Diagnosis of DHTR

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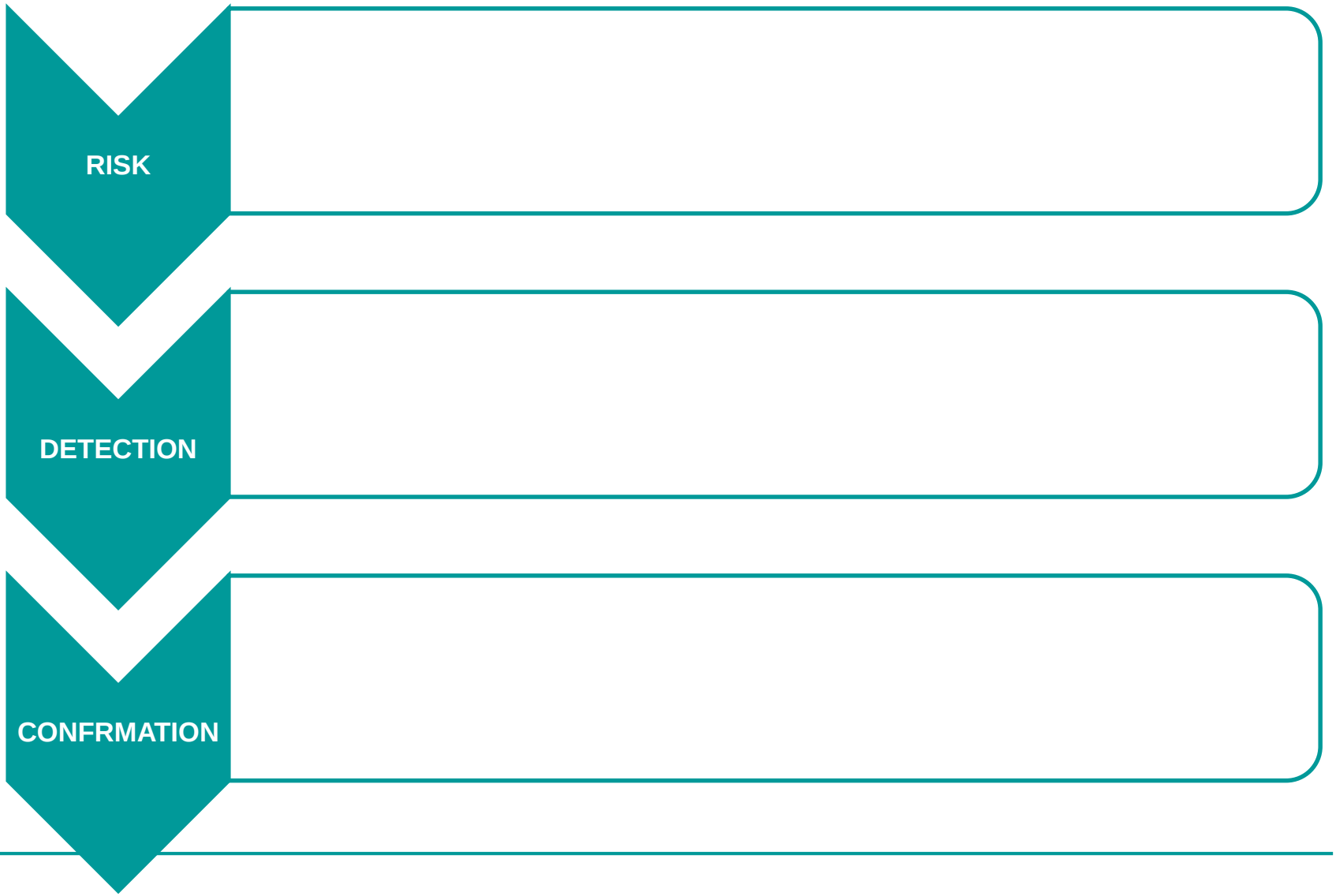
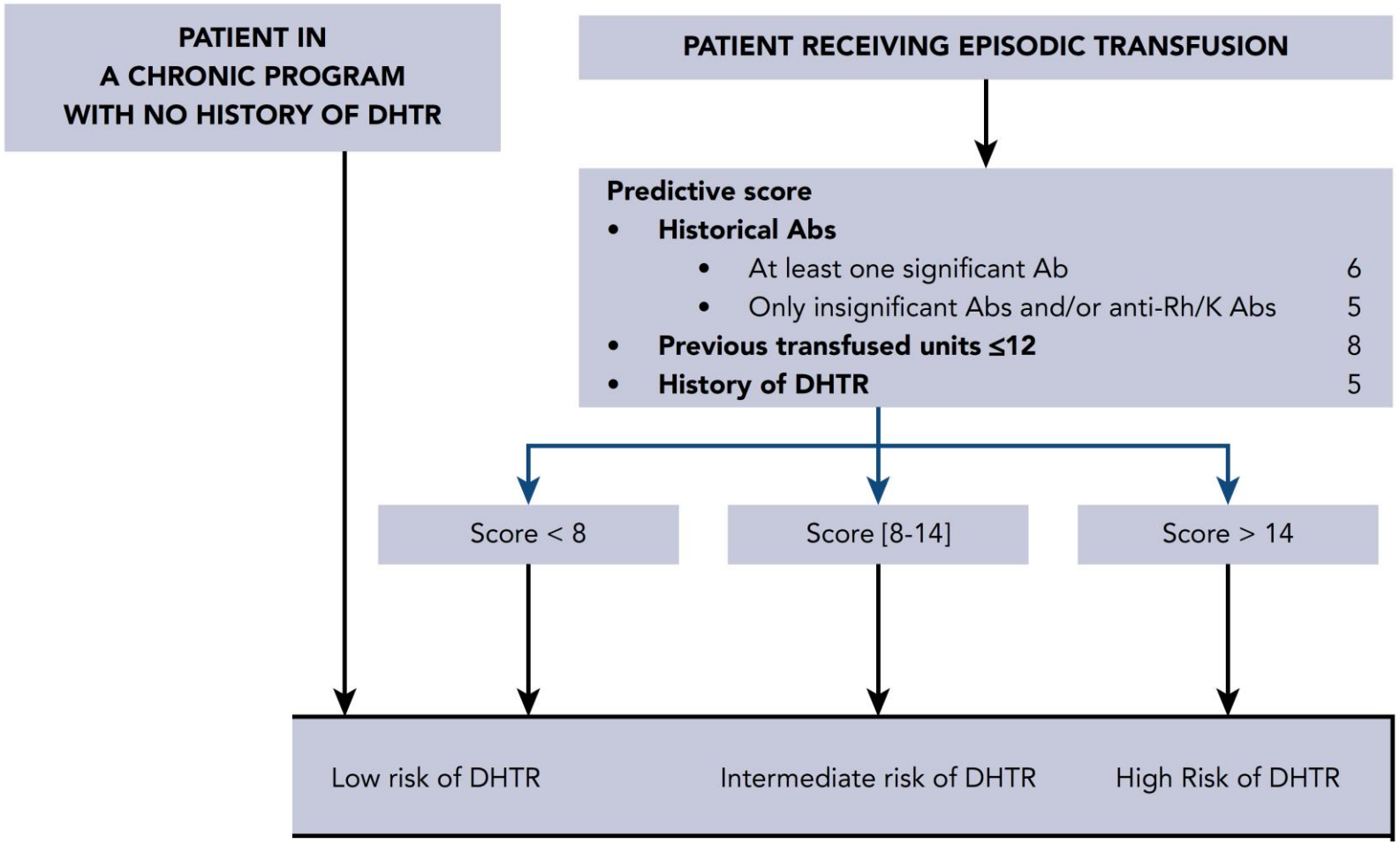
Stepwise approach



Risk factors

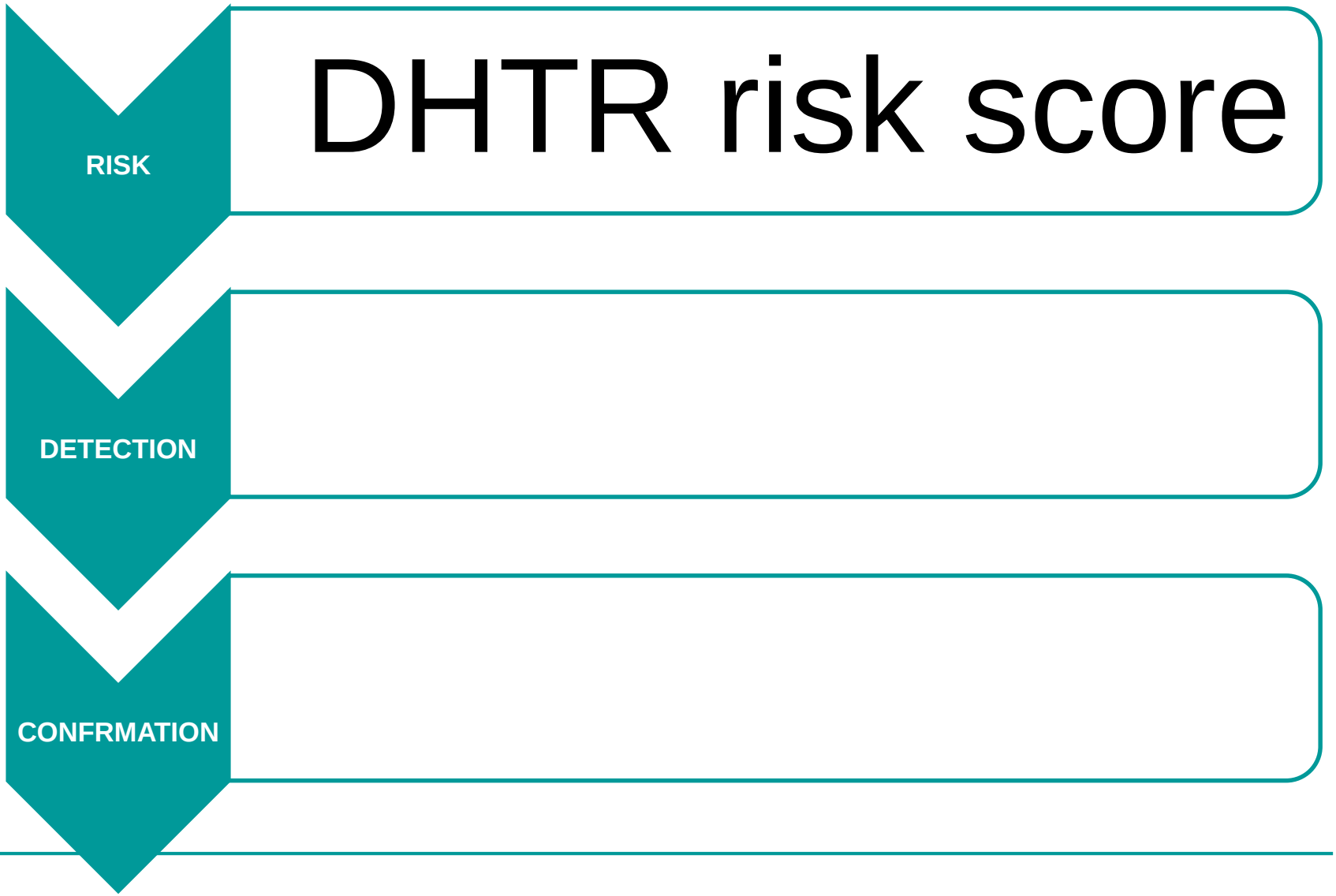
- History of immunization
- History of DHTR
- Transfusion for an acute complication
- Lower cumulative number of transfused units (<12 units)

DHTR risk score



Pirenne, Blood 2018

Stepwise diagnosis



The sickle cell hemolytic transfusion reaction syndrome

L.D. Petz, L. Calhoun, I.A. Shulman, C. Johnson, and R.M. Herron

TABLE 1. Components of the sickle cell HTR syndrome

1. Manifestations of an acute or delayed HTR.
2. Symptoms suggestive of a sickle cell pain crisis that develop or are intensified during the HTR.
3. Marked reticulocytopenia (a significant decrease from the patient's usual absolute reticulocyte level).
4. Development of a more severe anemia after transfusion than was present before. A rapid drop in Hb and Hct can occur when hemolysis of donor RBCs is accompanied by suppressed erythropoiesis, as sickle cell RBCs have an intrinsically short survival. In some patients, it is possible that hyperhemolysis of autologous RBCs (bystander immune hemolysis) may play a role in the decrease in Hb and Hct, although more definitive documentation of this phenomenon is necessary.
5. Subsequent transfusions may further exacerbate the anemia and it may become life-threatening or even fatal.[7,8]
6. Patients often have multiple RBC alloantibodies and may also have autoantibodies,[9-12] which makes it difficult or impossible to find compatible units of RBCs. However, in other patients, no alloantibodies are demonstrable,[13] or patients may have alloantibodies for which antigen-negative RBCs are readily obtainable.[14,15]
7. Serologic studies may not provide an explanation for the HTR.[8,13-15] Even RBCs that are phenotypically matched with multiple patient antigens may be hemolyzed.[14]
8. Recovery manifested by reticulocytosis and gradual improvement in Hb may occur only after the withholding of further transfusion. The administration of corticosteroids appears to be an important therapeutic measure in some patients.[10,11,13,15]
9. After a recovery period, similar symptoms may recur following subsequent transfusions, although other patients tolerate further transfusions without incident.[13]

Petz, Transfusion 1997

4 prominent features

- Particular timeframe
- Acute SCD symptoms
- Worsening anemia
- No alternative cause is more likely

Petz, Transfusion 1997

Timeframe

- After the index transfusion
- Variable from one study to another
  - Reported from Day-1 to Day >25

    Narbey, AJH 2017
  - In general Day-3 to Day-21

    Habibi, AJH 2016

    Mekontso Dessap, AJH 2016

Acute SCD symptoms

- Development or intensification of
  - VOC,
  - ACS, or
  - MOF

Worsening anemia

- ↓ Hb level
  - below the pretransfusion level
  - decrease relative to the value recorded after the index transfusion >25-30% ?

Vidler, Bjh 2015

Narbey, AJH 2017

- ↑ intravascular hemolysis
  - hemoglobinuria
  - jaundice
  - ↑ lactic dehydrogenase
    - twice above the baseline value?

Vidler, Bjh 2015

  - ↑ bilirubin
    - above the baseline value

De Montalembert, Haematologica 2011

- ↓ reticulocytes

No other obvious cause

- Cases are usually excluded if an alternative cause for symptoms or worsening anemia seems more likely, e.g.,
  - Perioperative blood loss,
  - Transient red cell aplasia due to Parvovirus B19

Vidler, Bjh 2015
Mekontso Dessap, AJH 2016

Stepwise diagnosis

RISK

DHTR risk score

DETECTION

Prominent features

CONFRMATION

Confirmation by biological tests

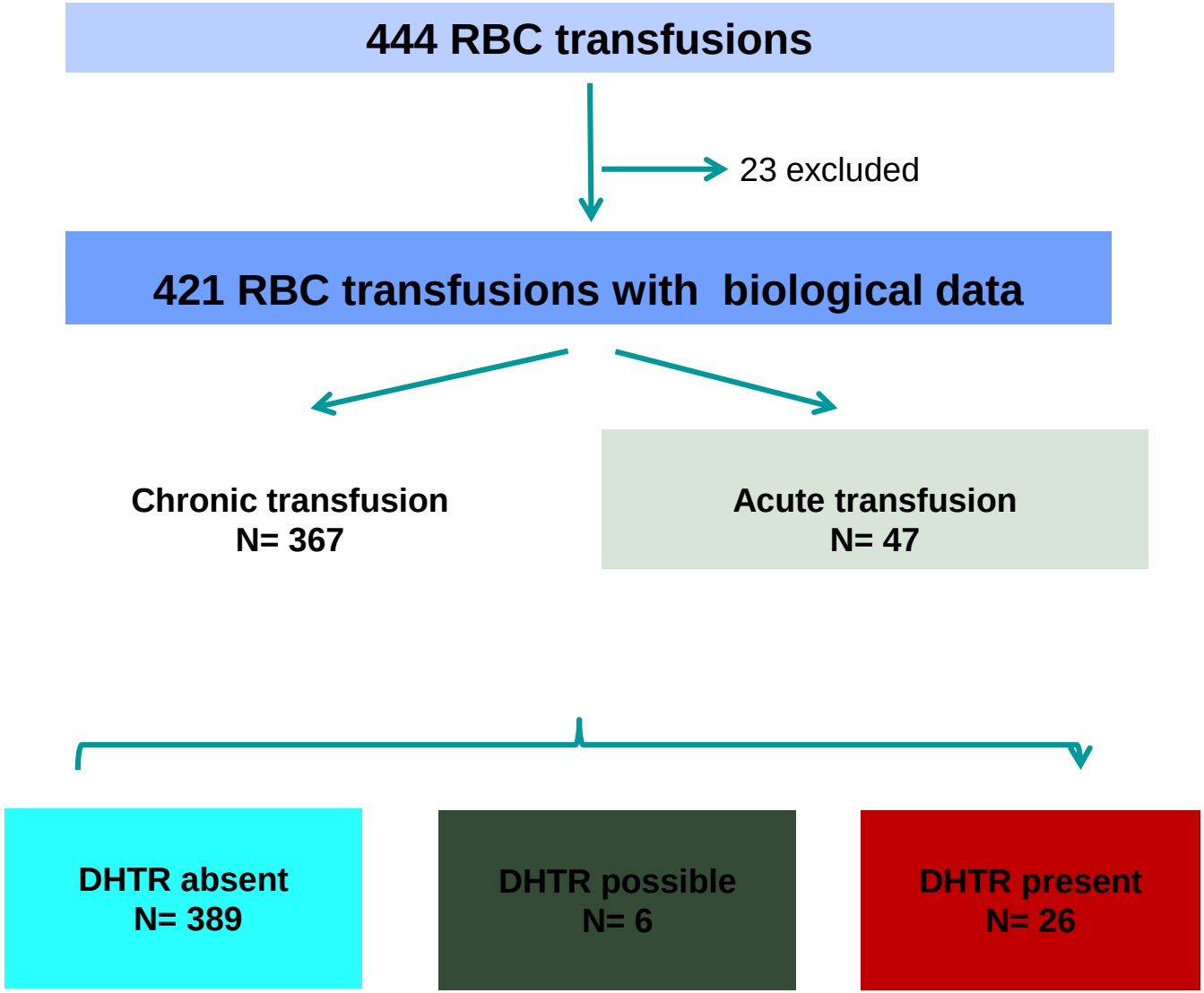
- New RBC immunization

RESEARCH ARTICLE

AJH

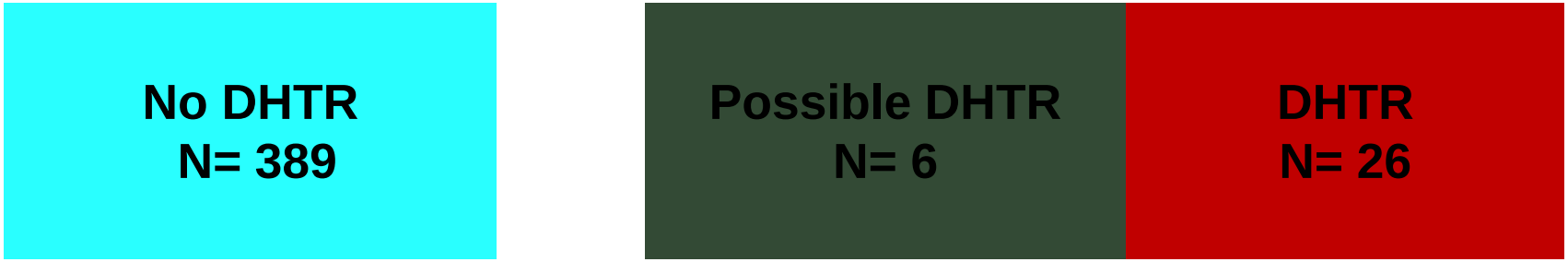
A diagnostic nomogram for delayed hemolytic transfusion reaction in sickle cell disease

Armand Mekontso Dessap,[1,2] France Pirenne,[3,4] Keyvan Razazi,[1,2] Stéphane Moutereau,[5] Shariq Abid,[1] Christian Brun-Buisson,[1,2] Bernard Maitre,[1,6] Marc Michel,[7] Frederic Galacteros,[4,8] Pablo Bartolucci,[4,8] and Anoosha Habibi[4,8]*



Mekontso Dessap, AJH 2016

New immunization



Positive screening test after the index transfusion

45 (12%) 23 (72%)

New antibody

0/45 12/23

Mekontso Dessap, AJH 2016

Confirmation by biological tests

- New RBC immunization
  - *The results of post-transfusion immunohematology analyses **were NOT** taken into account to confirm the diagnosis of DHTR, because no antibodies are detectable in the course of DHTR in many cases*.

    Narbey, AJH 2017

- HbA fall

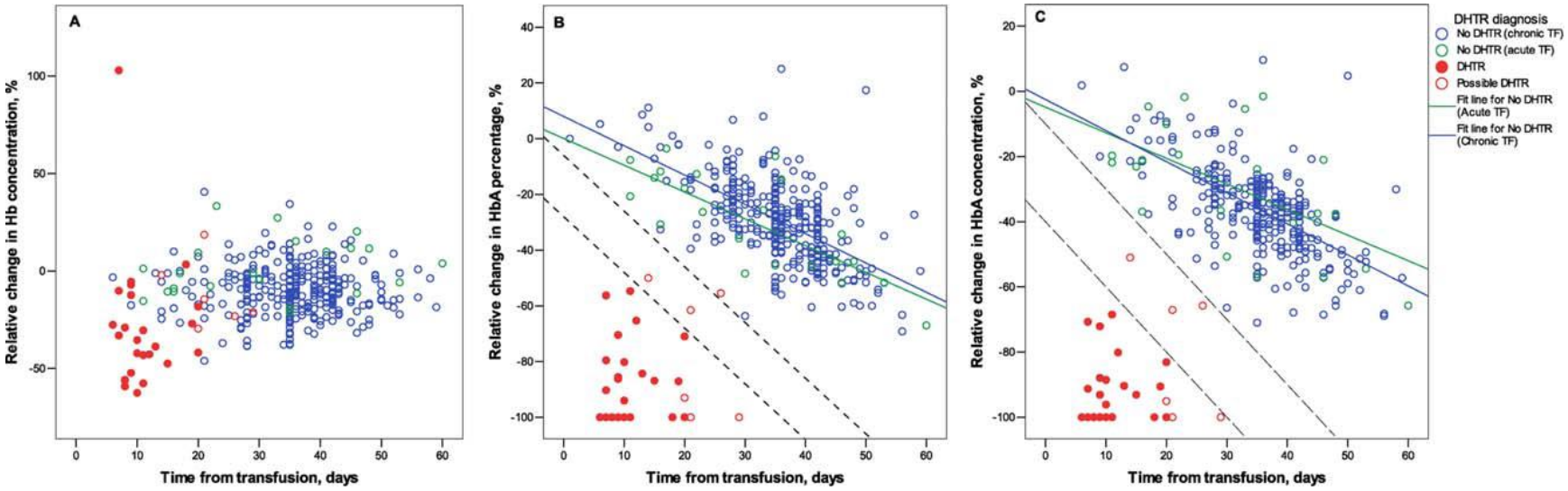
Fall in Hb and HbA

TABLE I. Biological Data According to Delayed Hemolytic Transfusion Reaction Diagnosis

	Delayed hemolytic transfusion reaction		
	Absent ($n = 389$)	Present or possible ($n = 32$)	p value
Hb concentration (g dL^{-1})	8.6 [7.8–9.7]	6.4 [5.2–7.5]	<0.001
Lactic dehydrogenase (IU L^{-1})	397 [298–531]	873 [597–1415]	<0.001
Total bilirubin (mmol L^{-1})	36.0 [22.0–56.0]	49.5 [33.3–77.0]	0.046
Delta Hb concentration (%)	−9.3 [−17.3 to −1.1]	−29.5 [−43.1 to −12.3]	<0.001
Delta HbA percentage (%)	−30.1 [−39.5 to −19.7]	−91.7 [−100.0 to −73.1]	<0.001
Delta HbA concentration (%)	−36.0 [−44.6 to −28.4]	−95.1 [−100.0 to −83.1]	<0.001

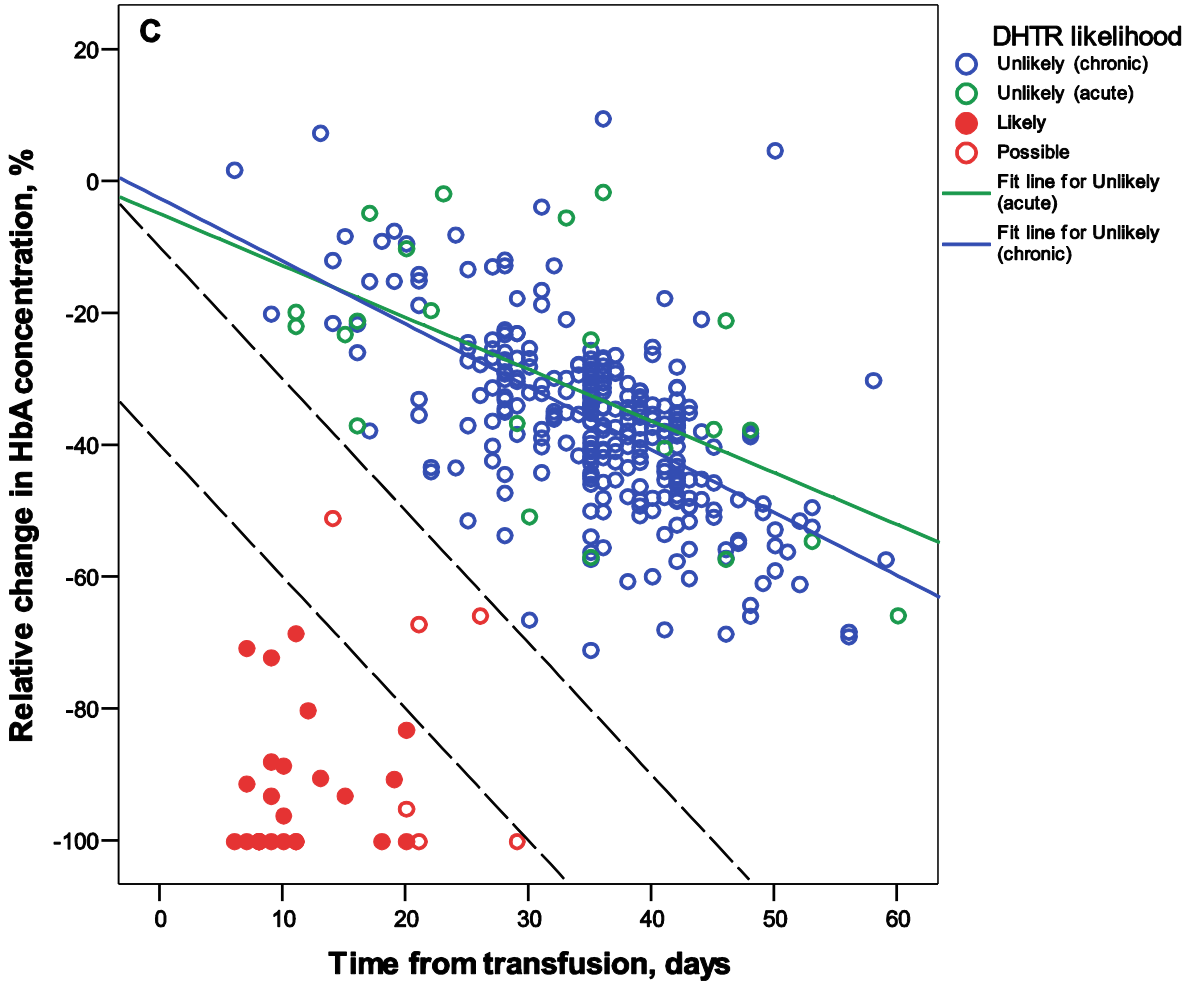
Mekontso Dessap, AJH 2016

Relative change in Hb and HbA for DHTR diagnosis



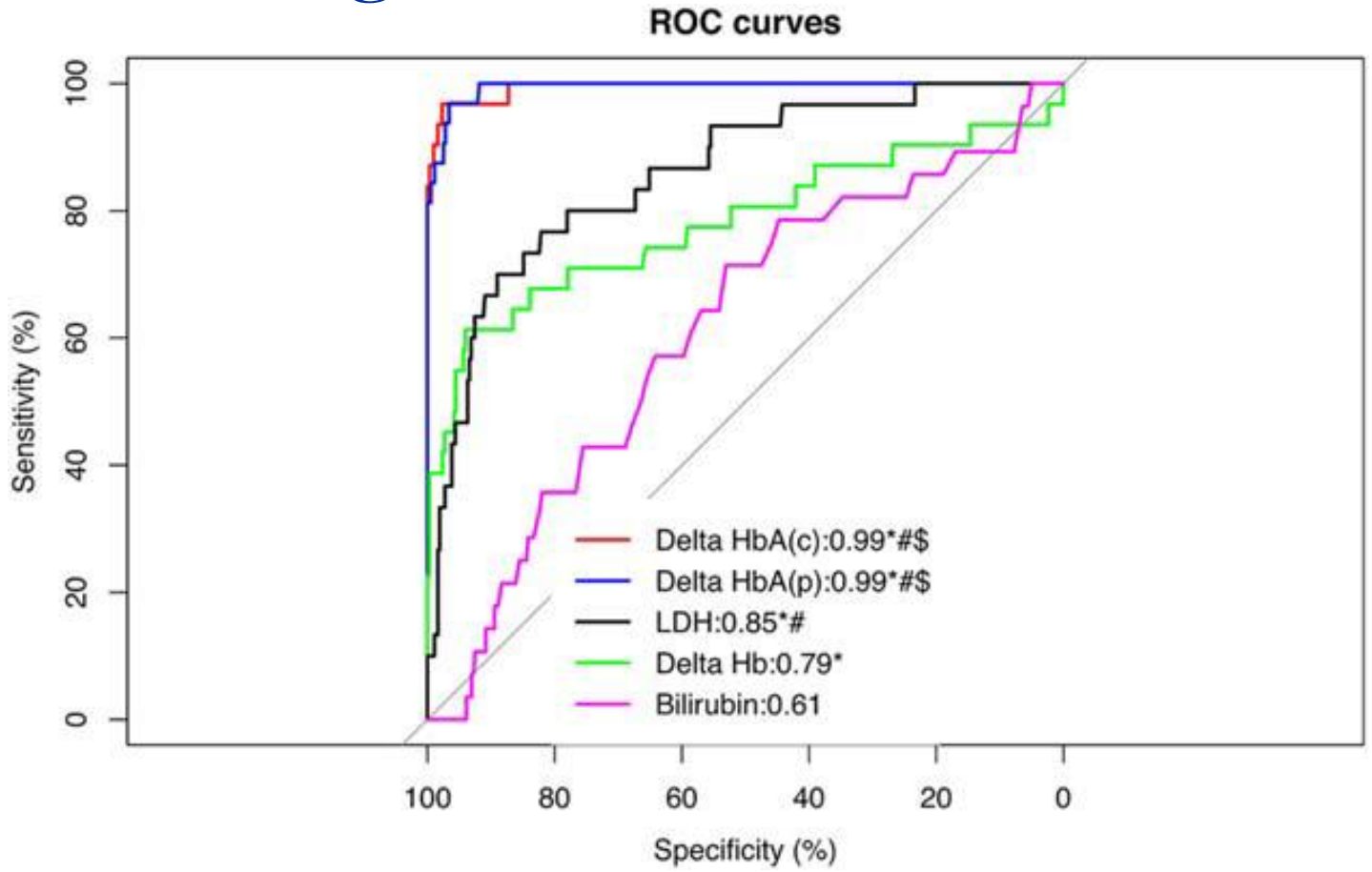
Mekontso Dessap, AJH 2016

DHTR nomogram



Mekontso Dessap, Am J Hematol 2016

Relative change in Hb and HbA for DHTR diagnosis



Mekontso Dessap, AJH 2016

www.reamondor.aphp.fr/nomogram.php

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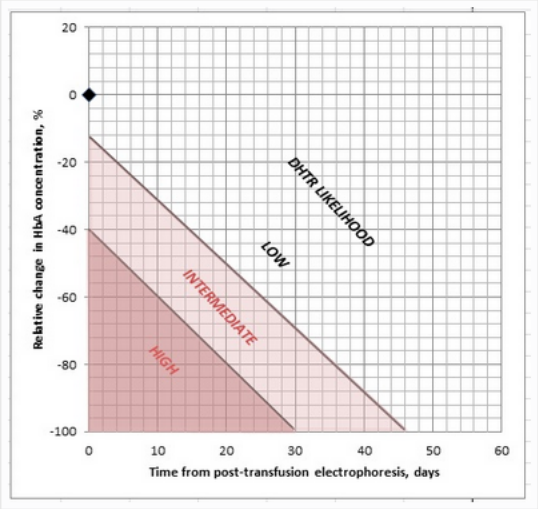
Accueil › Nomogram

Nomogram

Nomogram for the diagnosis of Delayed Hemolytic Transfusion Reaction as proposed by Mekontso Dessap et al, XXXXX :



Legend: This nomogram is proposed to estimate the likelihood of Delayed Hemolytic Transfusion Reaction (DHTR) in Sickle Cell Disease patients. To use the nomogram, the relative change in patient's hemoglobin A (HbA) concentration and the time interval since post-transfusion electrophoresis are plotted. If the resulting point is above and to the right of the upper limit line, DHTR likelihood is low. If the point is below and to the left of the lower limit line, DHTR likelihood is high. If the point is between the two lines, DHTR likelihood is intermediate. Patients withouth a post-transfusion hemoglobin electrophoresis cannot be evaluated with the use of the nomogram. The relative change in HbA concentration is calculated as 100*(HbA concentration at DHTR suspicion – post-transfusion HbA concentration) / post-transfusion HbA concentration ; with HbA concentration expressed in g/dL (percent HbA * total Hb in g/dL).

Download nomogram file

Service de Réanimation Médicale

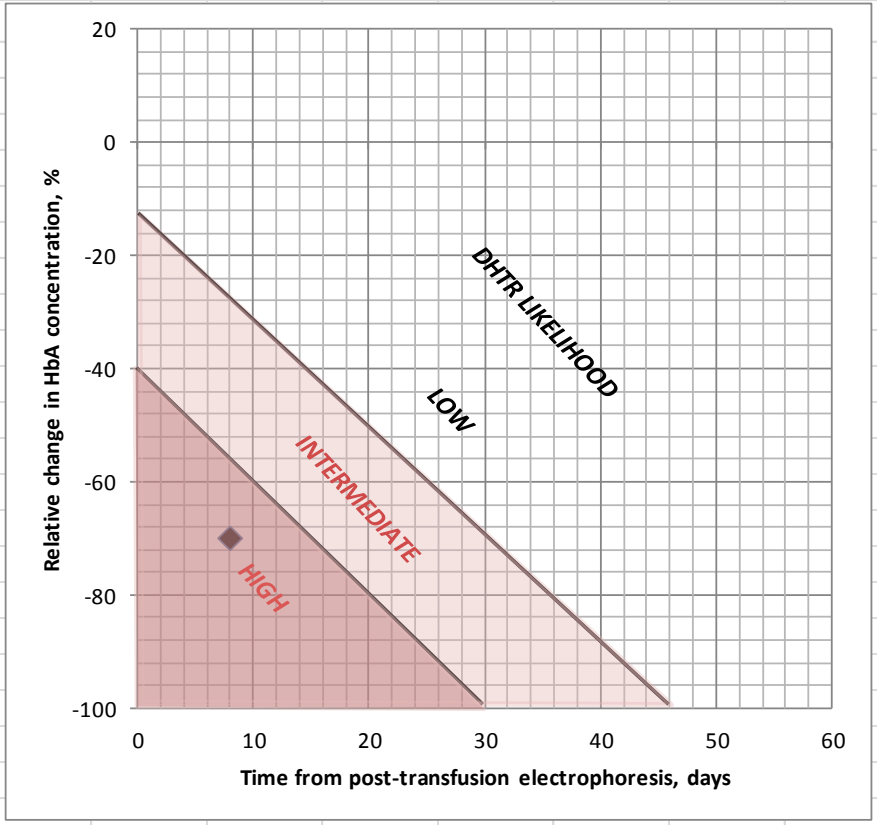
CHU - Albert Chennevier - Henri Mondor

Nomogram for the diagnosis of Delayed Hemolytic Transfusion Reaction as proposed by Mekontso Dessap et al.

To use the nomogramm, fill the yellow boxes with apropriate values.

	1st assessment (AFTER the index transfusion)	2nd assessment (at DHTR suspicion)
Date	12/06/2016	20/06/2016
Total Hb, g/dL	8,0	6,0
HbA percentage, %	25,0	10,0

Legend:
This nomogram is proposed to estimate the likelihood of Delayed Hemolytic Transfusion Reaction (DHTR) in Sickle Cell Disease patients. To use the nomogram, the relative change in patient's hemoglobin A (HbA) concentration and the time interval since post-transfusion electrophoresis are plotted. If the resulting point is above and to the right of the upper limit line, DHTR likelihood is low. If the point is below and to the left of the lower limit line, DHTR likelihood is high. If the point is between the two lines, DHTR likelihood is intermediate. Patients withouth a post-transfusion hemoglobin electrophoresis cannot be evaluated with the use of the nomogram. The relative change in HbA concentration is calculated as 100*(HbA concentration at DHTR suspicion - post-transfusion HbA concentration) / post-transfusion HbA concentration ; with HbA concentration expressed in g/dL (percent HbA * total Hb in g/dL).



www.reamondor.aphp.fr/ nomogram.php

Stepwise diagnosis

RISK — DHTR risk score

DETECTION — Prominent features

CONFRMATION — ±New RBC immunization
HbA fall nomogram

Conclusions

- DHTR diagnosis is not consensual
- A stepwise approach seems reasonable
  1. A predictive score for DHTR risk assessment has been proposed
  2. The proeminent features for DHTR detection are simple to assess
  3. A nomogram for HbA fall has been proposed for DHTR confirmation
     - Importance of post tranfusion Hb electrophoresis