

## MINUTES OF THE 14<sup>TH</sup> ANNUAL GENERAL MEETING Zürich (Switzerland) – February 11<sup>th</sup>, 2018

Edited by : Pat Evans, Françoise COURTOIS, Barbara BUTZECK

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### Agenda: **Appendix 1**

**Presents:** ABELE Maria (Hungary), BRISSOT Pierre (France), BUTZECK Barbara (Germany), COURTOIS Françoise (France), DON HOWARD (UK), ERSÖZLÜ SARA (SWITZERLAND), EVANS Robert (UK), EVANS Patricia (UK), GIRELLI Domenico (Italy), HEAD David (UK), HORN SCHLEGEL Gerda (Switzerland), LOREAL Olivier (France), Mc GRATH Ann (Ireland), MILMAN Nils (Denmark), MULLETT Margaret (Ireland), PINEAU Brigitte (France), PORTO Graça (Portugal), RYAN John (UK), SANCHEZ Mayka (Spain), SORRILL Robert (Italy), STAKVIK Dag Erling (Norway), SWINKELS Dorine (Netherlands), TOSKA Ketil (Norway), TRYGVE TONNING Nils (Norway), ZOLLER Heinz (Austria).

**Excused:** ALTES Albert (Spain), BARDOU-JACQUET Edouard (France), COUESLANT Béatrice (France), DELWART Bernard (Belgium), DISTANTE Sonia (Norway), PIPERNO Alberto (Italy), RIALLAND Jean (France), TEIXEIRA Emerencia (Portugal), VANCLOOSTER Annick (Belgium).

**Invited:** FISCHER Roland (Germany), FINZEL Stephanie (Germany), MORETTI Diego (Switzerland), SCHEIBER-MOJDEHKAR Barbara (Austria)

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### Welcome

The 2018 AGM of EFAPH has taken place in conjunction with the EIC Congress in the ETH, Zurich, Switzerland. The Chair of EFAPH, Barbara Butzeck, opens the meeting by thanking the members in attendance, invited guests and Dr Diego Moretti from ETH. New member representatives are Dr. Sara Ersözlü for Switzerland, accompanied by Gerda Horn, chair of the Swiss HH group and Hank Jacobs from HVN (The Netherlands, not present but represented by Prof Dorine Swinkels). Barbara Butzeck and Françoise Courtois wish to step down from their positions as President and Secretary respectively and a transition process to find replacements has begun.

### 1.EFAPH, activity report from June 2017 to February 2018: Dr Françoise Courtois, Général Secretary (*Appendix 2*)

As usual the Board and Executive Committee have been very busy this year with several meetings and telephone conferences. Progress is now described for relationships with European Health Organizations:

- **EURORDIS**

Maria Abele (Hungary) and Françoise Courtois will attend the ECRD in Vienna in May 2018. The main topics will include an ePAG Meeting, structuring research and diagnostics, new drugs, the digital patient and quality of life. An exceptional grant has been awarded to Maria to cover the expenses for the ECRD as she has been strongly involved in Hungarian research and diagnostics and may train to eventually replace Françoise. In October 2017, Brigitte Pineau (FFAMH) attended the Council of European Rare Disease Federations. This is a huge organization with 2 platforms enabling patients and associations to communicate worldwide (Rare Connect Platform) and allowing patients to participate in EURORDIS surveys (Rare Barometer Voices). The meeting also included the European Patient Advocacy Groups (ePAGS) which have a number of programmes including webinars, mentoring and leadership programmes. This is a good vessel for communication and sharing. Events organized under the EURORDIS umbrella included the French Alliance in December 2017 in Paris with Rare Disease Day being held on 28<sup>th</sup> Feb 2018.

- **European Patient's Forum (EPF)**

EFAPH thanks Annick Vanclooster for her work and for attending the 2017 AGM. However she may be stepping down so EFAPH needs at this point to consider whether to remain in EPF. EPF is a powerful European umbrella organisation giving EFAPH a lot of support over 11 years. However, EPF has become large and bureaucratic and the interests of EFAPH and EPF may be diverging. EFAPH must decide whether to stay, resign or change the type of membership. To stay as a full member but by reducing the activities would be probably the best solution. Perhaps a volunteer (any offers?) could read the weekly newsletter and report its contents back to the Secretary.

- **EuroBloodNet**

Prof Graca Porto attended the second Scientific and Strategic Board meeting in Brussels in September 2017. Prof Dorine Swinkels attended the first Board of Network Meeting in Paris in November 2017. HH comes under the anaemias and iron disorders section. A website ([www.eurobloodnet.eu](http://www.eurobloodnet.eu)) has an inventory of diseases, data, facilities and experts. There is also a telemedicine platform to discuss and share clinical cases in a testing phase at present. Patients must be represented as per the Patient Advocacy Groups. However the organization needs more experts, for us, HH experts as well as 2 patient representatives as there are lots of thalassaemia patients but no genetic iron overload patients. Prof Girelli is willing to help. Prof Zoller asked about the inclusion of patients who have rare liver diseases often with a haematological bias.

- **HH Arthropathy Research Initiative**

Two meetings were held in 2017 with financial support from EFAPH, HVD and Haemochromatosis UK. 2-3 meetings are planned in 2018 in London, EULAR and Freiburg. HARI gave a presentation at a workshop at ACR in San Diego in 2017. Dr Patrick Kiely has offered to share his experience in lectures. A publication 'Treatment of HH Arthropathy, Advice for Patients' has been prepared and translated into several languages. Forthcoming projects include an information sheet about HH and osteoporosis and an awareness paper entitled 'Could it be Haemochromatosis?'. See also Dr Finzel's talk below.

- **Finances**

EFAPH urgently needs to attract more funding- see treasurer's report below

- **Achievements, projects, follow-up**

New Associations: HVN (Haemochromatose Verenigen Nederland) is a new member since January 2018

Sweden: membership application at an advanced stage (see Ketil Toska's talk below)

Romania: still trying to find contacts and support

HBA: The French Belgian Association is being supported by EFAPH as it has only a few active members. One solution might be to merge with the Flemish Association.

- **HemoNews**

Edition 6 is due hopefully in April 2018. We hope it is useful and interesting. Please send us short articles- stories of human interest, news items, photos ... at any time! Surely someone has some funny photos from the 2017 awareness week?

- **HH Week and Awareness Campaigns**

European HH Week/World Iron Week: HI and EFAPH will join forces for this week (June 4<sup>th</sup> until 10<sup>th</sup>, 2018). EFAPH needs to know about shared experiences on regional and national levels and how to co-ordinate EU and International experiences.

- **An important question**

Margaret Mullett (Irish Association) asks: what about heterozygotes with hyperferritinaemia but no symptoms? EFAPH needs to have a consensual position on this question. Perhaps it could be a topic for inclusion at the Biolron Meeting in Heidelberg in 2019 where the next EFAPH and HI AGMs will be held.

### **The activity report is unanimously approved**

## **2. EFAPH, financial report (Dag Erling Stadvik, Treasurer – Beatrice Coueslant Assistant treasurer) (Appendix 3)**

*The income for the fiscal year 2017 amounts to € 4,815. Of which :*

-memberships	2,100,00
-grants	2,500,00
-financial income	215,00

*The expenses for the fiscal year 2017 amount to € 7,222. Of which :*

-travel	1,148,00
-AGM Munster	3,654,00
-printing/communication documents, mail	1,911,00
HARI expenses	321,00
-bank fees	188,00

*Comment on EFAPH financial status from the treasurer: Cash situation at present is 'safe' but decreasing every year unless more grants/revenue are obtained. There were suggestions from the audience for fundraising- coffee mornings, mini-marathons etc. There was general agreement that in applying for grants, companies preferred to see a project involved. The question was raised as to whether EFAPH needed to develop rules for grant applications.*

*EFAPH warmly thanks Béatrice Coueslant for having maintained all the accounts this year.*

### **The financial report is unanimously approved.**

## **3. What is new in HH ? Report from the EIC (Pr Graça Porto, IMBC Porto, Portugal)**

Graça thanked Diego Moretti for a great EIC Meeting at the ETH and drew attention to two papers in the Masterclass preceding the EIC Meeting given by Profs Pierre Brissot (The Pioneering Role of Rennes in Haemochromatosis: the HLA discovery and more ....) and Domenico Girelli (Diagnosis of Atypical Iron Overload Disorders by Next Generation Sequencing, NGS). She then grouped meeting presentations on HH into 5 sectors: diagnosis, treatment, prognosis, pathogenesis and penetrance.

**Diagnosis:** The increasing importance of NGS was stressed as a means of explaining the variable phenotype of HH.

**Treatment and Prognosis:** There was an important paper on regression of fibrosis from the group of Prof Edouard Bardou- Jacquet and a poster from HI on therapeutic guidelines for treatment. Vifor International introduced their work on an oral ferroportin inhibitor able to prevent iron overload in a mouse model of HH. The work of Infanti *et al* showed progressive decrease of non-transferrin bound iron and transferrin saturation during venesection.

**Pathogenesis and Penetrance:** Ferreira *et al* presented a new *in vitro* model under development for arthropathy in the pathogenesis of HH. Disease modifiers which could affect the penetrance of the C282Y mutation included the role of Nrf2 and its alleles. Nrf2 is a protein transcription factor which affects expression of antioxidant response genes (work from Drakesmith and Porto laboratories). Finally Dr Tobiash from Prof Zoller's laboratory discussed the possible influence of other genetic polymorphisms in HFE HH.

Abstracts for posters and oral presentations at the meeting are available to download at [www.ironclub2018.ethz.ch](http://www.ironclub2018.ethz.ch)

#### **4. Haemochromatosis Research in Oxford: Looking to the Horizon (Dr John Ryan, University of Oxford, UK)**

Dr Ryan from Dublin is a consultant currently focussing on research in Oxford. He cited several problems in HH research including a disconnect between scientists and clinicians, lack of awareness of HH generally, incomplete penetrance, lack of new HH research including the effects of phlebotomy and a lack of funding. In Oxford, he has good collaboration with local patient groups, scientists and the OCMR MRI Institute. Using liver multiscan MRI, the ratio of liver fat to iron can be calculated, showing the extent of liver damage. He is also interested in the role of FGF18 in bone turnover and liver repair. This factor appears to be low in HH patients but increases towards normal values during venesection. After venesection, iron absorption increases but iron in faeces decreases. The importance of the gut microbiome is becoming increasingly recognized in HH. Looking to novel therapeutics, Dr Ryan recognizes three main areas: gene silencing, hepcidin agonists and restriction of iron absorption. He sees the greatest opportunities in the last option. During the discussion, Prof Zoller mentioned the influence of hepatitis C and the lack of a continuum of care for HH patients. Dr Ryan remarked that there are large differences in treatment worldwide with David Head (UK HH Society) suggesting a generalized map of procedures for patients and clinicians.

#### **5. Next Generation Sequencing for molecular diagnosis of atypical iron disorders: great advances but caution is needed (Pr Domenico Girelli, Verona, Italy)**

Prof Girelli basically presented his talk from the EIC Masterclass. He was introducing work on atypical disorders resulting in disturbances of iron metabolism rather than classical HFE HH. Diagnosis of these rare disorders is usually on the basis of clinical findings but Next Generation Sequencing (NGS) is useful for confirmation of diagnosis. This technique involves the sequencing of relevant sequences of the DNA or indeed whole genome sequencing. The DNA is fragmented into millions of sections which are then sequenced simultaneously and relevant sequences aligned with those from reference genomes. This method has led to advances in knowledge but there are some critical points. One example is in fact classical HH where a molecular diagnosis of the C282Y mutation by NGS gives no indication of the clinical presentation due to issues of penetrance. However, many clinical cases remain unexplained genetically even with this powerful technique. This may be due to problems with sensitivity or the presence of mutations in unknown genes not represented on gene panels used. The current diagnostic yield of NGS in rare diseases is far from 100% although the technique is useful for cascade screening in relatives. Byproduct generation of incidental findings such as the presence of other harmful genes (eg BRCA1 for female cancers) is an unresolved ethical issue.

#### **6. Haemochromatosis Arthropathy-Update on HARI-Projects (Dr Stephanie Finzel, University of Freiburg, Germany)**

Dr Finzel's talk was divided into 3 sections as below:

##### **1. Activities on treatment and early diagnosis of HH arthropathy (HA)**

Up to 75% of HH patients report joint pain even pre-diagnosis with a high degree of unawareness and uncertainty amongst physicians which can cause delays in diagnosis of up to 7 years. A diagnostic support paper 'Could it be HH arthropathy?' is being prepared for GPs and orthopaedic surgeons summarizing distinctive features of the arthropathy. These features were summarized into radiographical (eg hook-

like osteophytes, cysts), clinical (iron fist), demographic (onset in 5<sup>th</sup> decade normally but can present as early as the 3<sup>rd</sup> decade) and symptomatic (joint pain +/- morning stiffness, fatigue).

## 2. Activities on groundwork

In 1992 OMERACT (Outcome Measures in Rheumatoid Arthritis Clinical Trials) was set up as an informal international network with working groups and gatherings interested in outcome measurements across a spectrum of rheumatology intervention trials. The present momentum is to get an overview on HA features and facilitate pattern analysis especially in terms of imaging.

## 3. Outlook: studies on imaging in HA

Not all treatment centres have MRI facilities and patients may not be able to lie flat. Ultrasound can show joint skewing where there is a positive relationship between the degree of skewing and the pain intensity. High resolution peripheral quantitative CT gives high resolution images of peripheral bone in the extremities with high bone/soft tissue contrast using slice thicknesses of ~100 mm for a low radiation dose. Pilot studies are underway to determine the usefulness of this technology in HA imaging and diagnosis and if successful could lead to full clinical trials. This imaging can be performed during phlebotomy.

## 7. Non-HFE Registry Update: Prof Heinz Zoller, Med University of Innsbruck, Austria

Prof Zoller updated the audience on milestones and achievements of the Non-HFE Haemochromatosis Registry (<http://non-hfe.com>) which was launched in early 2016. By January 2017, a consortium agreement for members had been agreed and documents for patient ethical approval prepared. Later that year international and local regulations were developed and the first patients were registered into the study in early 2018. Thus far, the registry has a consortium agreement with Modena, Italy. Ethical approval to enter patient data into the database has been obtained for Innsbruck, Porto, Milan, Verona, Monza, with approvals pending for Nijmegen, Oslo, Oxford and Rennes. There will be a meeting in Innsbruck in late 2018. Howard Don of the British Society commented that the registry web page contains a statement that HH is rare and disputed this. Margaret Mullett from the Irish Association agreed with Howard. The frequency of HH is highly variable across Europe however Prof Porto commented that the disease might be considered generally rare if rare non-HFE forms of the disease were included.

## 8. New and potential new member

### 8.1 Associations Sweden (Ketil Toska, Norwegian Association)

Ketil Toska from the Norwegian Association spoke about the long term plan to help Swedish people form their own patient association and to then become members of EFAPH AND HI. Sweden has an estimated HH population of 35400 in a total population of 10.1 million inhabitants. The initial contacts were through Swedish people who had joined the Norwegian Association. Other contacts were built through Facebook where there are now 201 participants. Direct talks with doctors and hospitals in the Greater Stockholm area are now commencing and the prospective group have been given copies of the Norwegian and Danish statutes together with other useful material from the Norwegian group. It is hoped to found the Swedish Association later in 2018. There will eventually be an EFAPH initiative to meet with the group in Stockholm.

### 8.2 The Netherlands (HVN) No representative present to give a talk

### 8.3 Romania (Prof Robert Evans, UK)

Although there had been some preliminary work to set up a Romanian Association affiliated to EFAPH in 2008 in a workshop in Bucharest initiated by Francoise Courtois, Barbara Butzeck and Jean Rialland, very little progress had been made due to lack of contacts in Romania. The main contact was through Dorica Dan

(President of the Hungarian Alliance of RD)-~~lady~~ whose daughter had a rare disease (not HH) who attends EURORDIS Meetings. In 2017 there was a renewed contact not only with Dorica Dan but also through a visit to Bucharest of Prof R.Evans who visited the general hospital there and saw Dr Horia Bumbea who is a haematologist. He only has two HH patients but there may be more patients in the north of Romania especially close to the Hungarian border. Dr Bumbea said that he would contact other haematologists in Romania but has not responded since. In September 2018, Prof Evans will attend the Romanian Academy of Sciences Annual Meeting where he will give a brief overview of human iron metabolism and introduce the various forms of haemochromatosis concluding with a request for any available information regarding patient numbers, clinicians and demographics.

## 9. Relevant activities of National Associations

### 9.1 Getting health professionals to come to the fore: not a pie in the sky (Brigitte Pineau, president of the French Federation (FFAMH))

#### . A pilot experience:

In 2013 EFAPH and FFAMH launched the Yvelines Awareness Campaign by mailing an awareness document to 920 GPs followed by postage-paid reply card 5 months later to assess response. 39% of GPs replied and the regional hospital service involved was inundated with enquiries. However very few testing laboratories responded (17%) to give the increase in number of tests delivered as a result of the initiative.

#### . FERIF: Parcours Hemochromatose en Ile de France

Amid growing difficulties for patients to access healthcare, in 2016 FFAMH complained to the regional health authorities which led to the setting up of a Steering Committee comprising the major stakeholders. This resulted in a website, a 3-year phlebotomy-donation experiment involving hospital services dedicated to HH patients and an awareness campaign targeting 11000 GPs and specialist doctors in January, 2017. There will be a 5 year follow-up of data which will compare Paris with the rest of France with the prospect of expanding any advantageous findings throughout the whole of France.

#### . DetectFER

DetectFER organized a whole year project involving the French Medical National Council, Learned Societies, The College of Specialist Doctors and the College of Biologists. This included an awareness week for doctors in June 2017 including posters and video clips for GP surgeries resulting in newspaper promotions, inclusion on the facebook page of the Confederation of French Doctors College and inclusion on the Syndicat des Biologistes website. Additionally, FFAMH had stands in 10 Bretagne hospitals, published press articles and had video clips in many GP surgeries. Although this costly campaign had good success, it drew little response from laboratories in the Paris area and documents sent out to Biologists' Unions failed to reach their targets. It also failed to draw together biologists and doctors. More campaigns are envisaged to meet these goals and also to start a targeted screening program in the Paris area which will be extended to a national program in 2019. Brigitte thanked Françoise and Prof Brissot for all their help and involvement.

### 9.2 Hungarian HH patients allowed to donate blood (Maria Abele, president of the Hungarian Association HBE)

Maria Abele described the considerable achievement of the Association in getting acceptance of blood from HH patients' phlebotomies into the National Blood Bank from September 2017. Remarkably, discussions for this were begun in 2007 by Dr Judit Varkonyi- the Association's haematologist Honorary President. The argument against donation was that donations were not being made on a voluntary basis contrary to the ethos of the Blood Bank. This attitude persisted despite repeated representations by the HBE until a well-known Hungarian newspaper published an article describing the health story of an HH patient member of HBE. The same newspaper edition carried a story about the shortage of blood for blood banks in Hungary.

One week after this, Dr Varkonyi was told that phlebotomised blood was acceptable and donors now get a 'thank you' SMS from the Blood Bank when their blood is used!

### **9.3 Healthy Eating and Haemochromatosis: a new booklet (David Head, chief executive of the British Society, UK)**

David Head presented the Society's recently published booklet on 'Healthy Eating in Haemochromatosis' available on request and on the Society's website. This was prepared by professional dieticians as a response to the many requests for information on this topic received by the Society. The British Government publishes an 'Eat Well Guide' which formed the basis for the booklet. Basically patients are advised to eat a sensible healthy diet rich in fruits and vegetables with the following caveats: offal, alcohol and sources of vitamin C (with iron containing foods) should be avoided, with care advised in the taking food supplements as these may contain iron. The British Society thought that the cost of producing the booklet would be balanced by the benefits it would bring to patients. A further booklet is envisaged on venesection. After the talk there was some discussion about a section in the booklet which appears to suggest that eating foods with more non-haem iron is acceptable, this form of iron being less well-absorbed than haem iron. No consensus was reached about this.

### **9.4 Report from the Irish Association (Margaret Mullett)**

Margaret reported the success of the HH awareness day. There were also fund-raising events held throughout the year such as a National Ploughing Championship. Recently a charge of 80 euros per phlebotomy has been introduced in certain hospitals for a maximum of 800 euros per year. Newly diagnosed patients needing 4 venesections per month would spend 320 euros. Although there is some help available to those most in need, this charge could result in patients making decisions against attending phlebotomy appointments- a hugely retrospective step. Four ministers in the current Irish Government have HH and are leading complaints against the charge. Over 2400 people have signed a petition sent to the Minister of Health.

The Irish Blood Transfusion service will now accept venesection blood (from patients in the maintenance phase) which will be taken by their donation teams providing patients meet the established criteria for blood donors.

## **10. International HH Awareness week**

Prof Evans presented ideas from EFAPH and HI on what this week should involve. There has previously been some confusion between World Iron Week in May 2017 (HI) and HH European Awareness Day/Week in June 2017 (EFAPH). For this and subsequent years, it is proposed that HI and EFAPH join forces in the same week which would be the first week of June 2018. HI approached its members for suggestions about events to run in the week but is still waiting for responses. It would seem useful for both EFAPH and HI to employ common public releases. A common poster which could be taken to GP Surgeries and Pharmacies was proposed which would bear the logos of all participating member Associations. The title for each Association logo might differ as the word Awareness has no equivalent in some European languages. Other suggestions for the week included printed fabric shopping bags with the logos and publicity through local radio stations.

Regarding the submission of the HI Patient Treatment Guidelines for journal publication, delegates emphasized that the publication should be in a journal which has open access and applies no copyright restrictions.

Dr Barbara Butzeck closes the meeting and thanks all participants for their commitment and participation.

1. **May 2019: Bioiron Heidelberg (Germany) – EFAPH + HI AGMs**
2. **2020: EIC in Oxford, UK**
3. **2021 EIC Badalona (Barcelona region) ? (suggestion from Dr Mayka Sanchez)**

**Annexes: (\*)**

1. Agenda
2. EFAPH Annual Activity report 2015-2016
3. EFAPH Financial report



**Barbara BUTZECK**  
(EFAPH Présidente)

**Françoise COURTOIS**  
(EFAPH Secrétaire Générale)

*(\*) the different presentations are available : please, ask for them to the General Secretary*

