ADVERSE EFFECTS OF TRANSFUSION REACTION

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- Acute transfusion reaction occur in 1 to 2% of transfusion patients.

- With the exception of Hypersensitivity reaction and febrile non haemolytic transfusion reaction all are potentially fatal and require urgent treatment.

- With rapid recognization and management , we can save the life of patient.

- Delay and failure to do correct procedure are commonest cause of life threatening acute transfusion reaction.

- It is essential to monitor the transfusion patient closely to detect early sign and symptom of acute transfusion reaction. (especially within first 15 mins for each unit)

- In severe haemolytic transfusion reaction, signs and symptoms occur very quickly within minutes of infusing only 5-10 ml of blood.

- If you suspect an acute transfusion reaction, firstly check the blood pack labels and the patient's identity. If there is any discrepancy, stop the transfusion immediately.

- And report the doctor who is responsible and blood bank.

- Signs, symptoms and management depend on type of transfusion reaction.

I. Acute transfusion reaction (within 24 hrs)

a). Immunologic

1). Haemolytic transfusion reaction

2). Non haemolytic

- Febrile non h'lytic transfusion reaction
- Allergic (Hypersensitivity) reaction
- Anaphylaxis reaction
- Transfusion related acute lung injury

b). Non-immunologic

1). Bacterial contamination and septic shock

2). Heart failure due to fluid overload

3). Air Embolism

4). Complication due to massive transfusion

(Acidosis, Hyperkalaemia, Citrate toxicity and Hypocalcaemia,Depletion of platelets & coagulation factors, DIC, Hypothermia)

II. Delayed transfusion reaction (>24 hrs)

a). Immunologic

1). Delayed h'lytic reaction

2). Post transfusion purpura

3). GVHD

b). Non-immunologic

1). Transfusion related infection

HIV, hepatitis B & C, Syphilic

2). Iron overload

Depend on severity

1. Mild reaction- mild hypersensitivity reaction
2. Moderately severe reaction

- moderately severe hypersensitivity

- febrile non h'lytic reaction

- early bacterial contamination

III. Severe Life-threatening reactions

- h'lytic transfusion raction

- bacterial contamination and septic shock

- fluid overload

- Anaphylactic reaction

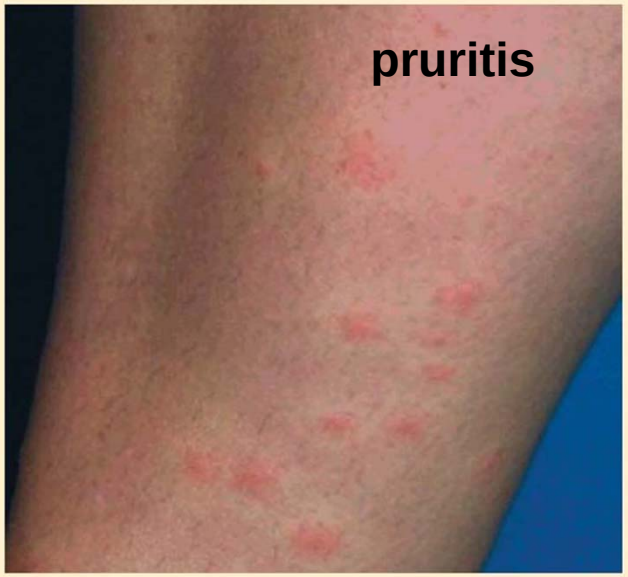
- Transfusion related lung injury

I. HYPERSENSITIVITY REACTION

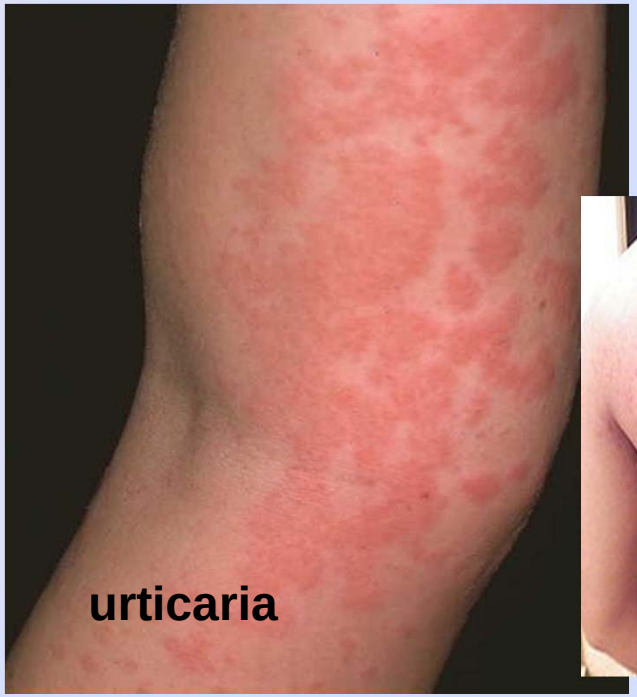
- Presence of antibody in patient blood to the plasma protein of donor blood with the release of histamine.

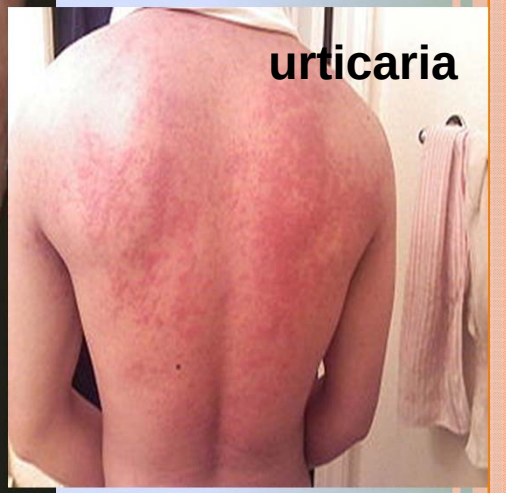
- Localized cutaneous reaction (urticaria, rash, pruritus)

FIGURE 1.
Papular urticaria, usually caused by mosquitoes or chiggers.

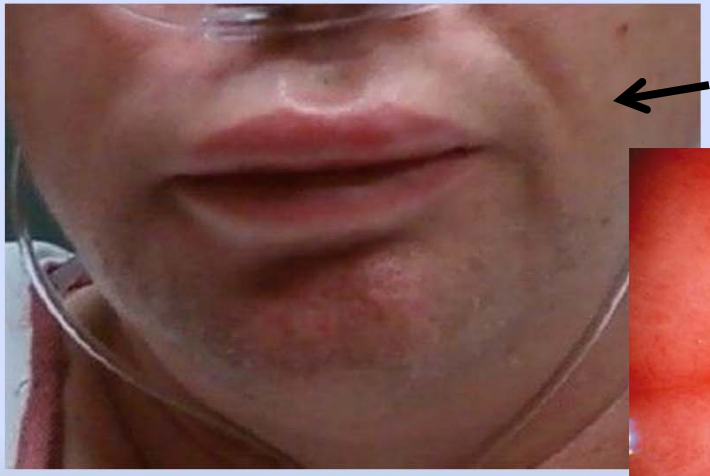


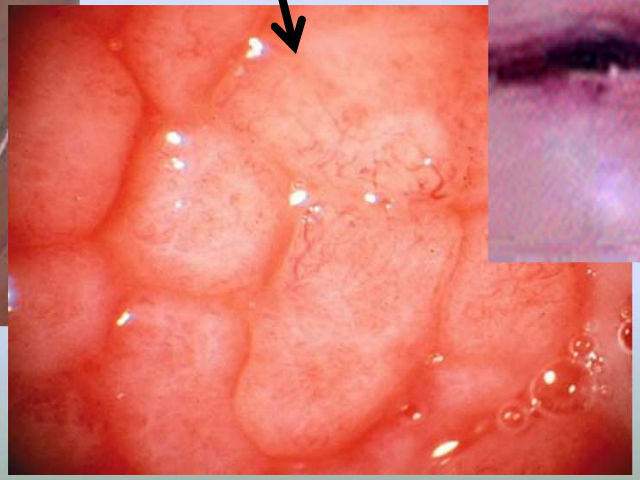
Source: NZ DermNet, www.dermnetnz.org.

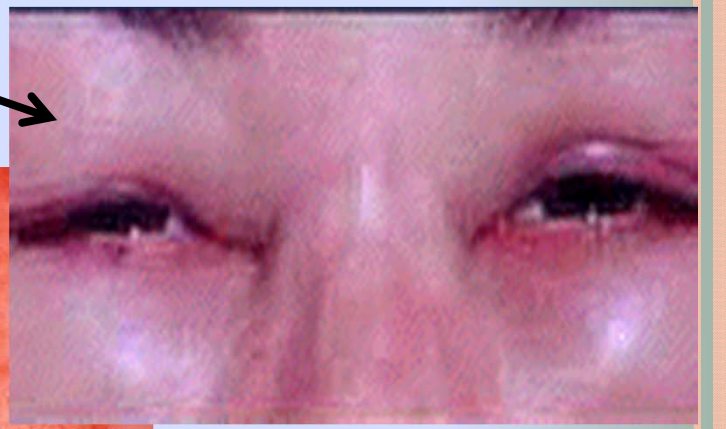




Angioedema







I. HYPERSENSITIVITY REACTION

- Mild or moderately severe reaction

Prevention

In previously experienced patient → give antihistamine IV 30 min before transfusion

II. Febrile Non H'lytic Trnsfusion Reaction

- Moderately severity 1-2%
- Caused by cytokine released form leucocytes in stored blood or presence of antibody in the patient to infused white cells + platelets.
- S/S occur 30-60 mins after the start of transfusion

II. Febrile Non H'lytic Trnsfusion Reaction (FNHTR)

- Seen in
  1. multiparous female
  2. previously transfused patient
  3. common in patient with repeated blood transfusion (AA, Thalassaemia)

- Rarely severe, But important to differentiate from h'lytic transfusion reaction & bacterial contamination, underlying cause (malaria).

II. Febrile Non H'lytic Trnsfusion Reaction

- Fever
  - >1*C above base line
  - early transfusion on 1-2 hr later

- Bacterial Contamination
  - >40*C, severe rigor
  - hypotension

II. Febrile Non H'lytic Trnsfusion Reaction

Prevention

If the patient is a regular transfusion and has had two or more reaction in the past.

1). Give antipyretic (Paracetamol) 1 hr before transfusion

2). Repeat 3 hr after the start of transfusion

3). Transfuse slowly

4). Keep the patient warm

5). Centrifuge + remove the plasma and buffy coat

6). If possible →

- Use washing method
- Use transfusion set with leucocyte filters

III. ANAPHYLACTIC REACTION

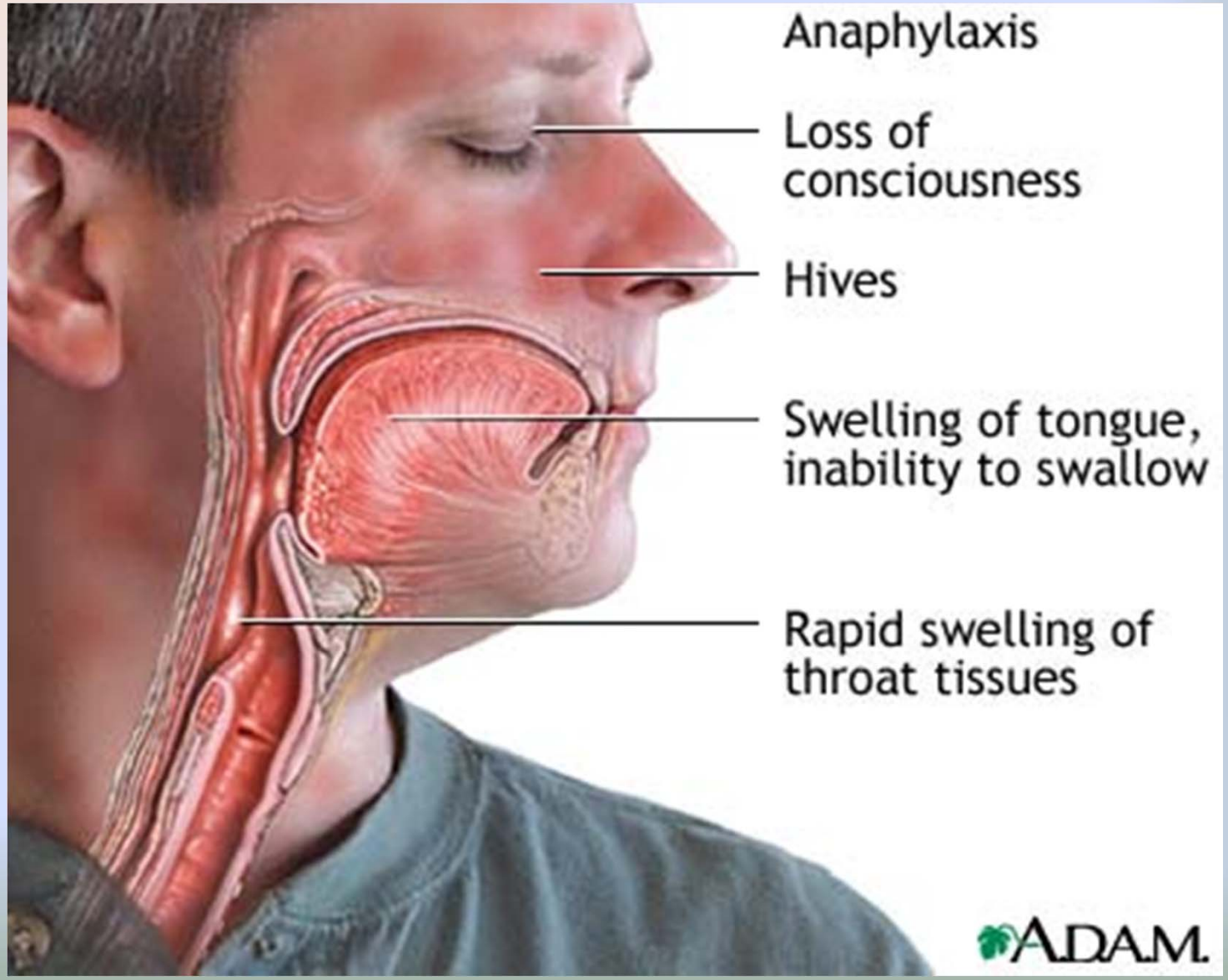
- Due to antiIgA antibodies in patient serum which react with IgA in the transfused blood
- Person who lack IgA in their serum

  - no previous history of transfusion
  - antibody in serum, react with IgA
  - antibody titre is high
  - no fever

- Passive transfer from donor

  - high titre of Ab in donor plasma which can present within patient blood as long as 90 days, and reacts with IgA present in blood unit transfused later.

Signs of anaphylaxis



IV. Fluid Overload

- Too much fluid is transfused

- Too rapid

- Underlying disease such as (RF, Chronic severe anaemia, underlying CVD eg. IHD)

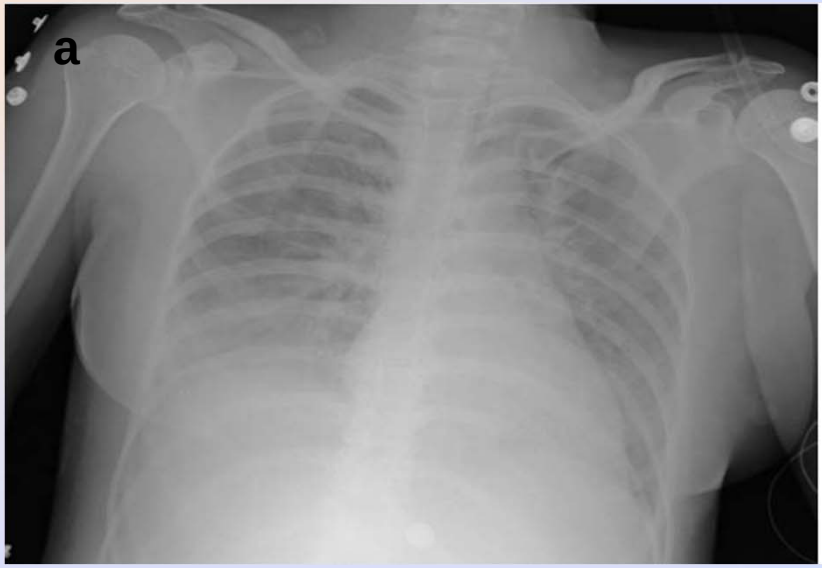
- Packed red cells, slowly, diuretics for prevention

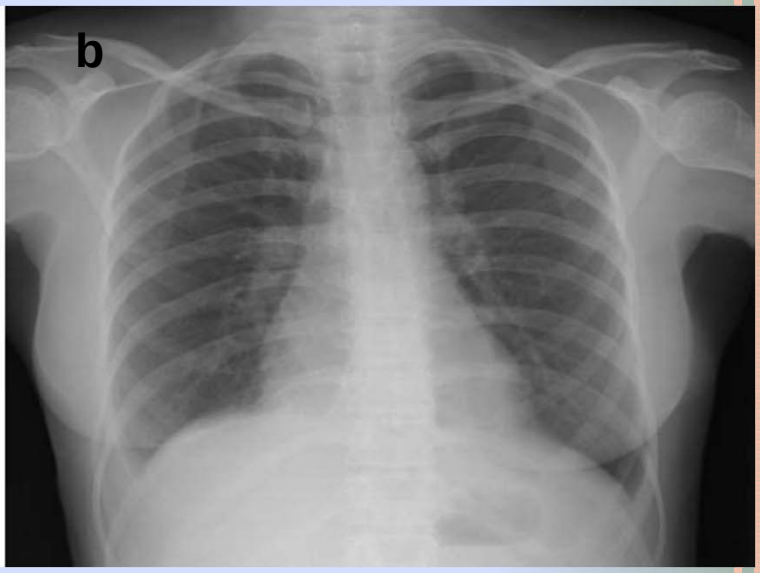
V. TRANSFUSION RELATED ACUTE LUNGS INJURY (TRALI)

- Caused by donor plasma that contains antibodies against the patient leucocytes.
- Donor – multiparous women
- Within 4 hr of transfusion →acute respiratory distress, chest pain, dyspnoea, hypotensio

V. Transfusion Related Acute Lungs Injury

- CXR → Bilateral pulmonary opacity
- No specific therapy
- Respirator support in ICU
- Donor must be removed permanantly





(a) Bilateral patchy alveolar infiltrate in TRAL (b) Complete resolution

Criteria for the diagnosis of TRALI

- No acute lung injury immediately before transfusion
- New acute lung injury:
  1. acute onset lung injury,
  2. no circulatory overload or PA pressures <18mmHg,
  3. bilateral pulm infiltrate on Cxr,
  4. Hypoxemia:Pa02/FiO2 <300, or sat <90% on RA.
- Onset within 6 hours after transfusion
- No temporal relation to an alternate risk factor for acute lung injury

Popovsky TP et al TRALI; definition and review. Crit care Med 2005

VI. Bacterial Contamination and Septic Shock

- Moderately severe or life threatening reaction

- Blood may become contaminated by

1).from donor skin during blood collection

2).bacteremia in donor at the time of donation

3).defect or damage blood bag

4).improper storage

5).warming blood

6).delay in initiating blood transfusion

7).transfusion over >4 hr

VI. Bacterial Contamination and Septic Shock

- Usually sings and symptoms appear rapidly after starting transfusion
- High Fever >40*C, rigor, hypotension
- High dose IV antibiotics

VII. Massive or Large Volume Blood Transfusion

- <24 hr (70 ml/kg in adult, 80-90 ml/kg in child)
  - Acidosis
  - Hyperkalaemia
  - Citrate toxicity + Hypocalcaemia (Citrate bind Ca*)
  - Depletion of fibrinogen, coagulation factors, platelets (<48 hr) → Fresh frozen plasma platelets rich plasma
  - Hypothermia

VII. Massive or Large Volume Blood Transfusion

- Microaggragates
  - In stored blood, microaggregates of WBC + platelets may be present.
  - In massive transfusion, these microaggregates fuse and embolize to lungs causing ARDS
  - Prevention → Buffy coat depleted packed red cells

VIII. HAEMOLYTIC TRANSFUSION REACTION

Aetiology

I. Blood group incompatibility—

-most cases are caused by infusion of incompatible red cells .

-Ab in patient's plasma react the corresponding antigen on donor red cells and cause haemolysis of donor red cells.

-ABO and Rh incompatibility.

-Sometime, antibody in patient's plasma against other blood group antigens of transfused blood.

VIII. HAEMOLYTIC TRANSFUSION REACTION

II. Transfusion of haemolysed blood

- improper storage

- heating >50*C

- contamination with organisms

(1)CAUSES OF BLOOD GROUP INCOMPATIBILITY

I. Avoidable
II. Unavoidable

I. Avoidable

Ward	Clerical error
Blood bank	**Clerical error** **Techanical error**

CAUSES OF BLOOD GROUP INCOMPATIBILITY

Ward

- Taking blood from wrong patient
- Labelling error of blood sample bottle
- Errors in blood request form
- Inadequate checks of blood against the patient's identity
- Giving blood to wrong patient

CAUSES OF BLOOD GROUP INCOMPATIBILITY

Blood Bank

- wrong labelling blood bag

- errors in grouping and matching

- errors in handling blood sample

CAUSES OF BLOOD GROUP INCOMPATIBILITY

II. Unavoidable

- Transfusion reaction occur despite of careful clerical errors and technical errors.

(proper technique, careful recording, interpretation)

-Due to very low level of iso-agglutinations in recipient's serum below the sensitivity of the Agglutination Test.

BLOOD GROUP INCOMPATIBILITY

- Major
- Minor

1). Major

- Destruction of donor cells
- By antibody in patient's plasma which react with Ag on donor red cells cells
- ABO or Rh incompatibility
- may be due to rare antibodies of other blood group system

BLOOD GROUP INCOMPATIBILITY

2). Minor

- Less severe
- Destruction of recipient cells
- By antibody in donor's plasma which react with Ag on recipient's RBC
- Group O is transfused to a recipient other than O (universal donor)
- Rarely severe but sometime fatal.

BLOOD GROUP SYSTEMS

- 400 antigen on red cell membrane
- Each Ag has specific antibody
- Naturally occuring antibody (IgM) acquired alloantibody (Ig G)
- Immune system recognize foreign Ag and produce antibody when expose to red cells

COMMON BLOOD GROUP

ABO	1901
Rh	1939
Lewis	1946
MNS	1927
P	1927
Lutheran	1945
Kell	1946
Kidd	1950
Duffy	1951
Deigo	1955
Dombrock	1965

I. ABO Blood Group

ABO Ag on RBC

Blood Group	Ag on RBC	Antibody in serum
A	A	B
B	B	A
O	-	A,B
AB	A,B	-

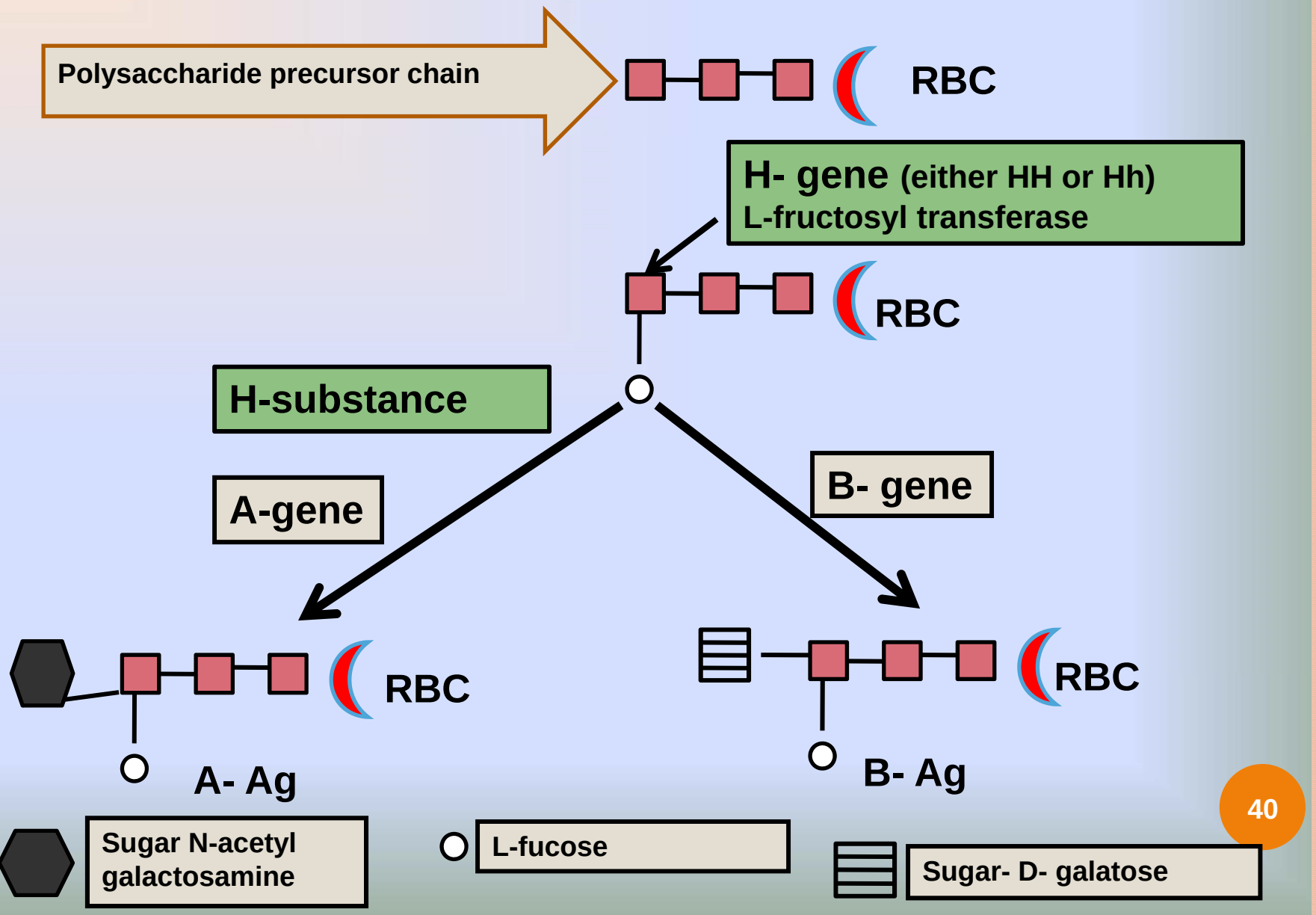
I. ABO Blood Group

- Presence of A,B Ag on RBC depend on inheritance of allelic gene A,B and O.
- H gene is for the precursor substance (H) from which A,B Ag are formed.
- A,B gene produce specific enzyme transferase which add the specific sugar to precursor substance (sub: H) and produce A or B Ag.

I. ABO Blood Group

Gene	Enzyme	Added sugar
A	•N-acetyl-galactosaminyl transferase	•N-acetyl galactosamine
B	•Galactosyl transferase	•D-galactose
H	•Frucosyl transferase	•Fucose

EXPRESSION OF ABH ANTIGEN ON RBC



I. ABO Blood Group

- O gene is silent.
- So, does not alter the structure of H substance
- So, group O individual have large amount of H substance on RBC membrane

Blood group	Ag
A	A,H
B	B,H
O	H
AB	A,B,H

I. ABO Blood Group

Bombay Blood Group

- ✓ Some individuals do not inherit on H gene (hh genotype).
- ✓ Do not produce H substance
- ✓ No A or B Ag on RBC membrane
- ✓ So, blood group O (Bombay O)
- ✓ No H gene → no H substance → anti H antibody
  - Ig M, naturally occurin antibody
  - Active in 37*C
- ✓ O blood group to bombay O → can cause HTR
- ✓ So Bombay O to Bombay O

I. ABO Blood Group

Para-Bombay

- Some individuals inherit mutant gene and produce low level of H substance on RBC
- So, H substance is completely used by A or B Ag
- So, no H Ag on RBC
- So, anti H antibody
- Weaken than Bombay O

I. ABO Blood Group

Subgroups

- A phenotype can be divided into A_1 and A_2 depending on the structures of precursor substance (straight chain, branched chain)
- 80% → A_1 AB → A_1B

  20% → A_2 A_2B
- 3% of A_2 → anti A_1 antibody which react with A_1 25% of A_2B red cells Ag
- A_1 to A_2 with anti A_1 → HTR (rare)
- 1 active at low Temp 2 99% → A_1
- No clinical significant

II. Rh Blood Group

- Ag – D, C, c, E, e
- D Ag is most potent immunogen
- Rh +ve → D Ag +ve

  Rh –ve → D Ag –ve
- 70% of Rh –ve can produce anti D if Rh +ve blood is given.
- C, c, E, e Ag → anti D Ab after transfusion

Rh +ve	Rh –ve
Dde	Dce
DcE	dCe
Dce	dcE
DCE	dCE

II. Rh Blood Group

Rh Antibody

- Ig G, alloantibody
- Occur after blood transfusion, pregnancy
- Next transfusion → HTR

Weak D

- Weak expression of D antigen
- Cause negative reaction with anti D during grpuping
- After transfusion to Rh –ve patient, cause production of anti D

III. OTHER BLOOD GROUPS

1). Lewis blood group system

Ag – lea, leb

phenotype

- le (a+b-)
- le (a-b+)
- le (a-b-)
- le (a+b+)

lewis antibody - + in le (a-b-)

- Ig M, naturally occuring
- cause HTR if le Ag + blood

III. Other Blood Groups

2). kell system

Ag – K, k, Kp, Js

phenotype – K+k-, K+k+, K-k+

- Kp (a+b-), Kp (a+b+), Kp (a-b+)
- Js (a+b-), Js (a+b+), Js (a-b+)

3). Kidd system

Ag – Jka, Jkb

phenotype – Jk (a+b-), Jk (a-b+), Jk (a+b+), Jk(a-b-)

III. Other Blood Groups

4). Duffy system

Ag – Fya, Fyb

phenotype – Fy (a+b-)

- Fy (a+b+)
- Fy (a-b+)
- Fy (a-b-)

5). P blood group system

Ag – P, P1

phenotype – P1 (P, P1Ag)

- P2 (only P Ag)

6).Diego system

- Ag-Dia, Dib

III. OTHER BLOOD GROUPS

ANTIBODY

- IgG
- Allo antibody
- Occur after taransfusion or pregnancy
- Cause HTR in next transfusion
- P antibody→ delayed HTR

FEATURES OF ACUTE LIFE-THREATENING TRANSFUSION REACTIONS

	FNHTR	Acute IV heamolysis	Bacteria Contamination	TRALI	Anaphylaxis	Fluid overload
Cause	Cytokine From luecoantibody to WBC & platelet	Infusion of incompatible blood	Skin, blood pack, thaw, handling	Antibody in donat plasma to patient's WBC	1. IgA deficiency 2. Antibody to IgA	Too much, too rapid (A, Heart, Reanl)
Timing	Usually towards the end 5-10% up to 2 hrs after transfusion	50-100ml of RBC Usua ml)lly required	During or up to 8 hr after transfusion	Within ½ - 4 Hr after starting of trnsfusion (10-15 ml)	Early within a minute	
fever	+	++	++	++	--	--
Chills& rigor	++	++	++	++	--	--
Hypotension, shock	--	++	++	++	++	--

FEATURES OF ACUTE LIFE-THREATENING TRANSFUSION REACTIONS

	FNHTR	Acute IV haemolysis	Bacterai contamination	TRALI	anaphylaxis	Fluid overload
S/S of Haemolysis		++, Hburia,Back pain, Coomb's Test +				
DIC		++	++			
Oliguria, Renal failure		++	+		+	
Dyspnoea, Respiratory distress	+	++	--	++, cyanosis++ CXR- diffuse opacity	+ airway obstruction	++
Cutaneous					Prutitis, urticaria	
GI,N,V	+	++	+	-	NVD.abodminal pain	--

SIGNS, SYMPTOMS & MANAGEMENT

I. Mild reactions	Signs	Symptoms
Mild hypersensitivity reaction	-Rash -Urticaria	-Pruritus -Itching

MANAGEMENT

I.

1). Slow the transfusion

2). Give antihistamines (IM) (0.1 mg/kg)

3). Continue transfusion at normal rate if there is no progression of symptoms after 30 mins

4). If no clinical improvement within in 30 mins or if signs and symptoms worsen, treat as moderate severe reaction.

SIGNS, SYMPTOMS & MANAGEMENT

II. Moderately Severe reaction	Signs	Symptoms
1.Moderately severe H/S reaction	-Flushing -Urticaria	-Anxiety -Pruritus
2. Febrile non H'lytic reaction	-Rigors -Fever	-Palpitation -Mild dyspnoea
3. Early bacterial contamination	-Restlessness -Tachycardia	-Headache

MANAGEMENT

II.

1). Stop the transfusion.

2). Replace the giving set and keep IV line with N/S.

3). Give antihistamine IV or IM, oral or rectal antipyretic (Paracetamol) (500mg – 1g in adult). AVOID ASPIRIN

MANAGEMENT

4). Give IV corticosteroid and bronchodilation if there are anaphylactic features (bronchospasm,stridor).

5). **Notify team leader or senior doctor and blood bank.**

6). **Send the blood unit with giving set, freshly collected urine and new blood samples (1 clotted and 1 anticoagulant) from the vein opposite the infusion site with appropiate request form to blood bank for investigation.**

MANAGEMENT

7). Collect urine for next 24 hr for evidence of haemolysis and send to lab.

8). If there is no clinical improvement within 15 mins or patient's condition deteriorate, treat as severe reaction.

SIGNS, SYMPTOMS & MANAGEMENT

III. Severe Life-threatening	Signs	Symptoms
1. H'lytic transfusion reaction	-Rigor -Fever	-Anxiety -Chest pain
2. Bacterial contamination and septic shock	-Restlessness -Hypotension	-Pain near the infusion site -Respiratory distress
3. Fluid overload	-Tachycardia	-Loin / Back pain
4. Anaphylactic reaction	-Hburia	-Headache
5. Tansfusion related lung injury	-Unexplained bleeding (DIC)	-Dyspnoea

MANAGEMENT

III.

1). Stop the transfusion. Replace the giving set and keep IV line open with normal saline.

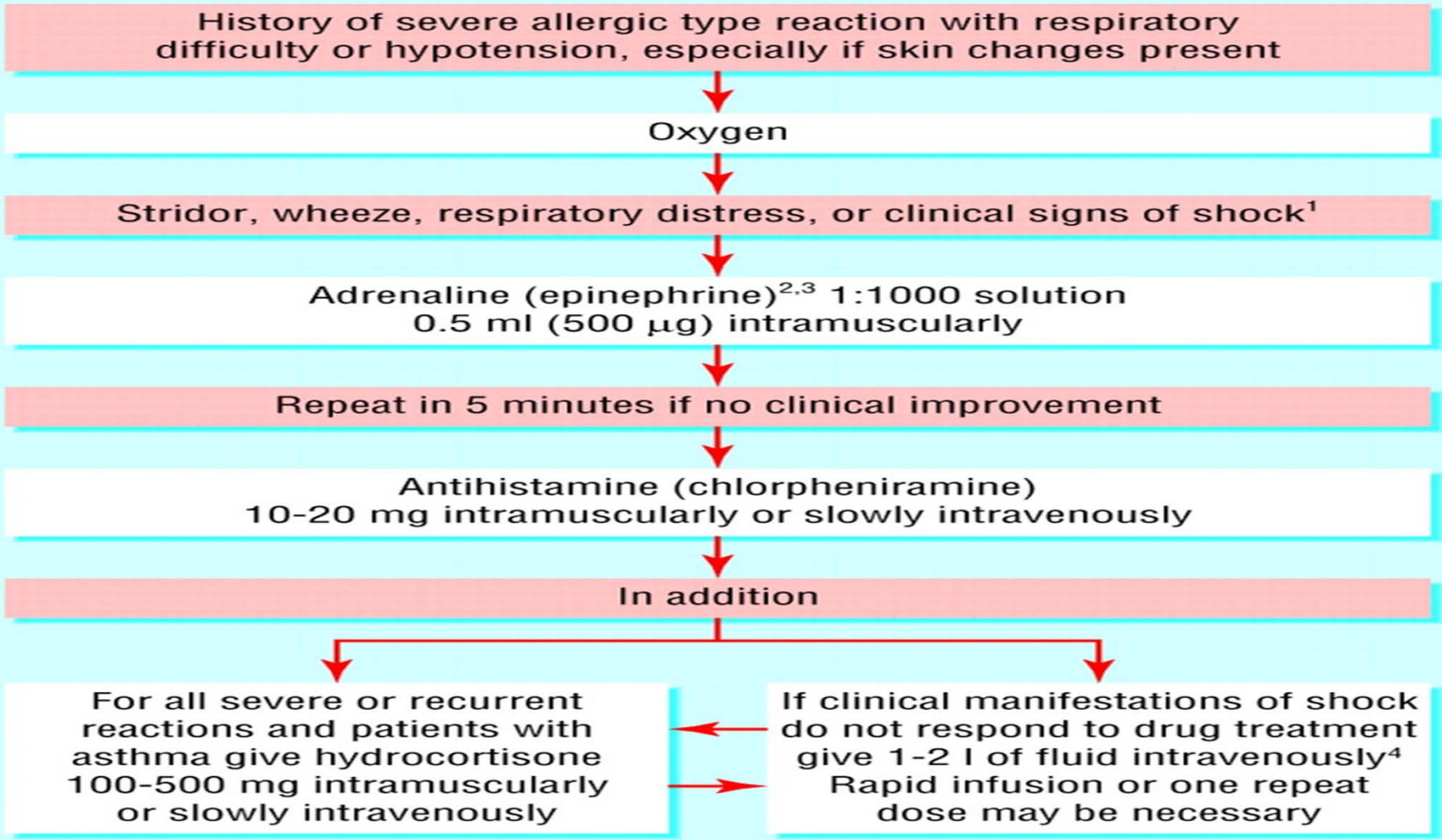
2). Infuse normal saline to maintain systolic BP (initial 20-30 ml/kg). If hypotension present, give over 5 mins and elevate patient's legs.

MANAGEMENT

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

4). Give 1:1000 Adrenaline 0.01 mg/kg body wt by IM.

5). Give IV Corticosteroid and bronchodilators if there are anaphylactic features (bronchospasm, stroidor).



1. Inhaled β_2 agonist such as salbutamol may be used if bronchospasm severe and does not respond rapidly to treatment
2. If profound shock immediately life threatening give cardiopulmonary resuscitation or advanced life support if necessary. Consider giving adrenaline 1:10 000 solution slowly intravenously. Hazardous and recommended only for experienced physician. Note different strengths used for intramuscular and intravenous routes
3. If treated with Epipen, 300 µg will usually be sufficient. A second dose may be required. Half doses of adrenaline may be safer for patients taking tricyclic antidepressants or β blockers
4. Crystalloid may be safer than a colloid

Source: Bmj.com

MANAGEMENT

6). Give diuretics: eg. Frusemide 1 mg/kg IV to prevent renal failure.

7). Notify the doctor responsible for the patient and blood bank immediately.

MANAGEMENT

8). Reassess if hypotension present,

- give further saline 20-30 ml/kg IV over 5 min

- give inotrope support of circulation.

dopamine, dobutamine infusion and adrenaline 1:1000 by IM injection(0.01 mg/kg)

9). Assess for bleeding from puncture site or wound for DIC. If present, give PRP or FFP. Monitor regularly coagulation status of patient.

MANAGEMENT

10). If urine output fall or lab evidence if ARF (Ur, Cr , K+), Treat as ARF.

11). If bactiraemia is suspected, blood spectrum Antibiotics IV.

12). Check first sample of urine for sign of Hburia and collect 24 hr urine.

13). Intake – output chart.

INVESTIGATION IN ACUTE TRANSFUSION REACTION

1). Record

a). Type of transfusion reaction

b). Length of time after start of transfusion that the reaction occur

c). Volume, type and numbers of blood products transfusion.

INVESTIGATION IN ACUTE TRANSFUSION REACTION

2). Take the following sample and send them to the blood bank for laboratory investigation.

a). Immediate post transfusion samples (1 clotted and 1 anticoagulated EDTA) from the vein opposite the infusion site for

- full blood count
- coagulation screen
- direct antiglobulin test (DAT)
- Urea, Creatinine, Electrolytes

INVESTIGATION IN ACUTE TRANSFUSION REACTION

b). For blood culture in blood culture bottle

c). Blood unit and giving set containing red cells and plasma residues from transfused donor blood.

d). First specimen of patient's urine

INVESTIGATION IN ACUTE TRANSFUSION REACTION

3). 12 hr and 24 hr after the start of reaction, give blood samples (1 clotted and 1 antigoaulated) from vein opposite the infusion site.

4). Patient's 24 hr urine sample.

MONITORING THE TRANSFUSED PATIENT

1). For each unit of blood transfusion, monitor at the following stage

- Before starting the transfusion
- As soon as transfusion started
- 15 min after transfusion
- At least every hour during transfusion
- On completion of transfusion
- 4 hr after transfusion

MONITORING THE TRANSFUSED PATIENT

2). At each of these stages, record the following on the patient chart

- general appearance
- temperature
- BP
- pulse
- respiratory rate
- urine output

MONITORING THE TRANSFUSED PATIENT

3). Record

- Time of transfusion started
- Time of transfusion completed
- Volume and type of all products transfused
- Any adverse affected.

DELAYED TRANSFUSION REACTION

1). Delayed haemolytic reaction

- patient has previously immunized to red cells Ag during pregnancy or previous transfusion, but has low level of antibody.

- After repeated transfusion, rapid secondary immune response and raised antibody level and cause haemolysis.

DELAYED TRANSFUSION REACTION

1). Delayed haemolytic reaction

- Fever, Anaemia, Jaundice, Hburia after 5 – 10 days.

- Usually no treatment.

- Treat only if hypotension and renal failure.

DELAYED TRANSFUSION REACTION

2). Post transfusion purpura

- Female
- rare but potentially fatal
- Ab against the platelets in recipient
- severe thrombocytopenia 5-10 days after transfusion
- bleeding, reduced PC $<100*10^9$ /L
- High dose steroid
- PRP

DELAYED TRANSFUSION REACTION- GVHD

3). GVHD

- rare but potentially fatal
- Immunodeficient patient (drugs, diseases, BM type)
- Blood from donor with compatible HLA gene
- Donor T lymphocytes proliferate and attach the recipient tissue.
- Fever, skin rash, desquamation, diarrhoea, hepatitis, pancytopenia.
-No specific Tx, only supportive

Bone marrow aplasia is the primary cause of death

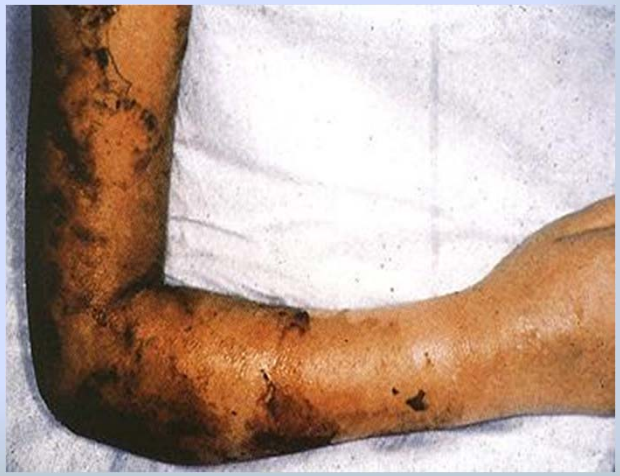
CLINICAL PRESENTATION

Skin: **Swollen, erythroderma and bullae formation- most common**

GI: **Diarrhea and abdominal cramps**

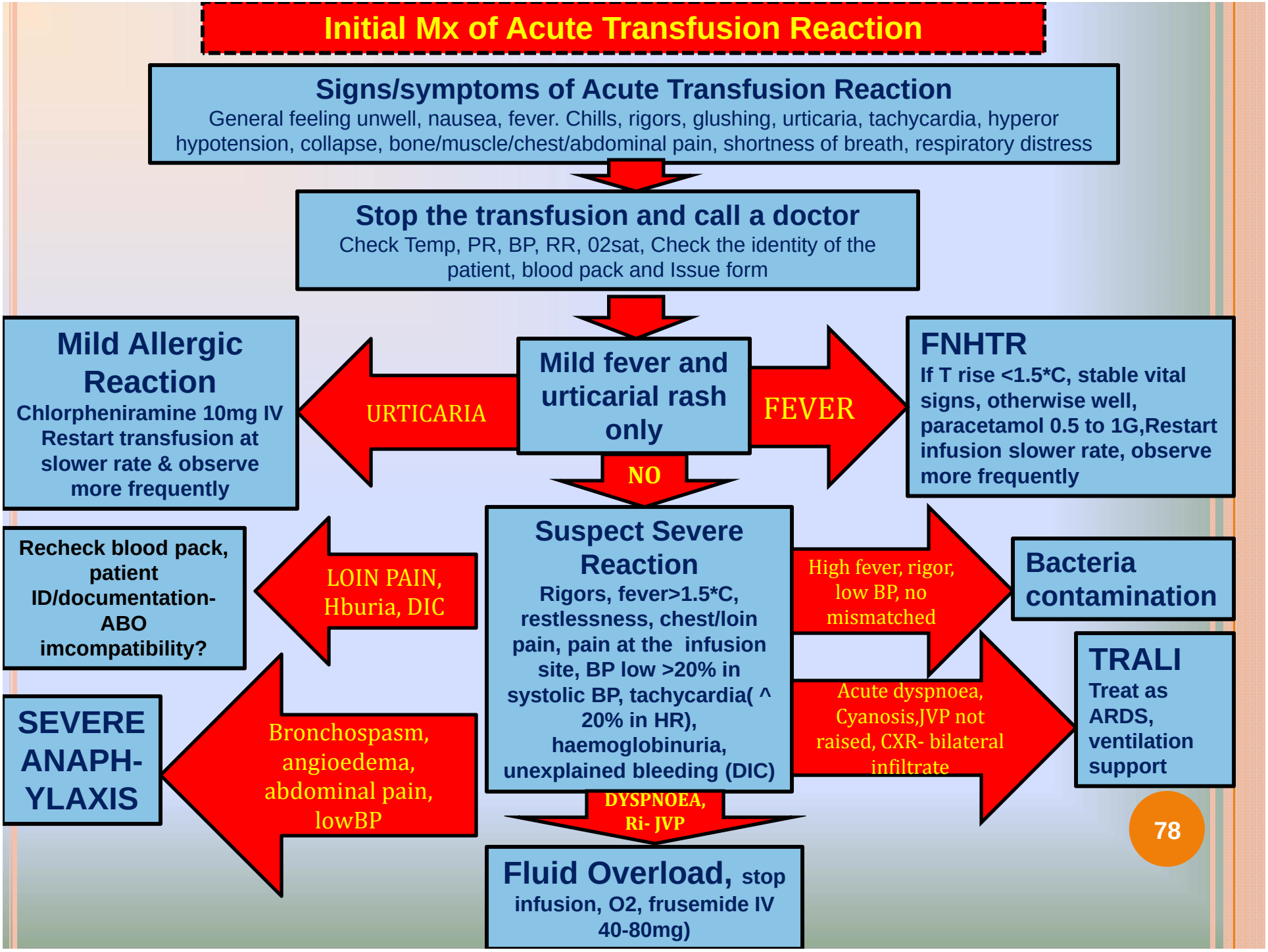
Liver: **Elevated LFT and Hyperbilirubinemia**

Heme: **Bone marrow aplasia, persistent thrombocytopenia**



Skin manifestation of GVHD
Generalized swelling, erythroderma and bullous formation

Initial Mx of Acute Transfusion Reaction



THE END!

IMΦ

Thank you

for your attention !