



University Hospital Pontchaillou
Inserm 991
Rennes (France)



**Current concepts in iron metabolism
relevant to transfusion and haemovigilance**

Paris

March 11 2016



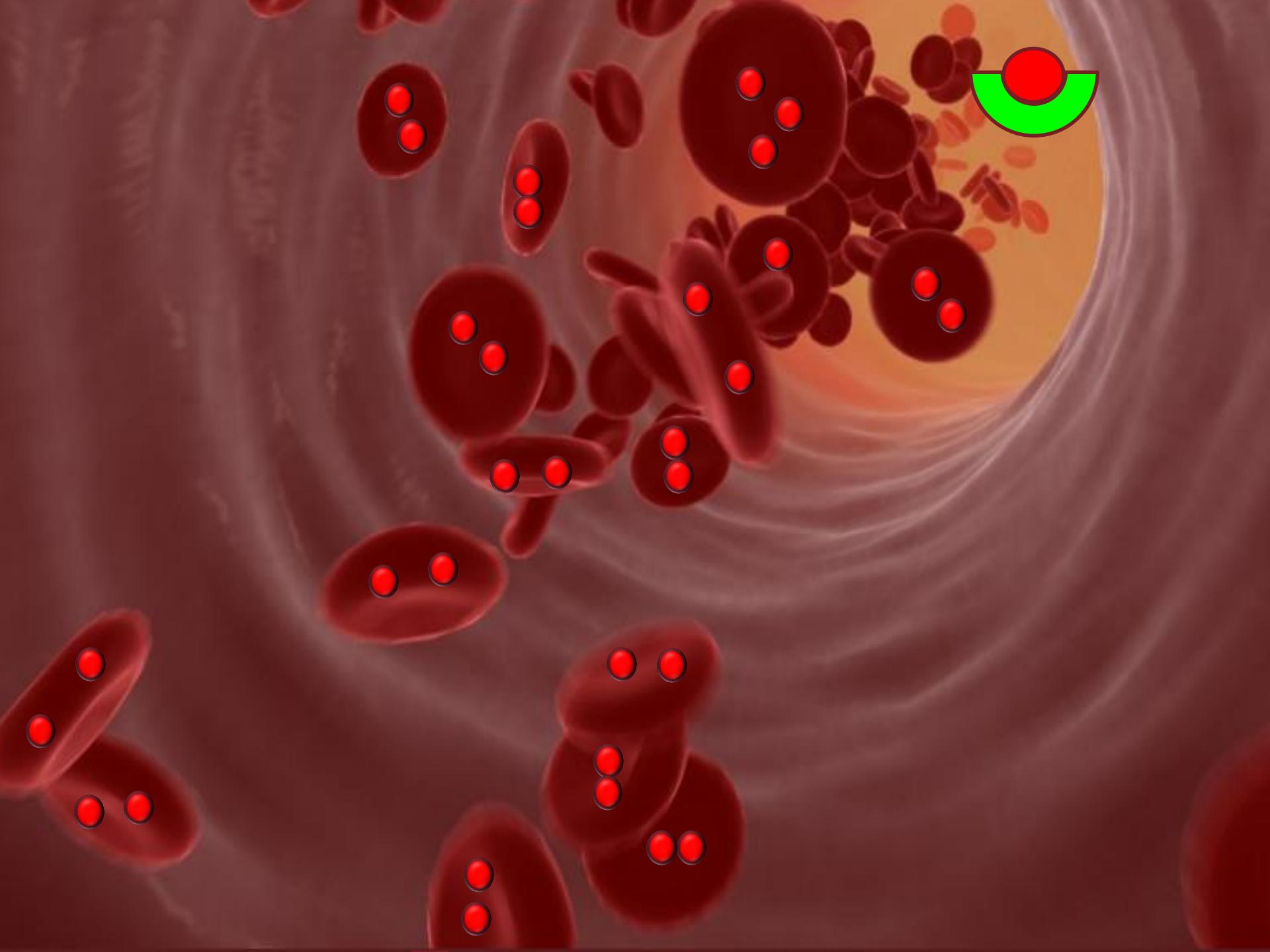
Iron metabolism

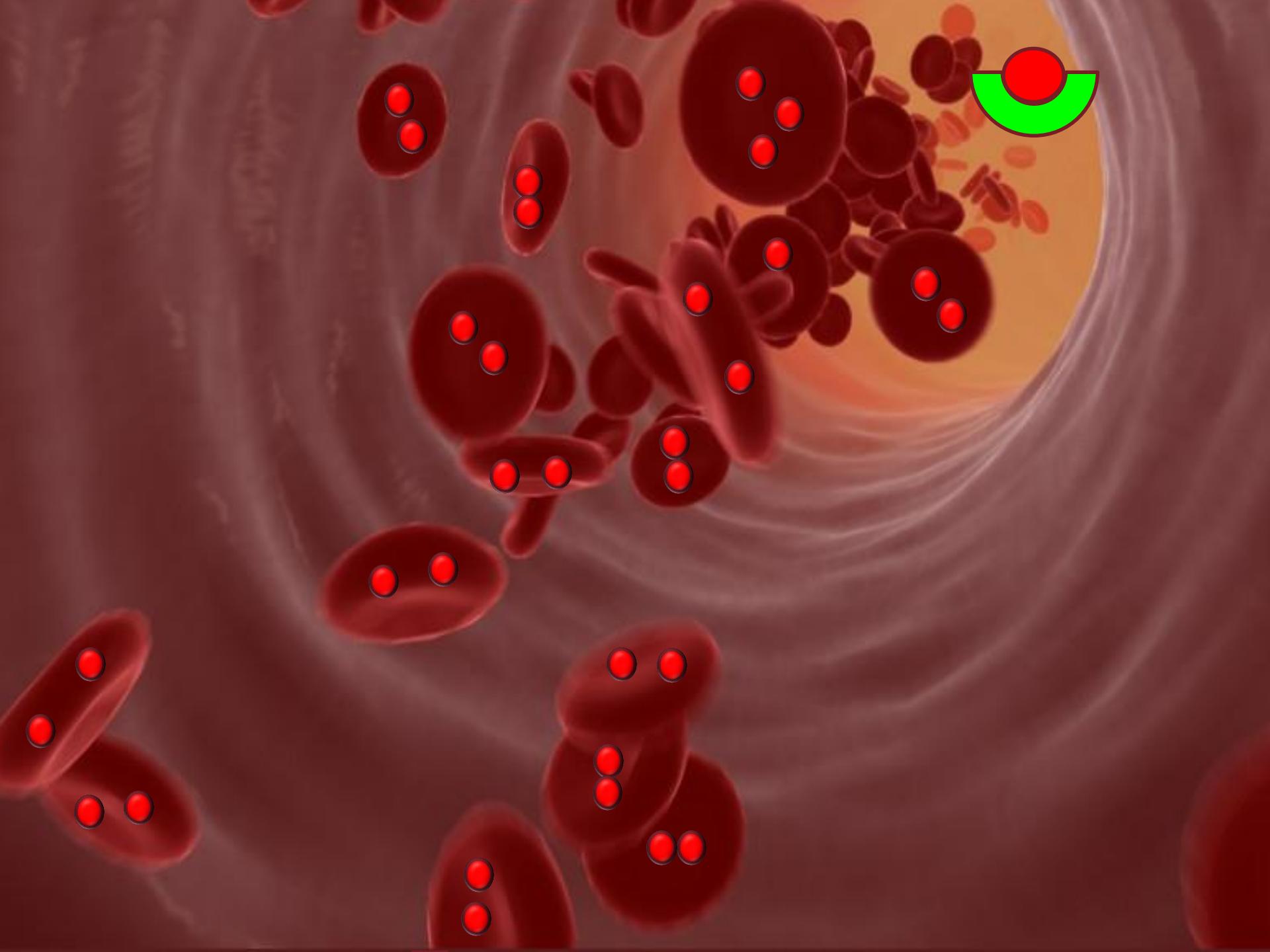
Classical background

Recent advances

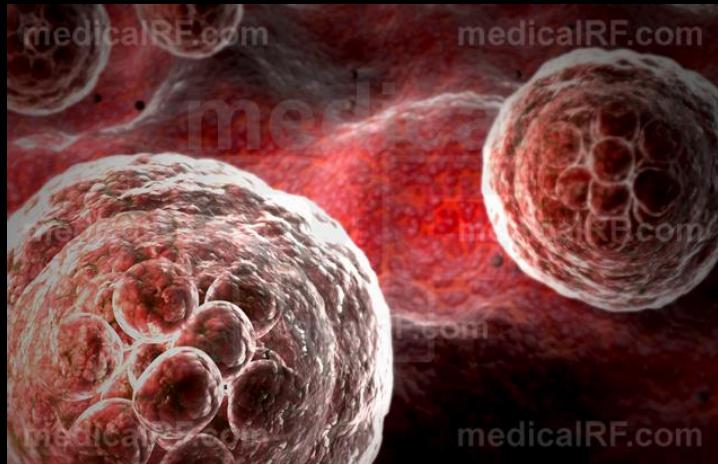
Relevance to transfusion and haemovigilance



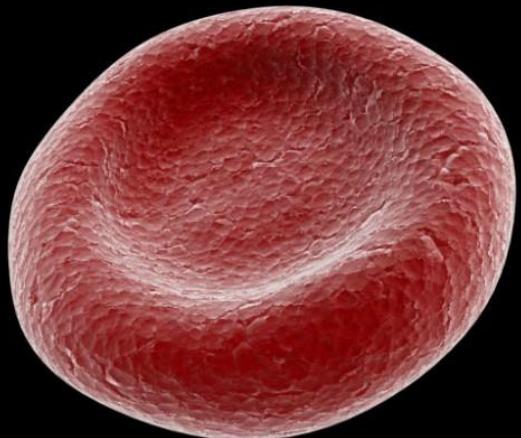


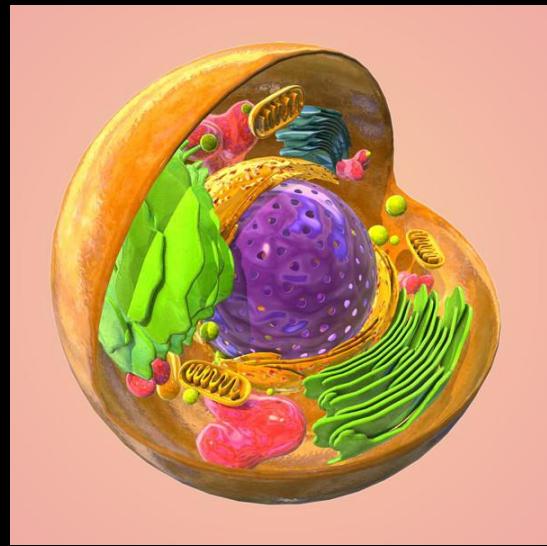
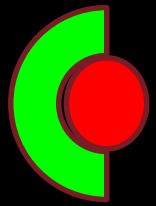


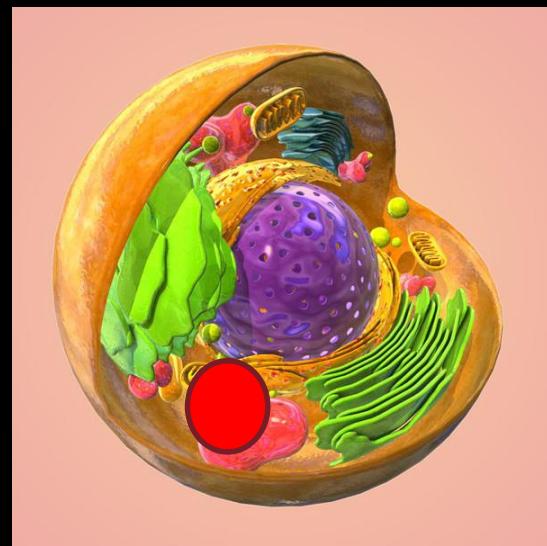


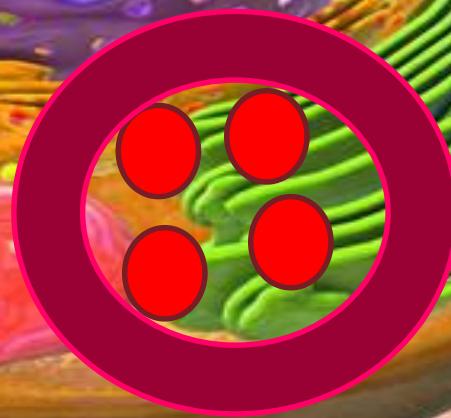
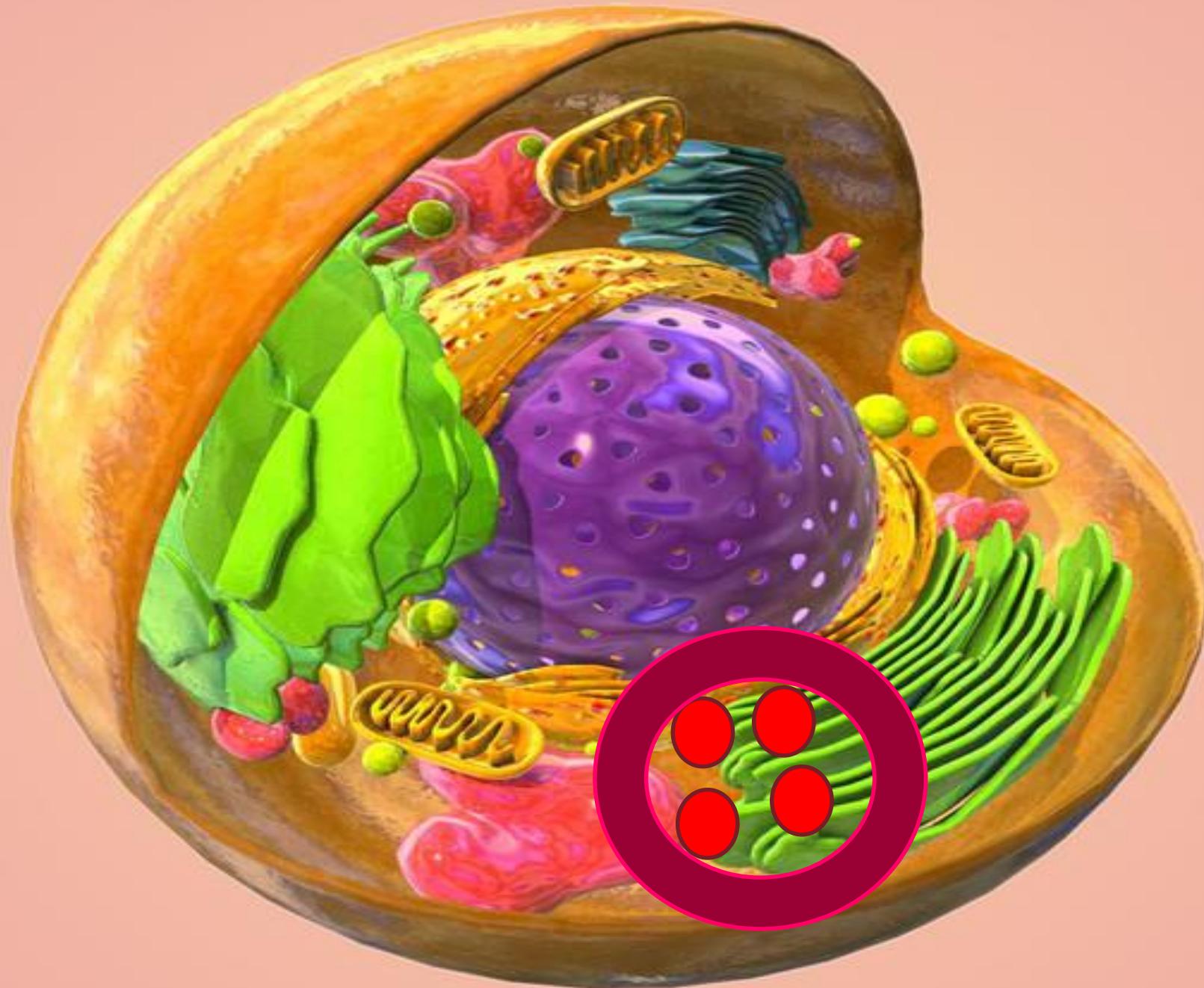


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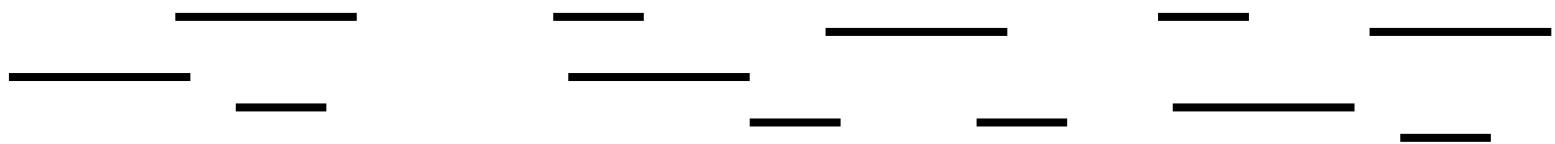
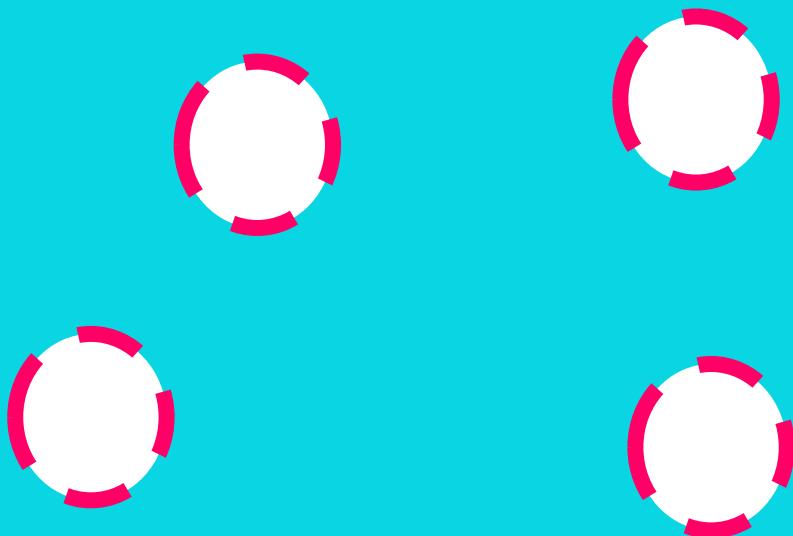




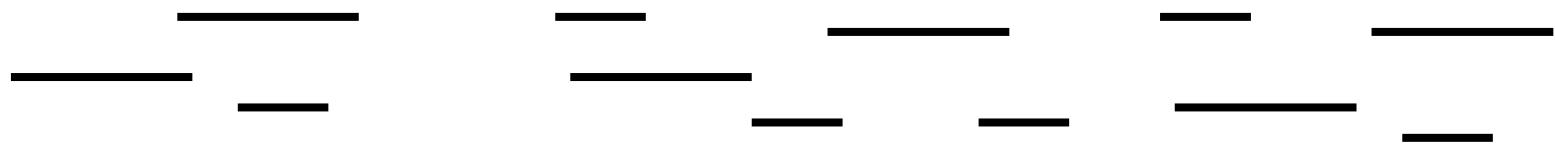
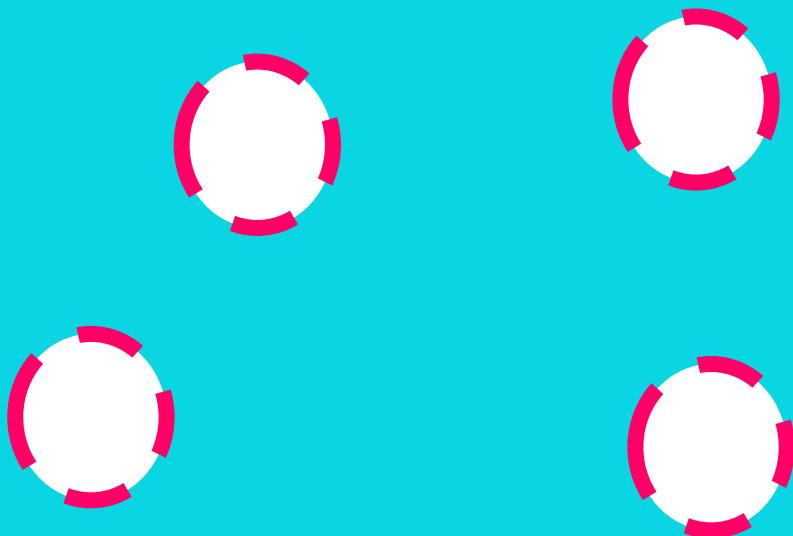


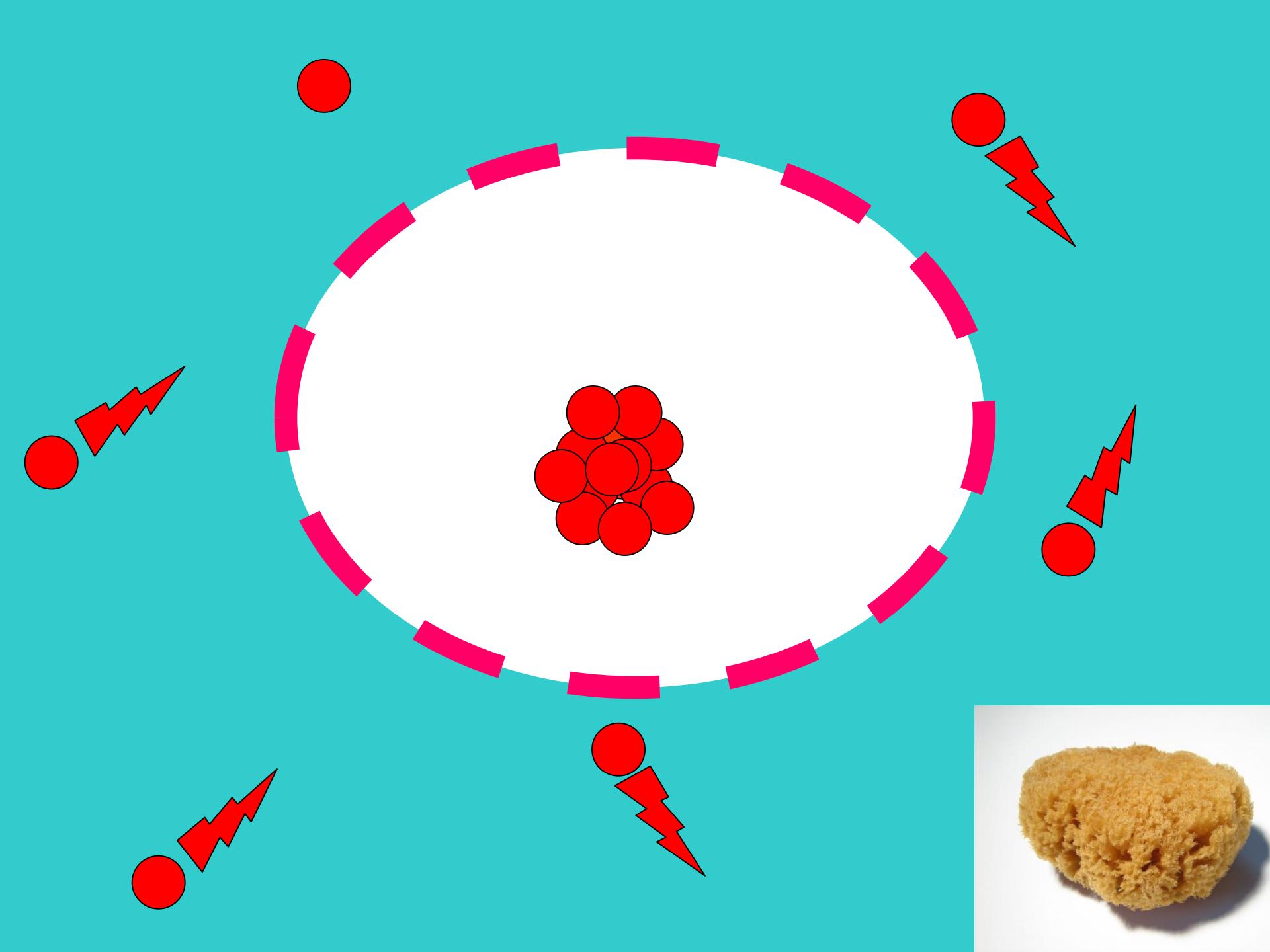


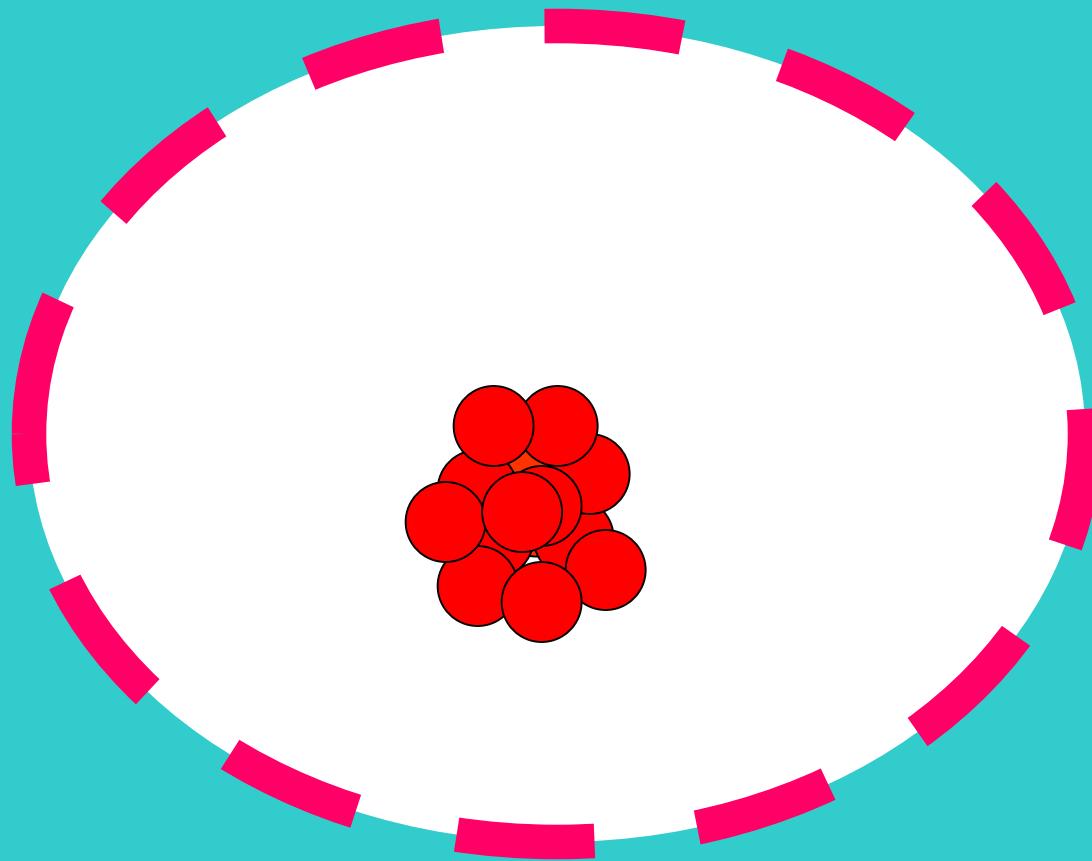
CELL

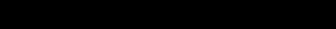
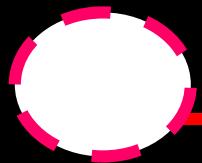
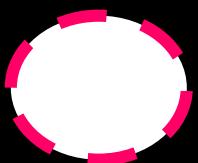


CELL



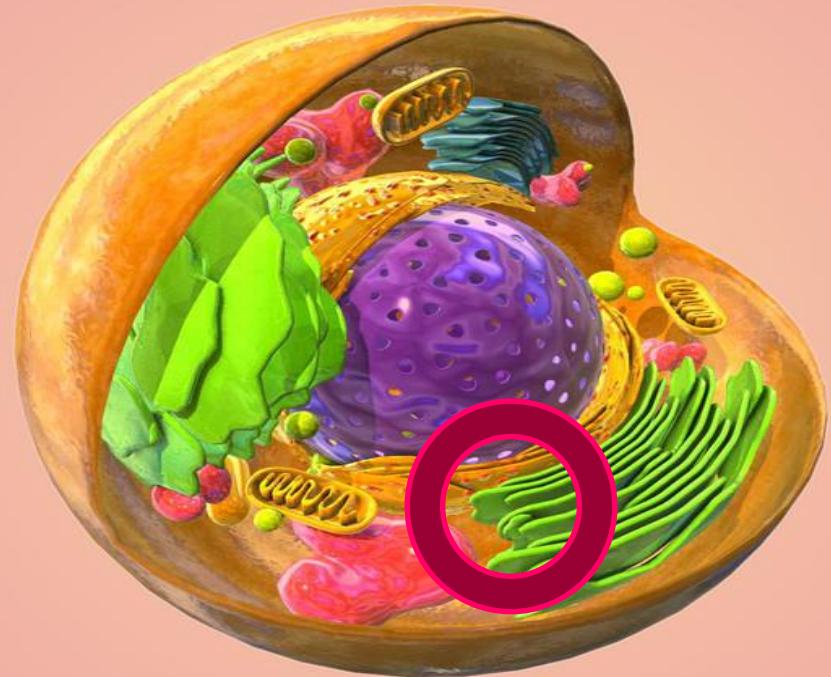








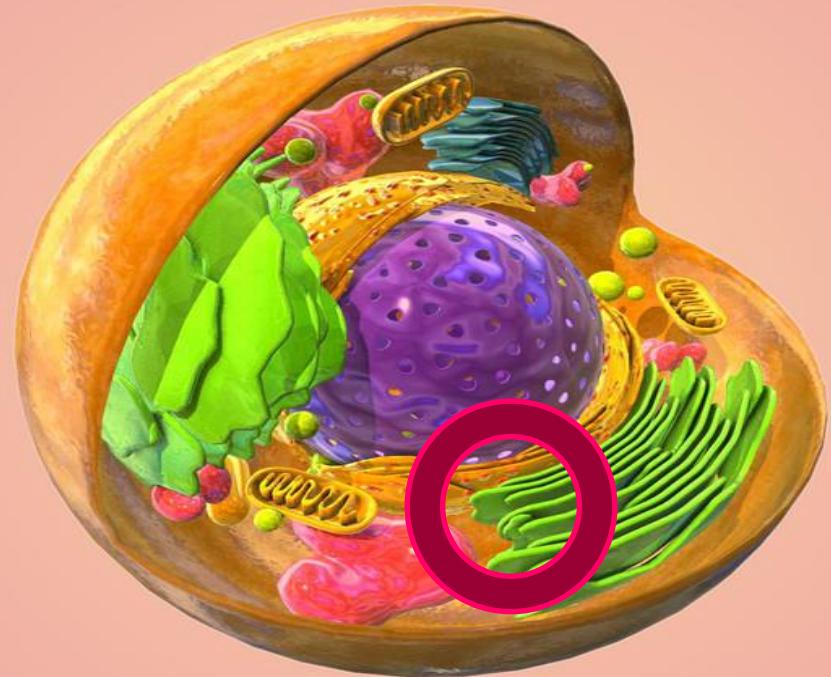
Transferrin



Ferritin



Transferrin



Ferritin

Iron metabolism

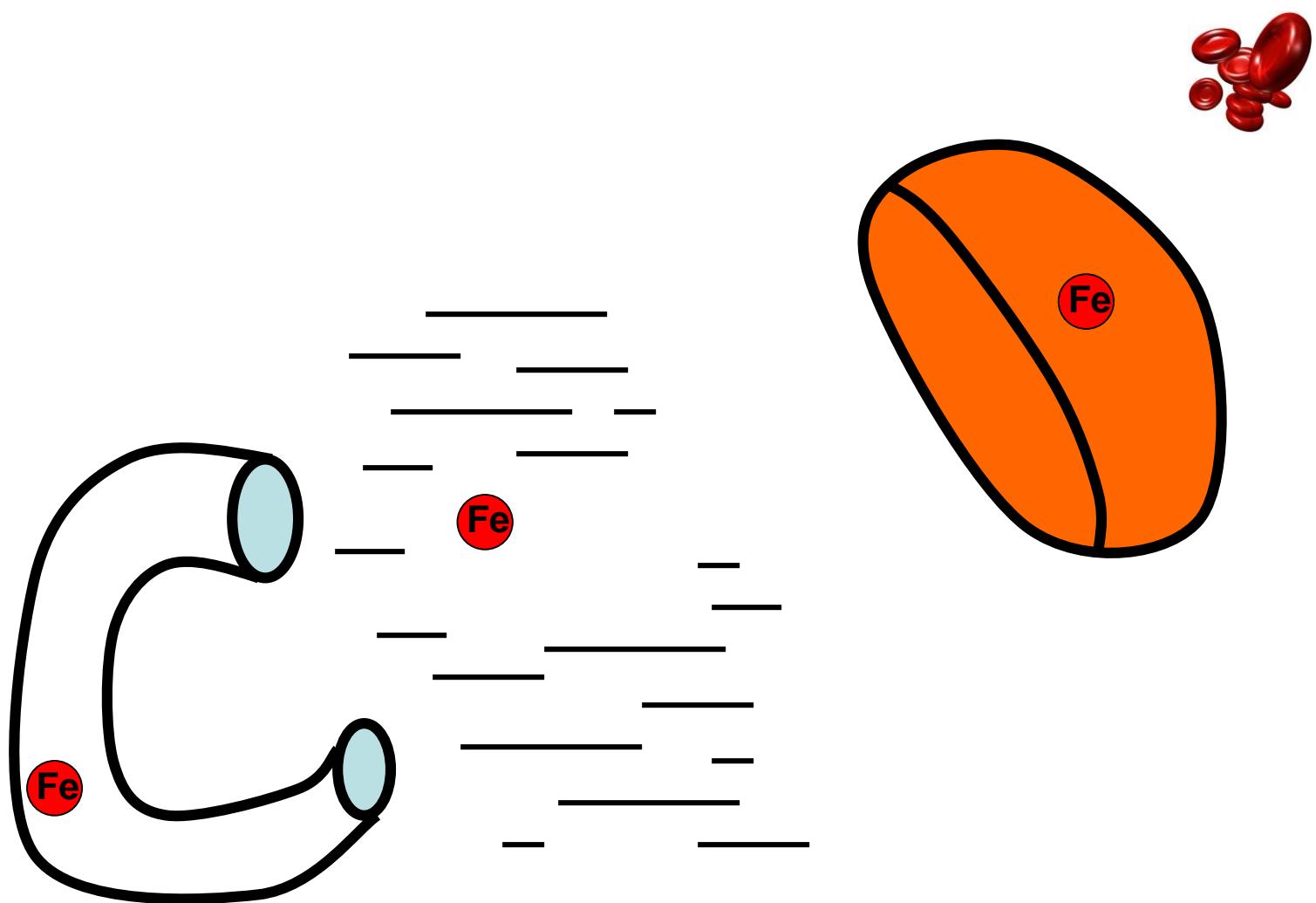
Classical background

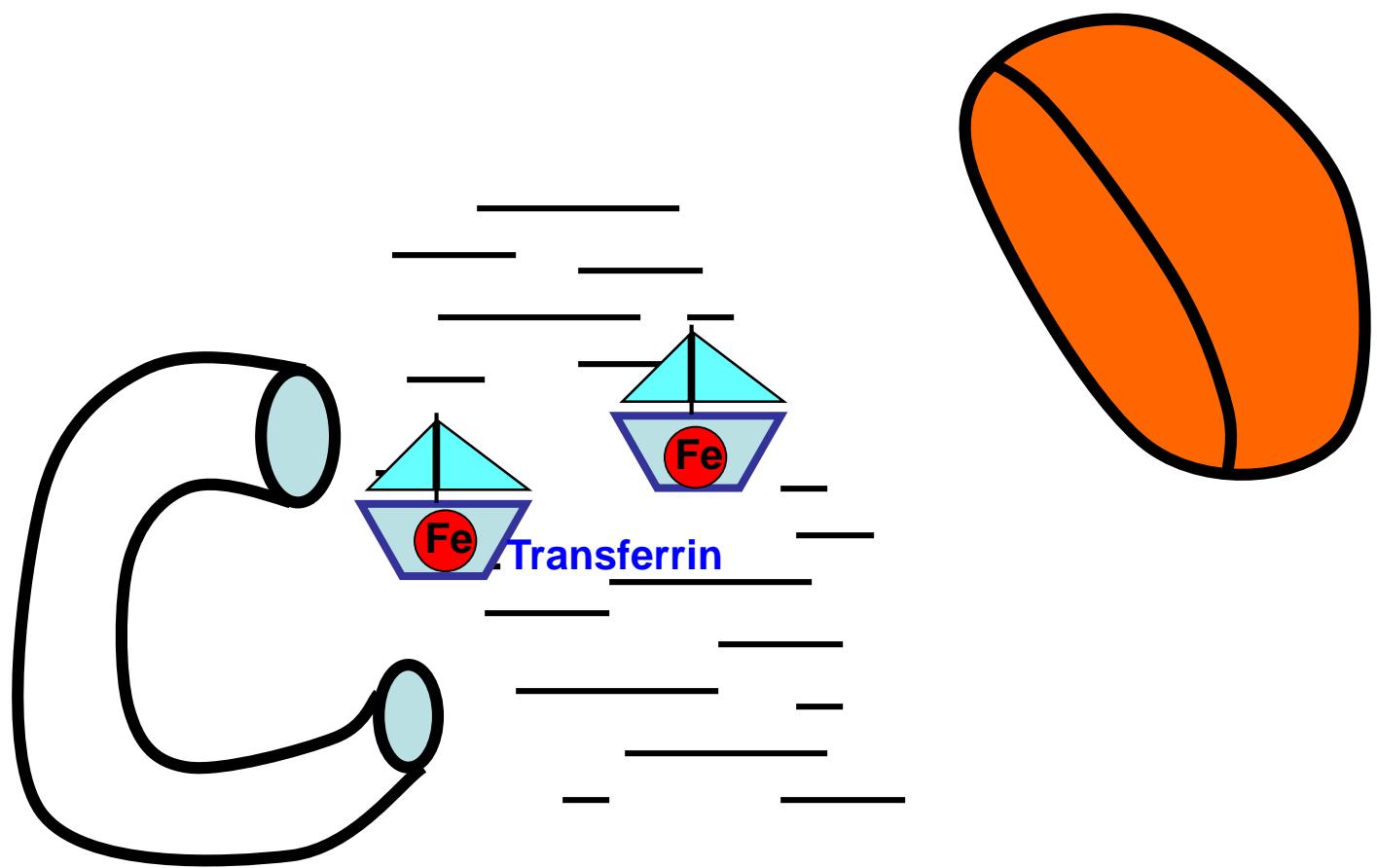
Regulation

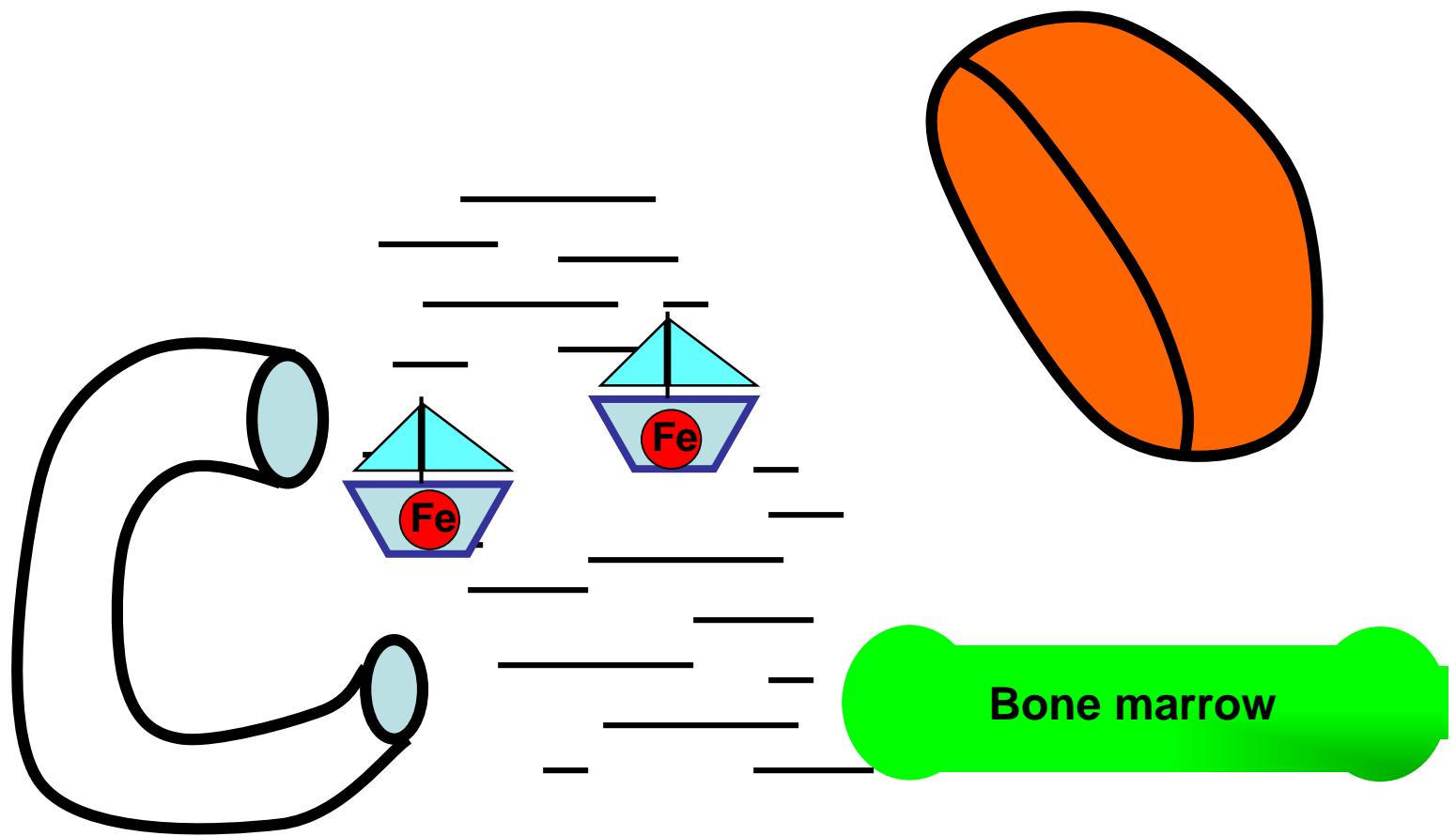
Recent advances

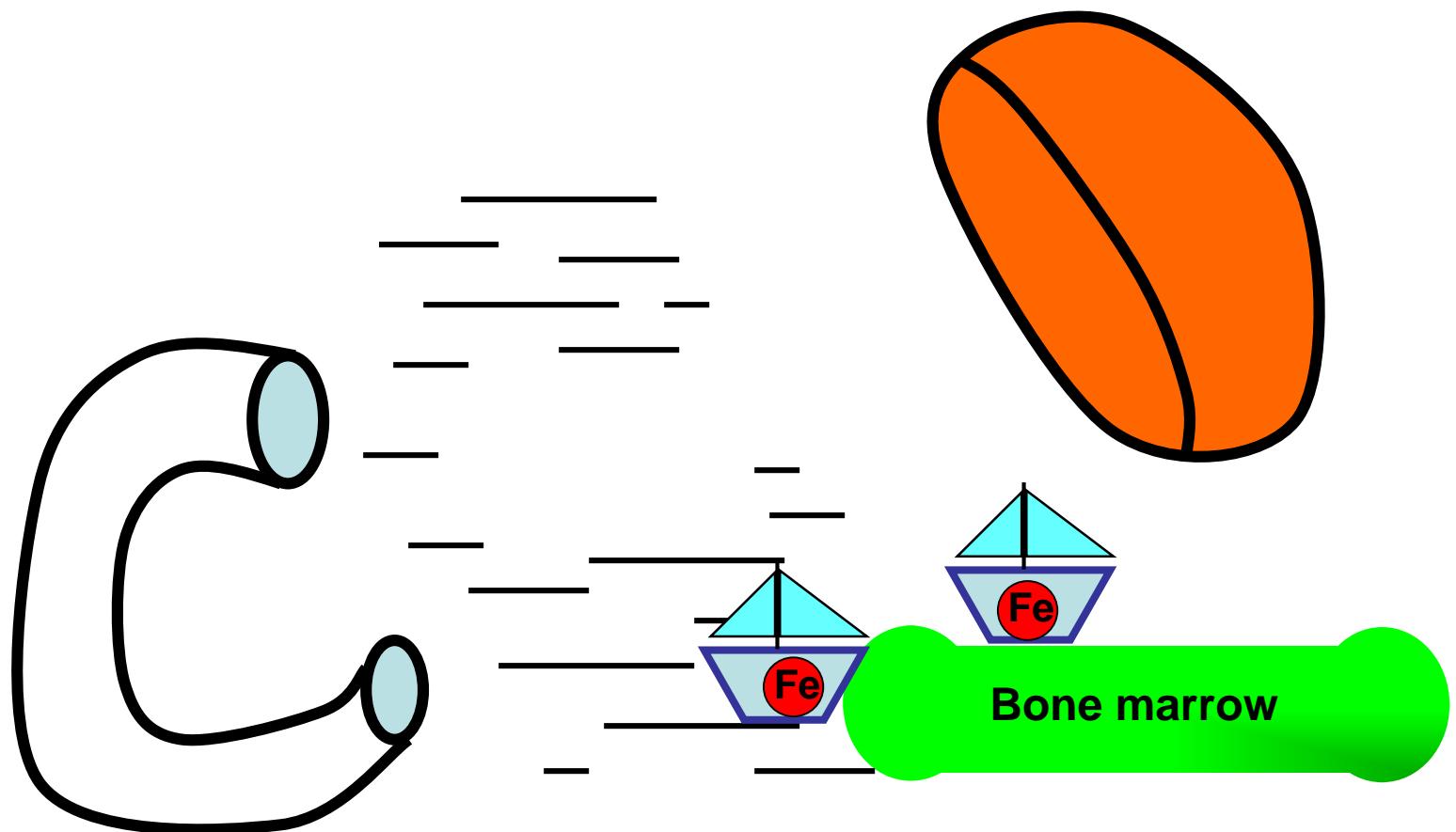
Toxicity

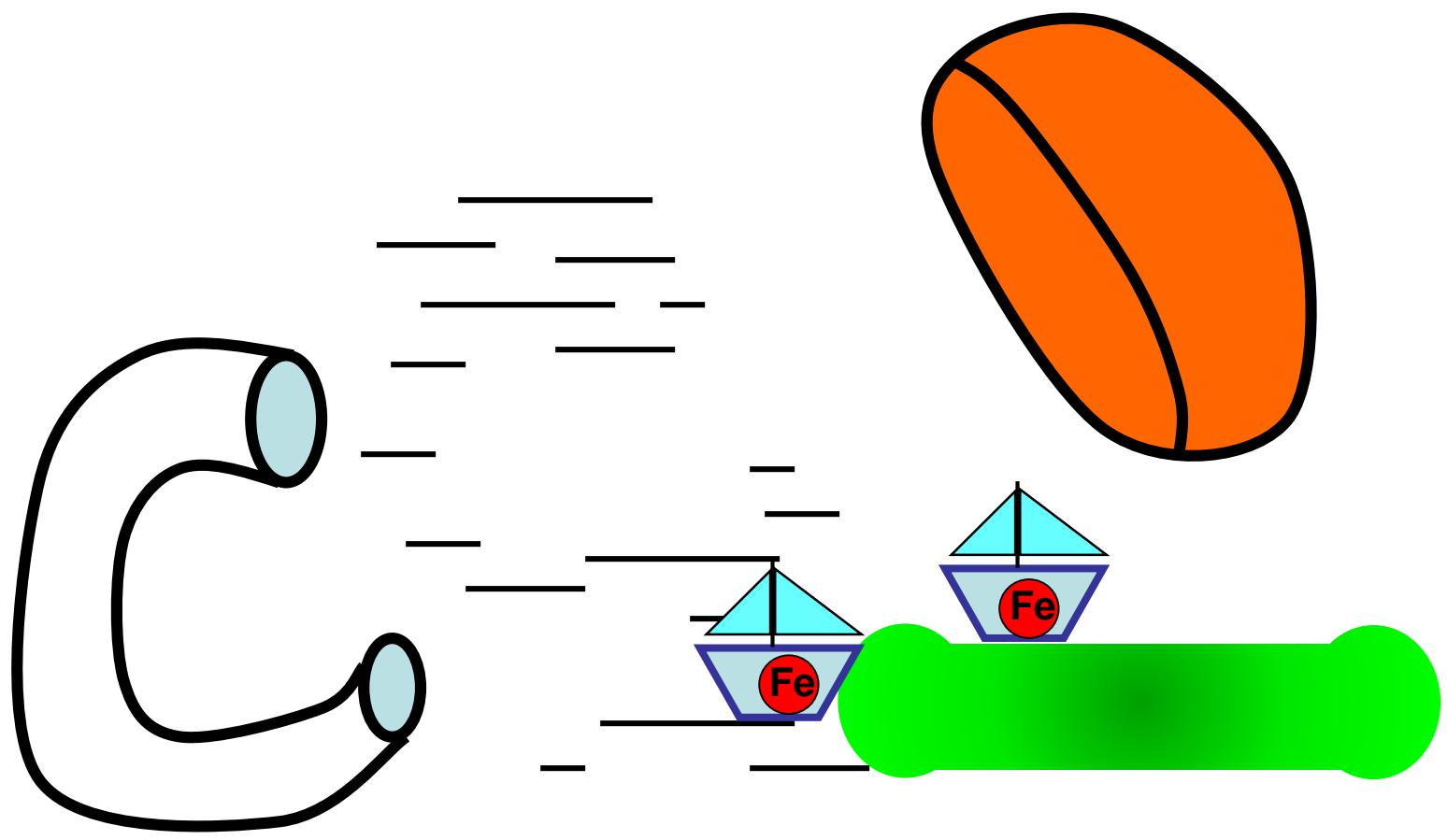
Relevance to transfusion and haemovigilance

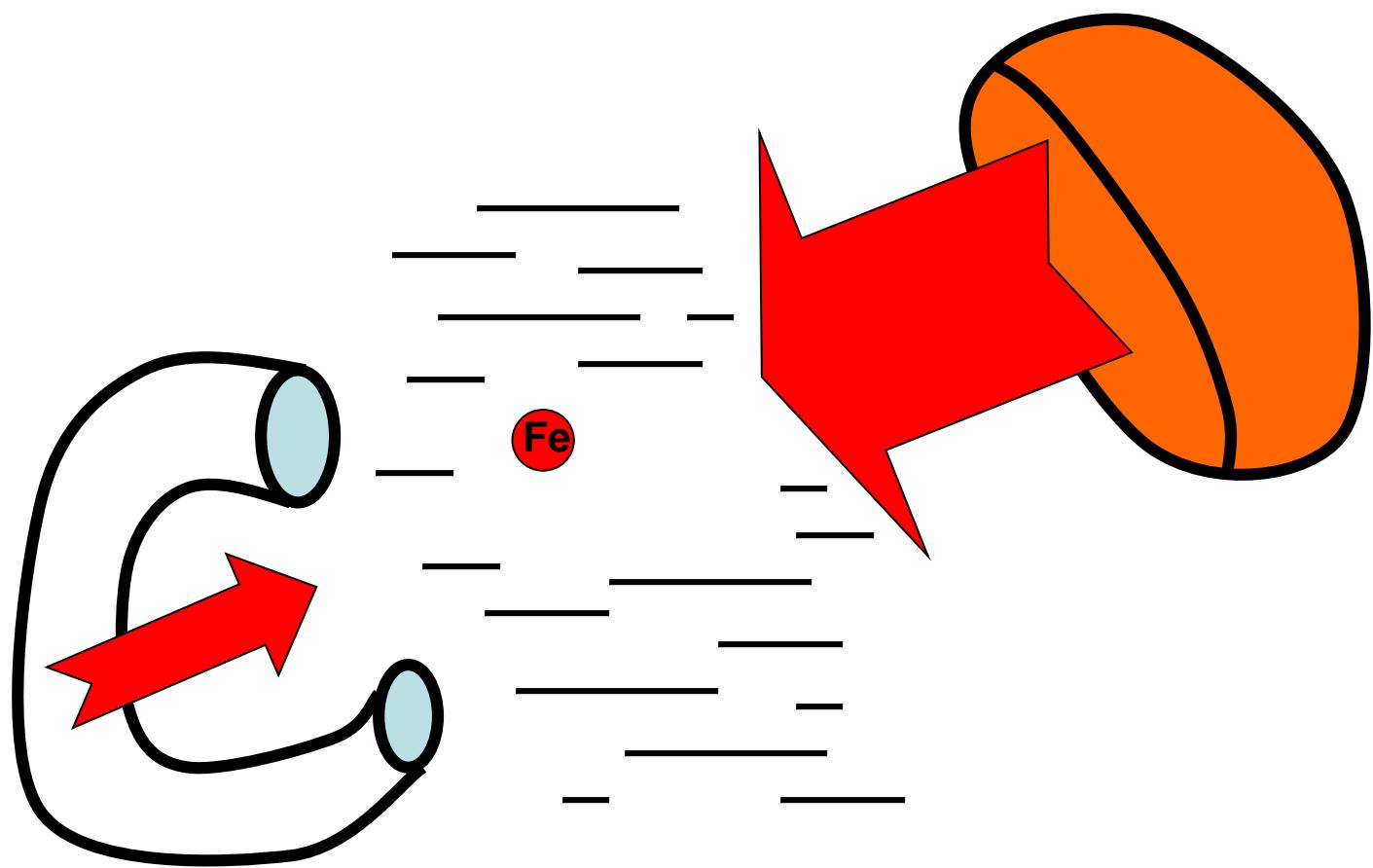








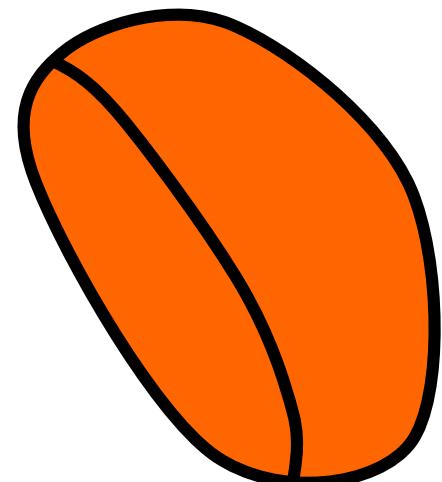
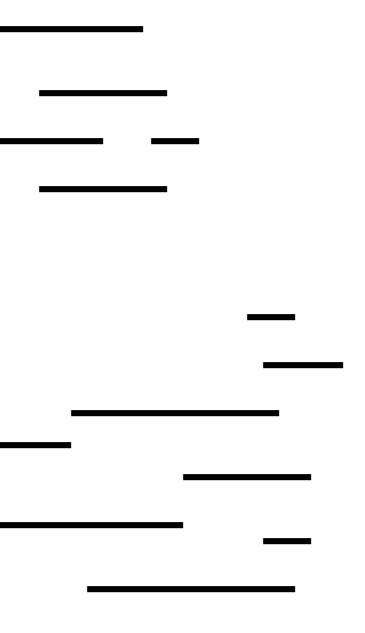
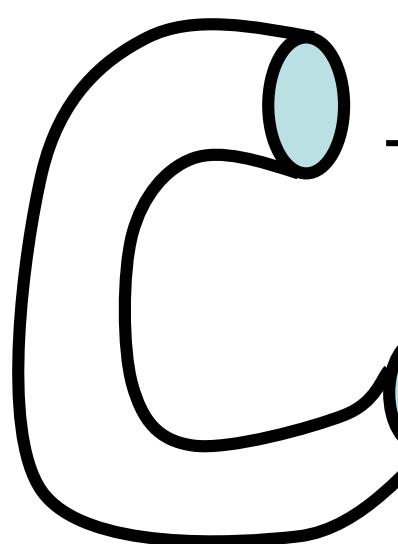


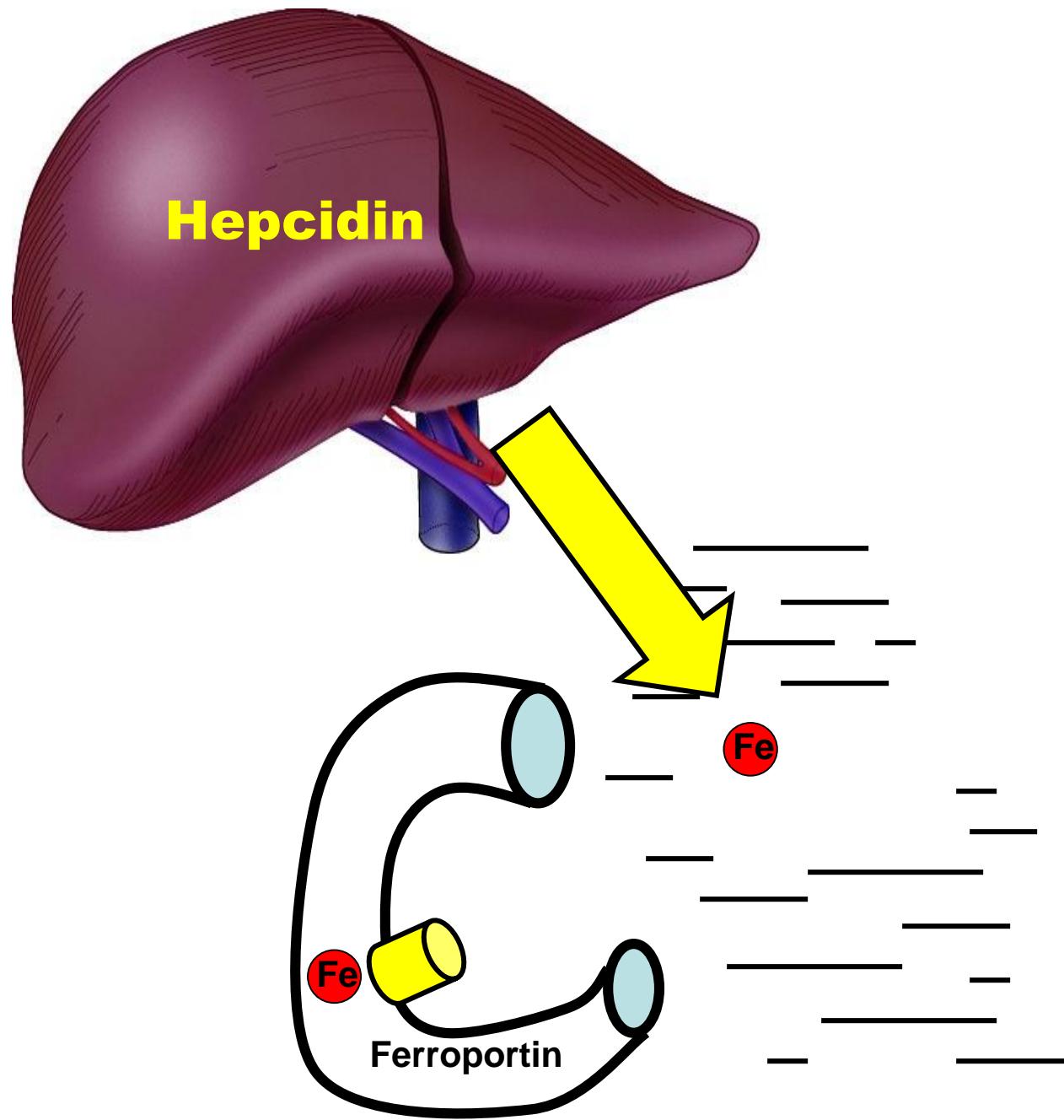


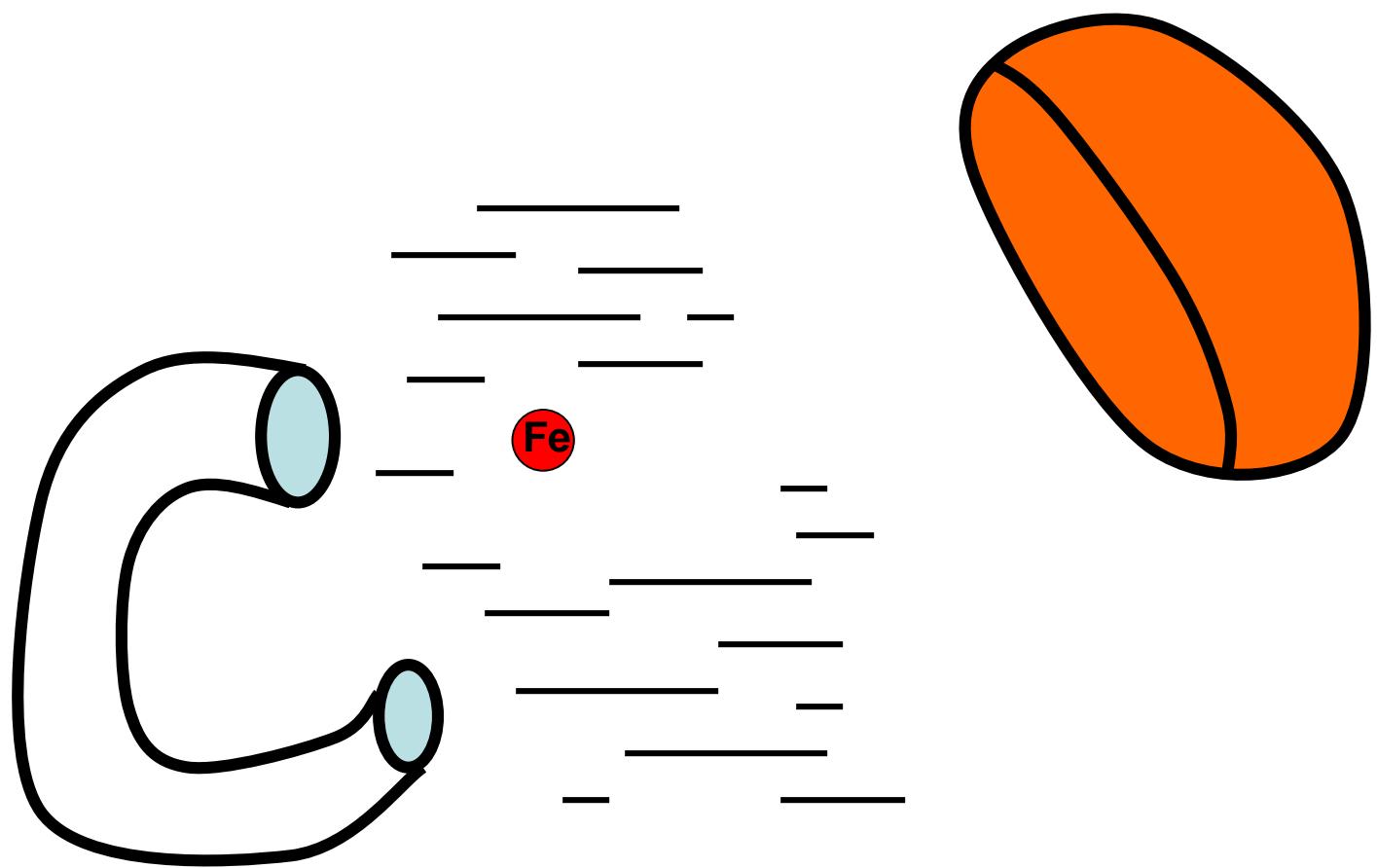


Hepcidin

An anatomical illustration of a dark red liver. A blue and red tube-like structure representing the hepatic artery and portal vein enters the liver from the bottom. The word "Hepcidin" is written in yellow capital letters on the upper left side of the liver.



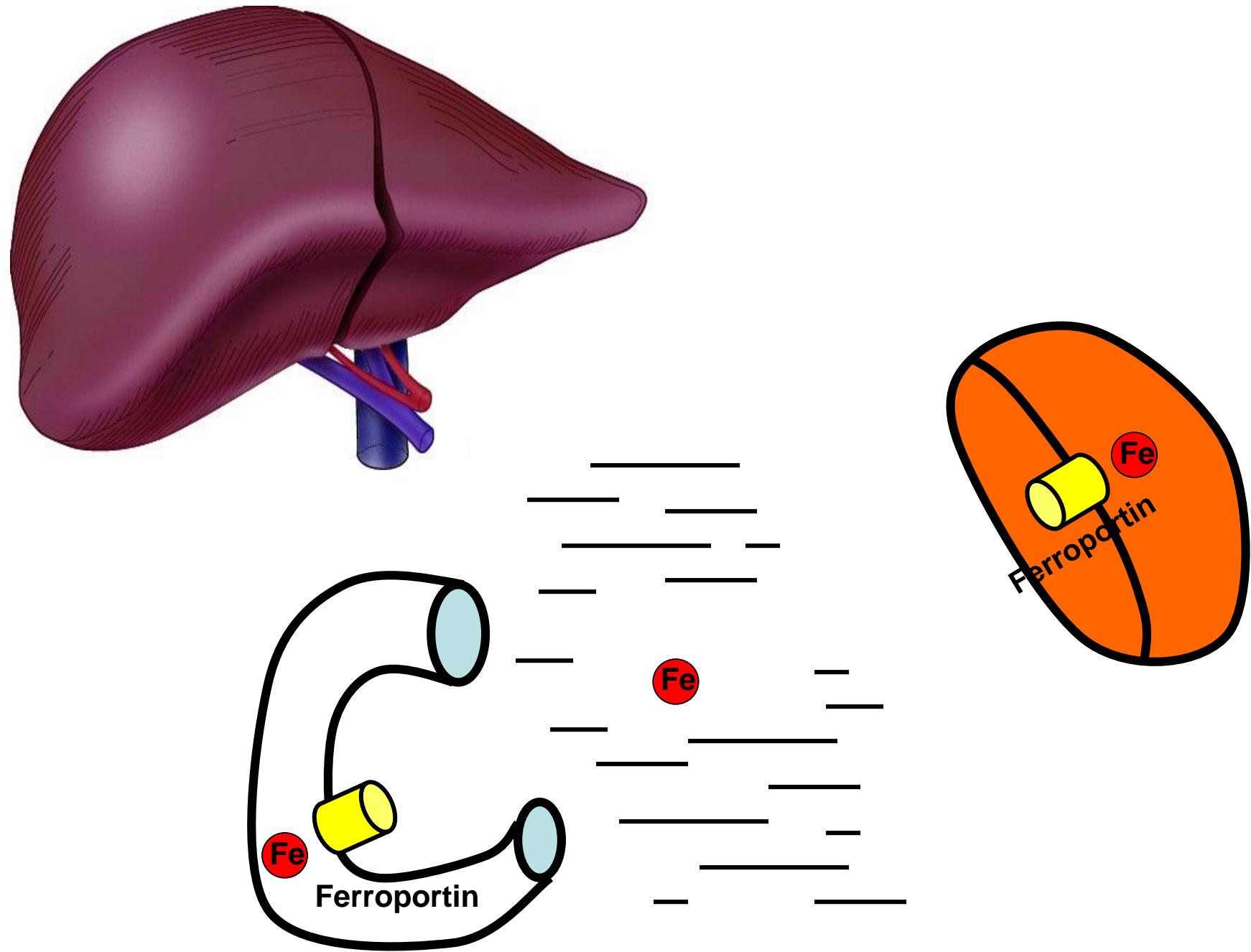


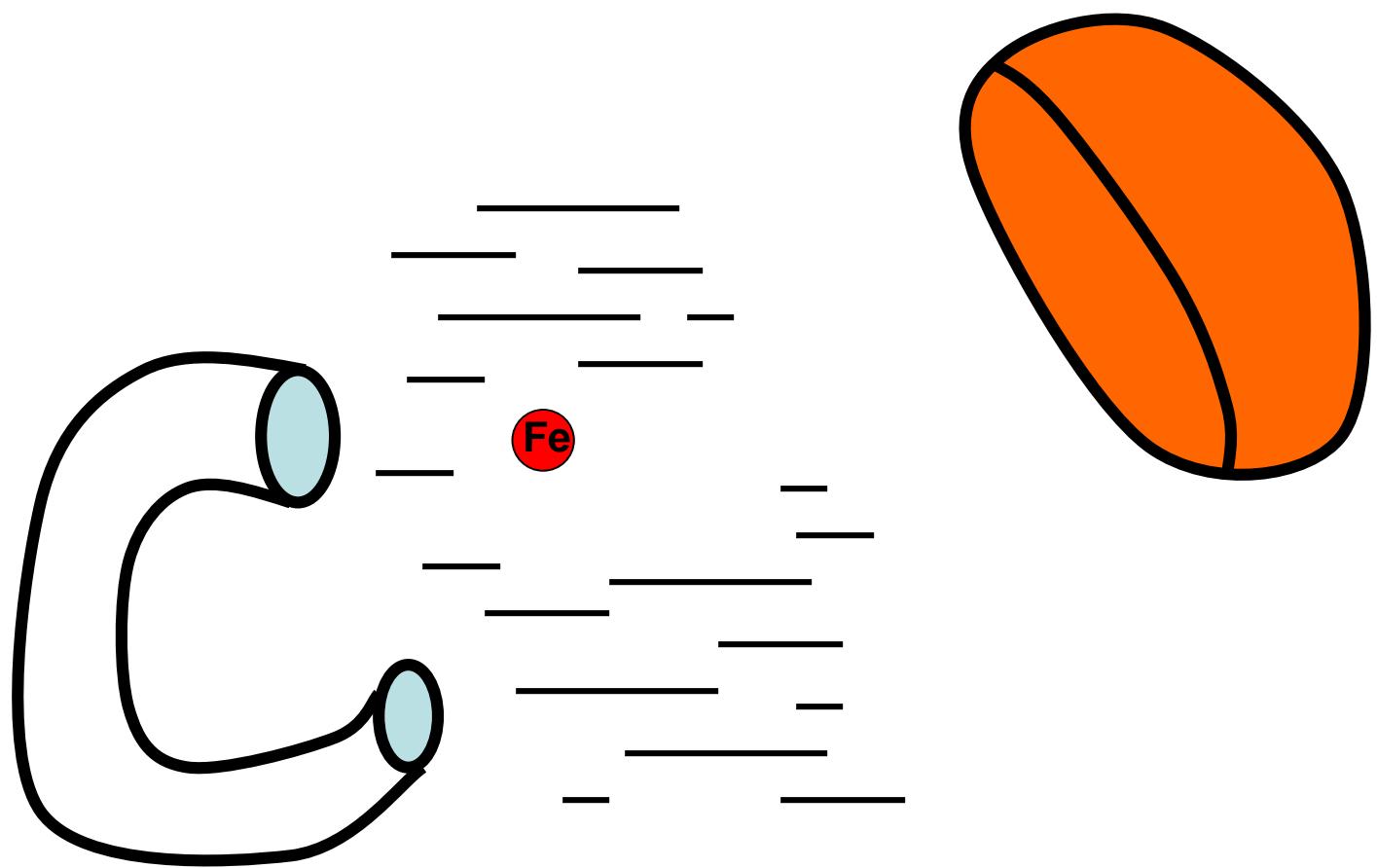


Hepcidin

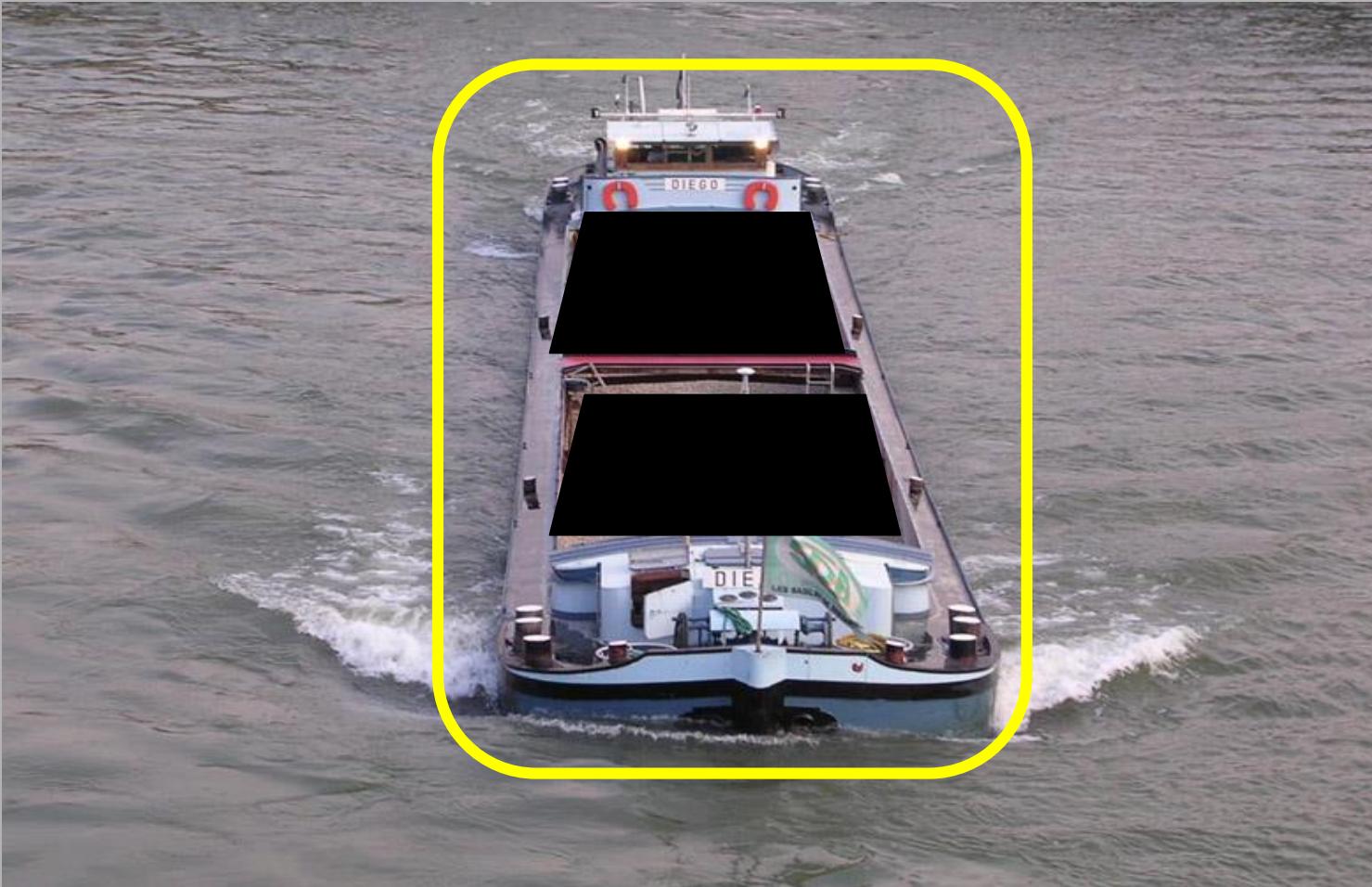
This diagram illustrates the mechanism of hepcidin in regulating iron homeostasis. At the top left, a detailed illustration of a liver is shown with the word "Hepcidin" written in yellow text. A large yellow arrow points downwards from the liver towards a stylized representation of a red blood cell. Inside the red blood cell, there is a red circle labeled "Fe" (iron). The path of the arrow is marked by several horizontal black dashed lines, indicating its trajectory through the extracellular space. To the right of the red blood cell, there is a large orange oval, likely representing a macrophage or another type of cell involved in iron storage.

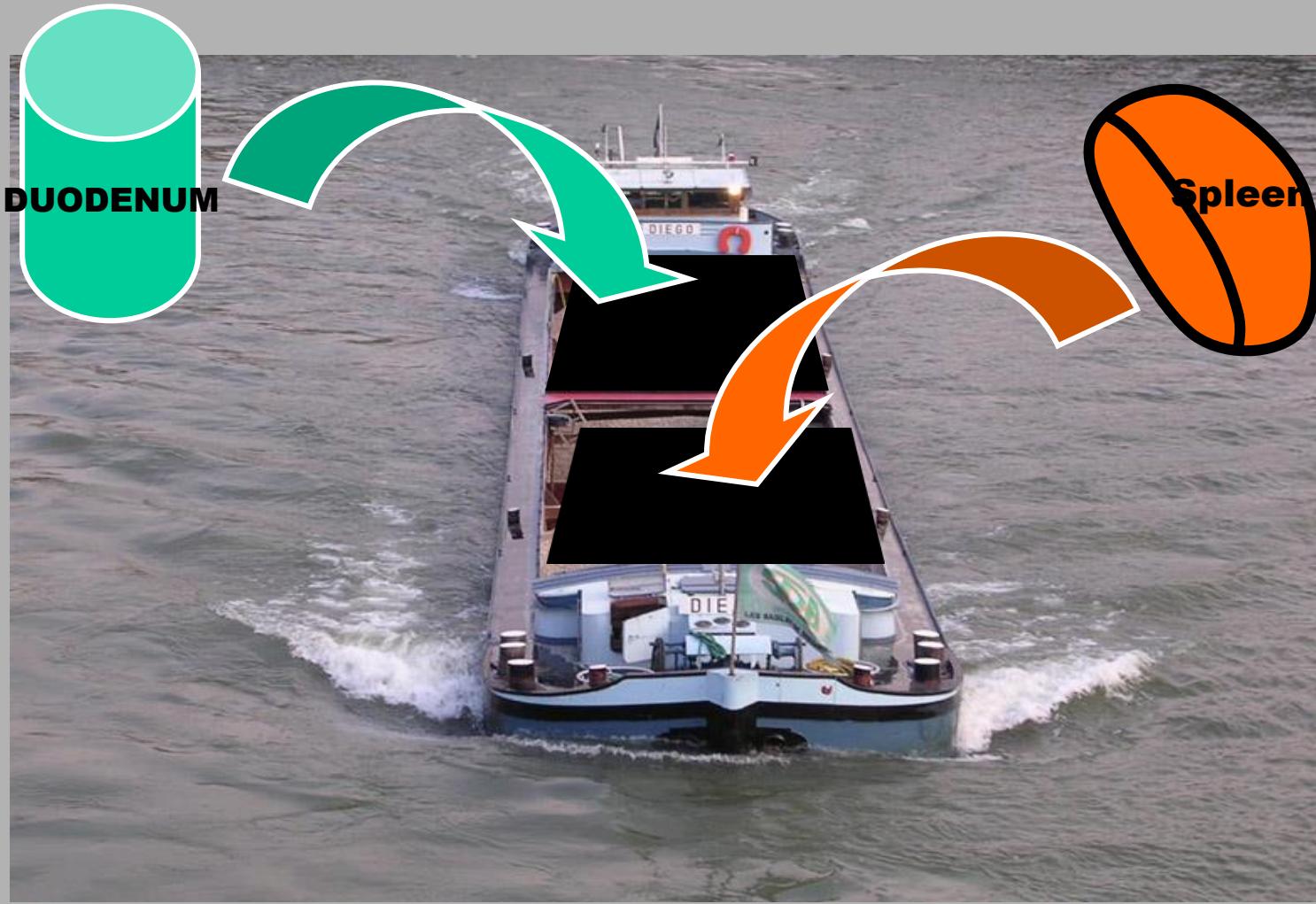
Fe





Transferrin

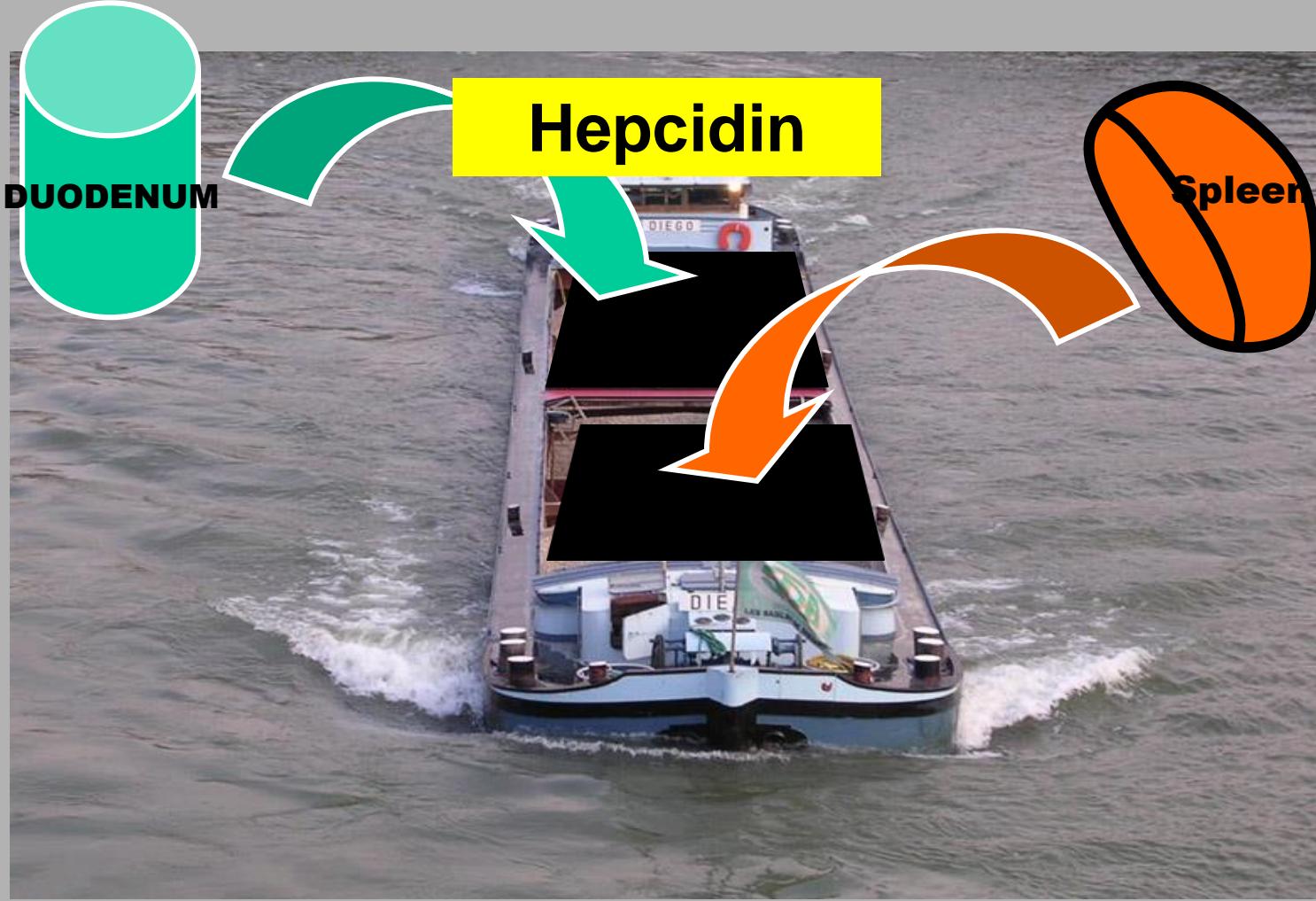




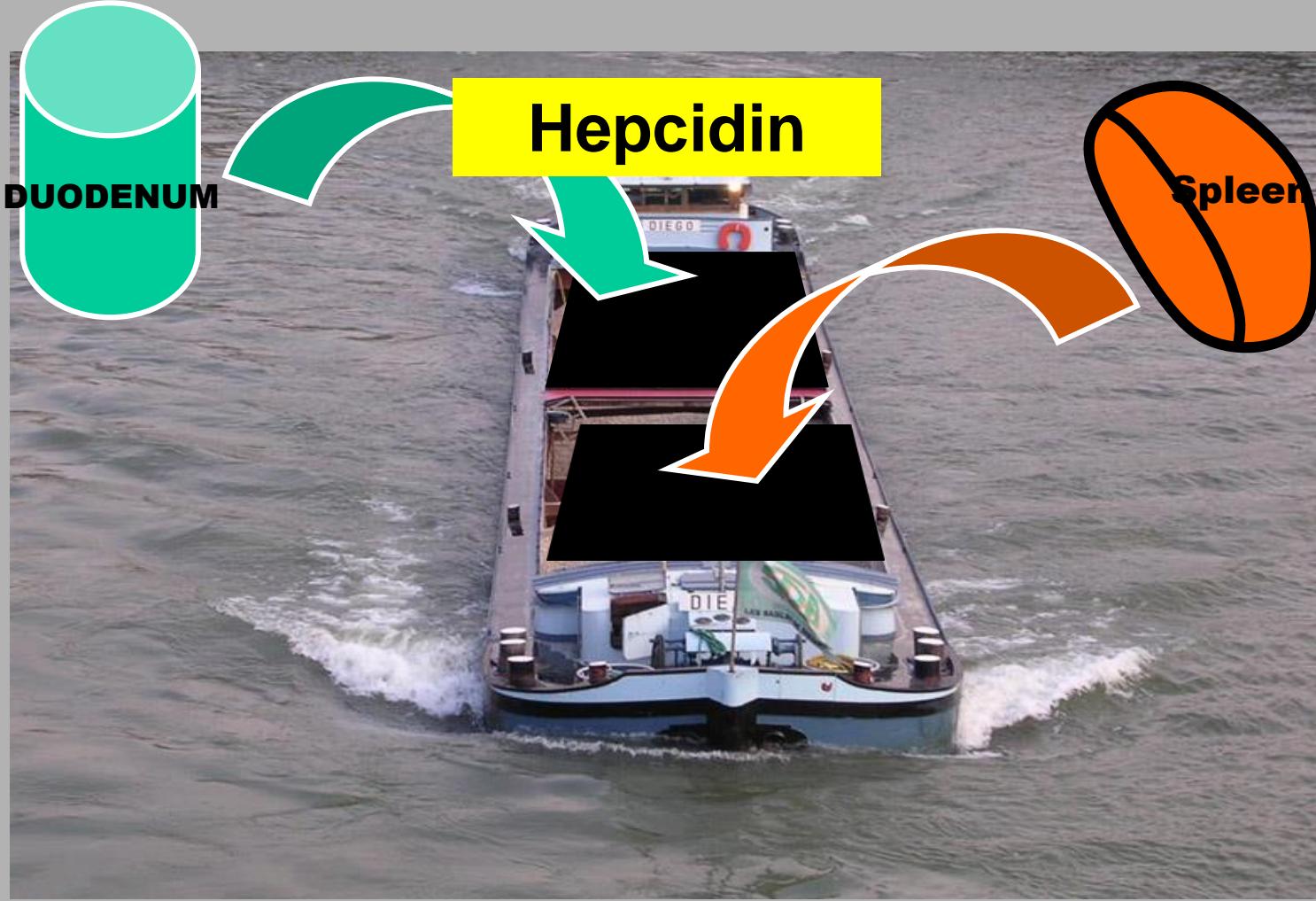
Transferrin saturation (%)



Transferrin saturation < 45%



Transferrin saturation (%)



Transferrin saturation (%)

Iron metabolism

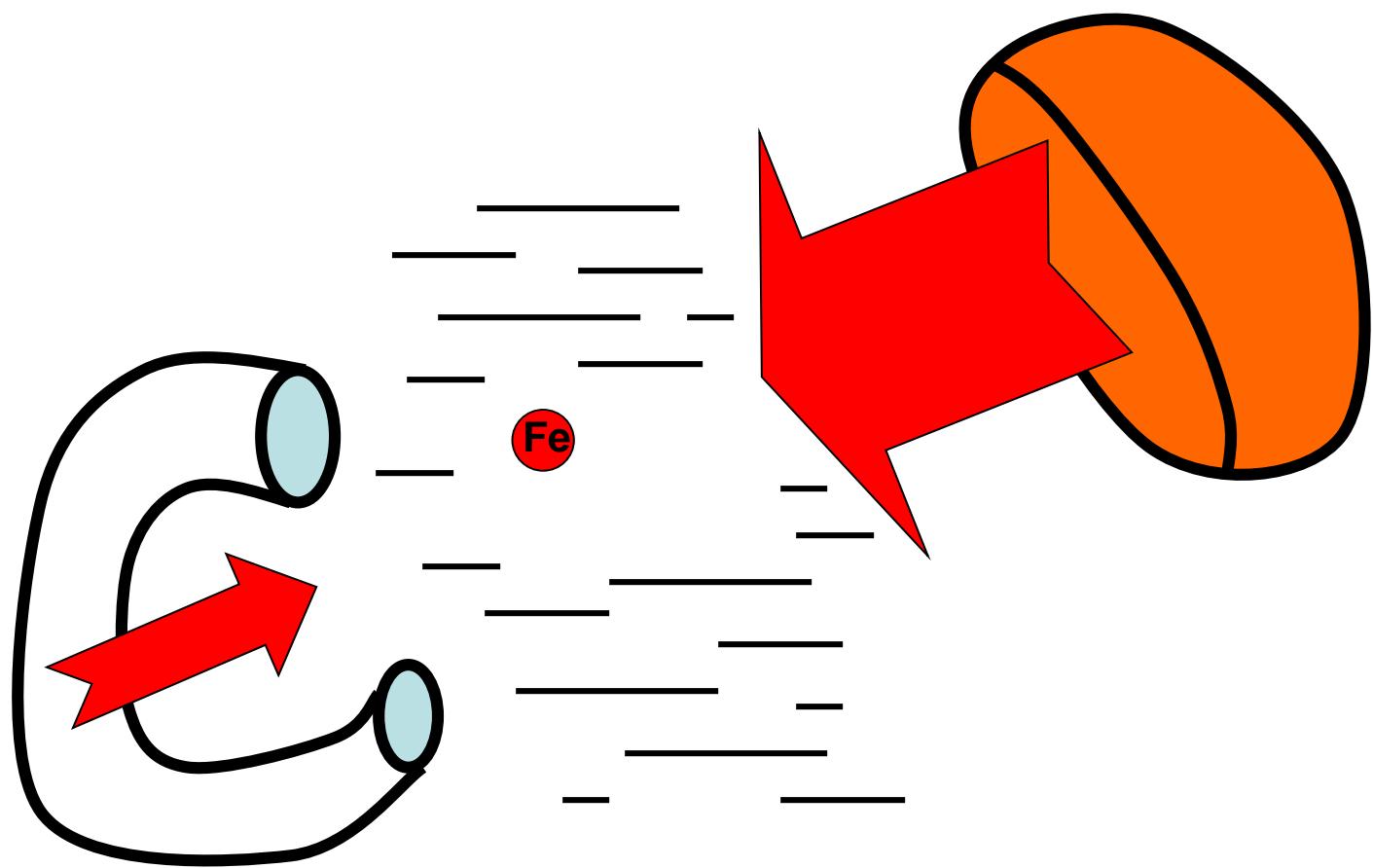
Classical background

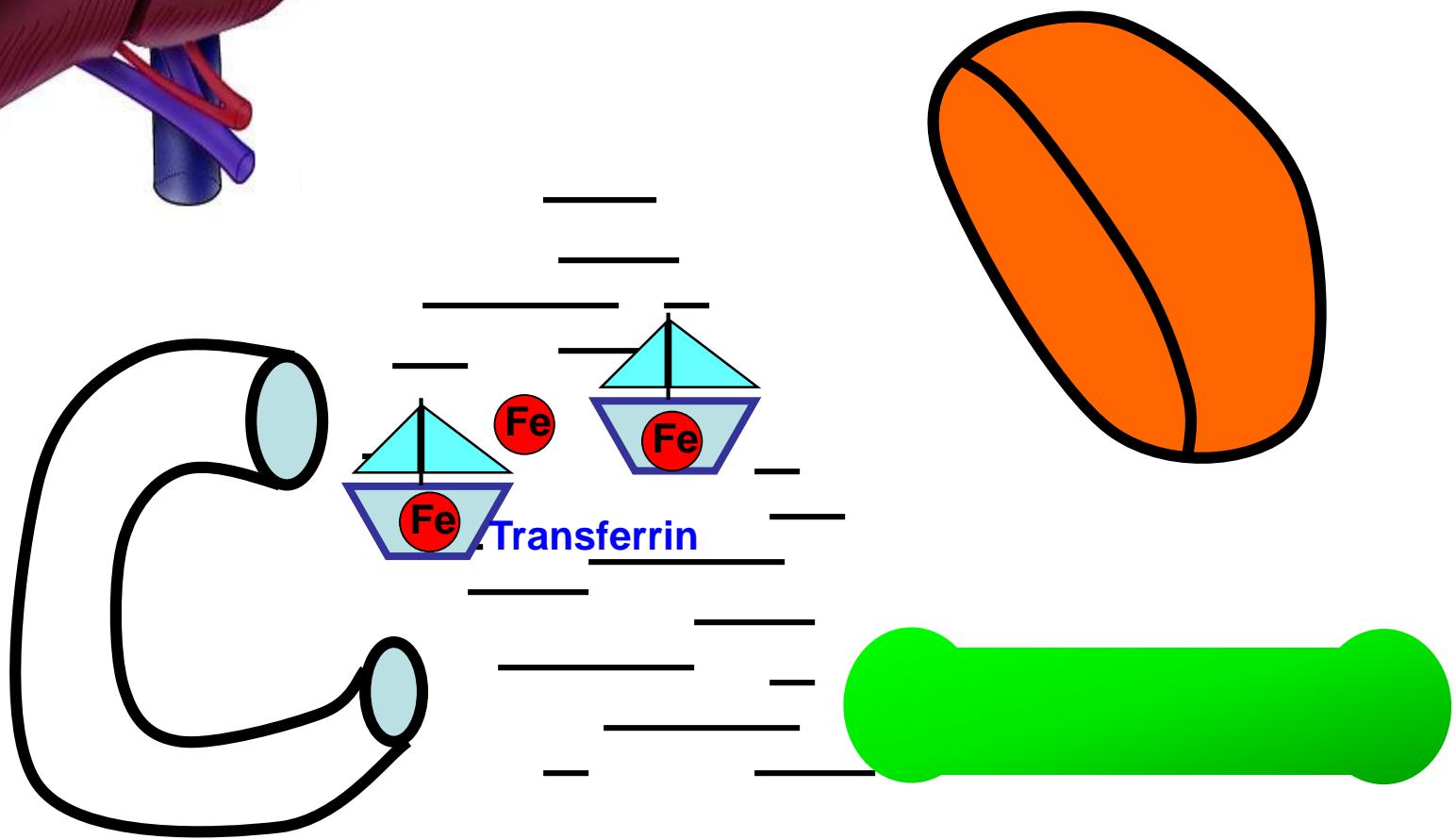
Regulation

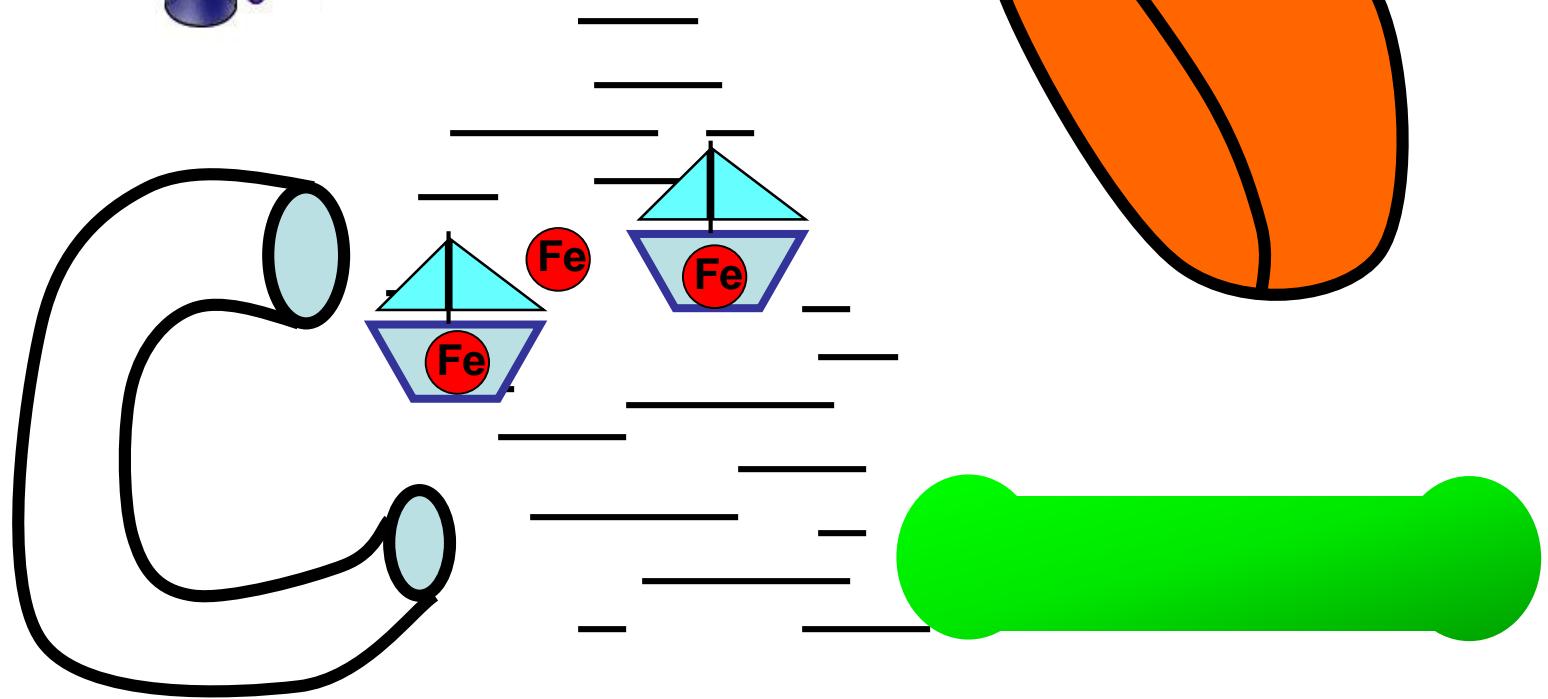
Recent advances

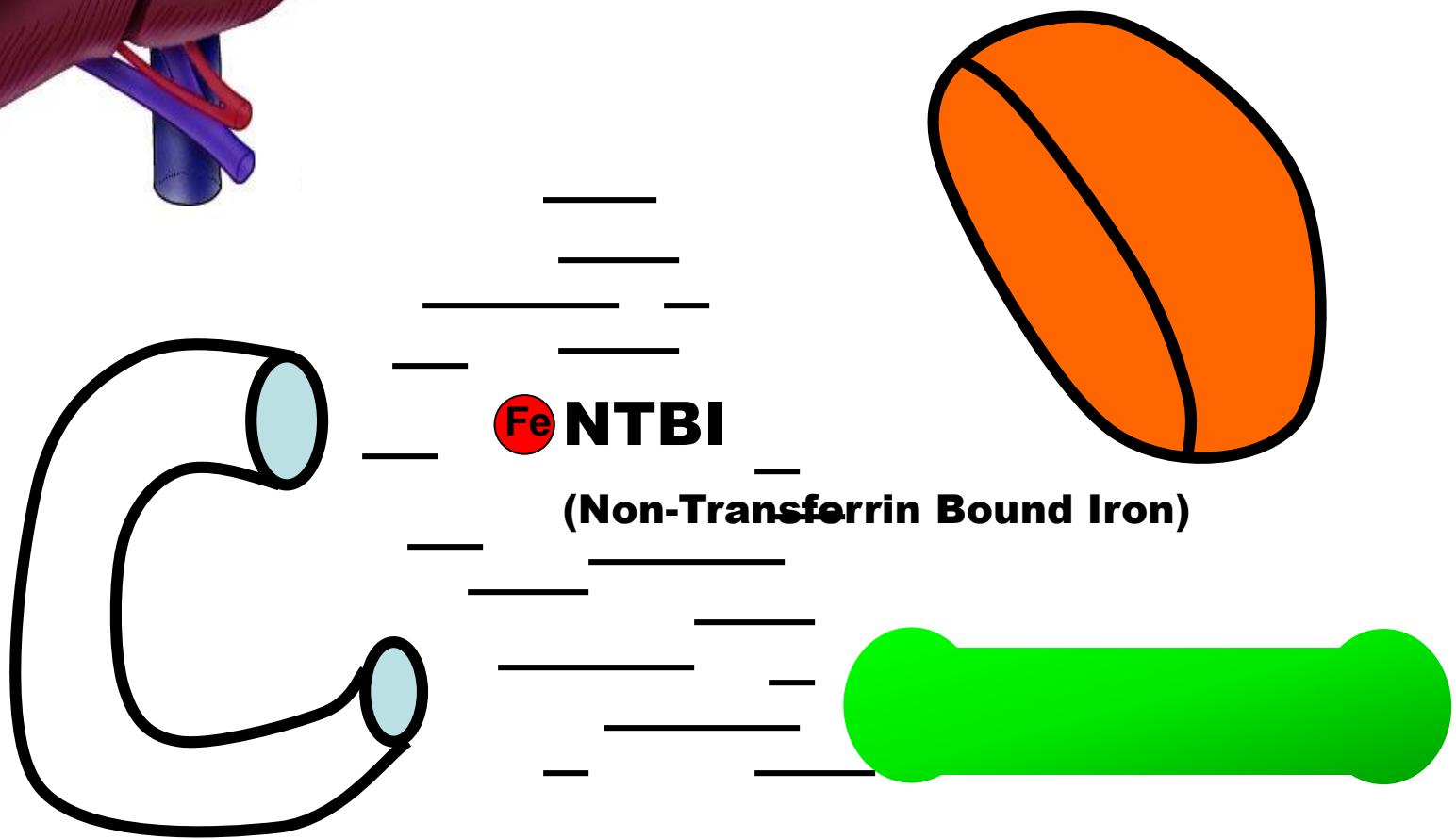
Toxicity

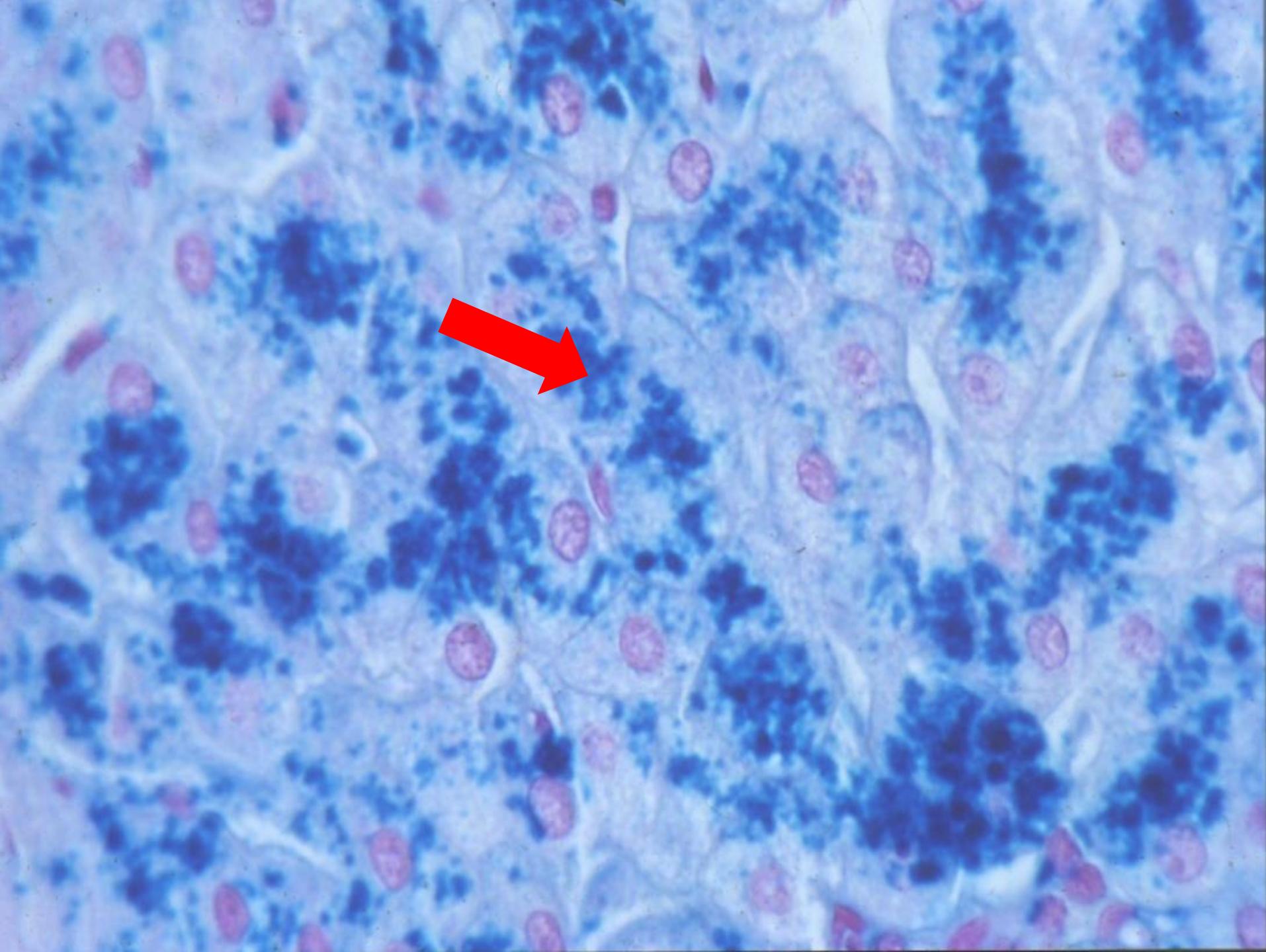
Relevance to transfusion and haemovigilance

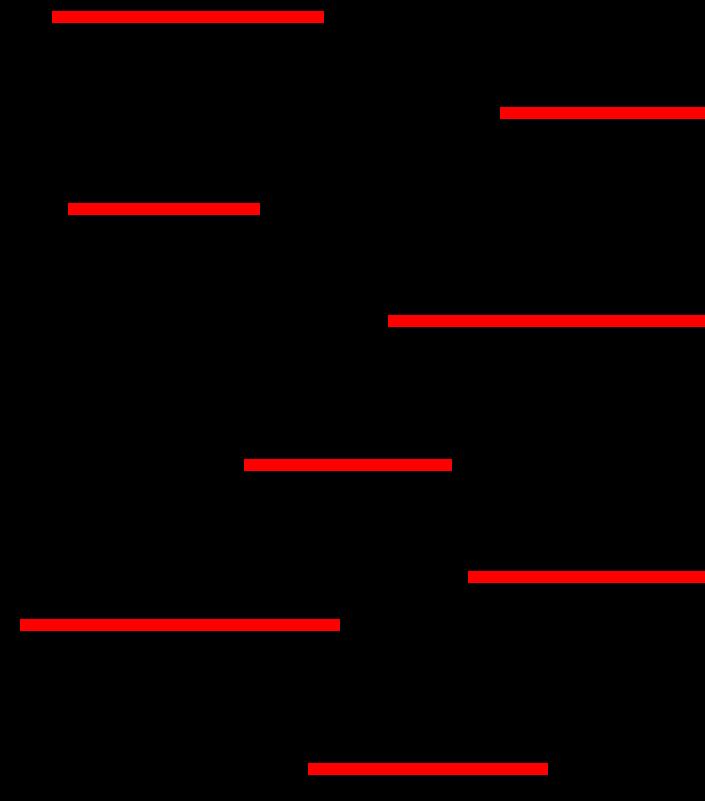
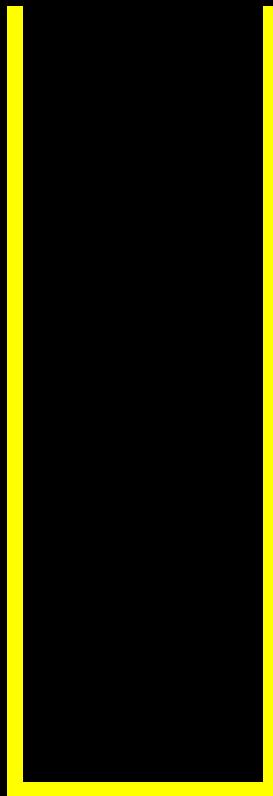


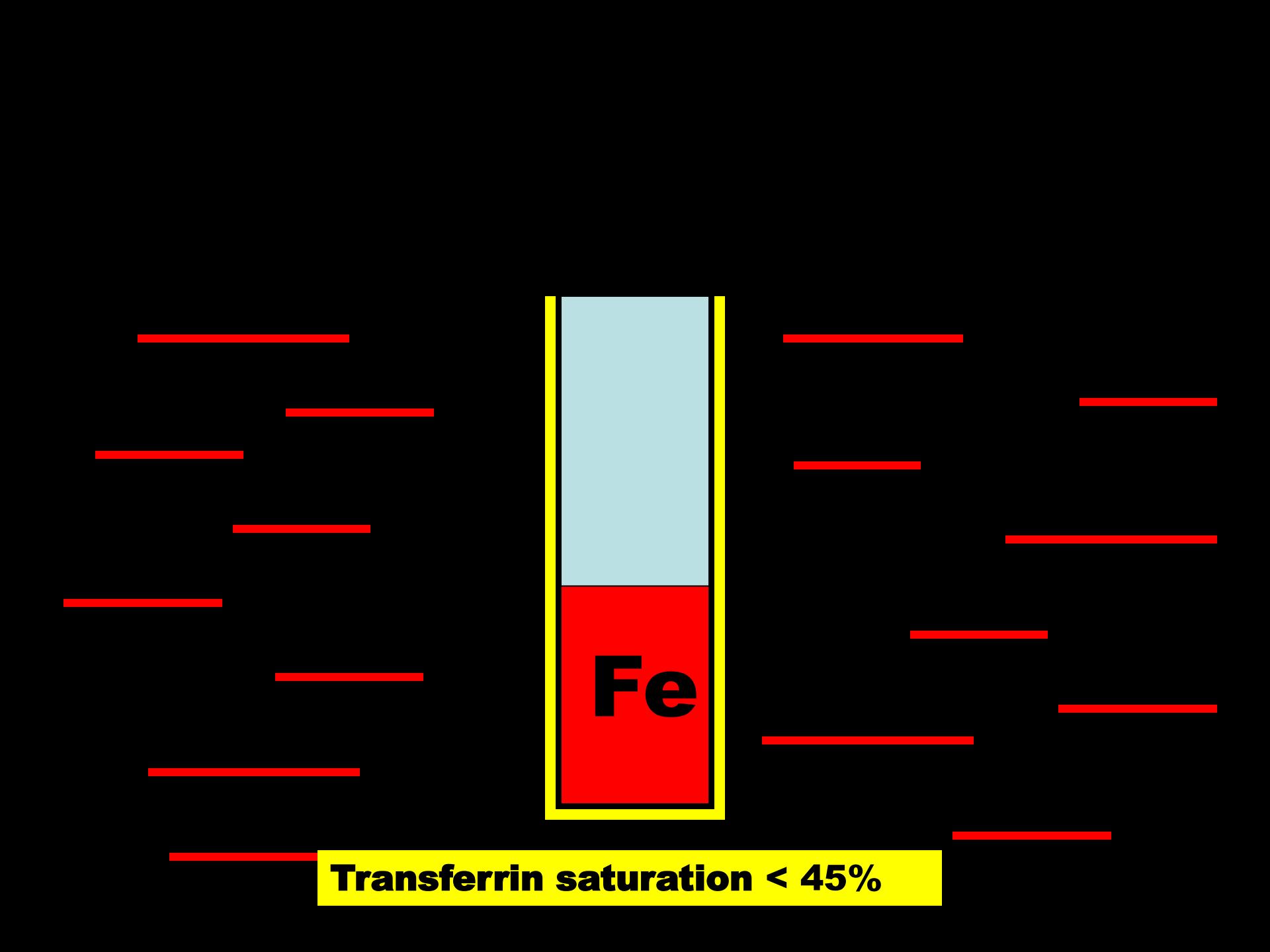










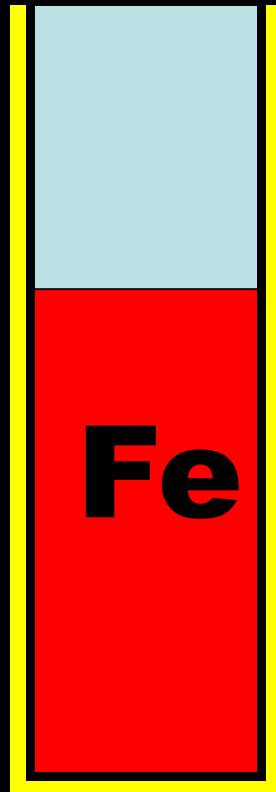


Fe

Transferrin saturation < 45%

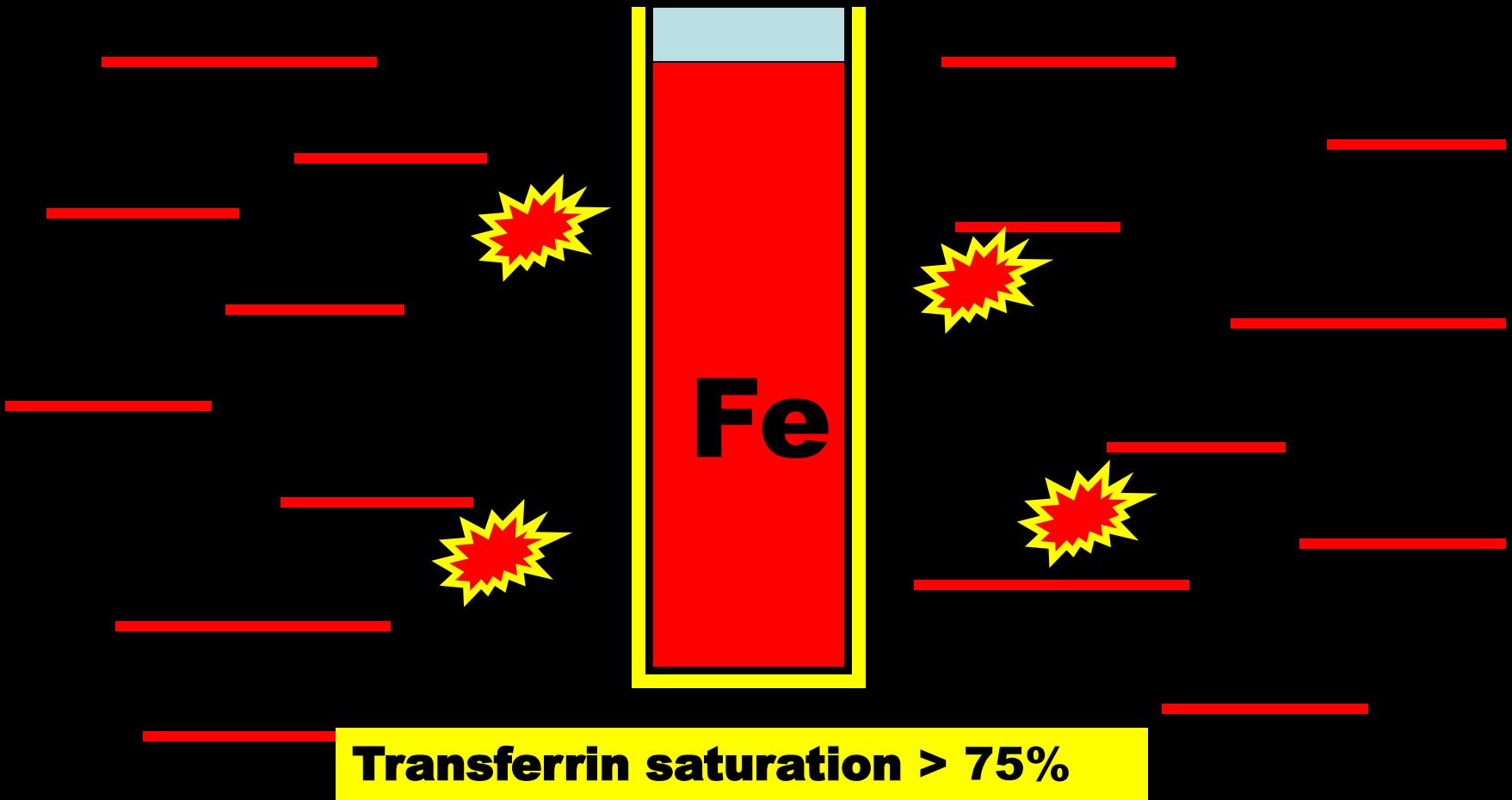
NTBI

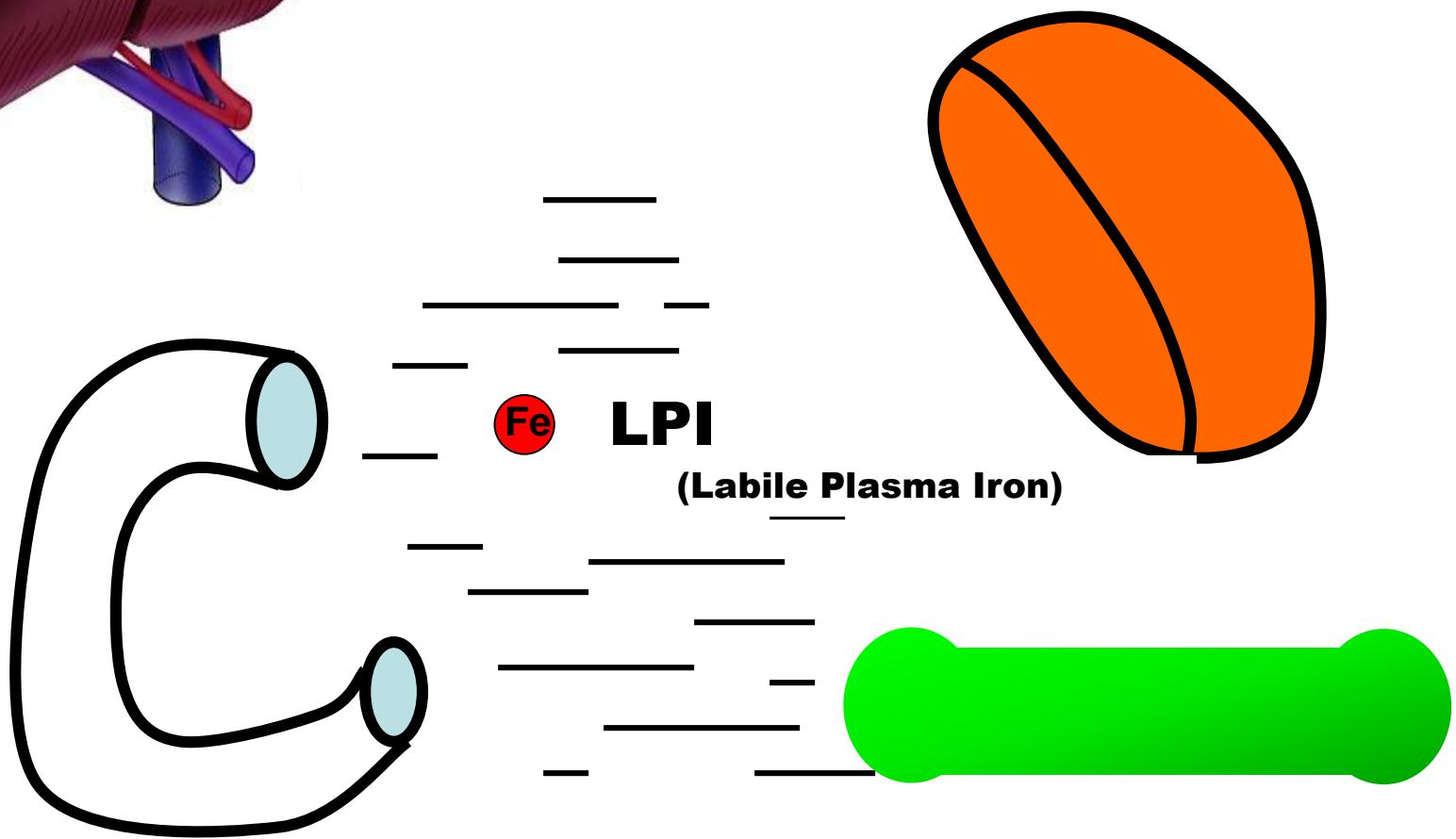
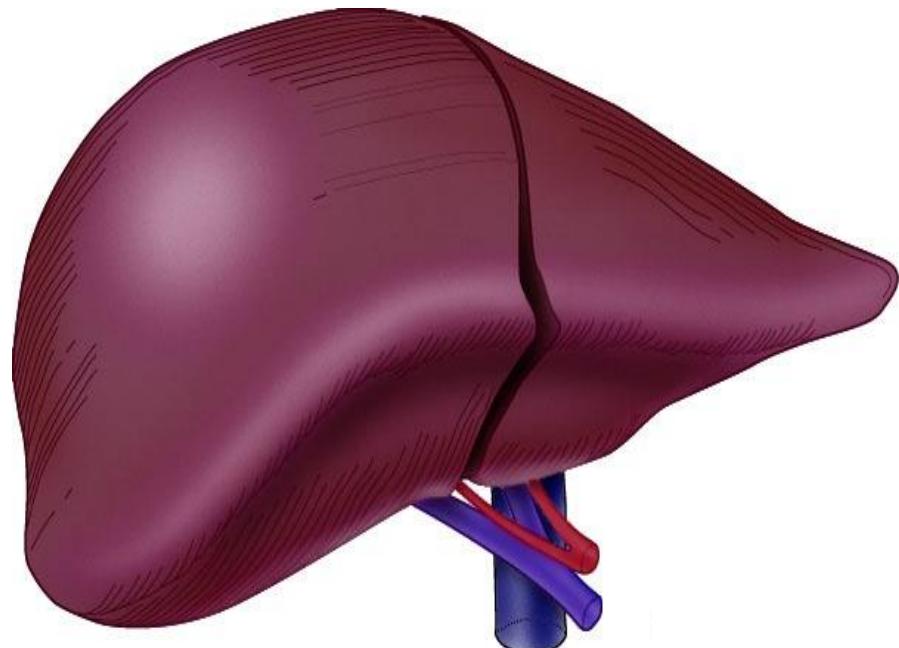
(Non-Transferrin Bound Iron)

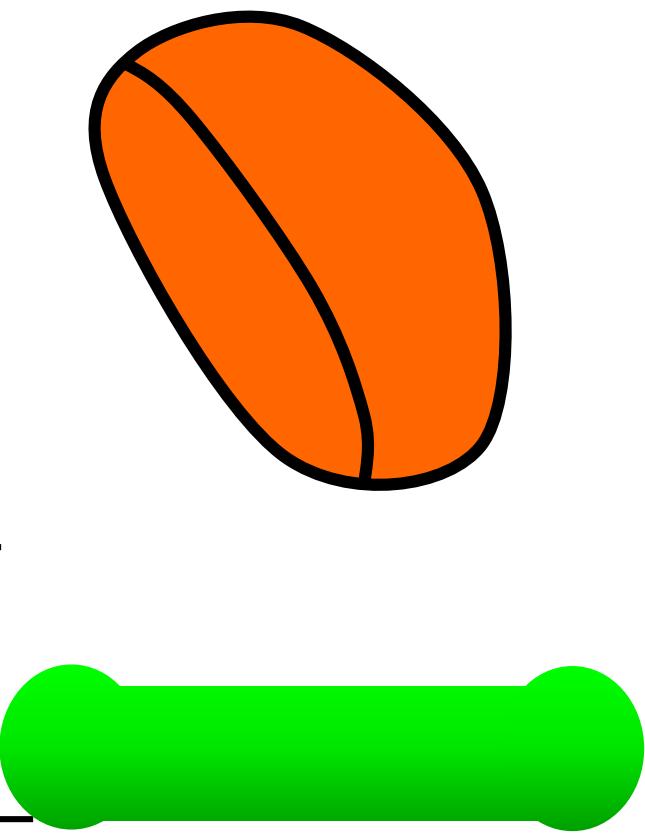
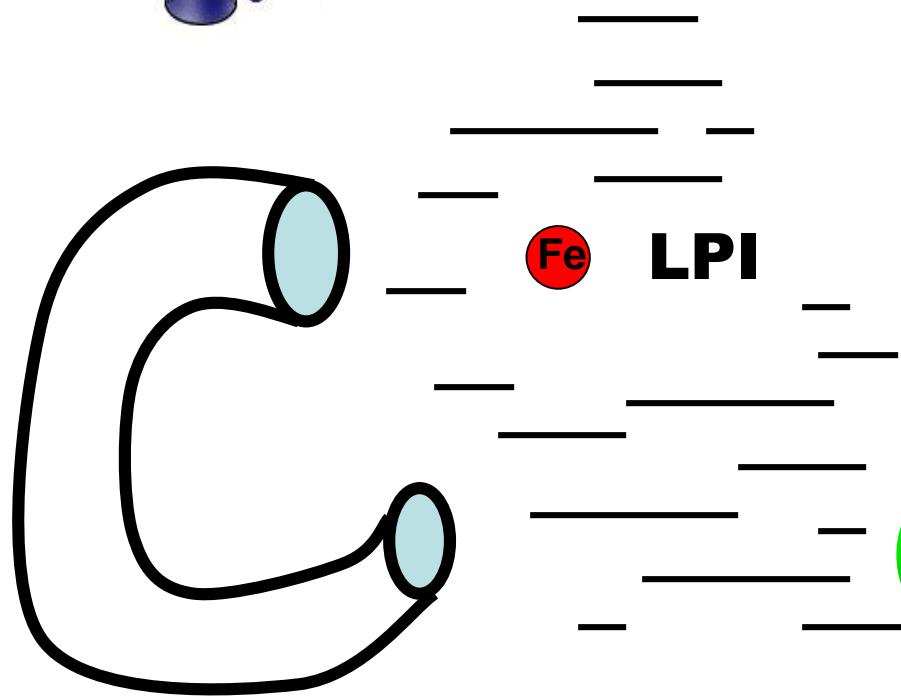
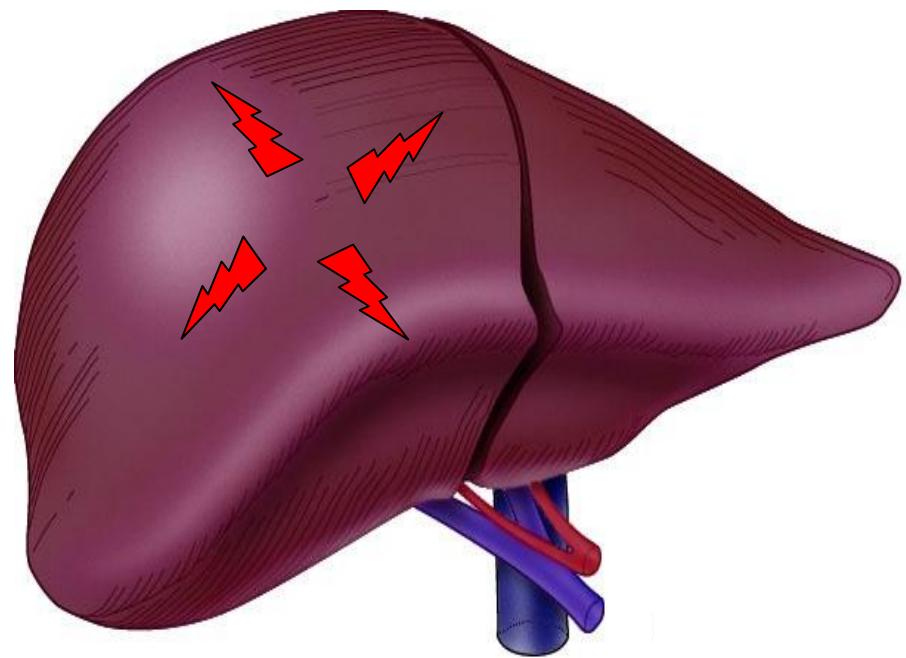


Transferrin saturation > 45%

LPI (Labile Plasma Iron)





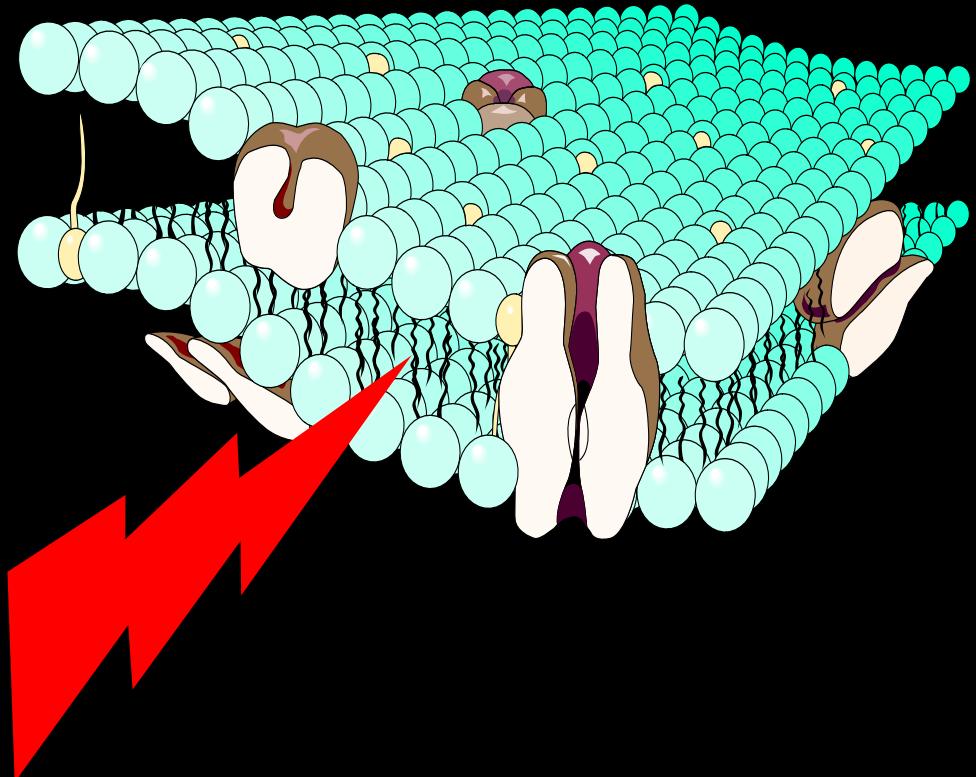


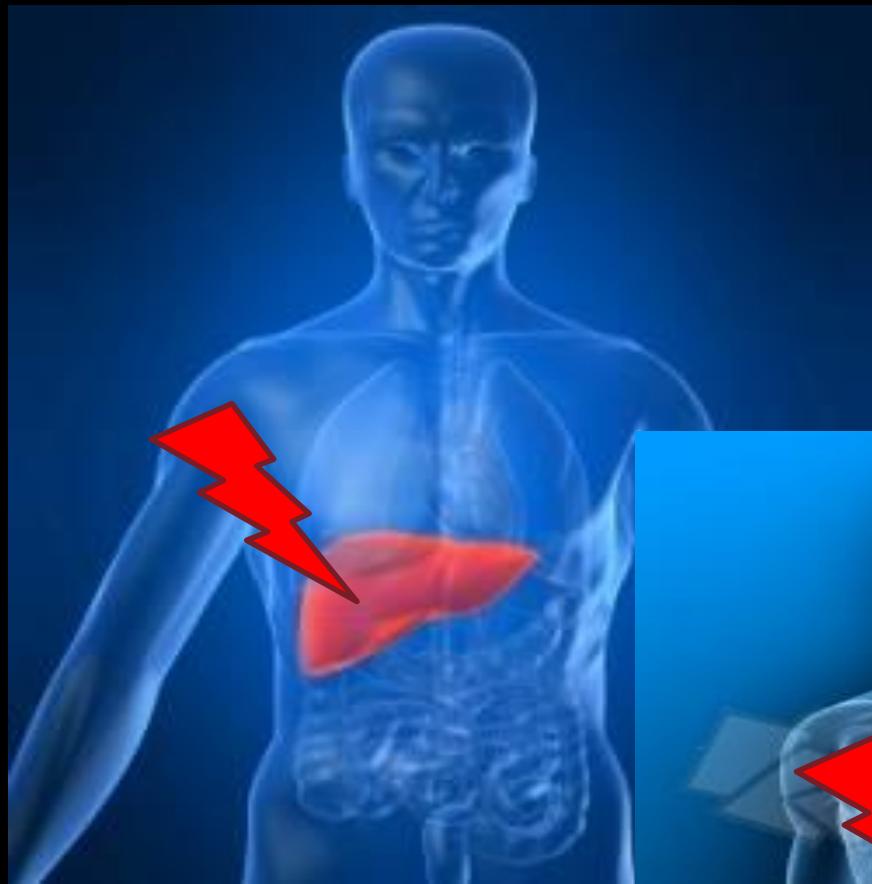


LPI



Reactive
Oxygen
Species





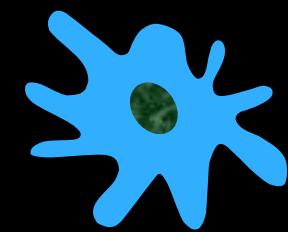
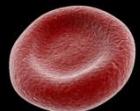
Iron metabolism

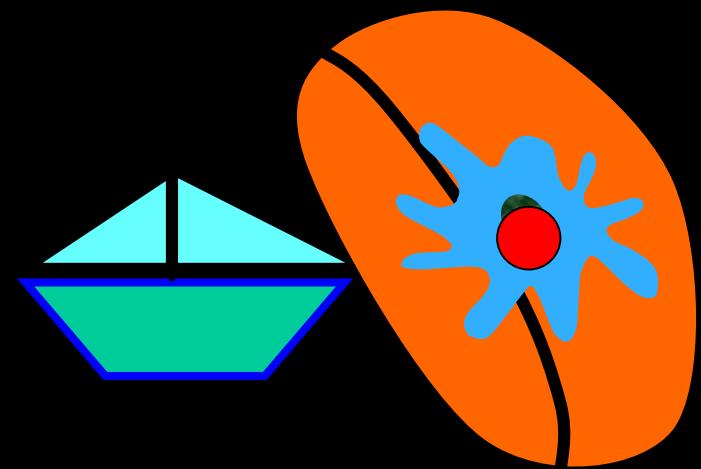
Relevance to transfusion and haemovigilance

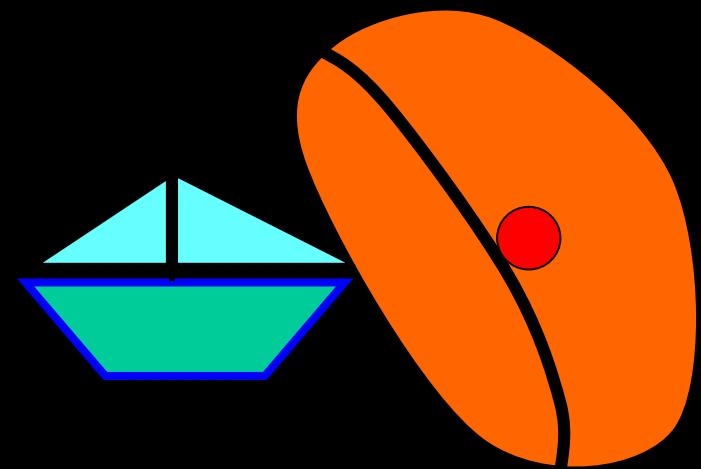
The fate of transfusional iron

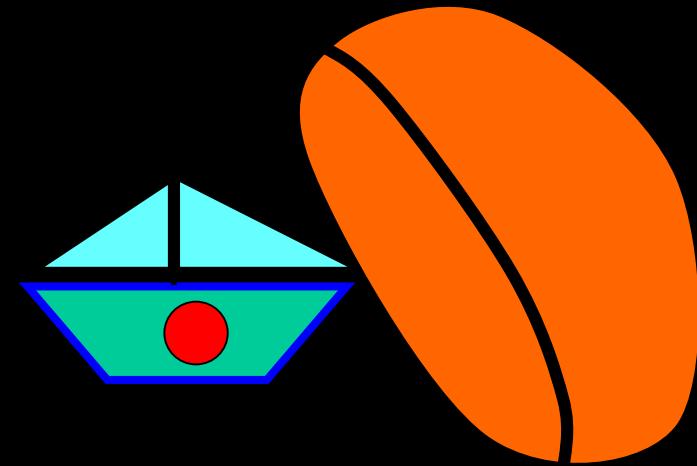
Damaging impact of transfusional iron

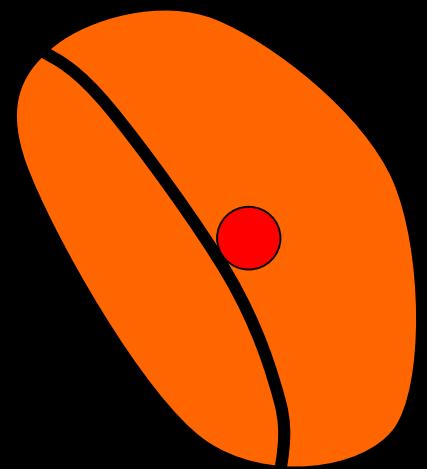
« Iron clinical attitude »

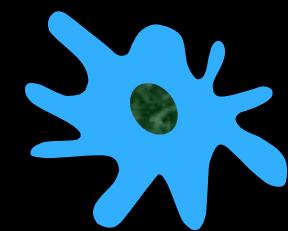
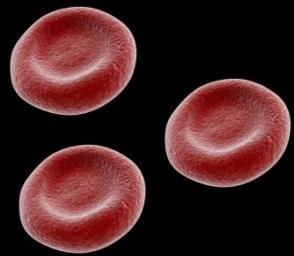


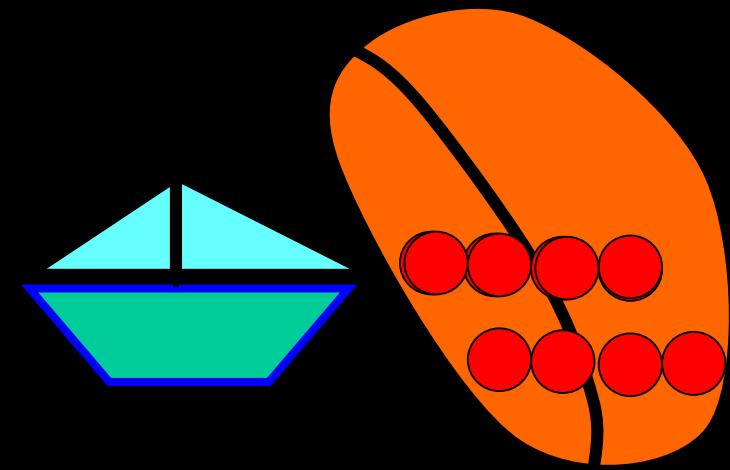


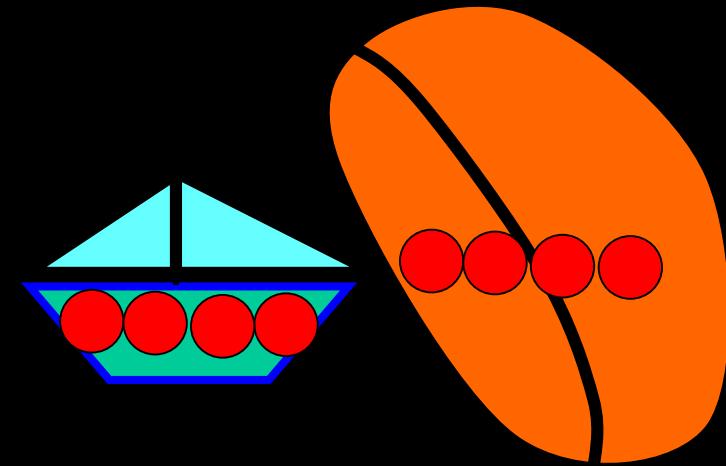


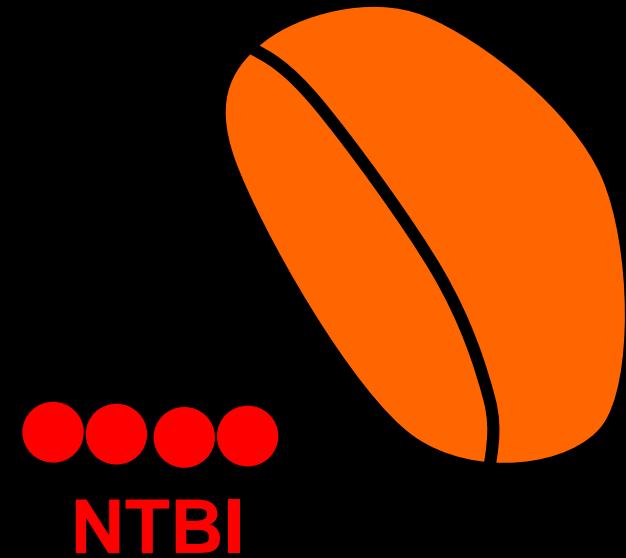


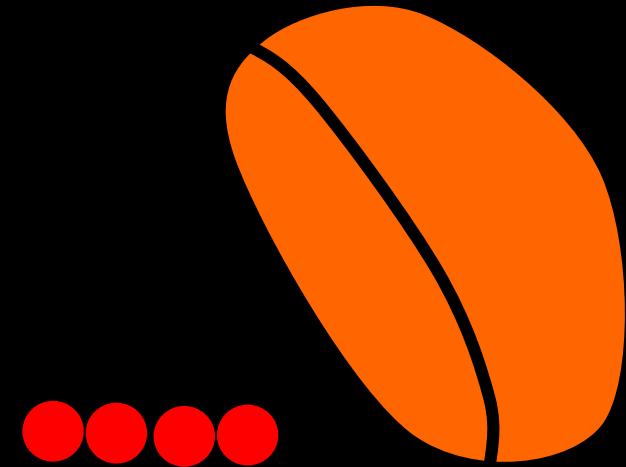












NTBI

Iron metabolism

Relevance to transfusion and haemovigilance

The fate of transfusional iron

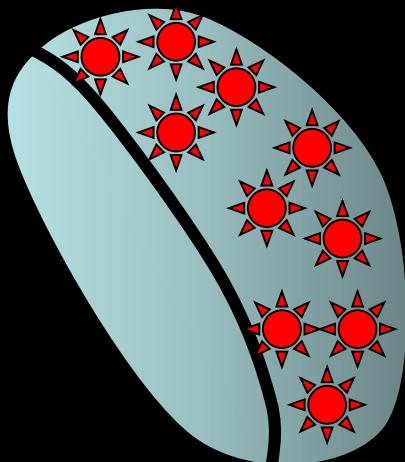
Damaging impact of transfusional iron

« Iron clinical attitude »

Chronic anemia



« FIRST ORGAN IRON HIT »

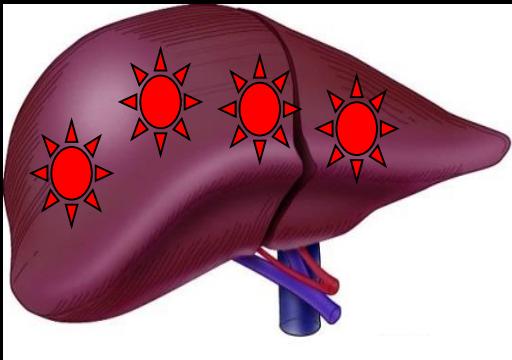


Iron overload

Chronic anemia

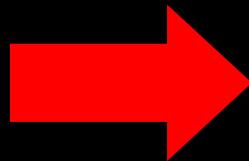


« SECOND ORGAN IRON HIT »
(NTBI)

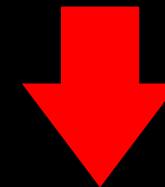
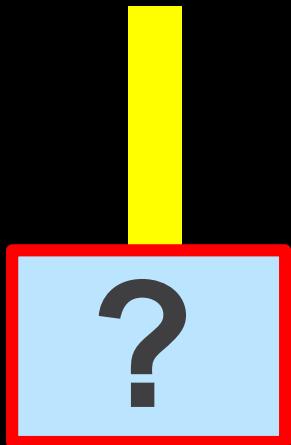


Iron overload

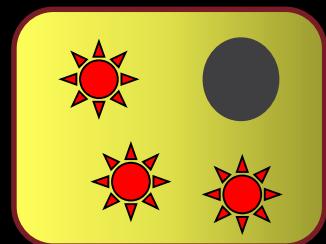
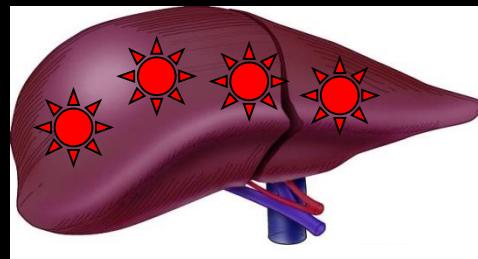
Chronic anemia



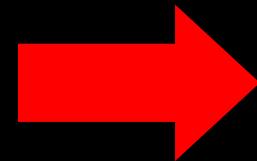
Anemia



Iron overload



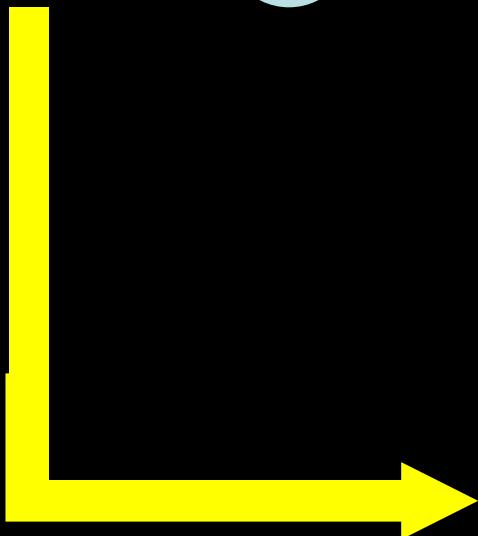
Chronic anemia



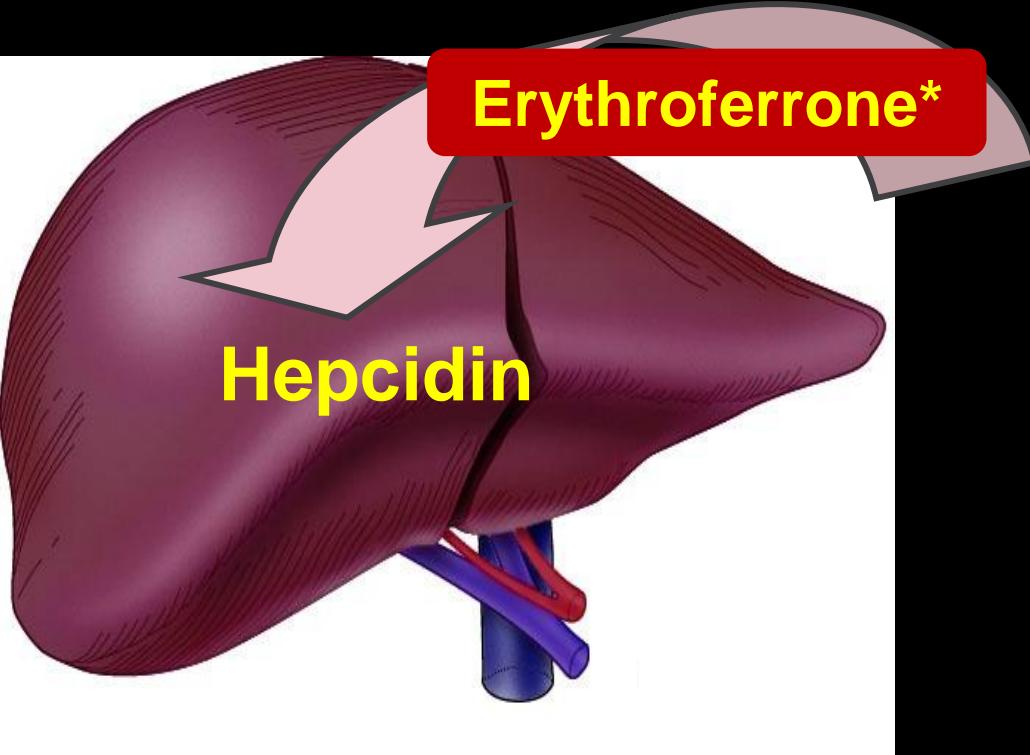
Anemia



Dyserythropoiesis

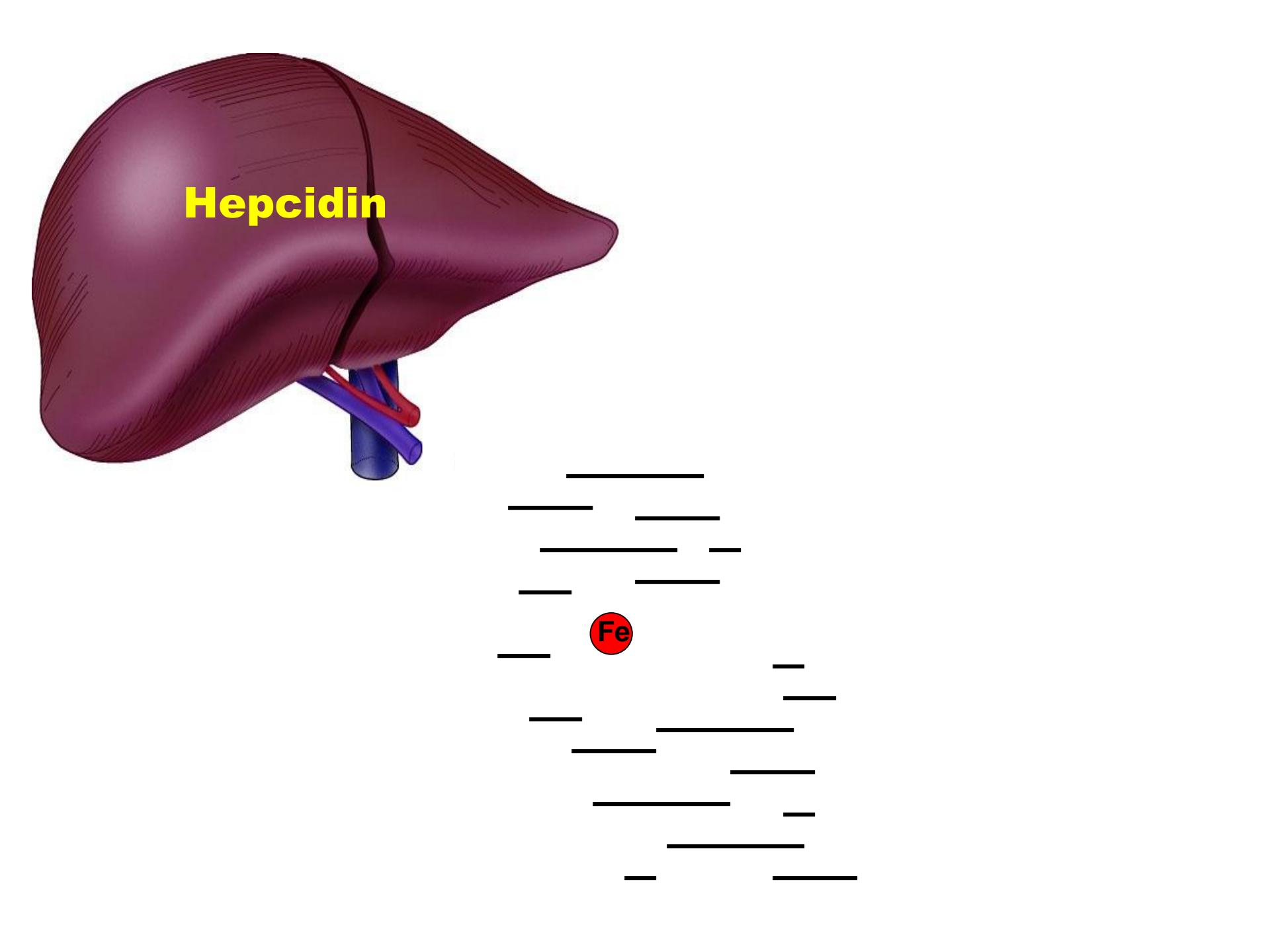


Iron overload



Dyserythropoiesis

* Kautz L et al Nat Genet 2014 : 46: 678-84

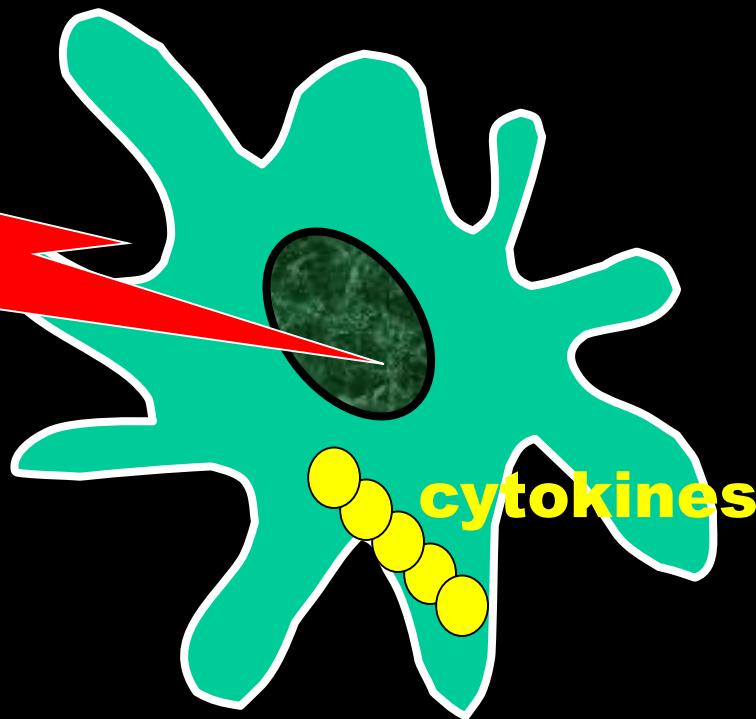


Hepcidin

Fe

Inflammation

IRON



**Systemic
inflammation**



Infection



Iron



Iron metabolism

Relevance to transfusion and haemovigilance

The fate of transfusional iron

Damaging impact of transfusional iron

« Iron clinical attitude »

Ferritin

MRI
(Magnetic resonance imaging)

1. Increased serum ferritin



Iron

2. Increased serum ferritin



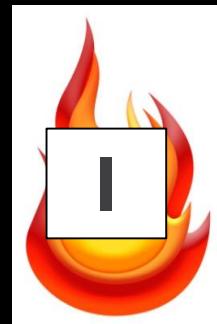
Iron



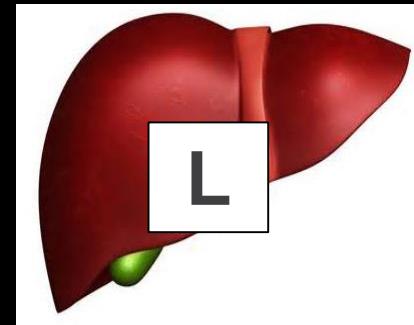
M



A



I



L

1. Increased serum ferritin

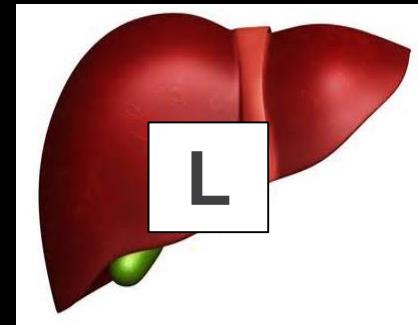
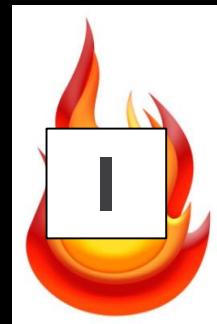


Iron

2. Increased serum ferritin



Iron



1. Increased serum ferritin

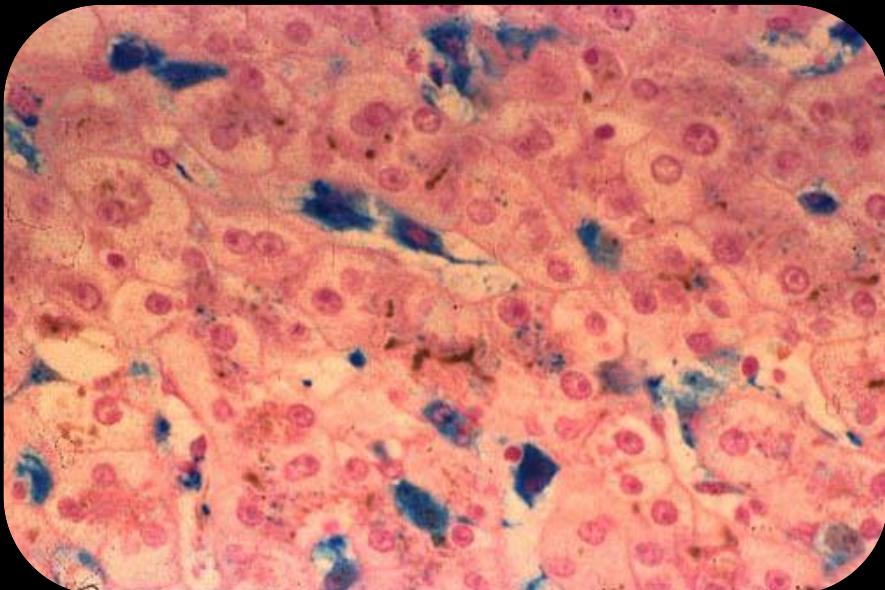


2. Increased serum ferritin

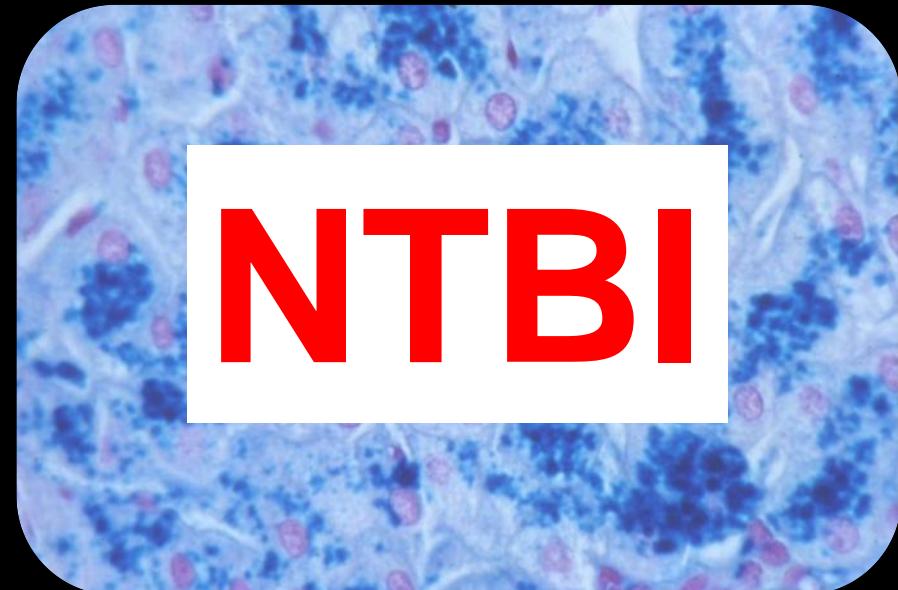


3. Hyperferritinemia level depends on cellular iron distribution

Macrophagic siderosis



Parenchymal siderosis



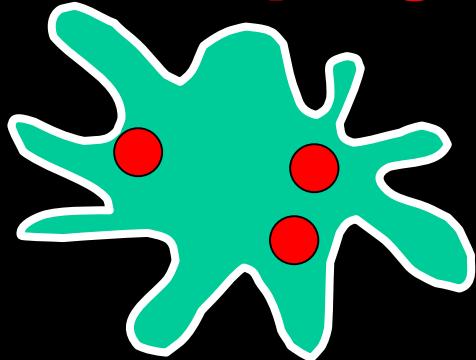
**Transfusional first cellular
hit**

**Transfusional second cellular
hit**

Dyserythropoiesis

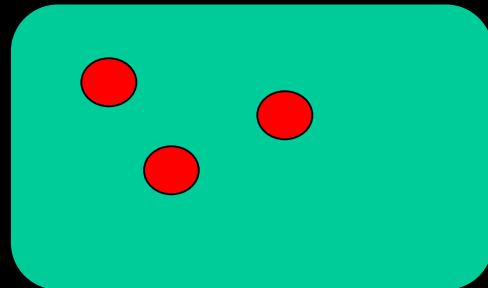
Serum ferritin is more elevated in macrophagic than in parenchymal siderosis for the same degree of iron excess

macrophage



Serum
ferritin

hepatocyte

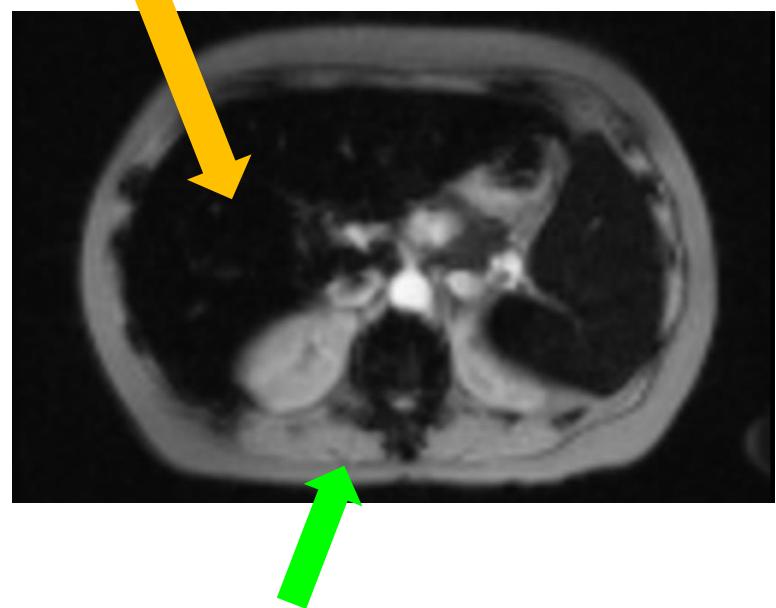
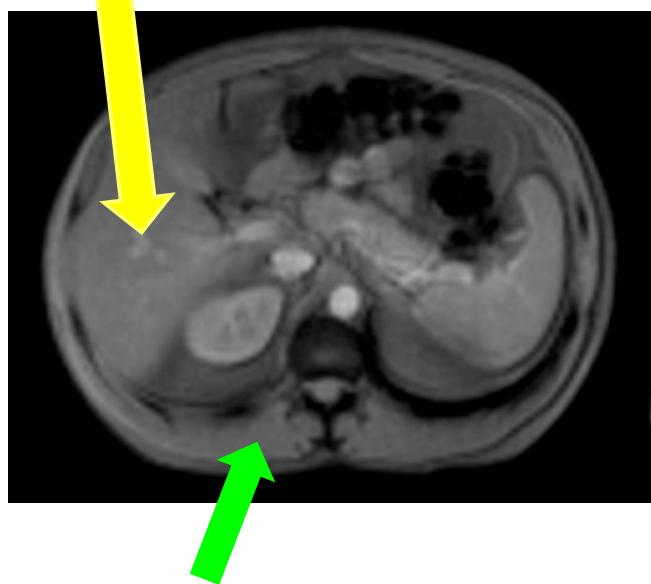


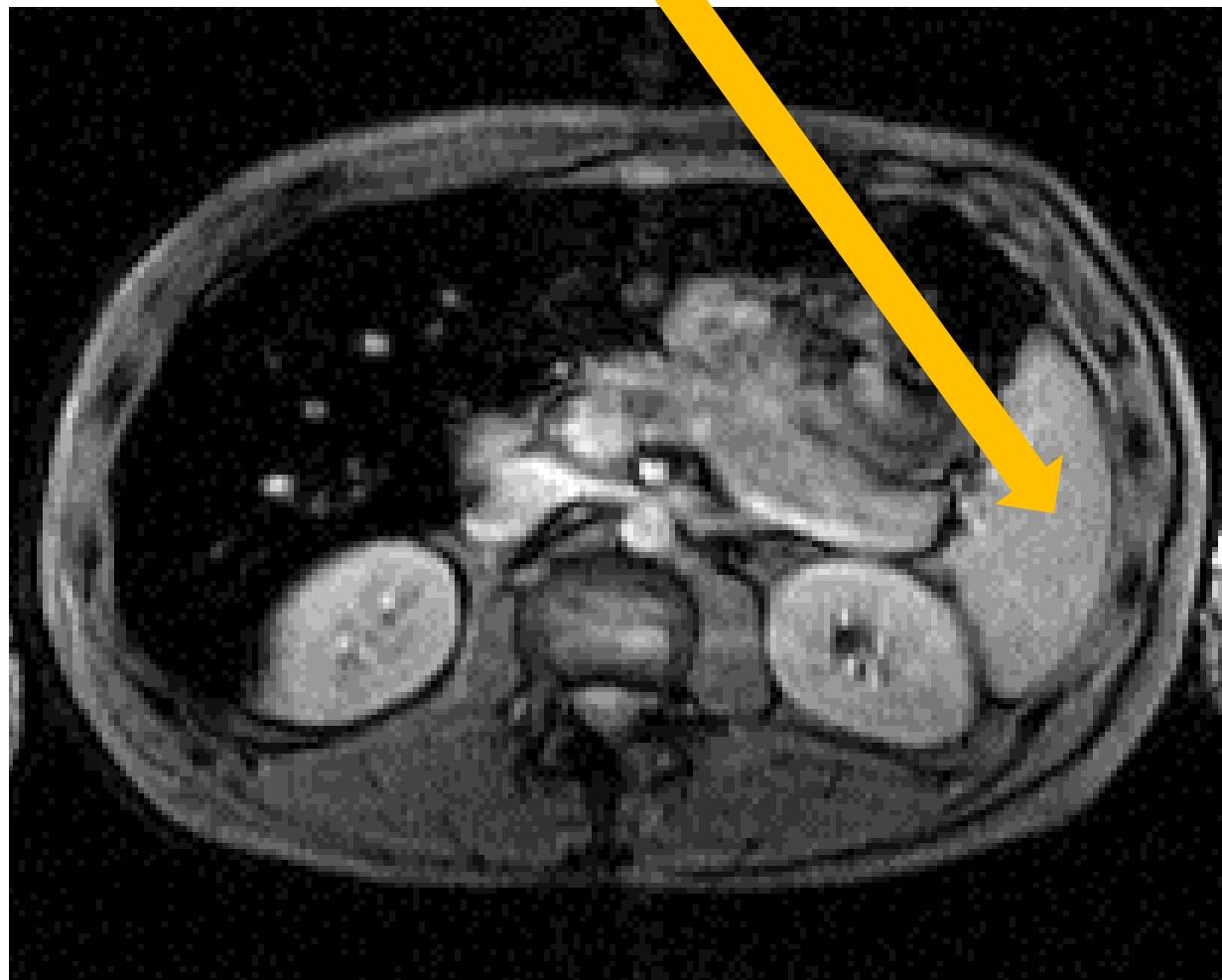
Serum
ferritin

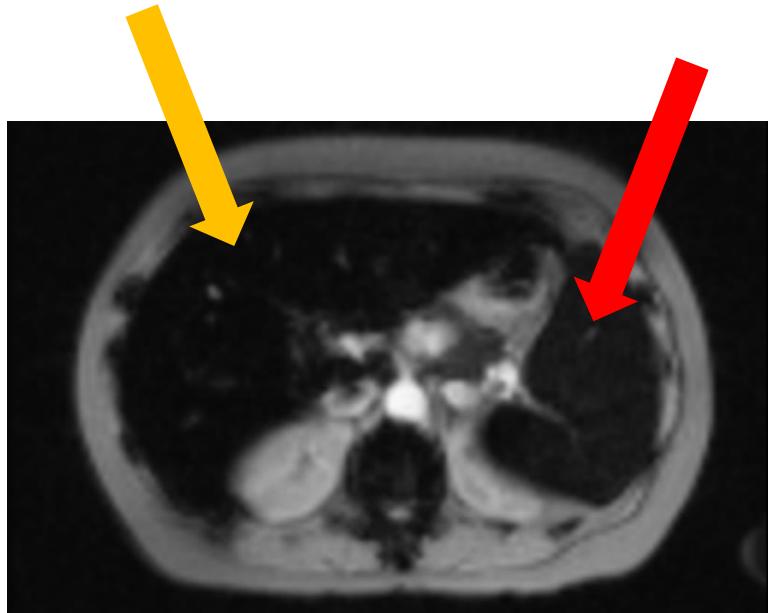
Ferritin

MRI

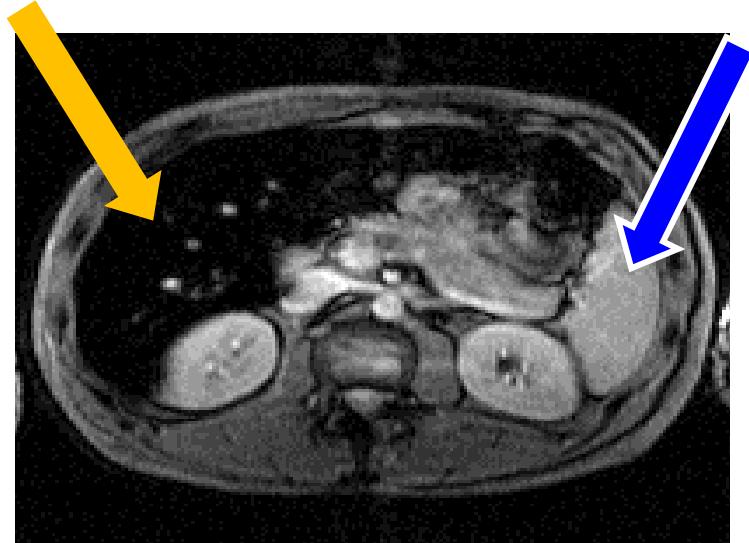
MRI







Transfusional iron overload



Dyserythropoiesis

**Transfusion not
responsible !**

Conclusions

In terms of iron :

- The human body ensures a finely tuned regulation, in a very conservative way
behaving as if iron was as precious as...gold
- The transfusional process may disturb this equilibrium, leading to deleterious iron excess
- The «transfusion physician» must therefore be careful about iron status

HAEMOVIGILANCE

« Iron vigilance »