Haemochromatosis: A changing world

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HFE-related Haemochromatosis

C282Y/C282Y
Evolving concepts and practices
Patho-physiology

Diagnosis

Treatment
Hepcidin

Ferroportin

C282Y/C282Y

Fe

Bone marrow
HFE mutation (C282Y/C282Y)
HFE mutation (C282Y/C282Y)
HFE mutation (C282Y/C282Y)

Bone marrow
HFE mutation
(C282Y/C282Y)

Fe

Bone marrow
HFE mutation (C282Y/C282Y)

Fe

Bone marrow

Fe

Fe

NTBI (non-transferrin bound iron)

Fe

Brissot P

Biochem Biophys Acta

2010
HFE mutation (C282Y/C282Y)
HFE mutation (C282Y/C282Y)

Fe

Bone marrow

LPI (labile plasma iron)

Cabantchik ZI Best Pract Res Clin Haematol 2012
Le Lan C Blood 2005
HFE mutation (C282Y/C282Y)

Bone marrow

Fe
LPI

Cabantchik ZI Best Pract Res Clin Haematol 2012
Le Lan C Blood 2005
HFE mutation (C282Y/C282Y)

Bone marrow

Cabantchik ZI Best Pract Res Clin Haematol 2012

Le Lan C Blood 2005
Phenotypic variability

Iron overload

Visceral target
Hepcidin promoter
(Island ML Haematologica 2009)

Low CD8
(Costa M Plos One 2013)

(Dostalikova-Cimburova M J Cell Mol Med 2014)

(Detivaud L Blood 2005)

(Girelli D J Hepatol 2009)

(EPO)
(Liu Q JCI 2012)
Phenotypic variability

Iron overload

Visceral target
cirrhosis

PNPLA3
Valenti L
WJG 2013

PCSK7
Stickel F
Hum Mol Genet 2014
Patho-physiology

Diagnosis

Treatment
Clinical exam.
Clinical exam.

Biology
Biochemical analyses
Transferrin saturation $> 60\%$
LPI = labile plasma iron.
Transferrin saturation > 75%

LPI (Labile Plasma Iron)
Ferritin
Ferritin
Ferritin
black liver + white spleen
=parenchymal iron overload

black liver + black spleen
=macrophagic iron overload

(www.radio.univ-rennes1.fr)

Hernando   J Magn Reson Imaging   2014
Bone marrow

Hepatocyte

Fe

Venesection
FUTURE
Today

Chelation
Deferasirox

Phatak P
Hepatology
2010
Tomorrow
Hepcidin supplementation...
Liver transplantation cures...the liver and the disease!
HFE
HFE-related Haemochromatosis
C282Y/.......
Frequent HFE mutation
H63D
Rare HFE mutation

C282Y/R226G
(Cézard C
Blood Cell Mol Dis 2014)
Rare HFE-Haemochromatosis (C282Y/rare mutation)

«Classical» HFE-Haemochromatosis (C282Y/C282Y)

Hepcidin deficiency

Rare HFE-Haemochromatosis (C282Y/rare mutation)
Rare HFE-haemochromatosis
Non HFE-related Haemochromatosis
Increased iron entry
Hamp (hepcidin)

HJV (hemojuvelin)

TFR2 (transferrin receptor2)

Hepcidin deficiency
<30 years
Hepcidin supplementation...
Increased iron entry

HAMP (hepcidin)

TFR2 (transferrin receptor2)

HJV (hemojuvelin)

Camaschella C Curr Opin Pediatr 2011
Pietrangelo A Semin Liver Dis 2011
Decreased iron exit
Decreased iron exit

Ferroportin disease
Ferroportin dysfunction

Ferroportin mutations

Fe

C

C
Hepatocytic iron

Ferroportin mutations (type A)

NTBI
Visceral toxicity

LPI

Ferroportin mutations (type A)

Le Lan C Gastroenterology 2011
Decreased iron exit

Aceruloplasminemia

Anemia

↑ ferritin

Chelation