Ferriprox (deferiprone) today

(its relevance to DEEP)

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Agenda

- Safety in pediatric patients
- Main factors that could affect efficacy
- Other points to consider

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FERRIPROX (DEFERIPRONE)
SUMMARY OF PRODUCT CHARACTERISTICS

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients.

- History of recurrent episodes of neutropenia.

- History of agranulocytosis.

- Pregnancy.

- Breastfeeding.

- Due to the unknown mechanism of deferiprone-induced neutropenia, patients must not take medicinal products known to be associated with neutropenia or those that can cause agranulocytosis

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FERRIPROX (DEFERIPRONE)
SUMMARY OF PRODUCT CHARACTERISTICS

4.2 Posology and method of administration

- *Paediatric population*

  There are limited data available on the use of deferiprone in children between 6 and 10 years of age, and no data on deferiprone use in children under 6 years of age.

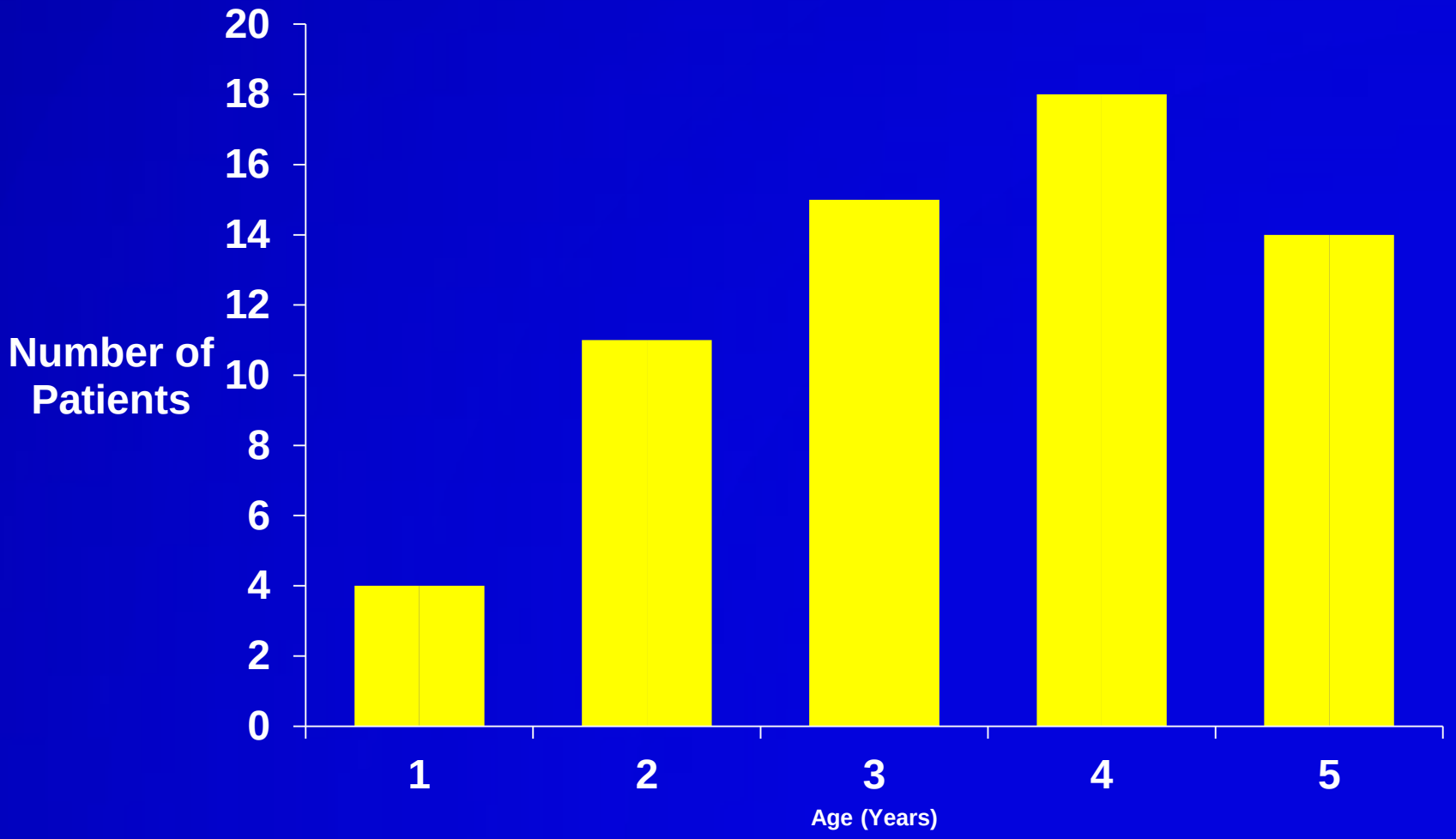
Pediatric (<16 years) vs. Adult Patients Pooled Clinical Trials Safety Data

	Ferriprox (All Doses)	
	Pediatric	Adult
N Exposed	223 (32%)	469 (68%)
Total Exposure (patient-years)	496	1046

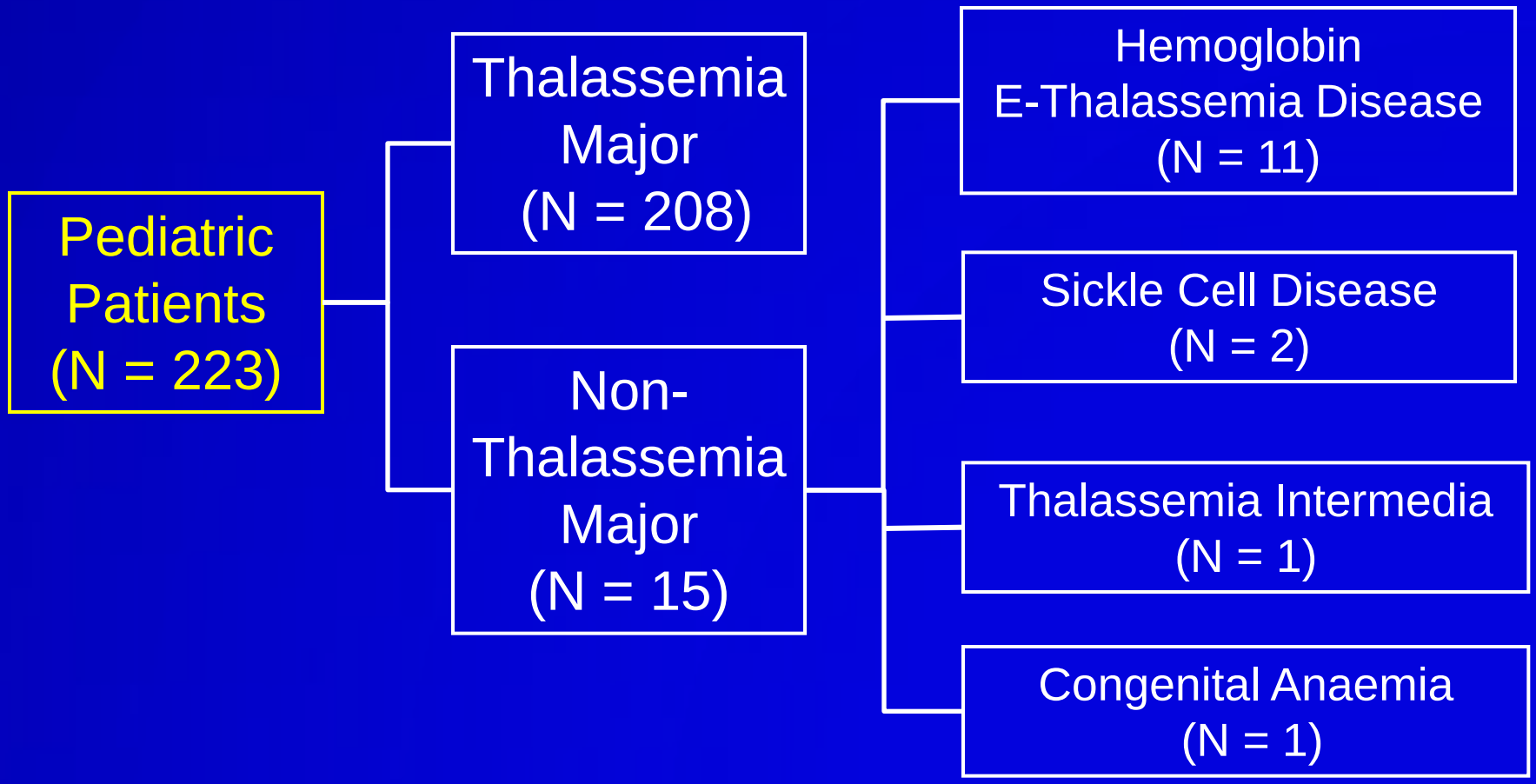
Pediatric (<16 years) vs. Adult Patients Pooled Clinical Trials Safety Data

	Ferriprox (All Doses)			
	Pediatric N=223			Adult N=469
	1-5 years	6-11 years	12-15 years	≥16 years
N Exposed	62	81	80	469
Total Exposure (yrs)	106	156	234.6	1046

Patients aged 1-5 in Pooled Safety Data



Primary Diagnosis
Pediatric Patients (<16 Years Old)

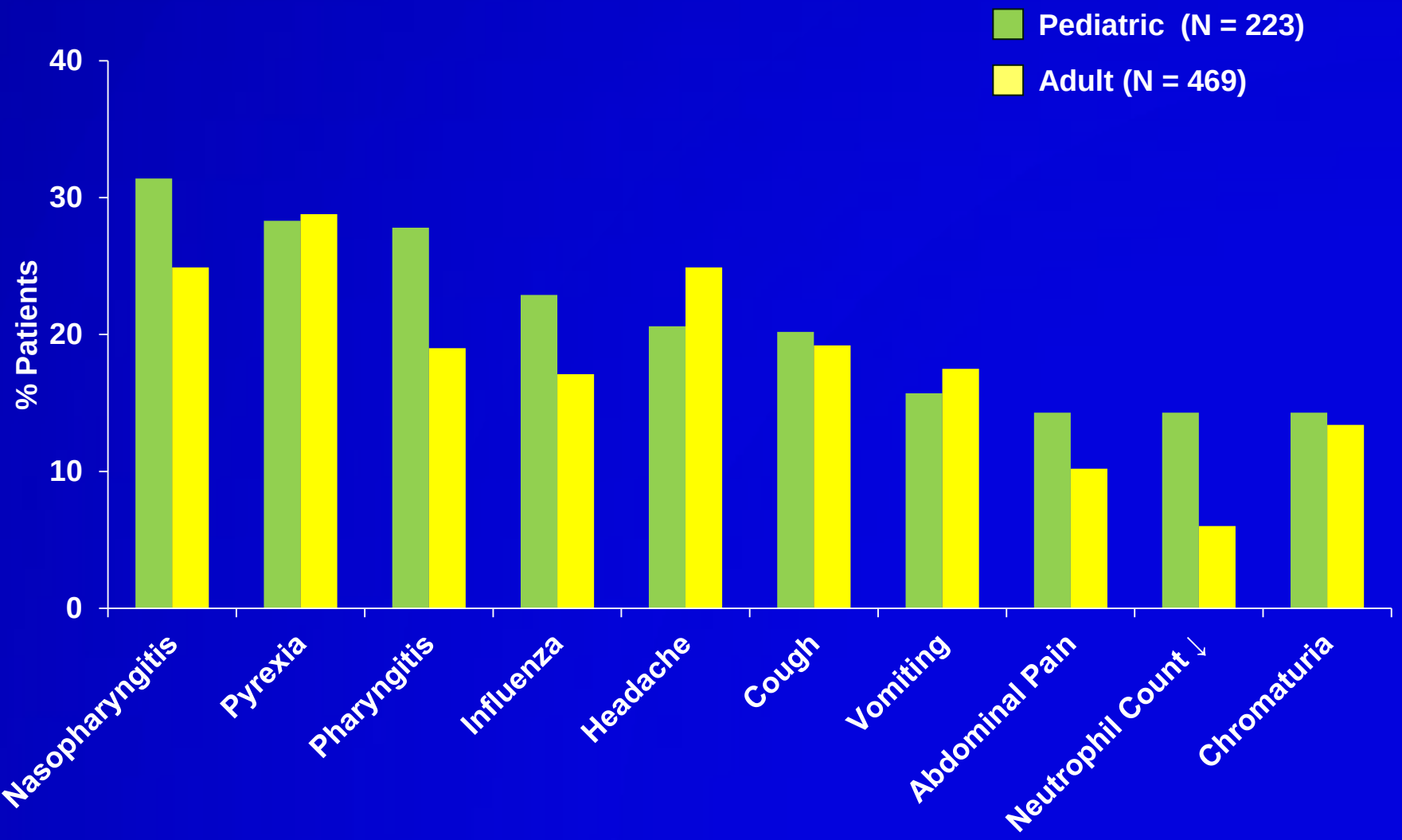


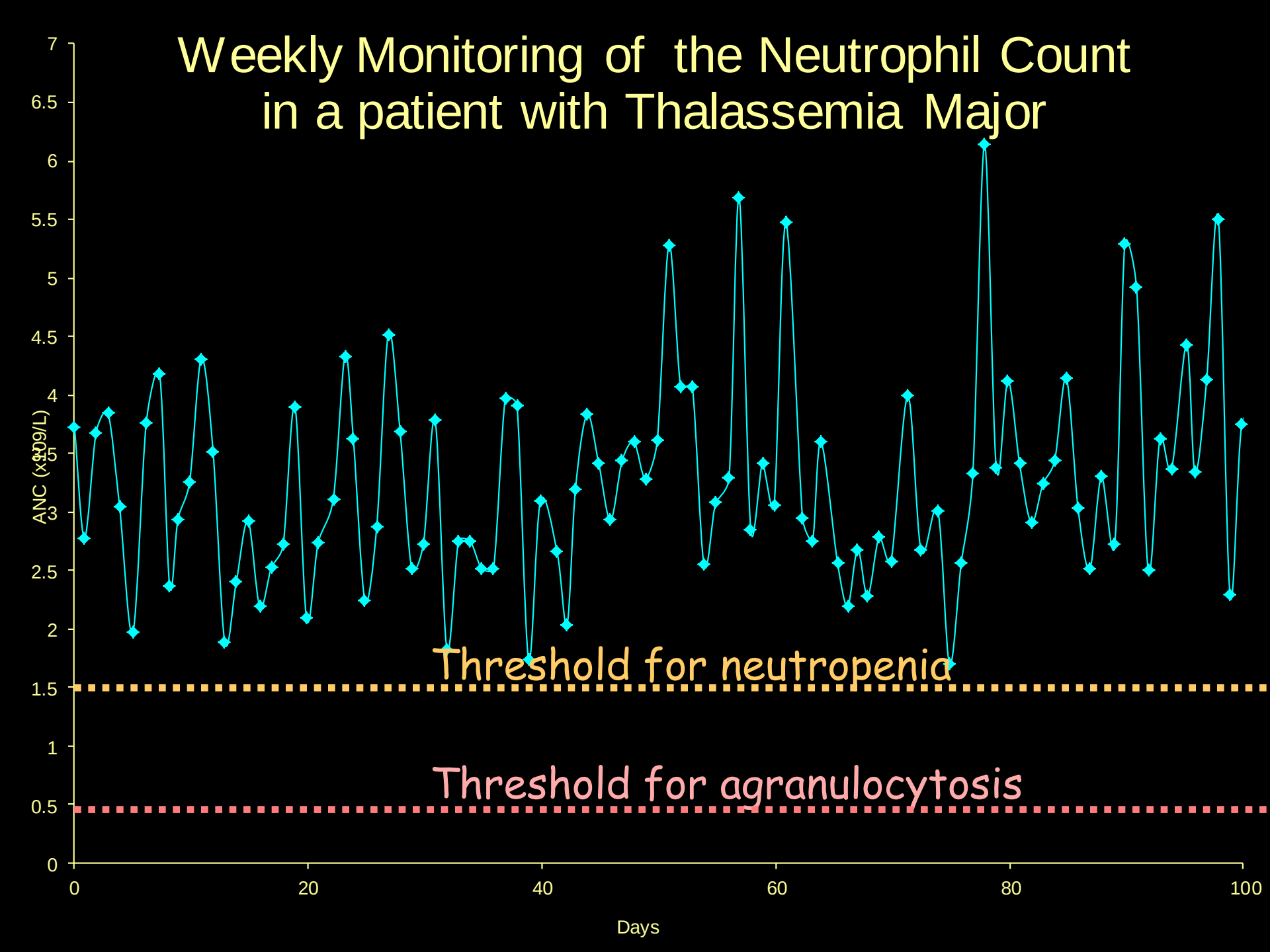
Pediatric Patients by Dose
Pooled Safety Data

	Ferriprox (all doses) mg/kg/d n=223 (%)			
	50 mg/kg/d	75 mg/kg/d	100 mg/kg/d	Combination Therapy
N patients	3 (1.3)	140 (62.8)	67 (30.0)	13 (5.8)

Top 10 Adverse Events, Irrespective of Causality in Pediatric vs. Adult patients

Pooled Safety Data




Weekly Monitoring of the Neutrophil Count
in a patient with Thalassemia Major
ANC (x10^9/L)
Days
Threshold for neutropenia
Threshold for agranulocytosis
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5
5.5
6
6.5
7
0
20
40
60
80
100

Prevalence of Neutropenia in the U.S. Population: Age, Sex, Smoking Status, and Ethnic Differences

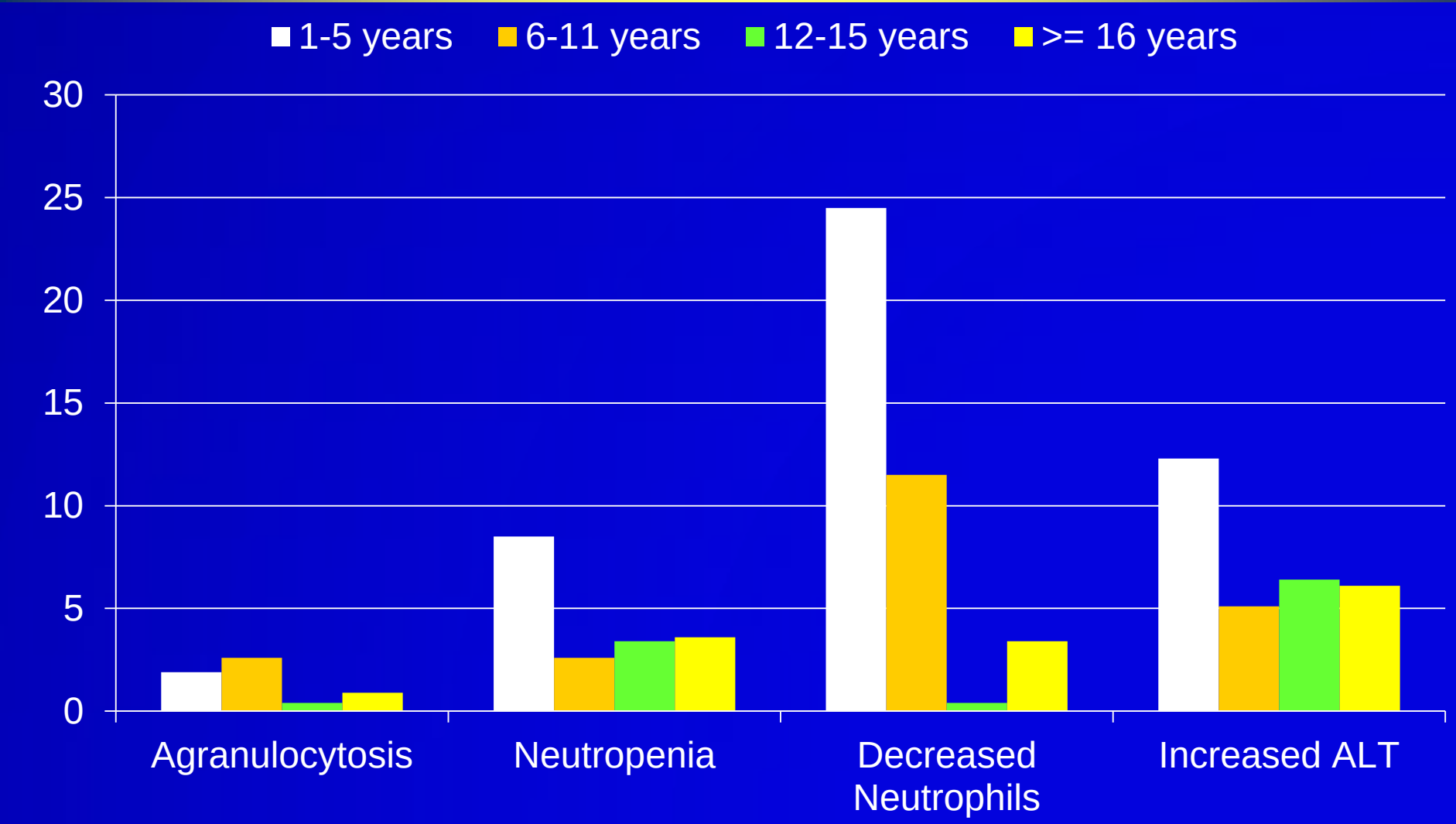
Matthew M. Hsieh, MD; James E. Everhart, MD, MPH; Danita D. Byrd-Holt; John F. Tisdale, MD; and Griffin P. Rodgers, MD

Table 3. Prevalence of a Neutrophil Count Less than 1.5×10^9 Cells/L

Variable	Prevalence, %* (95% CI)
Age	
1–2 y	7.24 (5.24–9.24)
3–5 y	3.70 (2.6–4.8)
6–8 y	2.25 (1.51–2.99)
9–11 y	2.73 (1.63–3.83)
12–14 y	2.21 (1.64–2.78)
15–17 y	1.51 (1.0–2.02)
18–24 y	0.66 (0.31–1.01)
25–74 y	0.72 (0.54–0.9)
≥75 y	0.50 (0.17–0.83)

Ann Intern Med. 2007;146:486-492

Rate of Specific Adverse Events Stratified by Age: Pooled Safety Data



Ferriprox
Safety in pediatric patients

Safety profile of Ferriprox in pediatric patients is comparable to that of adult patients

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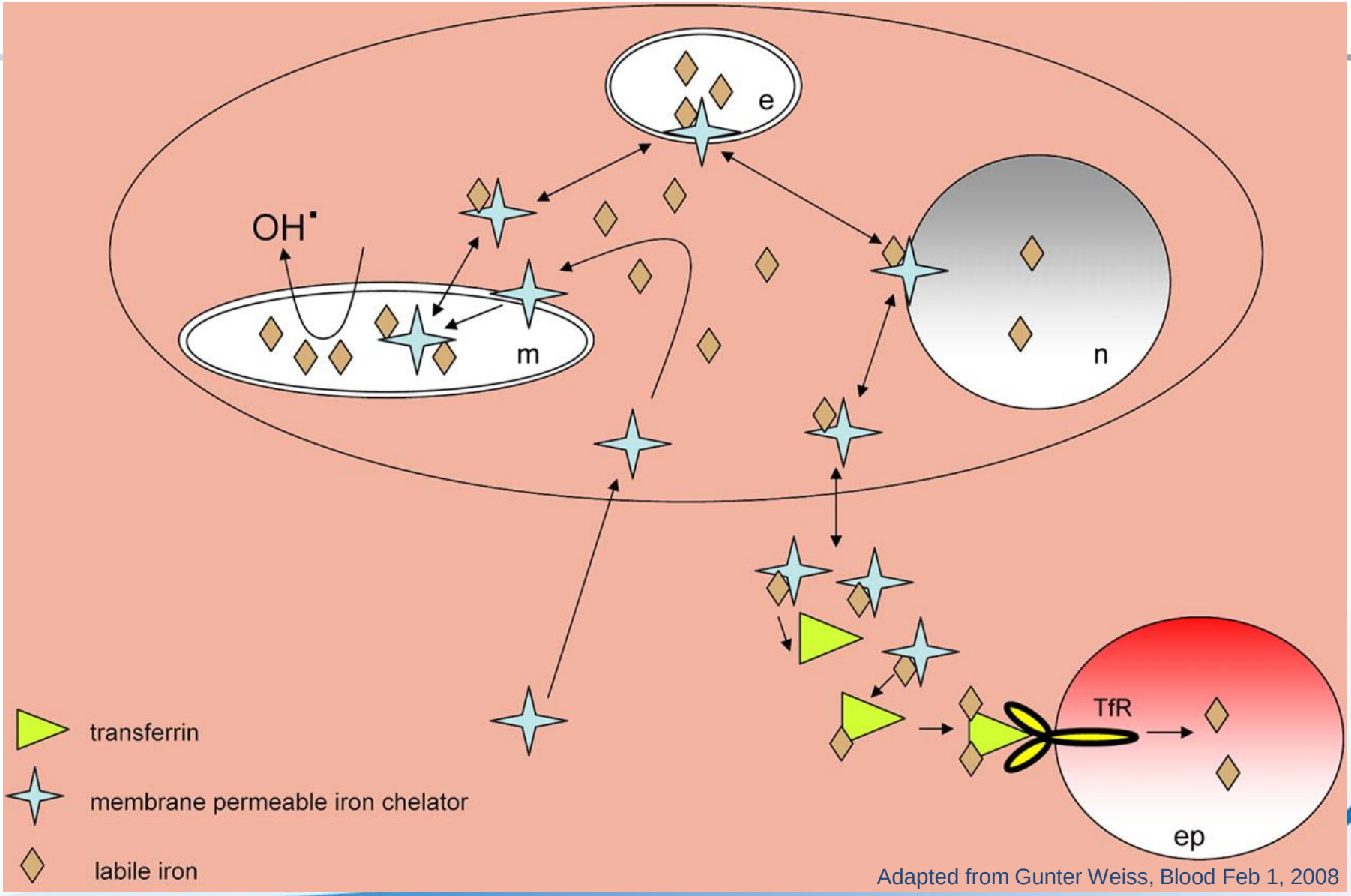
Physiochemical properties Comparison of three chelators

	deferiprone	deferasirox	deferoxamine
Molecular Weight	139	373	560
Partition Coefficient	0.18	6.3	0.02
Protein Binding	<10%	99% (albumin)	<10%
Charge of Chelator	neutral	negative	positive
pFe3+	19	22.5	26

Deferiprone can relocate labile iron from sites of regional iron accumulation to sites of iron consumption



Adapted from Gunter Weiss, Blood Feb 1, 2008

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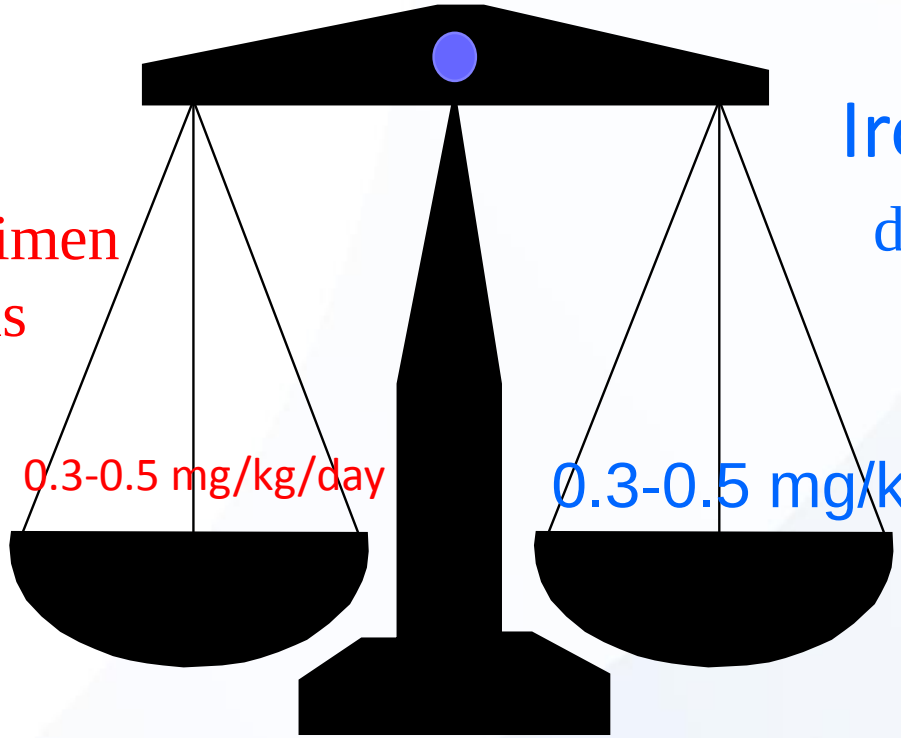
IRON BALANCE
IN TRANSFUSIONAL IRON OVERLOAD

Iron input

transfusion regimen
spleen status



Iron excretion

dose of chelator
compliance
iron overload

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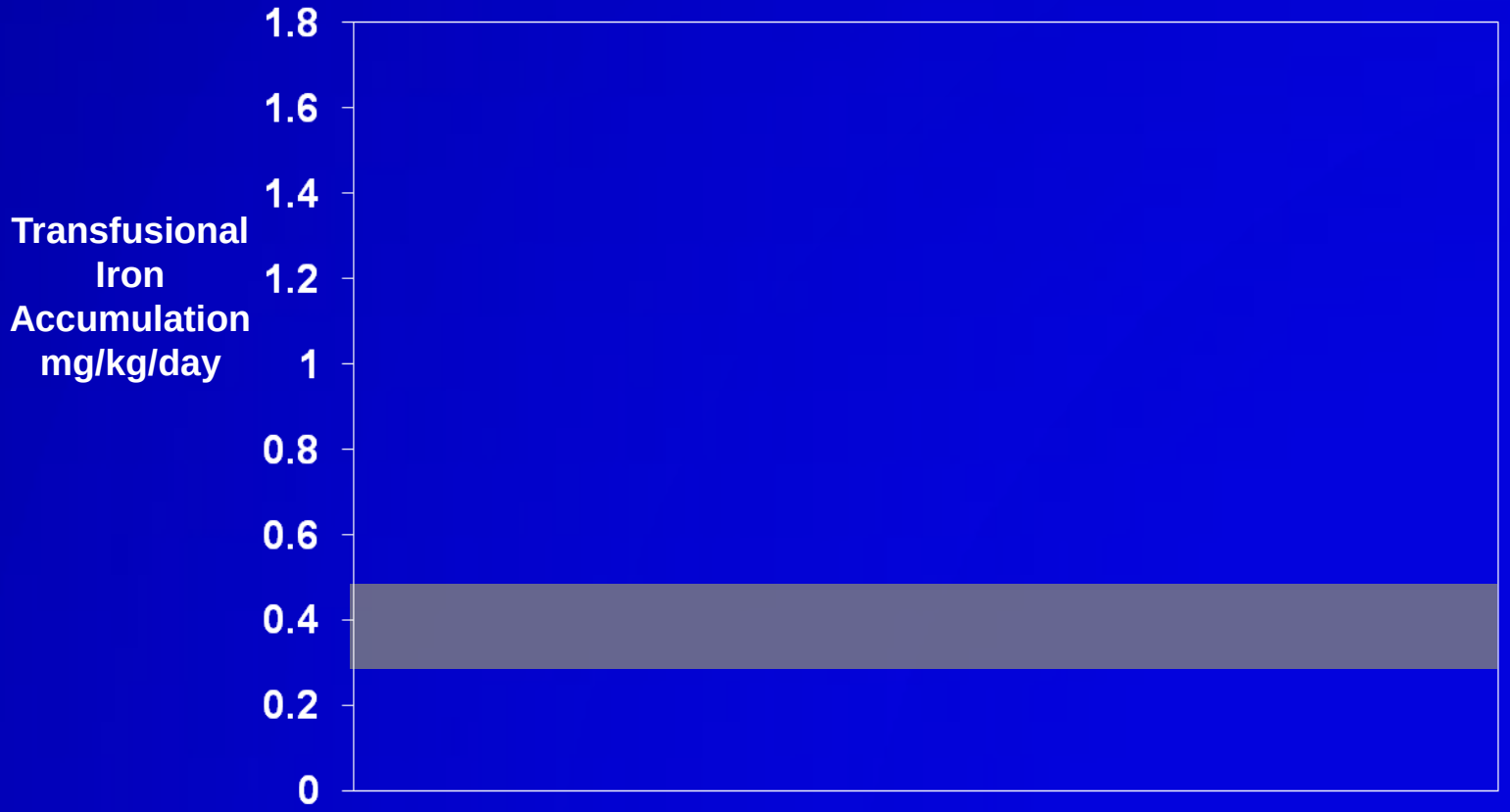
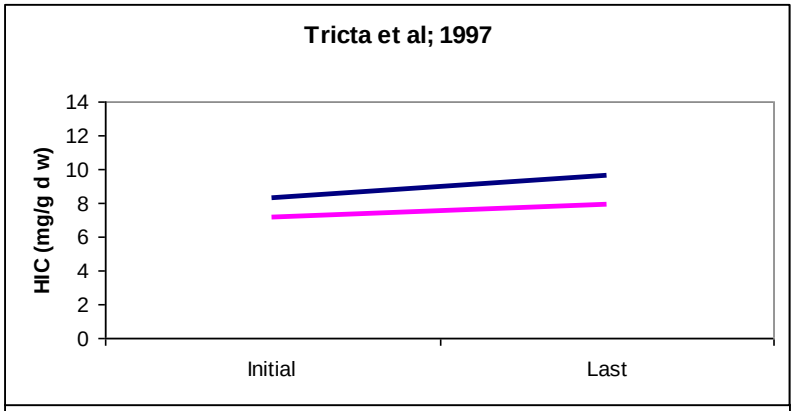
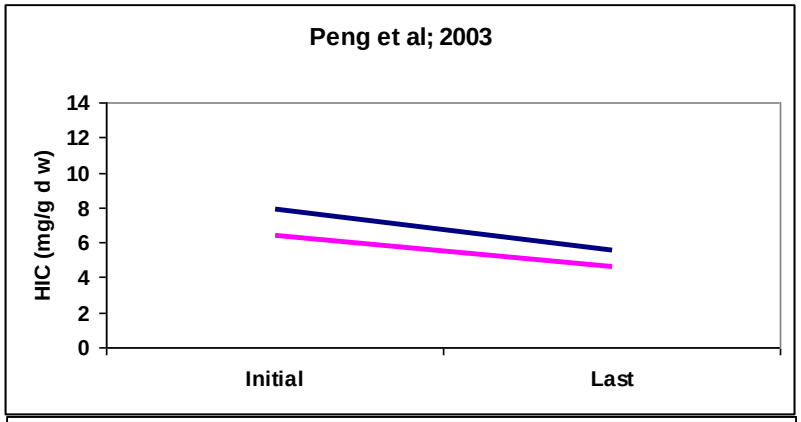
Transfusion Iron Accumulation vs Chelator-Induced Iron Excretion

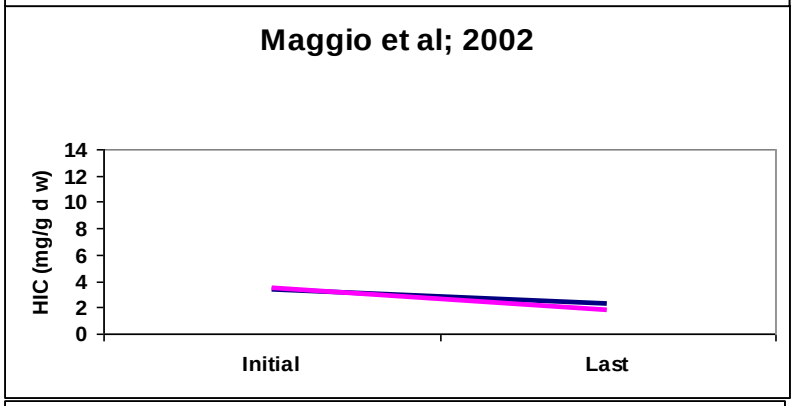


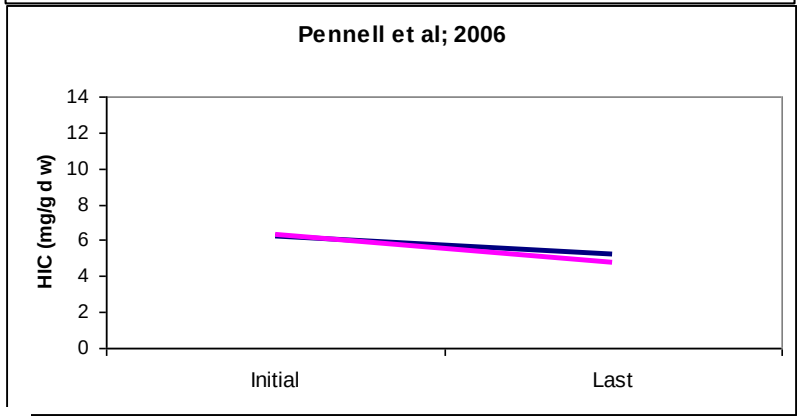
Adapted from Grady et al 2000, 2001, 2002; Galanello 2007

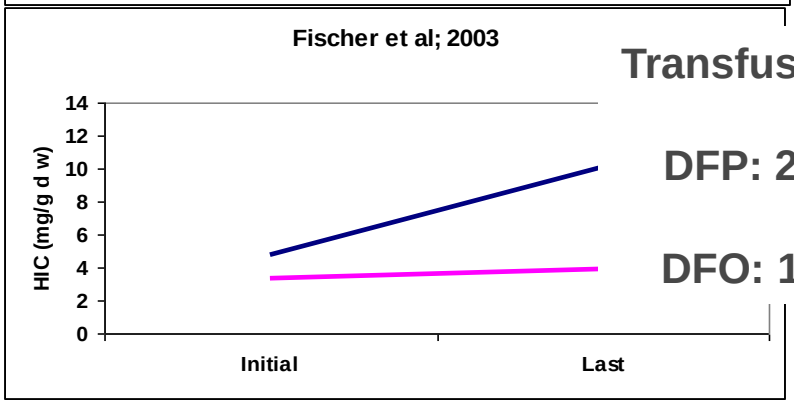
Deferiprone (DFP) is comparable to Deferoxamine (DFO) in Controlling Hepatic Iron Concentration











Transfusional iron input:

DFP: 24.4 ± 5.3 mg/d

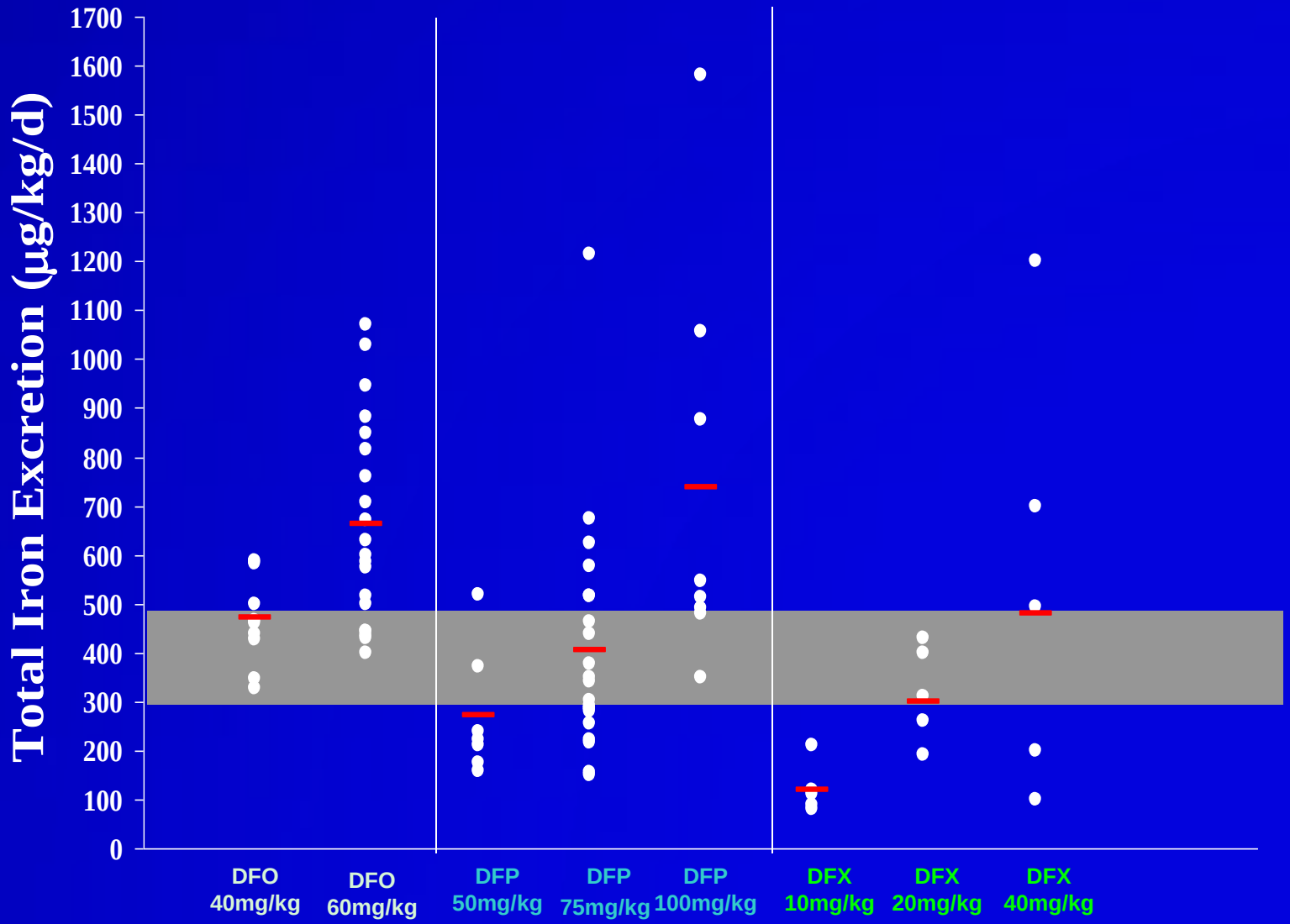
DFO: 18.9 ± 4.7 mg/d

29% higher in DFP-

than in DFO-patients

DOSE RELATED IRON EXCRETION

DFO= Deferoxamine; DFP= Deferiprone; DFX= Deferasirox



Adapted from Grady et al

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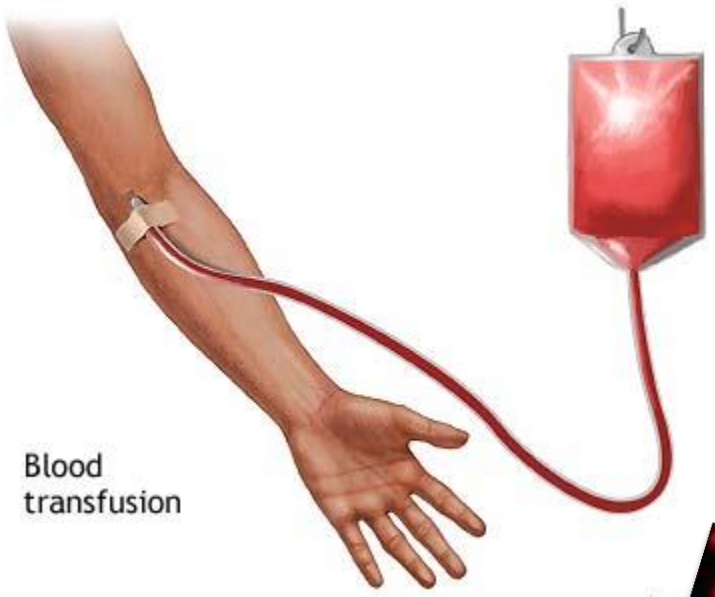
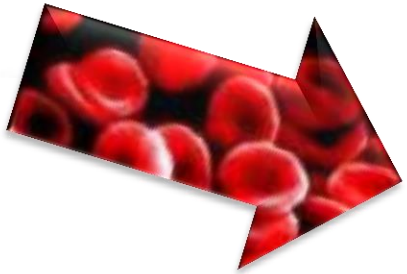
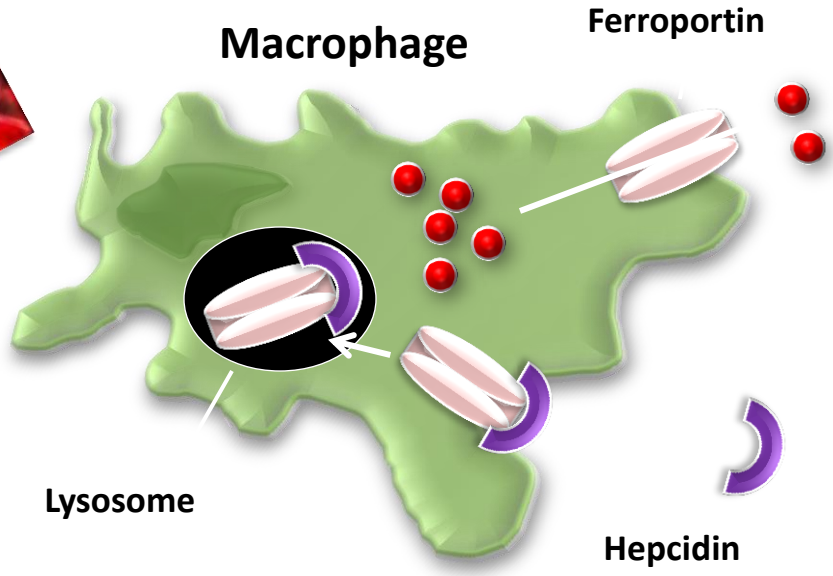
Transfusional Iron Overload



Each unit contains
200 - 250 mg of iron





Senescent RBC

Macrophages (Bone Marrow, Spleen, Liver)

Intra-cellular chelator

Chelator

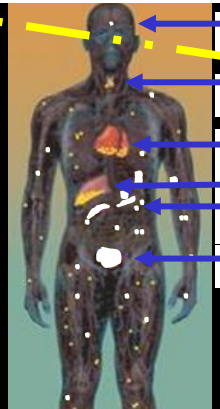
Extra-cellular chelator

Transferin

NTBI

LPI

Uncontrolled iron loading of organs



Pituitary

Parathyroid

Thyroid

Heart

Liver

Pancreas

Gonads

Chelator