BELGIAN CHARCOT FOUNDATION

FIGHTING MULTIPLE SCLEROSIS

Number **44**
November 2018

NEWSLETTER

Belgian Charcot Foundation
Public interest foundation

Under the Patronage of Her Majesty The Queen

Huart Hamoir Avenue 48
B - 1030 Brussels
Tél.: +32 2 426 49 30
Fax: +32 2 426 00 70
info@fondation-charcot.org
NN 468 831 484

www.fondation-charcot.org
IBAN : BE34 6760 9000 9090
BIC : DEGRBEBB

Photo Credit: iStock & Shutterstock
Responsible publisher: I.Bloem
Av. Huart Hamoir, 48 - 1030 Brussels

DONATE ON-LINE

Customised treatments: let's go!

Better diagnosis of MS, clearer definitions of the various MS phenotypes,improved knowledge of the genetic factors in susceptibility and prognosis. Over the past 20 years, our knowledge of the disease has greatly improved. As a result, we are now able to diagnose and define it more accurately despite its considerable heterogeneity and very different evolution from one individual to the next.

The latest **revision of the diagnostic criteria** (June 2018) is described with great precision by Dr. Brigitte Capron in this newsletter. These criteria remain based on two constants, on the one hand the requirement that lesions disseminate over time and space, and on the other hand the exclusion of other diseases which may cause symptoms similar to those of MS.

The various forms of MS were also redefined in a 2014 publication. We now know there is a "radiologically isolated syndrome", a "clinically isolated syndrome", and that "progression" may take various forms. The purpose of all these efforts is to catch the disease earlier and to treat it in a manner more appropriate to its evolution in each patient.

The genetic factors in susceptibility of the disease have been very widely studied and over 200 of them have been detected, each of which is of variable and often low importance. Importantly, the presence of these factors enhances the adverse effects of external environmental elements such as smoking. However, somatic mutations, especially in the DNA of immune cells from MS patients, remain unknown and require further study, which at present has barely begun. For this reason, the Belgian Charcot Foundation jury has decided to attribute **the Charcot Fellowship 2018-2022** to Lies Van Horenbeek, who is currently working in the laboratory of Professor An Goris at KU Leuven. Her research project is described in this issue.

All these subjects demonstrate the great vitality of MS research and the resulting practical applications in the day-to-day working lives of the clinical neurologists in charge of patients' diagnosis and care.

Prof. Christian Sindic
President

< < Join Us !

DIAGNOSTIC

The new diagnostic criteria for Multiple Sclerosis (MS)

In recent years, it has been shown that starting treatment early in MS patients significantly improves the long-term prognosis in the relapsing-remitting forms. It is therefore critically important that MS be diagnosed as soon as possible.

MS becomes "clinically definite" when the patient has presented 2 clinical symptoms, i.e. has had 2 attacks of the disease. Fortunately, it is now possible to treat MS after a single attack ("clinically isolated syndrome" (CIS)), provided it is recognised as such.

For this reason, periodic reassessment of the diagnostic criteria and their use on the basis of new data and innovative techniques enables the diagnostic criteria for MS to be improved. Around 30 world MS experts met in 2017 to revise the McDonald criteria, which had remained unchanged since 2010, in order to improve them. The purpose of these revisions is to facilitate an earlier diagnosis for patients with probable but unconfirmed MS according to the 2010 criteria, while maintaining the specificity of these criteria and enabling them to be applied appropriately in order to minimise diagnostic errors.

Identifying oligoclonal bands

The first major change concerns the identification of specific oligoclonal bands (OCBs) in the cerebrospinal fluid (CSF) which attest to the local synthesis of antibodies in the central nervous system compartment.

This enables a diagnosis of MS to be confirmed in the event that a CIS meets the MRI (Magnetic Resonance Imaging) criteria for spatial dissemination, i.e. at least 1 lesion in at least 2 locations typical of MS (provided no other valid diagnosis may explain the clinical manifestations). Formerly, temporal dissemination criteria (MRI or clinical) were mandatory to demonstrate the chronic and evolving nature of the disease.

Today, many studies have demonstrated that the presence of OCBs in the CSF is a predictor of the risk of a second attack. According to these revised criteria, therefore, the identification of OCBs in the CSF can replace the requirement that temporal dissemination be proven.

An image-based diagnosis (MRI)

The second notable change relates to the MRI criteria for temporal and spatial dissemination: according to the 2010 criteria, symptomatic spinal cord or brainstem lesions could not be taken into account to confirm temporal and spatial dissemination in CIS patients.

Further to the 2017 revision, no distinction is made between symptomatic and asymptomatic lesions to determine spatial and temporal dissemination: a symptomatic active lesion has the same value as an asymptomatic one. It should be noted that lesions of the optic nerve are not yet taken into account.

The locations required to meet the criteria for spatial dissemination include the ones flagged using the Barkhof image-based criteria: periventricular, juxtacortical, spinal cord or brainstem. However, histopathological studies have shown that cortical lesions are also typical of MS.

The improvement in the technical performance of MRI now enables them to be identified. For this reason, the 2017 panel of experts decided to include cortical as well as juxtacortical lesions in the image-based diagnostic criteria.

> *At this point in time, the true challenge is diagnosing MS on the basis of a single attack.*

To summarise: at this point in time, the true challenge is diagnosing MS on the basis of a single attack. The 2010 diagnostic criteria emphasised the importance of MRI in demonstrating the spatial and temporal dissemination of the disease to clinically confirm the suspected diagnosis: this requires that different areas of the central nervous system be involved (spatial dissemination) and that disease activity be diagnosed at different times (temporal dissemination).

The new 2017 criteria take into account the MS foci in the cerebral cortex, and temporal dissemination can be proven by analysing the SCF.

Dr. **Brigitte Capron**
Neurologist, CHU of Charleroi

▶ *The references of all the studies mentioned are available on request at the Belgian Charcot Foundation.*

With the support of

Biogen

Degroof Petercam

Join us for the 20km of Brussels 2019

Thanks to their involvement and their efforts, during the 2018 edition, the runners of the Charcot Team contributed to finance 268 days of research. A big thank you to all of you.

Next appointment: Sunday, May 19, 2019.
Register now on www.fondation-charcot.org

THE CLINICAL SUBTYPES OF MULTIPLE SCLEROSIS

A new classification

A precise description of the clinical subtypes of multiple sclerosis is necessary in order to better classify each patient's disease and better tailor their immunomodulatory therapy according to its course. The earlier classification of 1996 has been reviewed in 2013 and published in 2014 by Fred Lublin and co-workers.

The current classification of disease courses

The radiologically isolated syndrome. This consists in the incidental discovery of lesions highly suspected of being multiple sclerosis plaques but detected by brain magnetic resonance imaging (MRI) performed for any other reason, such as a headache, cranial trauma, a suspected pituitary tumour, etc. It involves patients who have never shown any symptoms of multiple sclerosis but who could potentially develop the disease later on.

The clinically isolated syndrome. This refers to persons experiencing a first inflammatory event in the central nervous system, displaying symptoms typical of multiple sclerosis. There is, however, no dissemination of lesions, either in the central nervous system (only a single lesion is detectable), or over time (there are no inactive previous lesions, and only one new active lesion). In the absence of such a dissemination in space and time, a multiple sclerosis diagnosis cannot be made.

Relapsing-remitting multiple sclerosis. This is the predominant form of multiple sclerosis (55%), with exacerbations ("relapses") varying in frequency and intensity. It can either be followed by a complete recovery or can leave permanent damage, but shows no worsening of symptoms between exacerbations. The symptoms appear and worsen in a few hours or in a few days and must persist for more than 24 hours without fever. This form of multiple sclerosis can be inactive, either spontaneously or thanks to immunomodulatory therapies, or active, if clinical exacerbations occur and/or if MRI shows new lesions when compared to previous imaging.

Progressive multiple sclerosis. This consists of a progressive increase of neurological deficits over the course of several months, either at the onset of the disease, without any initial exacerbation (primary-progressive type), or after a first phase of exacerbations and remissions (secondary-progressive type). At this time, we do not yet have specific and precise criteria to determine the moment of transition from the relapsing-remitting type to a secondary-progressive type.

This progression must be evaluated at least once a year using the "EDSS" disability scale and must be differentiated from the accumulation of deficits due to previous exacerbations. We can distinguish **four subtypes** for both the primary and secondary progressive types:

1. Active with progression
2. Active without progression
3. Inactive with progression
4. Inactive without progression
   (in this case, the disease is stabilised at a "plateau" which remains susceptible to changing later).

> *"The fact that the severity and activity of the disease can change significantly but unpredictably throughout its course must be emphasized*

The term "active" denotes the presence of exacerbations in addition to a progression and/or a change in the MRI. The term "progression" means the aggravation of symptoms over a period of several months, as measured by the EDSS scale.

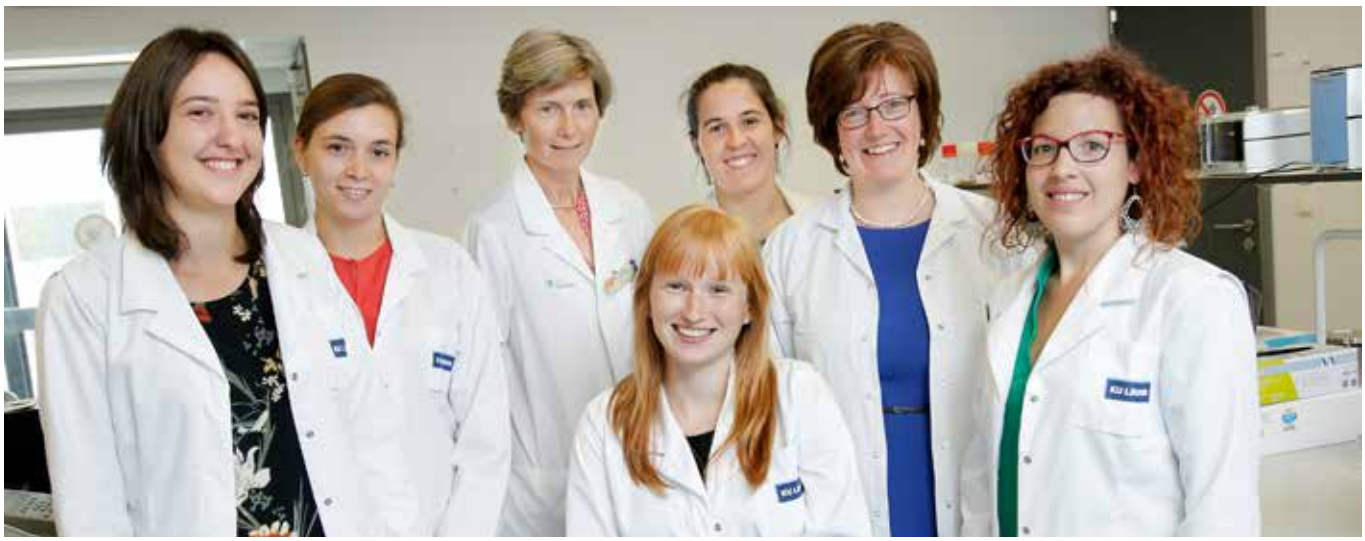
The fact that the severity and activity of the disease can change significantly but unpredictably throughout its course must be emphasized. The term "benign", with regard to MS, always refers to a retrospective diagnosis which can only be given after a disease'duration of 20 to 30 years.

It is therefore up to each patient and his/her neurologist to regularly determine, *together* and at least once a year, the course and characteristics of his/her disease.

Prof. Christian Sindic

CHARCOT FELLOWSHIP 2018–2022

Investing in research potential in Belgium



From left to right: Marijne Vandebergh, Klara Mallants, Prof. Bénédicte Dubois, Ide Smets, Prof. An Goris, Dr. Emanuela Oldoni and in the middle Lies Van Horebeek (laureate of the Charcot Fellowship 2018-2022)

The Belgian Charcot Foundation plays a key role in financing research in Belgium, whether basic, translational or clinical.

Since 2016, therefore, in addition to the large sums it devotes each year to basic research, the Foundation has decided to allocate a doctoral research grant every other year to young researchers (up to the age of 30) working in Belgium. Besides a financial grant of **200,000 euros over a 4-year period**, the recipient benefits from top-quality supervision within a renowned research team. The recipient of this year's second edition, **Lies Van Horebeek** (24), was officially awarded the doctoral grant on 16 October 2018 in the course of an academic session.

> *“ Her research project proposes a whole new explanation*

The research team of her supervisor Prof. A. Goris (KU Leuven) has already demonstrated that 200 genetic risk factors influence an individual's susceptibility to MS. Identification of these factors meant a big leap forward over the past 10 years and highlighted an important role of immune cells during disease development. As known genetic risk factors are not all explanatory, the next key question is: what triggers whether an individual with a certain load of known genetic risk factors does or does not get MS? Rather, the crucial question is: **why does a person with a particular predisposition due to hereditary genetic factors develop the disease at all?**

Lies Van Horebeek (KU Leuven) is a bioengineer whose research project proposes a whole new explanation. For a long time, it has been assumed that our genetic code is identical in all cells of our body. We are now starting to understand that our body actually is a mosaic of cells, which can differ slightly in their genetic material.

These genetic differences are not inherited from our parents but have arisen newly in a subset of our cells, and are called somatic variants. The role of these genetic variants in the susceptibility to autoimmune and neurological diseases is increasingly being uncovered. In her Master's thesis Biomedical Sciences, Lies has developed a method to detect such somatic variants in the immune cells of MS patients.

The PhD Fellowship of the Belgian Charcot Foundation will now enable Lies to investigate whether and how these somatic variants contribute to the development and the course of MS.

This will contribute to a better understanding of the disease. Lies will also investigate whether these variants can be used as markers for immune cells that play a role in disease development. If so, these markers would be useful to follow up a patient's response to treatment.

▶ *For further information, please visit : www.fondation-charcot.org*

WHAT IF YOU WERE THE ONE WHO FOUND THE ANSWER?

A BEQUEST CAN MAKE ALL THE DIFFERENCE. THINK ABOUT IT.

The solution to multiple sclerosis lies in research

You can play an essential part in this if:

- ✓ **you want to continue changing the world for the better even when you're no longer there**
- ✓ **you believe that only research will lead to solutions for a disease such as MS**
- ✓ **you are looking for a good cause that will respect your wishes**

So, why not support the Belgian Charcot Foundation by means of a bequest or donation?

In all cases, do not hesitate to seek legal advice. The first visit to a notary is free of charge. We are also available to answer any queries you may have, both by phone or face-to-face and in confidence. With the support of notaries, we ensure full compliance with the provisions specified by each testator.

Please do not hesitate to contact us for further information or a meeting:
Isabelle Bloem-Gonsette, Donation and Legacy Manager.
isabelle.bloem@fondation-charcot.org

The Belgian Charcot Foundation participates in the Testament.be campaign. Research requires considerable resources and we prefer to affiliate with a joint campaign, which is less costly, in order to devote most of our funds to MS research.

"With my husband, we thought it was important to choose a good cause to support, one we trusted. We have always worked hard and we know that the Belgian Charcot Foundation will put our money to good use." *Anne, 72*

"Thanks to research, I was given treatment and had an almost normal life. I'm lucky enough to have three wonderful children. For their sake, I hope that researchers can find solutions for an MS-free future."

Clara, 53

"I've seen what MS can do to a person's life. My decision to support research by including the Belgian Charcot Foundation in my will is a well-considered one; I want to help find a solution for all MS patients." *Pascal, 49*

"We have already made all our plans for our children and grandchildren. We added a bequest to the Belgian Charcot Foundation, as we want to 'invest in the future' and show our children that you need to be generous as well as provident. Multiple sclerosis can happen to anyone."

Georges, 84

"What if researchers could find a cure for MS thanks to my bequest?" *Ingrid, 51*

The Belgian Charcot Foundation complies with privacy legislation. You will find more information on how we manage personal data on: www.fondation-charcot.org.

FONDATION CHARCOT STICHTING