

HEMO NEWS

Bulletin n°3 March 2015 | The newsletter of European Federation of Associations of Patients with Haemochromatosis

THE PRESIDENT'S MESSAGE



Dr Barbara BUTZECK
(Germany)

2014 saw new impulses in EFAPH actions: The question of blood donation was approached. The collaboration with the "Etablissement Français du Sang" (EFS) was consolidated. A questionnaire regarding the acceptance of the blood of HH-patients in different EU countries was planned and presented at the AGM in Verona.

More and more rare forms of the diseases are coming into focus both on the patients' and researchers' side. The need for a network of Reference Centres or Centres of Expertise was confirmed.

I am looking forward to see you all at our next AGM on October 16th/17th 2015. The German HH-Association HVD as organizer will warmly welcome you in the City of Cologne, Germany. This meeting will be held together with the International Alliance of HH-Associations (IAHA). ■

SCOOP ABOUT HAEMOCHROMATOSIS ON THE "ROUTE DU RHUM" TRANSATLANTIC SAILING CONTEST!



Three days after Loïc Peyron (the winner of the race), on Thursday, 13th of November, Erwan Le Roux, won in the Multi 50 category on board FenêtréA-Cardinal. The standalone Breton crossed over the Atlantic in eleven days, five hours, thirteen minutes and fifty seconds. Note the new logo of the European Federation of Associations of Patients with Haemochromatosis (EFAPH).

The European and French Haemochromatosis Federations as well as

the associated regions/countries hail Erwan's victory and congratulate him wholeheartedly.

Well done, Erwan!

We are proud to count Erwan as one of our ambassadors. Thanks to him thousands of people have been made aware of haemochromatosis. The early diagnosis of the disease is necessary in order to avoid severe complications (joint pains, heart problems, diabetes, cirrhosis...). ■



The New Logo where besides the abbreviation EFAPH, the full name of the association was added to bring a better visibility on Haemochromatosis.

Welcome to HVV, EFAPH's 13th association!



At the beginning of 2014 the Flemish Association for Haemochromatosis Patients in Belgium called HV Vlanderen (HVV), joined EFAPH. The association was represented at the AGM in Verona by the treasurer Mrs. Annick Vanclooster who gave an interesting talk on key-interventions for treatment and follow-up of patients with HFE-haemochromatosis. ■

Calendar 2015

- June 2015:** European HH week
A multiregional registry of HH rare forms
- September 2015:** phase 2 of GPs awareness campaign (France & Europe)
- October 2015:** Cologne AGM (EFAPH + IAHA)
- 25th November 2015:** Yves Henry piano concert, salle Cortot, Paris 17^e
- December 2015:** Blood donation and hereditary haemochromatosis survey.

EUROPEAN IRON CLUB (EIC) 2014, MEETING IN VERONA, ITALY, SEPTEMBER 11-14

This four-day meeting took place at the Historical Palazzo della Gran Guardia. It was chaired by Pr. Domenico Girelli. It was devoted to the biochemical, physiological, genetic and clinical aspects of iron in both health and diseases in order to promote fruitful interaction between fundamental research and clinical practice.



Pr. Pierre Brissot (France)

Pr. Pierre Brissot, in charge of the Reference Centre for Rare Iron Overload Diseases of Genetic Origin, at Pontchaillou University Hospital in Rennes (France), pointed some highlights presented during the EIC.

- Some factors are likely to modify the expression of HFE homozygosity as only 30% of men and 1% of women with homozygous C282Y mutation get severe

iron overload. The phenotypic variability is modified by low CD8-T lymphocytes, through elevated S100 a9 calgranulin according to research carried out by Graça Porto's group. The role of CREBH (Pr. Antonello Pietrangelo's group) and chemokine CCL2 (Muckenthaler's lab) as modulators of iron overload has been studied using knockout mice. The co-factors for liver fibrosis are high alcohol consumption, fatty liver, the genetic factors NRF2 and PCSK 7 (Prs. Graça Porto's and Alberto Piperno's working group).

- Regarding diagnosis: Pr. Dorine Swinkels' group confirmed, in a multi-centered study, that plasma NTBI (non-transferrin bound iron) and labile plasma iron (LPI), which are potentially toxic forms of iron, are frequently observed when transferrin saturation levels are above 80%. This indicates that the evaluation of transferrin saturation may be of interest not only for the diagnosis but also for

the treatment.

Pr. Sonia Distante showed that lymphocytes from HH-Patients provide a suitable model for studying the effect of venesections on mitochondrial iron metabolism. ■



EFAPH'S GENERAL ASSEMBLY IN VERONA, 14 SEPTEMBER 2014

On occasion of the AGM, EFAPH's 10th anniversary has been duly celebrated!



- The statutory activity and financial reports were unanimously approved,
- Emerencia Teixeira (Porto, Portugal) was appointed corporate webmaster.

• Among the presentations the following can be pointed out:

- **Olivier Loreal**, further to a European symposium in Brussels (June 2014), has explained the framework set by the European Commission for the definition and project calls related to European Reference Networks (ERN). EFAPH plans to apply for a project "Rare Genetic Iron Overload Diseases European Network", managed by the Scientific Committee.

- **Blood Donation survey:** An online Survey titled "Actual situation of Blood Donation in Hereditary Haemochromatosis (HH) in Europe, using the Monkey Software, has been launched under the authority of EFAPH's Scientific Committee. It is implemented by Emerencia Teixeira (IBMC), Portuguese team. The objectives are:

- To know the current practices of blood donation from HH patients in different countries/regions from the perspective of the members of Patients' Associations;
- To understand how strongly the different policies may affect the effectiveness of treatment.

The member associations are expected to designate a coordinator for their country in order to disseminate the questionnaire. The target date for publication of the results is the fourth quarter of 2015. ■



12 participating countries.

A financial support is partially provided by EFS (French Blood Establishment)



WHEN HAEMOCHROMATOSIS CALLS...

How to aim towards an early diagnosis of genetic haemochromatosis at the family doctor level? Two thesis (DIAPHREG I and II) are led at Paris- Diderot University (Paris VII).

In May 2014, a first thesis (DIAPHREG I) defended by Dr. Manuela Condet, coached by Dr. Françoise Courtois (European/French Federations of Patients with Haemochromatosis-EFAPH/FFAMH), Dr. Laurence Coblenz-Baumann (methodologist) and Dr. Françoise Lecompte (general practitioner), highlighted the warning signs of genetic Haemochromatosis in homozygous (C282Y) patients by a qualitative survey.

The methodology relied on individual semi-directive interviews from a descriptive statistical analysis and a "text mining" mathematical approach. Eleven warning signs

have been evidenced. The majority of patients mentioned an extreme tiredness associated with joint pains in 80% of cases. Problems with nails, skin, hair as well as libido and behaviour changes have been declared in 1/3 of cases. A focused analysis of fatigue (the most frequent warning sign), has helped to clarify its specific characteristics. These data were included in a questionnaire which served as a basis for an extended quantitative survey: it will focus on 350 homozygous haemochromatosis patients, from 4 Parisian blood collection centres (survey DIAPHREG II). This survey started in January 2015. It will help to clarify the warning signs which should induce the general practitioner to diagnose haemochromatosis and to request screening before clinical complications appear. ■

pain,
fatigue,
sleep,
work,
phlebotomy...



LATEST MEDICAL ADVANCES

Hepcidin



Dr D. Johnstone
(Australia)

Most haemochromatosis patients manage their iron overload through routine venesection. But this is not feasible for everybody.

Some people have a strong aversion to needles, others do not have appropriate blood vessels, and others have non-iron-related anaemia that would be worsened by blood removal. There has been therefore considerable interest in ways of controlling hepcidin.

Hepcidin is a hormone produced by the liver and circulating in the bloodstream. Discovered in 2000 it appears to be the master regulator of body iron levels, controlling how much iron is absorbed from the diet and how much is released from the body's cells. Haemochromatosis patients naturally have low hepcidin levels and scientists believe that, by finding a way to increase hepcidin levels or activity, one should be able to restore normal iron control. A Boston research group recently screened 10,000 different chemicals to see how they affect the production of hepcidin.

Only 16 chemicals were identified with this capacity; 2 of them, ipriflavone and vorinostat, were particularly potent.

As this study only looked at the effects on cells grown in culture, a lot more work needs to be done to show that ipriflavone and/or vorinostat are safe and effective in animal models. But it may provide, in a few years' time, an alternative to regular venesection.

Courtesy of Dr D. Johnstone, Sydney Australia, and of Irish Haemochromatosis Association-IHA Newsletter ■

Factors influencing iron overload



Pr G. Porto
(Portugal)

All patients with classical haemochromatosis (HH) have the same ancestral mutation in the HFE gene. In 2002 it was shown that a large number of people with 2 copies of the C282Y gene do not develop iron overload.

So what are the modifiers of iron overload? They can be divided into 2 major categories: environmental and genetic. Environmental modifiers are relatively well

known and include, besides the effects of sex and age, the life-style habits, body weight, alcohol consumption, blood loss, etc...

Regarding genetic modifiers, a group of scientists in Portugal have for many years focused on the role of CD8 T lymphocytes and their research has shown that HH patients with a low number of circulating CD8 T lymphocytes have a more severe iron overload. These important cells of the immune system have been shown to be capable of taking up and retaining a toxic form of iron. Studies

involving HH patients also demonstrated that the low CD8 T cells numbers are "genetically determined" and that this characteristic is inherited together with the HFE mutation.

Many aspects are still to be researched: for instance the handling mechanism of the iron in circulation by CD8 T lymphocytes and if it is altered in HH patients.

Courtesy of Pr G. Porto-IMCB Porto University, Portugal, and of Irish Haemochromatosis Association-IHA Newsletter ■

The German Association

In 2014, the German Association HVD launched an approach to specialists in occupational medicine. This group of physicians often play the role of General Practitioners. During the German congress for specialists in industrial medicine in Dresden, April 2014, a poster about HH

early diagnosis was presented. This resulted in two studies starting at the end of 2014: 1. Immunological changes in the blood of HH-Patients. 2. Manganese and Iron in the brain of welders – in comparison to Parkinson and HH-Patients.



New!
EFAPH
sponsorship file
2nd version

The Hungarian Association



In Hungary, the public at large and General Practitioners are unaware of HH; during 2014, different actions were undertaken to improve their knowledge, in particular during the health-screening days (when people are sensitive to health problems). For these events, a special T-shirt with the logo of HBE was created.

A dynamic country: Portugal!



Emerencia Teixeira (APH) : EFAPH's webmaster

In addition to the above-mentioned survey on Blood Donation and to taking over the management of EFAPH's website, APH has organized for its 11th anniversary a symposium "Prevention of Risk or Risk Prevention?" targeted at GPs, sponsored by the Portuguese Association of General Practitioners. APH has issued a new booklet adapted from the original Australian document. A new slogan "1 in 500 Portuguese has a genetic risk for HH" is now widely used, amongst others on nice T-shirts. Worthwhile mentioning is also the contest by 100 students from 7 schools of V.N.Famalicao resulting in 27 videos/posters about HH.

A new president for HBA (Haemochromatosis Belgian Association).

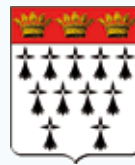


Bernard Delwart,
HBA president

In 2014, Bernard Delwart replaced Anne Saille, as President of HBA. He will benefit from the dynamic contributions of Tanguy de Decker (Treasurer) and Anne-Sophie Snyers (General Secretary). A project to raise the awareness of General Practitioners of one of the regions of French-speaking Belgium is starting by the end of the year.

The Swiss Association

The Swiss self-support group, active near St Gallen for years, has taken a big step forward by establishing a countrywide association, called Hämochromatose Schweiz, chaired by President Gerda Horn.



A meeting important to note:
The next General Assembly of EFAPH
in Cologne, Germany,
October 16th and 17th 2015.

A successful campaign to make General Practitioners (GPs) HH sensitive: the Yvelines pilot project

Too often in Europe GPs are unaware of the diagnosis of Hereditary Haemochromatosis (HH). This was acknowledged by the European Commission in February 2012 and 5 recommendations were issued assigning a priority to the early diagnosis of this disease. France was the first country to take action. A pilot campaign aimed at the 920 GPs in the Yvelines district (78) was launched in September 2013. They were sent a simple, didactic document featuring "what should be done so as not to omit a HH case" as well

as a list of the specialized departments and phlebotomy centres in the 78 District.

This action has had the following impact for the first 2014 half-year:

- 40% of the GPs have stated that they did receive the document, 95% of whom reported that they found it useful, among whom 50% stated having used it for a patient in the months that followed,

- 25% of the surveyed medical labs in the 78 District reported a + 5.7% increase in the number of ferritin tests and a +13.5 % in the

number of transferrin saturation tests.

- A 20% increase in genetic tests was reported by the 2 specialized labs (CERBA and BIOMNIS)*.

The outcome is very significant and led to the launching of similar campaigns in Brittany (December 2014) and in the Paris/Ile-de-France Region (year 2015). Some of EFAPH member countries will follow suit, within the next few months, Belgium in particular.

*1st semester 2014 vs. 1st semester 2013, Dr F.Courtois
- Savoir-Fer, FFAMH news bulletin (France).