

Abstract Book



MS

State of the Art

Symposium 2021



MS State of the Art Symposium

«MS and Infectious Diseases»

Dear Colleagues,

It is with great pleasure that we invite you to this year's «MS State of the Art Symposium», organised by the Swiss Multiple Sclerosis Society and its Scientific Advisory Board.

The main theme «MS and Infectious Diseases» revolves around the Covid-19 pandemic and Multiple Sclerosis. It is this very pandemic that forces us to carry out the 23rd annual symposium as virtual edition.

Jan Fehr and **Milo Puhan** will give clinical, epidemiological and health policy insights into the pandemic and discuss the «Corona Immunitas» research program in their joint talk. Covid-19 registries play an important role in documenting the disease. **Robert Hoepner** will elaborate on the European LEOSS registry, while **Céline Louapre** will give insights into the French COVISEP registry, a cohort study focussing on Covid-19 in persons with MS. As vaccinations for Covid-19 are currently being developed and distributed, questions of safety and effectiveness of vaccinations are highly prevalent among persons with MS. **Matthias Mehling** will discuss these implications by citing relevant studies. The third session of the symposium will focus entirely on MS. First, **Renaud Du Pasquier** will recapitulate the risk factors of PML in MS. Finally, **Andrew Chan** and **Anke Salmen** will give a joint speech on the current treatment landscape of MS and of Neuromyelitis Optica Spectrum Disorders.

For the first time, MS research projects that are supported by the MS Society will be displayed as short «**Poster Blitz**» presentations during the main session. In the coffee and lunch breaks, these projects will then be displayed in interactive, live **Poster Sessions**. You may join these virtual sessions and discuss the latest findings with the researchers.

In the breaks you will also have the opportunity to chat individually with other attendees and join virtual discussion tables.

On behalf of the organisers and speakers, we sincerely hope that the programme meets your interest and that you will be able to attend this virtual «MS State of the Art Symposium».

A white handwritten signature of Andrew Chan on a red background.

Andrew Chan
Swiss MS Society
Board of Directors and
Scientific Advisory Board

A white handwritten signature of Patricia Monin on a red background.

Patricia Monin
Swiss MS Society
Director

A white handwritten signature of Claudio Gobbi on a red background.

Claudio Gobbi
Swiss MS Society
Scientific Advisory Board

General Information

Date

Saturday, January 23th, 2021, 09.30 – 15.30

Virtual Symposium

www.ms-state-of-the-art.ch

Programme Committee

Andrew Chan, Bern

Adam Czaplinski, Zurich

Claudio Gobbi, Lugano

Roman Gonzenbach, Valens

Robert Hoepner, Bern

Ilijas Jelcic, Zurich

Jens Kuhle, Basel

Stefanie Müller, St. Gallen

Caroline Pot, Lausanne

Milo Puhan, Zurich

Anke Salmen, Bern

Organisation

Swiss Multiple Sclerosis Society and its Scientific Advisory Board

Contact

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Credits

The Swiss Neurological Society awards 5.0 credit points.



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Epidemiology, Biostatistics and Prevention
Institute

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University Hospital Bern
Department of Neurology

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University Hospital Bern
Department of Neurology
Medical Division Neuro

Renaud Du Pasquier, Lausanne

Lausanne University Hospital (CHUV)
Service of Neurology

Jan Fehr, Zurich

University Hospital Zurich
Department of Infectious Diseases
and Hospital Epidemiology

Robert Hoepner, Bern

University Hospital Bern
Department of Neurology

Céline Louapre, Paris (FR)

– Pitié Salpêtrière Hospital, Paris (FR)
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Matthias Mehling, Basel

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Milo Puhan, Zurich

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MS Researcher Poster Presentations

Maud Bagnoud, Bern

University Hospital Bern
Department of Neurology

Sandra Bigi, Bern

– University of Bern
Institute of Social and Preventive Medicine
– University Hospital Bern
Department of Neurology
and Department of Pediatrics

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Özgür Yaldizli, Basel

University Hospital Basel
Neurology Clinic and Polyclinic

Swiss MS Society: We care for persons with MS

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Information

We advise and accompany persons with MS and their relatives. They can count on our professional counselling services.

Research

MS research projects contribute to a better understanding of the disease, improve treatment and quality of life for persons with MS.

Awareness

The MS Society raises awareness for MS and promotes exchange with researchers, professionals and institutions.

Relieve

The «group respites» are highly appreciated by persons with MS and caregivers alike.

MS

Swiss
Multiple Sclerosis
Society



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Der Infyna Chic Einmalkatheter wurde mit Hilfe von Fachexperten entwickelt, um ein hohes Mass an Diskretion für Frauen, die Einmalkatheter verwenden, zu gewährleisten. Der Einmalkatheter hat nicht nur ein ansprechendes Design, sondern ist auch einfach in der Handhabung. Infyna Chic kann einer Frau helfen, sich besser damit zu fühlen, einen Katheter zu verwenden.

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Infyna Chic

Einmalkatheter

MS State of the Art Symposium

«MS and Infectious Diseases»

Session 1

Chairpersons:

Adam Czaplinski, Zurich
Britta Engelhardt, Bern

09.30 – 09.45

Christoph Lotter, Zurich
Welcome from the Swiss MS Society

09.45 – 10.30

Jan Fehr & Milo Puhan, Zurich
The Corona Pandemic and MS – First Line Clinical, Epidemiological and Health Policy Insights

10.30 – 11.00

MS Researchers
Poster Blitz - MS Society Research Projects at a Glance

11.00 – 11.30

Coffee Break & Poster Presentations

Session 2

Chairpersons:

Caroline Pot, Lausanne
Gabrielle Di Virgilio, Vevey

11.30 – 11.45

Robert Hoepner, Bern
Swiss Covid-19 Data in the European LEOSS Registry

11.45 – 12.00

Céline Louapre, Paris (FR)
The French COVISEP Registry

12.00 – 12.30

Matthias Mehling, Basel
MS and Vaccinations

12.30 – 13.45

Lunch Break & Poster Presentations

Session 3

Chairpersons:

Ilijas Jelcic, Zurich
Stefanie Müller, St. Gallen

13.45 – 14.15

Renaud Du Pasquier, Lausanne
Risk of PML in Multiple Sclerosis Therapies

14.15 – 15.00

Andrew Chan & Anke Salmen, Bern
Treatment Landscape of MS and NMOSD 2021 – Discussion

15.00 - 15.30

Christoph Lotter, Zurich
Goodbye & Networking



I am specialized in internal medicine and infectious diseases focusing on Global Health Challenges. I am currently the Head of the Department of Public Health at the Epidemiology, Biostatistics and Prevention Institute at the University of Zurich. Furthermore, I have an appointment as senior attending physician at the University Hospital Zurich working in the Division of Infectious Diseases and Hospital Epidemiology. I am investigator in the 2020 established «Corona Immunitas» Cohort Study.



My main research interest focuses on epidemiology of chronic and infectious diseases and on the development of tools to support preference-sensitive health care. I am currently principal investigator of the Swiss MS Registry and several other studies. In 2020, together with other colleagues from SSPH+ we founded the Corona Immunitas Initiative that unites Swiss national efforts to determine the spread of SARS-CoV-2 and development of immunity in Switzerland.

Jan Fehr & Milo Puhan, Zurich

The Corona Pandemic and MS –

First line Clinical, Epidemiological and Health Policy Insights

Prevention of infections and clinical care for patients with Covid-19 must go hand in hand in the Coronavirus pandemic. Prevention and care are closely intertwined since measures on the system and community level have immediate impact on the number and type of persons needing care. Insights from individual care provide much needed information on the nature and course of Covid-19, which in turn informs health policy decisions.

In this ping pong talk, we will discuss this interplay with insights from care at a tertiary care hospital, from a large Covid-19 testcenter and from the «Corona Immunitas» research program with its 40 studies and 30'000 participants.

This is an interesting and illustrative showcase of the interaction between science and decisions makers at the local, cantonal and federal level.

*Jan Fehr
University Hospital Zurich
Department of Infectious Diseases and Hospital Epidemiology*

*Milo Puhan
University of Zurich
Epidemiology, Biostatistics and Prevention Institute*

Poster Blitz – MS Society Research Projects at a Glance

The Swiss MS Society supports research projects in the field of Multiple Sclerosis with considerable financial contributions. The «Poster Blitz» gives a brief overview of a selection of current research projects. Given the virtual nature of the symposium, each project is introduced by a short video film. These projects are then displayed in interactive, live poster presentation sessions during the coffee and lunch breaks.

01 | Maud Bagnoud & Robert Hoepner, Bern

Investigation of Vitamin D Signaling via the Glucocorticosteroid Receptor

02 | Sandra Bigi, Bern

The Swiss Pediatric Inflammatory Brain Disease Cohort Study: A Nationwide Population-Based Registry to Enhance Epidemiological Knowledge and Improve Care of Pediatric Onset MS and Related Disorders.

03 | Matthias Mehling, Basel

Growth Differentiation Factor 15 is Increased in Stable MS

04 | Sarah Mundt, Zurich

Neurodegeneration in MS: What is the Contribution of Phagocytes?

05 | Hideaki Nishihara, Bern

Advancing Human Pluripotent Stem Cell Derived Laboratory Models of the Blood-Brain Barrier to Investigate the Pathogenesis of Multiple Sclerosis

06 | Johanna Oechtering, Basel

Intrathecal Immunoglobulin M Synthesis is Associated with Higher Disease Activity and Severity in Multiple Sclerosis

07 | Nadine Patt, Valens

High-Intensity Interval Training and Energy Management Education, Compared with Moderate Continuous Training and Progressive Muscle Relaxation, for Improving Health-Related Quality of Life in Persons with Multiple Sclerosis – Study Protocol of a Randomized Controlled Superiority Trial with Six Months' Follow-Up

08 | Sylvain Perriot, Lausanne

Deciphering Reactive Astrocyte Phenotypes Associated with Neuroinflammation and Multiple Sclerosis

09 | Jana Remlinger, Bern

Investigation of CNS Autoimmunity with Focus on Involvement of the Visual Pathway

10 | Nicholas Sanderson, Basel

The Significance of IgM in CSF of Patients with Multiple Sclerosis

11 | Guillaume Thévoz, Lausanne

The Impact of Dietary Factors and Circadian Rhythms on Fatigue in Multiple Sclerosis

12 | Valentin von Niederhäusern & Josefine Ruder, Zurich

B Cell Immune Reconstitution after Autologous Hematopoietic Stem Cell Transplantation in Multiple Sclerosis

13 | Viktor von Wyl, Zurich

Impact of Covid-19 on the Daily Lives of Persons with MS during the First Lockdown

14 | Özgür Yaldizli, Basel

Value of Serum Neurofilament Light Chain Levels as a Biomarker of Suboptimal Treatment Response in MS Clinical Practice



I am the head of the neuroimmunological outpatient department and study center at the University Hospital Bern. I work as a clinician treating patients with neuroimmunological diseases, mainly Multiple Sclerosis. Here my main interest is to improve the actual situation for each individual patient in order to reduce the burden of the disease. From a researcher's perspective, my research group and I focus on translational aspects, meaning to combine clinical data with laboratory findings. My areas of interest are efficacy and safety of immunotherapies especially glucocorticosteroids and Vitamin D as well as all aspects of Multiple Sclerosis associated MS fatigue.

Robert Hoepner

Swiss Covid-19 Data in the European LEOSS Registry

The «Lean European Survey on SARS-CoV-2 infected patients» (LEOSS) registry is an international registry investigating the effect of SARS-CoV-2 infections. A subcohort of this registry has focused on people with Multiple Sclerosis (MS) and several Swiss MS Centers participated.

Within the oral presentation data of Swiss MS patients in regard to disease course of Covid-19, immunotherapies and MS related factors will be presented. Epidemiological data of the patient cohort will also be highlighted. In addition, a special focus will be set on the infection rates of Covid-19. Infection rates of Swiss MS patients will be compared with those of the general population, to investigate if people with MS had been at higher risk of a Covid-19 disease.

*Robert Hoepner
University Hospital Bern
Department of Neurology*



As a clinical neurologist and researcher in the field of MS, I am particularly interested on bringing novel technical developments in MR imaging to investigate MS pathophysiological mechanisms with a particular emphasis to cortical pathology, quantitative markers of demyelination/remyelination and neuroinflammation. Since 2015, I am medical coordinator of the Neuroscience Clinical Research Centre (CIC Neuroscience) at the Paris Brain Institute (ICM), conducting more than 80 clinical trials in the field of neuroscience. Since 2018, I also coordinate together with Prof Gilles Edan (Rennes, FR) the national clinical research network FCRIN4MS.

Céline Louapre

The French COVISEP Registry

Background — Risk factors associated with Covid-19 severity in patients with multiple sclerosis (MS) begin to be identified from several cohort studies. Disease modifying therapies (DMTs) may modify the risk of developing a severe Covid-19 infection, beside identified risk factors such as age, disability and comorbidities. The objective of this study was to describe the clinical characteristics and outcomes in patients with Covid-19 and to identify the factors associated with COVID-19 severity.

Methods — This multicenter, retrospective, observational cohort study (COVISEP registry, NCT04355611) included patients with MS presenting with a confirmed or highly suspected diagnosis of Covid-19 between March 1, 2020 and November 10, 2020. The main outcome was Covid-19 severity assessed on a 7-point ordinal scale (ranging from 1: not hospitalized, no limitations on activities, to 7: death; cutoff at 3: hospitalized, not requiring supplemental oxygen). We collected demographics, neurological history, Expanded Disability Severity Score (EDSS), comorbidities, Covid-19 characteristics and outcome. Univariate and multivariate logistic regression models were used to estimate the influence of collected variables on Covid-19 outcome.

Results — A total of 565 patients (mean age: 43.8 years, female/male: 417/146, mean disease duration: 12.7 years) were analyzed. Ninety-one patients (16.1%) had a Covid-19 severity score ≥ 3 , and 13 patients (2.3%) died from Covid-19. 468 patients (82.7%) were on DMT. Multivariate logistic regression models determined that age (OR for 10 years: 1.68, 95% CI: 1.3-2.16), EDSS (OR for EDSS ≥ 6 : 3.7, 95% CI: 1.8-7.8) and cardiac comorbidity (OR: 3.1; 95% CI: 1.2-7.8) were independent risk factors for Covid-19 severity score ≥ 3 (hospitalization or higher severity) while DMTs (grouped according to immunosuppressive effect, or individually) were not significantly associated with a higher risk of Covid-19 severity score ≥ 3 .



I am a clinical neurologist with a specialization in neuroimmunology. I trained in neurology at the University Hospital in Tübingen (DE) and mainly at the University Hospital Basel. As a post-doctoral fellow, I worked at the Federal Institute of Technology Zurich (ETHZ) and at the Institute of Science and Technology Austria. I am the head of the hospital ward at the Neurology Clinic of the University Hospital Basel and a research group leader at the Department of Biomedicine of the University of Basel. My main research focus is the role of chemokines and chemotaxis in the pathogenesis of multiple sclerosis (MS) and how current MS immunotherapies impact on vaccine responses.

Matthias Mehling

MS and Vaccinations

Vaccinations are important measures of global health and currently prevent 2-3 million deaths every year from diseases like diphtheria, tetanus, pertussis, influenza and measles. Consensus exists among various international neurological societies and multiple sclerosis societies that all persons with multiple sclerosis (MS) should be immunized according to the local vaccine standards.

Physicians and other healthcare providers caring for persons with MS are often faced with questions concerning vaccinations in the context of MS: Do immunizations cause MS? Do vaccinations trigger MS relapses? How safe and effective are vaccinations in patients treated with disease modifying therapies (DMTs)?

During recent years, numerous studies addressing these questions have been published and will be summarized. Large, population-based studies have not uncovered a causal link between immunizations and the onset of MS. Also, no studies have identified a statistically significant relationship between standard vaccinations used in Switzerland and the occurrence of MS relapses. Immunization-induced immune responses have been studied in the majority of the currently approved DMTs. In these studies, differing immunological paradigms were used to quantify the magnitude of vaccine-specific immune responses.

These data and their consequences for vaccination strategies will be summarized. Finally, recent developments of SARS-CoV2 vaccination candidates and their implications for persons with MS are discussed.

*Matthias Mehling
- University Hospital Basel
Neurology Clinic and Policlinic
- Research Center for Clinical
Neuroimmunology and Neuroscience*



I am the Head of Neurology at the CHUV in Lausanne. In addition to my clinical duties, I run a laboratory of Neuroimmunology with a focus on the immune mechanisms in Multiple Sclerosis and progressive multifocal leukoencephalopathy.

Renaud Du Pasquier

Risk of PML in Multiple Sclerosis Therapies

Reactivation of JC virus in immunocompromised patients may lead to progressive multifocal leukoencephalopathy (PML). This disease is now well known by neurologists as it has been described in association with different treatments for Multiple Sclerosis (MS). Among them, the one that caused the highest occurrence of PML is natalizumab. However, mitigation and stratification of the risk have allowed to identify those patients who are more susceptible to develop the disease, making it safer to prescribe this drug to the others. Other drugs than natalizumab such as fingolimod or dimethyl-fumarate have also been shown to be able to trigger PML, even if at a rarer occurrence than natalizumab. PML has occurred in an anecdotal way with other MS treatments.

In this talk, I will recapitulate the essential clinical and neuroradiological features of PML in MS; review the latest evidence about the risk of developing PML with a given treatment; enumerate the risk factors; and try to provide an explanation for the underlying pathophysiological mechanism leading to PML in this or that treatment.

Finally, I will recapitulate the essentials in the management of PML in MS patients, paying a particular attention to the sometimes perilous immune reconstitution steps, also known as the immune reconstitution inflammatory syndrome (IRIS).

*Renaud Du Pasquier
Lausanne University Hospital (CHUV)
Service of Neurology*



I am Head of the Medical Division Neuro, Inselspital, University Hospital of Bern. After studying medicine and obtaining a doctorate at the University of Hamburg, I completed my specialist training at the University of Würzburg and continued my professional development as Senior Physician at the Universities of Göttingen and Bochum. I have published widely in the field of MS, including papers on molecular markers of disease progression and risk of immunotherapy, treatment optimisation and patient monitoring. I have been the Principal Investigator for several clinical studies in MS. I have also been involved in the development of national treatment guidelines.

Andrew Chan

Treatment Landscape of MS and NMOSD 2021

In the past year we have once again seen several additions to the armamentarium of approved disease modifying agents for MS. Most recently, two oral sphingosine-1 phosphate (S1P)-receptor modulators were approved for different indications in Switzerland (ozanimod, RRMS; siponimod, SPMS with focal disease activity). Especially the approval of siponimod for SPMS is remarkable, given that currently only few agents can be used in this indication; still, effect size in delaying disease progression is moderate.

Despite presumed similar mechanisms of action of S1P receptor modulators, pharmacodynamic differences indicate underlying heterogeneity between these substances, e.g. based on receptor specificity, pharmacokinetics/metabolization, and other biological characteristics. More experience is needed in order to evaluate if this will also translate e.g. in different side effect profiles. That the global safety profile of a substance cannot conclusively be assessed using data from clinical development programmes only was recently highlighted by the fact that agencies have reemphasized safety signals for some agents (dimethylfumarate, fingolimod) with longstanding use.

Until timepoint of writing, potential safety signals of certain immunotherapies (e.g. anti CD20) on the risk of Covid-19 are still preliminary. Still, Covid-19 has the potential to cause major changes in our clinical practice. Thus, one future milestone will be the response to a much hoped-for Covid-19 vaccine under different immunotherapies in MS. These aspects add further levels of complexity to individualized benefit-risk considerations that govern modern MS therapy.

*Andrew Chan
University Hospital Bern
Department of Neurology, Medical Division Neuro*



As deputy head of the Ambulatory Neurocenter and head of Infusion Unit at the Inselspital, University Hospital Bern, where I work since 2016, I am engaged in the diagnosis and treatment of patients with Multiple Sclerosis (MS) and other demyelinating CNS disorders as my special field of interest in Neurology. My research group focuses on antibody-driven CNS disorders and visual outcome parameters in animal models as well as clinical-translational research in the field of MS, Neuromyelitis optica spectrum disorders (NMOSD) and MOG-IgG-associated disorders (MOGAD). I took up my work as a neurologist and researcher at Ruhr-University Bochum, Germany, in 2007.

Anke Salmen

Treatment Landscape of MS and NMOSD 2021

Although not as prevalent as Multiple Sclerosis (MS), Neuromyelitis optica spectrum disorders (NMOSD) as an antibody-mediated inflammatory condition of the central nervous system (CNS) represent a neuroimmunological disease entity of high impact with necessity of both effective relapse treatment and immunotherapy.

However, differentiating NMOSD – aquaporin-4 antibody (AQP4-IgG) positive or negative – from MS and also from other novel entities such as MOG-IgG associated disorders (MOGAD) is a challenge in clinical practice due to overlapping features and similarities, but also pitfalls in antibody detection assays.

Important lessons on relapse treatment of NMOSD are that the timing of sequential treatments can be even more important than in MS, but also that in defined cases, first-line plasma exchange might be indicated.

The immunotherapeutic treatment landscape has just been significantly broadened – at least for AQP4-IgG positive NMOSD – with several new agents approved or on their way, such as satralizumab (anti-IL6-receptor), eculizumab (anti-complement C5) or inebilizumab (anti-CD19). Given the long clinical (off-label) use of other immunotherapeutics, especially rituximab (anti-CD20), in this indication, the question is burning which treatment may be the right for which patient, with implications for both newly diagnosed, but also patients with established NMOSD diagnosis. Despite lacking data on direct comparisons of the different immunotherapeutics, clinical pathways and decision strategies need to be implemented. Again, in the light of a very new risk constellation in the SARS-CoV2 pandemic, risk benefit considerations are getting more and more complex.

*Anke Salmen
University Hospital Bern
Department of Neurology*

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MS Researcher Poster Presentations

The Swiss MS Society supports research projects in the field of Multiple Sclerosis with considerable financial contributions.

A selection of current projects is displayed in interactive, live poster presentation sessions. You may join these sessions and discuss the projects with the researchers.



01 | Maud Bagnoud, Robert Hoepner

Investigation of Vitamin D Signaling via the Glucocorticosteroid Receptor

Background — Several evidence suggest a beneficial effect of vitamin D (VD) on multiple sclerosis (MS) and its animal model, the experimental autoimmune encephalomyelitis (EAE). It is known that VD administration reduces the severity of the EAE in vivo. Interestingly, preliminary data from our group demonstrate that VD decreases EAE severity in wild type (WT) mice whereas this effect is abolished in T cell specific glucocorticoid receptor (GR)-deficient mice suggesting a possible role of the GR in VD efficacy. We aim to identify a potential role of the GR in VD signaling. In more details, we would like to determine if VD signals through the GR or if there is a GR-dependent regulation of the VD receptor in T cells.

Methods — Myelin oligodendrocyte glycoprotein (MOG35-55) EAE was induced in female C57BL/6JRj WT- and T cell specific GR-deficient mice. Four different concentrations of calcitriol (1-1000ng), the active form of VD, were then given orally after disease onset for three consecutive days. Furthermore, cell apoptosis and Treg differentiation were analyzed in vitro by flow cytometry with CD3+ T cells from both WT and T cell specific GR-deficient mice.

Results — Three days of calcitriol treatment (from 1ng/day to 100ng/day) significantly reduced EAE severity in WT mice whereas no significant beneficial effect was observed in T cell specific GR-deficient mice. In contrast, calcitriol treatment at a concentration of 1000ng/day worsened the disease in both genotypes. In vivo results were confirmed by in vitro experiments as calcitriol treatment significantly promoted apoptosis and Treg differentiation of CD3+ T cells from WT mice whereas these effects were abolished in CD3+ T cells from T cell specific GR-deficient mice.

Conclusions — Preliminary results showed that the GR appears to be required for proper VD effects. However, further investigations are needed to determine the exact role of the GR in VD signaling.

Maud Bagnoud
University Hospital Bern
Department of Neurology

Robert Hoepner
University Hospital Bern
Department of Neurology



02 | Sandra Bigi

The Swiss Pediatric Inflammatory Brain Disease Cohort Study:

A Nationwide Population-Based Registry to Enhance Epidemiological Knowledge and Improve Care of Pediatric Onset MS and Related Disorders.

Background and rationale — Pediatric onset MS (POMS) is a severe disease affecting children and adolescents in a period of essential brain development. This possibly leads to early cognitive impairment, which may impact school performance and vocational achievements. Timely diagnosis and treatment initiation as well as individually tailored management are important for a favourable disease course/ outcome. However, the diagnosis of POMS can be challenging, especially in young children, since their first demyelinating attack is often accompanied by unspecific symptoms also common to other inflammatory brain diseases (IBrainD). A systematic assessment of similarities and differences between clinical signs, symptoms, diagnostic workup, and management of POMS patients versus patients suffering from other IBrainD will enable faster and more reliable diagnosis. In Switzerland, there is neither epidemiological data nor information on health care management and disease outcome of POMS patients. Therefore, we are setting up a national registry, which will allow a deeper understanding of POMS epidemiology, clinical presentation, and management. Ultimately, the registry will improve the care of Swiss POMS patients.

Aims and methods — The registry pursues the following goals:

- 1) Gathering representative, population-based epidemiological data on pediatric MS and other IBrainD in Switzerland.
- 2) Monitoring treatment, clinical course, education, social aspects, and outcomes of pediatric MS patients.
- 3) Providing a platform to facilitate national and international collaboration.

The registry will thereby address the increasing requests for medical trial participation and promote the exchange with existing adult registries (Swiss MS Registry). By design, the registry is set up as a cohort study with prospective and retrospective data collection. The following patients qualify for inclusion: All patients living and/or treated in Switzerland with POMS or another specified IBrainD with an onset before the age of 18. Excluded are patients with 1) neurological symptoms due to infectious diseases of the CNS; 2) genetic/metabolic causes of central demyelinating diseases; 3) neurological symptoms due to Guillain-Barré-Syndrome. Demographic and medical data as well as data from questionnaires will be centrally collected. Statistical analyses include descriptive statistics, univariate analysis, regression modelling, and statistical methods appropriate for longitudinal data.

Significance and feasibility — The study benefits the Swiss POMS patients by:

- 1) enabling faster diagnosis and improved care through enhanced epidemiological knowledge;
- 2) facilitating access to national/international clinical trials;
- 3) increasing the awareness of POMS in Switzerland.

Feasibility is ensured by embedding the study in a large, highly specialized national network.

Sandra Bigi

– *University of Bern*

Institute of Social and Preventive Medicine

– *University Hospital Bern*

Department of Neurology and Department of Pediatrics



03 | Matthias Mehling

Growth Differentiation Factor 15 is Increased in Stable MS

Background — Multiple Sclerosis (MS) is a chronic inflammatory demyelinating disease of the CNS. The disease course in MS is highly heterogeneous. Monitoring subclinical disease activity is a major challenge for clinicians caring for patients with MS. Identification of biomarkers that indicate disease activity in individual MS patients is largely an unmet need. Growth differentiation factor 15 (GDF-15) is a transforming growth factor-beta-related cytokine and counteracts LFA-1-dependent extravasation of leukocytes into inflamed tissues, hereby limiting tissue destruction. The objective of our study was to assess whether serum concentrations of the anti-inflammatory cytokine growth differentiation factor 15 (GDF-15) differ in patients with highly active MS vs patients with stable MS and healthy controls (HCs).

Methods — GDF-15 concentrations were measured by ELISA in serum and CSF in a cross-sectional cohort of patients with MS, patients with other inflammatory neurologic diseases (OIND), patients with noninflammatory neurologic diseases (NIND), and healthy controls (HC). Serum GDF-15 concentrations were measured in a longitudinally sampled cohort of clinically and radiologically well-characterized patients with MS and corresponding controls.

Results — Cross-sectionally measured median serum GDF-15 concentrations were significantly higher in patients with OIND ($n = 42$) (600 pg/mL, interquartile range [IQR] = 320-907 pg/mL) compared with HCs ($n = 29$) (325 pg/mL, IQR = 275-419 pg/mL; $p = 0.0007$), patients with NIND ($n = 46$) (304 pg/mL, IQR = 245-493 pg/mL; $p = 0.0002$), or relapsing MS ($n = 42$) (356 pg/mL, IQR = 246-460 pg/mL; $p = 0.0002$). CSF and serum concentrations of GDF-15 were correlated ($r = 0.41$, 95% CI = 0.25-0.56, $p < 0.0001$). In a longitudinally sampled cohort of patients with MS ($n = 48$), deeply phenotyped with quantitative clinical and MRI assessments, mean GDF-15 concentrations were significantly higher in patients with a stable disease course (405 pg/mL, SD = 202) than in patients with intermittent MRI activity (333 pg/mL, SD = 116; $p = 0.02$).

Conclusions — Serum GDF-15 concentrations are increased in patients with MS with a stable disease course. These data suggest that GDF-15 may serve as a biomarker for disease stability in MS.

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04 | Sarah Mundt

Neurodegeneration in MS: What is the Contribution of Phagocytes?

Background — Multiple sclerosis (MS) is a chronic inflammatory, demyelinating disease of the central nervous system (CNS). During the course of the disease, patients often experience a transition from a so called relapsing remitting (RR) disease to a progressive course of MS where neurodegeneration and failure of brain compensatory reserve become prominent features leading to irreversible neurological disability. This discrimination between the two phases is therapeutically highly relevant as disease-modifying drugs that not only prevent acute MS relapses but also counteract MS progression and neurological disability are essentially unavailable so far. Identification of mechanisms responsible for disease progression are among the main unmet needs in MS. Our focus is on the role of CNS resident and infiltrating mononuclear phagocytes that have been previously suggested to play a major role in the transition from acute to progressive disease.

Methods — Up-to-date, the unambiguous identification of distinct phagocyte subsets in inflammation has been challenging due to overlapping marker expression and limited dimensionality in cytometric and histologic approaches. Using multiparameter single-cell cytometry approaches in parallel with genetic fate mapping and RNA sequencing approaches, we and others have started to systemically distinguish and characterize the spectrum of myeloid cells in CNS pathologies, in particular in experimental autoimmune encephalomyelitis (EAE), the mouse model for MS. Using the NOD mouse model of chronic progressive EAE, we will characterize phenotypic and functional changes of mononuclear phagocytes that occur during the transition from acute to progressive EAE. Using CreLoxP mediated gene ablation we systematically interrogate previously known and newly identified phagocytic effector mechanisms that might be involved in neurodegenerative disease progression.

Results — Our preliminary data point towards a strong reduction of CNS inflammatory infiltrates during chronic/progressive EAE. In contrast, retained monocytes derived cells (M_{DC}s) and resident phagocytes (border-associated macrophages (BAMs) and microglia) stay in an activated state which might contribute to worsening of disease symptoms. In contrast to what has been reported in the literature, we find that Cybb (Nox2) (a subunit of the NADPH oxidase) expression in phagocytes is not required for ROS production and does not play a non-redundant role in the pathogenesis and progression of EAE.

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05 | Hideaki Nishihara

Advancing Human Pluripotent Stem Cell Derived Laboratory Models of the Blood-Brain Barrier to Investigate the Pathogenesis of Multiple Sclerosis

Background — Human induced pluripotent stem cell (hiPSC)-derived blood-brain barrier (BBB) models have proven to be useful to study disease pathomechanisms and drug delivery into the central nervous system. Currently available hiPSC-derived BBB models are well characterized with respect to diffusion barrier properties and specific transporters, however little is known about their expression of adhesion molecules, which limits their usage for studying BBB-immune cells interactions. We investigated adhesion molecule expression on presently available hiPSCs-derived BBB models. Furthermore we aimed to advance hiPSCs-derived BBB models for studying immune cell interactions.

Methods — We employed two established methodologies to investigate adhesion molecule expression of hiPSC-derived brain microvascular endothelial-like cells (BMEC-like cells). The Unconditioned Medium method (UMM) differentiates hiPSCs to a mixed endothelial cell/neuronal progenitor culture in unconditioned medium before selectively expanding endothelial cells in endothelial cell specific medium. In contrast, the Defined Medium method (DMM) employs a chemically defined method, where hiPSCs progress to BMEC-like cells via sequential Wnt and RA signaling pathway activation.

Results — BMECs differentiated by UMM or DMM did not show expression of the BBB adhesion molecules observed in vivo that are necessary for BBB-immune cell interactions. We therefore established a novel protocol to differentiate hiPSCs to BMEC-like cells, namely the Extended Endothelial cell Culture Method (EECM) with good barrier properties and mature tight junctions. Importantly, EECM-BMEC-like cells exhibited constitutive cell surface expression of ICAM-1, ICAM-2 and E-selectin. Pro-inflammatory

cytokine stimulation increased cell surface expression of ICAM-1 and induced cell surface expression of P-selectin and VCAM-1. Coculture of EECM-BMEC-like cells with hiPSC-derived smooth muscle-like cells or their conditioned medium further increased induction of VCAM-1. Functional expression of endothelial ICAM-1 and VCAM-1 was confirmed by T-cell interaction with EECM-BMEC-like cells. Finally, we verify their capability to support immune cell migration by investigating T-cell interaction with EECM-BMEC-like cell monolayers under physiological flow.

Conclusions — We present a novel protocol for hiPSC-derived BMEC-like cells that are suitable to study immune cell interaction with the BBB in an entirely autologous fashion. This has allowed to differentiate healthy control- versus MS-derived hiPSCs into EECM-BMEC-like cells to investigate potential intrinsic alteration in MS-derived in vitro model of the BBB.

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06 | Johanna Oechtering

Intrathecal Immunoglobulin M Synthesis is Associated with Higher Disease Activity and Severity in Multiple Sclerosis

Background — Biomarkers predicting acute inflammatory activity and chronic worsening of multiple sclerosis (MS) are in need for individually adapted therapy (precision medicine). We aimed to determine how in relapsing MS (RMS) intrathecal immunoglobulin M (IgM) synthesis, in addition to presence of IgG synthesis, is associated with 1.) time to first relapse, 2.) degree of neuronal damage, 3.) MRI disease activity, 4.) clinical disability, and 5.) choice of therapy.

Methods — Cerebrospinal fluid measurements, clinical, MRI data as well as Serum neurofilament light chain (sNfL) concentrations from 530 patients with RMS in the observational longitudinal Swiss MS Cohort Study were included. Patients were either untreated or under disease modifying therapies (DMTs) according to national treatment algorithms. Patients were categorized by presence or absence of oligoclonal IgG bands (OCGB), and intrathecal IgG and IgM fraction (IgGIntrathecal Fraction (IF), IgMIF). Time to first relapse and associations with sNfL-Z-scores, total and new/enlarging T2w lesions, MS Severity Score (MSSS), and first initiation of a high efficacy therapy were analyzed in uni- and multivariable (adjusted for age at first symptoms, sex and DMT category) statistical models.

Results — By categorical analysis, the median time to first relapse in patients with IgMIF was 28 months shorter (HR 1.944 [CI 1.237; 3.054], $p < 0.01$) and they had on average a 1.11 steps higher MS Severity Score ([CI 0.382, 1.843], $p < 0.01$) compared to patients without any immunoglobulin synthesis. Moreover, they had more yearly

new/enlarging T2w lesions with an incidence ratio of 3.13 ([CI 1.29; 7.58], $p=0.01$), higher sNfL-Z-scores and higher total T2w lesion counts (IR 2.53[CI 1.63, 3.93], $p<0.01$). Eventually, those patients with additional IgMIF+ also had a shorter interval from disease onset to a first relapse (HR 1.944 [CI 1.237; 3.054], $p<0.01$). These associations were absent, or smaller by a similar level degree, in patients only positive for OCGB or OCGB/IgGIF. Furthermore, quantitative analyses revealed that in patients with $\text{IgMIF} \geq \text{median}$, time to a first relapse and to escalation to high efficacy therapy was 32 (HR 1.851 [CI 1.172, 2.922], $p<0.01$) and 203 (HR 2.347[CI 1.325, 4.156], $p<0.01$) months earlier, respectively, versus those with $\text{IgMIF} < \text{median}$; similar dose-dependent associations were found for MRI disease activity and sNfL-Z-scores. Again, no corresponding correlations of these measures with IgGIF levels were observed.

Conclusions — Intrathecal Immunoglobulin M synthesis is a biomarker associated with higher clinical (relapse, progression) and paraclinical (MRI lesional load, neuronal loss) disease activity and severity, and earlier escalation to high efficacy DMTs and may be useful for therapeutic decision making in early MS.

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07 | Nadine Patt

High-Intensity Interval Training and Energy Management Education, Compared with Moderate Continuous Training and Progressive Muscle Relaxation, for Improving Health-Related Quality of Life in Persons with Multiple Sclerosis –

Study Protocol of a Randomized Controlled Superiority Trial with Six Months' Follow-Up

Background — Persons with multiple sclerosis (PwMS) often have a reduced aerobic capacity and report fatigue as their most disabling symptom impacting their health-related quality of life (Hr-QoL). Guidelines and systematic reviews recommend a multidisciplinary rehabilitation approach for a successful symptom management, but strong evidence to date is available only for unimodal interventions (exercise or energy management programs). The aim of this study is to evaluate the effect of high-intensity interval training (HIIT) + inpatient energy management education (IEME) versus moderate continuous training (MCT) + progressive muscle relaxation (PMR) on the Hr-QoL in PwMS after a 3-week inpatient rehabilitation stay and at four and six months' follow-up.

Methods — A two-armed, single-blinded randomized controlled superiority trial design is adopted. 106 PwMS-related fatigue (Expanded disability status scale ≤ 6.5) are recruited at the Valens clinic and randomized into an experimental (EG) or a control group (CG). Participants in the EG perform HIIT three times and IEME twice per week during the 3-week rehabilitation stay. HIIT contains of five 1.5-min high-intensive exercise bouts at 95–100% of the maximum heart rate (HRmax) followed by active breaks of unloaded pedalling for 2min at 60% of HRmax on a cycle ergometer. IEME consists of a 1-hour individual session, followed by five 1-hour group ses-

sions and concludes with a 0.5-hour individual session. Participants in the CG perform MCT three times and PMR twice per week during the 3-week rehabilitation stay. MCT contains of 24-min continuous cycling at 65% of HRmax. PMR consists of six 1-hour group sessions. In addition to the study interventions, all participants receive their individual rehabilitation program. The primary outcome is the Hr-QoL (total score of 36-item short form health survey, SF-36) assessed at baseline (T0), three weeks after T0 (T1), and at four (T2) and six (T3) months after T0. Secondary outcomes comprise cardiorespiratory fitness and inflammatory markers (measured at T0 and T1), fatigue, mood, self-efficacy and occupational performance (measured at T0, T1, T2 and T3).

Conclusion —This study will provide new information on a multimodal therapy approach and will further help to improve exercise recommendations for PwMS. IEME will help PwMS to efficiently set regular sequences of exercise in their daily routine to build up long-term fitness and thus to have more energy available for an active and satisfying everyday life.

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08 | Sylvain Perriot

Deciphering Reactive Astrocyte Phenotypes Associated with Neuroinflammation and Multiple Sclerosis

Background — Astrocytes occupy a central place in neuroinflammatory diseases such as multiple sclerosis (MS). Depending on the context, astrocytes can modulate their phenotype and become either pro or anti-inflammatory, but they can also become neurotoxic or neuroprotective. In human MS, there is actually very few data assessing the exact role of astrocytes.

Methods — To address this question, we have developed a new system to study human astrocytes. We harvested blood cells from healthy donors and MS patients, reprogrammed them into induced pluripotent stem cells, and developed a protocol to differentiate them into resting astrocytes. We then stimulated these astrocytes with different cytokines implicated in MS: IL-1b, TNF α , IL-6 and a combination TNF α /IL-1b, and we assessed astrocyte phenotype by RNA sequencing.

Results — Transcriptomic analysis of reactive astrocytes showed first that each of these three cytokines leads to the modulation of a specific set of genes, triggering a unique activation profile of astrocytes. Second, gene ontology analysis revealed that IL-6 triggered the upregulation of genes mainly involved in cell adhesion, CNS development and ion transport, while TNF led to a downregulation of these same genes. In addition, IL-1 β and TNF α led to the upregulation of genes mainly involved in the inflammatory response, interferon signaling and defense against viruses.

Conclusions — In conclusion, we found very diverse phenotypes of reactive astrocytes hinting for different functions depending the microenvironment of neuroinflammation. We are now analyzing the response of astrocytes to the cerebrospinal fluid of different categories of MS patients (relapsing-remitting and progressive) and will compare them to patients suffering from non-inflammatory diseases. This next set of experiment will bring us a step closer to decipher the profile of reactive astrocytes in the different stages of MS and hold great promises to understand their net contribution to the pathogenic mechanisms within the central nervous system.

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09 | Jana Remlinger

Investigation of CNS Autoimmunity with Focus on Involvement of the Visual Pathway

Background — In autoimmune demyelinating disorders of the central nervous system (CNS), the visual system is a prominent target during disease attacks leading to potentially irreversible impairment. Retinal degeneration might serve as a generalizable biomarker of neuronal loss. Thereby, functional and structural parameters can be measured easily and reproducibly, also in animal models. However, sparse data comparing different autoimmune demyelinating CNS disorders in patients and murine models are inconclusive. Here, we compare antibody- and non-antibody-mediated murine experimental models of CNS demyelination. This will increase the understanding of different pathomechanisms associated with antibodies against myelin oligodendrocyte glycoprotein (MOG-IgG) or aquaporin 4 (AQP4-IgG) or unspecific isotype antibodies (Iso-IgG), especially focusing on the visual outcome.

Methods — Murine chronic active MOG35-55 experimental autoimmune encephalomyelitis (EAE) was induced with additional administration of AQP4-, MOG- or Iso-IgG shortly before onset of disease symptoms. Visual outcome was assessed longitudinally (baseline, acute and chronic disease phase) via optomotor reflex (OMR) and optical coherence tomography (OCT). Histological correlates of disease manifestations in the spinal cord and optic nerve were quantified using immunohistochemistry for immune cell infiltration, Luxol Fast Blue/PAS staining for demyelination and immunofluorescence for complement deposition. Additionally, the number of retinal ganglion cells (RGC) was quantified on retinal flat mounts.

Results — Disease severity was highest after application of MOG-IgG compared to AQP4-IgG or Iso-IgG. Both, MOG-IgG and AQP4-IgG administration increased disease incidence compared to Iso-IgG (95% and 89 % vs 60%). Histological correlates of demyelination, macrophage and T cell infiltration in spinal cords and optic nerves were found in all groups. RGC numbers were decreased in chronic MOG-IgG-exacerbated EAE compared to the acute phase. While no clear difference in visual acuity between the groups at the measured time points was observed, it declined in both antibody-exacerbated models over time. Longitudinal evaluation of retinal morphology is ongoing.

Conclusions — Previous findings that administration of MOG-IgG worsens the disease course of EAE was confirmed and corroborated by histopathological infiltrates of macrophages and T cells as well as demyelination of the spinal cord. Even though systemic administration of AQP4-IgG did not aggravate disease symptoms compared to Iso-IgG, the incidence was increased suggesting different pathophysiological mechanisms. Differences between the model systems regarding the manifestations in the visual system are currently further investigated.

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10 | Nicholas Sanderson

The Significance of IgM in CSF of Patients with Multiple Sclerosis

Background — Oligoclonal antibodies in the CSF (oligoclonal bands) are a characteristic feature of MS. Most widely examined clinically are oligoclonal bands of the IgG class, but some patients also have oligoclonal bands of the IgM class, and these have been associated with more aggressive disease course but also with reduced risk of progressive multifocal leucoencephalopathy (PML) under natalizumab. We recently discovered that IgM antibodies from the CSF of patients recognize a primitive neuroectodermal cell line (PNET). We are trying to exploit this fact to identify the target antigen of these antibodies.

Methods — We have isolated a monoclonal IgM antibody from the CSF of a patient that shows the same binding characteristics as the polyclonal IgM from the CSF. We have used this antibody to immunoprecipitate the target antigen from the PNET cell line, and have identified candidate antigens by mass spectrometry. In parallel, using next generation sequencing, we have identified the subset of membrane proteins that are expressed on the PNET cell line, but not on other cell lines that are not recognized by the antibody.

Results — We have identified five candidate target antigens that are transmembrane proteins expressed on the PNET cell line and over-represented in immunoprecipitate from the monoclonal antibody. We are currently preparing stably transfected cell lines expressing these target antigens, so that we can screen the original cohort of CSF samples to identify which is the common target antigen.

Conclusions — We have isolated and recombinantly produced a monoclonal antibody from a single CSF B cell that recapitulates the binding characteristics of the crude CSF. We hope to be able to use this to identify the antigen bound by oligoclonal IgM, and thereby gain insight into the influence of oligoclonal IgM on prognosis and PML susceptibility.

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11 | Guillaume Thévoz

The Impact of Dietary Factors and Circadian Rhythms on Fatigue in Multiple Sclerosis

Background — Multiple sclerosis (MS) is a chronic inflammatory and autoimmune disease that affects the central nervous system. Fatigue is a common debilitating symptom experienced by patients with MS. However, it is a difficult symptom to treat efficiently. Recent studies suggest that food intake could impact fatigue. When assessing eating habits, researchers have classically focused on food content (i.e. calorie and macronutrient intake), but for other diseases such as the metabolic syndrome, a new dimension is being explored, the timing of caloric intake sometimes dubbed «chrononutrition». The underlying idea that the timing of calorie intake over the 24h cycle might interact with the circadian rhythm and have additional effects on metabolism and neurological diseases may be the reason for this increased interest in eating patterns. We aimed to assess the relationship between the timing of food intake and fatigue among patients with MS. We hypothesized that MS patients with a shorter eating duration feel less fatigue than those who eat over a longer time of the 24h cycle.

Methods — We recruited 34 MS patients and assessed the MS-related fatigue using a validated questionnaire, the EMIF-SEP which is composed of 40 items, each question graded from 0 (no fatigue) to 3 (maximum fatigue) with a maximum score of 120 and a minimum score of 0. To evaluate the timing of food intake we used a smartphone app allowing participants to take timestamped pictures of what they eat and drink. Based on this remote data collection, we estimated the eating duration and eating patterns over one month of observation.

Results — The mean age of our participants was 35.9 years old (\pm SD 9.7) with 26 women for 8 men. Participants were diagnosed with MS within 38.2 months, with a median of 30 and an IQR of 28.3 months,

with a relapsing-remitting form (n=32) or a clinically isolated syndrome (n=2). The mean EMIF-SEP score was 36.4 (\pm SD 19.2, EM) with a mean eating duration of 14h22 (\pm SD 1h26). We observed that the eating duration was negatively correlated with MS-related fatigue with a Pearson correlation coefficient of -0.41 ($p = 0.03$).

Conclusions — Contrary to our hypothesis, we found a negative correlation between fatigue and eating duration in MS. This might be correlated with altered circadian rhythms in MS patients who would have less opportunity to eat. The study limitations are the small sample size, the short duration of the assessment, the absence of progressive forms of MS, and the low level of fatigue score. This exploratory observational study of fatigue and eating duration in MS needs to be further evaluated with regards to sleep quantity and quality.

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12 | Valentin von Niederhäusern, Josefine Ruder

B Cell Immune Reconstitution after Autologous Hematopoietic Stem Cell Transplantation in Multiple Sclerosis

Background — Autologous hematopoietic stem cell transplantation (aHSCT) has first been applied to mostly advanced multiple sclerosis (MS) patients over 25 years ago and has since been performed with great success. The underlying rationale for aHSCT in MS patients is the depletion of autoreactive lymphocytes by the conditioning regimen and subsequent immune reconstitution with a new and tolerant adaptive immune system. On the basis of the current understanding of MS pathogenesis, previous research has mainly focused on the mechanism of T cell reconstitution, thereby showing that T cell repertoire renewal is almost complete for CD4+ T cells while clonal persistence was seen in CD8+ T cells. Although multiple lines of evidence are supporting a central role of B cells in MS, only a small number of aHSCT studies have focused on B cells, mainly limited to studying major subpopulations by flow cytometry. Results from this work suggest a fast recovery of total B-cell numbers with a predominance of naïve B cells early post-transplantation, while data on their functional phenotypes and on immune repertoires are lacking.

Methods — To understand the immune reconstitution of the B cell compartment in greater detail, we performed longitudinal multidimensional flow cytometry analysis combined with immunoglobulin heavy-chain (IgH) repertoire sequencing on 20 MS patients before and after aHSCT. Follow-up timepoints included 1, 3, 6 and 12 months post transplant and are combined with an extensive dataset of clinical parameters.

Results — Recovery of total B cell numbers took place rapidly, reaching normal levels within the first 3 months following aHSCT. Transitional immature B cells were amongst the earliest cells to repopulate, showing a peak at the 3 month visit. The memory B cell (MBC) compartment reconstituted slowly after transplantation with absolute numbers still being below normal levels 1 year post-aHSCT. Early B cell reconstitution of naïve and memory subpopulations was strongly correlated with CMV status resulting in a significantly slower reconstitution in patients with CMV reactivation. Longitudinal mutation analysis showed a significant reduction of mean number of mutations post-aHSCT in all switched memory B cell subpopulations. This finding indicates persistence of a highly mutated memory B cells despite extensive conditioning that are only slowly outnumbered by newly emerging B cells that only slowly acquire mutations with accumulating antigen exposure.

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13 | Viktor von Wyl

Impact of Covid-19 on the Daily Lives of Persons with MS during the First Lockdown

Background — The first lockdown due to the Sars-CoV-2 pandemic, occurring between March and May 2020, caused significant disruptions to daily life routines, especially for persons with Multiple Sclerosis (MS). During this first lockdown phase, the Swiss Multiple Sclerosis Registry (SMSR) performed a nationwide electronic survey among its 1'700 online participants. The survey covered mental health issues (by use of the Beck Depression Inventory), problems accessing health care and treatment during the lockdown, and the general impact of Sars-CoV-2 on people's lives as a free text field.

Methods — We analyzed the free text information about life impacts using natural language processing tools. We included statements that contained at least 10 words. French and Italian texts were translated into German using DeepL. For each statement, a polarity score was calculated (reflecting negative or positive emotions in a text). Topics were extracted using Non-Negative Matrix Factorization (NMF). Analyses were performed using Python and R.

Results — We included 639 surveys of at least 10 words in length. The NMF analysis yielded four topic groups with similar use of key words.

- 1) Topic communication/contacts, n=119 entries, mean polarity score (mps) -0.16, key words: contacts, missing, colleagues, telephone.
- 2) Topic social aspects, n=274, mps -0.08, key words: family, relatives, home, contact.
- 3) Topic work, n=146, mps -0.11, key words: work, home, home office.
- 4) Topic daily routine, n=200, mps -0.07, key words: errands, week, partner, walk.

Conclusions — The text analysis identified four major topics and influences of Sars-CoV-2 on the daily lives of persons with MS. The methodology will be useful to analyze and draw comparisons with a SMSR follow-up study, released during the second pandemic wave in November 2020.

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14 | Özgür Yaldizli

Value of Serum Neurofilament Light Chain Levels as a Biomarker of Suboptimal Treatment Response in MS Clinical Practice

Background — Serum neurofilament light chain (sNfL) reflects neuro-axonal damage and may qualify as a biomarker of suboptimal response to disease modifying therapy (DMT). The aim of this study was to investigate the predictive value of sNfL in CIS and RRMS patients with established DMT for future MS disease activity in the Swiss MS Cohort Study.

Methods — All patients were on DMT for at least 3 months. sNfL was measured 6 or 12-monthly with the NFlight® assay. The association between sNfL and age was modeled using a generalized additive model for location scale and shape. Z-scores (sNfLz) were derived thereof, reflecting the deviation of a patient sNfL value from the mean value of same age healthy controls (n=8865 samples). We used univariable mixed logistic regression models to investigate the association between sNfLz and the occurrence of clinical events (relapses, EDSS worsening [≥ 1.5 steps if EDSS 0; ≥ 1.0 if 1.0-5.5 or ≥ 0.5 if >5.5]) in the following year in all patients, and in those fulfilling NEDA-3 criteria (no relapses, EDSS worsening, contrast enhancing or new/enlarging T2 lesions in brain MRI, based on previous year). We combined sNfLz with clinical and MRI measures of MS disease activity in the previous year (EDA-3) in a multivariable mixed logistic regression model for predicting clinical events in the following year.

Results — sNfL was measured in 1062 patients with 5192 longitudinal samples (median age 39.7 yrs; EDSS 2.0; 4.1% CIS, 95.9% RRMS; median follow-up 5 yrs). sNfLz predicted clinical events in the following year (OR 1.21 [95%CI 1.11-1.36], $p < 0.001$, $n = 4624$). This effect increased in magnitude with increasing sNfLz (sNfLz > 1 : OR 1.41 [95%CI 1.15-1.73], $p = 0.001$; > 1.5 : OR 1.80 [95%CI 1.43-2.28], $p < 0.001$; > 2 : OR 2.33 [95%CI 1.74-3.14], $p < 0.001$). Similar results were found for the prediction of future new/enlarging T2 lesions and brain volume loss. In the multivariable model, new/enlarging T2w lesions (OR 1.88 [95%CI 1.13-3.12], $p = 0.016$) and sNfLz > 1.5 (OR 2.18 [95%CI 1.21-3.90], $p = 0.009$) predicted future clinical events ($n = 853$), while previous EDSS worsening, previous relapses and current contrast enhancement did not. In NEDA-3 patients, change of sNfLz (per standard deviation) was associated with a 37% increased risk of clinical events in the subsequent year (OR 1.37 [95%CI 1.04-1.78], $p = 0.025$, $n = 587$).

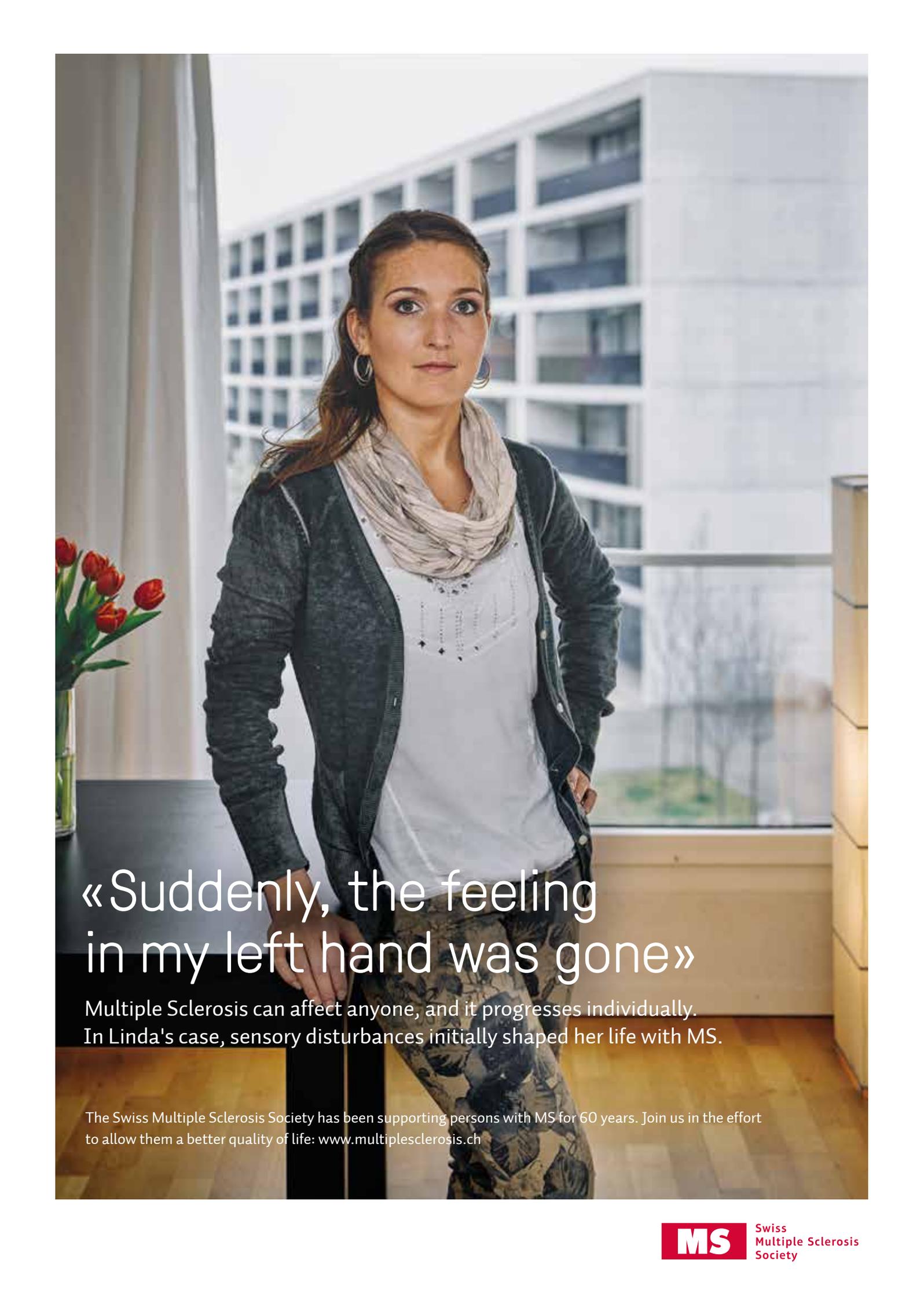
Conclusions — Our data support the value of sNfL levels, beyond the NEDA-3 concept, for treatment monitoring in MS clinical practice.

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We thank you for
your participation in the
virtual symposium.

See you next year at the
24th «MS State of the Art Symposium»,
Saturday, January 29, 2022

Kind regards
Swiss Multiple Sclerosis Society

A woman with long brown hair, wearing a grey jacket, a white top, and a light-colored scarf, stands on a balcony. She is looking directly at the camera. In the background, there is a modern building with many windows. To the left, there is a vase with red tulips on a dark table.

«Suddenly, the feeling in my left hand was gone»

Multiple Sclerosis can affect anyone, and it progresses individually.
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