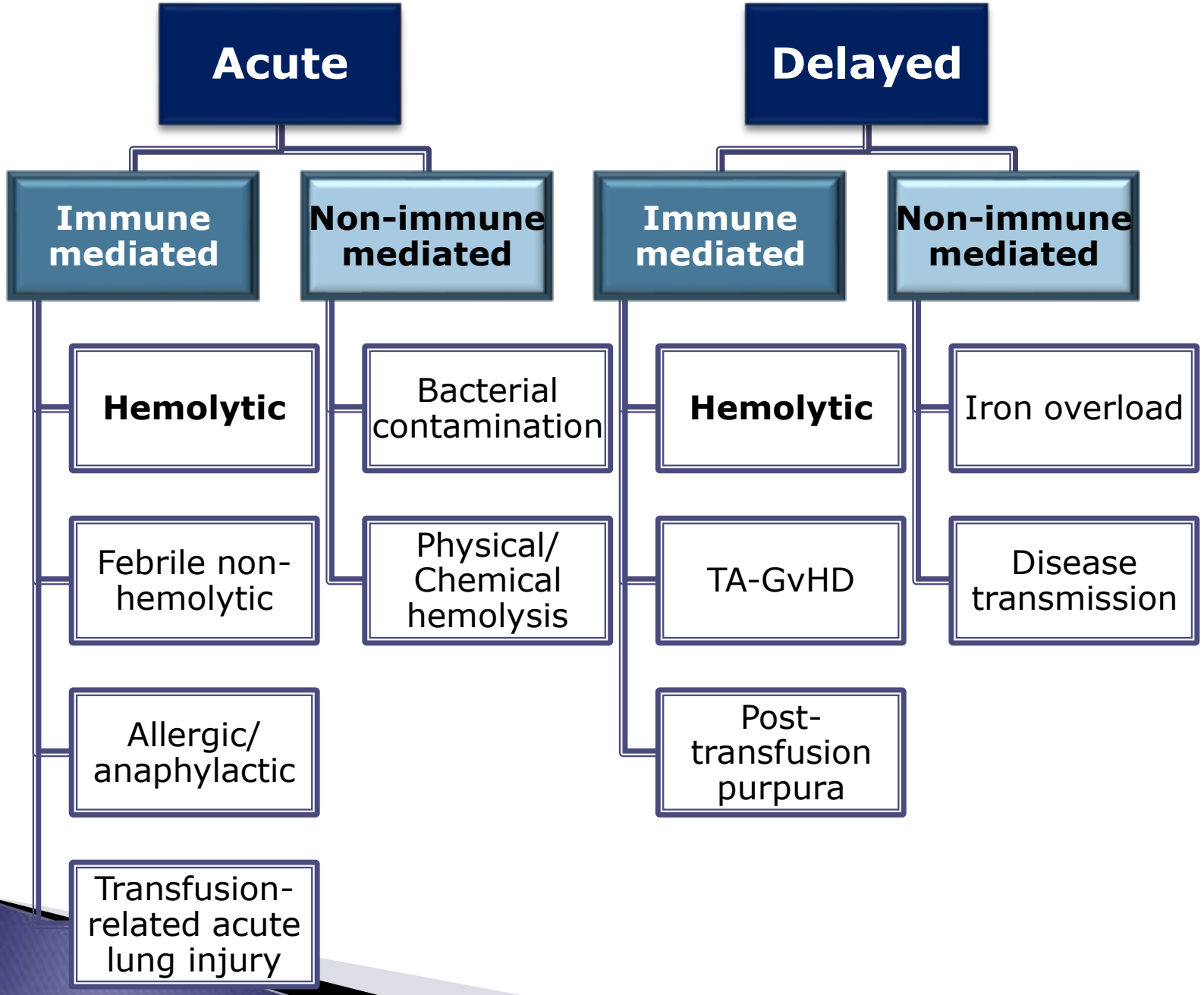
Hemolytic Transfusion Reaction

ANNIE NGUI (102456)

Introduction

- Transfusion reactions are defined as adverse events associated with the transfusion of whole blood or one of its components
  - range from mild to life threatening reactions

- Classification:
  - Immune mediated transfusion reaction
    - typically occur due to mismatch or incompatibility of the transfused blood product and the recipient
  - Non-immune mediated transfusion reaction
    - usually caused by the physical effects of blood product or the transmission of disease


Acute
Delayed
Immune mediated
Non-immune mediated
Immune mediated
Non-immune mediated
Hemolytic
Bacterial contamination
Hemolytic
Iron overload
Febrile non-hemolytic
Physical/ Chemical hemolysis
TA-GvHD
Disease transmission
Allergic/ anaphylactic
Post-transfusion purpura
Transfusion-related acute lung injury

Hemolytic Transfusion Reaction

- Accelerated destruction of red blood cells in recipient receiving blood transfusion
  - due to immunological incompatibility between blood donor and recipient
- Classified according to the time of onset:
  - **Acute hemolytic transfusion reaction**
    - during transfusion or within 24 hours of transfusion
  - **Delayed hemolytic transfusion reaction**
    - more than 24 hours after transfusion, typically 3-10 days (up to 28 days)
- Occur intravascularly or extravascularly in reticuloendothelial system

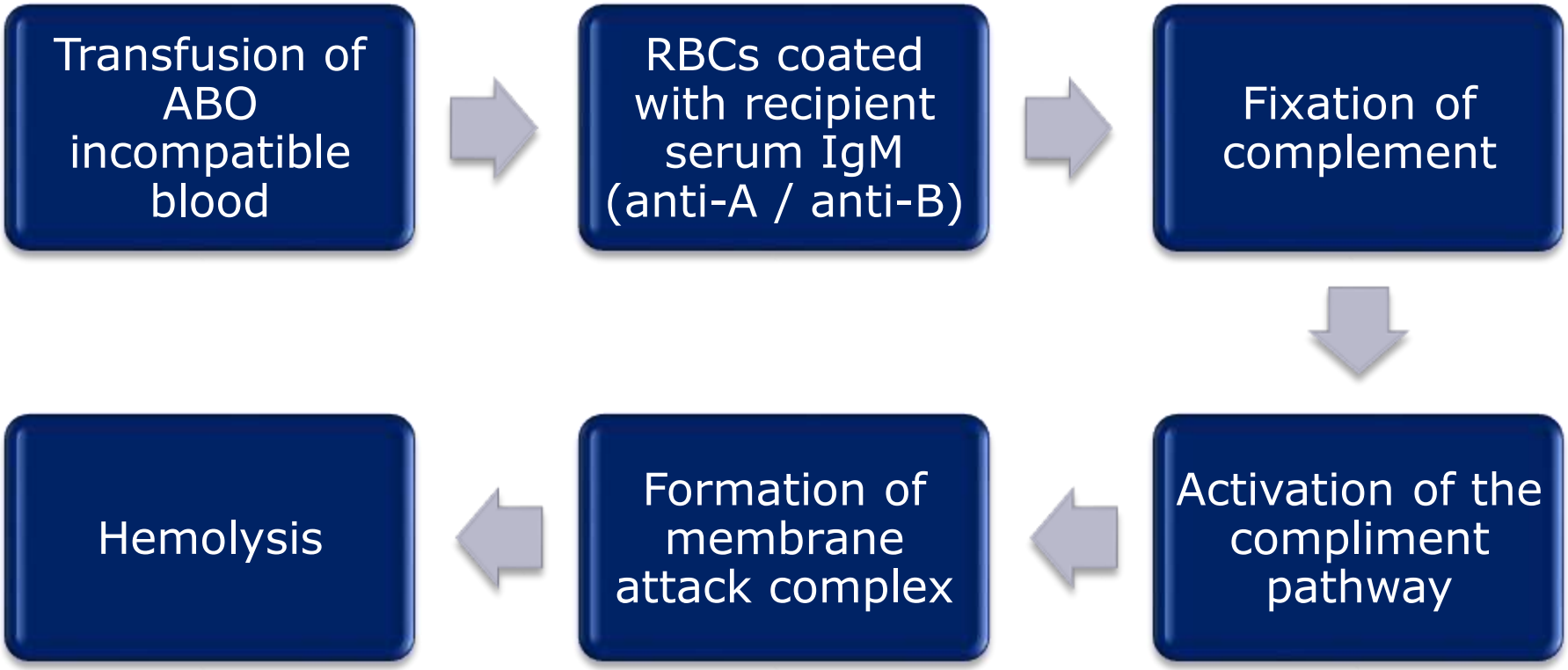
Acute Hemolytic Transfusion Reaction

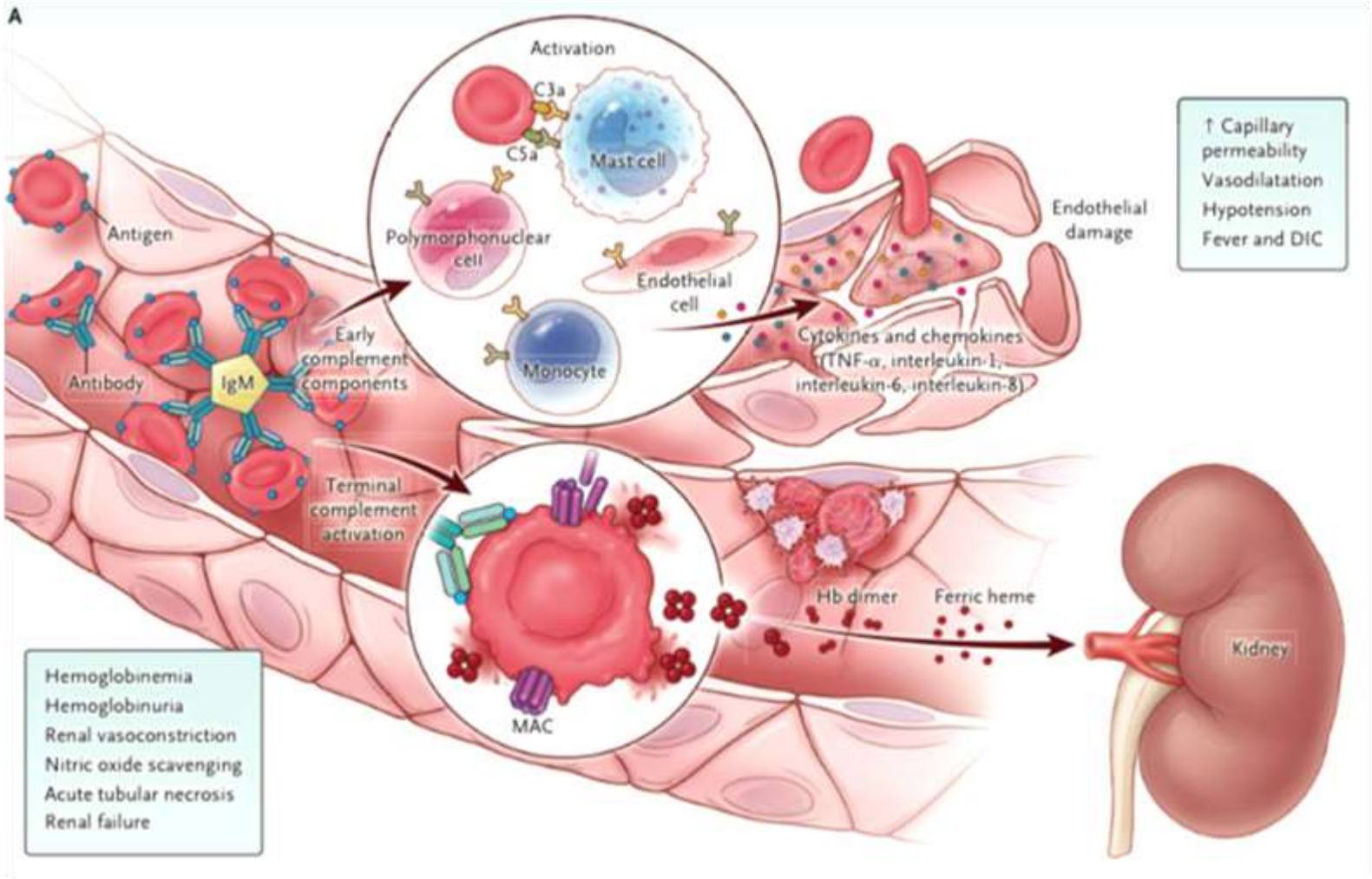
- Red blood cells destruction MOSTLY occur intravascularly via complement activation
  - ABO incompatibility (IgM)
  - non-ABO incompatibility (IgG): anti-Jk^a, anti-K
    - High titre of these antibodies cause complement fixation and hemolysis
    - Uncommon
- Sign and symptoms may present after infusion of as little as 5-10 ml red cells especially in ABO incompatibility

- Acute hemolytic transfusion reaction caused by transfusion of significant incompatible plasma
  - Occurs less frequently
  - Due to minor ABO mismatch
    - e.g. transfusion of O Positive plasma containing products (FFP, cryosupernatant, platelets) into A Positive patient
      - causes hemolysis of patient's own red cells especially in smaller patients (neonate, infant or child)
  - Clinical symptoms are identical to transfusion of incompatible red blood cells depending on the volume and titre of anti-A and anti-B antibodies

- Causes:
  - ✓Improper identification of patient during sample collection
  - ✓Improper labelling of patient’s sample or blood product
  - ✓Improper blood typing of patient’s sample or blood product and crossmatching
  - ✓Improper bedside checking or identification of the recipient or blood product at the time of transfusion

Intravascular Hemolysis




A
Activation
C3a
C5a
Mast cell
Polymorphonuclear cell
Endothelial cell
Monocyte
Antigen
Antibody
IgM
Early complement components
Terminal complement activation
MAC
Endothelial damage
Cytokines and chemokines (TNF-α, interleukin-1, interleukin-6, interleukin-8)
↑ Capillary permeability
Vasodilatation
Hypotension
Fever and DIC
Hb dimer
Ferric heme
Kidney
Hemoglobinemia
Hemoglobinuria
Renal vasoconstriction
Nitric oxide scavenging
Acute tubular necrosis
Renal failure

Delayed Hemolytic Transfusion Reaction

- Caused by anamnestic response to foreign antigen that the recipient was previously exposed to (primary alloimmunization)

- Common antibodies (IgG)
  - Kidd (anti-Jk^a, Jk^b, Jk^3)
  - Rh (anti-D, C, c, E, e)
  - Duffy (anti-Fy^a, Fy^b)
  - Kell (anti-K, k)

- Red cells destruction occur extravascularly

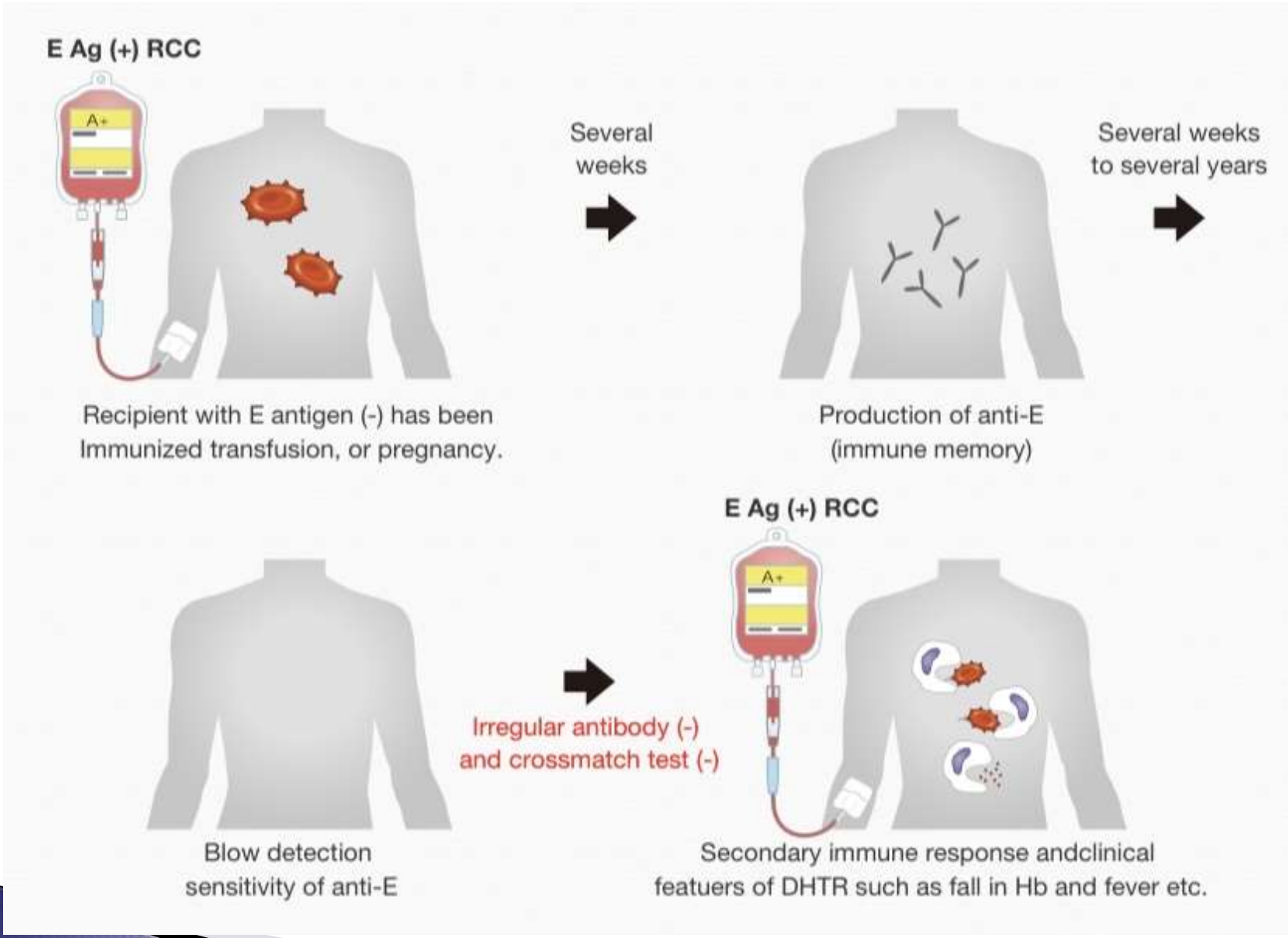
Extravascular Hemolysis

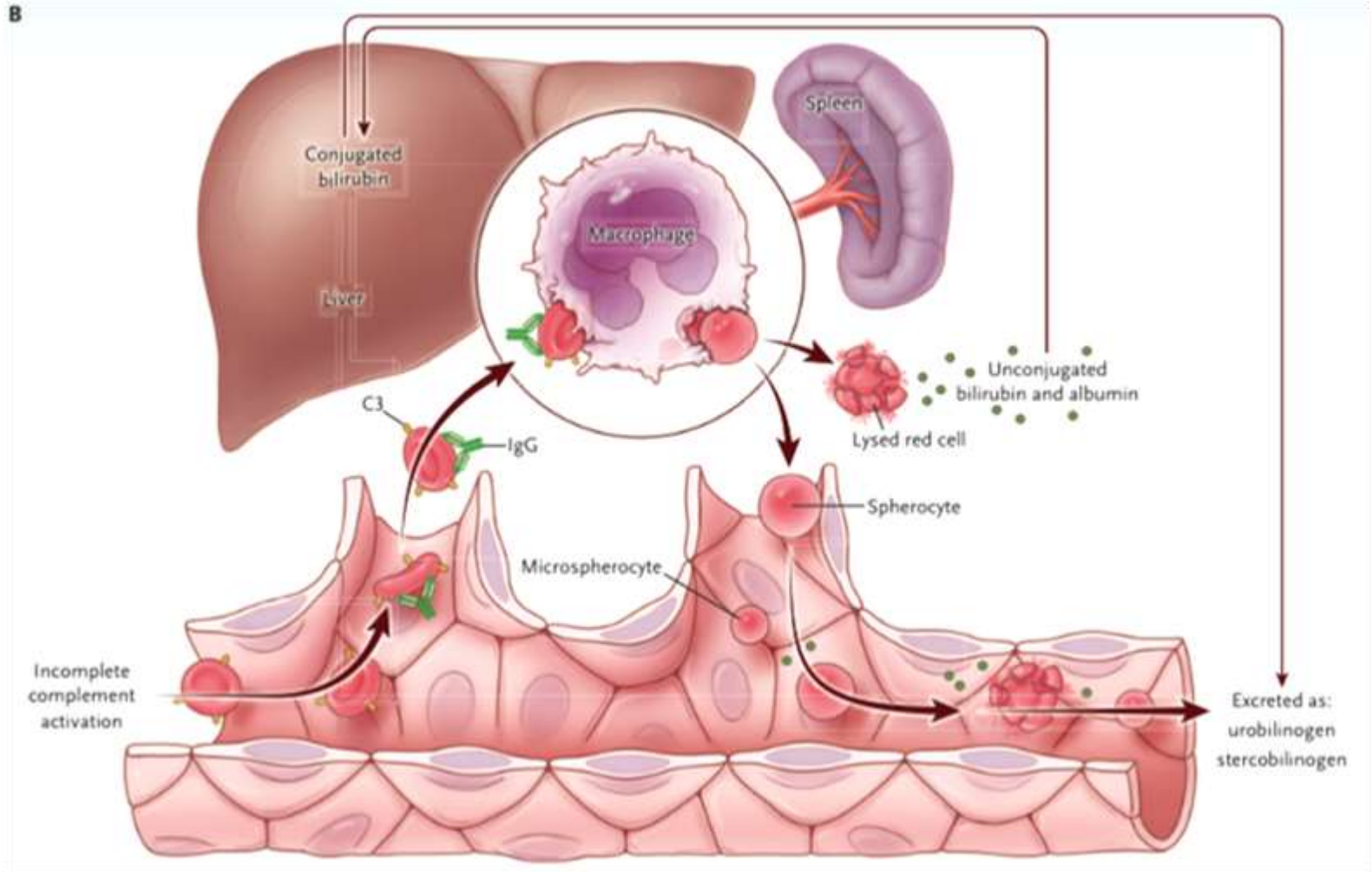
Prior red cell exposure through pregnancy or transfusion
→ sensitization to minor red blood cell antigens
→ primary immune response
→ alloantibody formation

Alloantibody titer decreases over time with no re-exposure
→ pre-transfusion testing becomes negative

Re-exposure to antigens by transfusion or pregnancy
→ anamnestic response
→ production of IgG
→ IgG will bind to the antigen on RBCs

IgG-coated RBCs removed from circulation
→ taken into the reticuloendothelial system
→ phagocytosed in the liver or spleen by macrophages
→ Hemolysis


E Ag (+) RCC
A+
Several weeks
Several weeks to several years
Recipient with E antigen (-) has been Immunized transfusion, or pregnancy.
Production of anti-E (immune memory)
E Ag (+) RCC
A+
Irregular antibody (-) and crossmatch test (-)
Blow detection sensitivity of anti-E
Secondary immune response andclinical featuers of DHTR such as fall in Hb and fever etc.


B
Conjugated bilirubin
Liver
Spleen
Macrophage
Unconjugated bilirubin and albumin
Lysed red cell
C3
IgG
Spherocyte
Microspherocyte
Incomplete complement activation
Excreted as: urobilinogen stercobilinogen

Sign & symptoms

Acute Hemolytic Transfusion Reaction	Delayed Hemolytic Transfusion Reaction
▪ Fever, chills ▪ Oozing or pain from IV site ▪ Flank pain ▪ Back pain ▪ Nausea, vomiting ▪ Hypotension ▪ Bronchospasm ▪ Red/Dark coloured urine	▪ Fever ▪ Progressive anemia ▪ Jaundice ▪ Malaise

Complication

- Shock
- DIC
- Renal failure

Rarely occur in DHTR

Management & Treatment

Acute Hemolytic Transfusion Reaction

- Stop transfusion immediately
- Blood unit must be checked again to ensure that it corresponds with patient's details
- Inform the physician for further management
- Replace IV set and start saline infusion
- Provide oxygen/ventilatory support if necessary
- Supportive care to maintain blood pressure
- Maintain urine output >1ml/kg/hr using diuretic
- Manage DIC and hemorrhage if present

Delayed Hemolytic Transfusion Reaction

- Symptomatic or supportive care
- Monitor renal function
- Provide antigen negative blood if transfusion required

Investigation

- The blood unit and post-transfusion blood samples and urine of the patient should be sent to laboratory immediately and 24 hours after transfusion (if requested by the physician)

- Transfusion reactions investigation include:
  - Blood grouping
  - Direct coombs
  - Antibody screening
  - Crossmatch

  } both pre-transfusion and post-transfusion sample

  - Renal profile
  - Full blood picture
  - Coagulation profile
  - Urine FEME
  - Blood culture of blood bag

Laboratory Findings

Acute Hemolytic Transfusion Reaction

- Hemoglobinemia
- Hemoglobinuria
- Positive/Negative DAT test
- Hyperbilirubinemia
- Elevated LDH
- Decreased haptoglobin
- Peripheral blood smear shows schistocytes, spherocytes

Delayed Hemolytic Transfusion Reaction

- Positive DAT test
- Hyperbilirubinemia
- Elevated LDH
- Decreased haptoglobin
- Positive antibody screening
- Peripheral blood smear shows spherocytes