

Carence martiale des maladies chroniques

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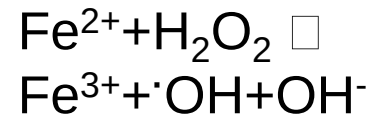
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Le fer est un élément paradoxal

- **Indispensable à la vie**
- Permet le transport d'O₂
 - *Hémoglobine*,
 - *Myoglobine*

- **Potentiellement toxique**
- Peut générer un stress oxydant

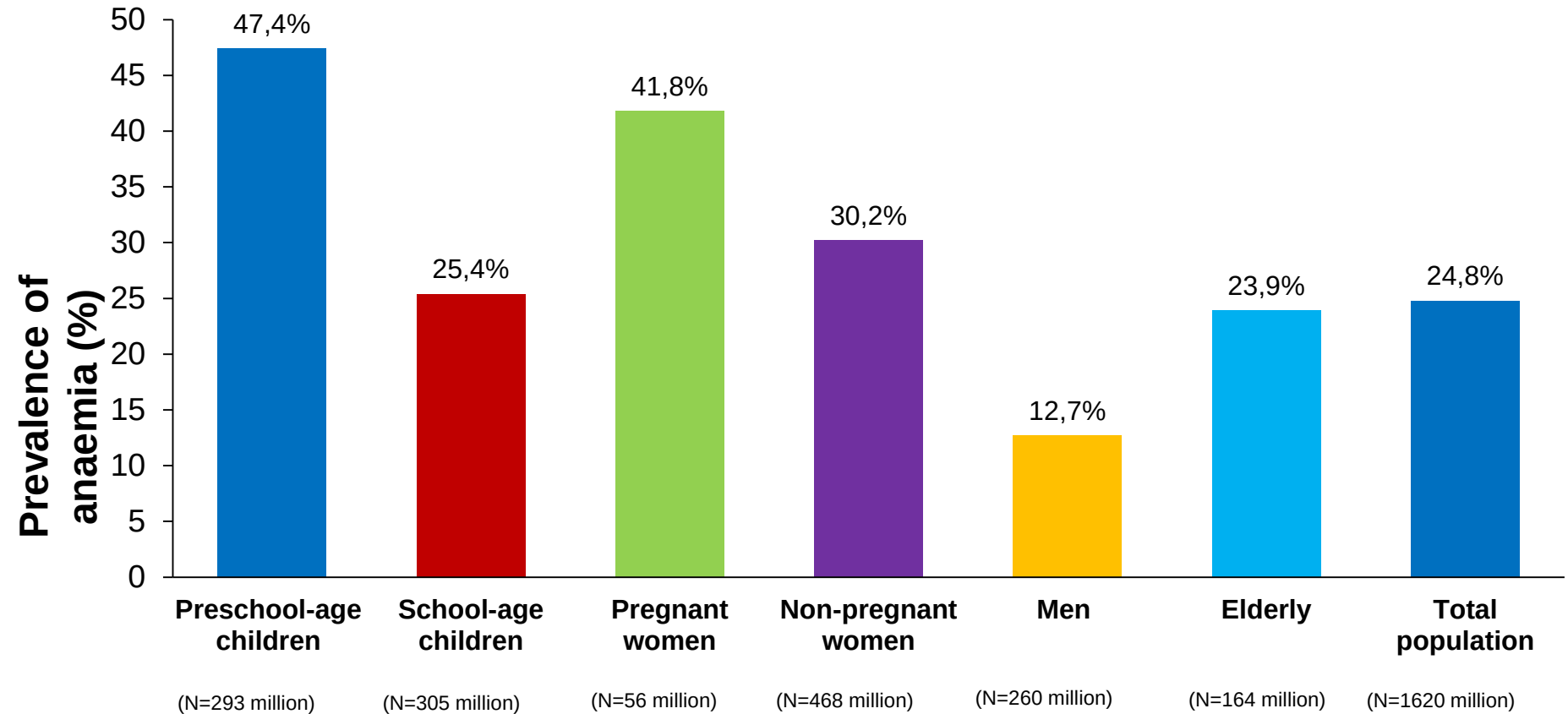


- Cofacteur de nbres réactions enzymatiques,
- Constituant indispensable des protéines « héminiques », dont les cytochromes

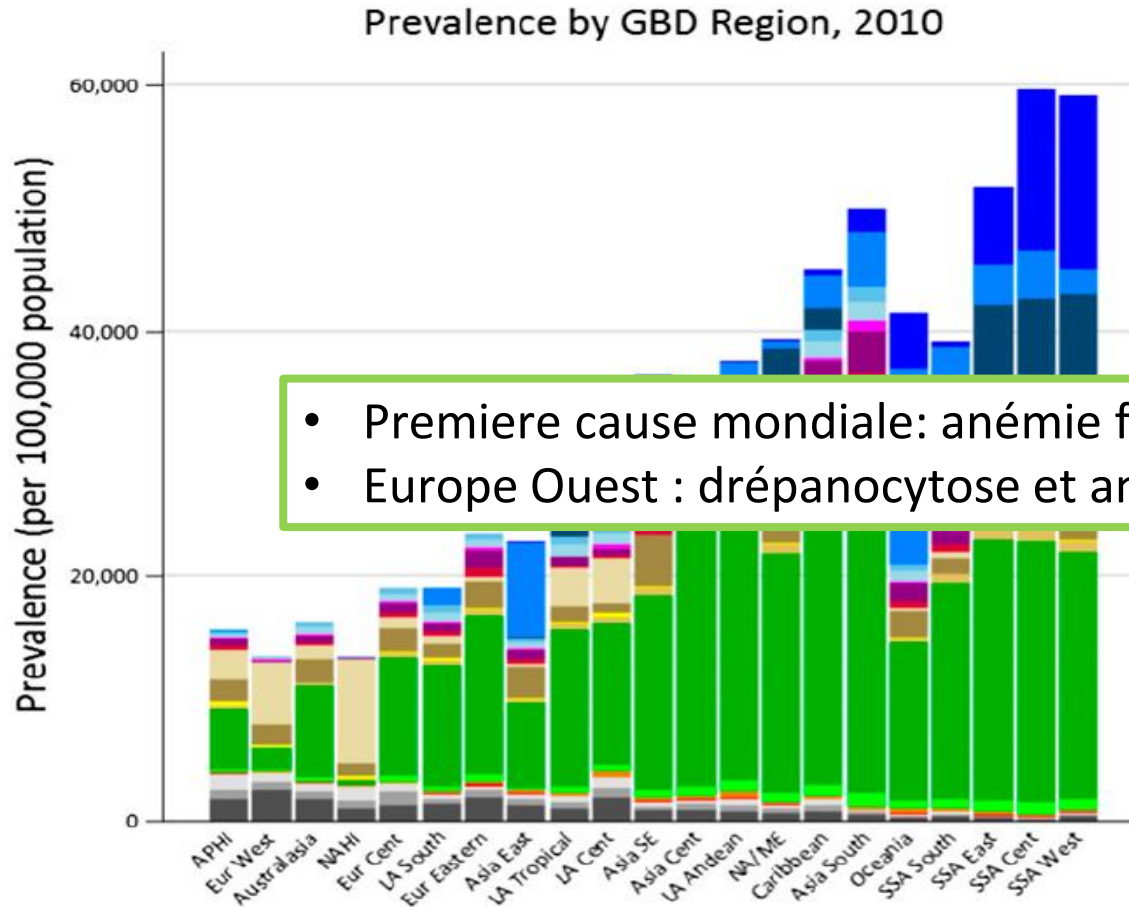


- « Toxicité » utile pour les défenses de l'organisme (PN...)

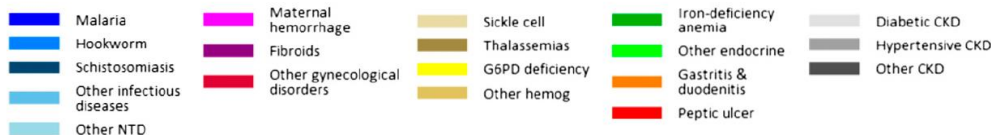
Global anaemia prevalence



Anémie, prévalences par étiologie et région



- Première cause mondiale: anémie ferriprive
- Europe Ouest : drépanocytose et anémie mal. chron.



La carence martiale: définition et conséquences ?

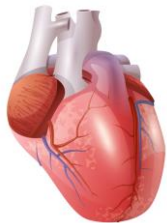
- **Iron deficiency is a health-related condition in which iron availability is insufficient to meet body needs**
- **Iron deficiency can be present with or without anaemia**

Importance of iron for functioning and survival across all levels of complexity of living structures

Iron is critical for optimal functioning and survival



- Mitochondrial dysfunction
- Deranged activity of enzymes
- Abnormal transport and structural proteins
- Apoptosis



- Tissue remodelling
- Impaired organ efficacy



- Impaired exercise capacity
- Reduced work efficacy
- Impaired cognitive performance and behaviour
- Increased morbidity and mortality

Cells

Tissues

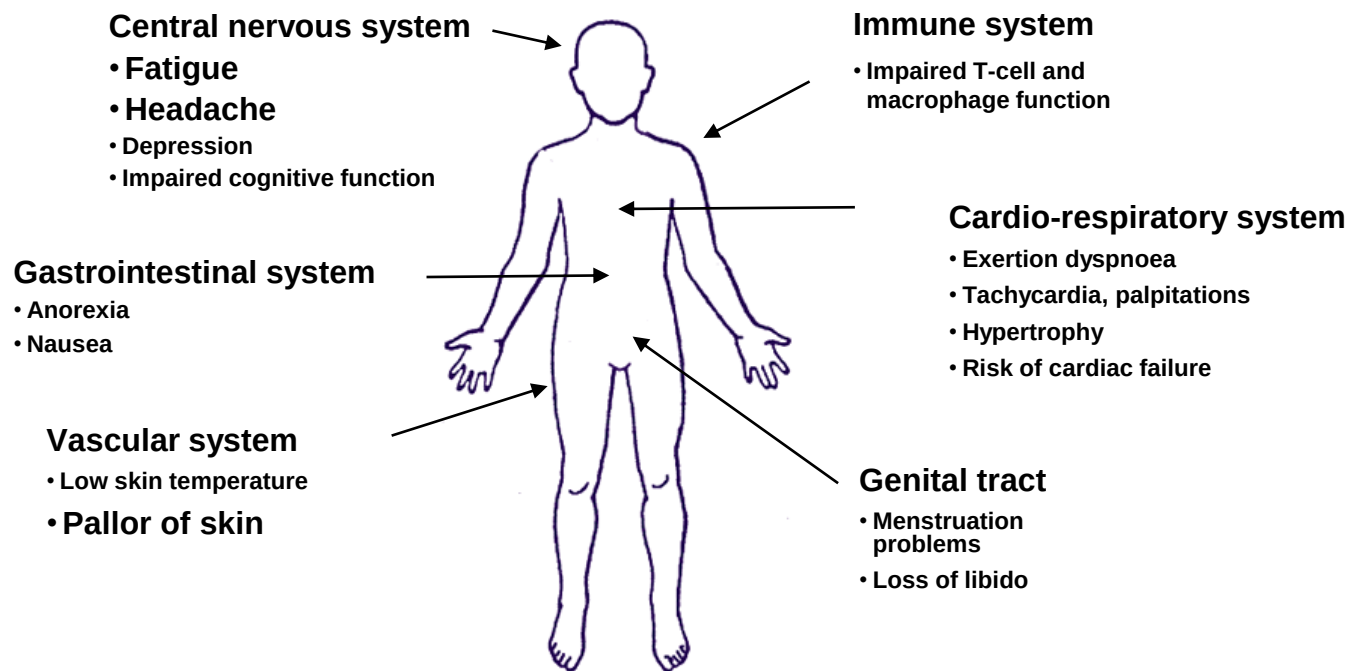
Organs

Body

Population

Clinical consequences of anaemia and iron deficiency

anaemia (very frequent 40-60%)



Most common causes of iron deficiency/iron deficiency anaemia

Blood loss

- Heavy or prolonged menstrual bleeding
- Heavy uterine bleeding
- Delivery
- GI tract disorders/bleeding
- Surgery
- Blood donation
- Haemodialysis

Increased iron demand

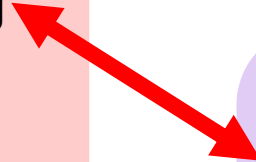
- Infancy, adolescence
- Pregnancy
- Endurance sport

Decreased iron intake

- Poor diet
- Vegetarian diet
- Disease-related anorexia (cancer)
- Eating disorder

Decreased iron absorption and utilization / release

- Inflammatory bowel disease
- Chronic inflammatory or malignant diseases
- Interaction food / drugs
- Malabsorption



Common causes of absolute and functional iron deficiency, and main biomarkers

Absolute iron deficiency

- Chronic blood loss
- Decreased iron intake
- Increased iron demand

- **Low TSAT**
- **Low serum ferritin**
- **High sTfR**

Functional iron deficiency

- Inadequate iron release
- Simultaneously increased iron need (e.g. due to ESAs)

- **Low TSAT**
- **Normal / high serum ferritin**
- **Normal sTfR**

La carence martiale: comment la diagnostiquer ?

Iron biomarkers according to the compartment

Cellular Iron

- Hb
- MCV, MCH
- Retics
- HypoRBC%
- ReticHb content
- Low Hb density%
- ZPP

Storage Iron

- Serum ferritin
- Bone marrow stain

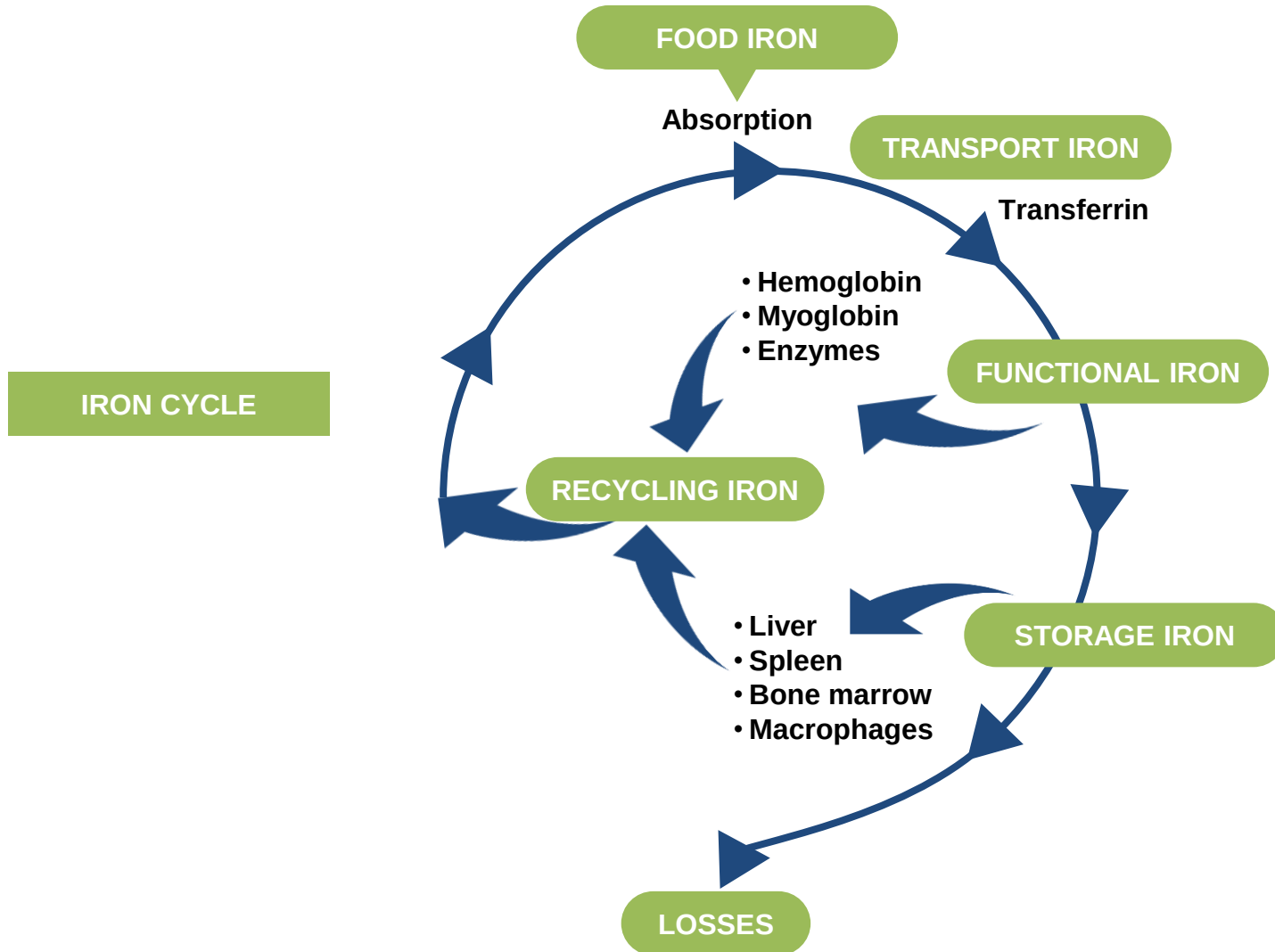
Transport Iron

- Tf, Tf sat,
- sTfR, sTfR/ferritin

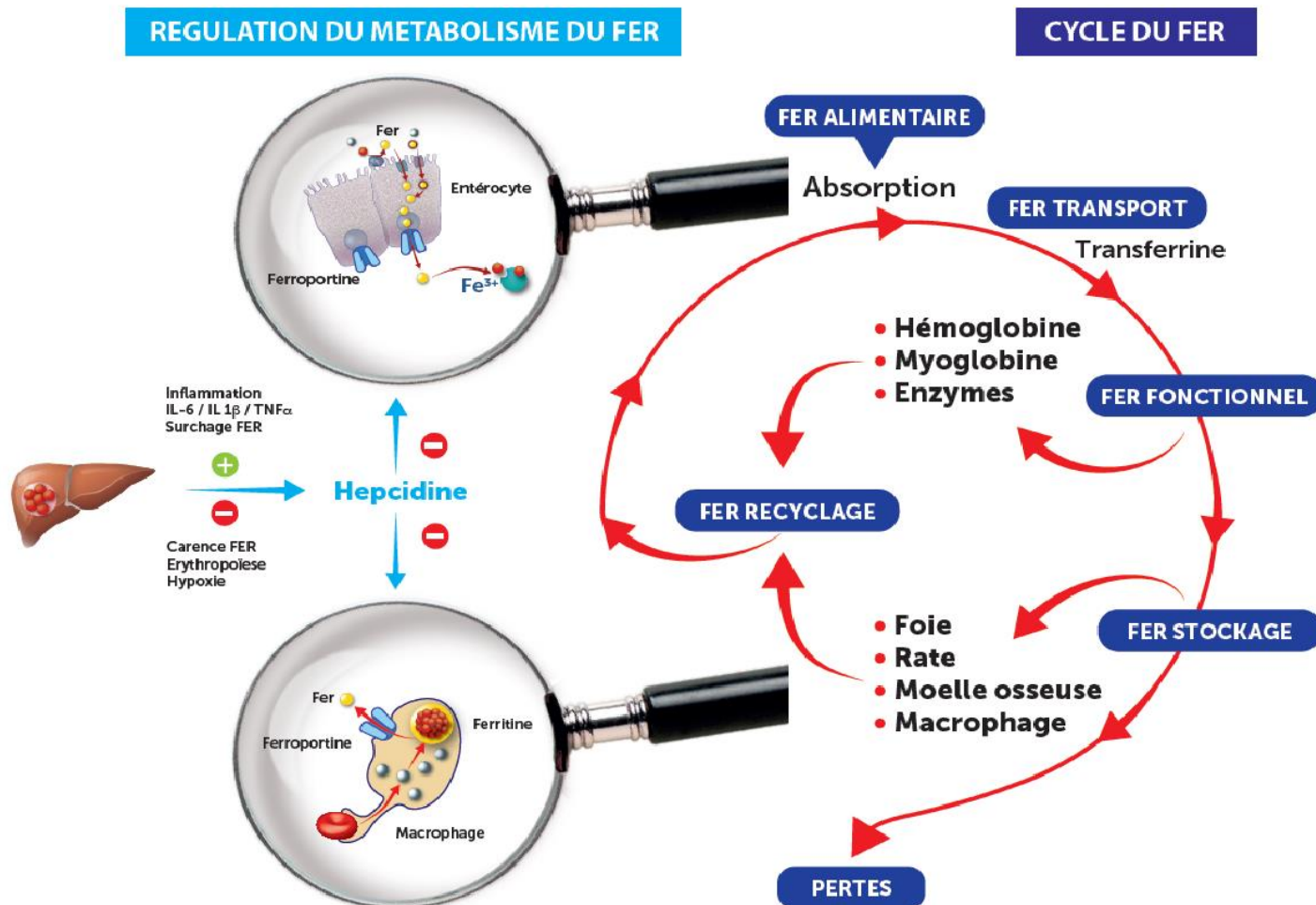
Other tests

- Epo, Hepcidin
- ESR, CRP

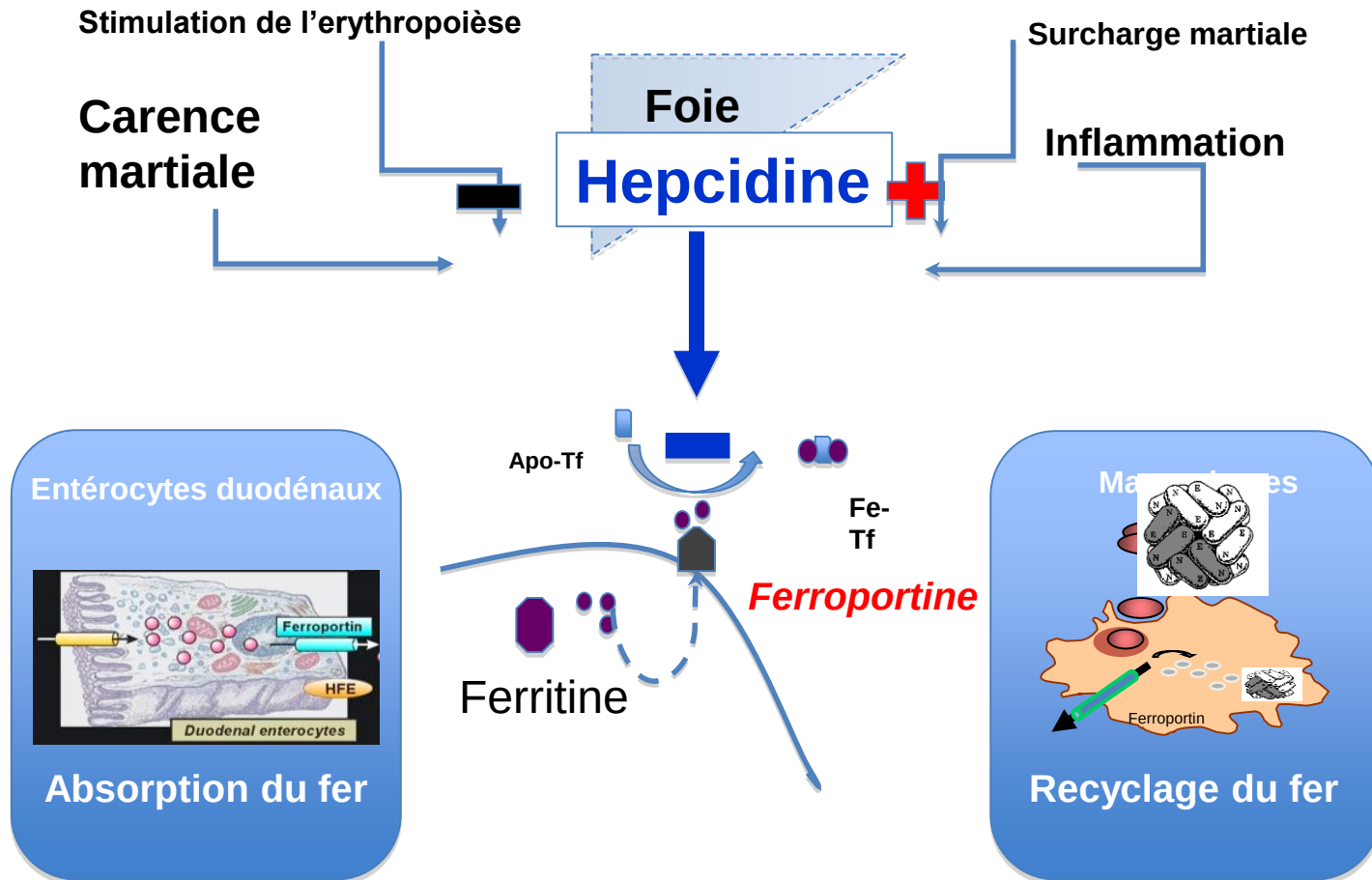
Régulation du métabolisme du fer: un circuit fermé



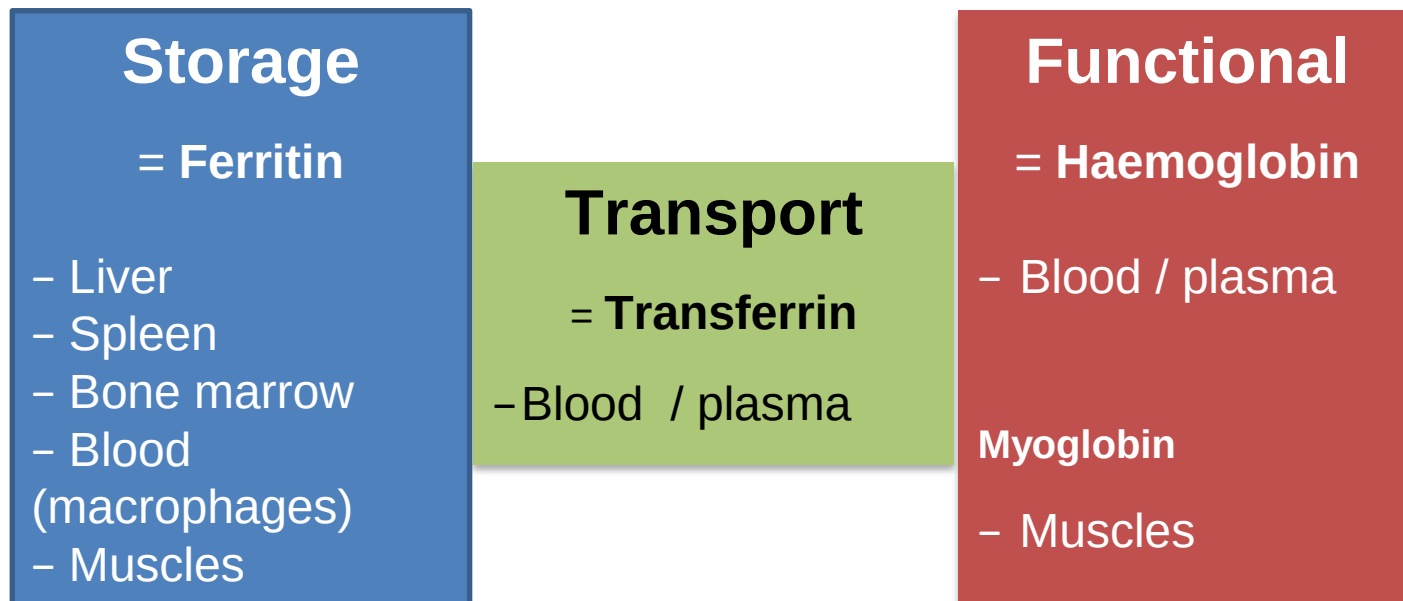
Régulation du métabolisme du fer



L'hépcidine contrôle le métabolisme du fer via la ferroportine

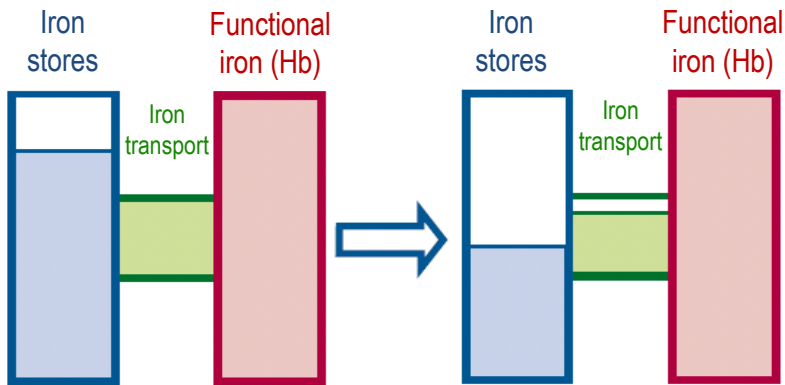


Body iron distribution and biomarkers



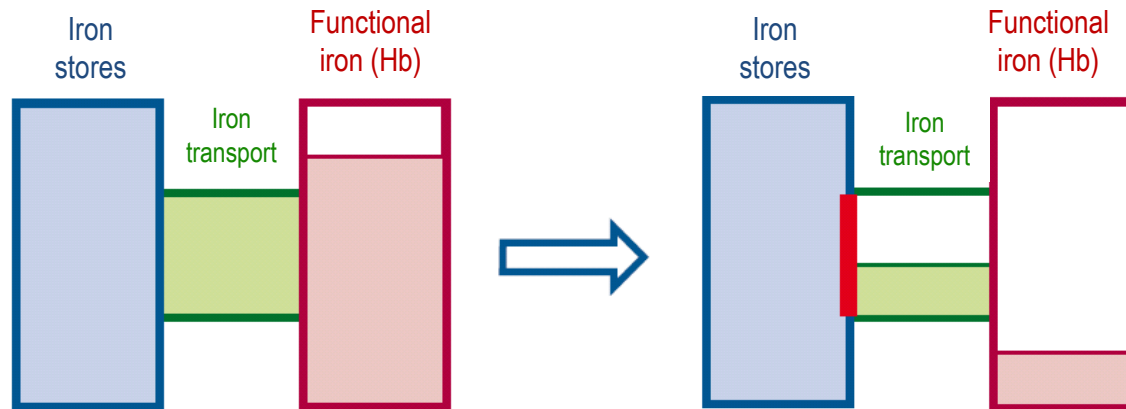
Total body iron: 3–4 grams (30–45 mg iron/kg)

Absolute iron deficiency: Decreased levels of iron stores lead to reduced iron availability for normal erythropoiesis



-  Ferritin
-  TSAT

Functional iron deficiency: Inadequate iron available for normal erythropoiesis, although iron storage is adequate



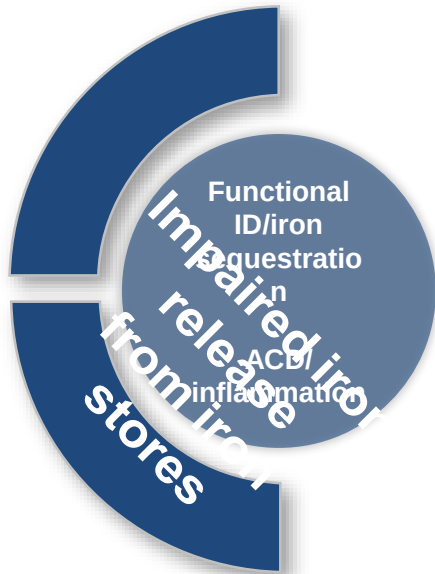
- Ferritin: normal, or high
- ☐ ☐ TSAT

Traitements par fer: utilisation des biomarqueurs en vraie vie (EGB 2006-2013) en France

Biomarqueur	Bilan avant traitement			Bilan après traitement			Bilan avant <u>ET</u> après traitement	
	n	(%)		n	(%)		n	(%)
CST	1677	(1,0)		863	(0,5)			
Ferritine	56081	(33,8)		24952	(15,0)			
CST ou ferritine	57510	(34,6)		25654	(15,5)		12161	(7,3)

Tous traitements par fer – Echantillon total, n=166 015 épisodes; CST, coefficient de saturation de la transferrine
EGB, échantillon généraliste des bénéficiaires de l'assurance maladie

Causes of functional ID/iron sequestration

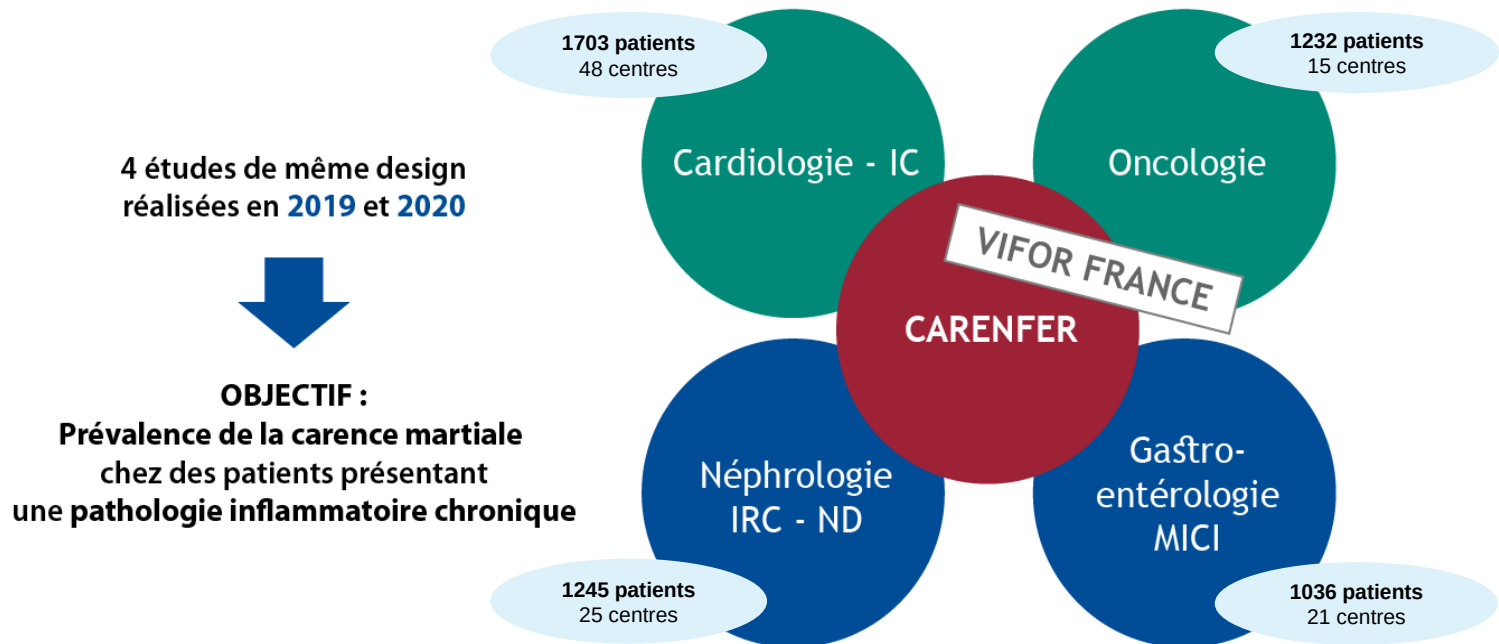


- Chronic kidney disease (CKD)^{1,2,3}
- Chronic heart failure (CHF)²
- Inflammatory bowel disease (IBD): Crohn's disease (CD)/ulcerative colitis (UC)^{2,3}
- Autoimmune diseases eg rheumatoid arthritis (RA)^{1,3}
- Other chronic viral, fungal, bacterial or parasitic infections^{1,3}
- Cancers (haematological malignancies and solid tumours)^{1,3}
- Obesity^{1,2}

□ In GI diseases, inflammation may progress to erosions and ulcers, which can lead to perforations and bleeding causing absolute ID⁴

Absolute and functional ID are not exclusive conditions but can be present at the same time

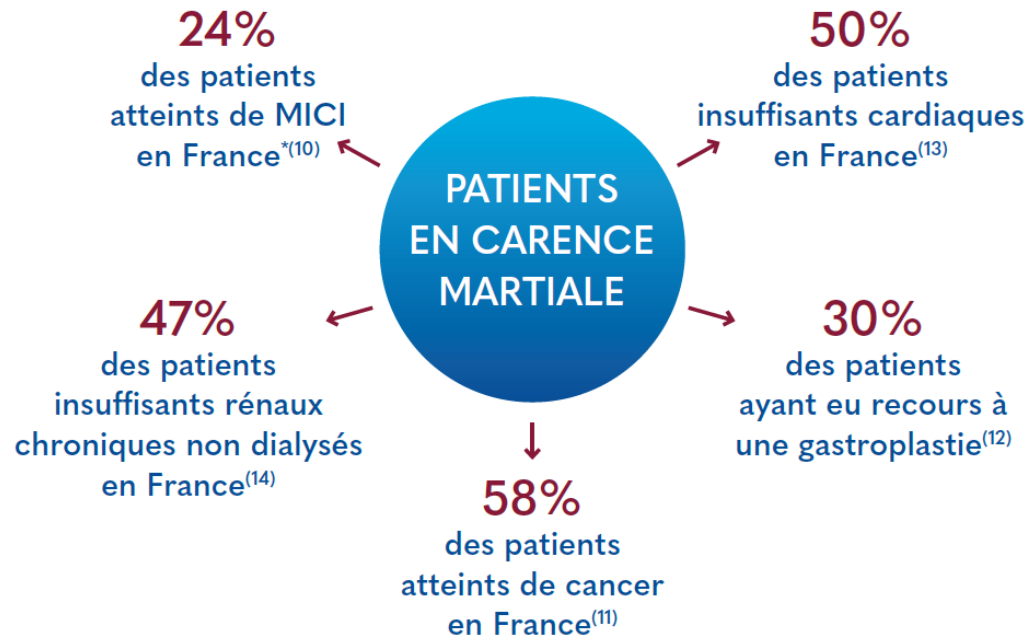
Prévalence de la carence martiale au cours des maladies chroniques en France 2019-2020, *Programme CARENFER n= 5216 patients*



Prévalence de la carence martiale au cours des maladies chroniques en France 2019-2020, *CARENFER*

Carence martiale = 1^{ère} cause d'anémie dans le monde⁽²⁾

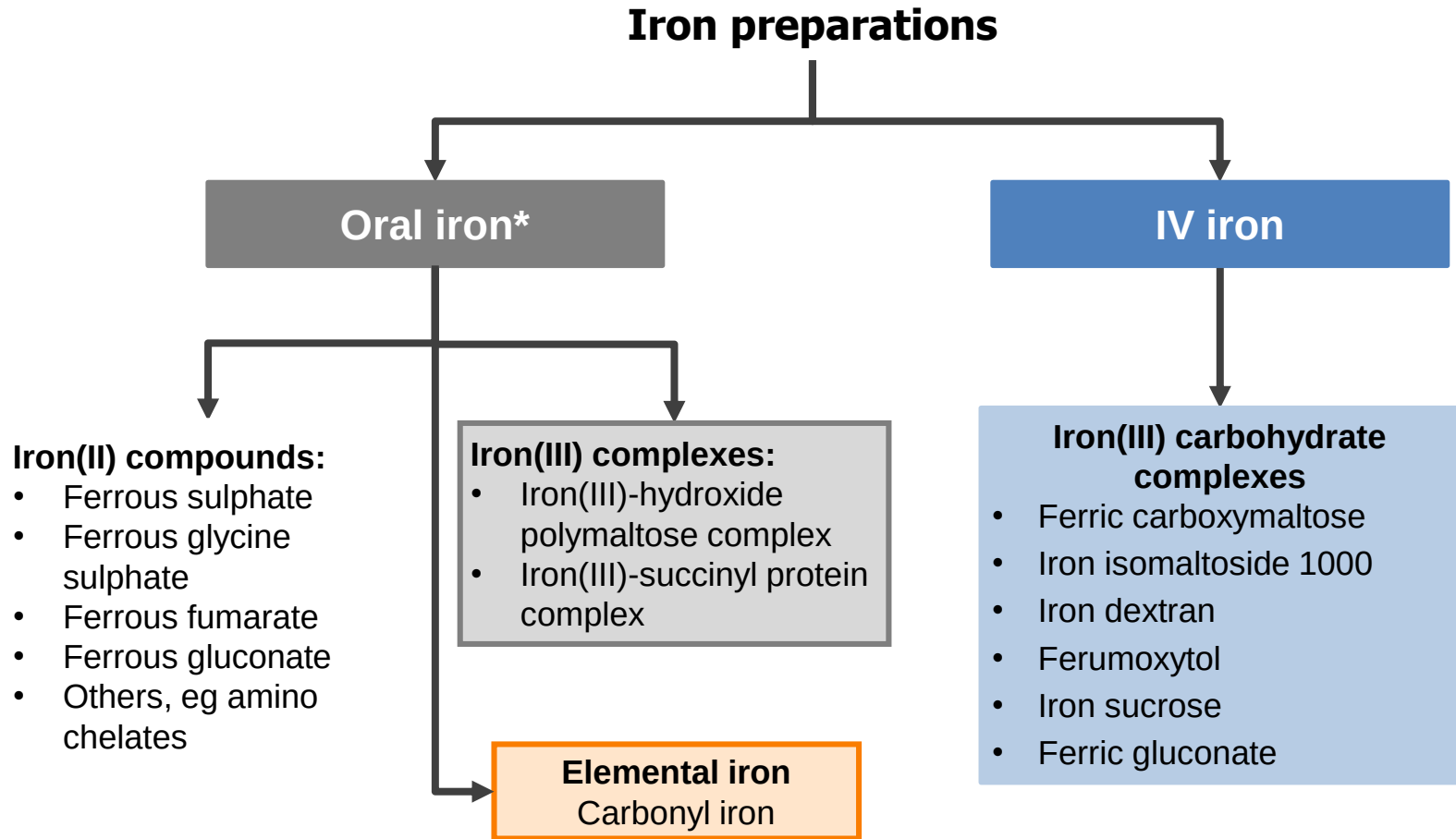
Elle est la carence **la plus fréquente** et touche plus particulièrement les enfants, les adolescents, les femmes enceintes et en âge de procréer.⁽²⁾



* Les patients atteints d'une maladie modérée voire sévère présentent un risque accru de développer une carence martiale (OR: 3.66; IC 95% 24.4-61.2; p = 0.007)

La carence martiale: comment la traiter ?

Treatment of Iron deficiency



*With/without folic acid

IV, intravenous

1. Fehr J et al. *Praxis* 2009;98:1445–51; 2. Gordeuk VR et al. *Am J Clin Nutr* 1987;46:1029–34; 3. Aapro M et al. *Ann Oncol* 2012;23:1954–62; 4. Auerbach M et al. *Hematology Am Soc Hematol Educ Program* 2010;2010:338–47

Carence martiale absolue versus fonctionnelle: implications thérapeutiques

ABSOLUTE

- inadequate body iron stores
- (ferritin < 100 µg/L)
- hepcidin levels low

Oral or i.v. iron

FUNCTIONAL

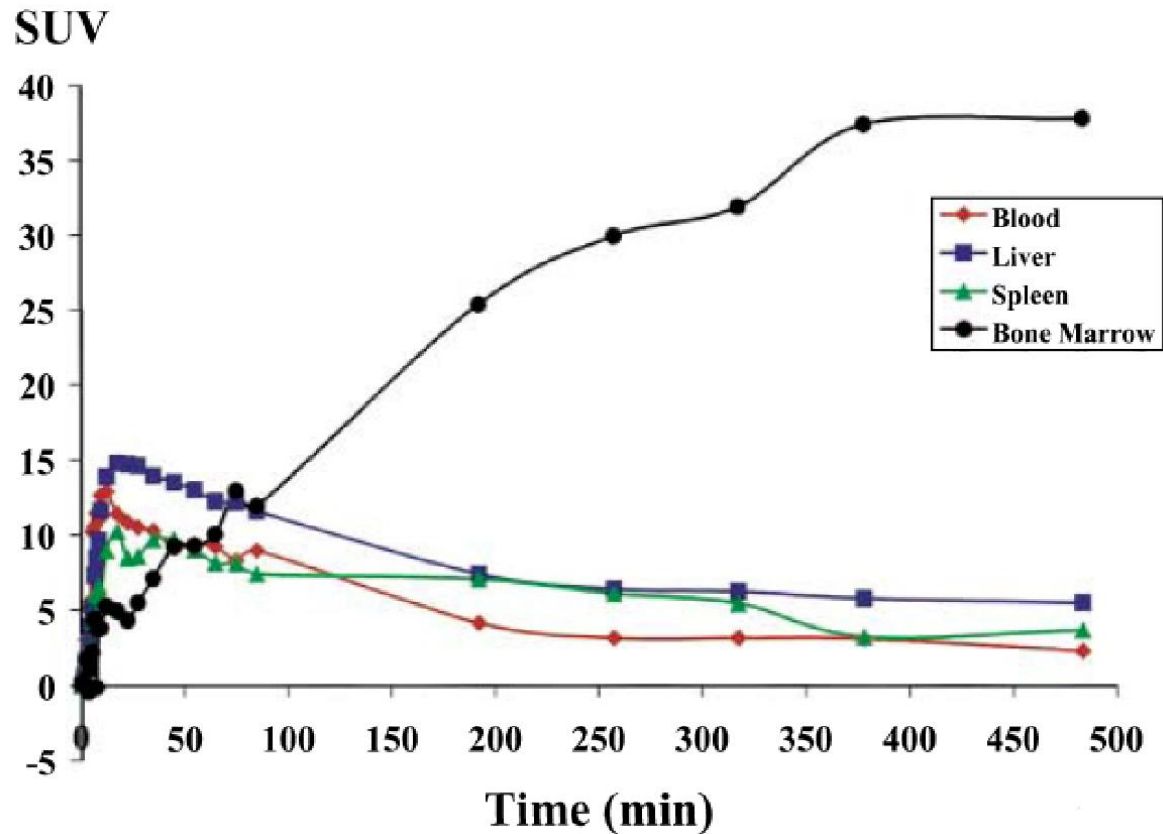
- adequate total body iron stores
- (normal or high ferritin)
- hepcidin levels high
- failure to release Fe rapidly enough to satisfy demands of bone marrow

Only i.v.

iron

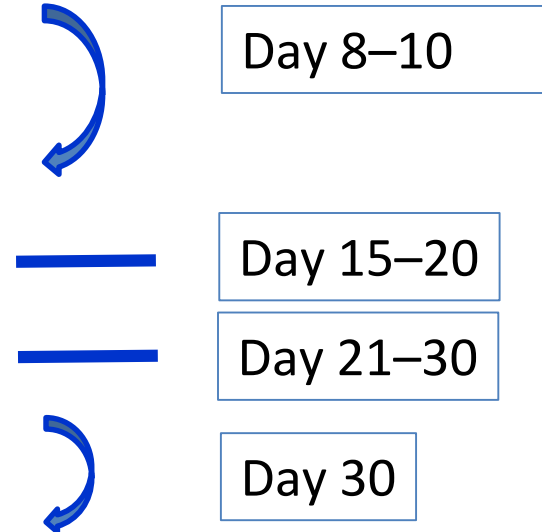
Où va le Fer après une injection i.v. ?

Distribution et accumulation dans la moelle osseuse



Quels biomarqueurs du Fer utiliser pour le suivi post-thérapeutique ?

- Tf sat (TSAT)
- sTfR
- sTfR/log10 ferritin
- Haemoglobin
- Ferritin
- MCV
- MCH



Carence martiale: conclusion

- La carence martiale est fréquente, avec ou sans anémie.
- **Faire le diagnostic** de carence martiale est simple: ferritine, saturation Trf.
- **La stratégie thérapeutique** de correction de la carence martiale adaptée au mécanisme: absolu vs. fonctionnel.
- Une augmentation modérée de l'hémoglobine et/ou du Fer "utilisable" entraîne une réduction significative des symptômes.