Irish Haemochromatosis Association

Carmichael Centre, North Brunswick Street, Dublin 7

WELCOME TO THE SUMMER NEWSLETTER 2016

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LAUNCH OF AWARENESS CAMPAIGN AT NATIONAL STUD FRIDAY 29TH MAY 2016

Irish champion jockey, Ruby Walsh and "Hurricane Fly" together with Sophie and Leah Mullett at the launch of Awareness Campaign.

A campaign to reduce the numbers of people suffering unnecessarily from Haemochromatosis was launched by Irish champion jockey, Ruby Walsh, at the Irish National Stud, Co. Kildare with dual champion hurdle winner "Hurricane Fly".
Dr Colm Henry, the HSE's Clinical Lead for Acute Hospitals said :
'We are delighted to add our voice to the IHA's promotion of public knowledge about this condition".
Professor Suzanne Norris, Consultant in Hepatology and Gastroenterology at St James's Hospital said that
'Ill -health from Haemochromatosis and the development of serious complications such as cirrhosis can be prevented by simple treatment. Life expectancy in treated non-cirrhotic patients is normal. Early diagnosis is therefore critical and Haemochromatosis is an ideal condition to consider for population screening in Ireland'.

DR ELEANOR RYAN, MSc., PhD., MATER HOSPITAL, DUBLIN

Dr Eleanor Ryan is the Senior Biologist at the Mater Hospital and is the author of over 70 research papers on HH. Eleanor has been responsible for ground-breaking research and at the AGM she gave us a fascinating overview of her work and that of her predecessors.

Landmark Events

1976: – First association of HLA (Human Leukocyte Antigen) with Hereditary Haemochromatosis (HH)
1996: – the HFE gene was discovered
2001: – Hepcidin controls iron metabolism

1976:

HLA, commonly known as tissue typing, is a group of procedures that determine the type of antigens on a person's cells. Before the discovery of the HFE gene, it could only be used for family screening once a clinically symptomatic family member had been diagnosed. For many years HLA typing was used to predict who might develop HH in a family.

20 years later

For the next 20 years the race was on to find the HH gene! The main contenders to find the gene were the Australians and French research teams.

Mater MD students looking for the gene were rather ambitious considering the team did not have the facilities to do this!

August 1996: –THE HH GENE WAS FOUND

Confirmation was provided by the Australians and French in November 1996

WHAT CHANGED AFTER HFE WAS IDENTIFIED ?

Discovery of HFE in 1996 changed how a diagnosis of HH was made. Comparisons between family members were no longer required. The identification of HFE served as a powerful stimulus for further studies to identify other genes/proteins that might be involved in iron homeostasis. Subsequently many more genes have been identified – including hemojuvelin (Type 2a) and hamp (Type 2b), transferrin receptor 2 (Type 3) and ferroportin (Type 4).

2001: MOST IMPORTANT WAS THE DISCOVERY OF HEPCIDIN

Hepcidin is a small protein produced in the liver that plays a critical role in the regulation of systemic iron homeostasis. This hormone has now been shown to play a major role in the control and regulation of iron absorption and a deficiency in hepcidin appears to be the root cause of most forms of HH.
Hepcidin levels in overweight and obese male C282Y homozygotes were significantly higher than in normal weight C282Y homozygotes. This may have implications regarding the usefulness of ferritin as a marker of when to start venesection treatment.

Dr Ryan and her team are now looking at Hepcidin and the Hepcidin/Ferritin ratio as potential new markers. They have been awarded a grant from the Mater Foundation to examine Hepcidin and Hepcidin/Ferritin ratio in C282Y HH patients. Ferritin is a marker of iron stores but may also be elevated in inflammation - thus a high ferritin in overweight/obese C282Y HH patients may be indicative of co-existent inflammation.

Recently the research efforts of Dr. Ryan and her team have involved looking at the relationship between hepcidin and other biochemical indices in iron loaded and non-iron loaded individuals with and without mutations in the HFE gene. They have shown that HFE genotype and serum ferritin are the most important determinants of hepcidin levels.

They have also shown that those with the greatest genotype risk for the development of iron overload (C282Y homozygotes) have the lowest hepcidin, and the highest transferrin saturation levels.

Sincerest thanks to Dr Ryan for sharing this very relevant information with us.

PRESENTATION BY PROFESSOR JOHN CROWE PhD., FRCPI

Professor John Crowe, Consultant Gastroenterologist, Mater Hospital, Dublin is one of the most esteemed researchers in the field of Haemochromatosis. He is an invited guest lecturer at the Australian Haemochromatosis Conference in Brisbane in August 2016.

In 2001, to investigate the prevalence of Haemochromatosis in Ireland, the research team in the Mater, led by Prof Crowe, extracted DNA from randomly selected cards of newborn babies and analyzed it for the C282Y and H63D mutations. Complete results were obtained from 800 cards.
It was found that;

- 1/ 86 of the sample carried two copies of the C282Y mutation,
- 1/ 60 were compound heterozygotes (C282Y/H63D)
- 1/5 were carriers of the C282Y gene.

Ireland has the highest prevalence of Haemochromatosis in the world. Professor Crowe mentioned that whereas gene frequency is high, disease frequency is low.
With regard to the diagnosis of Haemochromatosis:
If fasting Transferrin Saturation > 55% and Serum Ferritin >300ug/l in men and post menopausal women, a genetic test would confirm or deny a diagnosis of Haemochromatosis.
93% of Haemochromatosis patients are C282Y Homozygotes.
Prof Crowe discussed the frequency of venesection and mentioned that venesection increases iron absorption by 11% - 66% during venesection. Increases persisted for up to one year. He suggested that venesection in a hospital clinic should only be undertaken when Ferritin>300ug/l. This would diminish upregulation and reduce clinic attendance and cost. American Iron Overload Association recommends that ferritin be <50 ug/ litre. Many patients know the ferritin level at which they feel best and the consultant is guided by the patient's requirement.
If 500 ml's of blood are venesected, 200 mg of iron is removed. This is equivalent to 200 glasses of wine or 50 seven oz cuts of beef !
The IHA would like to thank Prof Crowe for his excellent presentation.

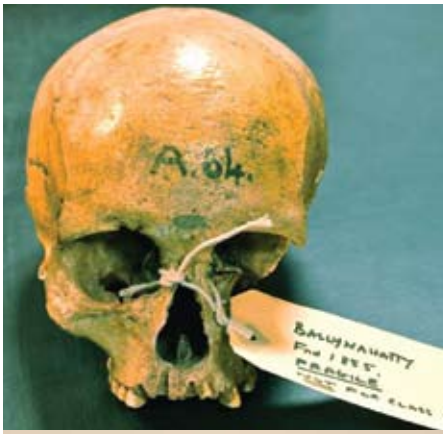
PRESENTATION BY PROFESSOR DANIEL BRADLEY TCD

Professor Dan Bradley is Professor of Population Genetics at Trinity College Dublin.

A team of geneticists from Trinity College Dublin led by Professor Bradley and archaeologists from Queen's University Belfast, has sequenced the first genomes from ancient Irish humans, and the new information is already answering key questions about the origins of Ireland's people and their culture.

A genome is an organism's complete set of DNA, including all of its genes. Evidence of massive migration to Ireland thousands of years ago has emerged from the sequencing of the first genomes from ancient Irish humans. These genetic influxes are likely to have brought cultural changes including the transitions to agriculture, bronze metal working and may even have provided the origin of western Celtic language.

The team sequenced the genome of an early farmer woman, who lived near Belfast some 5,200 years ago, and those of three men from a later period, around 4,000 years ago in the Bronze Age, after the introduction of metalworking. The H63D mutation was found when sequencing the genome of the woman farmer and the C282Y mutation was found in the Bronze Age men who lived over 4000 years ago.



The Ballinahhy Skull and a 3D model simulation of the head of the woman farmer.

Whereas the early woman farmer had black hair, brown eyes and more resembled southern Europeans, the genetic variants circulating in the three Bronze Age men from Rathlin Island had the most common Irish Y chromosome type, blue eye alleles and the most important variant for the genetic disease, haemochromatosis. The latter mutation is so frequent in people of Irish descent that it is sometimes referred to as a Celtic mutation.

This discovery therefore marks the first identification of an important disease variant in prehistory, according to the researchers. It has also demonstrated what a powerful tool ancient DNA analysis can provide in answering questions which have long perplexed academics regarding the origins of the Irish.

Thanks to Professor Bradley for presenting this information at the AGM

FALL FROM A HORSE LEADS TO A MORE SERIOUS DIAGNOSIS

If it wasn't for a fall from a horse, Sean Carter could have found himself with a more serious problem than just a sore back.

After a horse riding accident, Sean Carter suffered with backache and chest pain. He went to see his doctor after the fall, who enquired about his colouring. Confused, Sean asked the doctor if his colour was abnormal. The doctor told him that he had a bronze/grey pallor and that he would conduct a test to investigate. Due to the doctor's observations Sean, who was 45 at the time, was diagnosed with Haemochromatosis. Haemochromatosis, commonly known as the Celtic Curse, is a genetic condition where a person absorbs an excessive amount of iron from their diet. The iron is then stored in the body and it may affect the liver, heart, pancreas, endocrine glands and cause pain in the joints. The iron overload can lead to impaired function of those organs and eventually result in disease and organ failure.

More people in Ireland are affected by the disorder than in any other part in the world. About one in 86 people in Ireland are predisposed to have iron overload, but one in five people carry the gene. Since iron can build up slowly, symptoms might not appear until people reach 30 or 40 years old.

One indication of haemochromatosis is chronic fatigue, but when Sean experienced tiredness he just thought it came with his age. Other indications include skin pigmentation, abdominal pain, arthritis and diabetes. Many of the symptoms can be found in other disorders. However, when arthritis affects just the first two finger joints there's a high probability that it is haemochromatosis.

If the disorder is diagnosed early, the treatment is simple. A person gives blood to remove the excess iron. This is known as venesection and the numbers of units of blood that have to be taken depend on how high the iron level is at the time of diagnosis.

When Sean was first diagnosed his iron levels were very high and he gave 65 pints of blood in just 70 weeks! However, he has now dramatically reduced his iron levels and he just needs to gives blood a few times a year.

Since Sean's wife is a carrier of the gene, Sean made sure his four children were tested to see if they had the condition. One of them tested positive, but fortunately he was diagnosed early.

Sean, who is now 66, said its incredible how many people he knows who have the disorder. Since it's so common he believes that it is important to educate the community.

"When we first started raising awareness about ten years ago there was very little understanding of the disorder", Sean said. "Now people know about it because it is so common. We also encourage the relatives of those diagnosed to get tested".

This interview with Margaret Langevin was originally published in the Connacht Tribune on June 5th 2016.
Photo: Johnny Ryan Photography

HAEMOCHROMATOSIS AWARENESS DAY THURSDAY June 2ND

Sincerest thanks to all the people who helped man stands in 34 venues throughout the country.

It would not have been possible to organise the event without the support of members of the association and friends.
On June 1st Professor Suzanne Norris, Consultant in Hepatology and Gastroenterology at St James's Hospital and All Star Footballer, David Beggy, were interviewed by Mark Cagney on TV3 AM.
Radio interviews included Galway Bay FM, Clare FM, Kerry Radio , KCLR 96fm Kilkenny, South East Radio and Mid West radio.
Publications included *the Examiner, Cork Evening Echo, Connaught Tribune, Irish National Stud and Gardens and the Medical Independent.*

Phillipa Moran and Geraldine Mc Swiney, Dublin

Kathy and Pat O'Dwyer in Cork

Ann O'Sullivan Dooley & Majella O' Neill in Kilkenny.

Mary O' Rourke and Martin Monaghan manning the stand in Athlone.

Milo Walsh and Paddy Early in Waterford.

Nigel Connell and Joe Masterson in Navan.

ANNUAL GENERAL MEETING SATURDAY MAY 28TH 2016

Fran Mullaney, Prof Crowe and Margaret Mullett attending the AGM

The AGM of the Irish Haemochromatosis Association which took place on Saturday 28th May 2016 was attended by 70 people. Margaret Mullett gave the chairperson's report and the treasurer's report was given by Brendan Keenan. The board of directors agreed to stay on for another year.The IHA would like to thank the IBTS for once again making the centre available to us and for generously sponsoring morning coffee and lunch. We would also like to thank Dr Barbara Ryan, Professor John Crowe and Professor Dan Bradley for their excellent presentations.

NATIONAL GUIDELINES- MODELS OF CARE

A HSE multidisciplinary working group is developing Models of Care for patients with Hereditary Haemochromatosis. The final drafts will be discussed at the working party meeting on June 21st.
a) Model of Care for Hereditary Haemochromatosis
b) Model of Care for Therapeutic Phlebotomy
When signed off and published they will be available on line.
A GP Education Resource is also being made available which, once reviewed, will be uploaded onto the HSE website. Sincerest thanks to Dr Colm Henry and the working group. A special word of thanks to the project manager, Aisling Phelan, for her excellent work in progressing the agenda.

Shanaugh Gallagher

WOMEN'S MINI MARATHON JUNE 6TH

The IHA would like to thank all the ladies including Shanaugh Gallagher pictured above, who ran the Women's Mini Marathon for the IHA.

NATIONAL PLOUGHING CHAMPIONSHIP SEPTEMBER 20TH -22ND

The NPC will take place at Tullamore, Co Offaly from Sept 20th – 22nd. If you are available to help man a stand, please contact us by emailing margaretmmullett@gmail.com or by leaving a message on 01 8735911.