FONDATION CHARCOT STICHTING

58

Fighting multiple sclerosis

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FROM CHARCOT'S HISTORY TO TODAY'S RESEARCH

This issue of the Charcot Foundation Bulletin invites us to take a dual look at the history of neurology and multiple sclerosis.

On the bicentennial of the birth of Jean-Martin Charcot, the first to describe multiple sclerosis as a distinct clinical entity, we revisit his complex legacy. As the founder of modern neurology, he contributed to the advancement of medicine through observation and scientific rigor, but his work also fits into a context that today raises questions about our practices and ethics.

In the same spirit, we offer a historical overview of multiple sclerosis treatments. From the first empirical attempts to today's highly specialized therapies, the progress made has been considerable. These advances remind us how much each step forward depends on the accumulation of knowledge, the commitment of researchers, and the constant support of the community.

Finally, this Bulletin also marks an important milestone for our Foundation: the official launch of our new website, a veritable center of knowledge on multiple sclerosis. Designed as an evolution of the original site, it has been redesigned, enriched, and updated to continue to offer a reliable, clear, and accessible reference for everyone—patients, families, caregivers, and researchers.

Looking back helps us to better understand the present and prepare for the future. For nearly forty years, the Charcot Foundation has worked tirelessly to support research. In a context where public funding is becoming scarce and confidence in science is sometimes being tested, your generosity makes all the difference.

Thanks to you, we can continue to believe and work towards a future where multiple sclerosis is no longer a death sentence.

Prof. Dr. **Bénédicte Dubois**
PRESIDENT

The references for all studies mentioned in this newsletter are available upon request from the Charcot Foundation.

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CHARCOT: ONE NAME, THREE REALITIES... AND 200 YEARS OF LEGACY

The name "Charcot" can often be confusingly taken to refer to "Charcot's disease" (amyotrophic lateral sclerosis), the Charcot Foundation (which supports research into multiple sclerosis), and the man himself—Jean-Martin Charcot.

In November 2025, we will celebrate the bicentenary of his birth. It is a fitting moment to revisit the life of this brilliant, celebrated, and yet problematic neurologist at times.

Born in Paris in 1825, Jean-Martin Charcot is considered one of the founding figures of modern neurology. He was the first to recognise multiple sclerosis as a distinct disease, at a time when its highly variable symptoms were often misattributed to other conditions. He made the first clinical diagnosis of MS in a living patient in 1868 at Salpêtrière based on meticulous observation – a diagnosis that was later confirmed by autopsy. He rigorously described the histologic features of the disease, i.e. those now-famous demyelinating plaques in the brain and spinal cord, and produced himself remarkably precise drawings of the lesions which are still referenced in some medical texts today.

> Combining clinical observation with post-mortem investigation, this approach marked a turning point in the history of neurological pathology.

The very setting of the Salpêtrière sheds light on this development: Far more than a hospital, it was a city within a city, a place of care, but also of confinement. Thousands of women were institutionalised there for medical, social, or moral reasons.

Against this backdrop, Charcot devised a clinical method rooted in exacting observation, at a time when psychiatry was still in its infancy and often tainted by moral judgement. He drew, photographed, and categorised symptoms as one might classify specimens. From this ambiguous setting emerged a scientific revolution that was halfway between medical progress and institutional oppression.

Yet scientific advancement cannot be recounted without confronting its darker side. At the Salpêtrière, female patients (often poor women) were diagnosed with what was then termed "hysteria." They were institutionalised without genuine consent and were routinely showcased during Charcot's famous "Tuesday lectures." Hypnosis, convulsions, "theatrical" postures.

> These demonstrations captivated students and intellectuals from across Europe, including Freud, Babinski, and Gilles de la Tourette.

Long framed as educational exercises, these public sessions are now clearly seen as exploitative. They reflect how society at the time treated vulnerable women, namely as objects of curiosity, bodies to be studied, controlled, and displayed.

The scope of Charcot's immense scientific influence is inseparable from the duty to remember the women who were instrumentalised in its unfolding. He paved the way for a neurology grounded in observation, classification, and anatomical pathology.

He described amyotrophic lateral sclerosis (ALS), known in French-speaking countries as "Charcot's disease," a term often confused with MS, and trained generations of physicians. He also helped bridge medicine and fundamental science, at a time when mental illness was still largely broached through theological or legal doctrines.

1868
First clinical description of multiple sclerosis

1993
First effective treatment: beta interferon

2010
First oral treatment: fingolimod

2023
Confirmed link with the Epstein-Barr virus (EBV)

ANDRÉ BROUILLET - **UNE LEÇON CLINIQUE À LA SALPÊTRIÈRE** (1887)

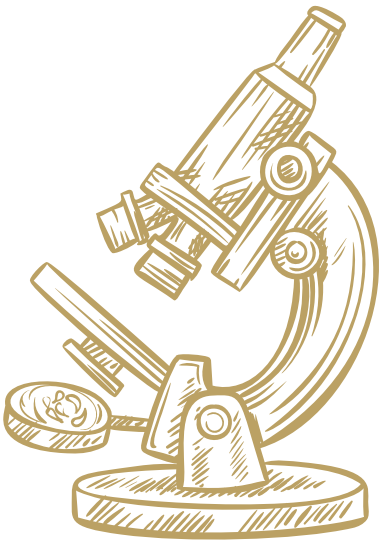
Charcot's many contributions include identifying primary lateral sclerosis and locomotor ataxia (linked to tertiary syphilis), as well as advancing the understanding of epilepsy, Huntington's chorea, and speech disorders. He was among the first to assert that certain neurological diseases had organic rather than spiritual or moral origins, thereby laying the foundations for a rational medicine of the nervous system.

Two centuries on, his legacy has to be viewed in all its complexity, with major advances for medicine, but also practices that cause discomfort and call for reflection. A comprehensive reckoning with this legacy is essential if we are to move forward on the ethical and scientific fronts.

For nearly 40 years now, Charcot's name has lived on in a very different way through the Charcot Foundation in Belgium, which supports researchers committed to deepening our understanding of multiple sclerosis.

This rigorous and dedicated research effort has one goal: to defeat the disease and improve the lives of the people affected.

We could never walk alone on this path. Your support, trust and commitment are essential, and we are grateful to have you on board.



↘ This article is based on public biographical sources and on Bernard Zalc's analysis (Brain, 2018), which retraces Jean-Martin Charcot's initial description of multiple sclerosis.

MS TREATMENTS OVER THE PAST 30 YEARS

Introduction

Treatment options for MS have evolved significantly over the past 30 years.

Prior to 1993, we could only offer corticosteroids and chemotherapy in the hope of influencing the course of the disease.

As of 2025, there are 16 different medicines registered in Belgium for the treatment of Relapsing-Remitting Multiple Sclerosis (RRMS). These are available in various forms such as tablets, injections and infusions.

Two of them can also be used in progressive forms of MS when there is evidence of inflammatory activity (ocrelizumab in primary progressive MS, siponimod in secondary progressive MS).

Viral hypothesis and the emergence of interferon

Researchers have for several decades suspected that viruses play a role in the development of MS. The antiviral effects of the human protein interferon formed the basis for research in the 1970s and 1980s.

Encouraging results from a large-scale, randomised, double-blind, placebo-controlled trial of interferon beta-1b in RRMS in 1993 marked a milestone in MS treatment. In July 1993, interferon beta-1b was approved by the FDA as the first medicine for RRMS.

> Subsequent studies with interferon beta-1b and interferon beta-1a confirmed a reduction in the number and severity of relapses in RRMS and the effects on visible pathology (imaging).

Animal model for MS

Experiments on laboratory animals, primarily mice, have contributed to a better understanding of disease mechanisms and the testing of new MS treatments.

Induced inflammation of the central nervous system, known as autoimmune encephalomyelitis, serves as a model for MS. Glatiramer acetate, a mixture of synthetic proteins resembling myelin, has been shown to mislead the immune system in animal studies.

Based on promising results in people with RRMS, this treatment was approved by the FDA in October 1995. Approval in Europe followed a few years later.

Medicines for immune-mediated diseases

Encouraging results in Crohn's disease, an inflammatory bowel condition, led to large-scale studies conducted on RRMS with natalizumab. The hypothesis that monoclonal antibodies targeting proteins on the surface of inflammatory cells could inhibit their passage through the blood–brain barrier was confirmed.

This highly effective (second-line) infusion treatment has been available in Belgium for RRMS since December 2007. Fingolimod, the first oral treatment for RRMS, followed in February 2012 as a second-line option, as it reduced inflammation significantly by retaining lymphocytes in the lymphoid organs.

Earlier research with this substance had focused on preventing rejection after kidney transplantation. This class of drugs has since been expanded to include ozanimod and ponesimod (first-line treatments for RRMS) and siponimod (for secondary progressive MS).

Expansion of treatment options in RRMS

- First-line treatments were expanded to include teriflunomide (2013) and dimethyl fumarate (2014), which were derived from medicines for psoriasis and rheumatism, respectively, with various immunomodulatory effects.

- Three different monoclonal antibodies targeting a surface protein (CD20) on B lymphocytes were added in second line therapy: ocrelizumab, ofatumumab and ublituximab. Their intravenous or subcutaneous administration leads to a marked suppression of inflammatory processes in RRMS.

- A measurable effect on progression was also demonstrated with ocrelizumab in primary progressive MS with inflammatory activity. Cladribine, an oral induction therapy administered in two yearly doses (half the dose in year 1, and the other half in year 2), primarily targets rapidly dividing immune cells in RRMS.

- Alemtuzumab is an intravenous third-line induction therapy with monoclonal antibodies against CD52+ immune cells. These medicines were originally investigated for MS because of their efficacy in haematological cancers.

What these medicines do and do not do

Current MS medicines successfully suppress the overactive immune response. There are however drawbacks and risks associated with immunosuppression.

Choosing the most suitable treatment for an individual is not straightforward due to the diverse mechanisms of action and the unpredictable course of the disease. Treatment response cannot be reliably predicted either at present.

Unfortunately, no medication has yet proven significantly effective in slowing the gradual progressive course, independent of inflammation. A new class of drugs, the BTK inhibitors, may offer hope on this front. To be continued!

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TRUSTING AND BELIEVING IN THE FUTURE

Contribute to research by donating to the Charcot Foundation.

Speed up research on multiple sclerosis and make a difference to thousands of lives. The Charcot Foundation is Belgium's only independent organisation dedicated to basic research on this disease.

Remember us in your will

3 REASONS

- MS remains incurable and very often develops into a disability, shattering the lives of thousands.
- All our current endeavours are bringing us closer to solutions: slowing down the disease, repairing its damage and hopefully, one day, curing it completely.
- We undertake to invest the full amount of your legacy in multiple-sclerosis research.

DUAL LEGACY

If you have no close relatives, dual legacy reduces the inheritance-tax burden while supporting medical research. For further information, we advise you to contact your notary.

Any questions?

Please contact us for a confidential answer.

isabelle.bloem@fondation-charcot.org
or by phone at +32 **(0)2 426 49 30**

Make a donation

1 day of research= 7€ /month on 1 year

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