



Hémochromatose : **Qu'y a t-il d'important et de nouveau en 2021 ?**

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**Journées Francophones de Biologie Médicale
Rennes
7 Octobre 2021**

Liens d'intérêt

- **Ionis Pharmaceuticals**
- **La Jolla Pharmaceutical Company**
- **Novartis**
- **Protagonist Therapeutics**

Quoi de neuf dans la définition de « l'hémochromatose » ?

Quoi de neuf pour le diagnostic?

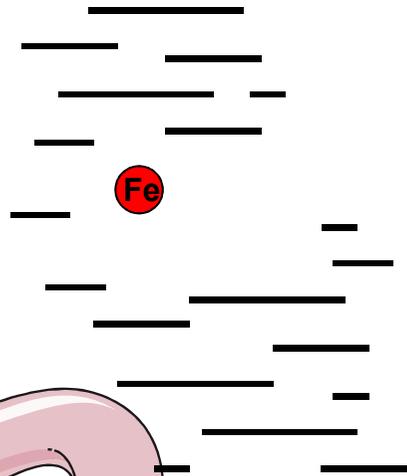
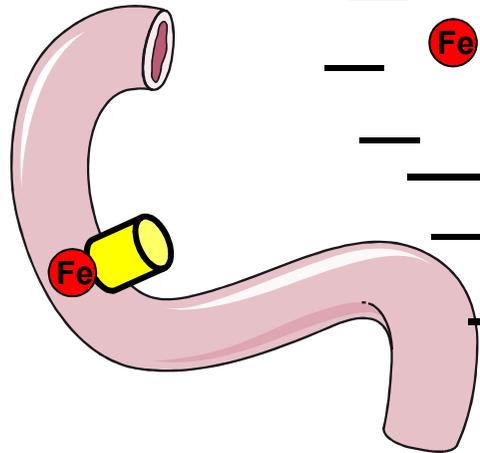
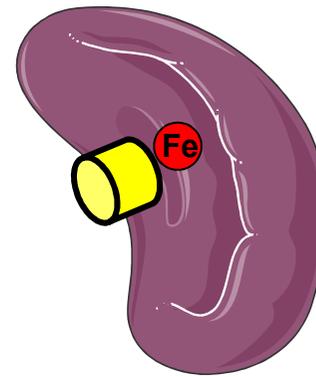
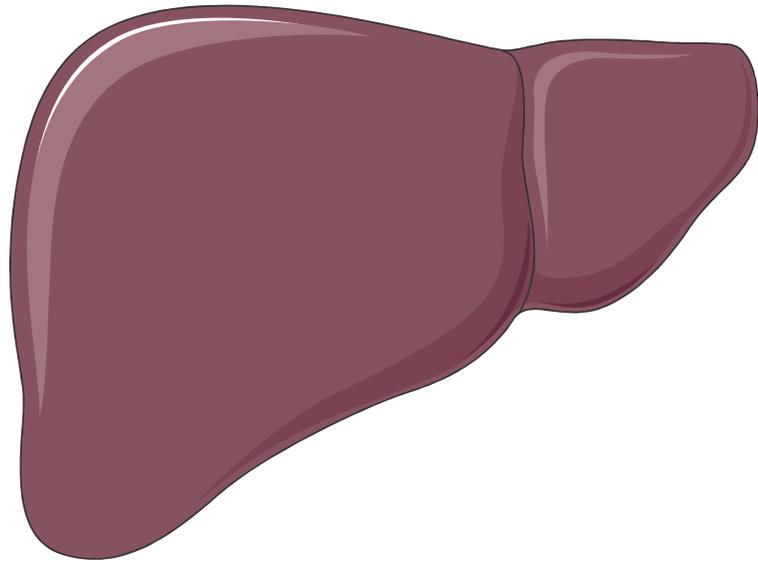
Quoi de neuf pour le traitement?

Surcharge en fer

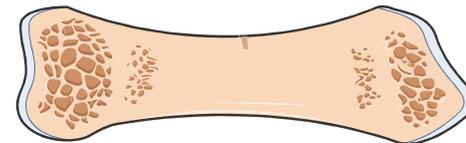
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graph TD; A[Surcharge en fer] --> B[Génétique]; A --> C[Déficit en hepcidine];
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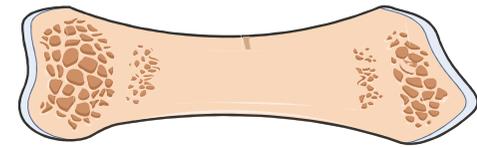
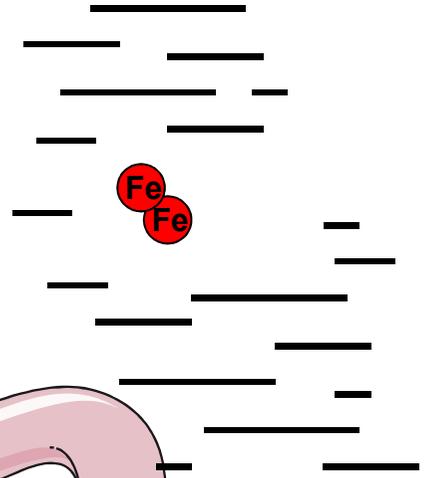
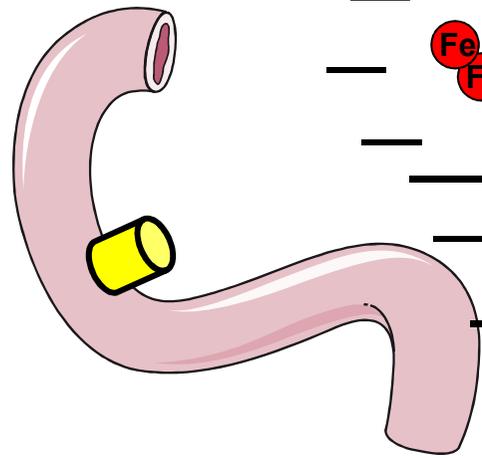
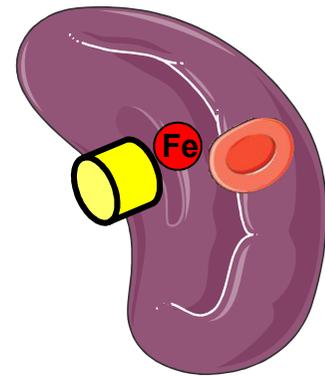
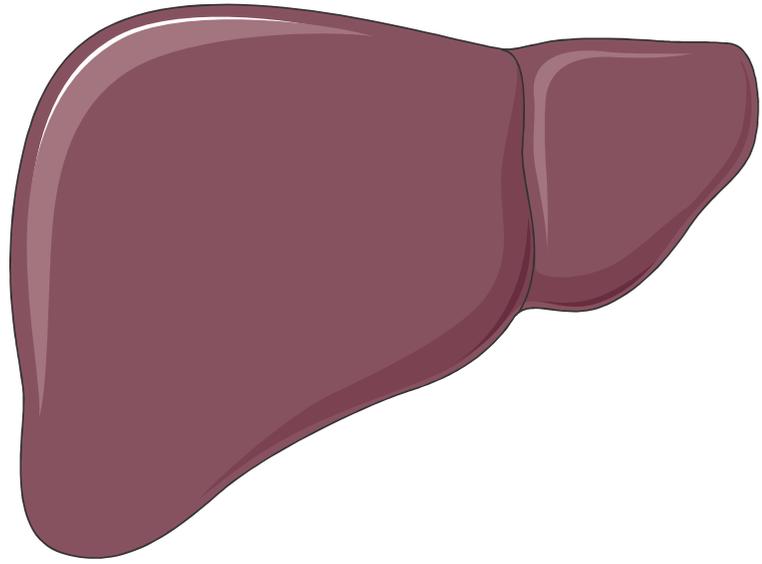
Génétique

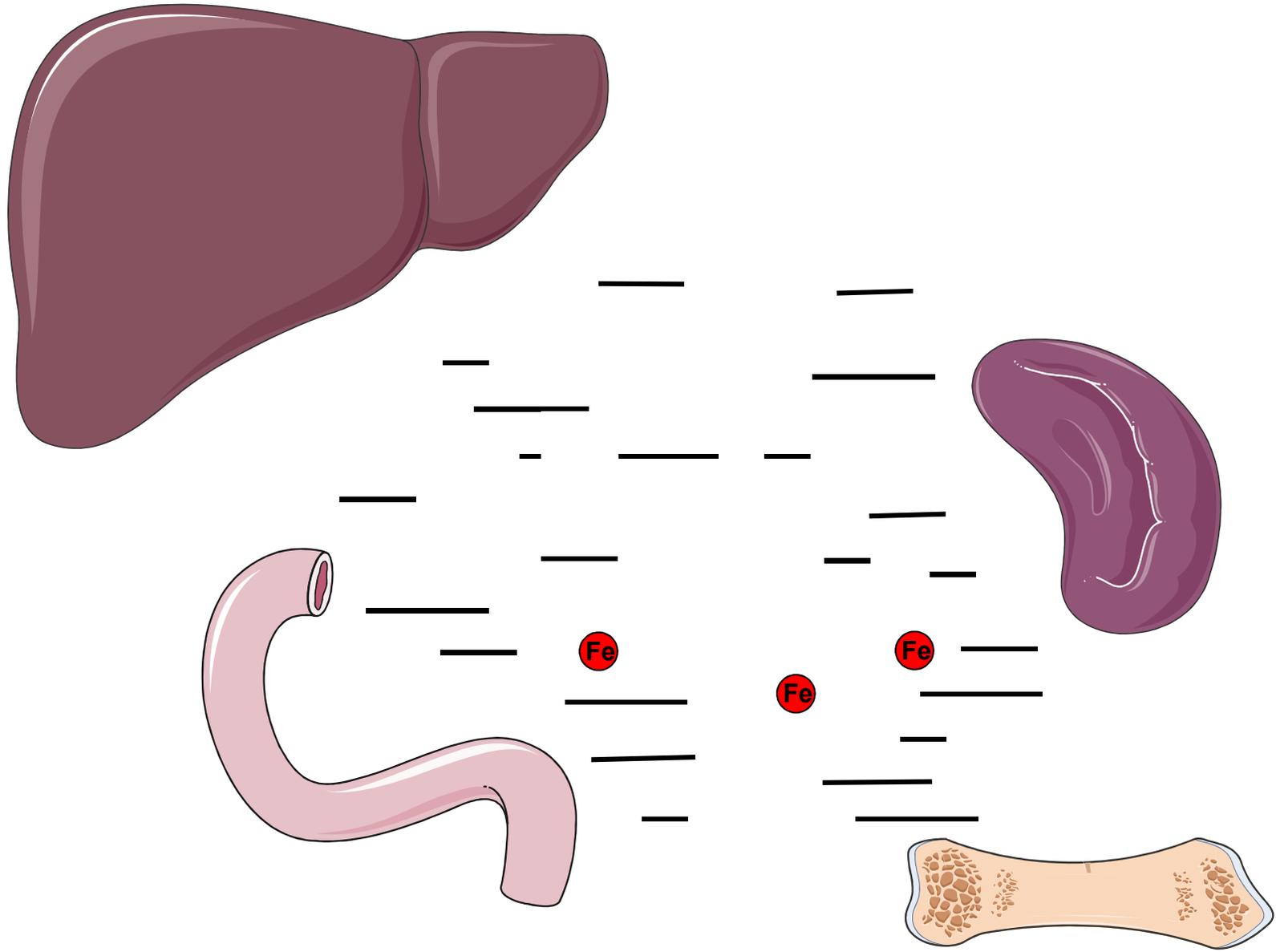
Déficit en hepcidine

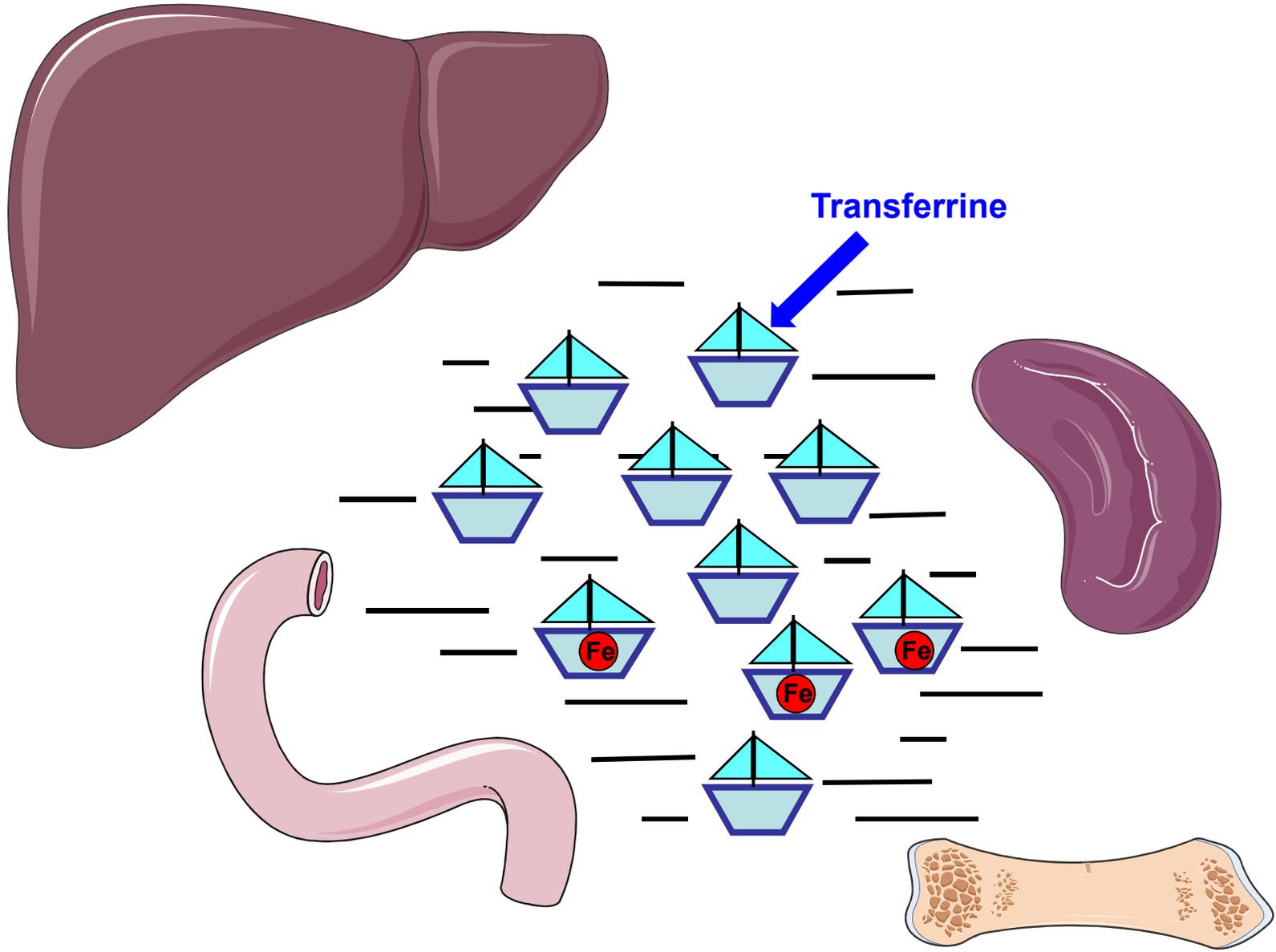


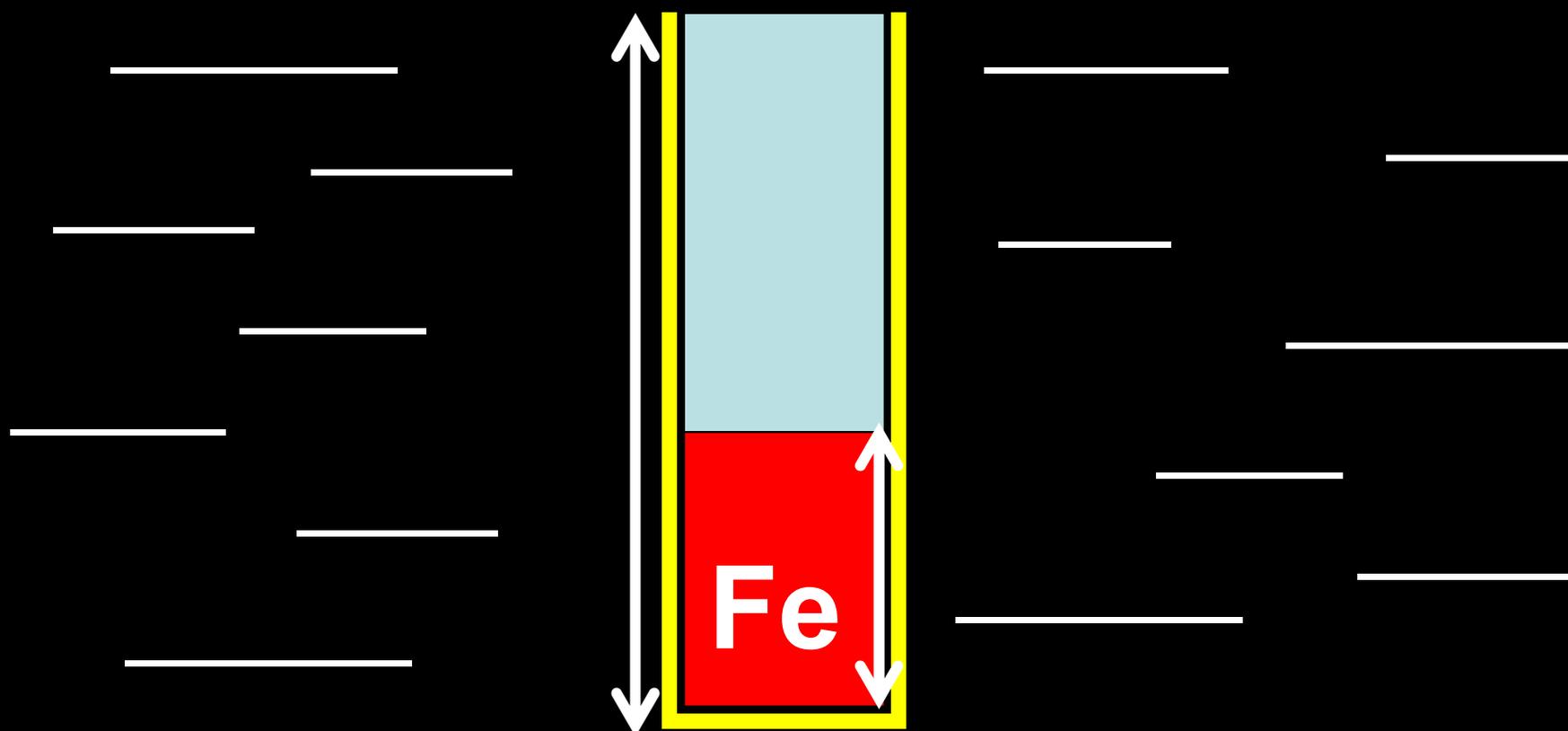
Fe



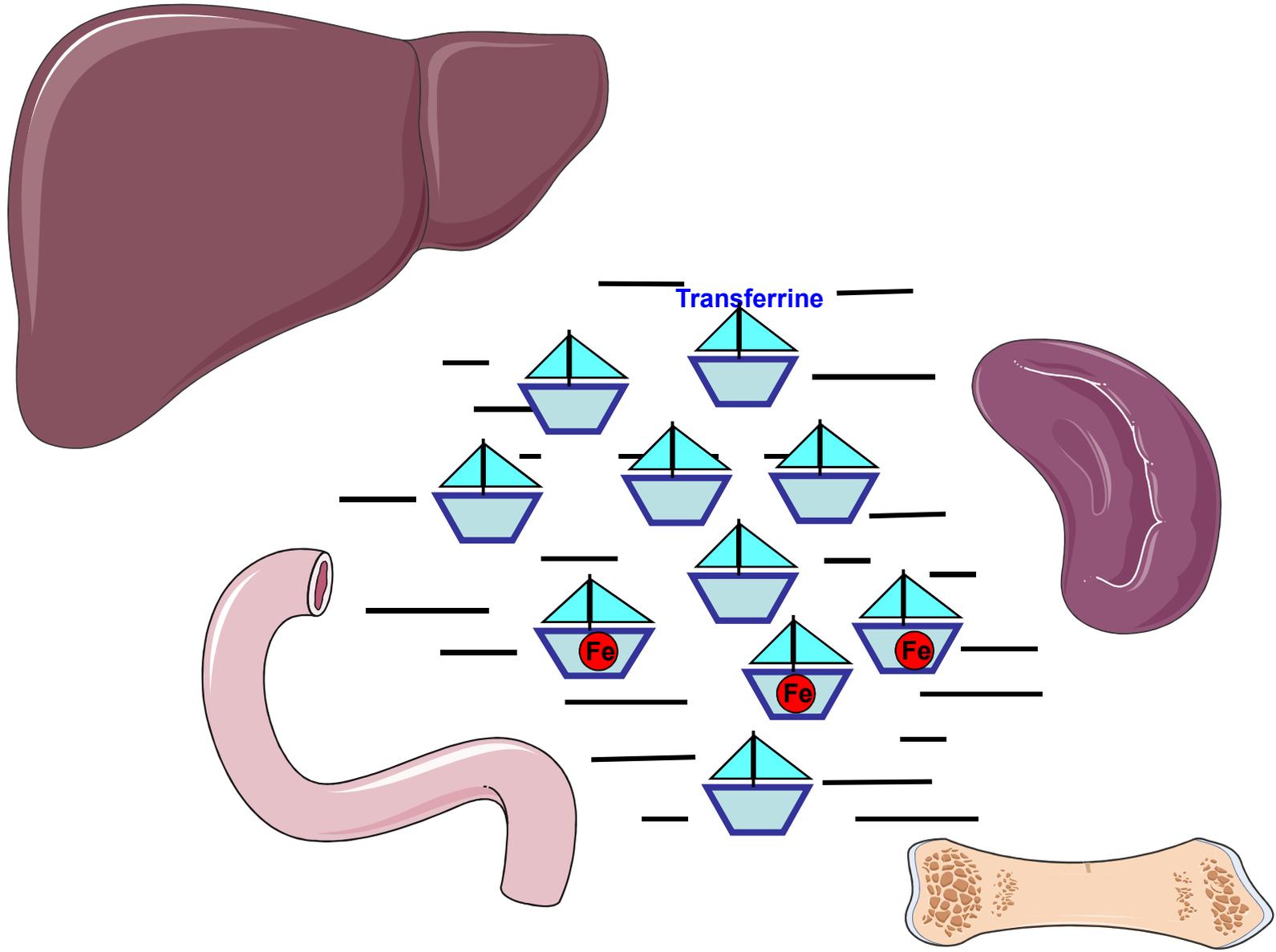


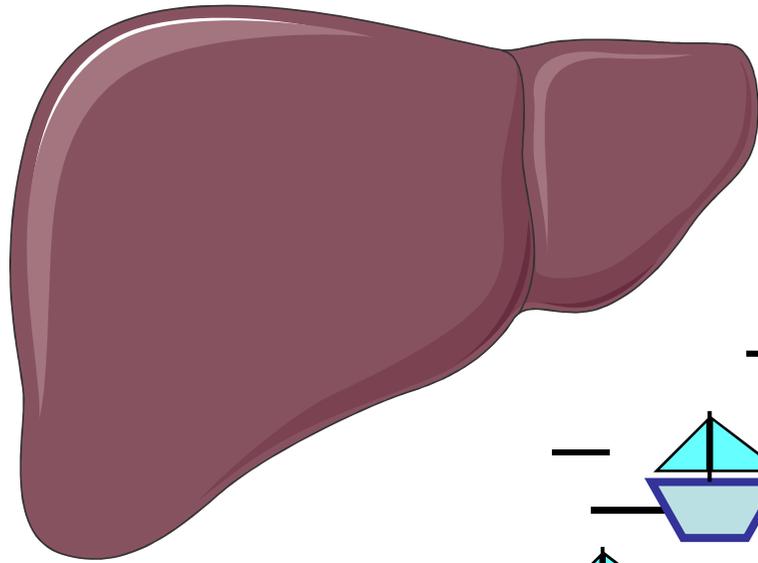




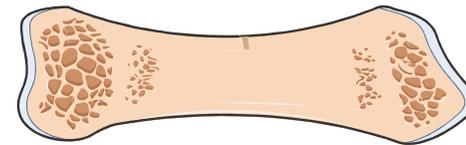
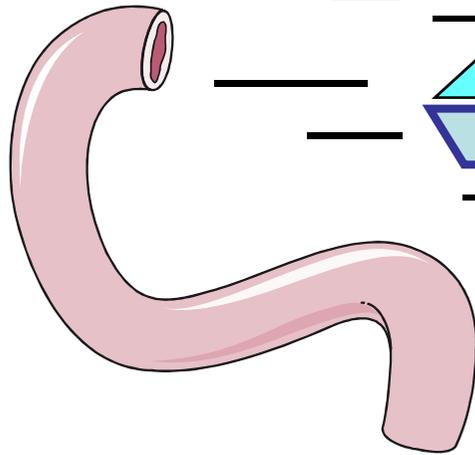
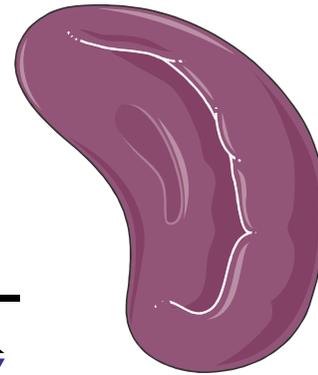
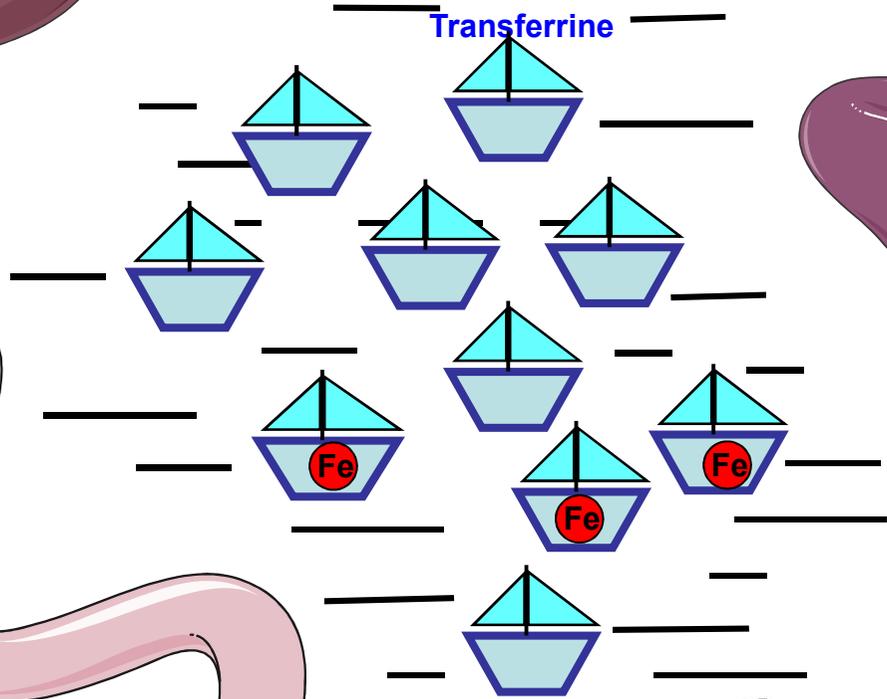


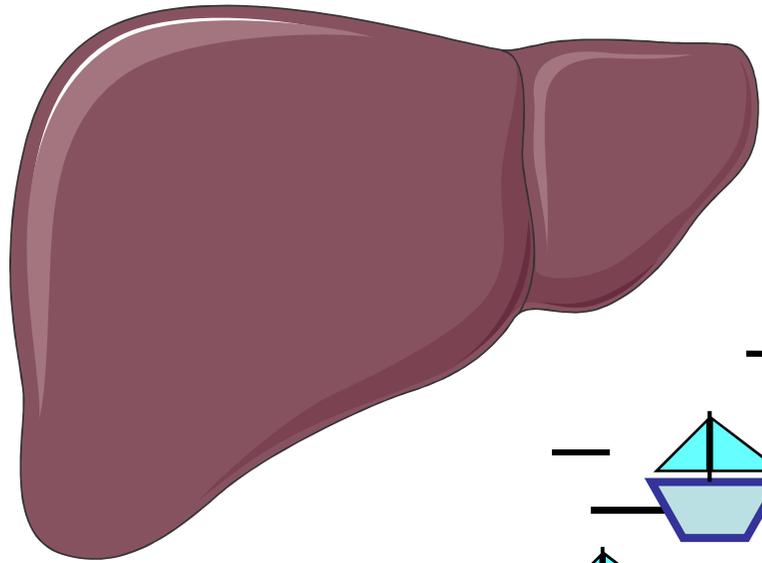
Saturation transferrine = $Fe/Tf < 45\%$



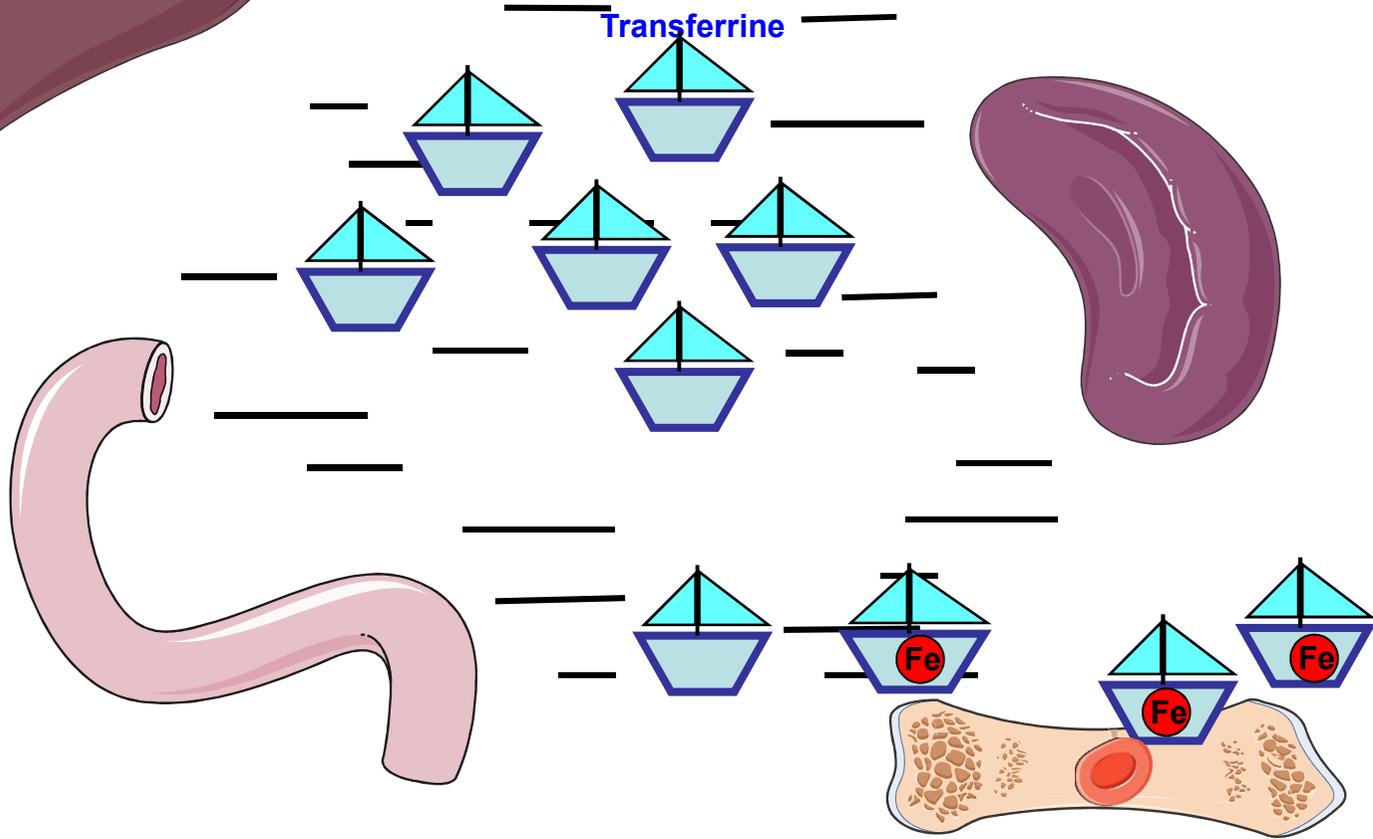


Transferrine





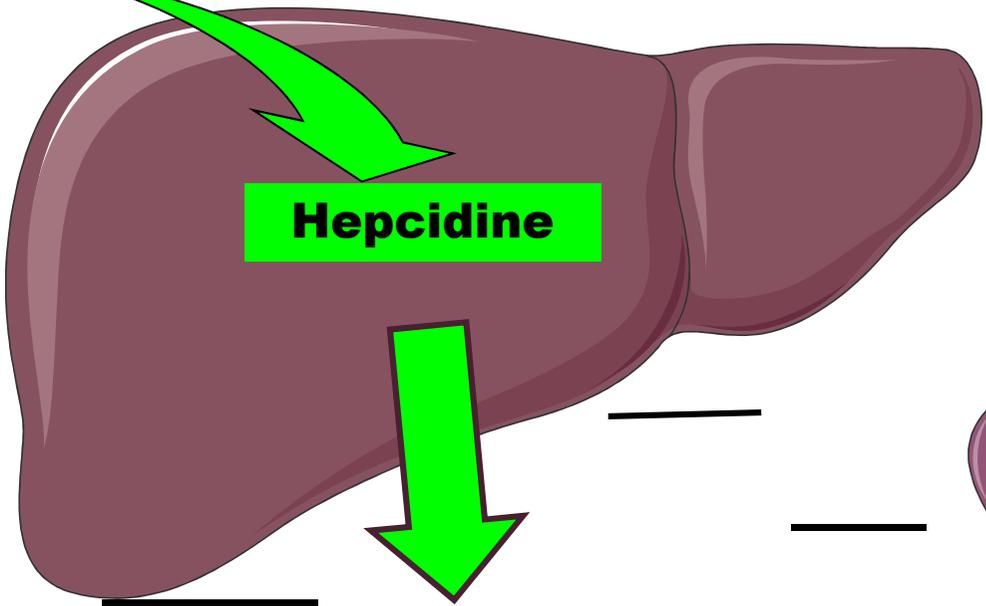
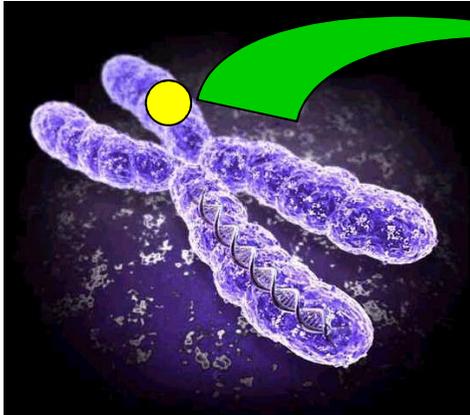
Transferrine



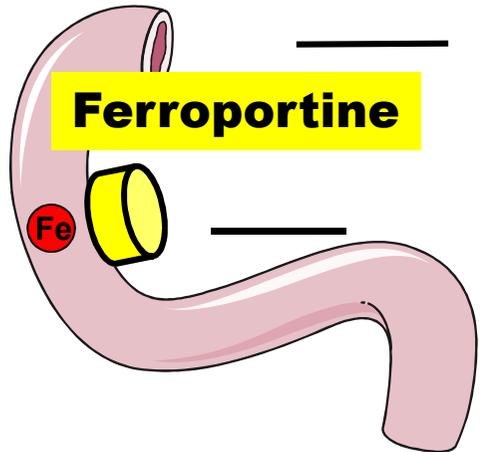
Hémochromatose

HFE:
C282Y/C282Y

Non HFE

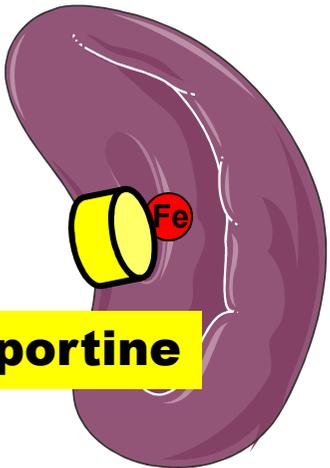


Hepcidine



Ferroportine

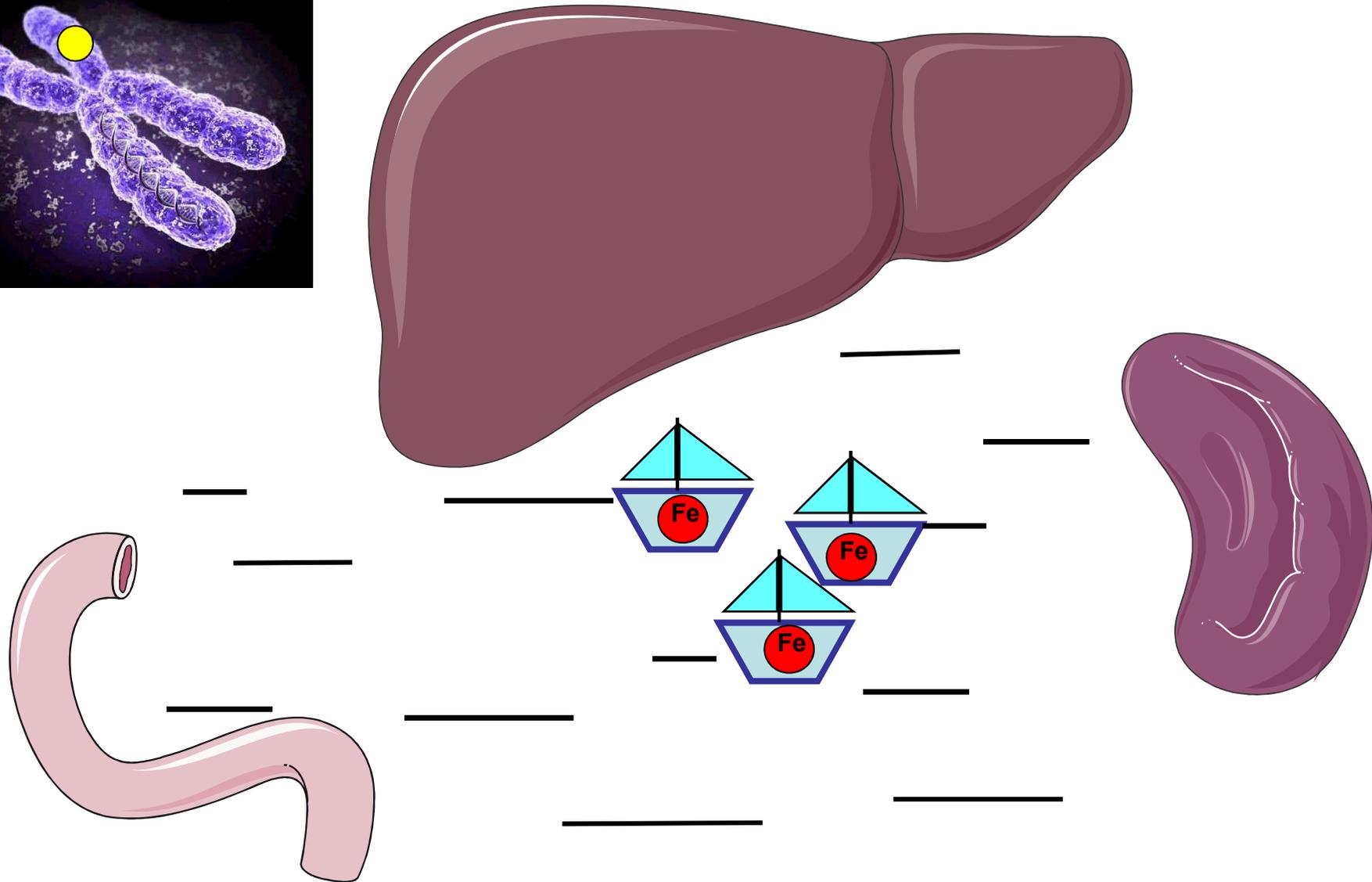
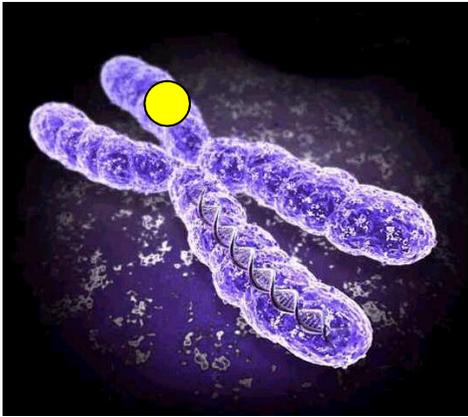
Fe

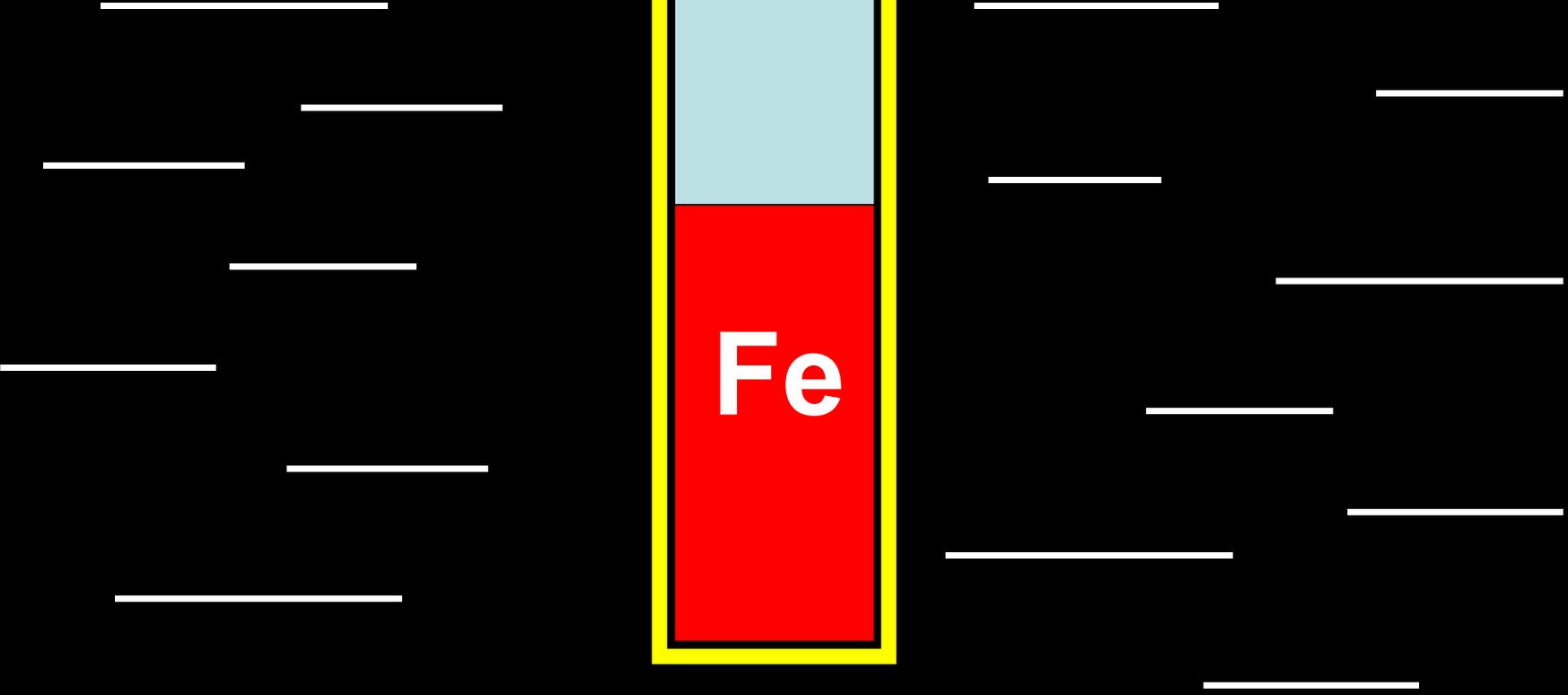
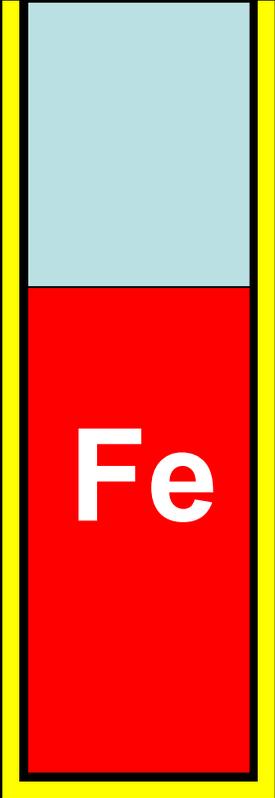


Ferroportine

Fe

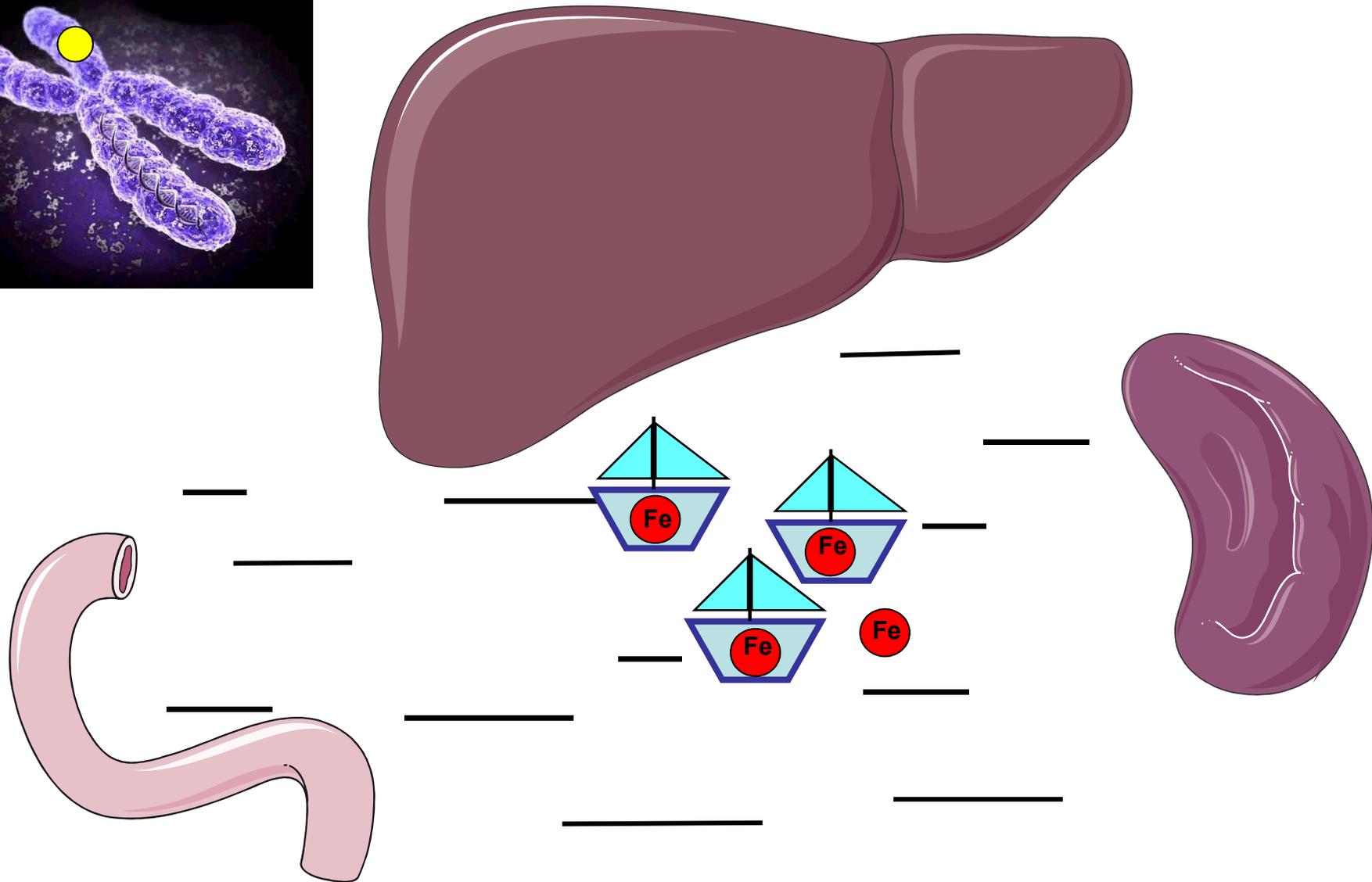
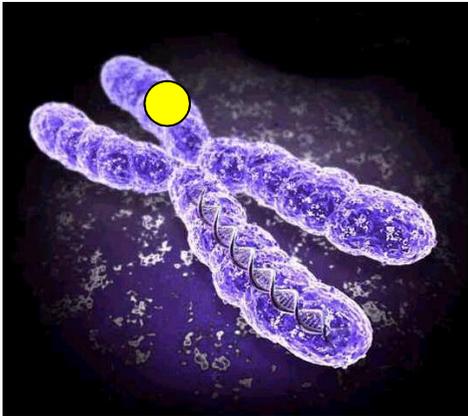
Hémochromatose



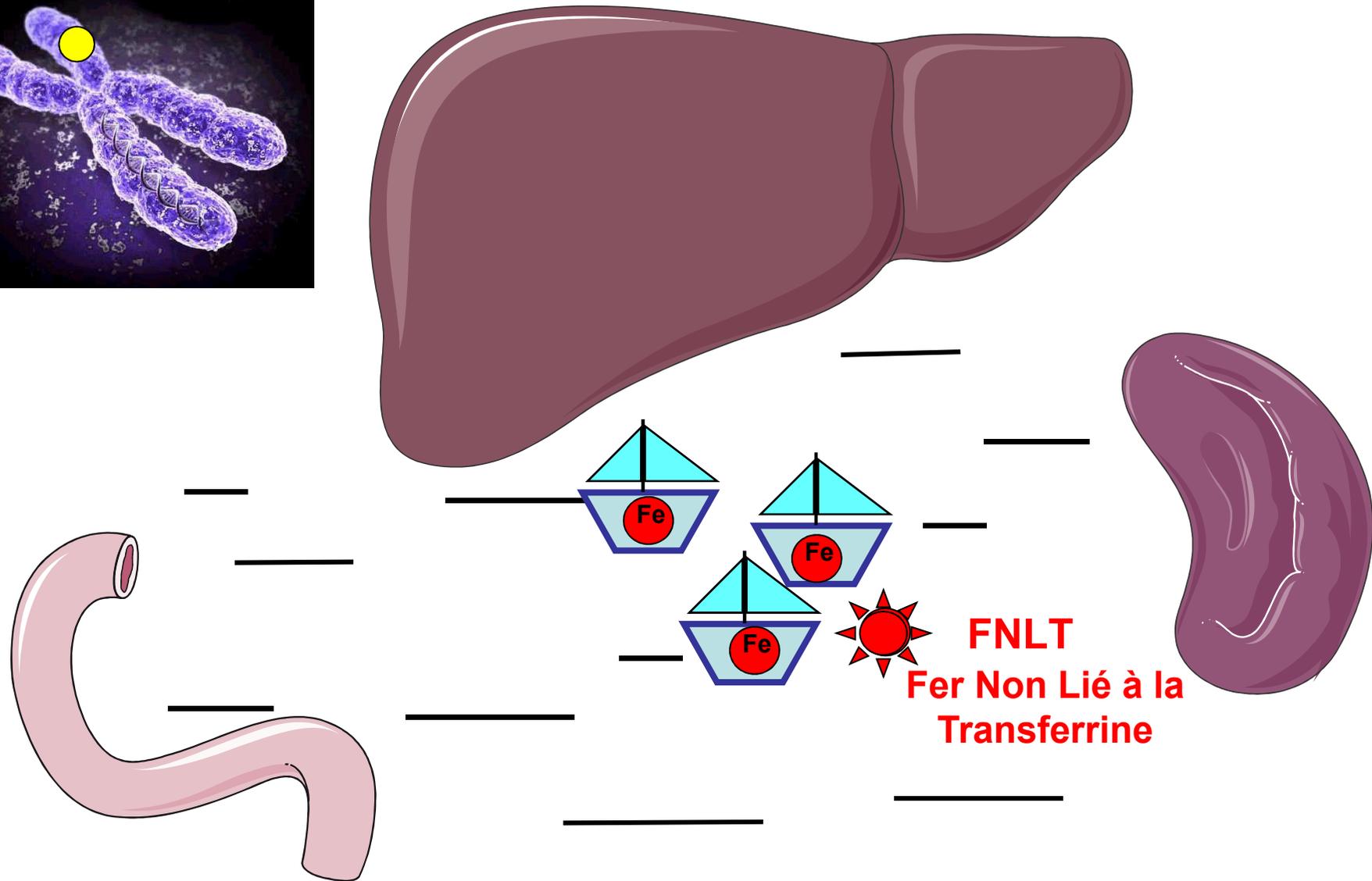
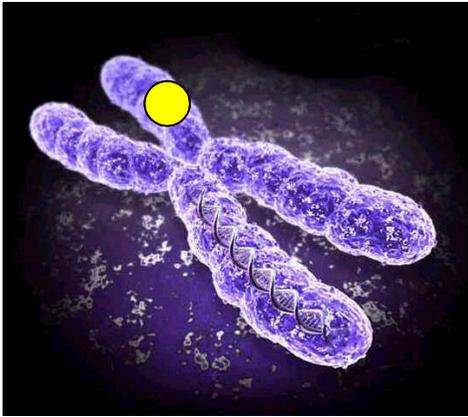


Saturation transferrine > 45%

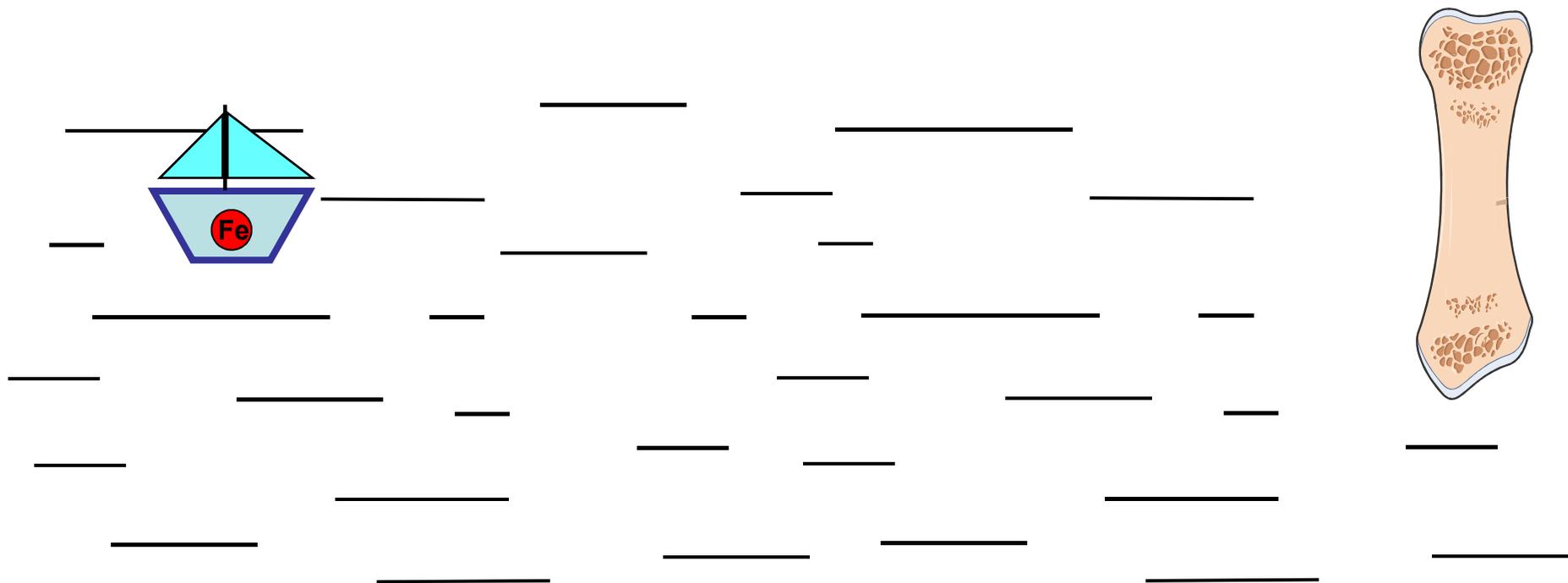
Hémochromatose



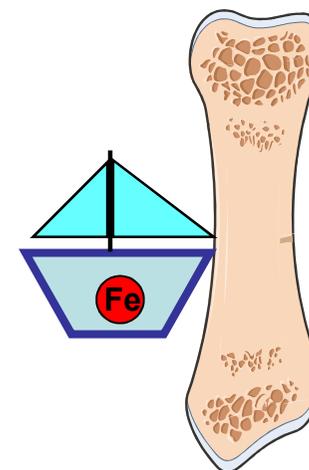
Hémochromatose



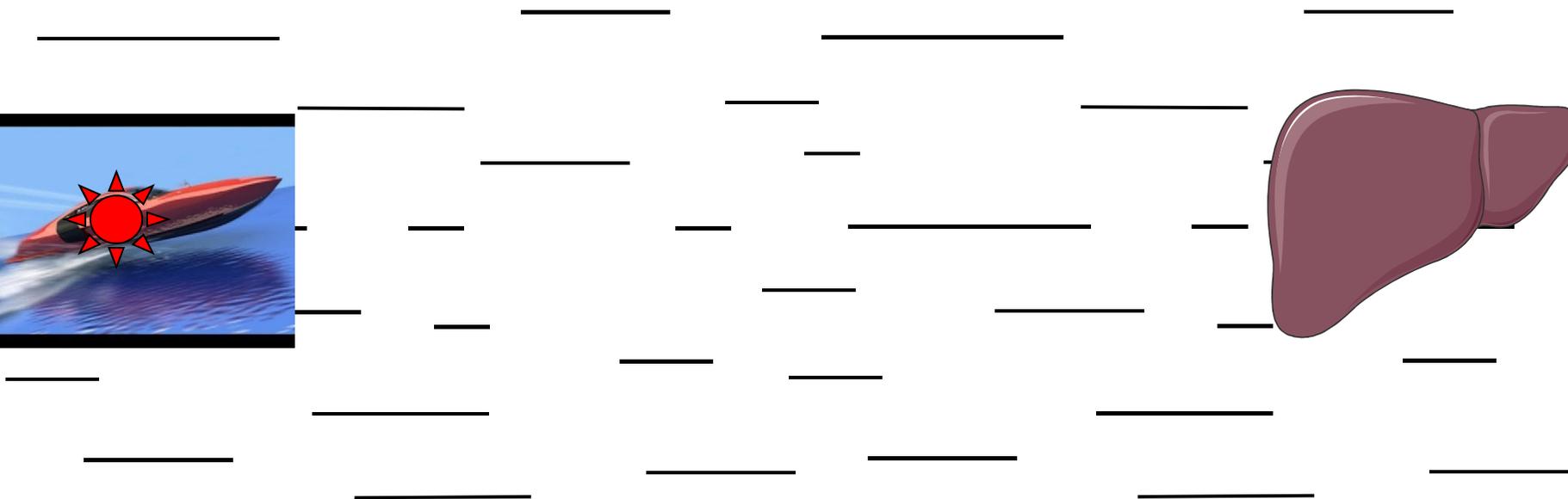
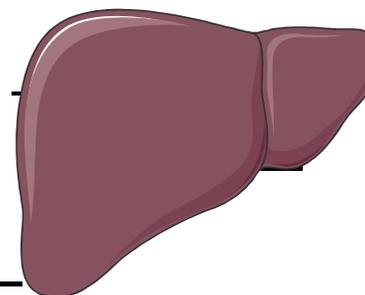
Fer lié à la transferrine



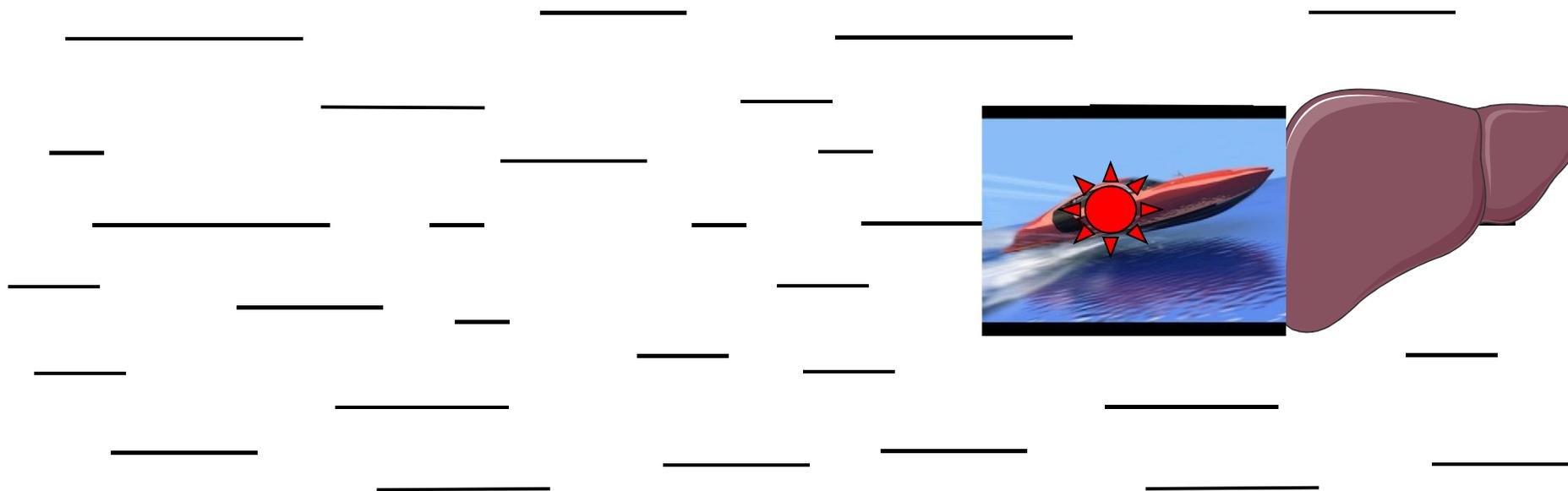
Fer lié à la transferrine



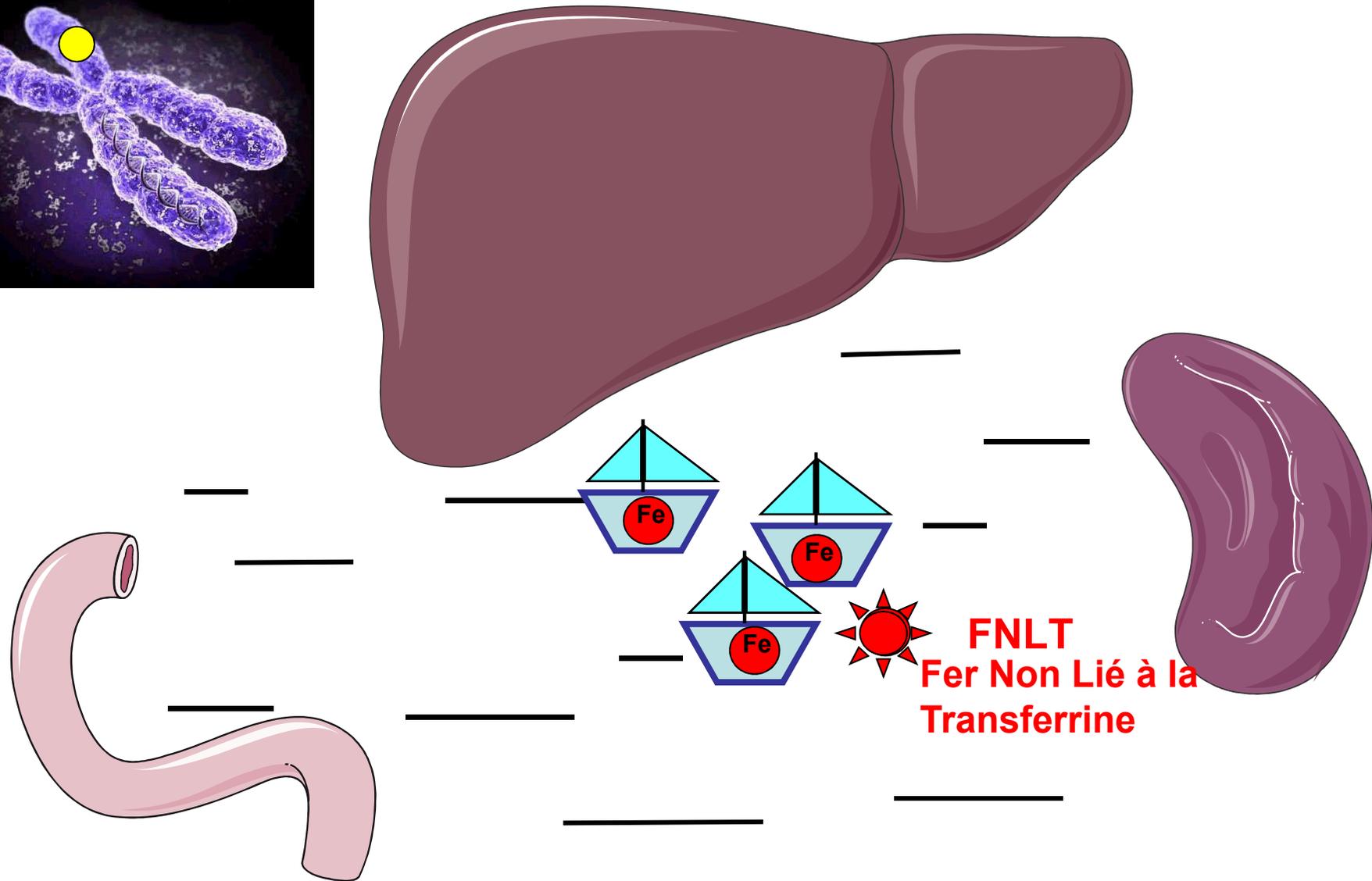
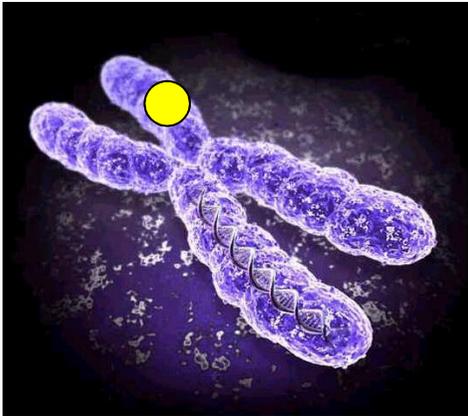
Fer Non Lié à la Transferrine (FNLТ)



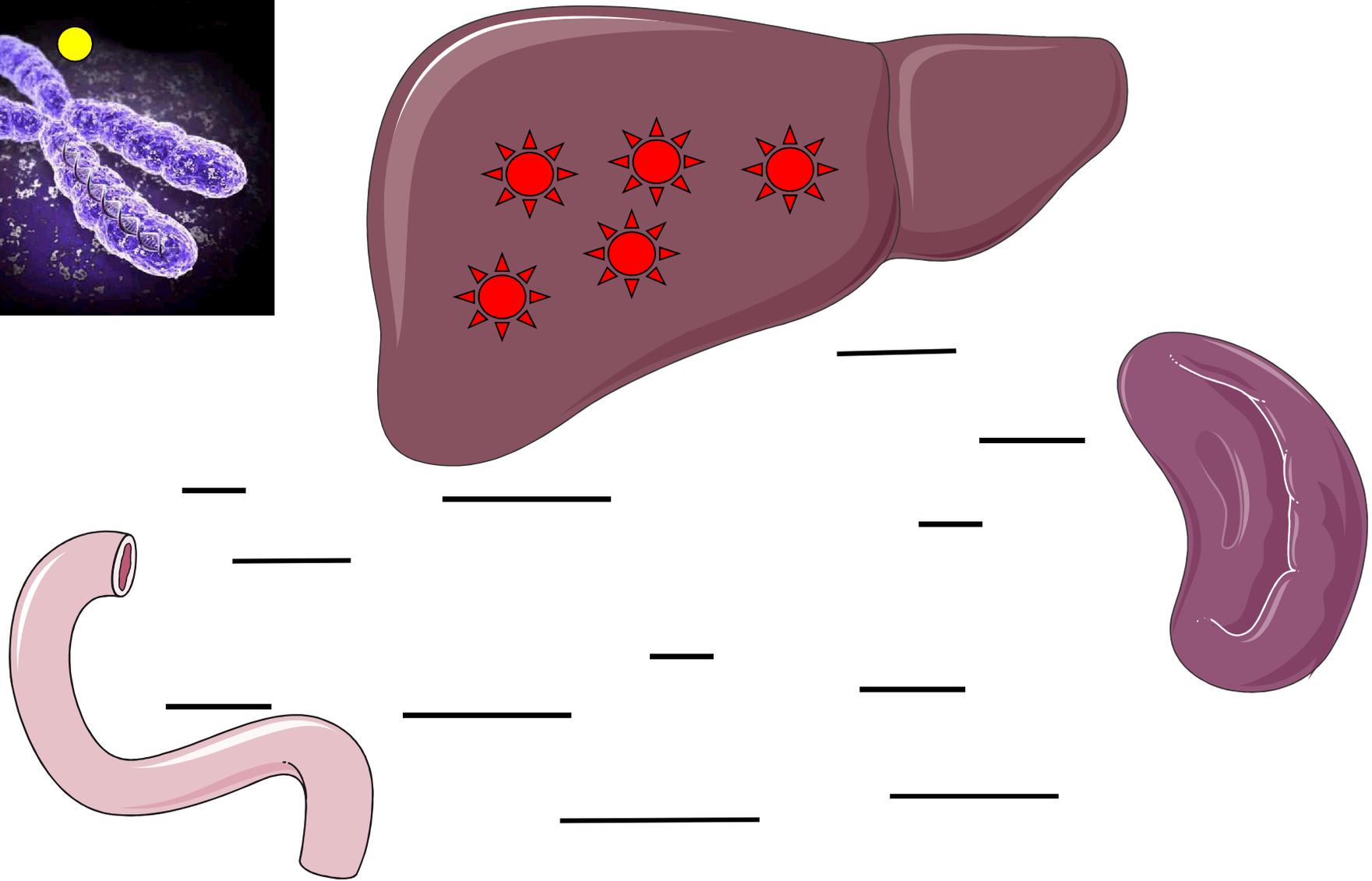
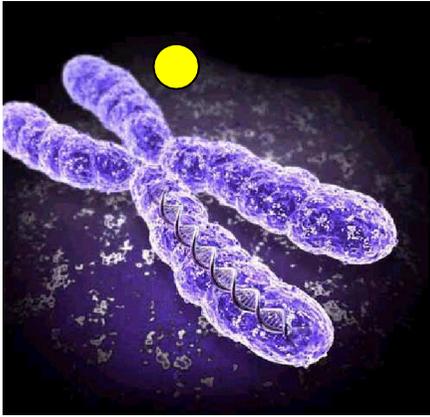
Fer Non Lié à la Transferrine (FNLТ)

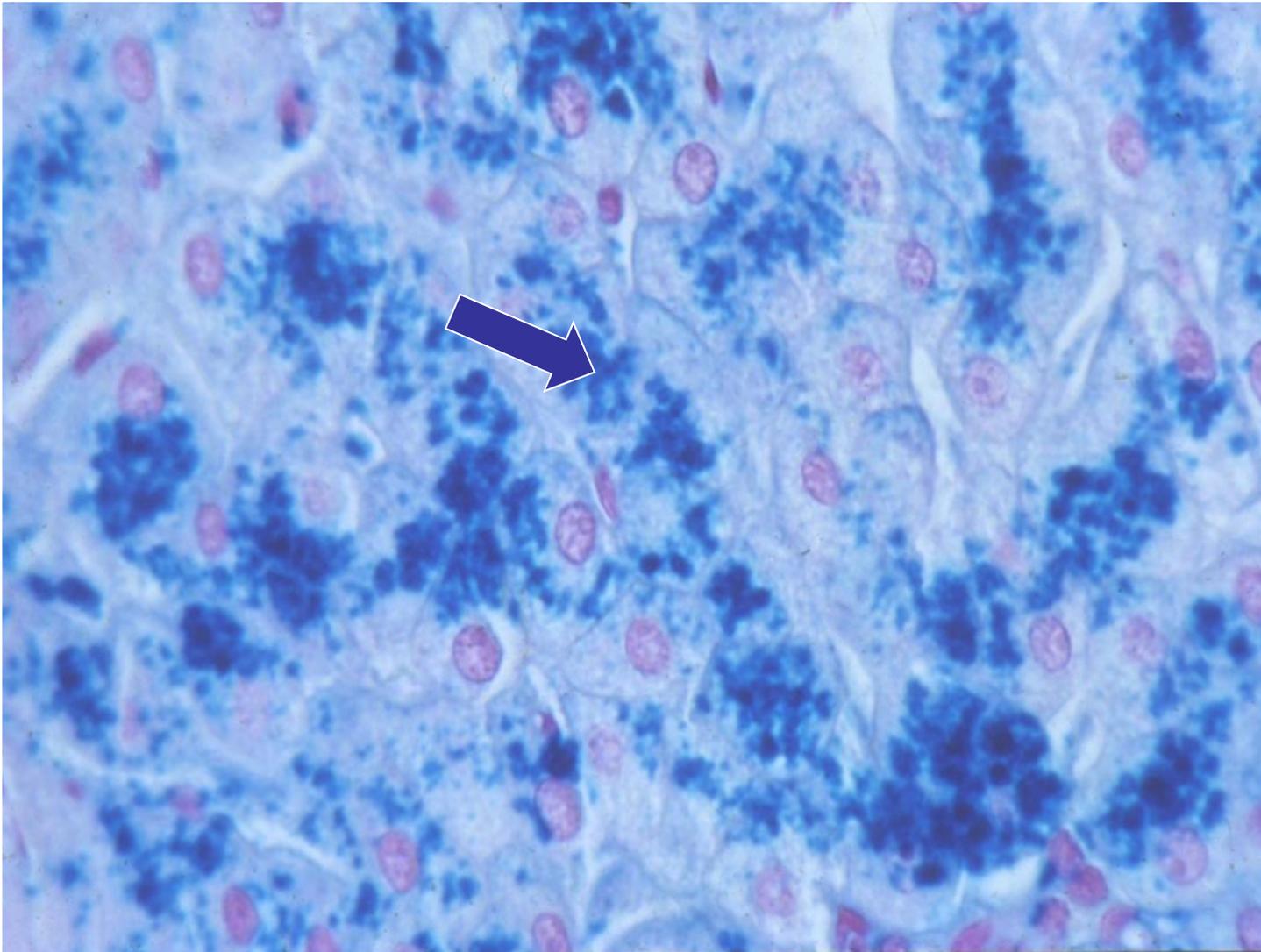


Hémochromatose



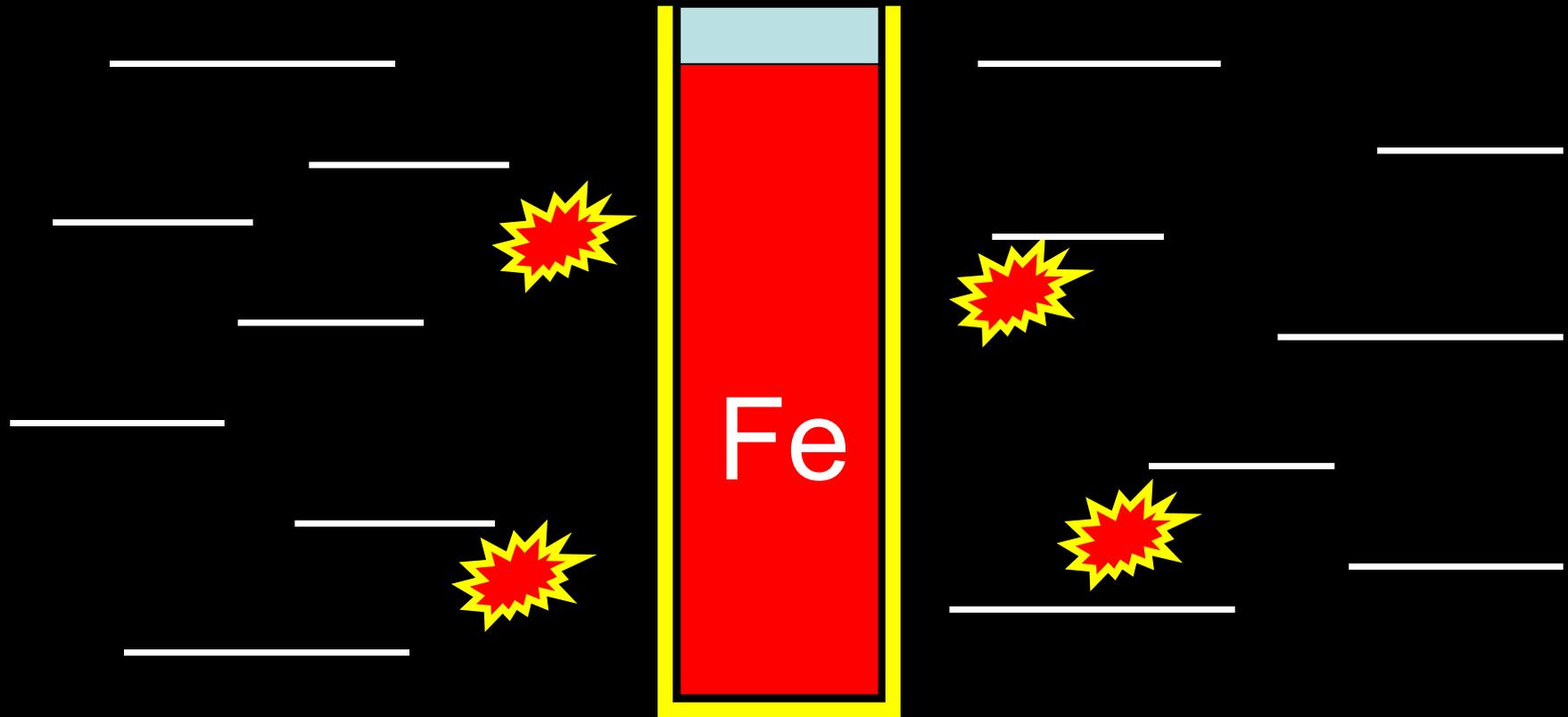
Hémochromatose



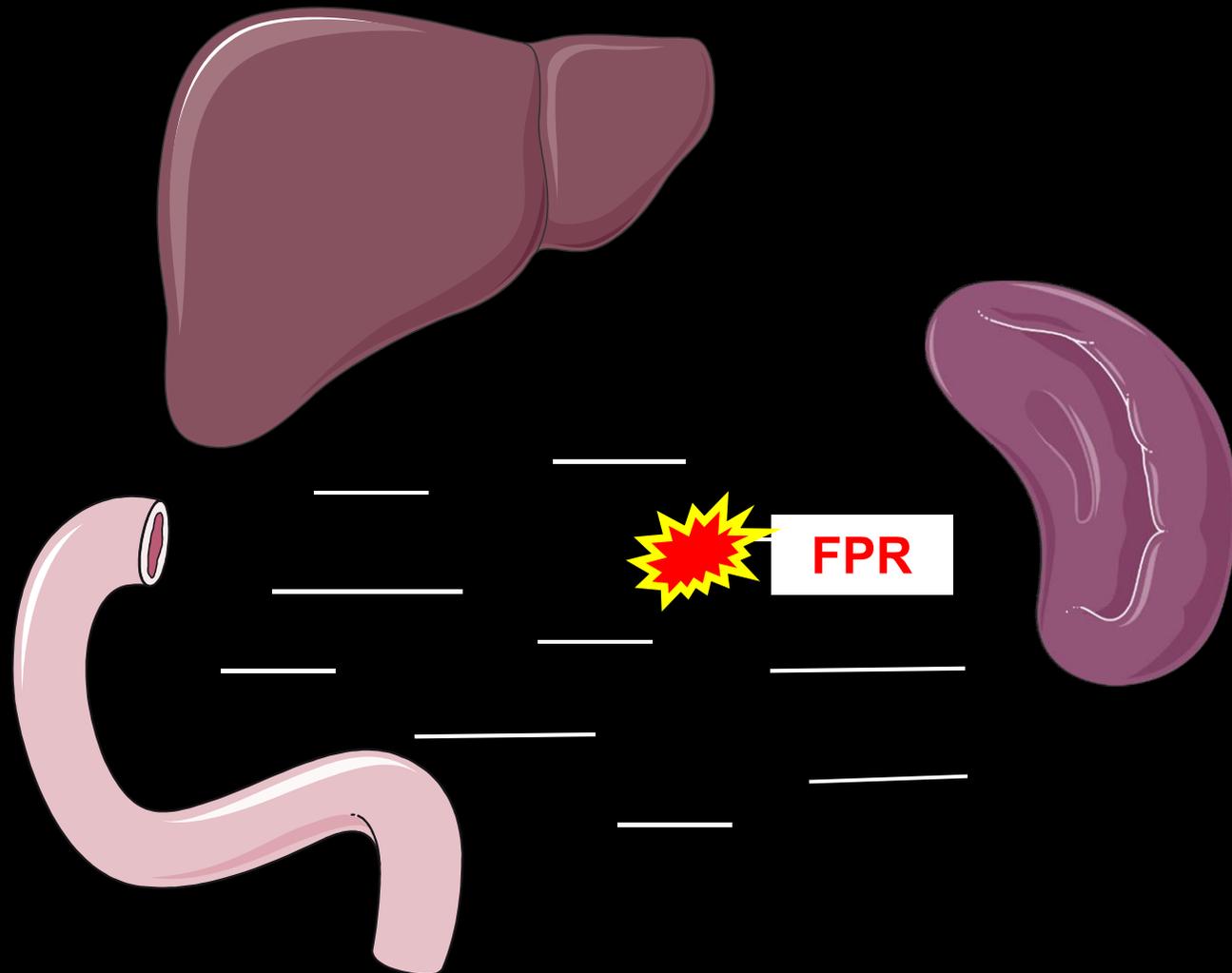


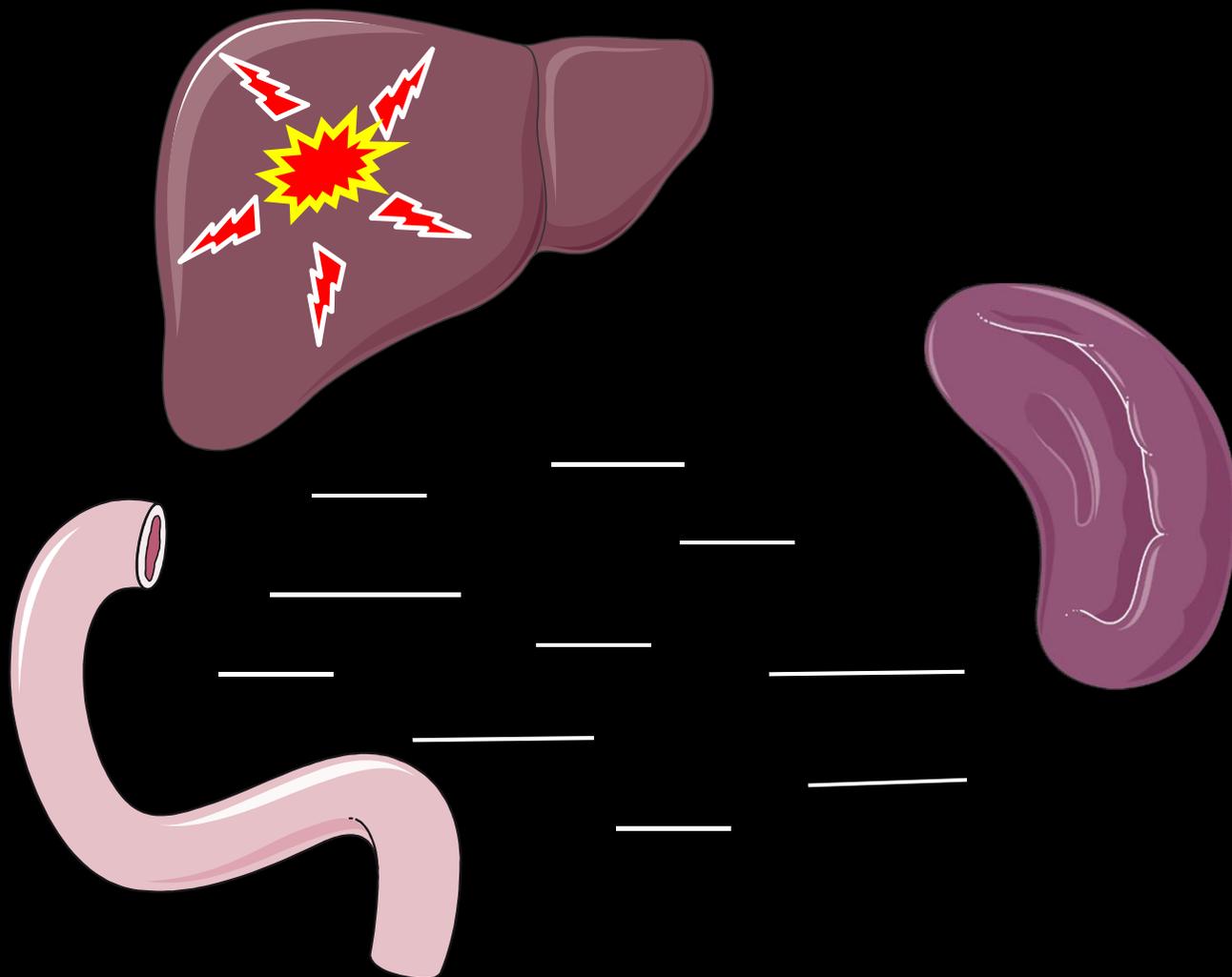
Surcharge hépatocytaire en fer

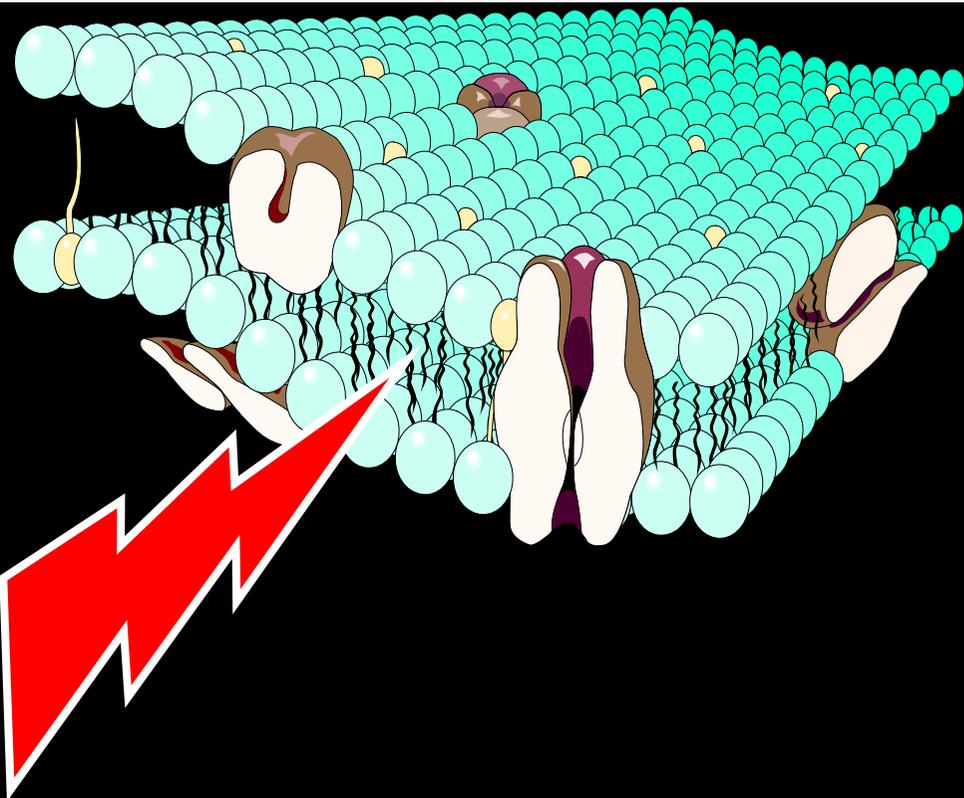
FPR (Fer Plasmatique Réactif)



Saturation transferrine > 75%



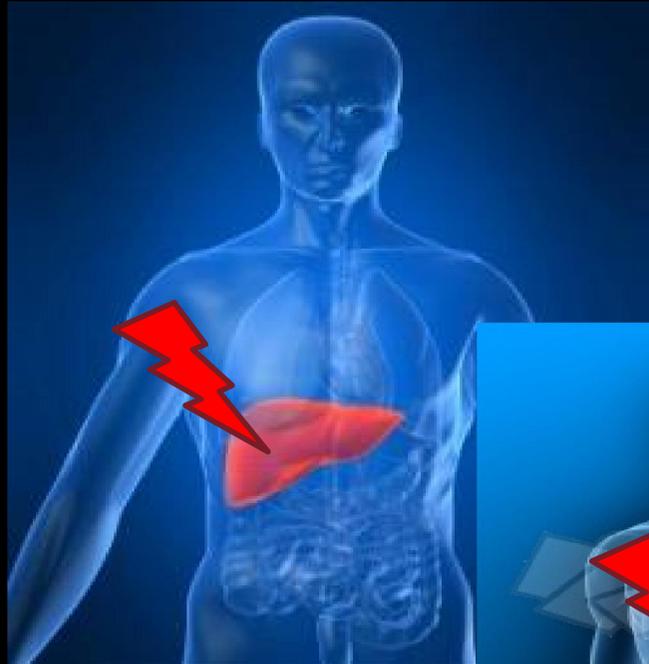




**Espèces
Radicales
Oxygénées**



FPR



Qu'est-ce que « l'hémochromatose » ?

Surcharge en fer

Génétique

Déficit en hepcidine

HFE (C282Y/C282Y)

Non-HFE (rare)

- Hémojuvéline (*HJV*)
- Récepteur Transferrine 2 (*TFR2*)
- ...

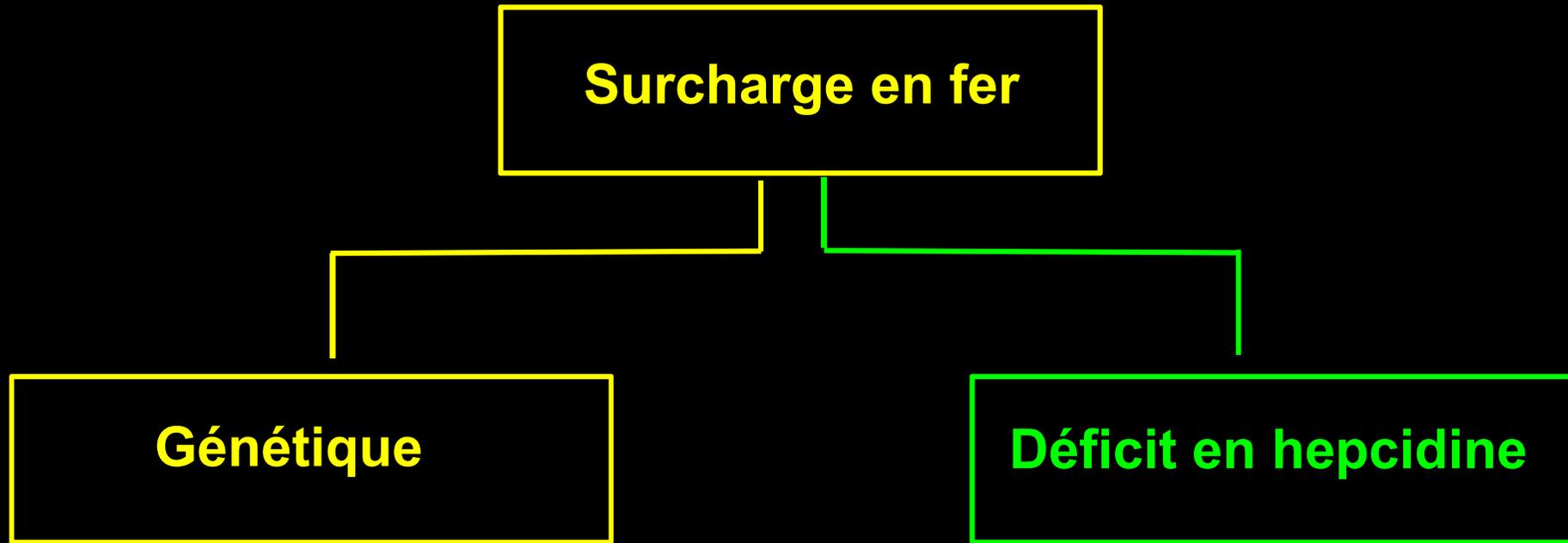
↑ Sat. transferrine

Pas de
surcharge
splénique

Surcharge
hépatique
en fer

**Qu'est-ce qui n'est pas de
« l'hémochromatose »?**

Qu'est-ce qui n'est pas de « l'hémochromatose » ?



Surcharge en fer acquise

- Transfusions
- Supplémentation parentérale en fer

Qu'est-ce qui n'est pas de « l'hémochromatose » ?

Surcharge en fer

```
graph TD; A[Surcharge en fer] --> B[Génétique]; A --> C[Déficit en hepcidine];
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Génétique

Déficit en hepcidine

Surcharge en fer génétique non hémochromatosique

Surcharge en fer

```
graph TD; A[Surcharge en fer] --> B[Génétique];
```

Génétique

**Maladie de la
ferroportine**

Quoi de neuf dans la définition de « l'hémochromatose » ?

Hémochromatose *HFE*

Quoi de neuf pour le diagnostic ?

Hémochromatose non HFE

**Surcharge en fer génétique non
hémochromatosique**

Quoi de neuf pour le traitement ?

Hémochromatose *HFE*

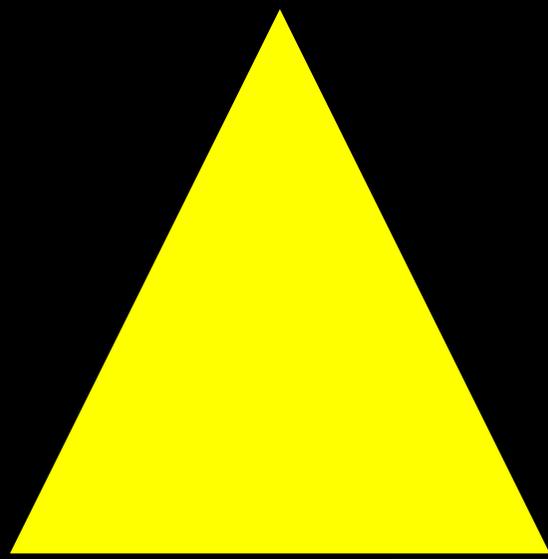
Diagnostic non invasif

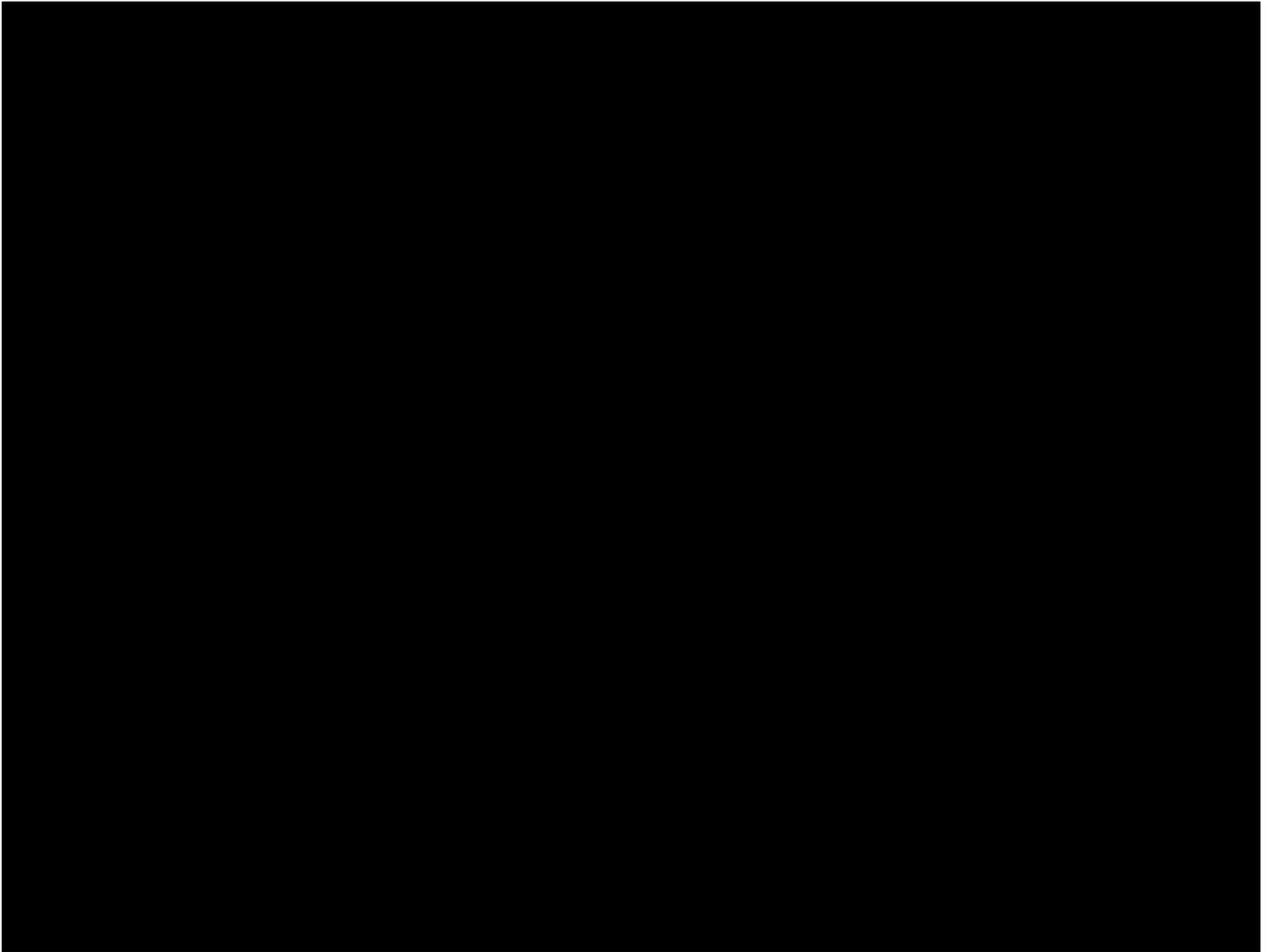


Clinique

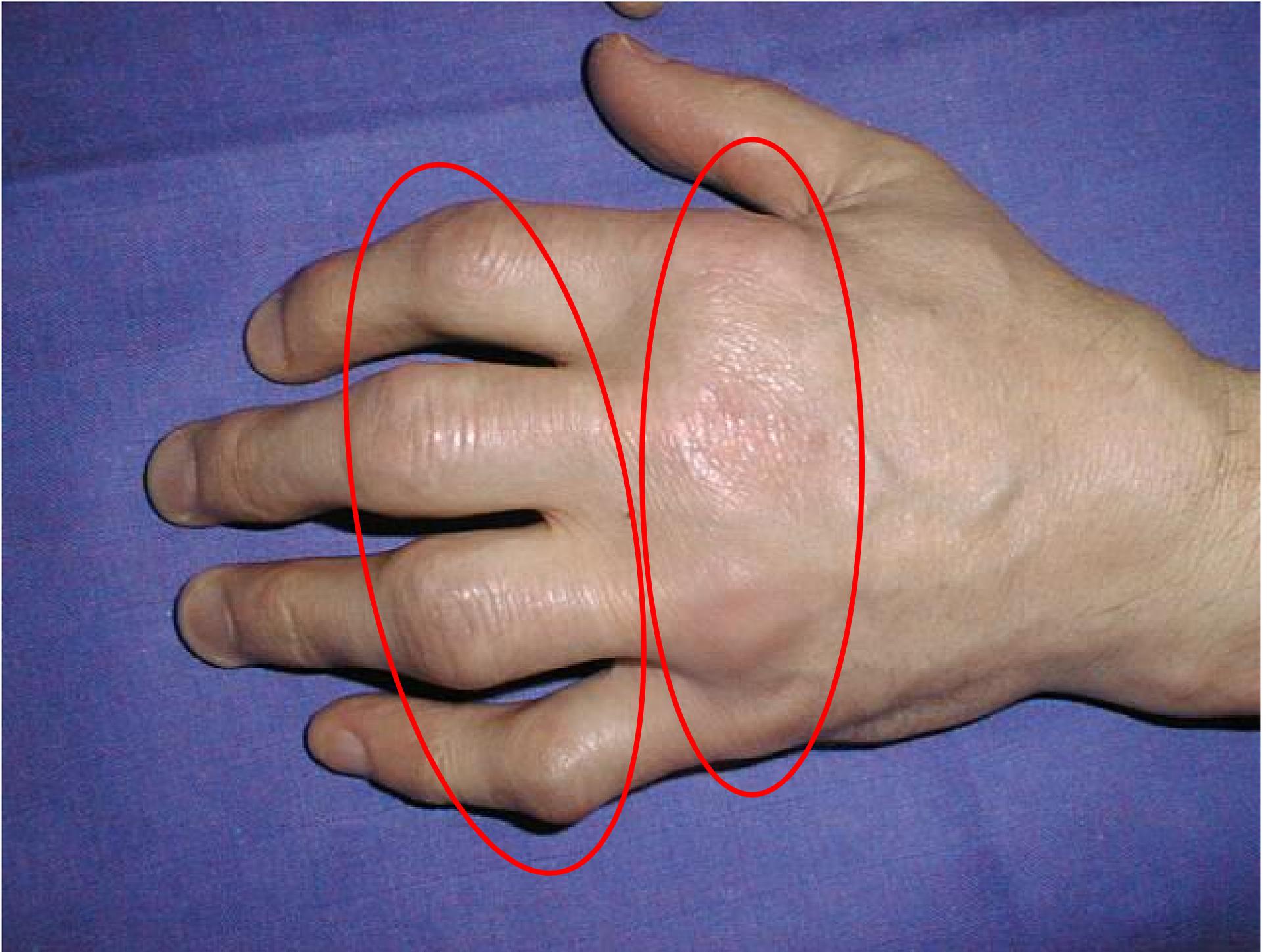
Imagerie

Biologie







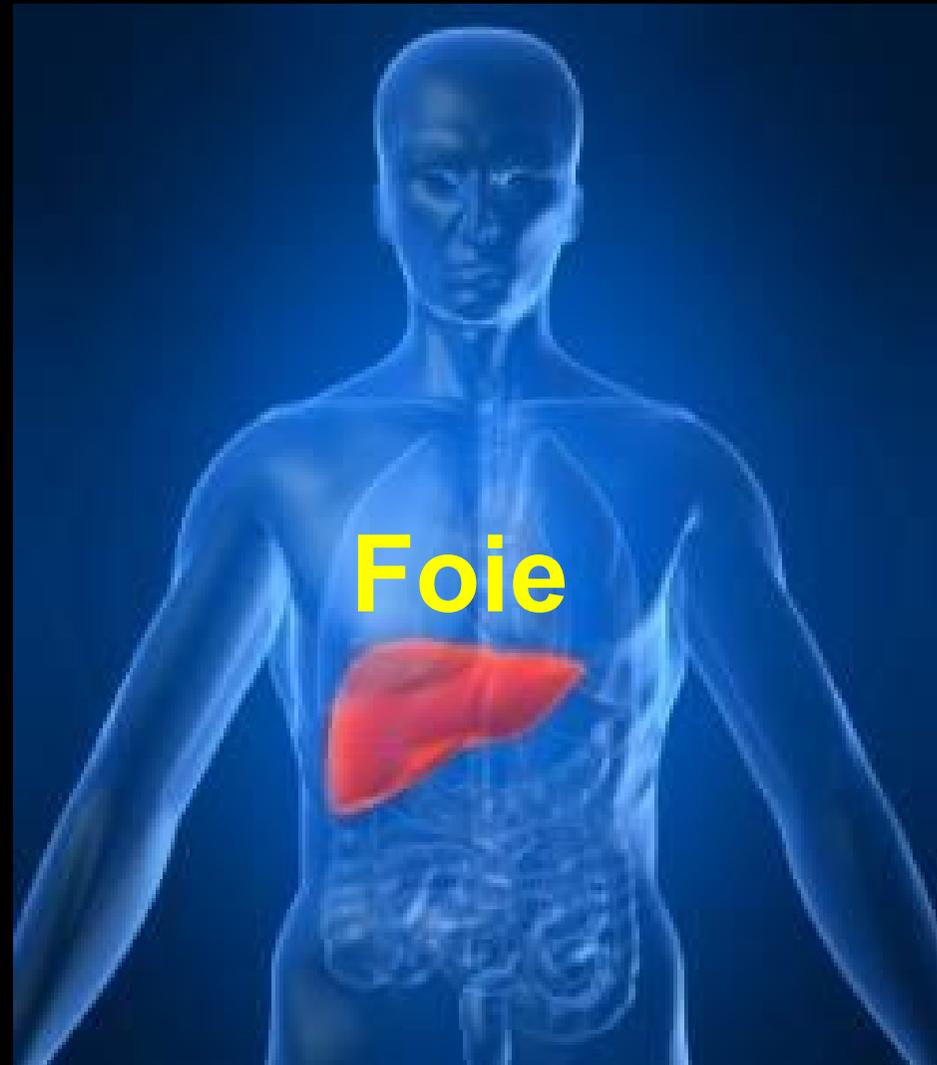


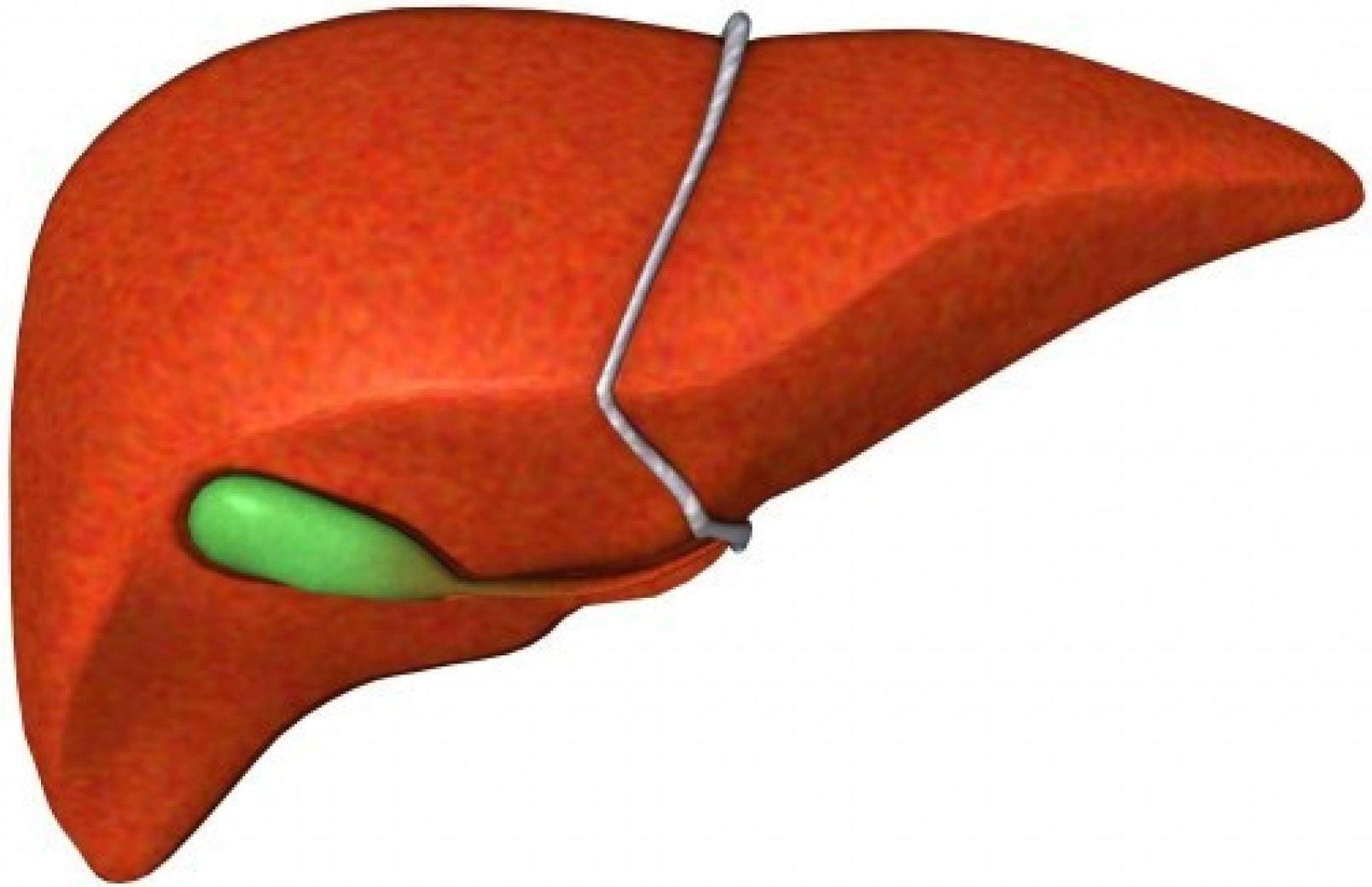


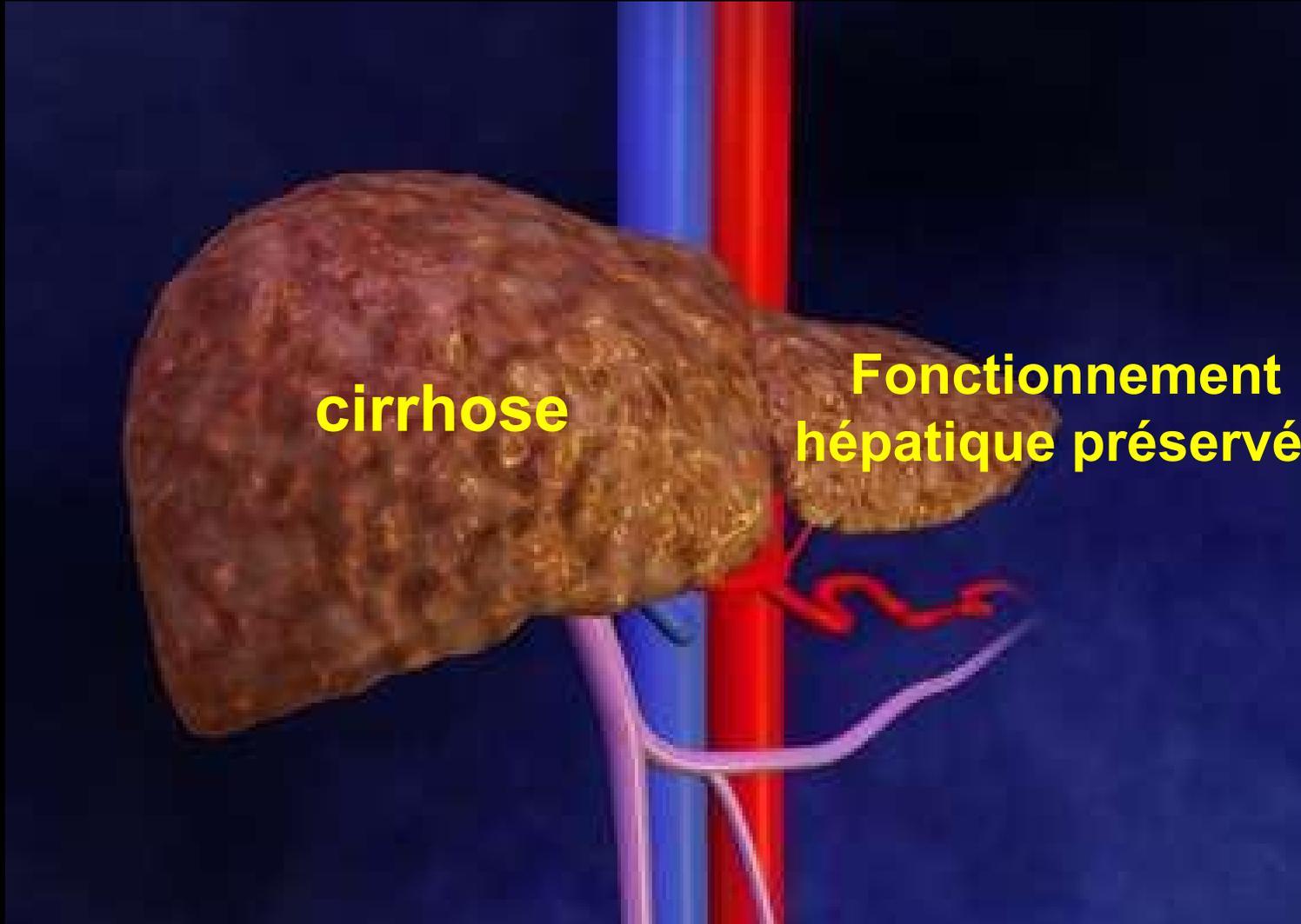


Ostéoporose









cirrhose

**Fonctionnement
hépatique préservé !**

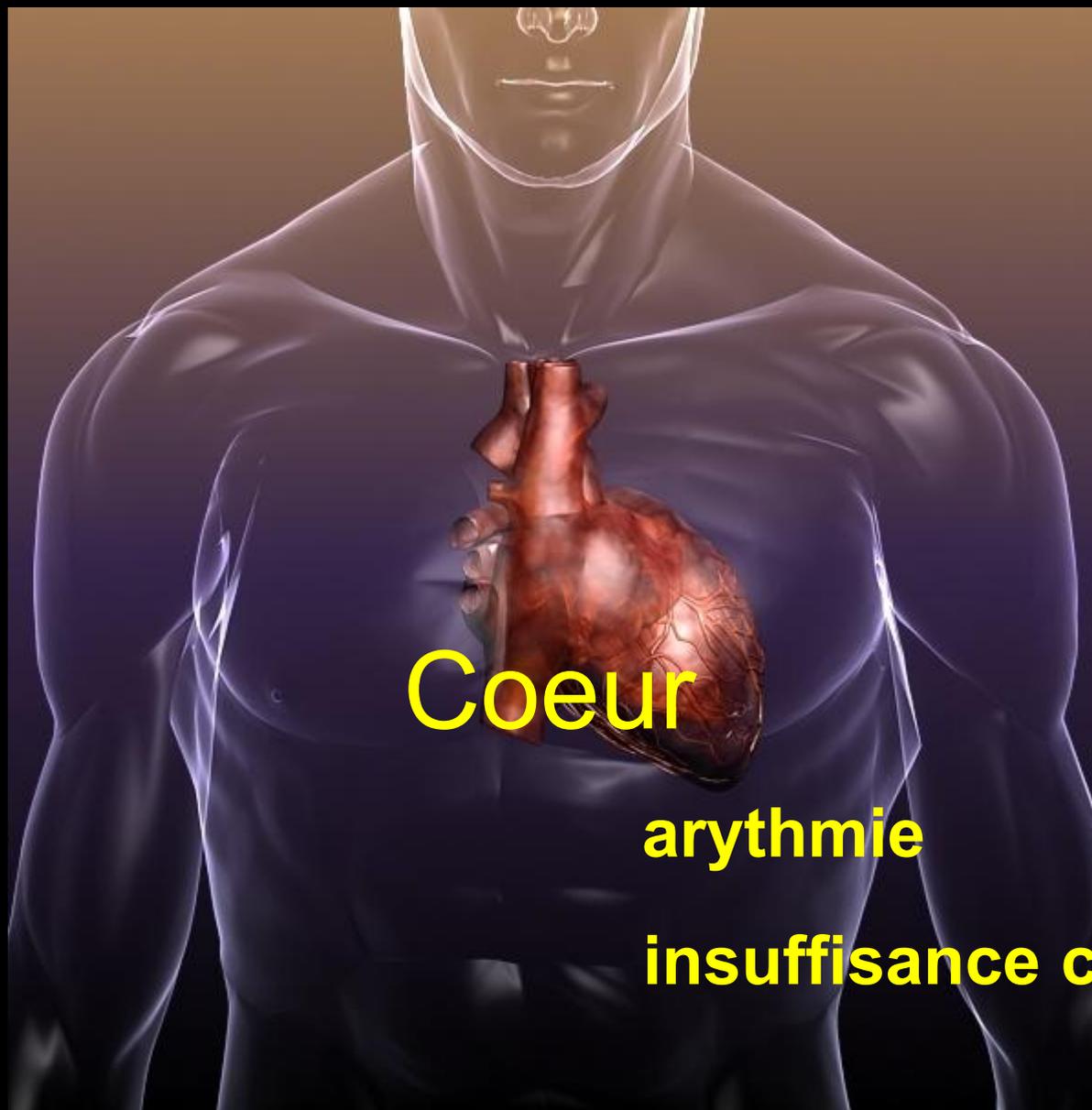




Pancréas



diabète

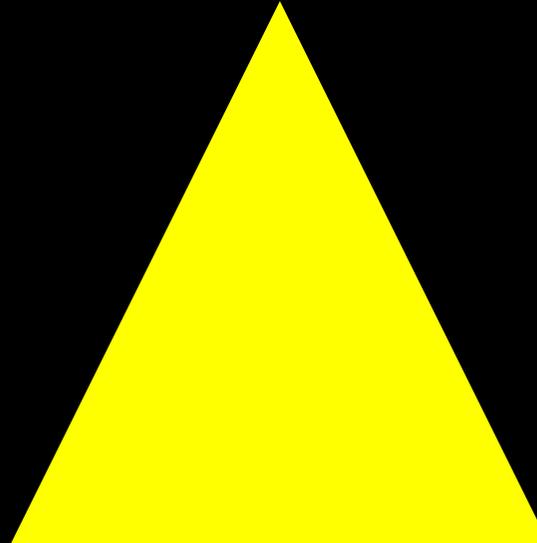


Coeur

arythmie

insuffisance cardiaque

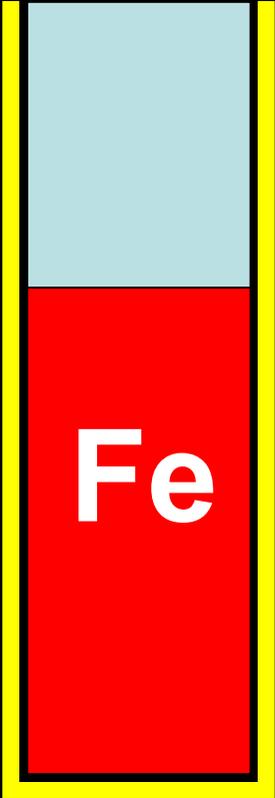
Clinique



Imagerie

Biologie

- **Saturation transferrine**
- **Ferritine**
- **Test génétique**



Saturation transferrine > 45%

> 60 % (H)
> 50 % (F)

2 examens !

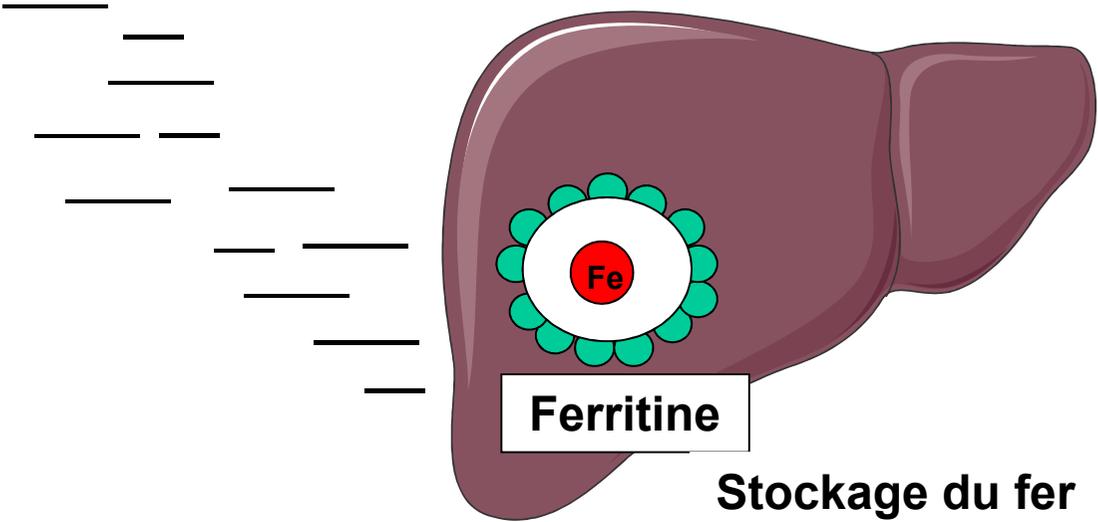
**Une saturation de la transferrine normale
exclut une hémochromatose**

Clinique

Imagerie

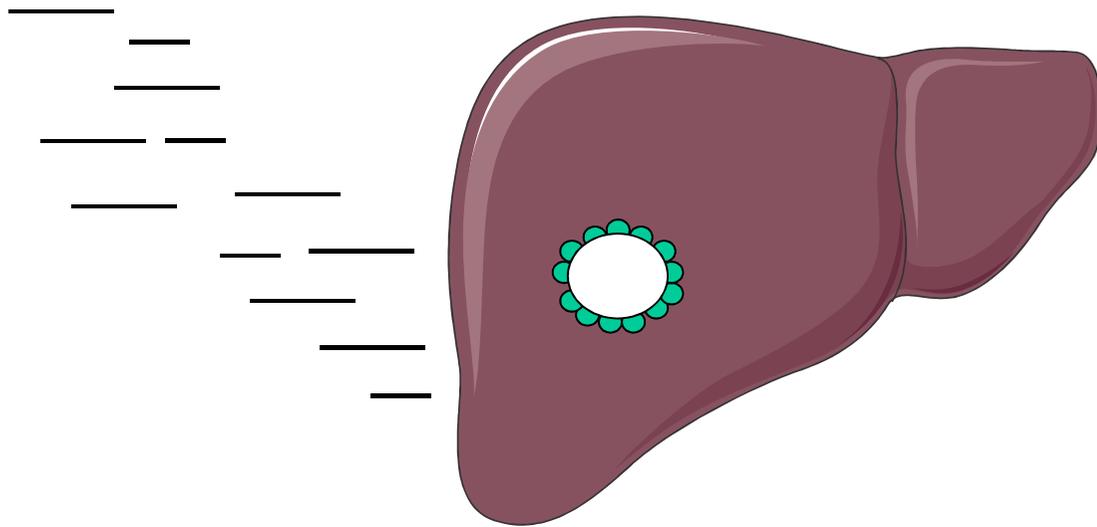
Biologie

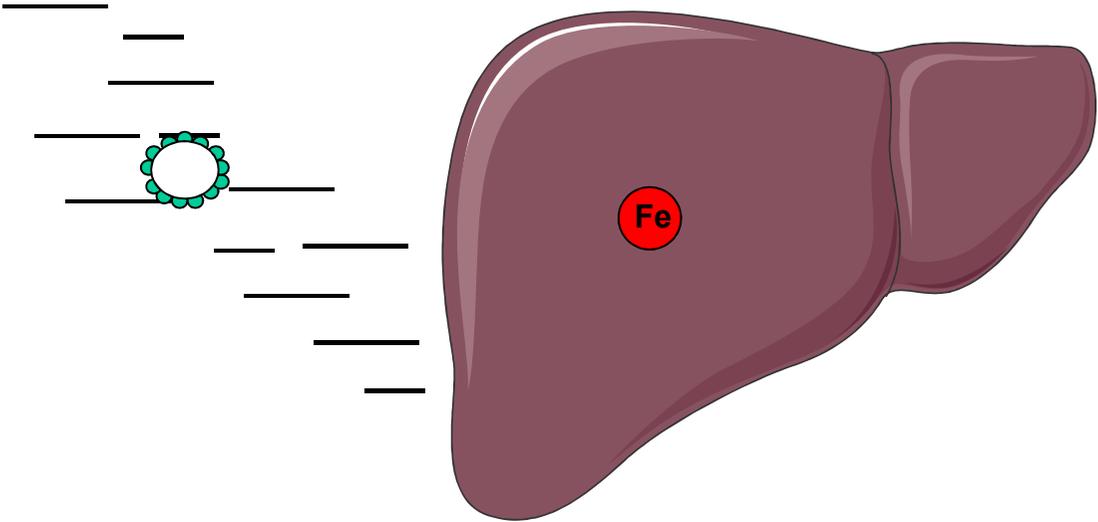
- **Saturation transferrine**
- **Ferritine**
- **Test génétique**

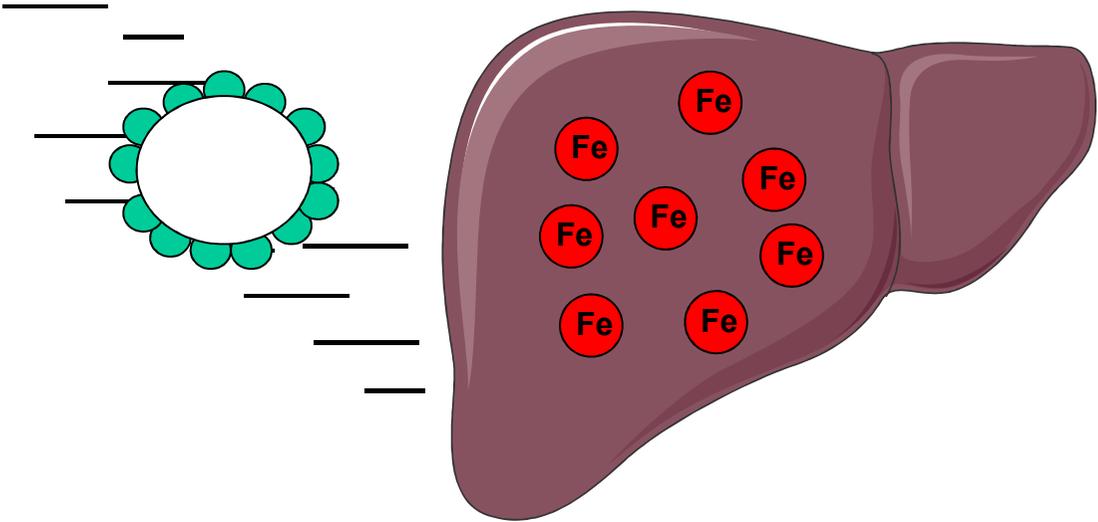


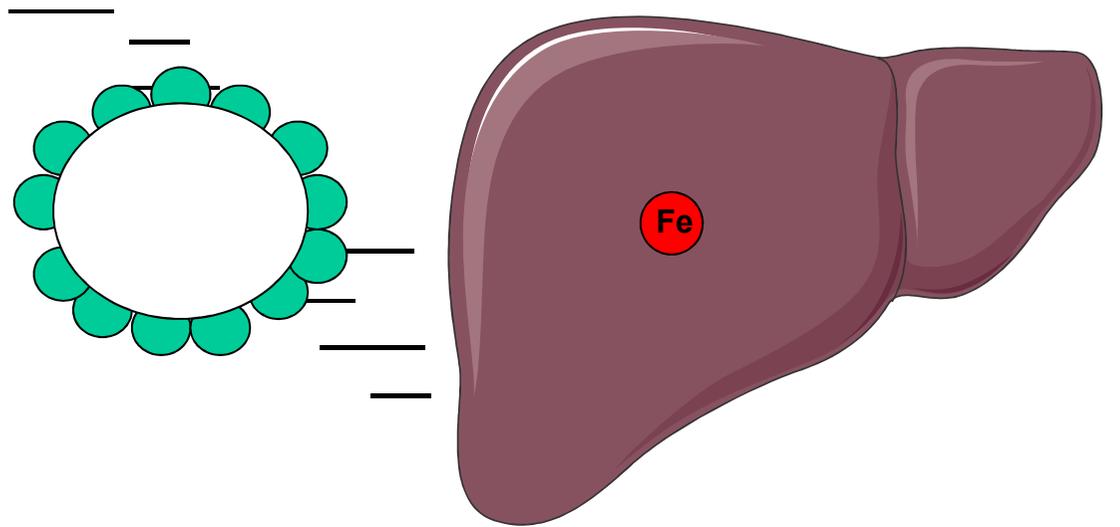
Ferritine

Stockage du fer









> 300 $\mu\text{g/L}$ (H)

> 200 $\mu\text{g/L}$ (F)



↑ Ferritine

Syndrome métabolique



Inflammation



Alcoolisme



> 300 µg/L (M)

> 200 µg/L (F)



↑ Ferritine

Syndrome métabolique



Inflammation



Alcoolisme



> 300 µg/L (M)

> 200 µg/L (F)



↑ Ferritine
Sat. Tf ?

Syndrome métabolique

Sat. Tf normale

Inflammation

Sat. Tf basse

Alcoolisme

Sat. Tf N ou peu élevée

Clinique

Imagerie

Biologie

- **Saturation transferrine**
- **Ferritine**
- **Test génétique**

C282Y/C282Y

H63D

H63D/H63D

S65C

C282Y/H63D ?

***Saturation
transferrine***

Ferritine

***Effet
« booster »***

Clinique

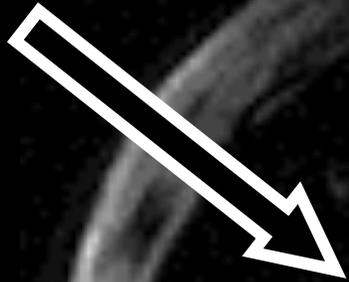
Imagerie

Biologie

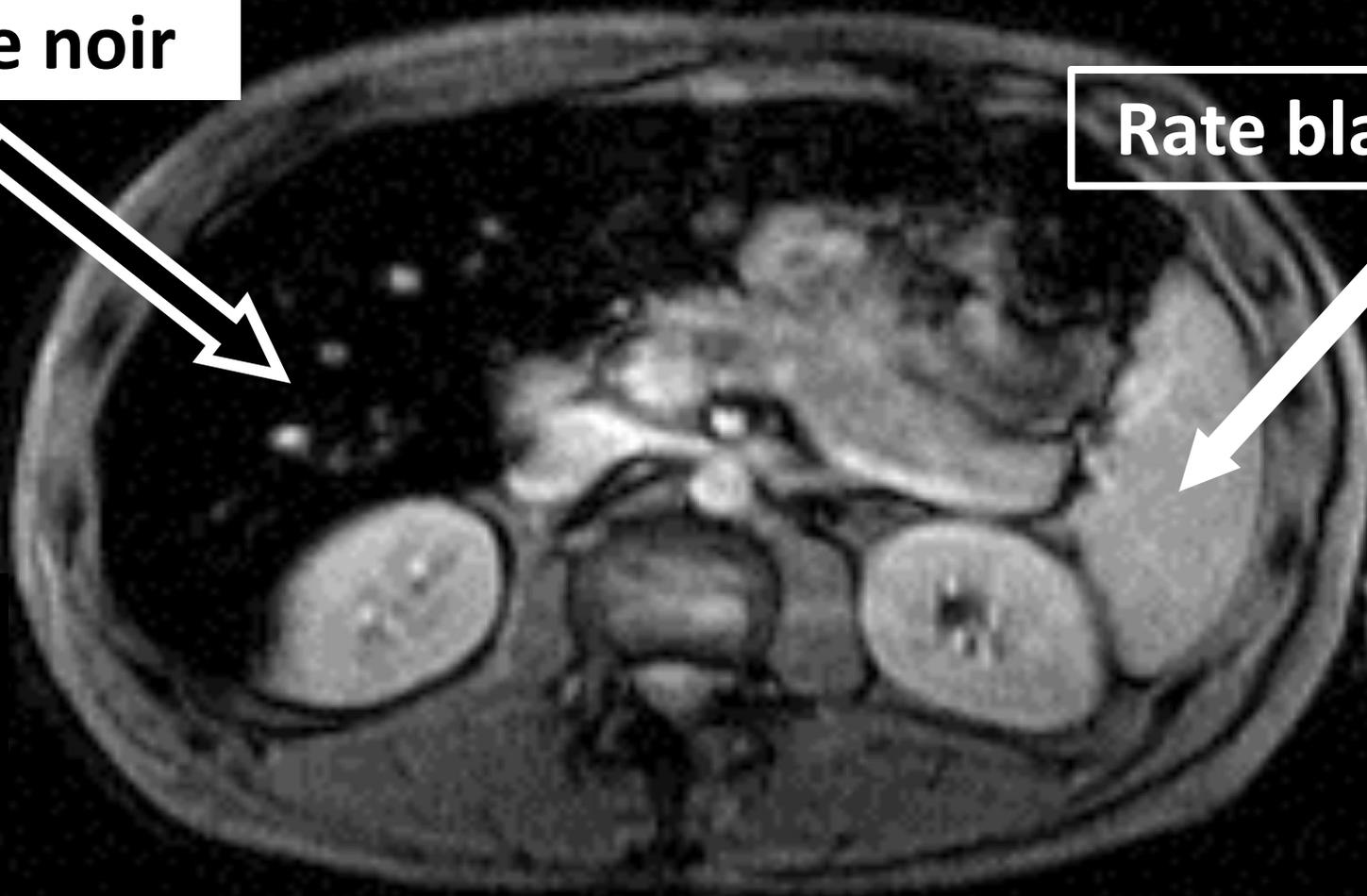
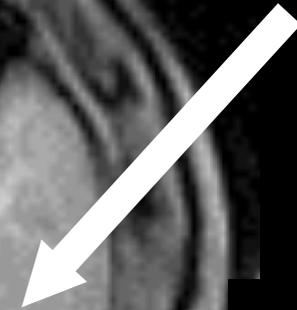
- **Saturation transferrine**
- **Ferritine**
- **Test génétique**

I.R.M. - Fer

Foie noir



Rate blanche



Quoi de neuf dans la définition de « l'hémochromatose » ?

Hémochromatose *HFE*

Quoi de neuf pour le diagnostic ?

Hémochromatose *non HFE*

**Surcharge en fer génétique non
hémochromatosique**

Quoi de neuf pour le traitement?

Hémochromatose *non HFE* (= non C282Y/C282Y)

(hémoujuvéline, récepteur transferrine 2 ...)

Similarités

« Syndrome d'hepcidino-déficience »

↑ Sat. transferrine

Clinique

Pas de surcharge
splénique

Surcharge
hépatique en fer

Imagerie

Biologie

Différences...

Hémochromatose *non HFE* (= non *C282Y/C282Y*)

(hémouvéline, récepteur transferrine 2 ...)

Différences

- Rare ...mais multi-ethnique
- Plus jeune (< 30 ans) « juvénile »
- Plus sévère
- Centre expert pour étude génétique

**Quoi de neuf dans la définition de « l'hémochromatose »
?**

Hémochromatose *HFE*

Quoi de neuf pour le diagnostic?

Hémochromatose *non HFE*

**Surcharge en fer génétique
non hémochromatosique**

Quoi de neuf pour le traitement ?

Surcharge en fer génétique non hémochromatosique

Surcharge en fer

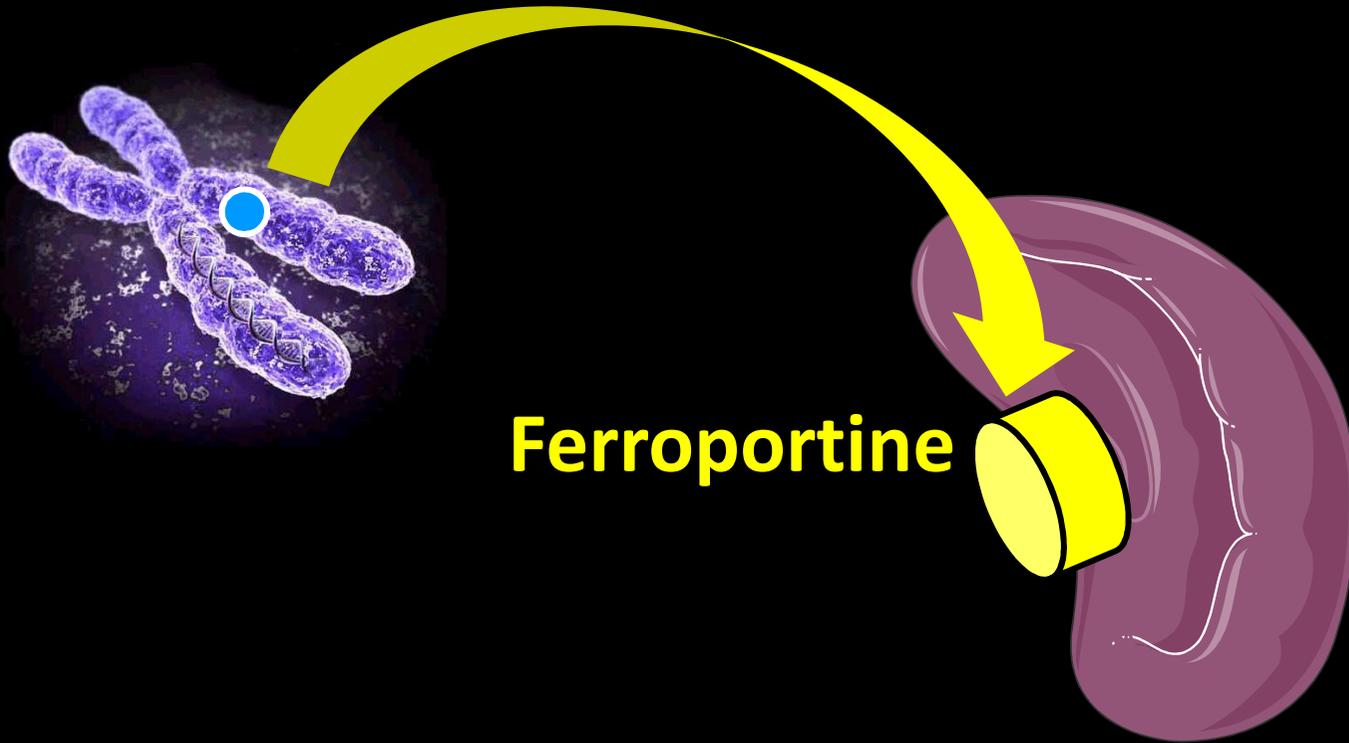
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graph TD; A[Surcharge en fer] --> B[Génétique]; A --> C[Déficit en hepcidine]; C --- D[Maladie de la ferroportine]
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Génétique

Déficit en hepcidine

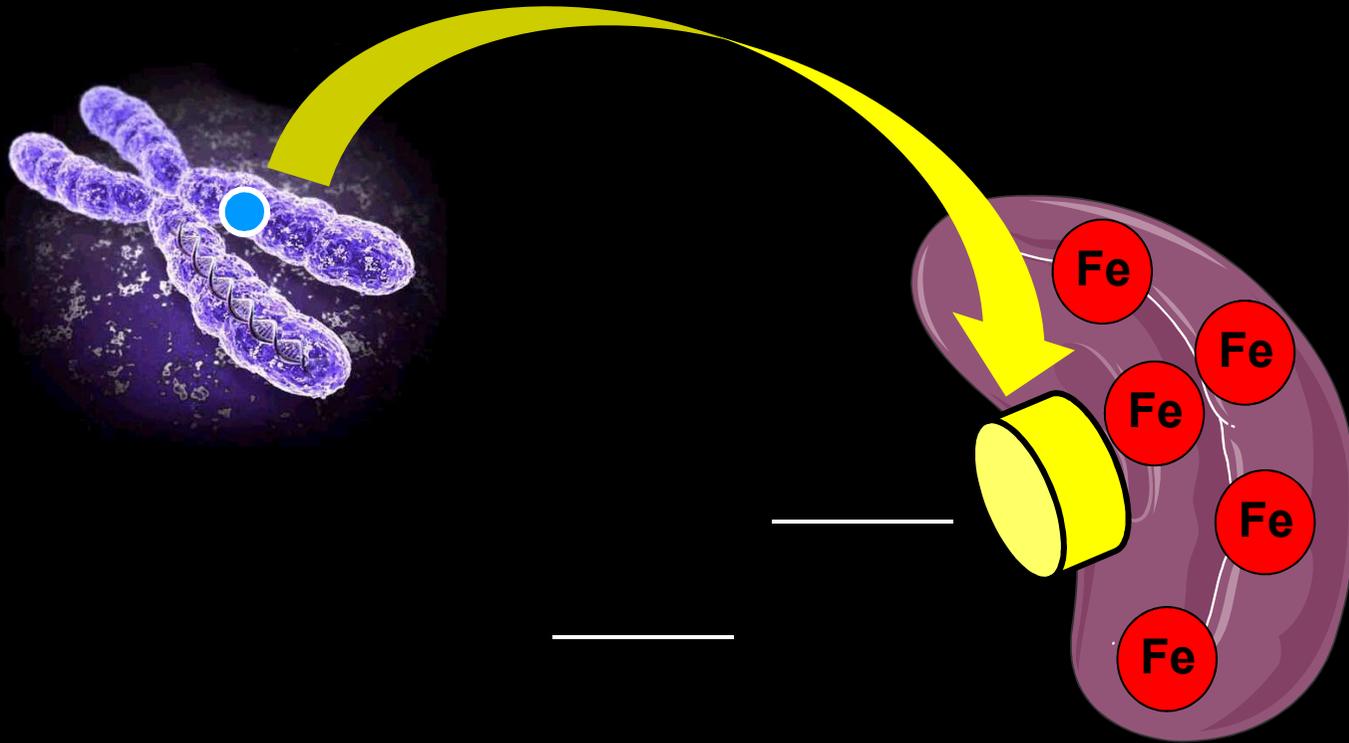
**Maladie de la
ferroportine**

Maladie de la ferroportine



Ferroportine

Maladie de la ferroportine



Saturation transferrine normale

Ferritine (très) élevée

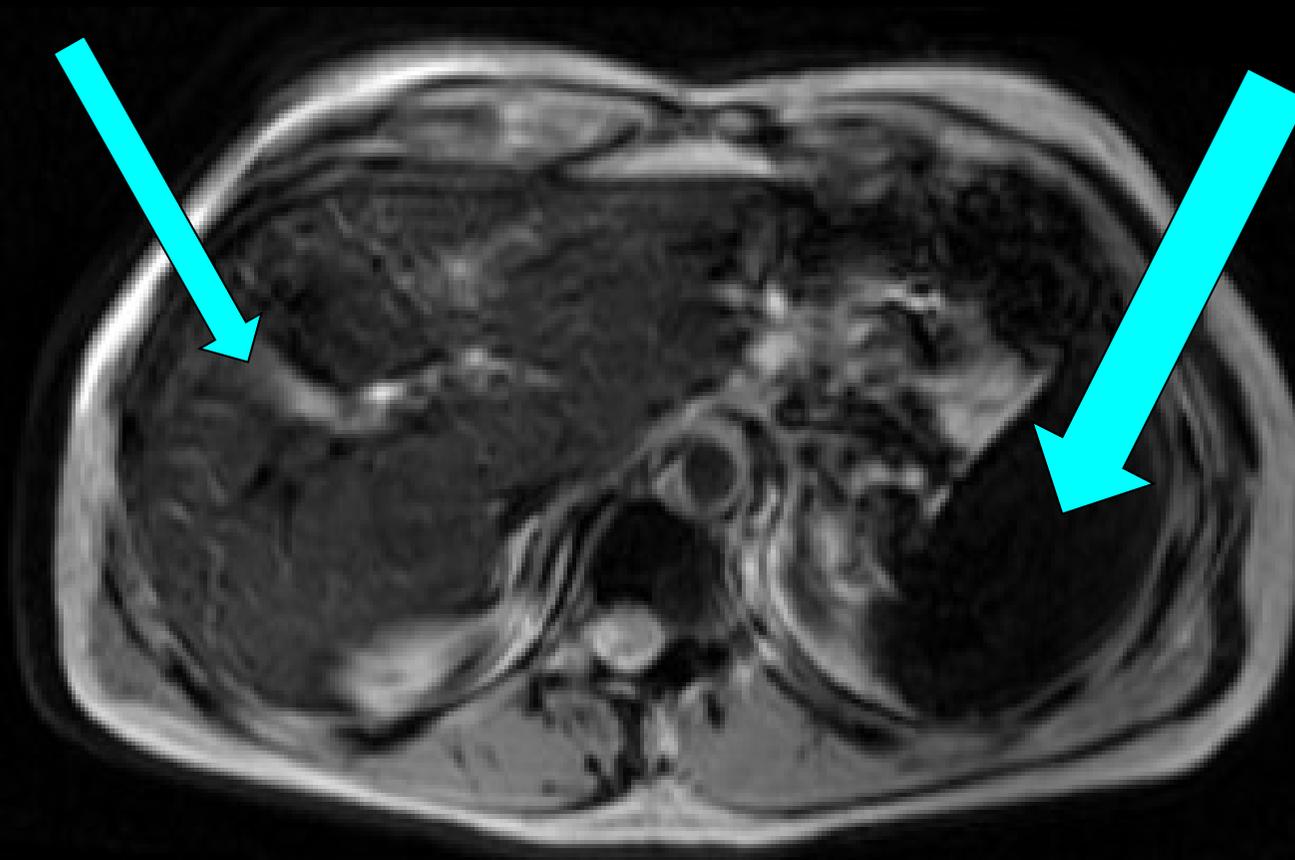
**Une saturation de la transferrine normale
exclut une hémochromatose**

mais

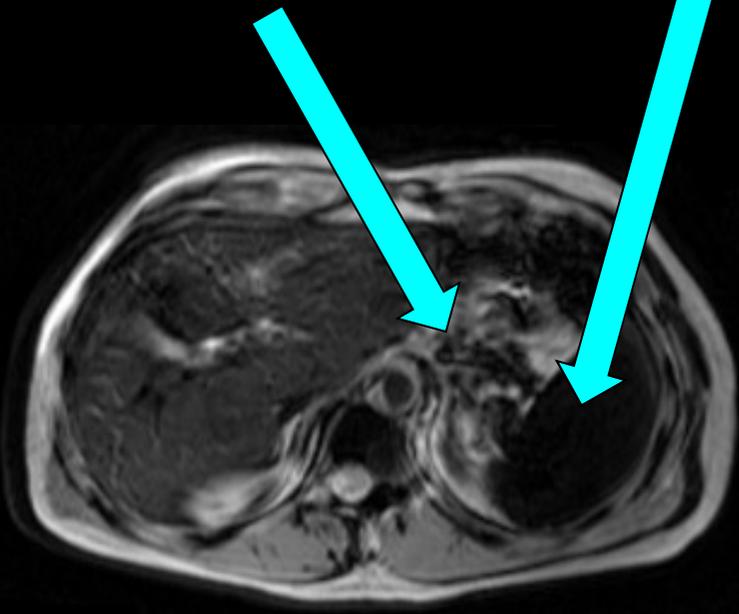
**Une saturation de la transferrine normale
n'exclut pas une surcharge en fer génétique non
hémochromatosique**

Foie gris

Rate noire

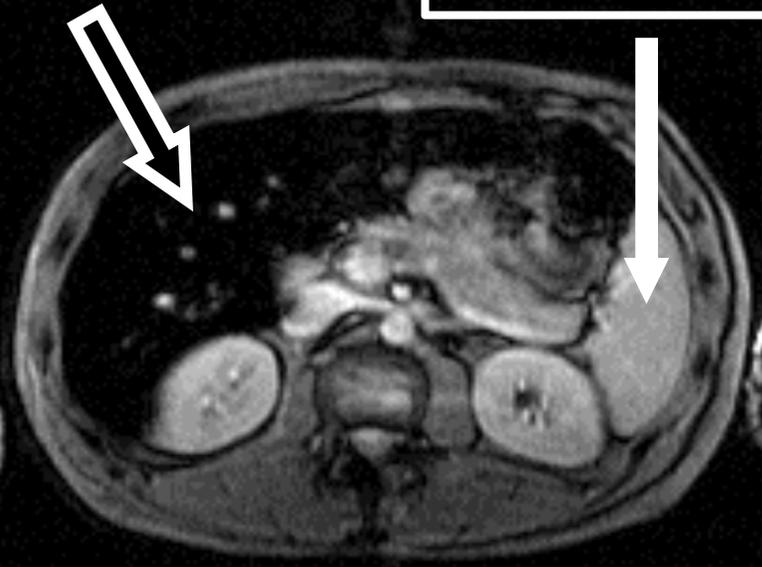


Foie gris **Rate noire**



Foie noir

Rate blanche



Quoi de neuf dans la définition de « l'hémochromatose » ?

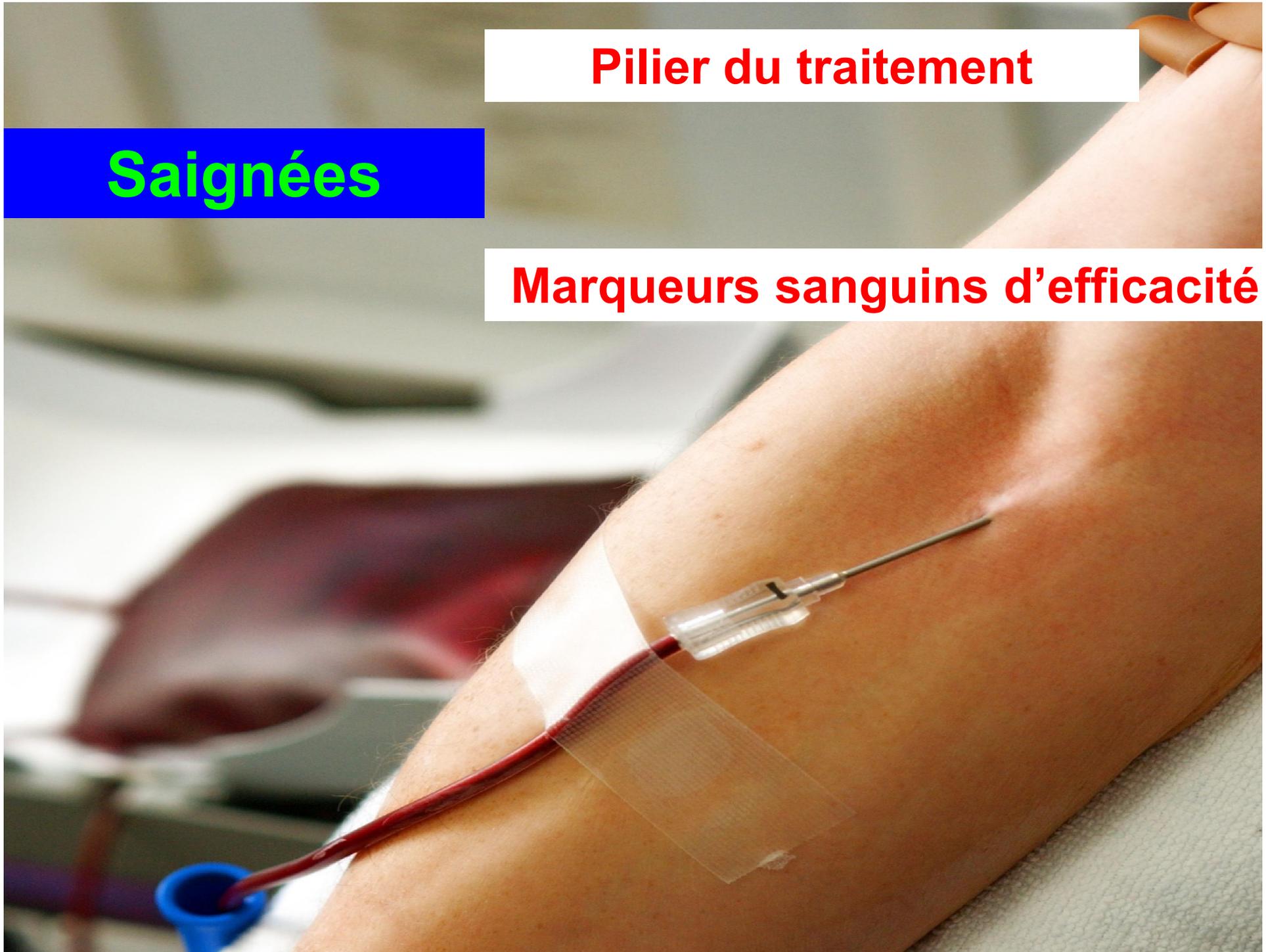
Quoi de neuf pour le diagnostic ?

Quoi de neuf pour le traitement ?

Pilier du traitement

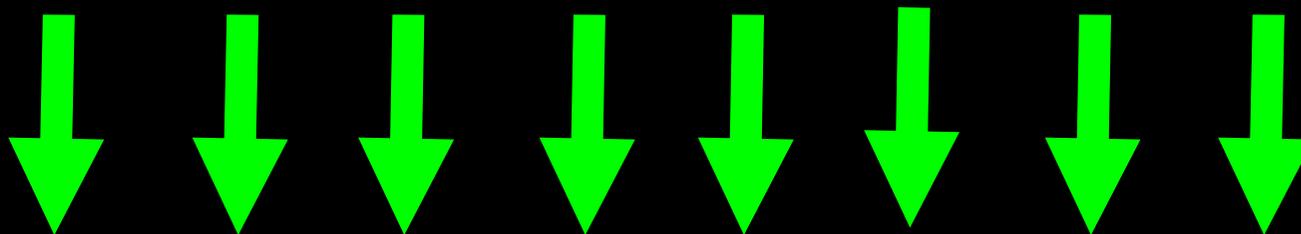
Saignées

Marqueurs sanguins d'efficacité



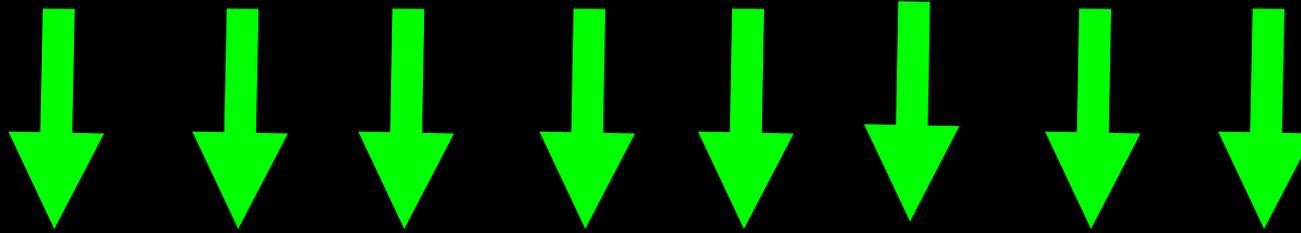
Phase d'induction

Saignées



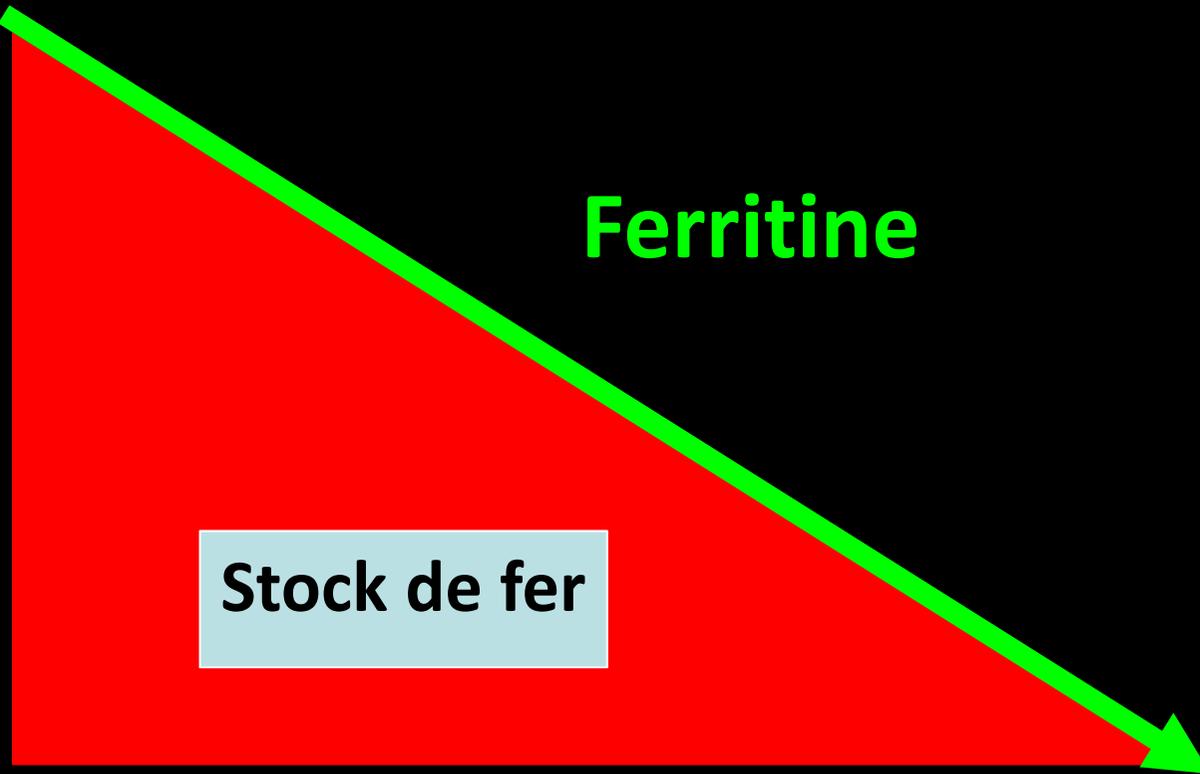
Stock de fer

Saignées



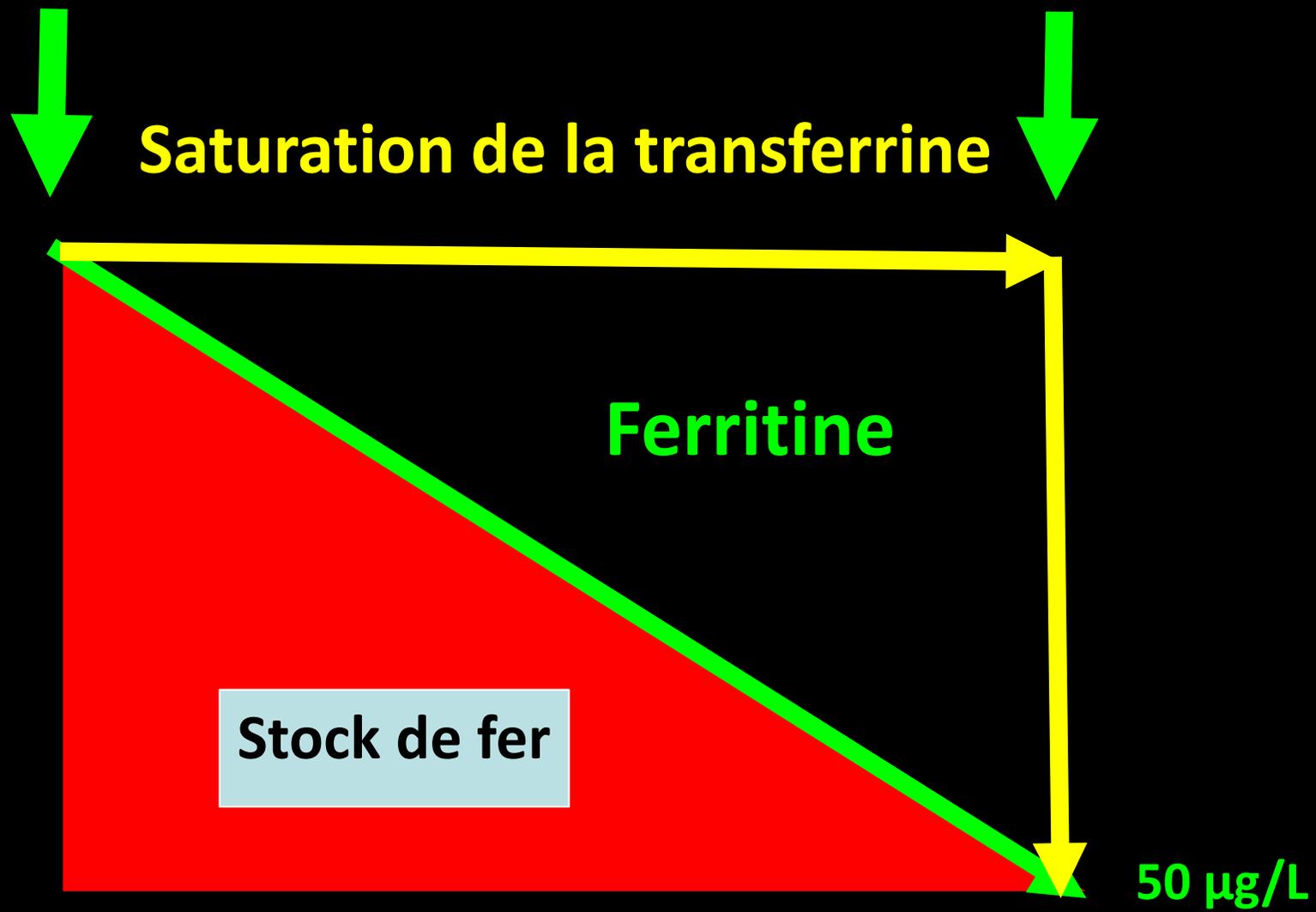
Ferritine

Stock de fer



Ferritine = efficacité

**Se méfier de la
Saturation de la transferrine !**



Traitement d'entretien

Ferritine
≤50



ST \leq 50%
Ferritine
 \leq 50



« Règle des 50 »

ST ≤ 50%

**Ferritine
≤ 50**

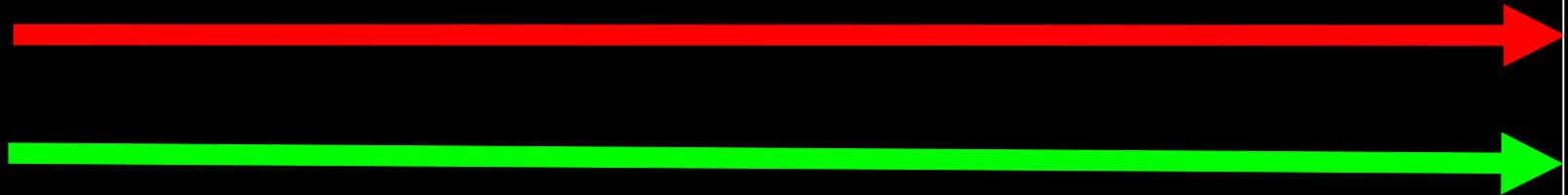


ST

> 75%

Ferritine

≤ 50



Une ferritine « normalisée » reste le but essentiel

mais

Ne pas oublier la saturation de la transferrine (2 fois par an)

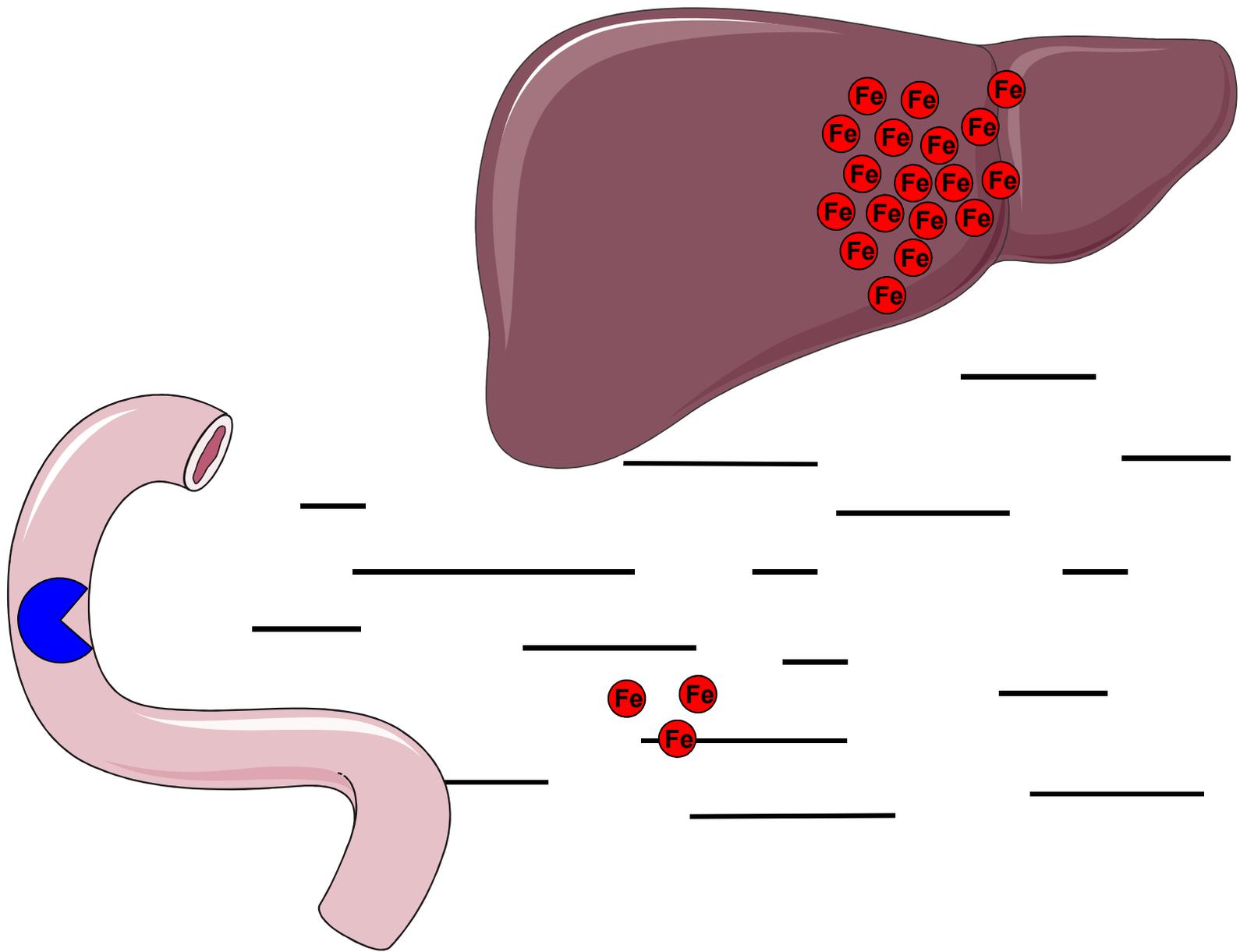
Autres traitements

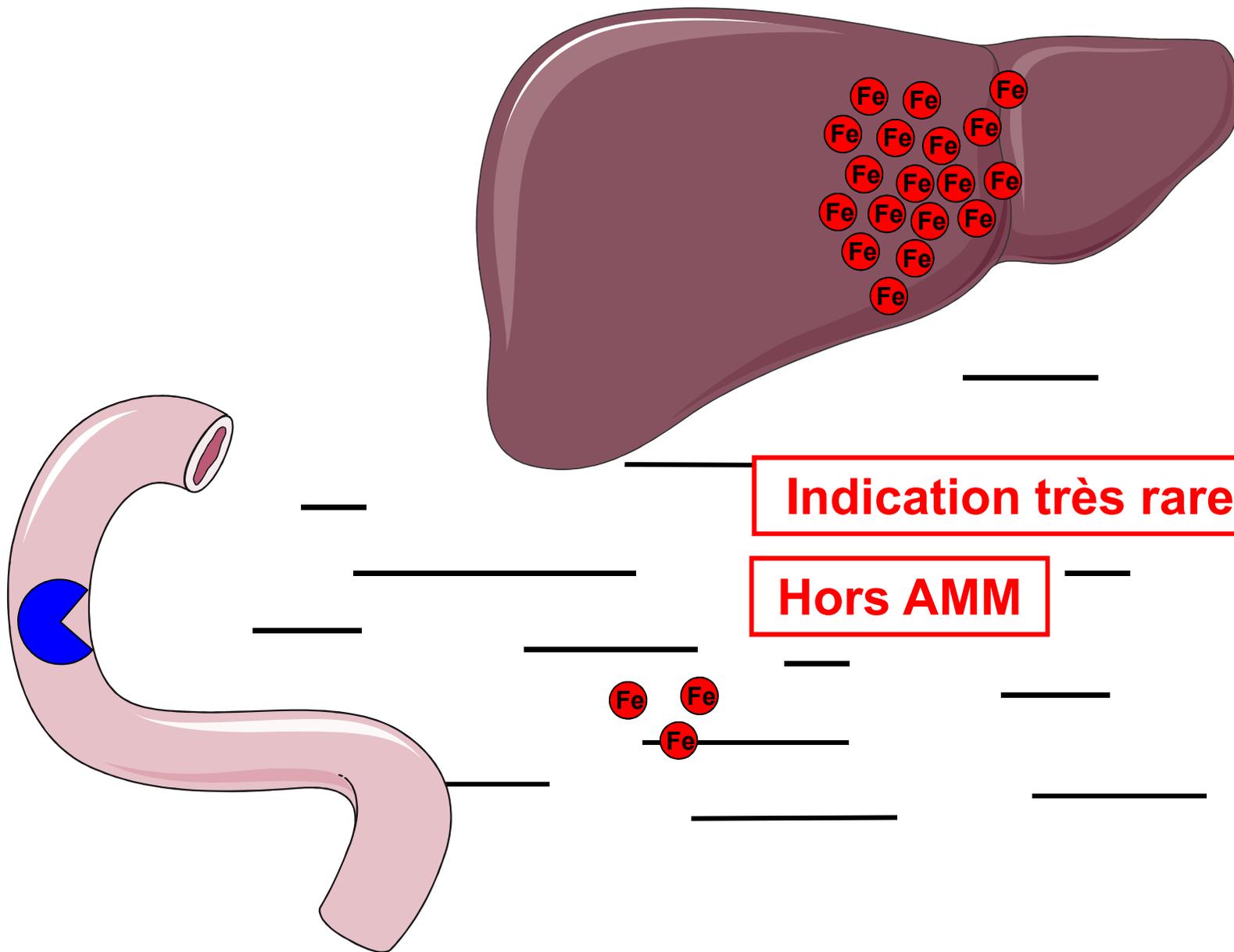


**« conséquence »
(= surcharge en fer)**



**Chélation orale
(déférasirox)**



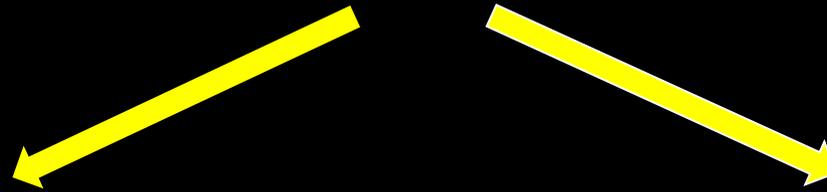


Indication très rare

Hors AMM

Fe
Fe
Fe

Autres traitements



« conséquence »
(surcharge en fer)

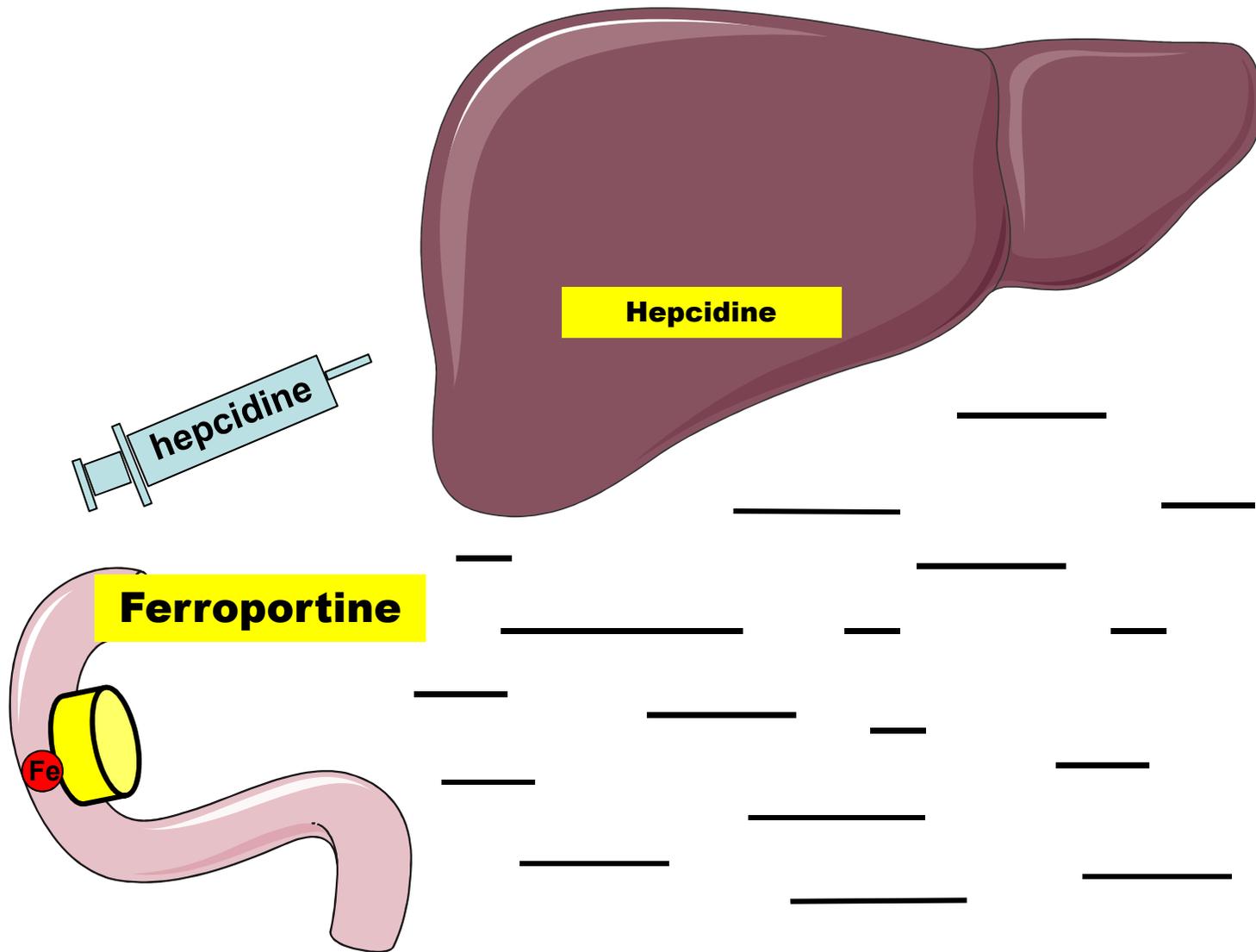


Chélation orale

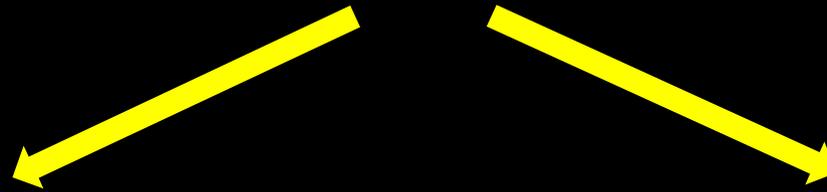
« cause »

(= déficit en hepcidine)

Supplémentation en hepcidine



Autres traitements



« conséquence »
(surcharge en fer)



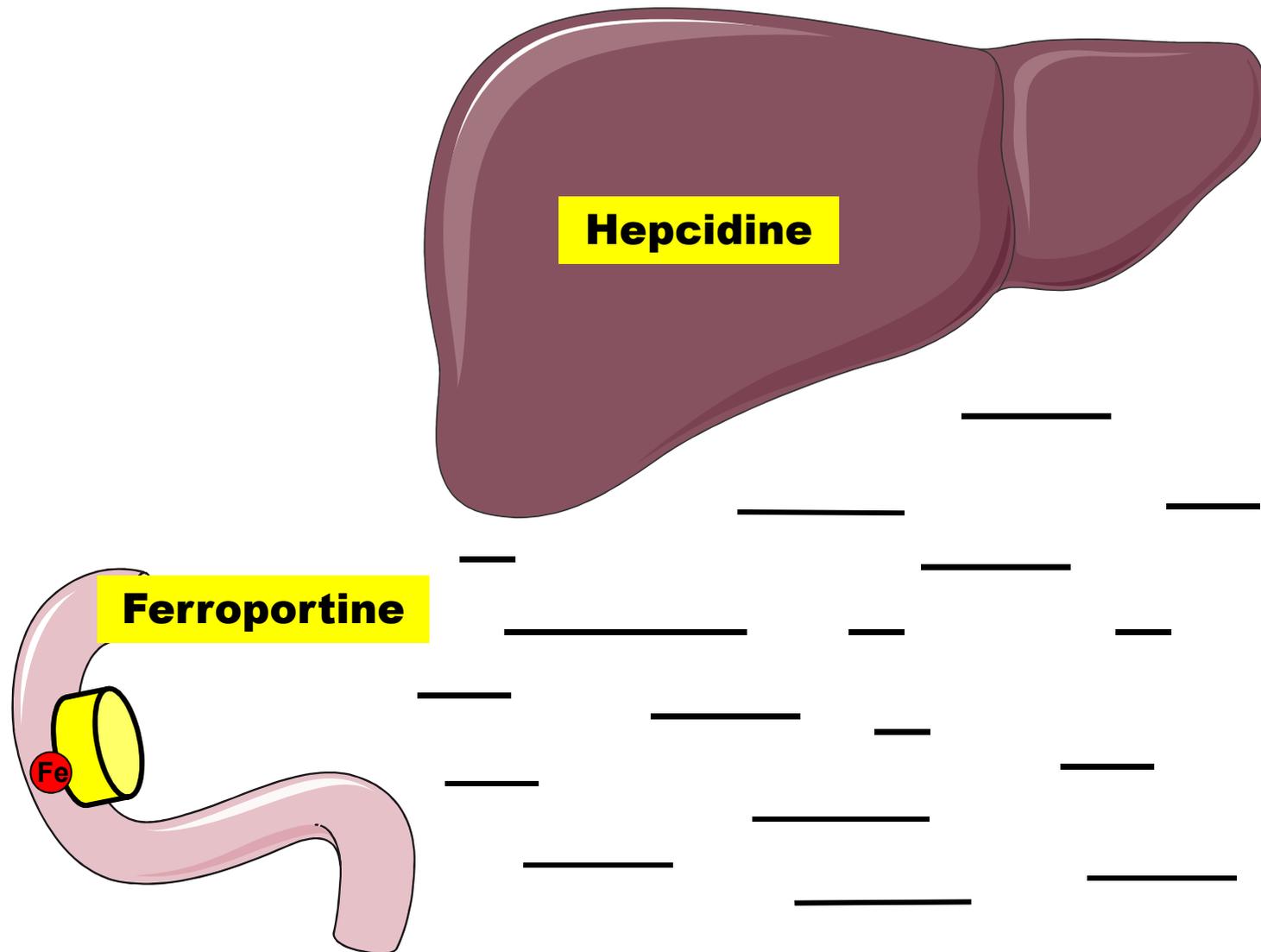
Chélation orale

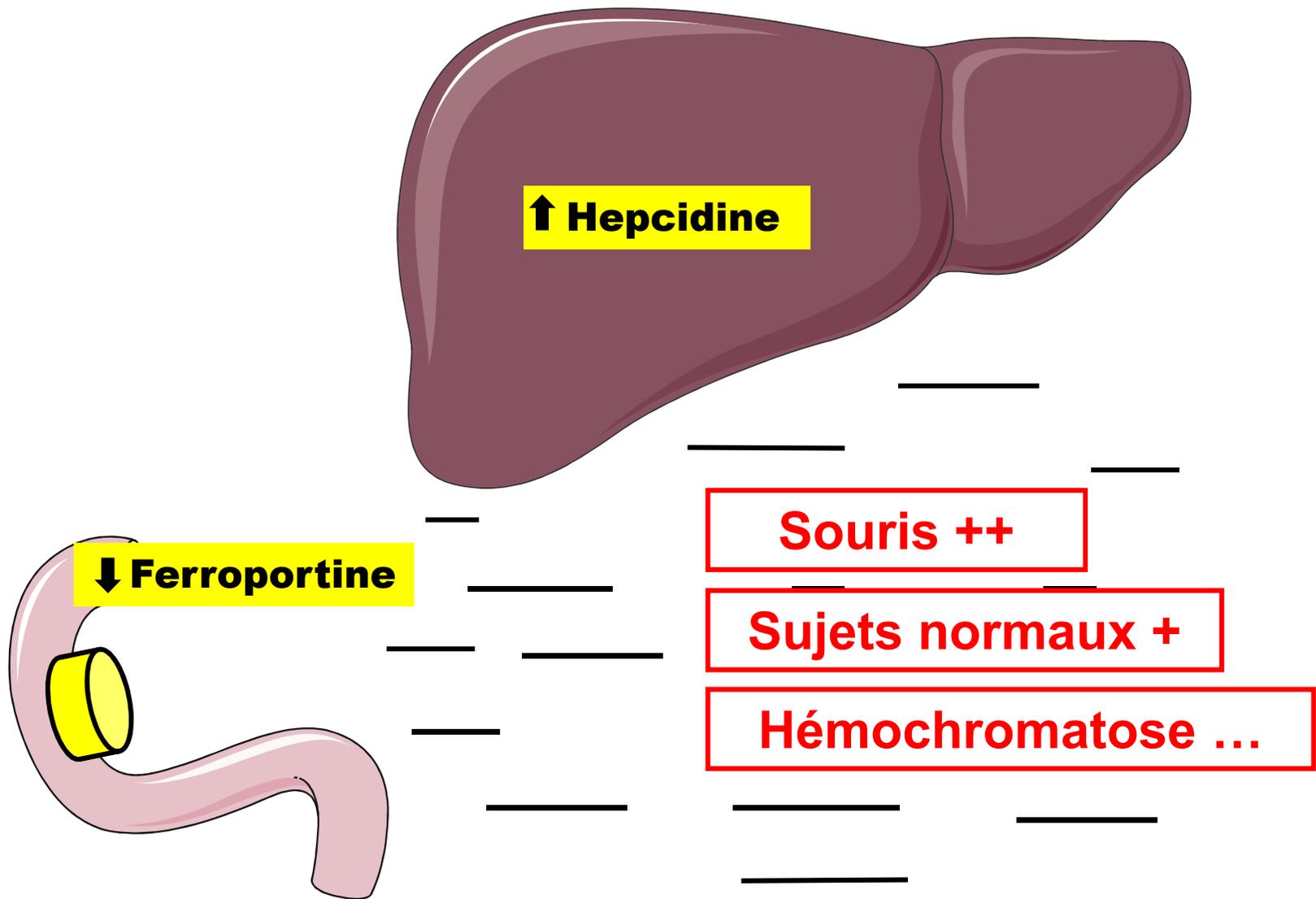
« cause »

(déficit en hepcidine)

Supplémentation en hepcidine

Inhibition de la ferroportine

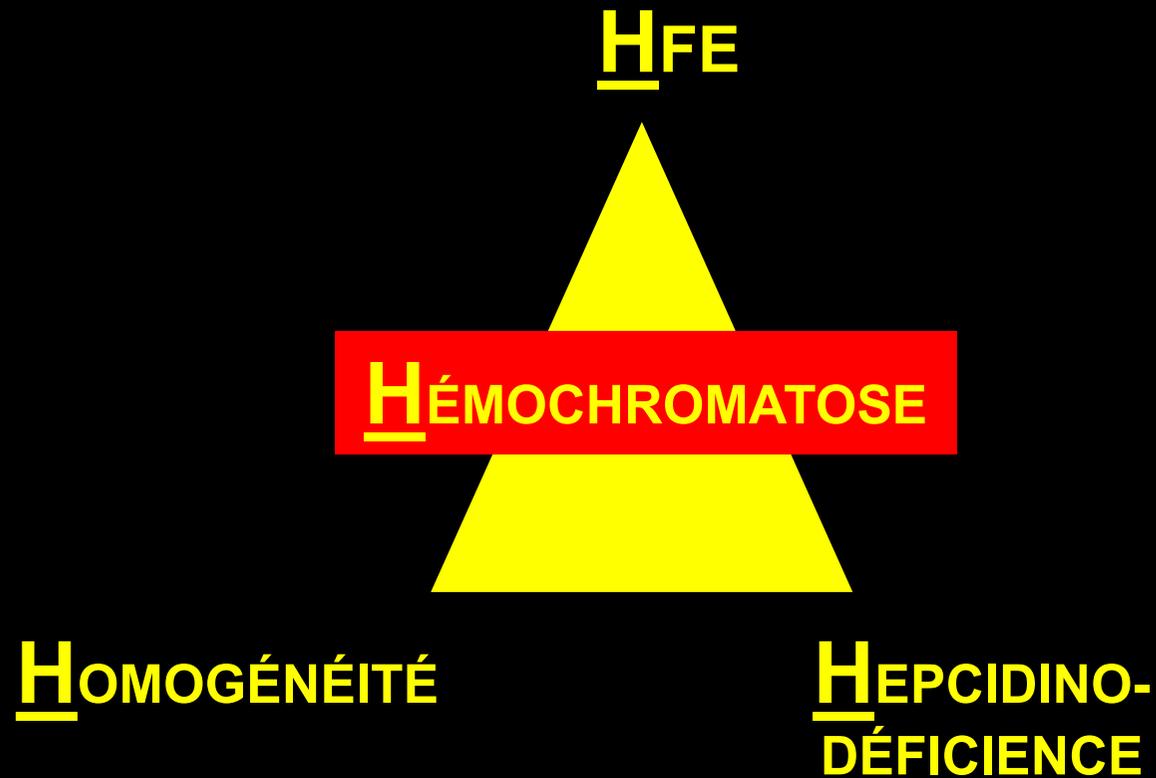




CONCLUSIONS

Les 4 « H » ...

CONCLUSIONS



Girelli D, Busti F, Brissot P et al.

Hemochromatosis classification: update and recommendations by the BIOIRON Society.

Blood (sous presse)

