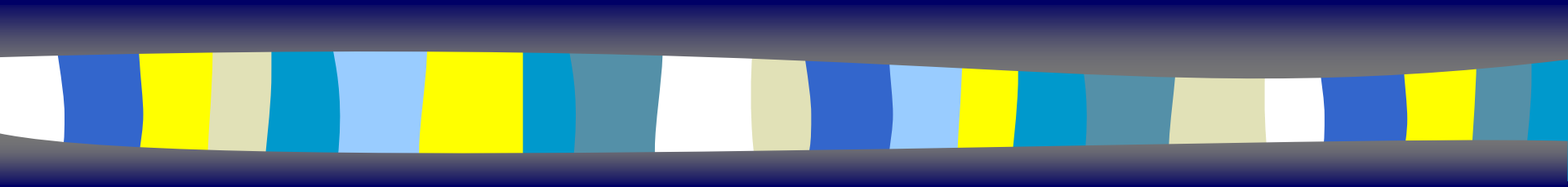


# Transfusion in Thalassemia



Ponlapat Rojnuckarin, MD, PhD  
Chulalongkorn University

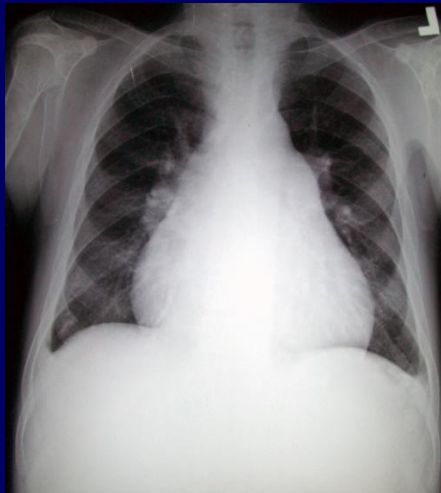
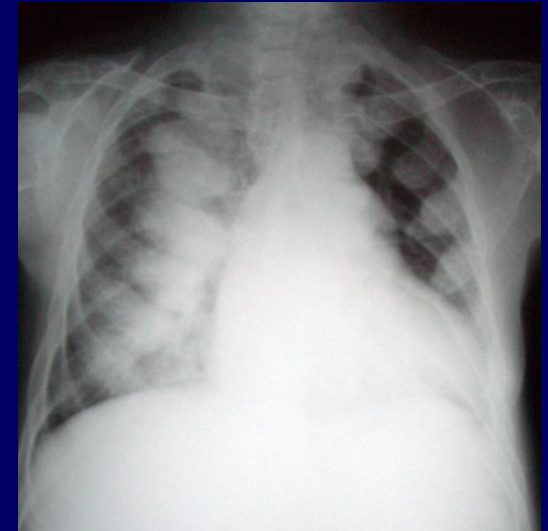
ในนาม: คณะทำงานการให้เลือดและมาตรฐานของเลือด  
สำหรับผู้ป่วยธาลัสซีเมีย



# Transfusion in Thalassemia

- Relieve Anemic Symptoms
  - Prevent compensatory mechanisms: Bone changes, Abnormal face, Extramedullary hematopoiesis, GI iron absorption
  - Suppress abnormal cell production: Thromboembolism, Gall stone
- Improved quality of life, Normal growth and development

# Prevention of complications





# Transfusion strategies

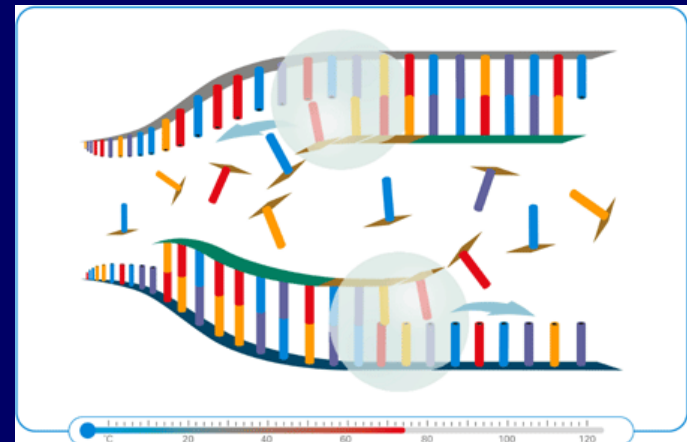
- **High transfusion** in severe thalassemia
  - Aim Hb > 8-9 g/dL (Western >9-10.5 g/dL)
  - Transfusion q 2-5 weeks with iron chelation
  - Best QoL, growth and development
- **Low transfusion** in thalassemia intermedia or inability to receive high transfusion
  - Aim Hb > 6-7 g/dL
  - Transfusion less frequently

**Consider clinical symptoms > Numbers**

ความพร้อมของผู้ป่วยและสถานพยาบาล

# Standard testing in donated blood

- ABO/Rh
- Antibody screening
- Infectious markers
  - Anti-HIV, HIV Ag, NAT (Nucleic acid test)
  - HBsAg, NAT
  - Anti-HCV, NAT
  - Syphilis



# Infectious transmission

- Window periods (Nucleic acid test: NAT)

HIV Ag	16 d	NAT	11 d
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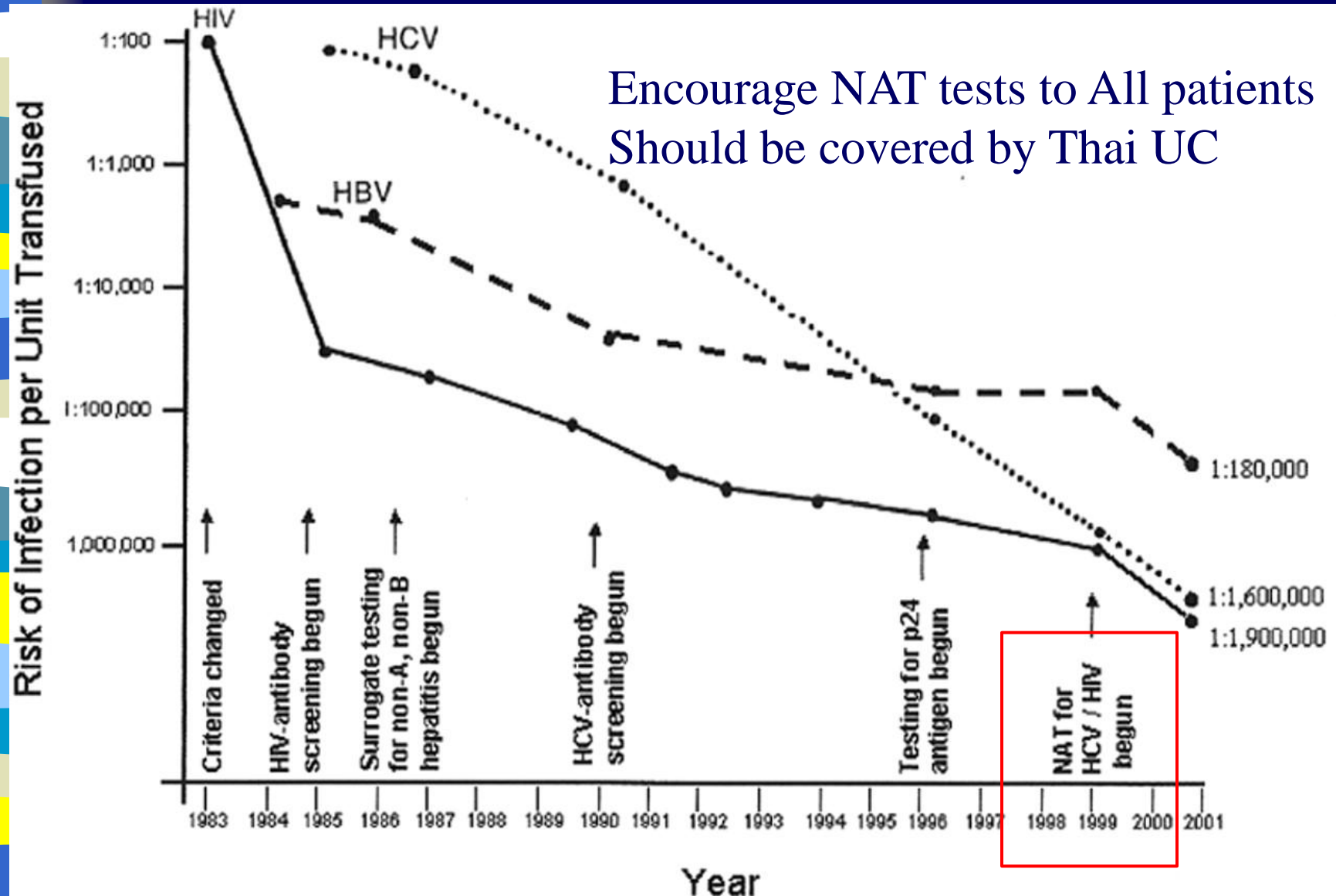
Anti-HCV	70 d	NAT	12 d
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HbsAg	56 d	NAT	33 d
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- Donor self exclusion is still required.



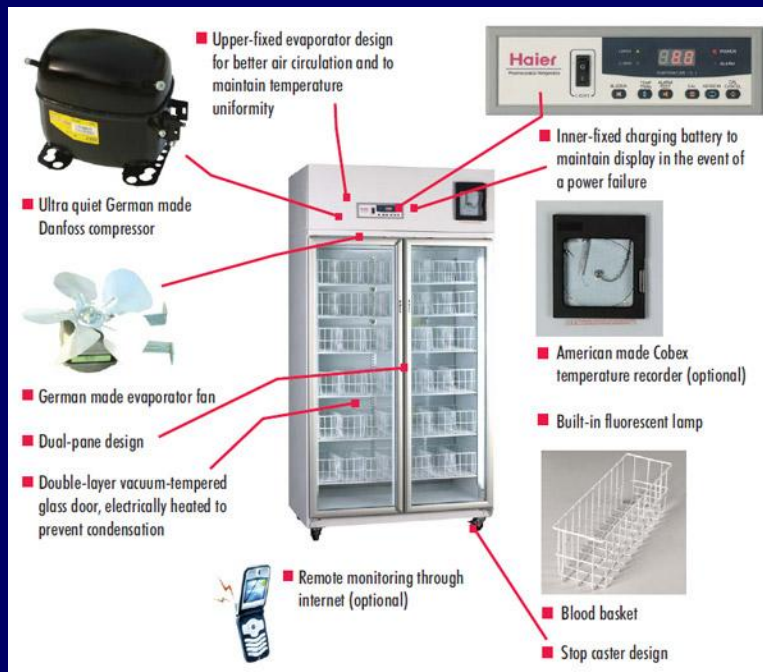
# Risk of transfusion (USA)





# Blood Component storage

- PRC 1-6 °C, 5 weeks
- Blood cold chain (1-10 °C)
- Monitored temperature







# Leukocyte-reduced products

- Leukocyte-poor PRC
  - Centrifugation,  $WBC < 5 \times 10^8$
  - Prevent febrile transfusion reactions
- Leukocyte-depleted PRC (Expensive)
  - Filtration,  $WBC < 5 \times 10^6$
  - Prevent febrile transfusion reactions
  - Prevent HLA alloimmunization (Anti-Plt)
  - Prevent CMV transmission

# Filtered blood products



- PRC or platelet concentrate
- Pre-storage filter (At blood bank)
  - Reduce cytokines that may cause febrile reactions
  - Cheaper than bedside filter
  - Do not know the exact demand
- Bedside filter
  - May cause hypotensive reaction

# Filtered blood products

- Plan for stem cell transplantation
- Hematologic malignancy that requires platelet transfusion

In order to save costs

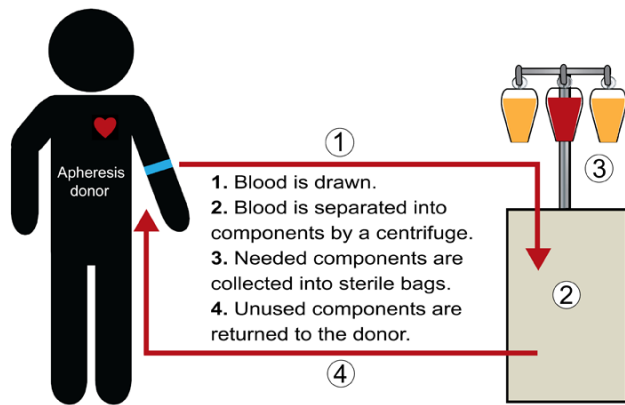
- Not use for palliative care
- Not use for general transfusion



# Single-donor PRC



- Apheresis and Return plasma and platelets to donors
- Equal to 2 units of PRC
- For antigen-matched transfusion, e.g. thalassemia to prevent alloimmunization
- Lower donor exposure





# ‘Fresh’ PRC for Thalassemia

- PRC stored for less than 7-10 days
- Circulate longer in recipients
- Modest decrease in blood requirement
- Should be considered in patients requiring frequent regular transfusion
- Disadvantages
  - Difficult blood management
  - Young child: wasted RBC, ↑ donor exposure



# Complications of Transfusion

- Iron overload (Iron chelation is required.)
- Infectious transmission
- Transfusion reactions
  - Febrile non-hemolytic transfusion reactions
  - Allergic reactions
  - Hemolytic transfusion reactions (immediate/delayed)
  - Bacterial contamination
  - Transfusion associated volume overload (TACO)
  - Post-transfusion hypertension, convulsion, cerebral hemorrhage
  - Hypotension (with ACEI Rx, bedside filter)

# Immediate Transfusion Reactions

	Fever Chill	Skin	Pain	Resp- iration	GI	Blood Pressure	Others
FNHTR	+	-	-	-	±	-	PRC/PLT with wbc
AHTR	+	-	+	+	+	↓	PRC, Bleed, Dark urine
TAS	+	-	+	+	+	↓	PLT > PRC, Sepsis
TRALI	±	-	-	+	-	↓	FFP/PLT, delay up to 6 h CXR: diffuse infiltrates
TACO	-	-	-	+	-	↑	Fluid imbalance, CXR
Allergic	-	+	-	+	+	↓	FFP, Platelets > PRC CXR: normal
Hypo- tensive	-	±	-	-	±	↓	ACEI, rapidly responds to transfusion cessation

GI, Gastrointestinal; FNHR, Febrile non-hemolytic transfusion reaction; AHTR, acute hemolytic transfusion reaction; TAS, Transfusion-associated sepsis; TRALI, Transfusion-associated acute lung injury; TACO, Transfusion-associated circulatory overload; Allergic, Allergic transfusion reaction; Hypotensive, Acute hypotensive transfusion reaction. Modified from Murphy MF, Pamphilon DH (ed). Practical Transfusion Medicine 3<sup>rd</sup> Ed, 2009





# Delayed transfusion reactions

- Delayed hemolytic reaction
- Alloimmunization: e.g. Platelet refractoriness (Anti-HLA or Anti-HPA)
- Post-transfusion purpura (Anti-HPA)
- Graft versus host disease (Prevented by irradiation)



# Acute Hemolytic Transfusion Reaction

- Incompatible red cells (ABO)
- Plasma or FFP with high-titer Anti-A (rare)
- ABO incompatibility 1: 33,000 - 1: 100,000
- ABO incompatible transfusion
  - 47% No harmful effect
  - 2-7% Death
- Death 1: 1,500,000 transfusion
- Death 10-30 cases/yr in USA



# Transfusion associated sepsis

- 1: 5,000 platelet units (RT storage)
- 1: 500,000 red cell units
- 1: 250 from surveillance culture
- Fever, Chills, Hypotension, Shock, DIC
- Mimic AHTR
- Culture positive (Blood bag and patients)
- High Mortality rate

# Preventive measures

2 separate occasions  
of blood draws



Diversion pouch to prevent  
Bacterial contamination  
from donor skin



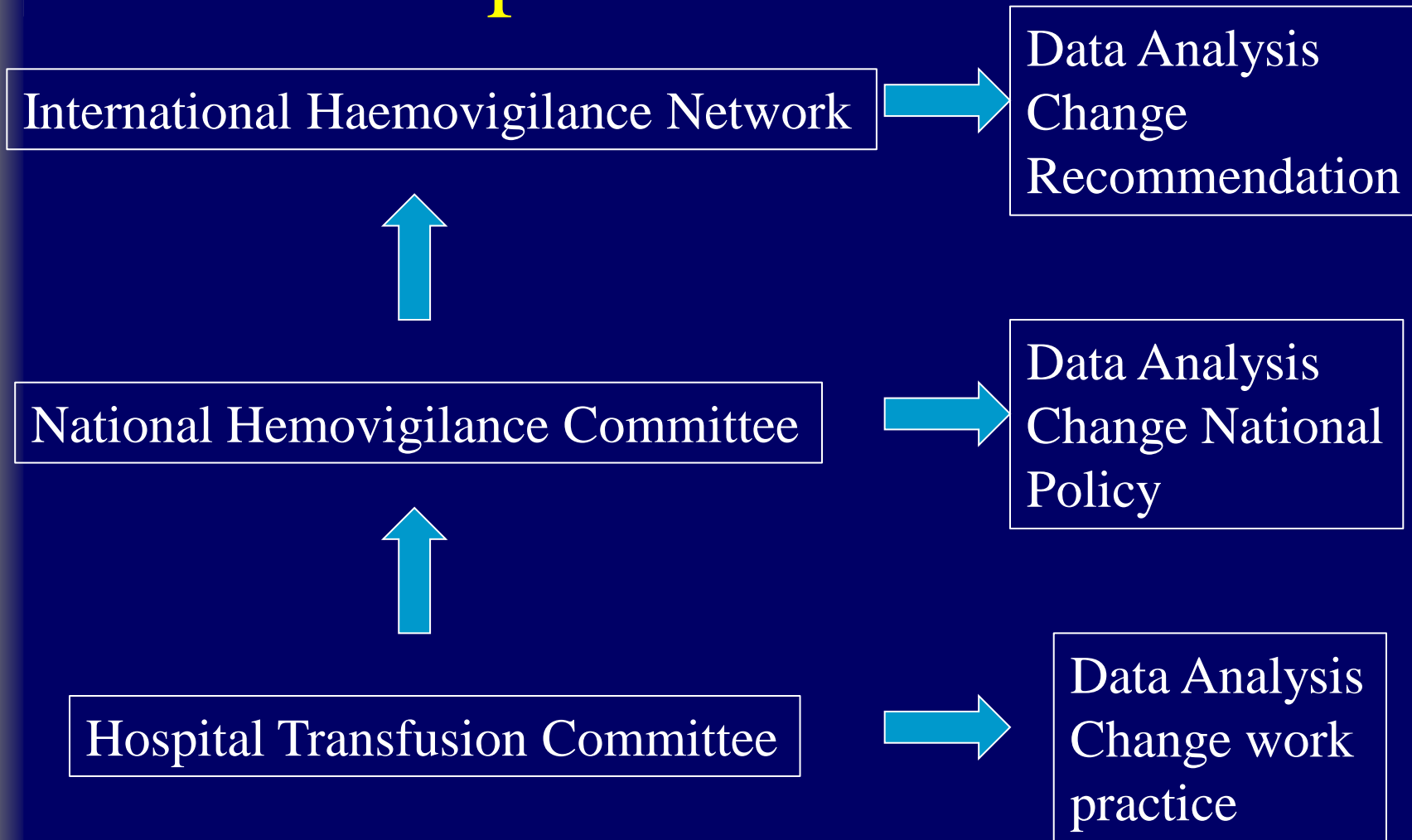
2 blood samples on the first  
Blood transfusion to prevent  
ABO incompatibility



# Hemovigilance

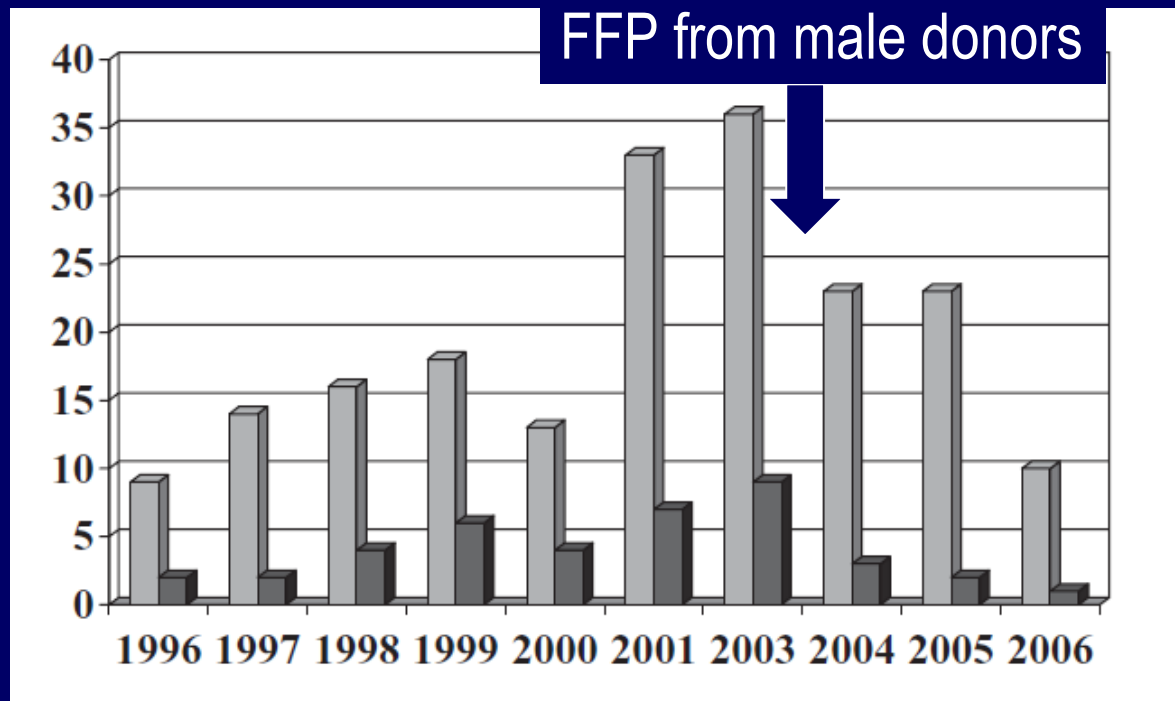
- Similar to Pharmacovigilance for drugs
- Record all adverse events in the whole process of transfusion, e.g. Donors, processing, storage, transfusion reactions
- Records include near miss
- No punishment
- Analysis for Prevention of future events
- Hospital, National, International levels

# Hemovigilance is the Quality Assurance process.



# National policy to prevent Transfusion Related Acute Lung Injury (TRALI) in UK

- Female donors may cause TRALI
- Policy: Male donors only







# Alloimmunization

- Pre-transfusion antigen typing\*: C, c, E, e and Mi<sup>a</sup> to give antigen-matched PRC
- Pre-transfusion antigen typing\*: Kidd, Duffy, Kell, MNS, Lewis and P to aid alloantibody identification
- Alloantibody screening in every cross-matching: Always give antigen-negative PRC
- Long-term records of known antigens and antibodies (Ab may become undetectable)

\*Cannot be done after regular transfusion

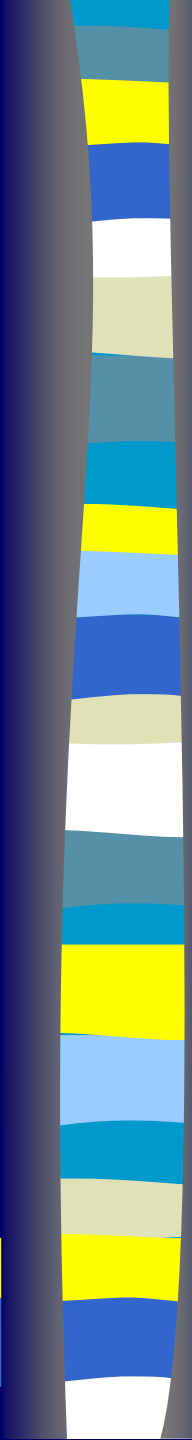


# Autoimmune Hemolytic Anemia in Thalassemia

- Often after transfusion → allo/autoimmunization
- Poor responsive to transfusion, low grade fever
- Direct Coombs test: Positive strongly

## Treatments

- Stop transfusion temporary if possible
- Short course of Corticosteroids



# Antigen typing in previously transfused patients

- Difficulties to find compatible blood in multiple alloimmunized patients
- Antigen typing by serology is complicated by transfused donor red cells in the patients
- May need genotyping (DNA from white blood cells is not affected by transfusion)

# Blood group Genotyping

Multiplex  
PCR



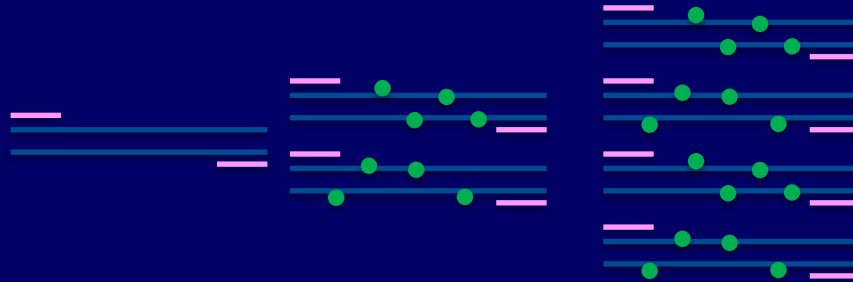
Hybridiz-  
ation



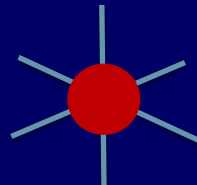
Labeling



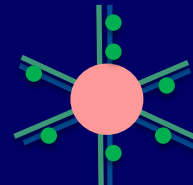
Signal  
detection &  
Data analysis



PCR product:  
biotinylated amplicons  
containing interrogated  
position

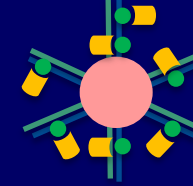
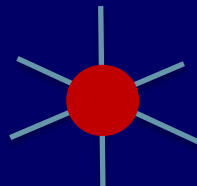


no presence of specific allele

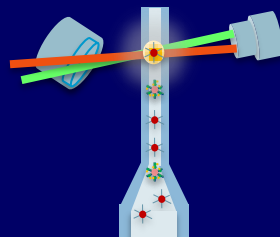


presence of specific allele

Alle-specific  
hybridization.  
Biotinylated amplicons  
bind to probes attached to  
fluorescently labeled  
beads



SAPE binds to biotin



Signal is detected by  
Luminex. BIDS XT  
converts the signal into  
genotypes and predicted  
phenotypes. Reports are  
generated.

## Serological phenotyping

Rh	D, C, E, c, e
Kell	K
Kidd	Jka, Jkb
Duffy	Fya, Fyb
MNS	M, N, S, Mia
Diego	Dia
P1PK	P1
Lewis	Lea, Leb

## Genotyping

RhCE	C(RH2), E(RH3),c(RH4), e(RH5), CW(RH8), V(RH10), hrS(RH19), VS(RH20), hrB(RH31)
Kell	K(KEL1), k(KEL2), Kpa(KEL3), Kpb(KEL4), Jsa(KEL6), Jsb(KEL7)
Kidd	Jka(Jk1), Jkb(Jk2), JKB_null(IVS5-1a), JKB_null(871C)
Duffy	Fya(FY1), Fyb(FY2), FYB_GATA, FYB[265T]_FYX
MNS	M(MNS1), N(MNS2), S(MNS3), s(MNS4), U(MNS5), Mia(MNS7)
Diego	Dia(DI1), Dib(DI2)
Dombrock	Doa(DO1), Dob(DO2), Hy(DO4), Joa(DO5)
Colton	Coa(CO1), Cob(CO2)
Cartwright	Yta(YT1), Ytb(YT2)
Lutheran	Lua(LU1), Lub(LU2)



# Red cell genotyping in Chulalongkorn Hospital

- 62 Thalassemia patients
- Both Phenotyping and Genotyping
- 40% (25/62) discrepancies: Inconclusive serology or Different results
- Limitations: High costs, Need donors with matched genotype

Phandee Watanabunyongcharoen, MD  
Chumnumporn Prukpa, MSc



# Summary

- **Adequate transfusion** can assure Normal development and Quality of life
- **Quality of blood products:** Infectious markers (NAT), Blood cold chain, Leukoreduction, Error-free blood transfusion, Hemovigilance system
- **Further improvements:** Pre-transfusion rbc phenotyping and antigen-matched PRC, Single-donor red cells, Leukodepletion, Genotyping, etc.



# Acknowledgments

คณะทำงาน: การให้เลือดและมาตรฐาน  
ของเลือดสำหรับผู้ป่วยธาลัสซีเมีย



Blood Group genotyping



National Blood Centre  
(Luminex)

# Acknowledgments

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ศ พญ พิมล เชี่ยวศิลป์ ประธาน

ศ พญ ภัทรพร อิศรางกูร ณ อยุธยา

รศ พญ ศศิธร เพชรจันทร์

ผศ พญ กวิวัฒน์ วีรกุล

นพ จัตรชัย สวัสดิไชย

ศ นพ พลภัทร โรจน์นครินทร์

**Blood Group genotyping**

พญ พรรณดี วัฒนบุญยงเจริญ

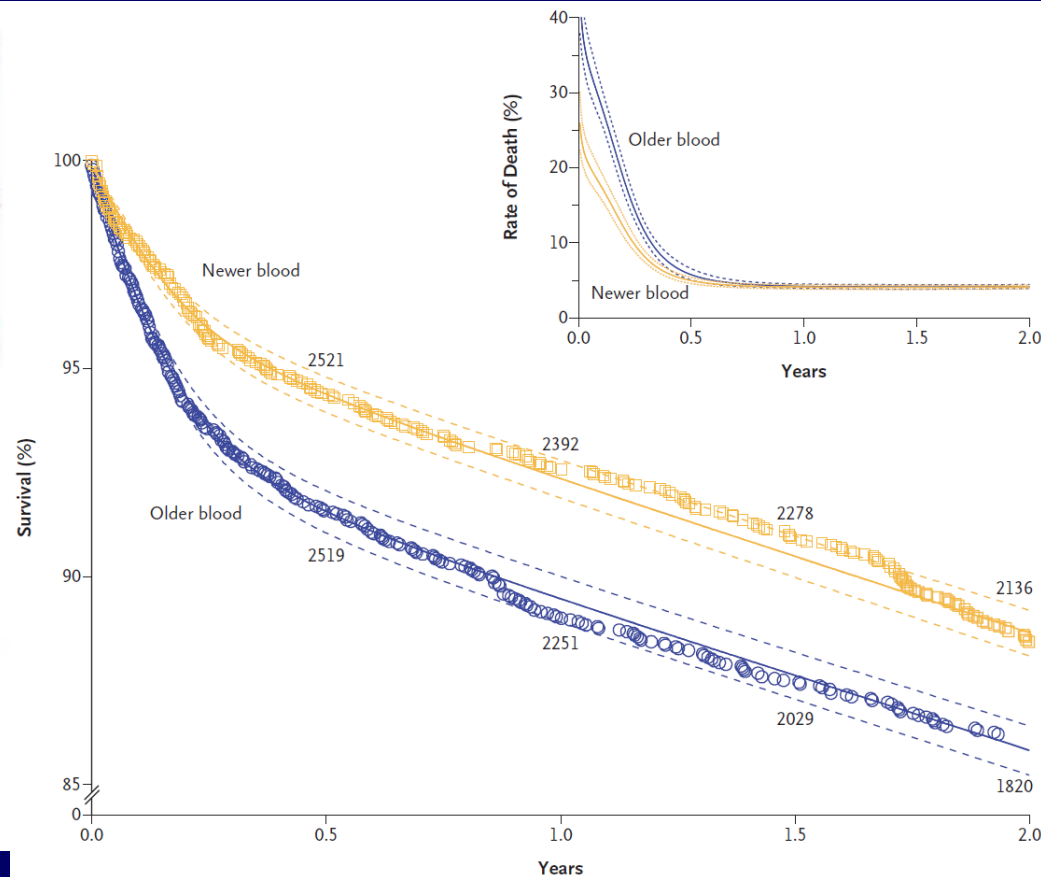
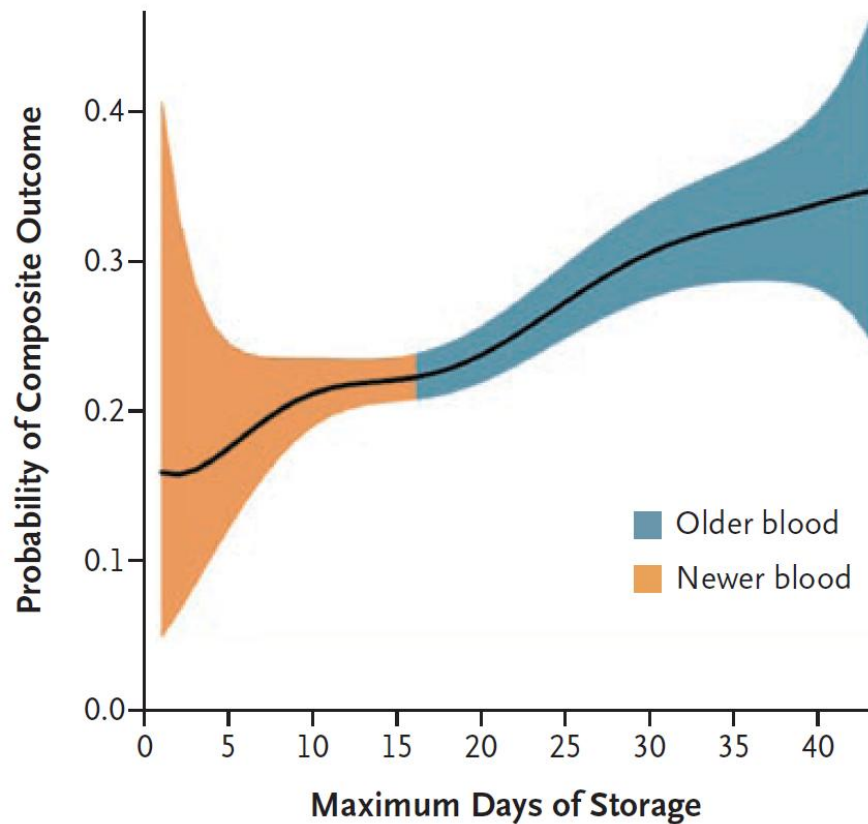
คุณ ชุมนุมพร พุกษา

Thank you  
Very much

# Preventable events

Types	Product	Process
TRALI	Yes	No
AHTR	No	Yes
TAS	Yes	Visual inspection
Anaphylaxis	No	No
TACO	No	Yes
FNHTR	Yes	No
TA-GVHD	No	Yes
PTP	No	No

# Old blood transfusion in cardiac surgery associated with poor outcomes



N = 3130  
Retrospective study

N Engl J Med 2008;358:1229-39.