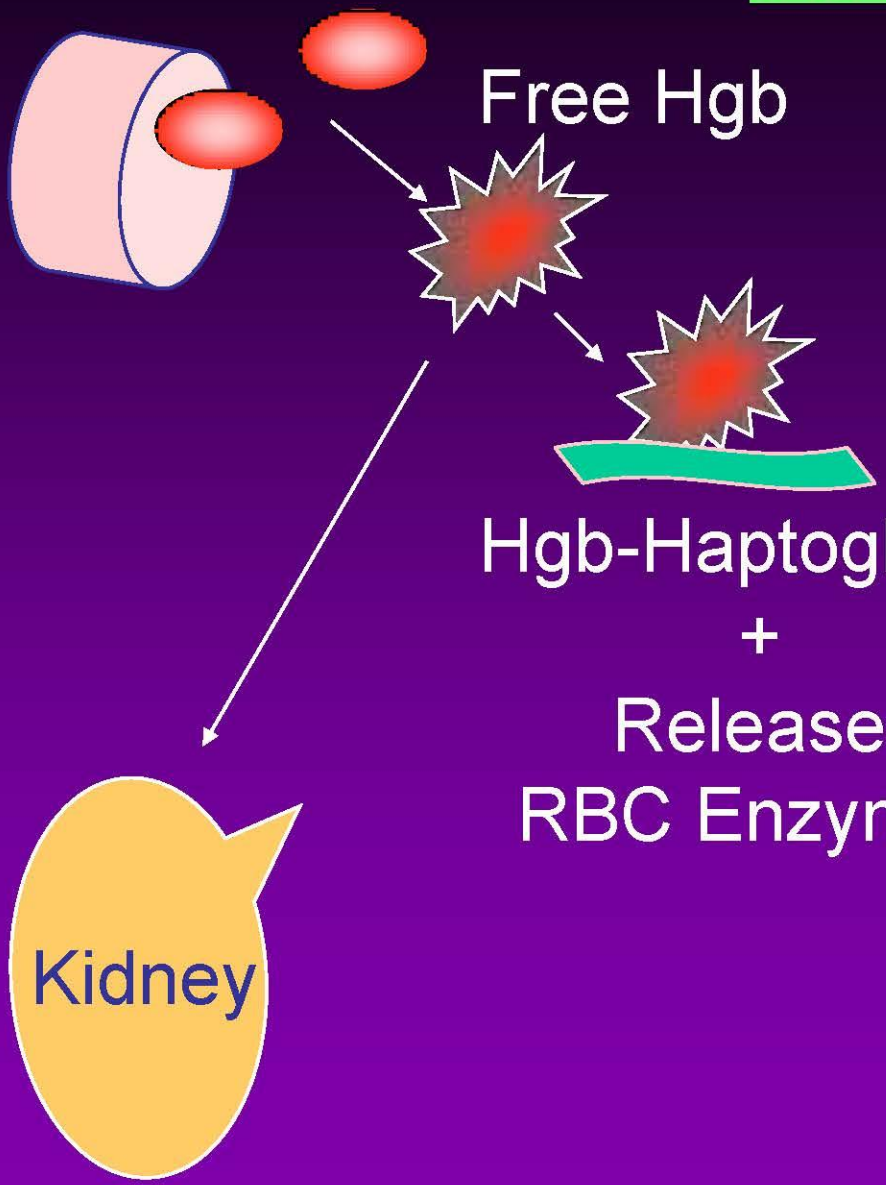
Indices (MCV, MCHC, MCH):

↑ MCV - reticulocytosis

↑ RDW - reticulocytosis

↑ MCHC - spherocytosis

Intravascular Hemolysis



↑ Plasma Free Hemoglobin

↓ Haptoglobin

↑ LDH
(LD1 > LD2)

Hemoglobinuria

Treatment of Hemolytic Transfusion Reactions

Treatment/Prophylaxis: Kidney

- Hydration
- Diuretics
- Possibly sympathomimetic (Dopamine)
  - Renal perfusion
- Nephrology consult

Treatment AHTR

- If shock
  - O2
  - Fluid resuscitation
  - Pressor support
    - MAP > 60 mm Hg or SBP >90 mm Hg
    - Dopamine 2 ≤ 5 mcg/kg/min
  - Steroids
    - Methylprednisolone 125 mg q 6 hrs

Treatment: Kidney

Hydration

- Normal saline
- Goal $\geq$100 mL urine/hr
- If oliguric, consider addition of diuretics
- If anuric, restrict after 1 liter

Renal: Ancillary Testing

Urinalysis

- Hemoglobinuria (NOT hematuria)
- Urobilinogen (acute hemolysis)
- Hemosiderin (chronic hemolysis)
- RBC casts
- Evidence UTI
  - Leukocyte esterase
  - Nitrate
  - WBC, RBC

DDx

Therapeutic Approach

***Keep urine output >1/ml/kg/hr with fluid & IV diuretic (furosemide)**

***Analgesic(may need morphine)**

***Low dose dopamine**

***Haemostatic components (PlT,Cryo,FFP) for bleeding**

Renal Ancillary Testing

Monitor renal function

- Electrolytes
- Urine output
  - Daily weights

Treatment: DIC

- Consider Heparin*
- Blood product support for bleeding
- Hematology consult

*If bleeding despite factor replacement

Non immune Hemolysis

***Improper shipping or storage temp.**

*** Using small needle size**

*** Improper use of blood warmer**

*** Bacterial contamination**

Exclude Nonimmune Hemolysis

- Examine tubing/blood set
- Review infusion sheet
  - Concurrent medications?
  - Incompatible solutions?
  - Use of blood warmer/infusion pump?
  - Flow rate/needle size?
  - Improper storage on-site?

Restarting transfusion

- **The potential restarting of transfusion is a critical question.**

- **On the other hand, if the patient is experiencing a serious reaction, giving the rest of the unit may lead to death.**
- **As a rule, once a reaction is suspected, the transfusion is stopped and never restarted. Another unit of blood is requested from the blood bank.**

- **The only exception is allow restarting product**
- **pruritus**
- **fever less than 1.5 has been made.**

IS THERE A ROLE FOR PREMEDICATION IN PREVENTING TRANSFUSION REACTIONS?

- Administering drugs in an attempt to prevent a possible transfusion reaction is becoming controversial.
- Hospitalists covering inpatient services at night may elect to premedicate before transfusion to lessen the chance of getting awakened during the night.
- Oncologists may not have time in their busy clinic schedules to deal with "nuisance" reactions

- When rapid RBC exchange is performed for sickle cell patients using apheresis technology, many practitioners choose to premedicate to avoid having to stop an urgent procedure and possible loss of special phenotype-matched RBC units.

- Although diphenhydramine and acetaminophen are effective for treating mild allergic and febrile reactions once they occur, it is a subject of debate whether they can prevent reactions.
-
- Three controlled trials consisting of 462 total patients suggest that premedication does not prevent mild allergic or febrile nonhemolytic transfusion reactions.

- **It is unlikely that premedication will obscure a true hemolytic reaction, so the issue is primarily one of administering drugs that may not be indicated, a question of both cost and risk-benefit ratio.**

Summary

- The importance of prompt recognition and reporting of suspected Transfusion Reactions cannot be over-emphasized.
- Assess reactions quickly and efficiently to rule out the most serious causes first
- Communicate results with responsible physicians so appropriate actions can be taken without unnecessary delay

Summary

- It is important to recognize the possible reactions that can be associated with blood transfusions
- If you suspect a reaction, stop the transfusion and assess the patient's vital signs, signs and symptoms as some reactions may be life-threatening
- Notify the blood bank if serious reactions are suspected

Take home message

Using appropriate transfusion strategy of transfusion and monitoring Of patients are very important in improving health related quality of Life.

Chronic Transfusion Reactions

- Alloimmunization
- Transfusion Associated Graft Verses Host Disease (GVHD)
- Iron Overload
- Transfusion Transmitted Infection
- Post Transfusion Purpura :

(Onset about 5-12 days after transfusion of cellular blood components ,

- Severe thrombocytopenia often with purpura and possibly other bleeding .
- Thrombocytopenia will persist for 1-2 weeks

General managements of Acute transfusion reactions

- **category 1: Mild reactions**
- Urticaria and itching are not uncommon reactions following transfusion. They arise as a result of hypersensitivity with local histamine release to proteins, probably in the donor plasma.
- **Signs and symptoms**
- Localised cutaneous reactions (urticaria and rash), often accompanied by pruritus (intense itching), occur within minutes of commencing the transfusion. The symptoms usually subside if the transfusion is slowed and antihistamine is given.

Management

1- Slow the transfusion.

2 -Give an antihistamine: e.g. chlorpheniramine 0.1 mg/kg by intramuscular injection.

3- Continue the transfusion at the normal rate if there is no progression of symptoms after 30 minutes.

4- If there is no clinical improvement within 30 minutes or if signs and symptoms worsen, treat the reaction as a Category 2 reaction.

Category 2: Moderately severe reactions

Signs and symptoms usually occur 30–60 minutes after the start of the transfusion.

Signs

- Flushing
- Urticaria
- Rigor
- Fever
- Restlessness
- Tachycardia

Symptoms

- Anxiety
- Pruritus (itching)
- Palpitation
- Mild dyspnoea
- Headache

1- Stop the transfusion. Replace the infusion set and keep the IV line open with normal saline.

3- Administer antihistamine IV or IM (e.g. chlorpheniramine 0.01 mg/kg or equivalent) and an oral or rectal antipyretic (e.g. paracetamol 10 mg/kg: 500 mg – 1 g in adults). Avoid aspirin in thrombocytopenic patients.

4- Give IV corticosteroids and bronchodilators if there are anaphylactoid features (e.g. broncospasm, stridor).

5- Collect urine for the next 24 hours for evidence of haemolysis and send to the laboratory.

6- If there is a clinical improvement, restart the transfusion slowly with a new unit of blood and observe carefully.

Category 3: Life-threatening reactions

The most common causes of life-threatening transfusion reactions are:

- Acute intravascular haemolysis
- Bacterial contamination and septic shock
- Fluid overload
- Anaphylactic shock
- Transfusion-associated lung injury (TRALI)

Signs

- Rigors
- Fever
- Restlessness
- Shock
- Tachycardia
- Haemoglobinuria (red urine)
- Unexplained bleeding (DIC)

Symptoms

- Anxiety
- Chest pain
- Respiratory distress/shortness of breath
- Loin/back pain
- Headache
- Dyspnoea

Management

1- Stop the transfusion and Check label and recipient identity

- Replace the infusion set and keep IV line open with normal saline.

2- Infuse normal saline to maintain systolic BP (initial 20–30 ml/kg). If hypotensive, give over 5 minutes and elevate patient's legs.

3- Maintain airway and give high flow oxygen by mask.

4 -Give 1:1000 adrenaline 0.01 mg/kg body weight by intramuscular injection.- Children 0.01mg/kg IM; min dose 0.1mL, max dose 0.5mL

5- Give IV corticosteroids (Consider iv Hydrocortisone 4mg/kg (200- 400 mg) and bronchodilators if there are anaphylactoid features (e.g. broncospasm, stridor).

6 -Give diuretic: e.g. frusemide 1 mg/kg IV or equivalent

7- Consider H1-antihistamine, eg Loratadine or Cetirizine 10 mg po for itch or angioedema.

o H2-antihistamine, eg Ranitidine may be added for severe reactions.

- Localised cutaneous reactions (urticaria and rash), often accompanied by pruritus (intense itching), occur within minutes of commencing the transfusion. The symptoms usually subside if the transfusion is slowed and antihistamine is given.

Management

1- Slow the transfusion.

2 -Give an antihistamine: e.g. chlorpheniramine 0.1 mg/kg by intramuscular injection.

3- Continue the transfusion at the normal rate if there is no progression of symptoms after 30 minutes.

4- If there is no clinical improvement within 30 minutes or if signs and symptoms worsen, treat the reaction as a Category 2 reaction.

THANK YOU!