Delayed hemolytic transfusion reaction in the French hemovigilance system

C. Rieux, G. Brittenham, D. Bachir, E. De Meyer, K. Boudjedir
for the French hemovigilance network

First Seminar on delayed hemolytic transfusion reaction in sickle cell disease patients
Monday, December 17th, 2018 - Créteil, France

French Hemovigilance System

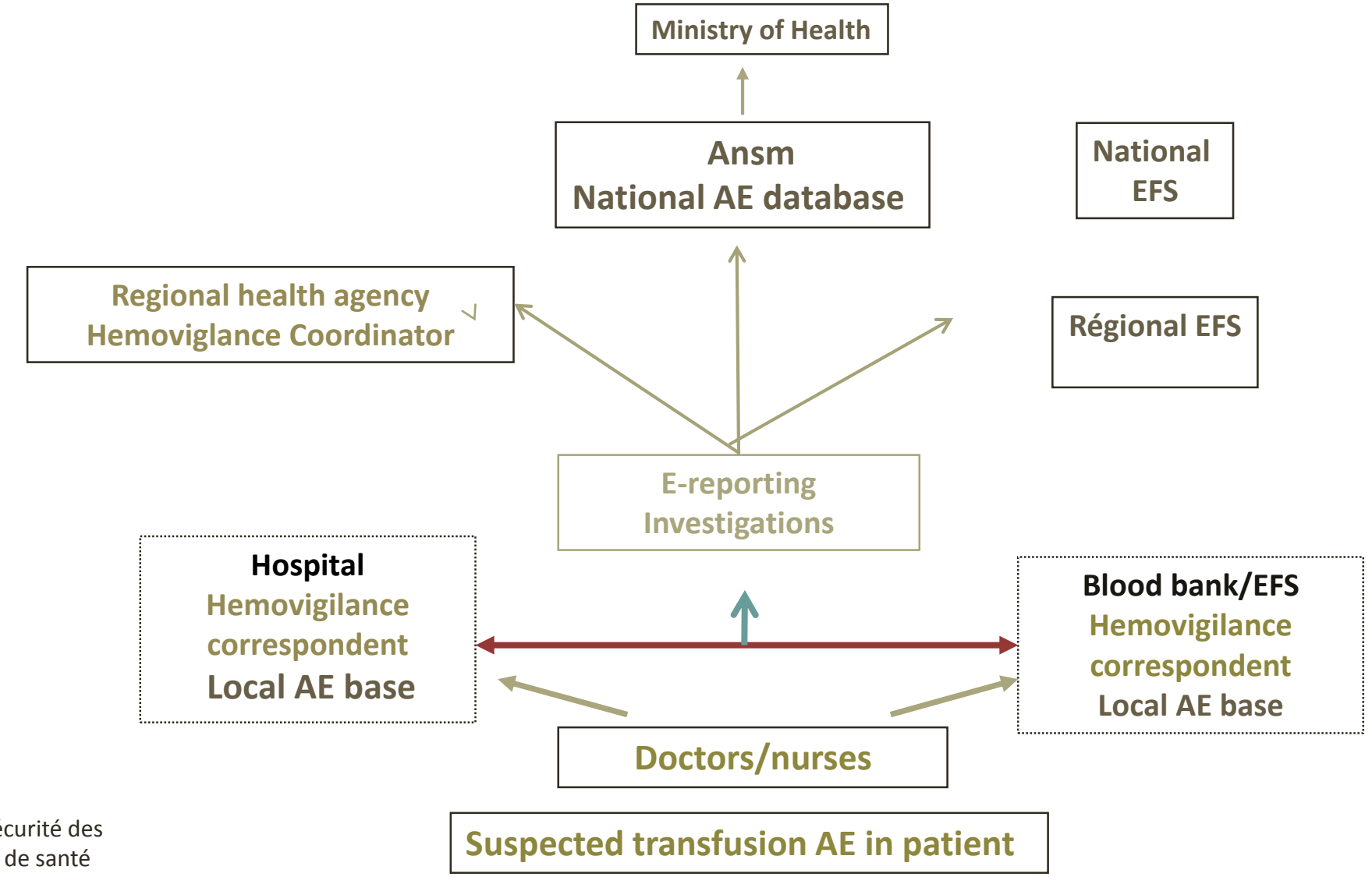
- Created in 1994

- Dedicated network for labile blood products
  - Red cells, platelets, granulocytes and plasma

➢ Tracability of all transfused labile blood products in France

➢ Mandatory reporting
  - Adverse events in recipients
  - Adverse events in donors
  - Errors in transfusion protocol
  - Post-donation events

Reporting process of AE in patients



Ansm Agence nationale de sécurité des médicaments et des produits de santé
EFS Etablissement français du sang
AE Adverse events

2017 main figures

	Number	Rate/ratio
Blood Labile Products	3 082 178	
Patients transfused	522 701	7,8/1000 inhabitant
Tracability	99.1 %	
Patients adverse events	7276	283,2/100 000 transfusions 166.6/10 000 patients
Non severe Death SCD patients	92.1% 6 84 (1%)	

ANSM Hemovigilance 2017 report

Major achievements of the French hemovigilance system

- Tracability : from 60% in 1996 to more than 99% since 2005

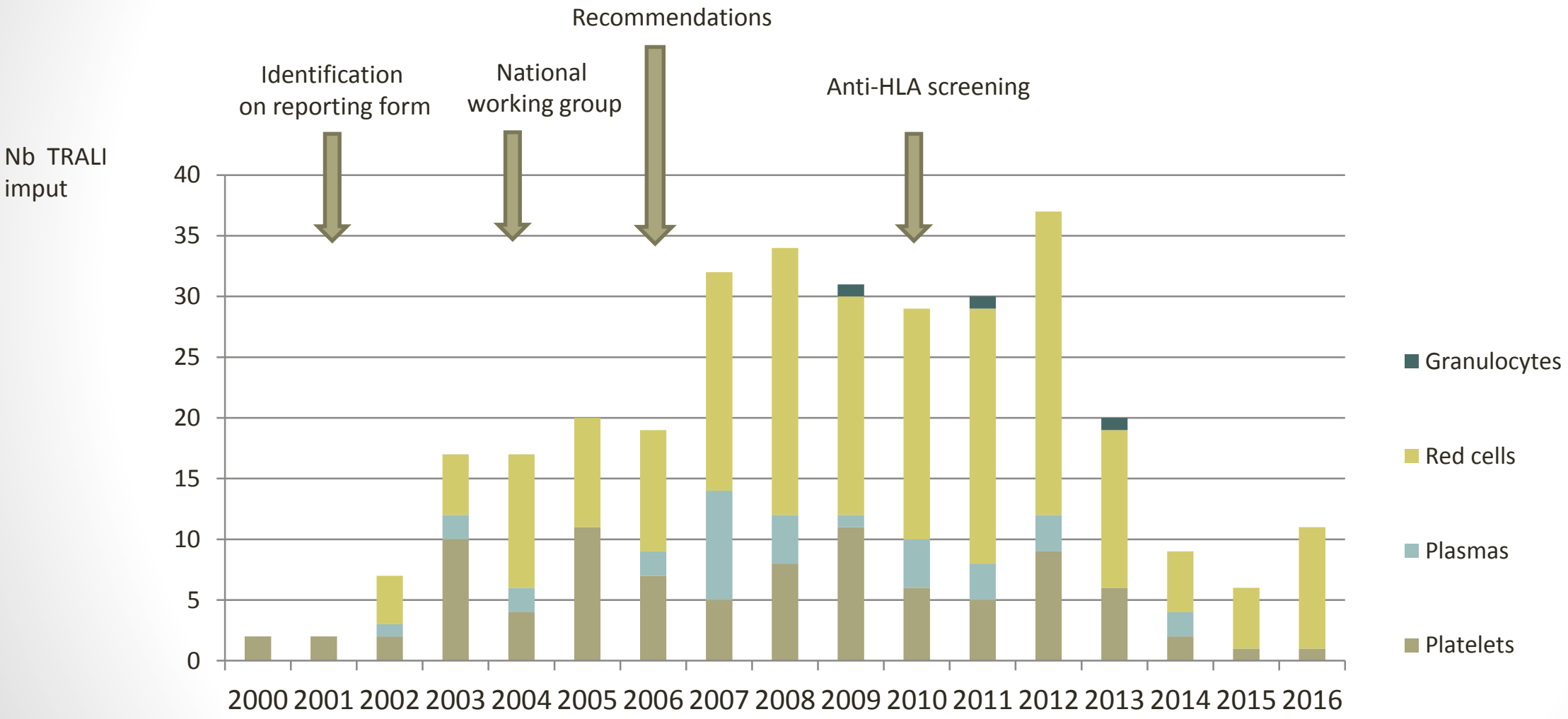
- Reduction of risks

	Incidence/ 100 000 LBP Number		Risk reduction
	2000	2015	**2000/2015**
ABO incompatibility Red cells and plasma	0,96 25	0,16 5	**6-fold**
Bacterial infection	0,78 20	0,16 5	**5-fold**

ANSM Hemovigilance yearly reports

- Recognition of unwell-known risks
  - TRALI
  - DHTR

TRALI



ANSM Hemovigilance yearly reports

DHTR : an under-reported event

- Under-recognized
  - Acute hemolysis in a chronic hemolytic disease
  - Mimics severe vaso-occlusive crisis
  - Link with transfusion not made because of delay
  - No alloimmunization found in some cases

- Under-reported
  - France : 2/3 of the cases identified after look-back review in a single center in France (*Habibi, Am J Hematol. 2016)*
  - UK : 47,8% were not diagnosed at the time of event *(Vidler, BJH, 2015)*

- Misclassification in the hemovigilance reporting

Hemolytic transfusion reactions

Intravascular hemolysis

Fever, pain, dark urine
Unconjugated hyperbilirubinemia
Increased LDH
Decreased hemoglobin level
Abnormal decrease of HbA

With or without alloimmunization

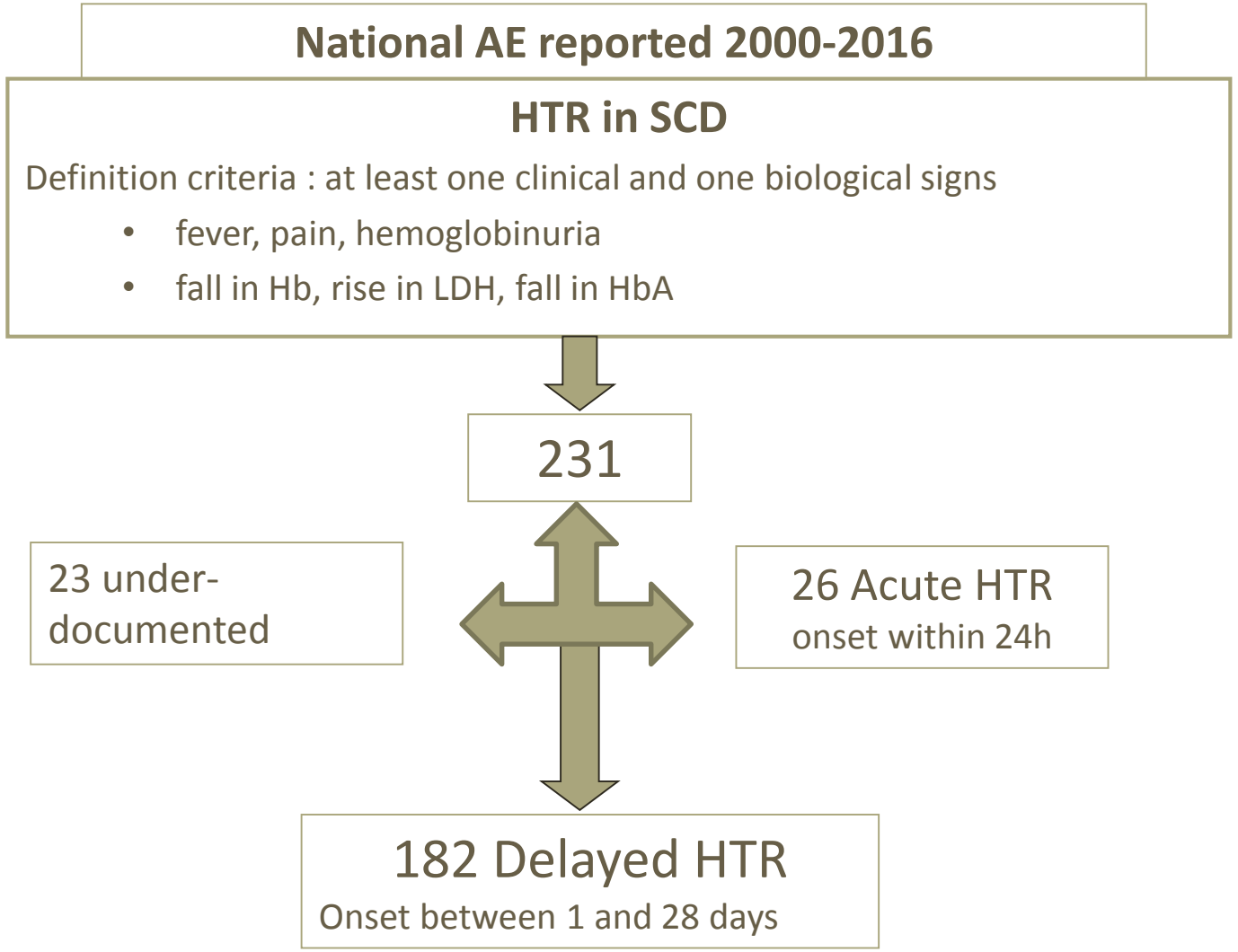
Acute HTR
Within 24h

Delayed HTR
> 24h to?

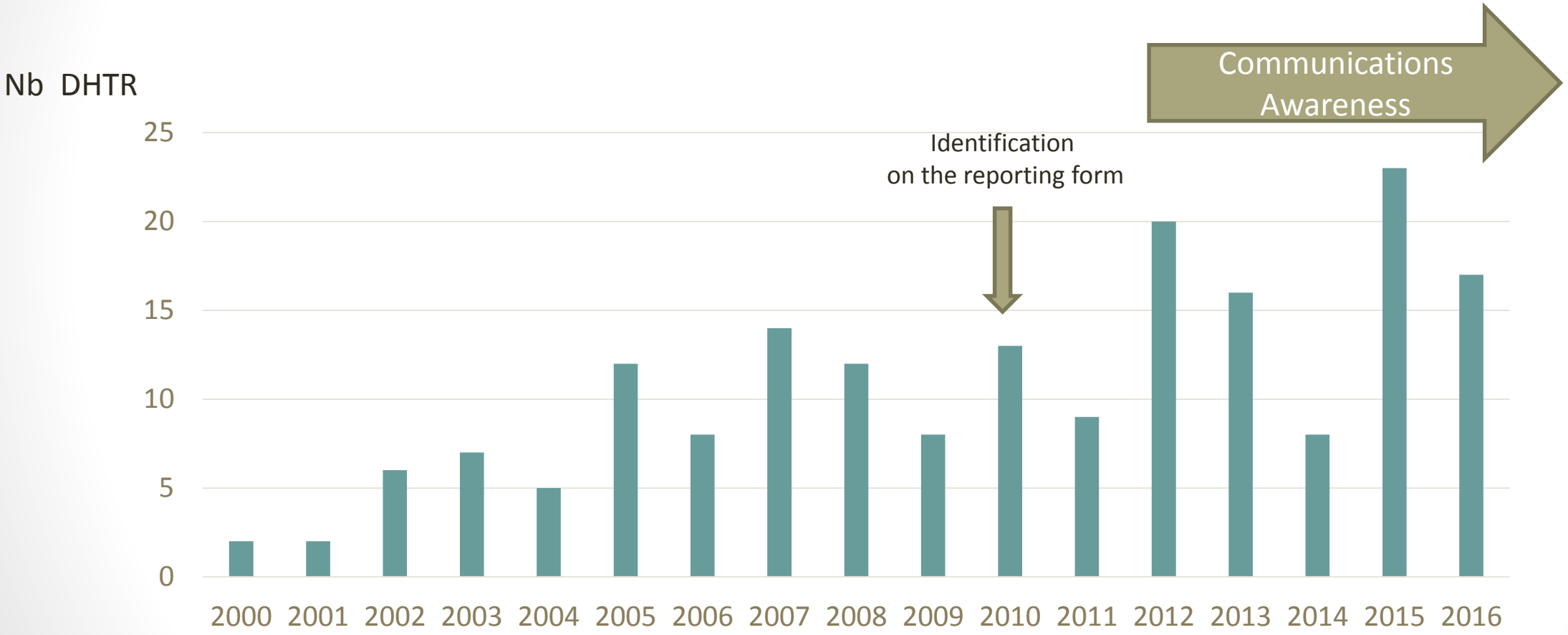
Hyper hemolysis syndrome

Destruction of autologous AND transfused RBCs
Post-transfusion Hb level lower than pre-transfusion level
Life-threatening complication
Compromised future transfusions for the patient

DHTR in the French hemovigilance database



DHTR in the French hemovigilance database



DHTR characteristics

N=182	
Sex ratio F/M	2.1
Median Age	26 years (1-76) 84.6 % < 40 years
History	
Allo-immunisation Previous DHTR	89 (48.9%) 37 (20.3%)
Transfusion indication (N=167)	
Acute setting Pregnancy	129 (77.3%) 35 (19.2%)
Median delay	8 days (2-29) 83% between 4 and 15 days
Mortality	10 deaths (5.5%)

Additional improvements (1)

- DHTR diagnosis and reporting
  - Elaborate guidelines for diagnosis and reporting
  - Develop specific DHTR form
    - Past history of transfusion and immunohematology
    - hemoglobin nadir, Reticulocytes count, LDH
    - Follow-up of hemoglobin A percentage (Nomogram, *Mekontso-Dessap, Am J Hematol. 2016)*
    - Immuno-hematological results

- Process of reporting
  - Exhaustiveness
  - Transfusion and management of patient in different settings
  - Eliminate duplicate reporting

Additional improvements (2)

- Data quality control
  - National reviewing expert group
  - Complementary documents (hospitalization charts and immuno-hematological results)
- National register of HTR
  - DHTR and AHTR
  - SCD patients and others
- National blood transfused patients register needed
- Epidemiological studies

Conclusion

- French hemovigilance system has one of the largest cohort of DHTR in SCD patients
- Importance of coordination between clinicians, transfusion specialists and hemovigilants
- Need for common approach of reporting in Europe, and others parts of the world including Africa

Thanks you

- Clinicians
  - SCD national reference center, CHU Henri Mondor, Creteil
- Transfusion specialists
  - EFS Henri Mondor
- French hemovigilance correspondants