

Managing *HFE*-related haemochromatosis

Scope

HFE-related haemochromatosis (type 1 haemochromatosis) is a genetically-determined iron overload disease (in individuals with the homozygous C282Y genotype), with autosomal recessive transmission, incomplete penetrance and variable expressivity. These guidelines concern the management of individuals with haemochromatosis who have just been diagnosed as homozygous for the C282Y mutation of the HFE gene.

■ **What should the initial assessment include?**

- Take a medical history of the individual who is homozygous for the C282Y mutation
- identify any risk factors for complications or aggravation of existing complications (excessive alcohol consumption, HVC infection, family history, etc.)
- carry out a clinical examination and iron tests (serum ferritin and serum transferrin saturation [STS]) if this has not already been done, and further tests if necessary (see Table I)
- determine the stage of disease severity (see Table I).

■ **When should patients be treated, and how?**

- Start induction therapy with phlebotomy in all patients at disease stages 2, 3 or 4, i.e. when serum ferritin is > 300 µg/L for men or > 200 µg/L for women (see Table I)
- only use iron chelation therapy in rare cases where the venous route is contraindicated or not feasible.

¹ For full guidelines (in English) and supporting scientific evidence (in French), *Prise en charge de l'hémochromatose liée au gène HFE (hémochromatose de type 1)* (October 2005) - www.has-sante.fr

■ Where should phlebotomy be performed?

In a healthcare organisation or authorised healthcare facility:

- do not perform phlebotomy in a day hospital when the patient's condition does not require any special management and the fees charged are not justified.

Only treat at home:

- after checking the patient's tolerance to treatment (at least 5 phlebotomies given in a healthcare organisation or healthcare facility)
- after a written treatment plan has been produced by a multidisciplinary and multiprofessional team and safety procedures, including management of waste, have been established
- after ensuring that a nurse will be present throughout the phlebotomy procedure and that a doctor would be able to attend quickly.

■ How should the patient be monitored?

- Start a monitoring record and ensure it is completed. The record is shared between the patient and the care team (e.g. a monitoring card)²;
- monitoring should be customised to the patient, depending on disease severity (see Table I)
- treat and monitor complications as per existing guidelines (i.e. guidelines not specifically related to the haemochromatosis)
- give the patient advice about risk factors such as alcohol abuse and viral liver disease (e.g. vaccination against hepatitis B).

■ What genetic counselling should the patient be given?

- Explain to the proband the benefits for their brothers and sisters, parents, children over the age of majority and other natural relatives and their children to have genetic testing. ***NB: the provision of appropriate information to relatives is the responsibility of the patient alone***
- all genetic tests should be accompanied by STS and serum ferritin determination.

² The card should include at least:

- the patient's details, weight and concomitant conditions;
- details of the different actors involved in care;
- blood pressure and heart rate at each phlebotomy;
- blood collection dates and volumes;
- results of serum ferritin and serum haemoglobin tests;
- a statement of the doctor's agreement concerning the phlebotomies and reasons for changes in treatment;
- a statement of any incidents and side-effects occurring during the phlebotomy procedure (safety)

Table 1. Standard factors in the management of HFE-related haemochromatosis

	Initial assessment: History, clinical examination, iron tests (serum ferritin and STS)	
	<i>No symptoms</i> <i>STS < 45%</i> <i>Serum ferritin normal</i>	<i>No symptoms</i> <i>STS > 45%</i> <i>Serum ferritin normal</i>
	STAGE 0	STAGE 1
FURTHER TESTS AT INITIAL ASSESSMENT	No further tests	
TREATMENT	No treatment	
MONITORING	<u>Every 3 yrs:</u> history clinical examination serum ferritin & STS	<u>Every year:</u> history clinical examination serum ferritin & STS

STS : Serum transferrin saturation

Table 1 (contd.) Standard factors in the management of HFE-related haemochromatosis

	Initial assessment: History, clinical examination, iron tests (serum ferritin and STS)	
	<ul style="list-style-type: none"> ▪ <i>No symptoms</i> ▪ <i>STS > 45%</i> ▪ <i>Serum ferritin raised</i> 	<ul style="list-style-type: none"> ▪ <i>Clinical expression phase</i> ▪ <i>STS > 45%</i> ▪ <i>Serum ferritin raised</i>
	STAGE 2	STAGES 3 & 4
FURTHER TESTS AT INITIAL ASSESSMENT	<ul style="list-style-type: none"> ▪ Look for the following types of disease: <ul style="list-style-type: none"> - pancreatic (fasting blood glucose); - liver (transaminases, ultrasound imaging in the event of clinical signs or cytolysis); - heart (ultrasound for stages 3 and 4); - gonads (testosterone assay, in men); - bone if there are concomitant predisposing factors for osteoporosis (bone densitometry). ▪ Refer to a specialist depending on clinical signs and symptoms and if there are abnormal laboratory values (particularly serum ferritin $\geq 1\ 000\ \mu\text{g/L}$). 	
TREATMENT	<p>Iron depletion therapy by phlebotomy (up to 7 mL/kg, not exceeding 550 mL)</p> <ul style="list-style-type: none"> ▪ <u>Induction phase</u> by phlebotomies not more frequently than once a week; continue until serum ferritin is $\leq 50\ \mu\text{g/L}$. ▪ <u>Maintenance phase</u> by phlebotomy every 2, 3 or 4 months (depending on the patient): maintain serum ferritin at $\leq 50\ \mu\text{g/L}$. 	
		Treatment of complications should depend on the clinical situation.
MONITORING	<ul style="list-style-type: none"> ▪ <u>At each phlebotomy</u>: history and clinical assessment. ▪ <u>During induction phase</u>: at start of treatment, check serum ferritin monthly during phlebotomy therapy until the threshold of $300\ \mu\text{g/L}$ in men and $200\ \mu\text{g/L}$ in women is reached. Below these values, monitor serum ferritin every 2 phlebotomies. ▪ <u>During maintenance phase</u>: monitor serum ferritin every 2 phlebotomies. Monitor haemoglobin during the week before phlebotomy. ▪ <u>Suspend phlebotomy</u> if haemoglobin is $< 11\ \text{g/dL}$. 	
		Monitoring of complications will depend on the clinical situation (e.g. screen for hepatocellular carcinoma in patients with cirrhosis, monitor diabetes, etc.)

STS : Serum transferrin saturation